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Topics in Regional Anesthesia

Edited by Víctor M. Whizar-Lugo, José Ramón Saucillo-Osuna and Guillermo Castorena-Arellano

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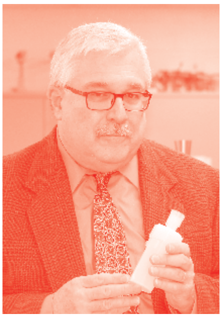



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Meet the editors

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Dr. Guillermo A. Castorena-Arellano graduated from Universidad Nacional Autónoma de México, and completed his residency in Internal Medicine, Anesthesia, and Critical Care at Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México City. He is a research fellow in Anesthesia at the Massachusetts General Hospital, Harvard Medical School, Boston. Currently, he is Professor of Anesthesiology at the Fundación Clínica Médica Sur-UNAM. Dr. Castorena-Arellano has many publications on anesthesia, pain, internal medicine, and critical care to his credit. He has edited a book on perioperative medicine and has given numerous conferences at congresses and meetings around the world. He is the past president of the Mexican Society of Anesthesia and the Mexican Society of Intensive Care Medicine.

José Ramón Saucillo-Osuna MD graduated from the Facultad de Medicina de la Universidad Autónoma de Guadalajara, and he specialized in anesthesiology at the Centro Médico Nacional de Occidente, Mexico. He is one of the most important pioneers in Mexico in ultrasound-guided regional anesthesia. Dr. Saucillo-Osuna has lectured at multiple national and international congresses and is an adjunct professor at the Federación Mexicana de Colegios de Anestesiología, AC, former president of the Asociación Mexicana de Anestesia Regional, and president of the Asociación Latinoamericana de Anestesia Regional Mexican chapter.

Contents

Preface

Born in 1946, I am privileged to be an aging baby boomer, one who has been fortunate enough to enjoy living in two very different centuries. In the 20th century, medicine received an ancestral legacy of knowledge full of illusions, professional ethics, and love for our profession. A time when the Hippocratic Oath was part of each of our medical actions, a time when in the operating room we used a manual cuff to measure blood pressure, a mercury thermometer, and a monitor with a screen so small and pale that it was difficult for us to see more than four PQRS complexes. Arterial blood gases were mandatory to determine perioperative oxygenation and acid-base status. We learned regional anesthesia from our mentors through anatomical references, and if we were lucky, using neurostimulation devices.

The end of the last century and the beginning of the 21st century were accompanied by enormous changes, including the development of new drugs and advances in technology previously unimaginable. Advances like pulse oximetry, capnography, and monitoring equipment integrated into compact and intelligent anesthesia machines that almost whisper in our ears the hemodynamic and metabolic changes of our patients, thus facilitating the modifications of our anesthetic plan. Ultrasound-guided regional anesthesia has been advancing by leaps and bounds, as has the use of new local anesthetics and adjuvant drugs.

Despite these advances, clinical anesthesiology continues to occupy a prominent place in the comprehensive management of each of our patients. Old, not so old, and new generations of anesthesiologists must observe the elementary principle *primum non nocere.*

This book, *Topics in Regional Anesthesia*, highlights the knowledge and experience of colleagues from diverse regions around the world, from sites with unlimited resources to places where the available technology is scarce. Undoubtedly, the current COVID health crisis has devastated all health systems, risking health workers, especially those anesthesiologists on the front lines. Regional anesthesia has once again demonstrated not only its technical benefits but has also become a powerful tool to reduce the possibility of contagion in this era of SARS-CoV-2.

As an editor, I want to thank my friends and co-editors Guillermo Castorena-Arellano and Ramón Saucillo-Osuna for their invaluable support in finishing the book, as well as the authors and friends who contributed to this project.

This book is dedicated to all doctors, especially my sister Blanca Whizar-Lugo, MD, who has died from COVID-19, and to all healthcare workers who continue to advocate for their patients during this frightening time, especially anesthesiologists and intensivist colleagues.

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Section 1

Introduction

Chapter 1

Regional Anesthesia in Times of COVID-19

Víctor M. Whizar-Lugo, Karen L. Iñiguez-López and Guillermo Castorena-Arellano

Abstract

The globalized coronavirus pandemic 2019 has kept us on our toes. Although confusion is widespread and there is a trend toward normalization of almost all human activities, outbreaks remain frequent. The majority of patients with COVID-19 have a trivial to moderate clinical course; a small group develops severe pneumonia and other life-threatening complications. Vaccination against this virus has contributed to better control of the pandemic, but there are no antiviral drugs that have demonstrated efficacy; therefore, the management of surgical patients confirmed or suspected of this disease is a challenge for health care workers, including the anesthesiologists, as well as the non-COVID-19 patients who at a given moment could become carriers or sick. General anesthesia produces aerosols and risks medical and technical personnel being infected, especially those who manage the airway. On the other hand, regional anesthesia has advantages over general anesthesia because the airway is not handled; however, its limited duration is the most important concern. It is reasonable that regional anesthesia occupies a preponderant place in the safe management of all patients, as long as the type of surgery allows it, the anesthesiologist has sufficient skills and patients accept the proposed technique. At this time of globalized crisis due to COVID-19, the intrapandemic anesthetic management of patients undergoing surgery continues to be a changing task, a challenge that has been solved as new data based on solid scientific evidence arise, besides the development of drugs, safer vaccines, equipment, and health prophylactic methods. There is a clear tendency to use regional anesthesia whenever this is possible.

Keywords: COVID-19, regional anesthesia, safety

1. Introduction

In early December 2019, the first cases of coronavirus disease 2019 (COVID-19) were reported in Wuhan, a city located in the Chinese province of Hubei. Most of these patients stated exposure to the Huanan seafood wholesale market selling several alive animals. On the eve of 2020, the WHO office in China was informed of cases of atypical pneumonia with mysterious etiology. Three days later, the first 44 patients with this new pathology were notified and a new member of enveloped RNA coronavirus was identified in bronchoalveolar lavage fluid from a patient in Wuhan and subsequently confirmed as the cause of this infection by the Chinese Center for Disease Control and Prevention. On January 7, 2020, the WHO named this virus a 2019 novel coronavirus (2019-nCoV). On February 11, 2020, the WHO named the illness associated with 2019-nCoV the 2019 novel coronavirus disease (COVID-19). On January 23, 2020, the central government of China imposed a lock-down in Wuhan and other cities in Hubei in an effort to quarantine the center of an outbreak of COVID-19; this action is commonly referred to as the Wuhan lock-down. The Huanan seafood market became recognized worldwide as the "Ground Zero" site of COVID-19. Since then, the disease has spread rapidly to all countries and territories of the planet—with the exception of Turkmenistan, North Korea, Tuvalu, and Nauru, which have reported no cases—becoming a pandemic that has devastated the world in all its activities and collapsing all health systems [1–5].

Although the available global statistics are approximations, as December 31, 2021; 287,574,670 cases had been recorded, with 5,449,965 deaths and 253,516,625 people recovered [6]. These data are changing every moment in relation to the virulence of the new strains, the worldwide resources for the comprehensive care of the population, and the attitude of the people. As COVID-19 spreads across the planet, perioperative medical and surgical personnel must prepare for the challenges associated with the best care for the pandemic. Rapid suspicion, diagnosis and isolation, proper clinical management, and prevention of disease transmission are vital not only for COVID-19 patients but also for other patients and healthcare workers (HCWs) who are at risk of transmission.

Professionals in perioperative areas, such as other specialties, have been developing timely guidelines based on experiences acquired since the beginning of this pandemic in such a way that peri anesthetic care is the safest and most effective for patients and health personnel. Care policies must be endorsed by hospital administrators, medical societies involved, governments, and the third-party payer, to establish an adequate consensus that can adapt to the frequent changes that are necessary for such a way that the infrastructure and available supplies are optimized.

At this time of the COVID-19 pandemic, we must consider five large groups of patients [7]—people with active COVID-19, patients with a history of remission of SARS-CoV-2, potential carriers, vaccinated and unvaccinated patients, and patients without COVID-19. The pre-anesthetic evaluation and perioperative anesthesiological management are based on these groups according to the type of urgent or scheduled surgery, the available resources, and, of course, the experience of each anesthesiologist.

This chapter reviews the actual role of regional anesthesia in the era of COVID-19, considering the different clinical scenarios that this pandemic has generated. Nowadays, there is no information on how regional anesthesia could affect patients with active COVID-19, those with the post-COVID-19 syndrome, carriers, or recently vaccinated people. Practical recommendations that guarantee both the safety of each patient and also of HCWs are addressed, as well as the protection of the equipment. More research is needed to justify the design of management guidelines in regional anesthesia based solidly on global scientific evidence.

2. SARS-CoV-2 virus

COVID-19 or coronavirus disease is caused by the SARS-CoV-2 virus that belongs to the betacoronavirus genus and shares high homology to the severe acute respiratory syndrome coronavirus (SARS-CoV) that occurred in 2003. This virus is closely related to SARS-CoV-1 and possibly originated either from bats or pangolins. Pneumonia and acute respiratory distress syndrome are the primary complications, although there are other disorders such as cardiovascular, hematological with lethal thrombotic complications, renal, gastrointestinal, hepatic, endocrine, and central nervous system diseases, just to mention a few. This sequence of events is due to the activation of immune responses that trigger uncontrolled massive inflammatory responses mediated by elevated serum levels of pro-inflammatory cytokines that can cause localized and systemic tissue damage. Eosinopenia and lymphopenia with reduction of CD4 + and CD8 + T cells, B cells, and natural killer (NK) cells have been identified in severe cases, severe disease suggests a reduction in NK cell number and function, resulting in decreased clearance of infected and activated cells. A higher ratio of neutrophils to lymphocytes has also been reported, being an indicator of inflammation and infection. COVID-19 patients display high levels of inflammatory cytokines and chemokines (IL-1, IP-10, MCP-1), with severe cases showing elevation in TNF alfa, IL-1, IL-6, IL-8, IL-10, MCP-1, and MIP-1A, leading to severe pulmonary damage and IL-1 has also been linked to the expression of thromboxane-A2 resulting in increased platelet activation and aggregation [8–11].

2.1 Variants

The evolution of the SARS-CoV-2 has been continuous with several variants emerging with unusual frequency. Although the clinical picture is similar, these genetic mutations have meant the prolongation of the pandemic with numerous unsolved effects and challenges. Omicron (B.1.1.529), the last variant that originated in South Africa in November 2021 has been classified as a concern variant, which, like the previous variants, has generated globalized uncertainty. These genetic mutations can affect the gene encoding the Spike (S) antigen with effects on preventive and therapeutic strategies known so far. The gold standard for the identification of variants is the sequencing of the entire genome, although recently real-time PCR techniques have been developed for the detection of specific mutations that can facilitate their identification.

Studying the variants could help assess risks and develop better treatment and prevention strategies [12–17]. An international classification system has been established to distinguish emerging variants of this virus into variants of concern (VOC) and variants of interest (VOI), which are listed in **Table 1**.

The under surveillance and de-escalated variants are also included in this classification. The classification of SARS-CoV-2 variants is continually modified

Variants of concern (VOCs)	**Date/Country**	**Mutations**
Alpha (B.1.1.7 lineage) Formerly GR/501Y.V1	UK Dec 2020	17
Beta (B.1.351 lineage) B.1.351 or Beta, or GH501Y.V2	South Africa Oct 2020	9
Gamma (P.1 lineage) Gamma or GR/501Y.V3	Brazil Dec 2020	10
Delta (B.1.617.2 lineage) Delta variant	India Dec 2020	10
Omicron	South Africa Nov 2021	> 30
Variants of interest (VOIs)		
Zeta (P.2)	Brazil April 2020	8
Epsilon (B.1.427 and B.1.429) CAL.20C/L452R	USA June 2020	5
Eta (B.1.525) and Iota (B.1.526)	USA Nov 2020	13
Lambda (C.37)	Peru Dec 2020	3
Kappa (B.1.617.1)	India Dec 2021	7

Table 1.
COVID-19 variants.

according to the genetic mutations of the virus and the WHO, CDC, and ESDC guidelines [16, 17, 18].

2.2 Clinical manifestations

COVID-19 is an infectious disease primarily of the respiratory system that is transmitted from animal to human and from human to human through air droplets, aerosols, and contaminated fomites. The most characterized symptoms are fever, cough, fatigue, dyspnea, sore throat, headache, myalgias, and arthralgias. Mild respiratory symptoms are the most frequent clinical manifestation; however, a broad plethora of signs and symptoms have been described, from asymptomatic patients to severe pneumonia, acute respiratory distress syndrome, respiratory failure, sepsis, and multi-organ failure. Even though the respiratory system is the most prominent target of SARS-CoV-2, the extrapulmonary damage is very extensive and devastating, contributing to its morbidity and lethality. Non-pulmonary manifestations are abundant and can affect systems, such as cardiovascular, central and peripheral nervous, hematological, digestive, hepatobiliary, renal, endocrine, olfactory, and taste disturbances, as well as skin signs [19–25]. **Table 2** lists the most frequent clinical manifestations of greatest clinical interest. The clinical picture varies according to its evolution, especially in seriously ill patients. These manifestations are usually modified with the various vaccination schemes.

2.2.1 Post-COVID-19 syndrome

The chronic post-COVID-19 syndrome is another aspect that is slightly known, as well as the psychological alterations secondary to the disease and the confinement that this pandemic has produced. SARS-CoV-2 fatality rates have been estimated between 1 and 7% [26], so there will be a large population recovered from COVID-19; patients who can acquire a multitude of long-term systemic disorders that are of paramount importance, especially when this group of patients undergoes

System	Associated manifestations/Lesions
Respiratory	Pneumonia, acute respiratory distress syndrome, respiratory failure, pulmonary microvascular thrombosis
Cardiovascular	Myocardial injury, acute coronary syndrome, myocarditis, Takotsubo cardiomyopathy, arrhythmias, heart failure, cardiogenic shock, and even sudden death
Hematological	Lymphopenia, neutrophilia, hyperferritinemia. Coagulopathy characterized by elevated D-dimer and an increased risk of VTE, PE, and DIC. Bleeding events
Neurology	Headache, dizziness, myalgia, anosmia, dysgeusia, encephalopathy, encephalitis, necrotizing hemorrhagic encephalopathy, spinal arachnoiditis, acute myelitis, stroke, seizures, rhabdomyolysis, Guillain-Barre, and Miller Fisher syndromes
Gastrointestinal, liver, and pancreas	Anorexia, nausea, vomiting, diarrhea, abdominal pain, gastrointestinal bleeding, hematochezia. Liver and pancreatic damage
Renal	Proteinuria, hematuria, acute kidney injury
Endocrine	Exacerbating hyperglycemia, euglycemic ketosis, and diabetic ketoacidosis
Skin	Acro-cutaneous (pernio or chilblain-like), maculopapular rash, vesicles, livedoid/necrotic lesions, exanthematous rashes, petechiae

VTE = Venous thromboembolism, PE = Pulmonary embolus, DIC = Disseminated intravascular coagulation.

Table 2.
Common disorders in patients with acute COVID-19.

System	Associated manifestations/Lesions
Respiratory	Restrictive abnormalities, reduced diffusion capacity, small airways obstruction, pulmonary fibrosis, reduced exercise capacity, pneumothorax, secondary infections, massive hemoptysis, pulmonary hypertension with or without evidence of thrombosis
Cardiovascular	Chest pain, dyspnea, palpitations, hypertension, myocarditis, pericarditis, postural orthostatic tachycardia syndrome, arrhythmias
Hematological	Prothrombotic state (deep vein thrombosis, venous thromboembolism), lymphocytopenia, thrombocytopenia, hemorrhage
Neurology	Headache, vertigo/dizziness, anosmia, ageusia, hypogeusia, dysgeusia, insomnia, memory impairment, inability to concentrate, global CNS dysfunction, encephalitis, ischemic stroke, intracranial hemorrhage, encephalopathy, seizures, peripheral neuropathies, autoimmune demyelinating encephalomyelitis, dysautonomia
Renal	Chronic renal failure, focal glomerulopathy, tubulo-reticular injury, proteinuria, hematuria
Endocrine	Post-COVID-19 primary type 2 diabetes mellitus, thyroiditis
Psychiatric, psychosocial manifestations	Chronic fatigue, cognitive dysfunction, sleep disturbances, memory impairment, burnout syndrome

Table 3.
Frequent clinical manifestations/lesions of the chronic post-COVID-19 syndrome.

surgical interventions. Post-COVID-19 chronic damage, to the cardiopulmonary, hematologic, renal, and neurological systems [26–30], is of special interest to the anesthesiologist. Of equal interest are the possible pharmacological interactions between the drugs that these patients have been taking during the acute and chronic phases and the drugs used in anesthesia. **Table 3** lists the most relevant alterations that should be detected in the pre-anesthetic evaluation. Laboratory tests that may persist altered in this syndrome and must be meticulously evaluated include hemoglobin level, erythrocyte sedimentation rate, white blood cell count, lymphocyte count, C-reactive protein, serum glutamic pyruvic transaminase, serum ferritin, prothrombin time, D-dimer, serum creatinine, as well as chest X-ray, CT or NMR.

2.3 Diagnosis

Clinical suspicion of infection with COVID-19 is the first step toward the diagnosis of this disease. However, the initial clinical picture can easily be mistaken with other viral diseases of the respiratory tract, and sometimes it can be totally asymptomatic. On the other hand, the available vaccines have modified the clinical manifestations. This makes it necessary to start a diagnostic approach with laboratory tests and thorax imaging (X-ray, CT, and NMR) at the slightest suspicion of COVID-19.

Although the gold standard test in the diagnosis of COVID-19 is PCR (polymerase chain reaction), it is also necessary to establish other techniques with high sensitivity and specificity that can be used on a large scale. Currently, there are three diagnostic tests used—nucleic acid detection tests (PCR), antigen detection tests (Ag), and antibody detection tests (Ab): IgM/A and IgG [31–33].

3. Risk of infection and death for the health personnel

Health personnel who work on the front lines caring for patients with COVID-19 have a high risk of contagion and death compared to those who work in non-COVID-19 areas, although physicians from all specialties may die from COVID-19. Lack of personal protective equipment was cited as a common cause of death. Although there are no reliable statistics, the published data mention figures of contagion and death not previously seen among HCWs, being emergency physicians, internal medicine, anesthesiologists, intensivists, pulmonologists, infectious disease specialists, primary care physicians, and nurses being the most affected [34–36]. The study of Ing and coworkers [37] reported 278 physicians who died from COVID-19 infection—the average age of 63.7 years, 90% male (235/261). General practitioners and emergency room doctors (108/254), respirologists (5/254), internal medicine specialists (13/254), and anesthesiologists (6/254) comprised 52% of those dying. Two percent of the deceased were epidemiologists (5/254), 2% were infectious disease specialists (4/254), 6% were dentists (16/254), 4% were ENT (9/254), and 3% were ophthalmologists (8/254). The countries with the most reported physician deaths were Italy (121/278; 44%), Iran (43/278; 15%), Philippines (21/278; 8%), Indonesia (17/278; 6%), China (16/278; 6%), Spain (12/278; 4%), USA (12/278; 4%) and UK (11/278,4%). In Mexico, the Mexican Federation of Anesthesiology AC has registered 62 anesthesiologists who died from COVID-19 since the beginning of the pandemic (Hernandez CE. Personal communication), although this figure could be higher since this association has only 5100 members and there are around 15,000 anesthesiologists in this country.

After the first outbreak in China, anesthesiologists in that country were the first to establish safety measures and online education for optimal perioperative management of patients with COVID-19: airway management, oxygen therapy, ventilatory and hemodynamic support, sedation, and analgesia, as well as attention to mental health aspects for workers in surgical areas and intensive care units [38]. After this publication, multiple recommendations appeared with two main goals: the safe management of COVID-19 and non-COVID-19 patients and the protection of all HCWs.

As these management guidelines were developed, the hospitals were reconfigured to increase their capacity to care for COVID-19 patients. "Not necessary" surgeries were postponed, supplies and personal protective equipment were provided to the staff, drugs were investigated for the disease and/or its complications, and preoperative tests were made mandatory for COVID-19, a practice which has generated much controversy, especially in countries with limited resources [31, 39]. On the other hand, asymptomatic carriers among the health personnel have been considered a risk of transmission of COVID-19, especially personnel working in emergency departments. An Egyptian study [40] revealed the prevalence of COVID-19 in asymptomatic HCWs in the emergency department of a tertiary care facility is 14.3% by RT-PCR. The study of Mostafa et al. [41] also done in Egypt included 4040 HCWs from 12 hospitals; 170 (4.2%) were positive for (RT-PCR) and rapid serological tests for IgM and IgG. Most of the infected HCWs were asymptomatic (116/170, 68.2%). The proportion of infection among the asymptomatic (n = 116/3424) was 3.4% (95% CI: 2.8–4.0). These researchers recommended to extend universal testing to all HCWs as infections among them may reflect community rather than nosocomial transmission. In a similar way to emergency physicians, anesthesiologists run a high risk of contagion since they are the providers of care both in the ICU and the perioperative areas and are exposed to the virus every day.

4. Returning to quasi-normal activities after shutdown

- COVID-19 has been and will continue to be an unexpected and catastrophic nightmare for healthcare systems around the world.

- The immediate cessation of elective care ordered by the governments had severe negative effects.

- The resumption of elective surgery during the various outbreaks and remissions of the pandemic has required adjustments to pre-pandemic routines.

All health systems on the planet have collapsed since the beginning of this pandemic; the rapid increase in critically ill patients exceeded the capacity of the emergency and intensive care services, which is why hospitals were transformed into COVID-19 care centers, new non-hospital areas were created or adapted to take care for these patients, and drastic preventive measures such as the social distancing policies, mandatory lockdowns, large isolation periods, confinement at home, home office work, mandatory face masks, frequent hand washing, and sanitation measures. Elective surgeries and many urgent procedures, as well as non-surgical medical hospitalizations, outpatient and home consultation, and the training of students, residents, and new specialists, underwent substantial changes which resulted in a serious increase in non-COVID-19 patient's morbidity and mortality. A systematic review of patients with an acute abdomen during the initial phase of the pandemic proposed that every effort be made to assess the feasibility of postponing surgery until the patient is no longer considered potentially infectious or at risk of perioperative complications. When surgery is necessary, the anesthesiologist and the surgeon must minimize the risk of exposure to the virus by involving the minimum number of personnel and reducing the time in the operating room. When there are no safety measures that allow safe laparoscopy, open surgery should be considered to decrease aerosols [42].

During the different stages of the pandemic, government hospitals and private health care institutions have been designing health care programs for COVID-19 and non-COVID patients in such a way as to return to normal pre-pandemic health care, or what we now know as the new health care routines. The surgeries of all specialties that had been suspended have been resuming a course quite different from the previously established sequences. New care guidelines have been oriented based on the experiences acquired since the beginning of this global health crisis, with the primary goal being to avoid contagion from other patients and health personnel without deterioration of the quality of care [43–45]. As soon as it was possible to adopt new safety measures for non-COVID patients and medical personnel, postponed surgeries that had endangered the lives of thousands of patients with cancers, cardiovascular disease, or organ transplant patients were restarted. Gradually, other types of surgeries were performed until hospital centers and outpatient and short-stay surgery units returned to the new normality. Management guidelines have also been issued to resume surgery in various specialties, with special care in pediatric and obstetric anesthesia [46].

The psychological disorders that the HCWs have undergone [47–49] are also of paramount importance for a reliable return to professional activities in anesthesia. Although for many physicians, returning to their pre-pandemic professional practice has been relatively quick and easy, for anesthesiologists who have been on the front line of this health crisis, returning to the anesthetic consultation, operating rooms, recovery areas or the ICU conveys still a high risk. Not only is it necessary to adopt the new guidelines, but it is prudent to prevent, diagnose and treat these psychological pathologies such as exhaustion, fear, anger, anguish, and uncertainty that are factors that could interfere with our professional performance. This almost "*two-year race is now a marathon that passes between nuclear reactors, next to war zones, of many unusual dangers*" where medical errors can flourish at any moment. As anesthesiologists, we must have the courage, resilience, determination, and conviction to continue with this new goal of providing safe anesthesia to each one of our patients in this era of COVID-19 [50, 51].

With the measures and precautions properly implemented it is now feasible and extremely safe without increased risk for patients to resume all surgical activities.

The health personnel of the surgical and recovery areas has been adapting to the new care guidelines that still have unresolved controversies [52]. Unfortunately, outbreaks with the new variants, including the new strain Omicron [19], continue to perpetuate the risks of contagion for HCWs, especially for professionals who manipulate the airway, which favors the use of regional anesthesia.

5. Clinical scenarios in the era of COVID-19

The COVID-19 health crisis has been changing the way we practice medicine. Fortunately, the WHO vaccination programs in agreement with the governments of almost the entire planet have reduced infections and positively modified morbidity and mortality figures. Some clinical scenarios can be considered in this era [7]: patients with active COVID-19, patients recovered from SARS-CoV-2, potential carriers, vaccinated and unvaccinated patients, and a majority group of patients without COVID-19. The pre-anesthetic evaluation and perioperative anesthesiological management are now based on these assumed groups, as well as on the type of urgent or scheduled surgery, on the available resources, and, of course, on the experience of each anesthesiologist.

5.1 Patients with active COVID-19

Despite the enormous number of clinical trials and vaccines available, unfortunately, we still lack an effective cure for COVID-19. Therefore, the anesthesiologic approach to these patients must be safe and effective for both the patient and the medical team. Transporting patients with active COVID-19 from their bed to the operating room and vice versa is a critical maneuver that requires both the patient and the HCWs to be properly protected and to do so through a pre-established route. An interesting experimental study showed that the surgical smoke generated by the electric scalpel and ultrasonic scalpel is not a risk factor; the coronavirus present in the smoke was unable to induce plaque formation in cultured cells. In addition, filtration of surgical smoke through a surgical mask effectively reduces the amount of viral RNA by at least 99.80% [53].

5.2 COVID-19 survivors

People who got COVID-19 and survived can be divided into two groups; recovery ad-integrum and those who develop the long-term disease. Those in the first group do not represent a special risk for anesthesiological management, but patients in the second group should be carefully evaluated for long-term cardiac, pulmonary, kidney, hematological, and neurological conditions.

5.2.1 Long term COVID-19 patients

Two years after the start of this pandemic, more than 287 million cases and 5.4 million deaths had been reported worldwide [6, 54]; approximately 253 million people around the world have recovered from Covid-19, of which 10 to 40% continued with symptoms of this disease for a few weeks to months. This is a new disease that has been called post-COVID-19, Prolonged COVID-19, or Post-acute COVID-19 syndrome [55–57].

COVID-19 long-term sequelae are yet unknown, but they can situate these patients at high risk when they undergo anesthesia and surgery [56]. The chronic post-COVID-19 lesions of greatest interest to the anesthesiologist are cardiovascular, pulmonary, kidney, hematological, and metabolic.

5.2.1.1 Cardiovascular

Up to 20–30% of hospitalized patients with COVID-19 have evidence of myocardial involvement, including acute myocardial injury, arrhythmias, cardiogenic shock, and even sudden death. Acute coronary syndrome (ACS) can be one of the initial presentations of COVID-19 infection which may range from ST elevation and myocardial infarction to Takotsubo cardiomyopathy [57]. The incidence of myocardial injury as reported in China increases with the severity of illness, uprising to 22.2% of patients needing ICU care [58]. Additionally, drug interactions with COVID-19 therapies can put the patient at risk for arrhythmias, cardiomyopathy, and sudden death [22]. A comprehensive cardiovascular review has been recommended in patients who recovered from heart injury due to COVID-19 since they may have residual damage even in asymptomatic patients, especially in search of arrhythmias and myocarditis [59, 60].

5.2.1.2 Lung

Mild to severe dyspnea are frequent manifestations of the post-COVID-19 syndrome. The lungs are the most damaged organs in patients with moderate to severe COVID-19; an undetermined percentage of recovered persons will develop structural pulmonary abnormalities that usually last for several months. The prospective study of Sonnweber et al. [61] with 145 patients with COVID-19 showed that 41% had respiratory symptoms 100 days after the onset of the disease—dyspnea reduced diffusion capacity in 21% of the studied cohort. The CT scans with alterations in 63%, with bilateral ground-glass opacities and/or reticulation of lower lobes. Other studies have found residual ground-glass opacities, consolidations, reticular and linear opacities, residual crazy paving patterns, melted sugar signs, and parenchymal fibrotic bands [62, 63]. A decreased lung diffusing capacity for carbon monoxide possibly due to loss of alveolar units with alveolar membrane damage was reported recently [64].

Long-term hematologic damage is not accurately recognized. It is unknown whether pulmonary thromboembolism in COVID-19 resolves completely in survivors or presents with long-term sequelae of lung parenchymal or pulmonary vascular damage or pulmonary hypertension. It is prudent to determine if there is thrombocytopenia, D-dimer levels, prothrombin time (PT) prolongation, international normalized ratio (INR), thrombin time (TT), and activated partial thromboplastin time (aPTT) reduction.

5.2.1.3 Kidney

Acute renal failure is a frequent complication in COVID-19 that affects up to 36.6% of patients, of whom the majority of survivors recover, but the long-term effects on renal function and risk of death are unknown. Patients at greatest risk of chronic kidney damage are older adults, African Americans, or those with diabetes and/or hypertension. Kidney impairment may be found 6 months after discharge.

5.2.1.4 Metabolic and endocrine disorders

Viral damage to the islets of Langerhans can lead to transient diabetes mellitus. Thyroid follicular damage, thyroiditis, hypothyroidism, as well as transient pituitary lesions, and damage to the hypothalamus-pituitary–adrenal axis leading to hypocortisolism and secondary hypothyroidism have also been found [64, 65].

5.3 Potential COVID-19 carriers

There is enough evidence that many COVID-19 patients are asymptomatic or have only mild symptoms, but they can transmit the virus to other people. There are difficulties in the detection of these asymptomatic carriers, which hinders the prevention and control of this pandemic [66]. A systematic review and meta-analysis [67] found that the proportion of asymptomatic among COVID-19 positive people is high with a substantial transmission potential in communities, therefore, asymptomatic carriers occupy a decisive place in the management of this global crisis.

5.4 Vaccinated and unvaccinated patients

Morbidity and mortality have decreased in vaccinated people due to vaccine-induced immunity against SARS-CoV-2. On the other hand, it has been shown that vaccinated people can be asymptomatic carriers, especially of the Delta variant, and they constitute another transmission factor [68]. During the last two outbreaks of the pandemic, unvaccinated people tend to develop more clinical complications, and their death rate is higher. This last group represents a management and contagion challenge similar to the beginning of this pandemic. Unfortunately, anti-vaccine people represent an important group and continue to be a factor that favors the persistence of this disease and only a few countries have taken drastic measures against this group.

In vaccinated patients, it is important to consider two facts—1) complications secondary to vaccines, especially the rare possibility of myocarditis and pericarditis that has been described after the application of COVID-19 mRNA vaccines (i.e., Moderna and Pfizer-BioNTech). This potential complication has been seen mainly in men under 30 years of age, which makes surveillance in this group of vaccinated people necessary [69, 70]. COVID-19 viral vector vaccines (i.e., Johnson & Johnson/Janssen and Oxford/Astra-Zeneca) use a modified version of adenovirus, which expresses a stabilized spike protein on its surface but is incapable of replicating. Similar to the Astra-Zeneca vaccine, the Johnson & Johnson vaccine was temporarily paused because of reports of thrombotic events. 2) The second point regarding vaccine is the time of vaccination in relation to the time of surgery anesthesia. To date, there are no scientifically proven guidelines on when to apply the vaccine in relation to the surgical moment. Some medical groups have recommended vaccination programs in this clinical setting [71, 72]:

- Surgery or urgent medical procedures should not be postponed based on the vaccination status
- Knowing the vaccination status of the potential patient is mandatory. It is ideal for patients to have a complete vaccination schedule prior to surgery. In special cases, a single dose of vaccine as early as possible before surgery should be considered. The earlier the vaccine can be given preoperatively, the greater the protection.
- Elective surgery does not contraindicate COVID-19 vaccination
- Vaccination should be done 2 weeks before surgery. If there is an adverse event related to vaccination, it is prudent to postpone surgery until the patient has recovered or the patient's condition has stabilized
- After surgery, it is recommended to wait at least 2 weeks before vaccinating, or until complete recovery in patients complicated by the operation

- Vaccination is recommended for patients with prior COVID-19 infection
- It is vital that vaccination reactogenicity (secondary reactions to vaccines) has been resolved before surgery
- Patients who need elective surgery should have priority to be vaccinated before the general population.

These recommendations could be modified in the near future when there are data based on new scientific evidence obtained from prospective studies. It is worthy to remember that vaccinated people can get COVID-19 and be carriers or have mild to severe manifestations.

5.5 Patients without COVID-19

Fortunately, this is the largest group in the midst of this health crisis. Theoretically, all patients without COVID-19 scheduled for an anesthesiological procedure could be managed as before this pandemic. However, in this era of COVID-19, there are many controversies, because scientific advances change every day, health systems have not yet recovered 100%, and many patients and HCWs are still afraid of contagion and death. The most cautious conduct is to manage each patient as if they were a potential transmitter of SARS-CoV-2. As above mentioned, there is evidence that COVID-19 carriers are asymptomatic, but easily transmit the virus to other individuals. It is this group of carriers that have forced us to handle ALL of our patients with widely recommended preventive recommendations.

At Lotus Med Group outpatient and short-stay plastic surgery unit, we suspended all activity for 6 weeks at the beginning of the pandemic. Before we restart the consultation and the surgery, we elaborated a plan for approaching our patients:

1. Most of the consultations—as they were partially done before the pandemic—would be online.
2. Only the patient would attend the face-to-face consultation.
3. Mandatory N95 mask in the waiting room, during the consultation, in the patient room, in the operating room as well in the recovery area.
4. Questionnaire about COVID-19.
5. Rapid blood test for COVID-19.
6. All personnel were protected with a mask, healthy distance, frequent hand washing, and sanitation of work areas.
7. Anesthesiologist with personal protection equipment.

This regulation was modified according to the new information available and the availability of resources. The rapid IgM and IgG serological tests were substituted by the RT-PCR, which must be performed between 3 and 5 days prior to the consultation/surgery. Patients with a positive result are postponed for surgery or consultation and must have another PCR test with a negative result. All staff received a PCR test and when vaccinations became available, all staff were vaccinated immediately.

Most of the surgical procedures performed in our unit are done with subarachnoid anesthesia [73]. General anesthesia is used only in breast surgeries, chest liposuctions, some cases of combined or very prolonged surgical procedures, or when there is a contraindication to regional anesthesia. All facial surgery is performed with local anesthesia and intravenous sedation, administering nasal oxygen with flows of 0.5–1 Lt/min.

6. General versus regional anesthesia

Under the current information, the type of anesthesia that we should use during this pandemic in the various clinical settings described is still controversial. Although general anesthesia is now safer than at the beginning of this crisis, the current trend is to use regional anesthesia whenever possible, ensuring the possibility that conversion to general anesthesia is not necessary.

- When the type of surgery allows, always use regional anesthesia during the COVID-19 pandemic

- If the patient has COVID-19, it is not a formal contraindication to perform regional anesthesia

- The most experienced anesthesiologist in the hospital should perform the anesthesia procedures

- The least number of HCWs in the operating room is recommended

- Whenever possible, informed consent should be obtained digitally

- Avoiding the aerosols found in general anesthesia can further protect HCWs and other patients [74]

During this time of COVID-19, we have two major scenarios in the practice of anesthesia: 1) Hospitals where there are well-established care programs for COVID-19 patients and people without this infection. These hospitals have personnel resources and supplies that vary according to each country and geographic region of the planet. The surgery programs have been gradually normalized according to their capacity and the level of infections by SARS-Cov-2. 2) On the other hand, outpatient and short-stay surgery units suspended their activities for short periods of time, but quickly resumed their activities during the pandemic due to the high demand for surgical patients referred from hospitals that limited their usual operating capacity due to being collapsed by COVID-19 patients [75, 76].

General anesthesia leads to the generation of aerosols, increasing the risk of COVID-19 contamination in operating rooms and recovery areas, significantly exposing healthcare teams to COVID-19 infection during tracheal intubation, extubation, and in the immediate period of recovery from anesthesia. The risk of transmission of acute respiratory infections to HCWs during aerosol-generating procedures, such as tracheal intubation, has been reported to be high. On the other hand, it is well known that general anesthesia decreases the immune response which could negatively interfere with the evolution of COVID-19 patients [77, 78]. Furthermore, general anesthesia has a higher risk of perioperative lung complications than regional anesthesia.

7. Regional anesthesia

Although some researchers have suggested that general anesthesia is safe for anesthesiologists and other HCWs, at this time of COVID-19, there is a clear tendency to use–whenever possible–the various regional anesthesia techniques [79–83].

The information available has focused on patients with active COVID-19 and post-COVID-19 syndrome. There is not enough information on the use of regional anesthesia in asymptomatic carriers, recently vaccinated and non-COVID-19 patients requiring anesthesia for surgery or any other medical procedures during this time of the pandemic. However, it is prudent to favor its use as a safe way to avoid possible infections in health personnel and to avoid complications for patients. A Turkish study [84] with 126 specialists in anesthesiology and resuscitation found that 42.6% had an increase in the use of regional anesthesia, compared to 57.3% who had no change. 74% were neuraxial anesthesia. The distribution of peripheral nerve blocks (PNBs) showed that upper extremity blocks were used at a rate of 64.9%, lower extremity blocks at 30.38%, and trunk blocks at 15%. Up to 44% of anesthesiologists used ultrasound guidance and 50% used both neurostimulation and ultrasound. An email survey of members of the American Society for Regional Anesthesia and Pain Medicine, UK Regional Anesthesia, and the European Society for Regional Anesthesia and Pain Therapy involving 729 anesthesiologists from 73 countries found that the use of regional anesthesia increased or remained the same, arguing that its use does not produce aerosols and reduces the risk of possible complications to patients. Only 2% of those surveyed decreased the use of regional anesthesia compared to the pre-pandemic period, being the most common reason for the possibility of urgent conversion to general anesthesia [85].

The following practical considerations are derived from the information available, the possibilities in the various clinical settings described above, the opinions of experts, and our experience.

7.1 General recommendations in the operating room

Before starting regional anesthesia, it is recommended to plan the available resources (staff, drugs, and equipment), appropriate clinical environment, suitable personal protective equipment for each case (in patients with active COVID-19 or carriers use PPE, goggles and N95 mask should be used throughout the perioperative period. In the other clinical scenarios described above, it is prudent to use minimal protective equipment that include goggles, N95 mask, face shield, surgical gown, and gloves), and evaluate meticulously the best regional anesthesia technique, as well as post-anesthetic care, always protecting patients and HCWs. All patients must be clinically monitored, in addition to being properly monitored with noninvasive blood pressure, electrocardiogram, respiratory rate, and pulse oximetry. If possible, carbon dioxide (CO_2) monitoring is recommended. Intraoperative oxygen administration should be avoided, and only if pulse oximetry is 90% or less should be given at low flows (0.5 to 1 Lt/min). Oxygen must be administered with nasal prongs (cannula) with a surgical mask layered over it. It is advisable not to use sedatives during regional anesthesia. When the patient is restless, sedation should be minimal to avoid respiratory depression and the need to administer oxygen and thereby increasing aerosol production. Patients should always keep their N95 masks on to prevent droplet transmission, and preferably not speak during their surgery. The use of long-acting local anesthetic (bupivacaine, levobupivacaine, ropivacaine, and etidocaine) prolongs the anesthetic effect of regional anesthesia. In addition to a sufficient and safe dose, the addition of an additive such as dexmedetomidine, clonidine, morphine, or fentanyl prolongs its duration [86, 87]. Nerve blocks should always be performed in the operating room, and preferably recover in the operating room to limit contamination and contagion. It is mandatory to limit the number of personnel to the minimum necessary. An HCW must be available to bring the necessary supplies to the operating room if required. It has also been recommended by various authors that regional anesthesia should be administered by the most experienced anesthesiologist. However, this negatively interferes with the learning of residents [88–90], which is why we consider it correct that an expert anesthesiologist support colleague in training as long as they follow the guidelines to avoid contagion and with the proper PPE [87].

7.2 Neuroaxial anesthesia

Epidural, subarachnoid, and combined spinal-epidural anesthesia can be used in all types of patients with maximum safety and efficacy during this pandemic [73, 78–84, 86, 87]. Major et al. found that during this pandemic laparoscopic gynecological surgery under general anesthesia is associated with higher mortality and pulmonary complications. These authors recommend the use of neuraxial anesthesia with low-pressure pneumoperitoneum ≤8 and in pelvic surgery, the Trendelenburg position of as much as 30–45° is essential [91].

Two years after the onset of the pandemic, there are many enigmas about the impact of the coronavirus 2019 on pregnant women, which have been considered at high risk due to the physiological changes of pregnancy and the effects on implantation, fetal growth and development, as well as the risk of infection in the newborn [92]. Anesthetic management guidelines for the mother-fetus-HCWs trinomial have been developed to reduce the possibility of contagion and complications of COVID-19 [93–95]. The available studies support the use of neuraxial anesthesia for labor, vaginal or cesarean delivery section, although the use of general anesthesia in urgent cesarean section continues to be the choice. Chen's retrospective study of 17 pregnant women found significant intraoperative arterial hypotension in 12 of 14 patients who received epidural anesthesia. Three patients were managed under general anesthesia. No newborns or HCWs were infected with COVID-19 [96]. Early epidural block minimizes the need for general anesthesia for urgent cesarean delivery. Depending on the hemodynamic status of each patient, a choice must be made between spinal, epidural, or combined spinal-epidural anesthesia, the latter with a very low spinal dose. Before doing a neuraxial procedure in these patients, it would be advisable to review the platelet count given that one-third of patients with COVID-19 infection have been reported to have thrombocytopenia compared with 7–12% of patients during pregnancy alone.

The possibility of neuroinfections (meningitis or encephalitis) after neuraxial analgesia/anesthesia is an unresolved topic, although it has been mentioned that this possibility is extremely low and there are no published cases with this complication [97]. At present, postdural puncture headache in patients with COVID-19, the epidural blood patch should be avoided [98], instead, regional analgesia can be used with peripheral blocks (greater occipital nerve block, lesser occipital nerve block, sphenopalatine ganglion block, and/or trigger point injections) [99, 100].

7.3 Peripheral nerve blocks

The introduction of ultrasound guidance has facilitated the development of new regional blocks with safe and effective results, for example, the erector spinae plane block, quadratus lumbar block, injection between the popliteal artery and the posterior knee capsule, pectoral nerve blocks, the transverse plane of the abdomen and many more [101]. The use of ultrasound guidance in peripheral nerve blocks performed by an expert anesthesiologist reduces the incidence of failure and complications. The ultrasound machine and all the accessories used must be properly protected with disposable plastic and be sanitized at the end of each nerve block. Murata et al. published some recommendations when using ultrasound-guided regional anesthesia [102] since the gel, the transducer, as well as the ultrasound machine used, are vectors that can transmit pathogens, including SARS-CoV2. Devices that only have contact with intact patient skin are classified as non-critical and can be sanitized with 70–90% alcohol, aldehyde, phenolic and quaternary ammonium-based disinfectants, and be used in conjunction with a single-use sterile transducer cover during the procedure. Needle guidance aids that are affixed to the transducer must be sterilized if re-used, but sterile and disposable attachments may be better suited for use in a pandemic. At the end of each regional block, the gel residues must

Planning	Equipment/supplies	Regional anesthesia	Comments
COVID-19 positive patients or persons under investigation			
Check COVID-19 status Examine cardiopulmonary, renal, hematological, metabolic, and neurological status Chest CT or NMR	HCWs with full PPE Protect and sanitize equipment	Not contraindicated	RA is contraindicated in severe cases with multiorganic failure Postpone surgery if not urgent 7 weeks or longer after infection
Post-COVID-19 patients			
Test Cardiopulmonary, renal, hematological, metabolic, and neurological status Chest CT or NMR Negative PCR test	MPPE	Not contraindicated Peripheral nerve blocks if possible	Neuraxial anesthesia could be contraindicated in dysautonomia and cardiac injury
Asymptomatic carriers			
Positive PCR, Antigen detection test, Antibody detection test	HCWs with full PPE Protect and sanitize equipment	Not contraindicated	Non-urgent or necessary surgery should be postponed until there is a negative PCR. In urgent surgery RA is preferable, Use full PPE
Patients vaccinated against COVID-19			
Negative PCR test	MPPE	Better option	Postpone surgery if there is an adverse vaccine reaction Vaccination should be done 2 weeks before surgery Vaccinated patients may have COVID-19 or be carriers
Non-COVID-19 patients			
Negative PCR test	MPPE	Best selection	Use your anesthetic of choice technique It is prudent to use minimum protective equipment Make a reasonable follow up of your patient via telephone/online in search for data from Covid-19

Patient with N95 mask at all times, nasal O2 only if necessary. RA = Regional anesthesia. PPE = Personal protective equipment. MPPE = Minimum personal protective equipment.

Table 4.
Recommendations for the management of regional anesthesia in the era of COVID-19.

be cleaned. If there are blood or body fluids on the transducer or its cable, they must also be decontaminated because they can be a vector for viral transmission.

A study to retrospectively analyze two cohorts of pre-pandemic vs. intrapandemic patients undergoing breast cancer surgery compared general anesthesia vs. paravertebral blocks and found that regional anesthesia significantly reduced hospital discharge time, the need for postoperative analgesics, time in the PACU, and the incidence of postoperative nausea and vomiting, concluding that this type of block offers safe anesthesia for patients and HCWs are not exposed to aerosols produced by general anesthesia, especially anesthesiologists [102].

Some nerve blocks can affect pulmonary function due to paralysis of the diaphragm or incidental pneumothorax. Brachial plexus block, stellate ganglion block, cervical epidural block, and thoracic subarachnoid anesthesia are procedures that could worsen borderline lung function in some patients with severe COVID-19 pneumonia, so these types of regional anesthesia should be avoided in these patients o meticulously adopt the recommendations to avoid these incidents.

There is always the possibility that regional anesthesia could fail. Before starting the surgery, it should be tested whether the dermatomes where the surgery will be performed have been adequately anesthetized. When the surgery is prolonged, conversion to general anesthesia is necessary. In both situations, the anesthesiologist must protect himself according to the established guidelines depending on whether it is a patient with active COVID-19 or one of the other scenarios described above, minimizing the production of aerosols. The possibility of systemic toxicity due to local anesthetics is remote, but if it develops it represents a true emergency that occasionally requires tracheal intubation. This emergency must be resolved in accordance with the established treatment protocols and the personnel must be properly protected to avoid becoming infected during the management of the airway [87].

Table 4 lists updated recommendations on the study, evaluation, and management of regional anesthesia in the various intrapandemic clinical scenarios. These are suggestions, which can be adapted to local needs and capabilities.

8. Conclusions

SARS-CoV-2 is the third coronavirus producing an outbreak of this century, and surely it will not be the last pandemic. The progressive appearance of variants, especially Delta and Omicron with a rapid transmission potential confirms that the pandemic is endless, with a greater negative impact which commits us to maintain prevention and management protocols in accordance with the recommendations dictated by experts. Perioperative SARS-CoV-2 infection increases postoperative mortality, which is why it has been determined that these patients should postpone elective surgery whenever possible. A prospective, multicenter, international study compared patients with and without COVID-19 undergoing urgent surgery, finding a 30-day adjusted primary mortality in patients without COVID-19 of 1.5% (95% CI: 1.4–1.5), while those affected by SARS-CoV-2 mortality was significantly increased in those who undertook surgery within 0–2 weeks, 3–4 weeks and 5–6 weeks of diagnosis (odds ratio (95% CI) 4.1 (3.3–4.8), 3.9 (2.6–5.1) and 3.6 (2.0–5.2), respectively). This study recommends that surgery should be postponed for at least 7 weeks after COVID-19 infection, and patients with ongoing symptoms ≥7 weeks from diagnosis may benefit from a longer delay [102]. Proper triage of urgent and non-urgent surgical patients is mandatory for the surgical team to minimize the exposure of HCWs and patients during this era. All patients with unknown COVID-19 status should be considered suspect and therefore essential precautions should be taken for their management.

Although a large number of patients affected by COVID-19 require urgent surgery under general anesthesia, an undetermined number of cases can be properly managed with regional anesthesia, especially those patients without severe respiratory failure, myocardial involvement, or coagulation disorders. Regarding the best anesthetic management of all types of patients in this era of COVID-19, we must identify all the available pieces and prudently put them together in a plan based on the evolutionary complexity of this pandemic puzzle, in such a way that patients, HCWs, and the use of supplies and medical equipment are optimized to the maximum. On the other hand, this goal should consider anesthetic management that reduces the possibility of perpetuating the global, regional and local spread of this virus. Regional anesthesia has come to reach a prominent place in the comprehensive management of these patients, and the various clinical environments must be considered, with obstetrics being a special group due to the particular physiological changes of pregnant women.

The coronavirus 2 pandemic will continue to change humanity and we as anesthesiologists will continue to run in this deadly marathon under new and changing health care modalities, whether in the perioperative areas, the emergency rooms, or the intensive care units. Undoubtedly, our professional practice will continue to be of very high risk, so the perioperative management of patients with COVID-19 and the various clinical scenarios that this health crisis has generated must keep us alert and in need of continuous updating.

Conflict of interest

There is no conflict of interest.

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Section 2

Ultrasound-Guided Regional Anesthesia

Chapter 2

The Tissue Plane

Philip Cornish

Abstract

In recent times, terms such as 'interfascial plane block' and 'fascial plane block' have become common in describing regional anaesthesia blocks such as transversus abdominis plane (TAP), serratus anterior plane (SAP) and erector spinae plane (ESP). In fact, none of these names accurately describes the applied anatomy involved in each named technique, as the acronym is only one part of the anatomic jigsaw puzzle. The correct term is 'tissue plane block', which derives from surgical terminology. The tissue plane is not new to regional anaesthesia, as it has been the endpoint of 'loss of resistance' and 'pop' techniques for many decades. However, the game-changer is that now we can see the tissue plane courtesy of ultrasound. The purpose of this chapter is to review the history of the tissue plane in relation to its use in regional anaesthesia, and to see how ultrasound has further advanced the regional anaesthesiologist's options in this regard. The chapter will also review how an understanding of tissue dynamics can further enhance our clinical results by manipulating the characteristics of the tissue plane.

Keywords: tissue plane, ultrasound-guided regional anaesthesia, applied anatomy, TAP block, ESP block, SAP block, rectus sheath block, tissue plane dynamics, dye studies, injectate, hydrodissection, nerve block

1. Introduction

> *'something old, something new, something borrowed, something blue...'*
>
> *18th Century English Rhyme*

'Something old' – it may have evolved over geological time, it may distort with congenital, surgical, traumatic or other influences, but fundamentally anatomy has been around for a long time. This was wittily expressed by Harrop-Griffiths and Denny [1] in relation to the introduction of ultrasound to regional anaesthesia when they suggested that there are 'no new blocks, just old anatomy'. These authors would undoubtedly agree though that how we look at anatomy can change, and indeed should change as study and scholarship advances our understanding.

'Something new' – the ability of ultrasound to visualise tissue planes provides a new, or more accurately, a newly appreciated target. The explosion of named techniques using ultrasound guidance in the last several years bears testimony to this development in regional anaesthesia practice.

'Something borrowed' - The 'tissue plane' is a concept borrowed from surgical practice [2–4] and it forms the foundation of modern surgical dissection technique. An alternative term for the same idea is the 'plane of dissection'. Surgeons also talk about 'creating' a plane of dissection or 'getting into the correct (tissue) plane' [4]. The key idea which surgeons are emphasising is that of dissecting between structures, and it matters little whether this is with a sharp (e.g., scalpel) or blunt (e.g., finger) instrument. In regional anaesthesia practice, the dissection occurs solely with a blunt (injected fluid) instrument and is termed 'hydrodissection'.

'Something blue' – it has been routine for many years in cadaveric anatomic studies in the regional anaesthesia literature to use methylene blue as a marker to track nerve block placement. These have in effect been studying spread of fluid along tissue plane/s. Once again, we find that this is not so much a new as an under-appreciated phenomenon. A note of caution however – early post-mortem changes in collagen change the structure of connective tissues [5, 6] and therefore the cadaveric model has an inherent flaw when it comes to assessing the dynamics of the tissue plane.

This chapter is divided into the following 10 sections: The tissue plane defined, History of the tissue plane in regional anaesthesia, The modern era of the tissue plane in regional anaesthesia, Tissue plane dynamics and some misunderstandings, Dye studies on tissue plane dynamics, High-definition ultrasound studies and the tissue plane, Tissue plane blocks versus compartment blocks, Systematic reviews, Research opportunities, and Conclusion.

2. The tissue plane defined

A tissue plane is defined as a potential space separating structures such as organs, muscles, nerves and blood vessels [7]. It frequently but not exclusively contains fine loose areolar tissue which is easily divided by both sharp and blunt dissection [2, 8]. The finer quality of these connective tissues contrasts to the much denser connective tissue that forms fascial boundaries, e.g. the prevertebral fascia. This is an important distinction as local anaesthetic will not diffuse across a fascial boundary.

Tissue planes are located throughout the body [2]. Examples include; providing a conduit for nerves, blood vessels and lymphatics from one body region to another e.g., within the femoral canal, [8]; dividing elements of a structure into its component parts, e.g., the brachial plexus [8, 9]; or where structures can be easily separated, e.g., between the fascicles of rectus abdominis muscle and the posterior rectus sheath [10].

The surgeon divides these tissues with scalpel, scissors, probe or finger and in so doing creates the plane of dissection in order to excise tissue or access an anatomic area. In surgical practice there is also a plane of dissection which creates less bleeding, the so-called 'avascular plane' [2]. By contrast the regional anesthesiologist injects a bolus of fluid which spreads along and through the tissue plane/s, not so much dividing as separating the tissues and then diffusing into the nerve/s to create a conduction block.

It is important to keep reminding ourselves that the tissue plane is a concept, not actual anatomy. It points towards tissues which are easily dissected/divided vs. tissues which are not. In regional anaesthesia the tissue planes of interest contain nerves. In this respect it is required to know which nerves may be blocked, where and what they innervate, how and where to access the tissue plane safely and how the tissue plane/plane of dissection will spread the injected solution.

3. History of the tissue plane in regional anaesthesia

While the tissue plane concept is fundamental to surgical dissection technique [2–4], the lack of emphasis on its importance in regional anaesthesia is perhaps ironic given the number of publications in the literature which have in fact related to it prior to the introduction of ultrasound [11–34]. Indeed, the terms 'loss of resistance' and 'pop' refer to techniques accessing tissue planes, although they have not traditionally been described in that fashion.

The lack of acknowledgement of the tissue plane concept changed abruptly in 2007 with the publication of TAP (transversus abdominis plane) block [35]. In this paper the authors described the tissue plane between the fasciae of internal oblique and transversus abdominis muscles as a 'fascial plane' and then called it the 'transversus abdominis plane'. The fascial plane label stuck as did the name TAP and the search was on for others which surfaced in quick succession [36–43]. This pursuit for new targets was undoubtedly promoted by the emerging use of ultrasound and it is fair to say that subsequently there has been an explosion of interest across the spectrum of practice [44–83]. The terms 'fascial plane block' and 'interfascial plane block' have been further promoted [84] although more recently 'tissue plane' has been used [9].

The common theme of course is that all of the above involves the study of tissue planes and their dynamics of solution spread. As in surgical practice the tissue plane concept has been and is fundamental to the practice of regional anaesthesia.

4. The modern era of the tissue plane in regional anaesthesia

In the modern era, the rules have changed with the introduction of ultrasound. Now we are able to directly visualise tissue planes and at least in theory, manipulate them to our clinical advantage. While we now have a significant advantage with this development, a greater need for understanding the concept and its relevance to regional anaesthesia has arisen. A headlong rush to discover and name new blocks has often preceded the basic scientific work that should have underpinned the practice. Soft endpoints (e.g., 'we have done 20 and they worked well') and generic terms (e.g., 'multimodal analgesia') have the potential to hide the fact that a particular technique does not achieve the intended effect.

Added to this is a confused nomenclature. Surgical specialties have long used the term 'tissue plane' with a clear understanding of its meaning and it would seem odd to borrow this concept and claim it for regional anaesthesia under revised names. That being said, this author would also argue that for historic reasons it is important to retain the original name of individual techniques since these are the names given by authors to their techniques and which have been accepted through a peer-review process.

In the following paragraphs, we examine several of these techniques through the lens of intended clinical application versus anatomic scientific foundations.

PECS block was originally published as a technique to provide analgesia following breast surgery [37]. The name refers to the tissue plane between pectoralis major and pectoralis minor muscles, and the aim is to block the medial and lateral pectoral nerves which derive from the brachial plexus. This creates somewhat of a dilemma as the pectoral nerves do not innervate the breast. There have been modifications since, possibly reflecting that fact and correcting the record somewhat.

The pecto-intercostal fascial block was first published as an analgesic technique for breast surgery [52] and anterior chest wall trauma [53]. It aims to block the anterior cutaneous sensory branches of the intercostal nerves where they penetrate the chest wall near the edge of the sternum. Whilst the cutaneous termination of the intercostal nerves T2-T6 do innervate the skin over the medial aspect of the breast, these same cutaneous sensory nerves do not innervate the bony structures of the anterior chest wall. Further study of the relevant tissue planes is awaited.

By contrast, the superior cluneal nerve block was first published as a very different type of anatomic study [85]. These nerves derive from the first three lumbar dorsal rami and innervate the skin over the buttock area. This technique creates a plane of dissection just deep to the superficial layer of the thoracolumbar fascia in its inferolateral aspect. The authors of that paper first studied a cadaveric model, but then in recognition of the inherent flaws of such modelling repeated the block in volunteers with accompanying mapping of sensory loss against potential surgical incisions. The accompanying editorial suggested that new techniques required similar basic science study so that in the clinical environment, we know exactly what we are doing and what we can expect to achieve [86].

Erector spinae plane block (ESP block), an injection into a tissue plane deep to the erector spinae group of muscles, has quickly become one of the most popular techniques since its first description [60]. It was almost immediately accompanied by multiple case reports with dramatic claims of efficacy [87–90]. There followed several quite different randomised controlled trials with claims of efficacy [91–94], and the indications for the technique have multiplied almost exponentially [95]. The source of greatest debate has seemed only related to the mechanism of action. A cadaveric study [65] disputed the theory that there was adequate spread of local anaesthetic to the ventral rami and instead suggested local anaesthetic spread to the lateral cutaneous branches of the ventral rami through the lateral aspect of the tissue plane. The original authors then followed up with their own cadaveric study [66] showing spread to the ventral rami and hence providing a mechanism of action for their observed results. The tie breaker in this debate was a volunteer study [96] which demonstrated inconsistent spread of injectate to the ventral rami. Hence the enthusiasm to use ESP block has far outrun our understanding of the technique. Can this enthusiasm cause harm? Yes, by lack of effect or failure to use alternative techniques of known efficacy. Some hospitals now run programs using continuous ESP block for rib fractures – one wonders how they work when the ribs are innervated by the ventral rami, and the lateral cutaneous nerves neither pass through the erector spinae group of muscles nor innervate the ribs. Hence the exact role of ESP block remains uncertain.

Continuous rectus sheath block has re-emerged as an option for analgesia post-midline laparotomy. The modern version of placement is a surgical technique, where a plane of dissection is developed between the rectus abdominis muscle and the posterior rectus sheath with a catheter placed in the ensuing compartment for upper abdominal procedures [10], and a plane of dissection developed between the rectus abdominis and the anterior rectus sheath for lower abdominal procedures [97]. It took little time for ultrasound-guided versions of the same technique to emerge [38, 39], although for the majority of placements there is little logic in placing the catheters percutaneously after the wound has been surgically closed [98]. It is suggested that an approach with ultrasound might be indicated if there is intraabdominal sepsis or adhesions making surgical access to the tissue plane unwise or impossible. In this scenario, avoidance of lateral approaches to the rectus sheath is recommended due to the risk of perforation of the epigastric vasculature. There have now been two dye studies confirming the spread of local anaesthetic throughout the developed tissue planes for rectus sheath block [99, 100]. One study demonstrated that inferior to the arcuate line where the posterior rectus sheath is less distinct, a tissue plane containing the relevant abdominal wall nerves lies between rectus abdominis muscle and the transversalis fascia [99], while the other demonstrated the importance of volume to ensure spread of solution across the tissue plane [100]. It is important to note that both of these studies used boluses and this has management implications for continuous systems.

Pericapsular nerve group (PENG) block is a recently published tissue plane block. First described in 2018 [69] it has been accompanied by multiple clinical reports and recently a randomised controlled study in the hip fracture population [101]. Whilst it appears remarkably effective for analgesia for hip fractures, the reasons for this are yet to be fully answered. It purports to block just the sensory branches to the hip joint from the femoral and obturator nerves [69]. Could there also be spread further posteriorly to include the superior gluteal nerves? A dye study [102] sheds some light on the characteristics of spread in this tissue plane deep to iliopsoas muscle. In this study, the needle was slightly more caudad to the site of PENG block but in the same plane and suggested that restriction of spread of injectate was only possible with small volumes. Larger volumes could spread to reach the femoral nerve, defeating the purpose of the technique. In this respect, is this tissue plane limited anteriorly by iliopsoas muscle fascia or by fascia iliaca, the latter being suggested by the spread characteristics of the larger volume in the study?

The IPACK block (infiltration between the popliteal artery and the capsule of the knee) for analgesia post-total knee joint replacement was introduced in 2019 as a cadaveric study [103] although there had been keen interest in this area in the years prior but without an accepted name for the technique [104–106]. A plane of dissection is developed deep to the popliteal artery with the intention to bathe the articular sensory branches of the knee joint in local anaesthetic as they traverse this area to reach the joint capsule. Since 2019 there have been over 10 randomised controlled trials [107–118] and 3 meta-analyses [119–121] reflecting widespread interest in techniques which might provide pain relief without hindrance to ambulation post-total knee joint replacement. There has also been widespread adoption of the IPACK block as reflected by reports of programmes in the literature [122, 123]. It is therefore somewhat concerning that the meta-analyses are not supportive of the technique, at least in its current format. Has enthusiasm outweighed clinical realities in this particular circumstance? Is this a technique that has yet to find its real indication? Or could the literature somehow not be accurately reflecting current effective clinical practice?

5. Tissue plane dynamics and some misunderstandings

In 2006 we published a paper in Anesthesiology which was provocatively entitled ‘The Sheath of the Brachial Plexus: Fact or Fiction?’ [7]. It may have been better entitled ‘The Sheath of the Brachial Plexus: Actual Anatomy or Concept?’, as negative reaction to the title may have distracted from what we believed to be the importance of the paper. This was a discussion about tissue planes and their significance to the practice of regional anaesthesia and to our knowledge the first time this had been directly addressed in the literature.

The notion of the brachial plexus ‘sheath’ has been attributed to various authors [124–126]. Two of these authors were in fact referencing the brachial fascia which is the deep investing fascia of the arm [125, 126], and one also referenced the intermuscular septum of the arm [126]. This is confusing as neither fascia is in intimate relationship with the neurovascular bundle.

Winnie [11] subsequently suggested that the ‘sheath’ was merely the final part of a tubular prolongation of the prevertebral fascia and promoted the concept of a continuous fascia-enclosed space extending from the cervical transverse processes to several centimetres into the arm. He likened brachial plexus anaesthesia to epidural anaesthesia where, once the space had been entered only a single injection was needed, an analogy intended to stop practitioners performing multiple injections which thereby increased the chances of neural injury. Various publications subsequently presented findings which significantly modified his concept [14, 16, 18, 20, 23, 28, 68].

The discussion section in our paper addressed tissue planes and their dynamics. The tough tissues of the prevertebral fascia give way rapidly to much thinner, softer and translucent connective tissues which encircle and entwine the brachial plexus and blood vessels [8]. As a collective, these thin and translucent connective tissues form the tissue planes of the brachial plexus. Indeed, in the current age of ultrasound-guidance the presence of these tissue planes is well accepted [9].

Within the tissue planes there may be minimal room for expansion at any one point and therefore flow has to occur along the tissue planes according to resistances encountered along the way [7]. The layers of connective tissue are not homogeneous, do not necessarily interconnect, and can hinder or prevent diffusion. Injection at one point does not guarantee spread elsewhere [8]. At the level of the trunks and divisions of the brachial plexus, the neural elements reorganise significantly and their associated tissue planes interconnect. This is readily observable during surgical dissection [8]. This arrangement allows for a more even spread of solution, a feature which has indeed been observed clinically [9, 127–130]. The belief that supraclavicular blocks are more effective because the neural elements are closer together [131] is better explained by the interconnection of tissue planes at this level. By contrast, at axillary level where the nerves do not interconnect and the tissue planes containing each nerve are largely separate [14, 16, 18], efficacy is lower unless each nerve was blocked separately. Side effect profiles can also be explained by spread of injectate via tissue planes, e.g., phrenic paresis with subomohyoid suprascapular nerve block [132].

The sheath concept also does not take into account the impact that surrounding rigid anatomy has on flow dynamics. Our work on the 'axillary tunnel' [133] calculated the dimensions of the tunnel and explained the significant impact of the varying dimensions. The injected dye did not spread as in a cylindrical tube but followed the contours of the rigid anatomy. The volume of the axillary tunnel at any one point was less than 10 ml, and so flow inevitably occurred along the tunnel. The tunnel had two constrictions and flow of injectate from the needle tip could be anterograde, bidirectional or retrograde depending on where the point of injection occurred in respect of these constrictions. The more lateral constriction was clearly the obstruction to flow at this lower level [133] rather than the head of the humerus as previously described [134]. Historic dye studies of the brachial plexus [11, 134] fitted with our predictions of flow patterns based on the contours of the rigid anatomy.

The CT dye studies from the axillary tunnel work also revealed the reason we were able to avoid the phrenic nerve during anaesthesia and analgesia for shoulder surgery [135]. We were manipulating the tissue planes of the brachial plexus by injecting into the tissue planes posterior to the artery, with retrograde spread restricted to these same tissue planes, well away from the anteriorly situated phrenic nerve. This phenomenon has subsequently been demonstrated by another group [136].

Given that brachial plexus regional anaesthesia had been based for many years on the concept of the sheath, it was unsurprising that a cadaveric study was subsequently published demonstrating apparent macroscopic evidence of the brachial plexus sheath [137]. We had significant issues with this evidence, including: 1. a significant connective tissue structure was demonstrated covering the emerging nerve roots in the root of the neck, but this was the prevertebral fascia. There were difficulties with calling this the brachial plexus sheath, partly because it already had an anatomic name. 2. the brachial plexus, as revealed prior to disappearing from view under the clavicle, was covered by a thin layer of opaque connective tissue. It was agreed by both sets of authors that this was what had been identified as the enveloping tubular structure called the sheath. This opaque connective tissue enveloping the plexus in the cadaver was remarkable for its difference to the equivalent tissue in a patient undergoing surgical dissection of the plexus [8], and we believe that this most likely reflected post-mortem changes in connective tissues [5, 6]. Interestingly, not all investigators using cadaveric specimens have encountered an opaque layer of connective tissue surrounding similar major nerves or plexuses. Indeed, they have echoed our words of 'thin, transparent and fragile' when describing such connective tissues [138].

We concluded that tissue planes, in conjunction with the influence of surrounding rigid anatomy, provided a better explanation for outcomes in brachial plexus regional anaesthesia than the concept of a sheath.

6. Dye studies on tissue plane dynamics

The regional anaesthesia literature already has a reasonably large number of dye studies [11–34, 44–51, 54–68, 70–83] and they encompass most of the techniques in current common usage. One could be forgiven for believing that we now have most of the answers, but this is an area where for various reasons there is still room for improvement. Our work on the axillary tunnel raised some generic questions to be answered in other areas – under what conditions do flow characteristics change, can flow characteristics be manipulated to clinical advantage and what anatomic features can be disadvantageous in terms of flow characteristics? These questions infer that the tissue plane is a dynamic environment and that this can be used to clinical advantage.

It has been unusual in this type of research work to use any model other than cadavers but for various reasons these cannot provide an accurate replication for clinical application. Connective tissue changes in quality and appearance very soon after death [5, 6]. As pointed out by Ivanusic et al. [65] it is also not possible to investigate for any block-related phenomenae that may be linked to physiological occurrences such as breathing in a dead body. Specific block-related positioning is not possible in cadaveric specimens. At best, with carefully planned and executed dissection, cadaveric models provide a sort of basic static road map of where fluid may spread and what nerve/s might be blocked.

In the above context a dye and latex study by Mayes et al. [139] investigated serratus anterior plane block (SAP) as a potential analgesic technique for rib fractures. It demonstrated a clear plane of dissection between serratus anterior and the external intercostal muscle/ribs, bathing the lateral cutaneous branches of the intercostal nerves in solution as per the description in the original publication [42]. This means that the technique will not provide analgesia for rib fractures, a conclusion framed by the authors in subtle language [139], because the intercostal nerves which innervate the ribs will not be blocked. Does trauma to the chest wall provide a pathway to these nerves? This is unlikely and not a dependable mechanism in this author's opinion. Can solution track along the lateral cutaneous branches to the intercostal nerves of origin? This again is unlikely as it requires the passage of these nerves through the muscle layers of the chest wall to be the path of least resistance as the injected fluid flows through the tissue plane. It is up to those who wish to prove any of these mechanisms to create the models and test their hypotheses.

Another technical issue at play in dye studies relates to where the tip of the catheter is located when injections are made. In a study on continuous parasacral sciatic nerve block [31], the investigators used 8 ml of dye for confirmation of location of their perineural catheters. In our work on the axillary tunnel [133], we realised that we could only locate the tip of the catheter by using a much smaller volume of injectate of 2 ml, a larger volume obscuring the location.

Adductor canal block [54] has gained popularity as an analgesic technique post-total knee joint replacement due to less motor block than femoral nerve block [140] albeit with some accompanying loss of pain relief [140, 141]. There have been several dye studies examining this technique [142–145], with ensuing cautions about volume used, where the injection is placed to limit spread of injectate beyond the adductor canal, and consideration of the impact of tourniquets on the spread of solution. However, there has been no work directly measuring the potential volume of the canal, nor how this might change with application of a tourniquet, nor what flow restrictions if any are present, all of which would require 3-dimensional imaging. This is a more costly investigative modality but provides much more information.

The cadaveric dye studies of ESP block [64, 65] and the subsequent volunteer study of ESP block [96] have been discussed earlier in this chapter. Perhaps this illustrates the peril of having cadaveric studies as stand-alone evidence of efficacy. The volunteer study certainly seems to be one potential bridging option to clinical practice but may not always be possible due to safety considerations. Some authors do combine their cadaveric studies with a clinical case series as additional evidence, but is this practice consistent with the current ethical standards in human research? Multiple pathways are probably likely required to establish efficacy and safety across the range of techniques and indications prior to widespread adoption in clinical practice. In this respect, randomised controlled trials are only as good as the science which underpins them.

7. High-definition ultrasound studies and the tissue plane

There have now been several studies examining nerves of the upper and lower extremities and the soft tissues which surround and envelope these nerves [146–149]. These have given rise to the term ‘paraneural sheath’ of the sciatic nerve [146] and brachial plexus [149] respectively. In one recent study, the sonographic imaging was correlated with histologic specimens [149] to demonstrate what the authors described as ‘fascial tissue planes’ within the paraneural sheath.

It is to be noted on the images of the brachial plexus [149] that the pectoral fascia is much more visible, i.e., it exhibits greater anisotropy, than the tissues within the plexus complex. This is not artefactual – fasciae such as the pectoral or prevertebral are much sturdier connective tissue structures than the relatively fragile connective tissues surrounding the brachial plexus. The imaging also demonstrates both the tissue planes of the plexus and the phenomenon of injected fluid separating the tissue planes as it flows through the length of the plexus complex. The ‘paraneural sheath’ has the same anisotropy as the tissue planes within the neurovascular bundle, i.e., the same type of tissue, which is quite distinct from fascial tissue. This study demonstrates very well some characteristics of the dynamics of the tissue planes of the brachial plexus.

8. Tissue plane blocks versus compartment blocks

In some literature it has been suggested that the local anaesthetic fills a compartment to achieve its effect, particularly where the injection is made within the fascia enclosing muscles such as rectus abdominis or perhaps even the erector spinae plane block [150]. The actual phenomenon can be viewed on ultrasound in real time as the injected solution can be seen to develop a plane of dissection between the muscles and the fascia or bone. Once again, the concept of the tissue plane becomes the focus of our attention.

9. Systematic reviews

There have been a number of systematic reviews over the last few years which have not specifically mentioned tissue planes in the context of regional anaesthesia but which clearly relate to that concept [151–164]. These have all been procedure specific and, despite apparent clinical enthusiasm for the different techniques, are quite often neutral or negative in their recommendations. This may reflect the difficulties in the development phase of various techniques to which the author has alluded earlier in this chapter.

10. Research opportunities

There is a wealth of opportunity for further research in this area. Regional anaesthesia in some respects is in its infancy in understanding and manipulating tissue planes. Ultrasound allows novel tissue plane targets to emerge and the challenge is to fit these new techniques into practice in a scientifically sound fashion. Now more than ever we are required to learn anatomy from a different perspective; what nerve/s innervate this area/region? how do they get there? where can I access them? does this raise safety issues, and how are these overcome? how will the tissues spread the fluid I inject? are there potential complications from this? how do I answer these questions in a scientifically meaningful fashion? do I need to create a new technique when one already exists for my purposes?

I would venture to suggest that after the initial idea comes thoughtful reading, basic science preparation and careful analysis. This is all before consideration is given to conducting randomised controlled trials.

11. Conclusion

Although it has been suggested by many to be the era of ultrasound in regional anaesthesia, it could equally be termed the era of the tissue plane. This of course is courtesy of ultrasound, but the technology alone will not get us the results we want. It has been suggested that 'if we can see it, we can block it' [84], but this invites invocation of the old adage 'primum non nocere'. Was the block necessary? Did it add real benefit? All interventions risk harm. Perhaps we could change the saying to 'now that we can see it, how do we better understand what we are seeing, and how can this aid our practice?' The challenge is to methodically and responsibly work our craft so that it helps us as well as our patients.

Conflict of interest

The author declares no conflict of interest.

Notes/thanks/other declarations

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Chapter 3

New Application of Low-Molecular Weight Dextran as Local Anesthetic Adjuvant for Ultrasound-Guided Nerve Block

Masahiko Tsuchiya

Abstract

Advances in ultrasound technology and the increased risk of opioid overdose following surgery have expanded applications of nerve block for surgical cases, resulting in reevaluation of adjuvants used to potentiate local anesthetics. We have found that a mixture of local anesthetic with low-molecular weight dextran, one such local anesthetic adjuvant, greatly enhances analgesic duration and potency in patients receiving an interfascial compartment nerve block under ultrasound-guidance as well as those receiving a single peripheral nerve block. Notably, a compartment nerve block in the abdominal trunk with an extra-large amount of low-molecular weight dextran mixture, which results in a longer duration of the injected drugs at the injection site, provides good analgesia that is comparable to epidural anesthesia. Such a dextran mixture also suppresses systemic absorption of local anesthetics, thus reducing their systemic toxicity, which enhances regional anesthesia safety. Furthermore, it controls unintended spread of injected local anesthetics, thus increasing nerve block accuracy. In this chapter, recent findings regarding use of low-molecular weight dextran as a local anesthetic adjuvant obtained in our laboratory are presented.

Keywords: low-molecular weight dextran, ultrasound-guided nerve block, local anesthetics, adjuvant, regional anesthesia, anesthesia safety, toxicity

1. Introduction

Recent advances in ultrasound technology have improved the accuracy and reliability of nerve block procedures [1–3]. As a result, there has been a shift from general anesthesia alone to that in combination with a nerve block. In addition, important related issues are opioid abuse, which has become a matter of public concern [4], as well as possible reduction in the risk of cancer recurrence in patients undergoing surgery with regional anesthesia [5, 6]. Evidence suggesting that general anesthesia in combination with regional anesthesia is superior for intraoperative hemodynamic stability and postoperative recovery has been reported [7, 8] (**Figure 1**). Those findings further advanced the shift to application of nerve block with general anesthesia, thus techniques to modify the effects of local anesthetics including use of an adjuvant compound have also regained attention [9]. Dextran,

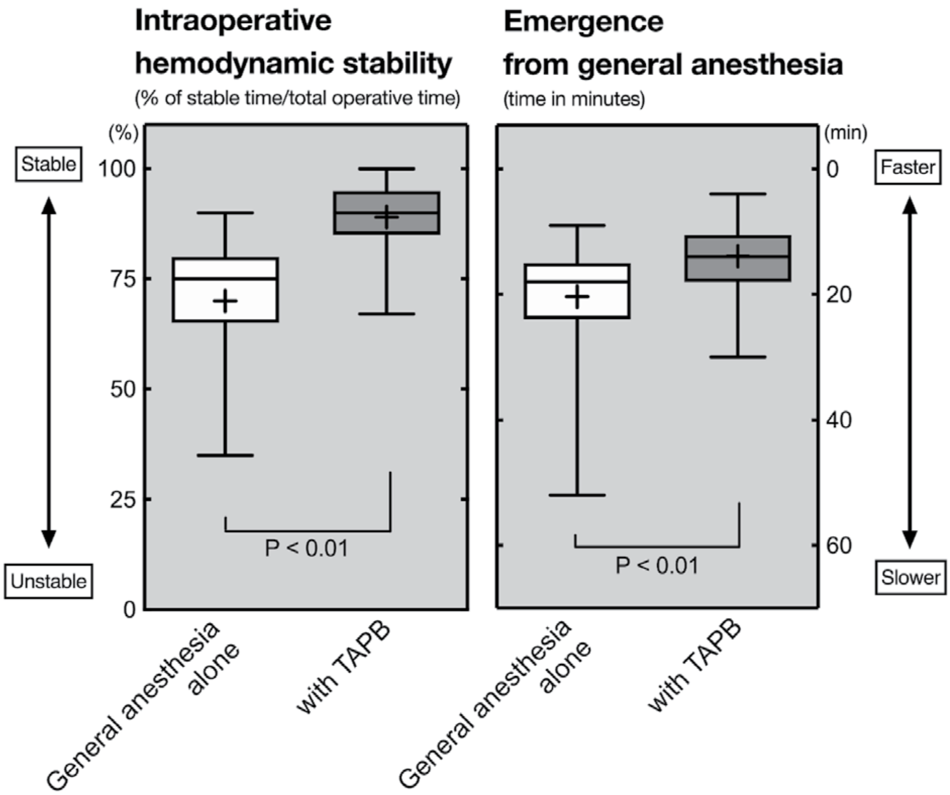

Figure 1.
Left panel: *Comparison of intraoperative hemodynamic stability between patients with general anesthesia alone (n = 35) and general anesthesia with a transversus abdominis plane block (TAPB) (n = 33) [8]. General anesthesia was maintained in the same manner with sevoflurane and remifentanil in both groups. The period during the operation when both systolic blood pressure and heart rate were within 70–110% of their pre-anesthesia value was defined as the hemodynamic stable time. The ratio of hemodynamic stable time to total operative time was used as an indicator of hemodynamic stability. The stability ratio was significantly higher in the group receiving general anesthesia with TAPB (91%, range 50–100%) as compared to general anesthesia alone (79%, range 40–91%), indicating greater hemodynamic stability with general anesthesia plus TAPB. Values are presented as the median and minimum-maximum range (mean value indicated by "+").* ***Right panel:*** *Comparison of anesthesia emergence time between the same groups shown in left panel. Anesthesia emergence time was defined as the time from completion of surgery to extubation. That was significantly shorter in the group receiving general anesthesia plus TAPB (14 minutes, range 4–30 minutes) as compared to general anesthesia alone (18 minutes, range 9–52 minutes). Values are presented as the median and minimum-maximum range (mean value indicated by "+").*

which is composed of complex branched polysaccharides derived from sucrose with various lengths and weights, is such a local anesthetic adjuvant and investigated many decades ago, though nearly forgotten in recent times.

Accumulated attention and increased need of regional anesthesia have resulted in development of new nerve block procedures, with transversus abdominis plane and quadratus lumborum blocks typically employed [8, 10] (**Figure 2**). However, these new types of nerve blocks require accurate injection of a sufficient quantity of local anesthetic into the targeted interfascial compartment. A compartment nerve block performed in this manner has potential to serve as a substitute for epidural anesthesia, the current gold standard method for surgical pain control. On the other hand, there is a risk of systemic toxicity of local anesthetics associated with this procedure because the drug is given in a large amount [11]. Furthermore, another weak point to be solved is insufficient analgesic duration for controlling postoperative pain when the nerve block is performed with a single injection.

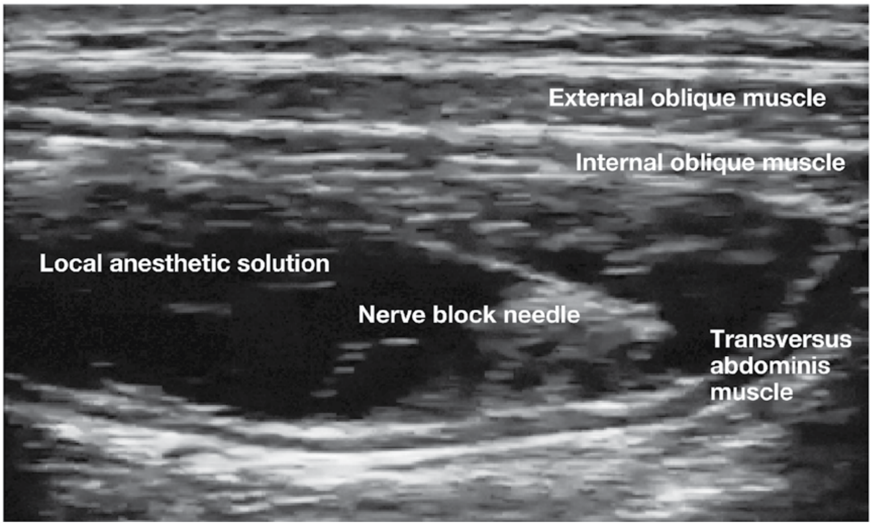

Figure 2.
Ultrasound image obtained during transversus abdominis plane block [8]. A local anesthetic solution was injected into the interfascial compartment between the internal oblique and transversus abdominis muscles.

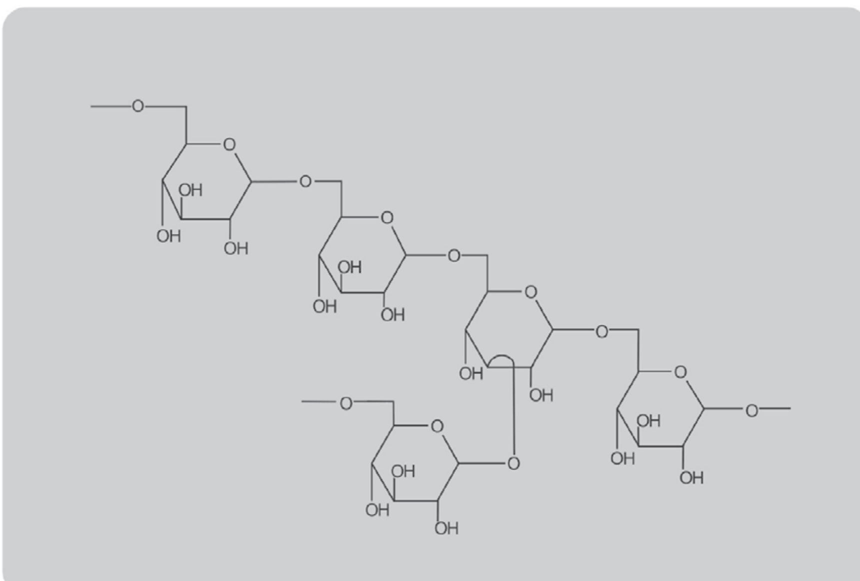

Figure 3.
Molecular structure of low-molecular weight dextran.

We recently performed a reinvestigation of dextran effects under modern clinical environments and found that low-molecular weight dextran, with an average molecular weight of 40,000 (**Figure 3**), used as a local anesthetic adjuvant resolves the disadvantages of a trunk nerve block by improving the potency and safety of the local anesthetic [10, 12–15]. In this chapter, effects and clinical applications of low-molecular weight dextran as a local anesthetic adjuvant are discussed based on recent findings obtained by our research team.

2. Toxicity of adjuvant adrenaline and prevention by low-molecular weight dextran

Adrenaline (epinephrine) is the oldest adjuvant given with local anesthetics and continues to be used. When used as an adjuvant it is typically applied with lidocaine, and known to induce vasoconstriction for reducing systemic absorption of the administered local anesthetic and enhancing the analgesia effects, and seems to be an optimal application. However, the combination of adrenaline and lidocaine does not always lead to good results.

Lidocaine has potent vasodilation effects, thus it can enhance the absorption of adrenaline into systemic circulation when a lidocaine-adrenaline mixture is administered. Wasa Ueda, presently professor emeritus and executive advisor of our research team, validated this issue in a clinical study, in which application of a lidocaine-adrenaline mixture for infiltration anesthesia was shown to significantly increase the plasma concentration of adrenaline in comparison with an infiltration injection of the same amount of a pure adrenaline solution [16] (**Figure 4**). An increase in adrenaline concentration in the circulation can increase blood pressure and heart rate, sometimes leading to severe lethal cardiac dysrhythmia. Such toxic effects of a lidocaine-adrenaline mixture are a significant problem for patients under general anesthesia using halothane, which has a characteristic property to increase sensitivity to adrenaline, whereas aggravating effects on circulation, such as increase in blood pressure, can still develop when the more recently introduced anesthetics desflurane and sevoflurane are used as an inhalant (**Figure 5**).

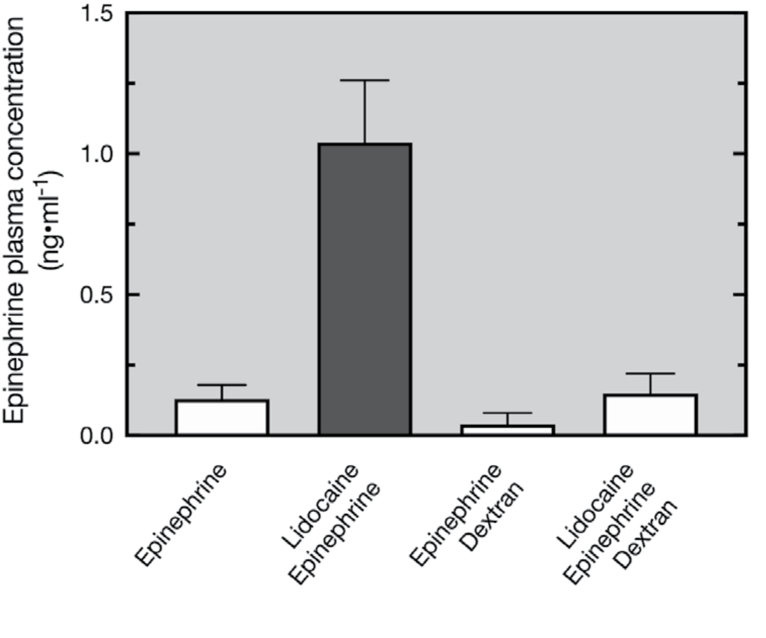

Figure 4.
Peak plasma concentration of adrenaline (epinephrine) following subcutaneous infiltrative injection of various adrenaline solutions in humans [16]. Each column indicates the following. (1) epinephrine: 1:200,000 adrenaline in normal saline solution. (2) lidocaine epinephrine: 1:200,000 adrenaline with 0.5% lidocaine in normal saline solution. (3) epinephrine dextran: 1:200,000 adrenaline with 10% low-molecular weight dextran in saline solution. (4) lidocaine epinephrine dextran: 1:200,000 adrenaline with 0.5% lidocaine and 10% low-molecular weight dextran in saline solution. The adrenaline concentration in the solutions was the same in all four groups. Values are expressed as the mean ± standard deviation. When adrenaline was subcutaneously injected with lidocaine (lidocaine epinephrine), the peak plasma adrenaline concentration showed an approximately 7-fold increase as compared with injection of the pure adrenaline solution (epinephrine). However, the presence of low-molecular weight dextran in the lidocaine adrenaline solution (lidocaine epinephrine dextran) suppressed the toxic increase in plasma adrenaline concentration.

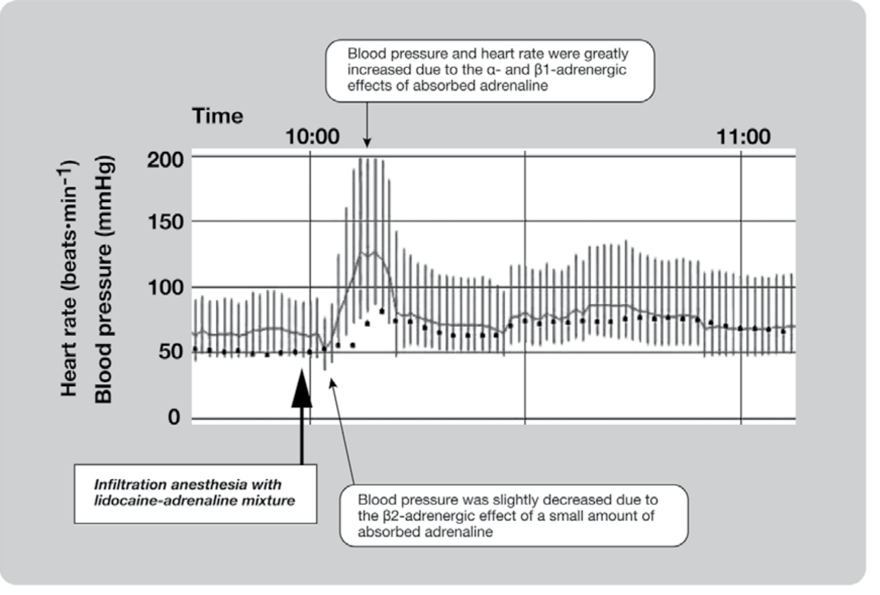

Figure 5.
Typical increases in blood pressure and heart rate with subcutaneous infiltration anesthesia using 20 ml of 0.5% lidocaine and 1:200,000 adrenaline in normal saline solution in patients receiving sevoflurane general anesthesia. Soon after injection of the lidocaine-adrenaline mixture, blood pressure was slightly decreased due to the β2-adrenergic effect of a small amount of absorbed adrenaline. Thereafter, blood pressure and heart rate were greatly increased due to the α- and β1-adrenergic effects of adrenaline.

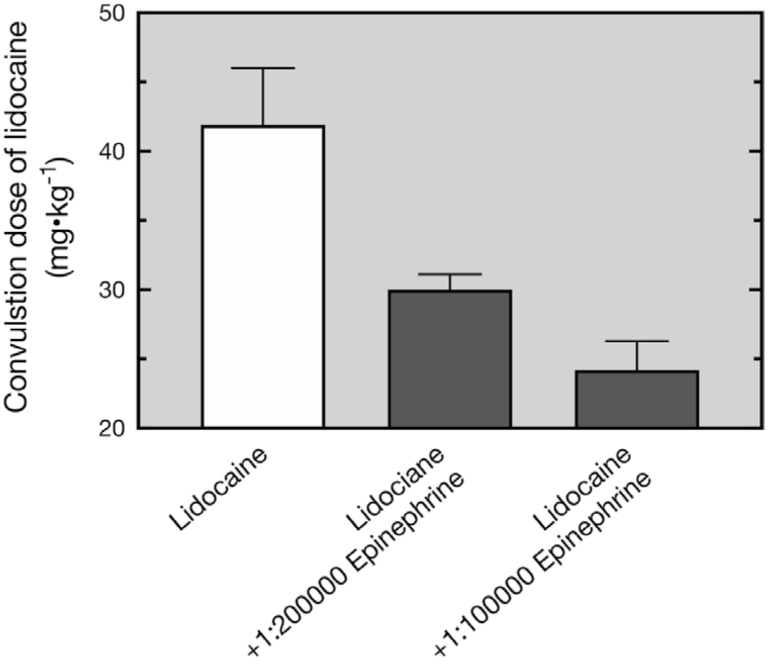

Figure 6.
Convulsion dose of plasma concentration of lidocaine in rat [17]. Male Wistar rats were divided into three groups and received continuous intravenous injections of 1.5% lidocaine, 1.5% lidocaine with 1:200,000 adrenaline (epinephrine), or 1.5% lidocaine with 1:100,000 adrenaline (epinephrine). Values are expressed as the mean ± standard deviation. The total lidocaine dose from the beginning of infusion of the lidocaine mixture to onset of generalized convulsions was analyzed. Addition of adrenaline to the lidocaine solutions significantly decreased the threshold of lidocaine-induced convulsions in a dose-dependent manner, indicating that adrenaline increased lidocaine systemic toxicity.

Furthermore, the presence of adrenaline decreases the threshold concentration of lidocaine to induce convulsions, leading to enhancement of the central nervous system toxicity of lidocaine [17] (**Figure 6**). Another study showed that concomitant administration of adrenaline with lidocaine increased the concentration of extracellular lidocaine in the brain [18], which may be another supporting mechanism by which adrenaline increases the toxicity of lidocaine for the central nervous system. Therefore, though this combination can be useful for regional anesthesia, a lidocaine-adrenaline mixture is not completely safe.

The Ueda research team found a solution to the hazardous risk of a lidocaine-adrenaline mixture, as addition of low-molecular dextran into the mixture was shown to suppress absorption of adrenalin into circulation [16]. The peak plasma adrenaline concentration with a lidocaine-adrenaline mixture with low-molecular weight dextran was 0.15 ± 0.07 ng•ml^{-1}, while that was 1.04 ± 0.22 ng•ml^{-1} with the standard lidocaine-adrenaline mixture (**Figure 4**). Thus, it was concluded that a lidocaine-adrenaline-dextran mixture is safe for application as regional anesthesia, which is now considered to be a landmark finding indicating an adjuvant function of low-molecular weight dextran to improve the safety of local anesthetic usage.

3. Early history of dextran as local anesthetic adjuvant and possible action mechanism

Apart from the effects of dextran on lidocaine-adrenaline mixtures, the first description of the adjuvant effects of dextran with local anesthetics can be traced back to the 1960s [19]. Thereafter, prolongation and enhancement of analgesia by dextran were studied, and some favorable results reported [20–22], with possible mechanisms for those actions also investigated. Dextran may form a water-soluble complex with local anesthetics that is slowly absorbed and remains at the injection site for a longer period with increased viscosity [23, 24]. Moreover, addition of dextran was shown to change the pH of a local anesthetic solution and that may further contribute to prolongation of action [25]. Despite these positive results, several studies that failed to find potential effects for analgesia with dextran have also been reported [26, 27]. As a result, along with the expanding applicability of general anesthesia for surgery, dextran has gone largely unnoticed and its adjuvant effects remain inclusive.

4. Adjuvant effects of low-molecular weight dextran with current nerve block techniques

Assuming an interaction of dextran with local anesthetics, its effectiveness as a local anesthetic adjuvant may be dependent on the type of nerve block employed and procedure used. Such nerve block dependency may induce inconsistent adjuvant effects, as shown in several previous studies. Because an interfascial compartment nerve block, such as a transversus abdominis plane block, is required to perform accurate injection of a large amount of local anesthetic solution into the targeted interfascial compartment, that is difficult to perform with a conventional landmark method. Fortunately, advancements in ultrasound guidance techniques have made this possible at a clinically acceptable quality. Consequently, an interfascial compartment nerve block has become popular. Maintaining the amount of injected local anesthetics in the compartment for a longer period is essential to induce sufficient analgesia in cases with such a compartment block, thus it is quite reasonable to assume that the possible fluid retention properties of dextran have a favorable impact. Based on findings obtained in previous studies reported by the

Ueda research team concerning use of a lidocaine-adrenaline mixture, we consider that low-molecular weight dextran is the most suitable local anesthetic adjuvant among the various dextran compounds available for interfascial compartment nerve block procedures currently used.

4.1 Pharmacokinetics and analgesia: transversus abdominis plane block and rectus sheath block cases

First, we investigated the adjuvant effects of low-molecular weight dextran when used for a transversus abdominis plane block and rectus sheath block [12]. Patients scheduled for a laparoscopic colectomy [age 66 ± 9.8 years, body weight 59 ± 11.7 kg, anesthesia time 322 ± 69 minutes (values shown as mean ± standard deviation)] received a combination of two bilateral interfascial compartment blocks, a transversus abdominis plane block and rectus sheath block. Following anesthesia induction, they received this two-block combination with either 0.2% levobupivacaine in a saline solution (control group: 20 ml × 4 injections = total 160 mg of levobupivacaine in saline; n = 27), or 0.2% levobupivacaine and 8% low-molecular weight dextran (LMWD) in a saline solution (LMWD group: 20 ml × 4 injections = total 160 mg of levobupivacaine in LMWD; n = 27). General anesthesia was maintained with sevoflurane and remifentanil, with 200 μg of fentanyl given at the end of surgery. Continuous intravenous infusions of fentanyl at 25 $\mu g{\bullet}hr.^{-1}$ and droperidol at 63 $\mu g{\bullet}hr^{-1}$ were postoperatively given for 24 hours as analgesia and antiemetic treatments.

There were no significant differences in regard to patient age, body weight, amount of intraoperative blood loss, or anesthesia time between the groups. Furthermore, no typical adverse effects, such as wound infection, delayed wound healing, tissue necrosis, or prolonged abnormal sensory disorder over the area of injection, or other systemic abnormalities were observed in either group. In the control group, the plasma concentration of levobupivacaine rose quickly just after performing the nerve block and reached a maximum at 51 ± 30 minutes (Tmax), while in the LMWD group, that rose in a more gradual manner with a significantly longer Tmax value (73 ± 25 minutes, $P < 0.05$ vs. control group) (**Figure 7**). The maximum concentration of levobupivacaine (Cmax) in the control group was 1410 ± 322 $ng{\bullet}ml^{-1}$, whereas that in the LMWD group was significantly lower at 1141 ± 287 $ng{\bullet}ml^{-1}$($P < 0.05$). Also, the area under the plasma concentration-time curve (AUC) from 0 to 240 minutes was significantly lower in the LMWD as compared to the control group (172,484 ± 50,502 vs. 229,124 ± 87,254 $ng{\bullet}min{\bullet}ml^{-1}$, $P < 0.05$). In contrast, the plasma levobupivacaine concentration in the LMWD group was higher than that seen in the control group after 1200 minutes. These results demonstrated that use of a low-molecular weight dextran mixture results in reduced systemic absorption of the local anesthetic from the injection compartment along with its longer retention in that compartment for more than 20 hours. Such a reduction in systemic absorption lowers the risk of local anesthetic systemic toxicity. In addition, the postoperative 24-hour numerical rating scale (NRS) for pain (0-no pain, 10-worst pain) demonstrated significantly better analgesia in patients with the local anesthetic mixture with low-molecular weight dextran as compared to those in the control group who received a standard local anesthetic solution (**Figure 7**). That result was considered to be due to extended presence of the injected local anesthetic in the injection compartment.

Together, our findings indicated that low-molecular weight dextran as a local anesthetic adjuvant provides great clinical advantages for enhancement of analgesia effect as well as reduction in systemic toxicity of a local anesthetic.

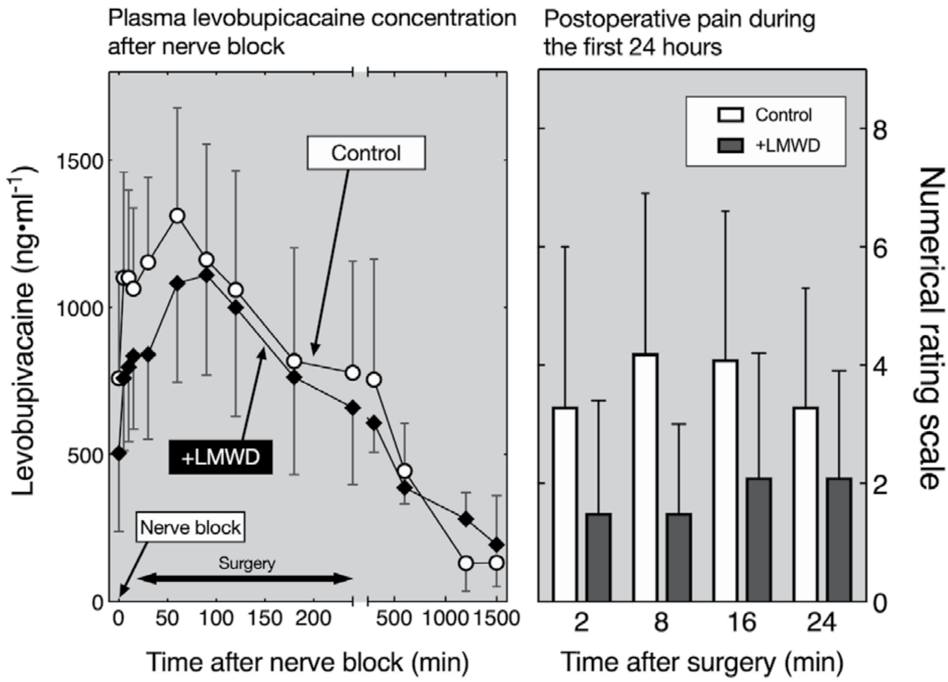

Figure 7.
Left panel: *Changes in levobupivacaine plasma concentration in patients receiving bilateral transversus abdominis plane blocks plus rectus sheath blocks with 160 mg of levobupivacaine [12]. For nerve blocks, the control group (n = 27) received nerve blocks using 80 ml of 0.2% levobupivacaine in a saline solution, while the +LMWD group (n = 27) received 80 ml of 0.2% levobupivacaine and 8% low-molecular weight dextran in a saline solution just before starting a laparoscopic colectomy. Values are expressed as the mean ± standard deviation. Addition of low-molecular weight dextran to the levobupivacaine solution was shown to lower the peak level of levobupivacaine plasma concentration, indicating that dextran suppresses systemic absorption of levobupivacaine from the injection site, which may prolong analgesic effects and decrease the systemic toxicity of levobupivacaine. After 1200 minutes, plasma levobupivacaine concentration in the +LMWD group was significantly higher than that in the control group, indicating longer retention of levobupivacaine at the injection site following its slow release.* ***Right panel:*** *Numerical rating scale (NRS) scores for postoperative pain in the same patients. Values are expressed as the mean ± standard deviation. NRS: 0, no pain, to 10, worst pain. NRS scores in the +LMWD group were significantly lower at each time point after surgery as compared to the control group (P < 0.01 at 2, 8, 16 hours; P = 0.035 at 24 hours).*

4.2 Extended retention time in injected area: quadratus lumborum block cases

To confirm the longer retention time of the local anesthetic and low-molecular weight dextran mixture at the injection site, a different group of cases that underwent a quadratus lumborum block, another type of interfascial compartment nerve block, were investigated [10]. A quadratus lumborum block using a low-molecular weight dextran mixture with ropivacaine was applied in 18 patients undergoing open abdominal surgery (age 67 ± 8.4 years, body weight 72.6 ± 4.6 kg, anesthesia time 429 ± 123 minutes) following anesthesia induction (**Figure 8**). One hundred ml of 0.1% ropivacaine and 8% low-molecular weight dextran in saline solution with 2 mg of morphine was injected into interfascial space posterior of the quadratus lumborum muscle (so-called QLB2 nerve block) on each side (total 200 ml in both sides). Anesthesia was maintained with desflurane and remifentanil. Postoperatively, intravenous flurbiprofen (50 mg) was given every 8 hours, with acetaminophen (15 mg•kg^{-1}) used as rescue treatment for pain.

No rescue drug was given to any of the patients on the first night after surgery and the NRS for pain (0-no pain, 10-worst pain) during that period was 2.2 ± 1.7.

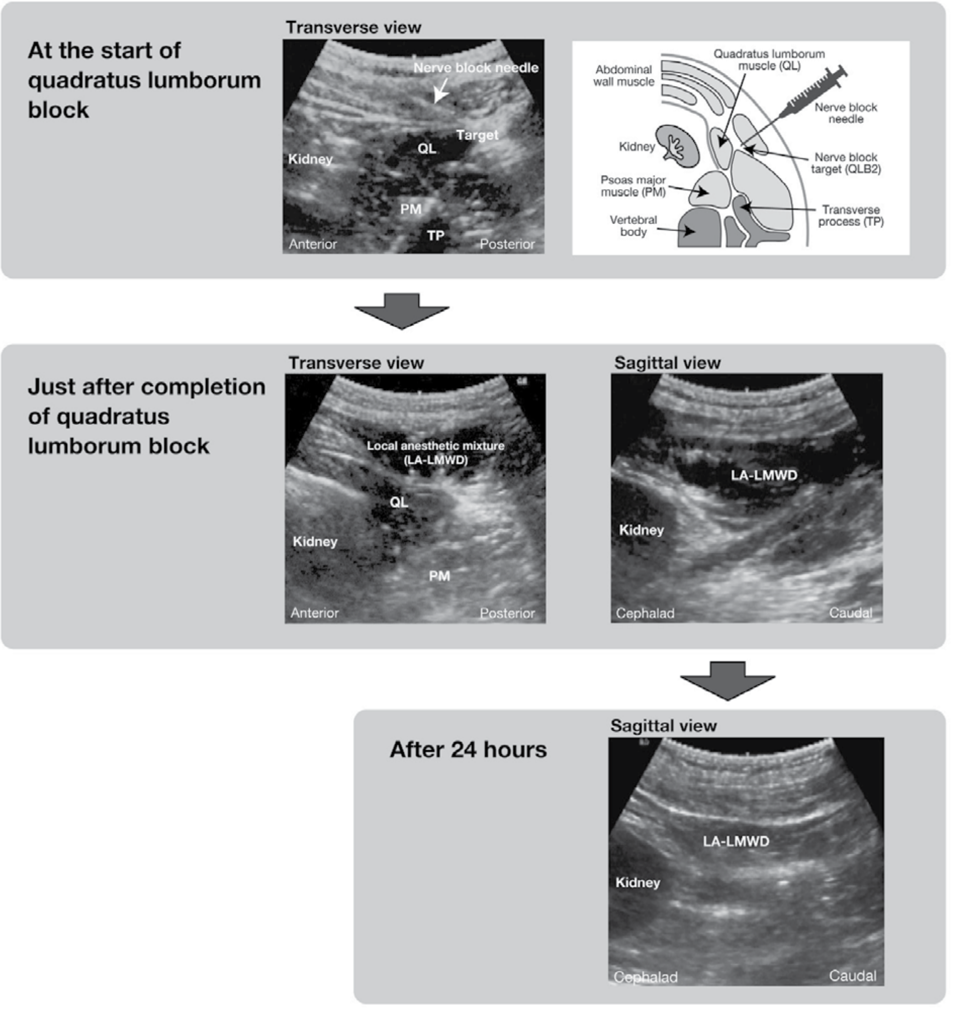

Figure 8.
Upper panel: *Transverse ultrasound image obtained just when nerve block needle reached target site in posterior quadratus lumborum block (so-called QLB2 nerve block) and related anatomical schema [10].* ***Middle panel:*** *Transverse and sagittal ultrasound images obtained just after completion of posterior quadratus lumborum block with 100 ml of 0.1% ropivacaine with 8% low-molecular weight dextran in a saline solution in the same patient shown in the upper panel. The injected local anesthetic mixture (LA-LMWD) was correctly and widely spread over the interfascial space posterior to the quadratus lumborum muscle.* ***Lower panel:*** *Sagittal ultrasound image obtained from the same injection site at 24 hours after completion of quadratus lumborum block in the same patient shown in the upper panel. Some of the local anesthetic mixture (LA-LMWD) remained. PM: psoas major muscle; QL: quadratus lumborum muscle; TP: transverse process.*

Each successfully walked more than 20 meters with less pain the next day. No local or systemic adverse effects from use of low-molecular weight dextran including tissue necrosis over the area of injection were observed. Ultrasound examinations performed after 24 hours indicated that some amount of local anesthetic mixture remained at the injected site (**Figure 8**). These findings well support the proposed mechanism of low-molecular weight dextran as an adjuvant that maintains the analgesic mixture at the injection site for an extended time, thus enabling longer lasting effects. The analgesia effect obtained with this method seems to be comparable with that with epidural anesthesia during the initial 24 hours follow surgery, thus is adequate for early postoperative pain control.

4.3 Guidance effect: erector spinae plane block cases

Findings obtained in transversus abdominis plane block, rectus sheath block, and quadratus lumborum block cases suggested that use of a mixture of local anesthetics and low-molecular weight dextran can provide good analgesia as part of an erector spinae plane (ESP) block in the same manner [14]. Thus, we applied such a block with a dextran mixture in patients undergoing video-assisted thoracic surgery (VATS) to confirm clinical feasibility and investigate the technical benefits of performing a nerve block with adjuvant dextran.

Five patients scheduled for video-assisted thoracic surgery for lung cancer (age 63 ± 7 years, body weight 59 ± 7 kg, anesthesia time 295 ± 94 minutes) received a unilateral erector spinae plane block just prior to starting surgery (**Figure 9**). Targeting the transverse process at the level of the thoracotomy incision, 40 ml of 0.3% ropivacaine and 7% low-molecular weight dextran in a saline solution were injected under ultrasound guidance. General anesthesia was maintained with

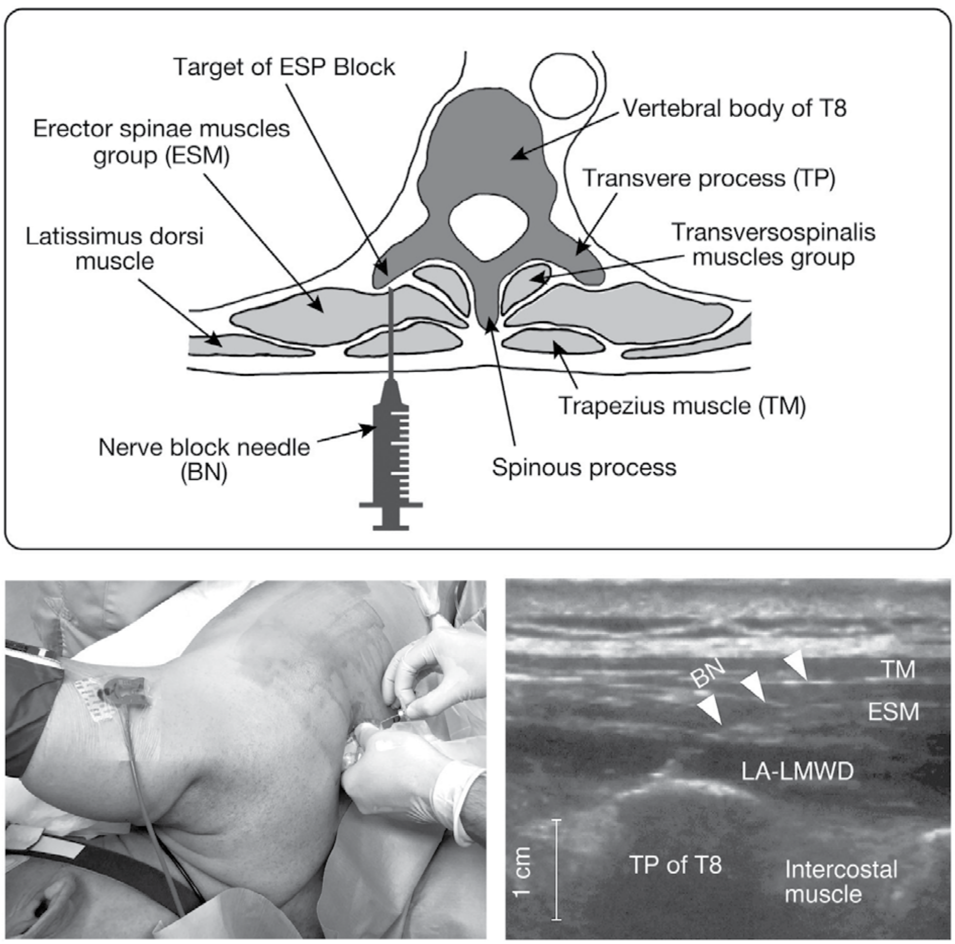

Figure 9.
Upper panel: *Anatomical scheme for erector spinae plane (ESP) block at T8 level of spine.* ***Lower left panel:*** *Positions of ultrasound linear probe and nerve block needle (BN) for ESP block targeting of the transverse process of T8 level of spine in patient positioned in a lateral decubitus position just prior to starting video-assisted thoracic surgery (VATS) for lung cancer [14].* ***Lower right panel:*** *Corresponding ultrasound image obtained during ESP block with use of linear ultrasound probe (8–13 MHz). A mixture of local anesthetic and low-molecular weight dextran (LA-LMWD) was shown spread on the compartment just above the transverse process. ESM: erector spinae muscles; TM: trapezius muscle; TP: transverse process.*

desflurane and remifentanil. Acetaminophen (15 mg•kg^{-1}) was also administrated at the end of surgery. For postoperative rescue analgesia, intravenous flurbiprofen (50 mg) was prepared.

During the first night after surgery, no additional rescue analgesic was given to any of the patients and the NRS pain score (0-no pain, 10-worst pain) was uniformly very low at 2.2 ± 1.1. No adverse effects were observed with use of the low-molecular weight dextran mixture, the same as seen in cases examined in our other nerve block studies that received a dextran mixture. As a control, we enrolled five patients who underwent our usual protocol for video-assisted thoracic surgery, general anesthesia combined with epidural anesthesia and 15 mg•kg^{-1} of acetaminophen, with postoperative continuous epidural anesthesia performed with 3 ml•hr.$^{-1}$ of 0.25% ropivacaine. The first night, NRS pain score (0-no pain, 10-worst pain) for those patients was 2.1 ± 1.2, indicating that an ESP block with a mixture of ropivacaine and low-molecular weight dextran has nearly the same analgesia effect as epidural anesthesia.

It should be noted that use of low-molecular weight dextran significantly increases the viscosity of the injection preparation. Should such a high-viscosity mixture be injected into the wrong portion of parenchymal tissue or an area outside of the target compartment, extra high pressure will likely develop. A large increase in injection pressure related to the site of injection can be a great help to avoid miss-injection, resulting in accurate compartment injection. This guidance effect may be related, at least in part, to the adjuvant effect of low-molecular weight dextran. In addition, the impact of injection pressure could be especially beneficial for novice practitioners learning nerve block procedures.

4.4 Inhibition of unintended spread: mandibular nerve block cases

Based on the above results obtained in our study of compartment nerve block cases, we also examined use of low-molecular weight dextran for cases with a single nerve block [15]. Patients undergoing a mandibular nerve block performed at a site close to the oval foramen from which the mandibular nerve appears were enrolled. In this target site, various nerves and vessels are closely assembled, thus accuracy is essential. However, a correct nerve block needle tip position alone is not sufficient for an accurate injection. In addition to that, spreading of the injected local anesthetic into the unintended surrounding area must be avoided for precision as well as safety, thus the high viscosity characteristic of a dextran solution may be best for such a procedure. Based on this speculation, we performed a study.

A mandibular nerve block was performed using a lateral extraoral approach with guidance using ultrasound imaging in 10 patients undergoing a parotidectomy under general anesthesia (age 60 ± 12 years, body weight 69.5 ± 14.6 kg, anesthesia time 227 ± 92 minutes). Following anesthesia induction, the head of the patient was turned according to the surgical site with the mouth open, then a convex ultrasound transducer was placed just below and parallel to the zygomatic bone (**Figure 10**). Next, a 23-gauge nerve block needle was inserted towards the dorsal edge of the plate, close to the mandibular nerve. When the needle touched the plate edge, 3 ml of a mixture of 0.3% ropivacaine and 7% low-molecular weight dextran in a saline solution was injected. The maxillary artery frequently appears in this section and should not be traumatized. Eighteen hours after surgery, the NRS pain score (0-no pain, 10-worst pain) was 1.2 ± 0.4 without use of a rescue drug, as compared to 2.7 ± 0.7 in our previous non-nerve block cases ($P < 0.01$). No side effects related to unintended spread of the injected ropivacaine were noted.

Performance of a mandibular nerve block using a mixture of ropivacaine and low-molecular weight dextran provided good postoperative analgesia, as well as

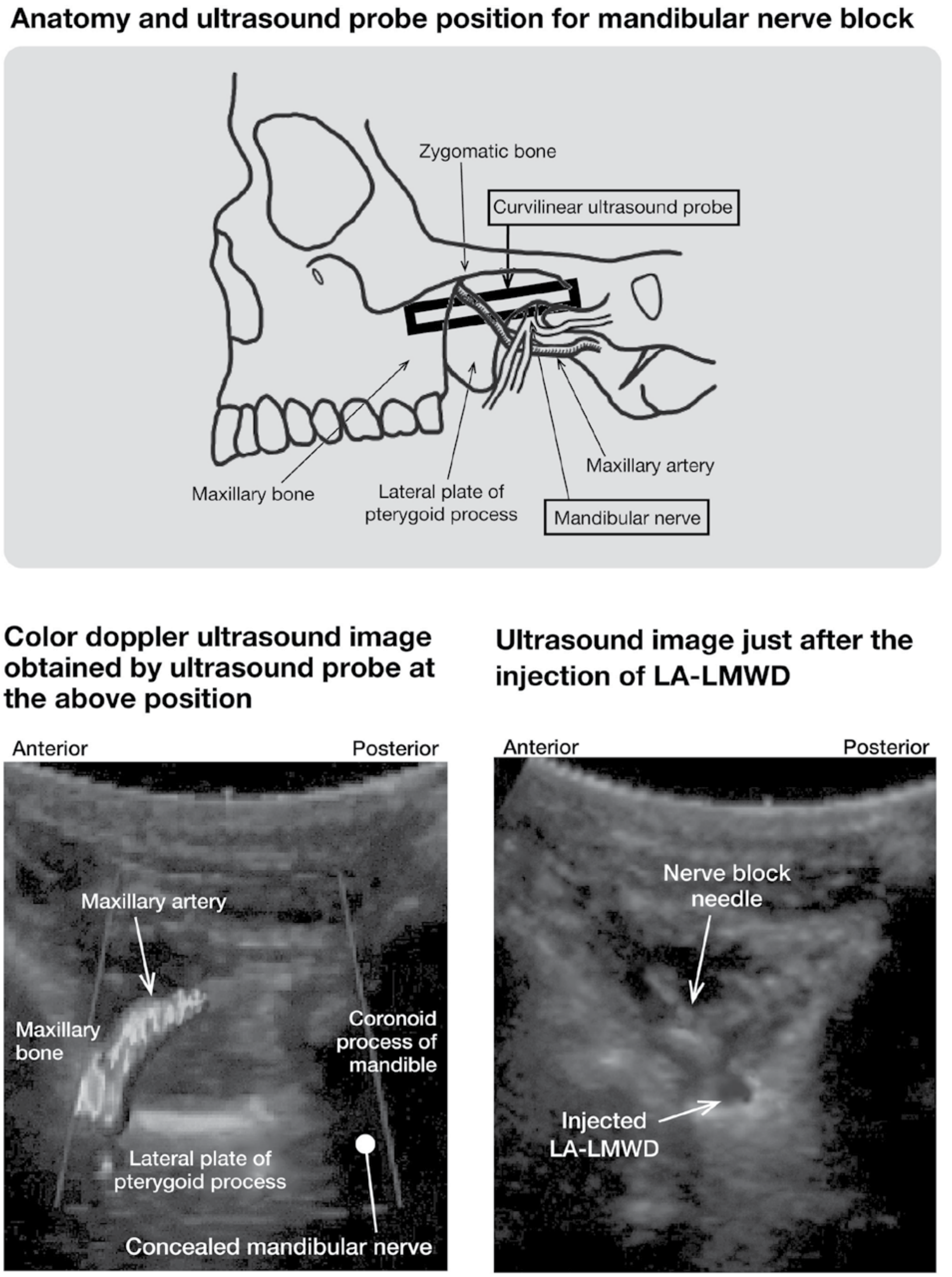

Figure 10.
Upper panel: *Anatomical relationships of mandibular nerve, lateral pterygoid plate, and maxillary artery. For a mandibular nerve block, the ultrasound probe is placed just below and parallel to the zygomatic bone [15].* ***Lower left panel:*** *Typical color Doppler ultrasound image obtained at 4.5 MHz with curvilinear ultrasound probe placed as shown in the upper panel. The maxillary artery is frequently visualized in such cases. The mandibular nerve could not be seen with this view due to acoustic shadows from surrounding bone.* ***Lower right panel:*** *Ultrasound image obtained at the moment when 3 ml of a mixture of ropivacaine and low-molecular weight dextran (LA-LMWD) was injected to the site close to the mandibular nerve emerging from the oval foramen.*

safety. These findings validated our speculation that such a dextran mixture enables an accurate single nerve block for enhancing analgesic potency of an injected local anesthetic without unintended spreading of the injectant.

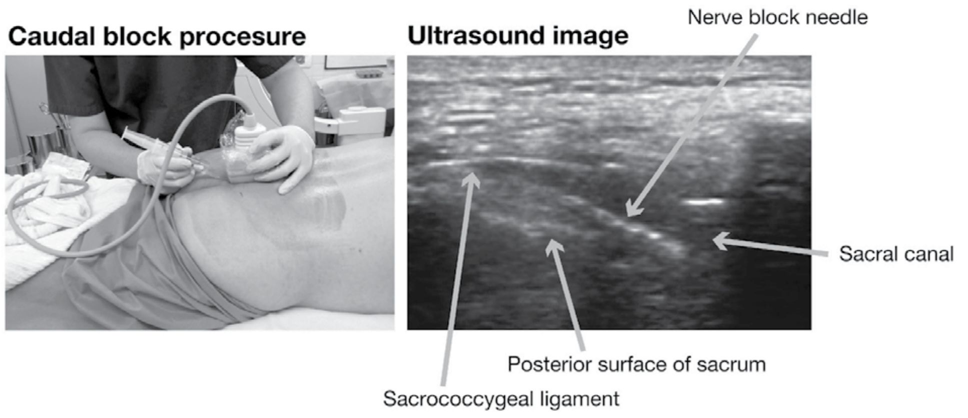

Figure 11.
Ultrasound probe positioning and block needle orientation during caudal block (left panel), and ultrasound longitudinal images obtained at the same moment (right panel) [2]. An ultrasound-guided caudal block procedure in adult patients is performed as follows. After prone positioning, the location and structure of the sacral hiatus are confirmed in ultrasound transverse and longitudinal images. Then, a 23-gauge nerve block needle is inserted in the direction of the sacral canal through the sacral hiatus while monitoring real-time ultrasound images. Next, the tip of the nerve block needle is inserted into the sacral canal approximately 0.5–1 cm ahead. After negative aspiration, a local anesthetic mixture is injected.

4.5 Advanced application of low-molecular weight dextran mixture

A local anesthetic and low-molecular weight dextran mixture can be used for a caudal block. Based on their experience, most anesthesiologists consider that a caudal block procedure in adults is generally not feasible and unreliable. However, an ultrasound-guidance technique makes such a procedure possible in adults and is rather easy to perform [2] (**Figure 11**). We consider that use of a block with a mixture that includes dextran can lead to a longer analgesia duration, thus is well applicable for gynecological, urological, and lower abdominal surgery procedures.

5. New local anesthetics with extended activities

Liposomal bupivacaine has recently become commercially available for use in cases with local infiltration anesthesia or a brachial plexus nerve block [28, 29]. Although this agent has shown excellent potential, it is quite expensive, and systemic or local toxicity occurring long after administration has yet to be determined. Low-molecular weight dextran was first used as an adjuvant more than half a century ago and its long history of clinical use, though recently limited in application, provides evidence of its therapeutic safety. Furthermore, it is inexpensive and approaches with it are easy to perform. Therefore, we consider that use of low-molecular weight dextran as a local anesthetic adjuvant remains beneficial even when compared with newer local anesthetics such as liposomal bupivacaine, with clinical condition a key factor for choosing the best method.

6. Conclusion

Findings obtained in our studies have demonstrated that low-molecular weight dextran functions as an effective adjuvant for potentiation of local anesthetic analgesia in patients undergoing an interfascial compartment nerve block, such as a transversus abdominis plane block, under ultrasound guidance. Notably, use of an abdominal trunk block with a large amount of a mixture of local anesthetic and low-molecular weight dextran, which allows the injected mixture to remain for a longer period at the injection site, provides good analgesia comparable to epidural anesthesia. The high viscosity of dextran can cause extra-high injection pressure when injected into the improper area or portion, alerting the practitioner regarding improper injection, a guidance effect and another practical advantage. Also, use of a dextran mixture may inhibit unintended spread of the injected solution and increase the accuracy of the intended nerve block. As a pharmacological safety aspect, use of a dextran mixture reduces the risk of systemic toxicity related to local anesthetics by suppressing their systemic absorption. All of these factors are significant clinical advantages gained by use of low-molecular weight dextran as a local anesthetic adjuvant when performing various nerve block procedures.

Abbreviations

ESP block	erector spinae plane block
LA-LMWD	local anesthetic and low-molecular weight dextran
LMWD	low-molecular weight dextran
NRS	numerical rating scale

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Chapter 4

Ultrasound-Guided Regional Analgesia for Post-Cesarean Pain

Pablo Santillán Roldan, Andrés Cepeda Mora, Pablo Armas Cruz, Lorena Guacales Zambrano, Geraldine Paredes and Andrea Campoverde Cajamarca

Abstract

Pain management after a surgical intervention is one of the fundamental pillars for optimal patient recovery. In obstetric patients, this management may affect the mother and the newborn. The gold standard for analgesic management is the use of intrathecal morphine due to its long-lasting effect; however, adverse effects related to the use of opioids are evidenced, whether administered intrathecally or systemically in case of contraindication to the neuraxial approach or if a long-acting opioid is not available. Cesarean sections have been associated with moderate-to-severe postoperative pain. Multimodal analgesic management seeks to minimize the undesirable effects on the mother-newborn binomial in order to increase maternal satisfaction. The most studied regional blocks for this surgery are the transversus abdominis plane block and the ilioinguinal-iliohypogastric block, which shows contradictory evidence at the time of evaluate pain where there is no significant difference compared with intrathecal morphine, but there were fewer side effects with the TAP block group when assessing pruritus, nausea, and vomiting. Quadratus lumborum and erectus spinae plane block demonstrate its usefulness with better pain management compared with TAP block regardless of them having a higher level of complexity due to the visceral pain control; but there is no evidence with methodologic quality enough that demonstrates better outcomes compared with intrathecal morphine.

Keywords: post-Cesarean pain, TAP block, ilio-inguinal, iliohypogastric block, ESP block, quadratus lumborum block

1. Introduction

Proper pain management after a surgical intervention is the fundamental pillar for optimal recovery, as in obstetric patients this aspect affects not only the mother but also the newborn. The gold standard for postoperative analgesic management is the use of intrathecal morphine since it has a long duration. However, adverse effects related to the use of opioids are evidenced, whether administered intrathecally or systemically in case of contraindication to the neuraxial approach, or if a long-acting opioid is not available. Cesarean sections have been associated with moderate-to-severe postoperative pain; therefore, improper management of analgesia would lead to chronic post-surgery pain, problems in breastfeeding, and

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the mother-newborn relationship, and it has even been considered a trigger for postpartum depression. Based on the foregoing, multimodal analgesic management seeks to minimize the undesirable effects on the mother-newborn binomial in order to increase maternal satisfaction and that the relationship between the mother and her newborn is not altered, since the regional analgesia techniques have gained territory by reducing the consumption of analgesics in the immediate postoperative period, and also are easy to perform procedures. Among the most studied we will review the more important aspects of the abdomen transverse plane (TAP), quadratus lumborum and erectus spinae plane blocks [1–7].

2. Transversus abdominis plane block

The TAP block had been described for the first time as an abdominal wall block based on anatomical landmarks to introduce local anesthetic (LA) into the TAP through the Petit triangle using the loss of resistance technique. The first ultrasound-guided TAP was described in 2007, since then it uses have become popular in upper and lower abdominal surgeries, although it has not been fully integrated into routine clinical practice [8].

The anterolateral abdominal wall consists of four muscles: rectus abdominis, external oblique, internal oblique, and transversus abdominis. The innervation of the abdominal wall and the underlying parietal peritoneum depends on the intercostal nerves (T7–T12) and the first lumbar root (L1). After their spinal emergence, the spinal nerves give a posterior branch and a lateral branch (which usually emerges at the level of the mid-axillary line) and ends in an anterior branch that joins in the linea alba with the anterior branches of the contralateral hemi body. The terminal branches of these nerves travel in the abdominal wall within a neurofascial plane located between the internal oblique muscle and the transversus abdominis muscle, and this space is named the transversus abdominis plane (TAP) [9].

The use of ultrasound allowed the development of new approaches, such as the subcostal, lateral, posterior or combinations such as dual TAP in which the possibilities of TAP block use have been increased [8].

There are three reported TAP block approaches: the posterior one, by anatomical landmarks in Petit's triangle, described by Rafi and McDonnell for analgesia of the lower abdominal quadrants (dermatomes from T11 to L1); the ultrasound-guided subcostal approach, described by Hebbard in 2008 for periumbilical and upper-quadrant analgesia of the abdomen (T10 to T6 dermatomes), and the lateral approach [10].

The subcostal approach targets the compartment of the transverse plane of the abdomen in the anterior abdominal wall, below the costal margin, anywhere between the xiphoid process and the anterior superior iliac spine. The lateral approach is directed to the compartment of the transverse plane of the abdomen in the lateral abdominal wall between the mid-axillary and anterior axillary lines. Finally, the posterior approach is directed to the compartment of the transverse plane of the abdomen at the level of Petit's lumbar triangle or the anterolateral aspect of the quadratus lumbar muscle (**Figures 1**–**3**) [11].

To perform these interfascial blocks, the abdomen is exposed between the ribs margin and the iliac crest, and it is recommended to use the high-frequency linear transducer (6–15 MHz), because the anatomical structures are relatively shallow [12].

Regarding the subcostal approach, initially a linear ultrasound probe with a sterile sheath is placed under the xiphoid process to view the linea alba. The probe is then directed obliquely down the costal margin while keeping the rectus

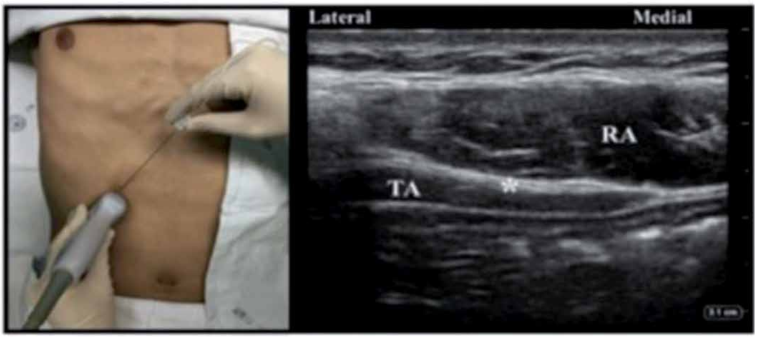

Figure 1.
Transversus abdominis plane block. Subcostal approach [11].

Figure 2.
Transversus abdominis plane block. Lateral approach [11].

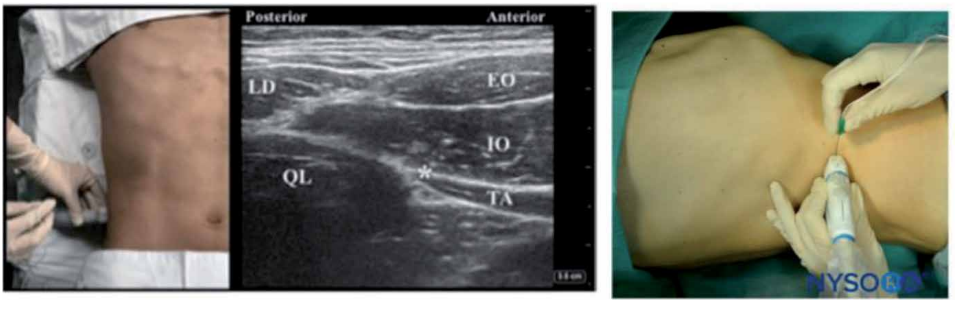

Figure 3.
Transversus abdominis plane block. Posterior approach [11].

abdominis muscle in view. The transverse abdominis muscle is seen below the rectus abdominis muscle. The probe is advanced further until the semilunaris (curved tendon intersection found on both sides of the rectus abdominis muscle) is seen. An echogenic needle is inserted into the plane until the tip of the needle reaches the fascia between the rectus abdominis and transverse abdominis muscles, while the local anesthetic is injected, the needle is advanced laterally, producing a lateral extension of the local anesthetic [13]. For the posterior approach TAP block, the linear transducer is positioned in the axial plane at the mid-axillary line and moved posteriorly to the most posterior limit of the TAP between the internal oblique and transverse abdominal muscles. The target is the rearmost end of the TAP. The needle is inserted in the mid-axillary line and advanced posteriorly until reaching the posterior end of the TAP [14].

The three muscle layers of the abdominal wall are identified: the external oblique muscle (most superficial), the internal oblique muscle (most prominent layer), and the transversus abdominis muscle. A 0.80 × 100 mm 21G short bevel needle is inserted in plane with the transducer. The insertion point is made slightly away from the transducer to allow better visualization of the needle. It is important to deposit the local anesthetic in a deep place in the fascia in such a way that it separates the internal oblique muscles from the transverse abdominis muscle, thus performing a "hydrodissection" (1–2 mL of saline solution or local anesthetic) that adequately exposes the plane. A total of 20 mL of local anesthetic is injected into the plane of each side [12].

Among RCTs comparing TAP versus intrathecal morphine, it has been demonstrated that there were no significant differences in VAS in pain at rest or in movement, nor any significant reduction in time to opioid rescue. It is well known that TAP prolonged the time to opioid rescue by 50%, increased early VAS at rest and on the move, and reduced PONV and pruritus in the TAP group. In the RCTs that compared TAP versus placebo TAP in Cesarean section with spinal anesthesia without intrathecal morphine, there is a decrease in opioid consumption in the first 24 h (18 mg vs. 13.5 mg; $p < 0.05$) and in the time to the first opioid rescue (2 h vs. 3 h, $p = 0.019$). However, no significant differences were found in VAS at rest or movement, as well as in the incidence of side effects of opioids. Baaj et al. demonstrated a significant reduction in opioid consumption in the first 24 h (25.89 mg vs. 62 mg, $p > 0.05$), as well as a 25% decrease in VAS at rest and in movement during the first 24 h, and a decrease in PONV [8].

In a study by Lopez et al. [9], 41 patients were included, 20 in the TAP group, and 21 in the group wound infiltration (WI). The analgesic efficacy obtained in both groups was similar, with a higher demand for additional analgesia in the postoperative period in the WI group at 10, 30, and 60 min, becoming statistically significant at 60 min. By means of a home telephone call at 24 h, a higher consumption of rescue analgesia was found in this group ($p < 0.05$). There were no differences in side effects or complications related to the ultrasound-guided regional technique. The degree of patient satisfaction with the anesthetic technique was similar for both groups. In the same way, Gao carried out a study where 100 patients who underwent Cesarean section were randomly classified into two groups. After surgery, one group underwent ultrasound-guided TAP block and the other group underwent patient-controlled intravenous analgesia (PCIA), and no significant differences were found in VAS scores between the groups ($p > 0, 05$). However, the incidence of postoperative complications in the TAP group was significantly lower than in the PCIA group ($p < 0.05$). Furthermore, patient satisfaction in the TAP group was significantly higher than in the PCIA group ($p < .05$) [15]. Also, in a study conducted by Dereu et al. [16], where patients undergoing Cesarean section were randomly assigned to one of two groups (quadruple blind): 100 mg of intrathecal morphine (ITM) was added to local spinal anesthetic or a bilateral TAP block with 20 ml of 0.375% ropivacaine +75 μg of clonidine on each side. About 24 hours after blocking, there was no significant difference between the ITM and TAP groups in the total number of patients who presented PONV: 17/92 patients and 27/88 patients in the TAP and ITM groups, respectively ($p = 0.065$). Pain scores at 6 h and cumulative morphine consumption at 24 h were lower in the ITM group ($p < 0.0001$ for morphine consumption at 24 h). The incidence of hypotension was higher in the TAP group. Maternal satisfaction was high and not different between the groups. As in the study by Ashok Jadon et al. [17], 139 mothers undergoing Cesarean section were randomized to receive a TAP block with 20 mL of 0.375% ropivacaine or 20 mL of saline. All subjects received a standard spinal anesthetic and diclofenac was administered for postoperative pain, found as a result that the median time to first analgesic request was prolonged in the TAP group compared with the control group ($p < 0.0001$); 11 h (8.12) and 4 h (2.5.6), respectively. The median doses of tramadol consumed in the TAP group was 0 (0.1) compared with 2 (1.2) in the control group ($p < 0.0001$). At all study points, pain scores both at rest and on movement were lower in the study group ($p < 0.0001$). Maternal satisfaction with pain relief was also higher in the study group ($p = 0.0002$).

Kakade and Wagh [18] evaluated the feasibility of TAP for postoperative analgesia after Cesarean section found that the duration of postoperative analgesia was significantly longer in the TAP block group compared with the control group (without block).

3. Ilioinguinal/iliohypogastric block

Both the iliohypogastric (IH) and ilioinguinal (II) nerves arise from L1 and emerge from the upper part of the lateral border of the psoas major muscle. Nerve II is smaller and runs caudal to nerve IH. Both nerves pass obliquely anterior to the quadratus lumbar and the iliac muscle and pierce the transverse abdominis muscle near the anterior part of the iliac crest. In the anterior abdominal wall, both nerves travel in the transverse abdominal plane. The IH nerve provides skin sensitivity to the groin region, and the II nerve provides skin sensitivity on the upper medial aspect of the thigh.

3.1 Blocking technique

The patient is placed in a supine position exposing the lower abdomen, the iliac crest and the groin area are the margins to be located, and the anterior superior iliac spine (ASIS) is marked. A high-frequency linear transducer is used, which is located obliquely along a line that joins the ESIA and the umbilicus, immediately superior and medial to the ESIA, to obtain a cross-sectional view of the nerves, performing an inspection from the iliac crest to the lower abdomen.

An attempt should be made to identify the three muscle layers: external oblique, internal oblique, and transverse abdominis, finding nerves II and IH inside the plane between the internal oblique, and the transverse abdominis on the ASIS. Many times, at this level the external oblique is visualized as a thin aponeurotic layer (**Figure 4**).

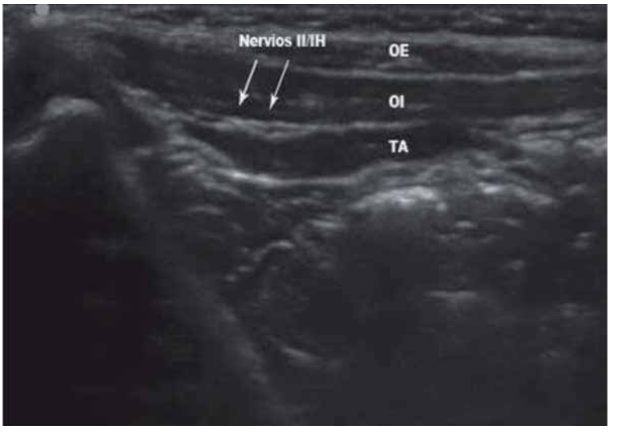

Figure 4.
Ilioinguinal/iliohypogastric nerve [19].

There is conflicting evidence when IL and IH nerve blocks are compared with TAP blocks. One study found significantly higher cumulative mean consumption of tramadol in 24 hours (63 mg vs. 27 mg) in the combined ILIH group compared with the TAP blocks, but there was no difference in time to first request for analgesia or in postoperative pain scores between groups. In a prospective non-randomized trial combining nerve blocks were associated with a reduction in cumulative consumption of tramadol in 24 h (37.25 mg vs. 52.45 mg) and a prolonged time to first analgesic request (14.09 h vs. 10, 71 h) compared with TAP blocks after elective Cesarean section. In both studies, there were no significant differences in pain scores between the groups at any time [19]. According to the study by Jin et al. [20], the score and cumulative morphine consumption were compared between the two groups (TAPB, transverse abdominal plane block; IHINB, iliohypogastric/ilioinguinal nerve block). Regarding the VAS score, there was no significant difference between the two groups in the first 12 h (all $p > 0.05$). However, the VAS score of the IHINB group was significantly lower than that of the TAPB group at 24 and 48 h after surgery ($p < 0.001$ for each). Similar to the VAS score, the cumulative total morphine consumption in the two groups was comparable at 12 h, while it was significantly lower for the IHINB group at 24 and 48 h after surgery ($p < 0.05$ and $p < 0.001$, respectively).

4. Quadratus lumborum block muscle

4.1 Anatomy

The quadratus lumborum muscle is part of the posterior abdominal wall and is located dorsal to the iliopsoas muscle. It has its origin in the posteromedial iliac crest in the iliolumbar ligament, and it inserts on the medial border of the twelfth rib (T12) and in the transverse processes of the first and fourth lumbar vertebrae (L1–L4), in the medial third of the iliac crest. Posterior to the quadratus lumborum muscle is the erector spinae muscle group, which consists of the multifidus, longissimus, and iliocostalis (**Figure 5**) [21–23].

The ventral branches of the spinal nerves (including the subcostal and iliohypogastric nerves) run between the quadratus lumborum muscle and its anterior fascia (**Figure 6**).

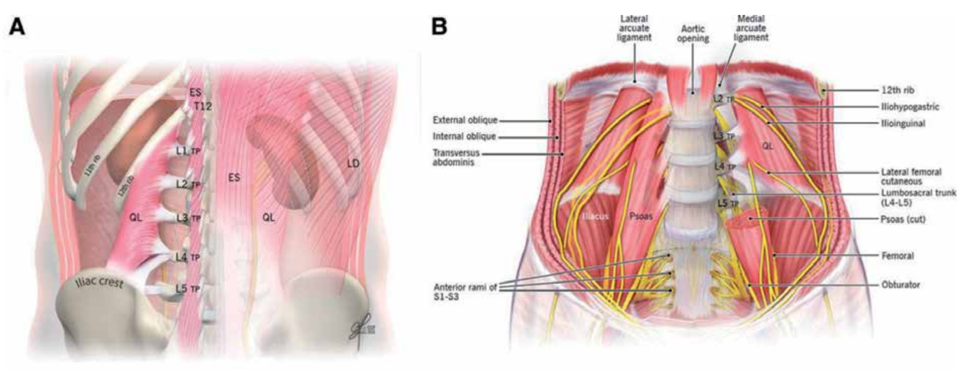

Figure 5.
Quadratus lumborum block. Anatomical concepts, mechanisms, and techniques. (A) A posterior diagram illustration of the musculature of the posterior abdominal wall. The quadratus lumborum muscle originates from medial border of the twelfth rib and lumbar vertebrae transverse processes and inserts into the posteromedial iliac crest. (B) An anterior schematic illustration of the musculature of the posterior abdominal wall. On the left, the psoas muscle has been removed to reveal the ventral rami of the spinal nerve roots and branches passing anterior to the quadratus lumborum muscle. ES, erector spinae; LD; latissimus dorsi; QL, quadratus lumborum; TP, transverse process (Cleveland Clinic Center for Medical Art & Photography © 2018).

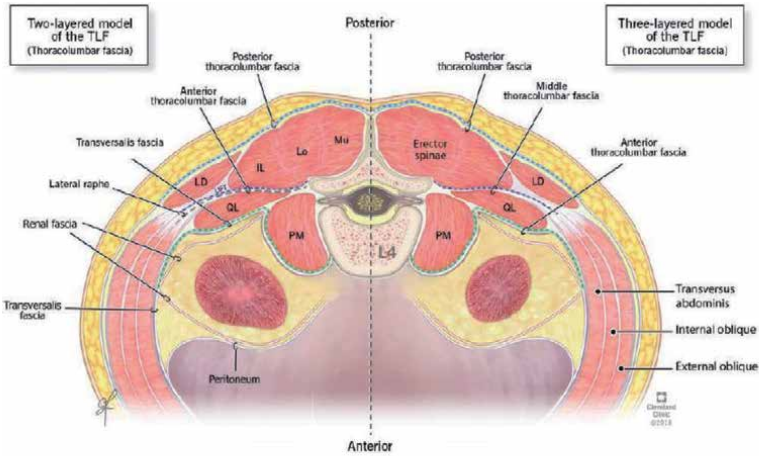

Figure 6.
A schematic illustration of cross-section at L4 level showing the quadratus lumborum muscle with the different layers of the thoracolumbar fascia. On the left, the two-layer model is depicted, where the purple dashed line represents the anterior layer of the thoracolumbar fascia, and the green dashed line represents the transversalis fascia. On the right, the three-layer model is depicted, where the purple dashed line represents the middle layer of the thoracolumbar fascia, and the green dashed line represents the anterior layer of the thoracolumbar fascia. The blue dashed line represents the posterior thoracolumbar fascia. IL, iliocostalis; LD, latissimus dorsi; Lo, longissimus; Mu, multifidus; PM, psoas major; QL, quadratus lumborum; TLF, thoracolumbar fascia. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2018. All Rights Reserved. showing the quadratus lumborum muscle with the different layers of the thoracolumbar fascia.

The quadratus lumborum muscle is surrounded by the thoracolumbar fascia (FTL) that comprises the multilayer fascia and aponeurosis with the two proposed models [21–23]:

1. Two layers: includes the erector spinae (posterior) and quadratus lumborum muscles (anterior or transversalis fascia). The transverse fascia separates the muscular layers of the kidney, which is located in the retroperitoneal abdominal space.

2. Three layers: the erector spinae muscles (posterior layer or FTL), erector spinae and quadratus lumborum muscles (intermediate layer), and the quadratus lumborum muscles and psoas (anterior layer), the anatomical relationships of the psoas major are important since housing the lumbosacral plexus and being so intimately located can become a route for local anesthetic to the lumbar plexus.

Knowledge of the anatomy of the thoracolumbar anterior fascia is important to understand the propagation after administration of the local anesthetic. The transverse fascia is divided into two layers: the inner layer that continues with the endothoracic and allows a cephalic spread of the local anesthetic (thoracic paravertebral space), and the outer layer that mixes with the arcuate ligaments of the diaphragm [21, 23, 24]. The abdominal aorta gives rise to the lumbar arteries from which the abdominal branches emerge, and these run lateral and posterior to the quadratus lumborum muscle.

4.1.1 Neurovasculature

On the ventral aspect of the quadratus lumborum muscle are the iliohypogastric, ilioinguinal, and subcostal nerves enveloped by the transversalis fascia. The sensory dermatome level involves T12–L2. There may be spread to the lateral femoral cutaneous nerve, the obturator, and the femoral nerve within the psoas (L4 and L5). On the dorsal aspect of the quadratus lumborum plane are the dorsal branches of the spinal nerves that innervate the erector spinae muscle and the sympathetic nerve fibers that innervate the muscles of the abdomen and innervate the thoracolumbar fascia [21–23].

4.1.2 Propagation and mechanisms of action

Dam et al. [25] documented that the block at the level of the iliac crest (L4) is spread in a thoracic paravertebral manner up to T9 and T10, as well as the approach at the level of L3 extended toward the thoracic paravertebral space.

4.2 Technique

The nomenclature for defining quadratus lumborum block is based on the anatomical location of the needle tip in relation to the quadratus lumborum muscle. Thus, we have a) lateral, b) posterior, and c) anterior quadratus lumborum. All blocks must be carried out under standard security and aseptic measures [23, 26]. Patient position can be prone, lateral, or sitting depending on patient and physician preferences.

Vision through ultrasound must be direct and with hydrodissection using a curvilinear low-frequency probe since it is a deeper block. The typical length of the needle used is 80–150 mm.

The most commonly used local anesthetics are 0.2–0.5% ropivacaine or 0.1–0.25% bupivacaine. The typical volume used varies from 0.2 to 0.5 mL/kg on each side.

4.2.1 Lateral or posterior quadratus lumborum block

The needle is placed lateral to the ultrasound probe in the anterior part in a posterior direction, and it crosses the external oblique (EO), internal oblique (LE), and transverse abdominal (TA) muscle. The final position of the needle is lateral to the quadratus lumborum (QL) (**Figures** 7 and **8**) [23, 26].

Figure 7.
Lateral or posterior quadratus lumborum blocks. Transverse transducer and anteroposterior needle trajectory are shown. The external image and ultrasound images show the ultrasound probe position with a solid arrow indicating the needle trajectory for a lateral quadratus lumborum block and the dashed line indicating the needle trajectory for a posterior quadratus lumborum block approach. The red-/blue-shaded area represents the spread of the local anesthetic.

Figure 8.
Quadratus lumborum block: A technical review.

4.2.2 Anterior quadratus lumborum block

An in-plane approach is performed using an anterior-posterior or posterior-anterior trajectory. The target of the local anesthetic is the posterior surface of the quadratus lumborum muscle. The position of the needle tip is between the erector spinae (ES) and the quadratus lumborum muscle (**Figures 9** and **10**) [21, 23, 26].

4.2.3 Subcostal block of the quadratus lumbar

Insertion of the needle is caudal to the transducer in a lateral or medial cranial direction, the deposit of the local anesthetic is between the quadratus lumbar and the psoas muscles (**Figure 11**) [23, 26].

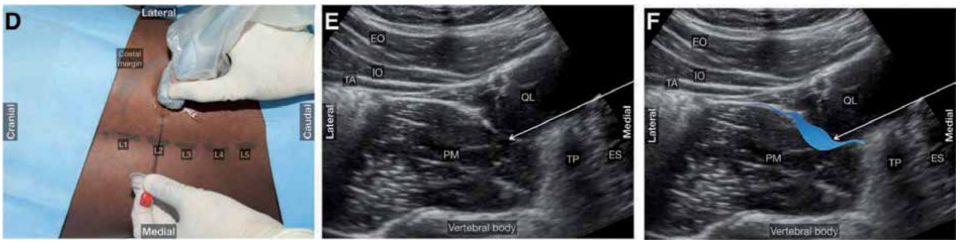

Figure 9.
Anterior quadratus lumborum block: transverse oblique paramedian approach. Transverse transducer and posteroanterior needle trajectory are shown. The external image and ultrasound images show the ultrasound probe position with an arrow indicating the needle trajectory. The blue-shaded area represents the spread of the local anesthetic.

Figure 10.
Quadratus lumborum block: A technical review.

Figure 11.
Anterior quadratus lumborum block: subcostal approach. Parasagittal oblique transducer and caudal-to-cranial needle trajectory are shown. The external image and ultrasound images show the ultrasound probe position with an arrow indicating the needle trajectory. The blue-shaded area represents the spread of the local anesthetic. EO, external oblique; ES, erector spinae; IO, internal oblique; PM, psoas major; QL, quadratus lumborum; TA, transversus abdominus; TP, transverse process.

4.3 Indications

It is indicated for lower abdominal surgeries, including Cesarean section, colostomy closure, hernia repair, gastrectomy, nephrectomy, hip replacement, above-knee amputation, iliac crest bone graft, and iliac and acetabulum fracture [23, 26, 27].

It has been shown that posterior quadratus lumborum block with 0.125% bupivacaine reduces opioid needs for 12 h postoperatively compared with placebo in patients who were administered the combination of bupivacaine 15 mg plus fentanyl 20 mμ. Similarly, Mieszkowski et al. [28] showed that the group that received the quadratus lumborum block (bupivacaine 0.375%, 24 mL) decreased the consumption of opioids (morphine 4 mg) vs. the placebo group that received the standard anesthetic technique (bupivacaine 0.5% 12.5 mg plus 20 mcg fentanyl).

While intrathecal morphine is the current standard drug, quadratus lumborum block offers superior pain control with fewer side effects. The study by Pangthipampai et al. [29] compared the pain-free period after Cesarean delivery among women in labor who received spinal block with 0.2 mg IT morphine, 0.2 mg IT morphine and bilateral QLB (bupivacaine 0.25% 25 ml), or alone. Using bilateral QLB (bupivacaine 0.25% 25 mL), it was concluded that quadratus lumborum block together with IT morphine had a longer pain-free period compared with standard IT morphine alone, but that quadratus lumborum block without association did not provide inferior pain compared with standard IT morphine. However, research by Irwin et al. [30] describes that there was no difference in pain scores up to 48 h after this block (40 ml of 0.25% levobupivacaine) or sham block after undergoing elective Cesarean section under spinal anesthesia and IT morphine.

4.4 Complications

- Lower limb weakness with delayed mobilization and prolonged hospital stays.
- Quadriceps weakness.
- Hypotension that may be related to the spread of the local anesthetic in the paravertebral spaces.
- Caution should be exercised with the toxicity of local anesthetics due to the volume used, especially in cases of bilateral blockade.
- Injury to the pleura, kidney, retroperitoneal hematoma, and nerve roots.

5. Erector spinae plane block

The erector spinae plane block (ESP) is an interfascial analgesic block first described by Forero in 2016 for the treatment of neuropathic thoracic pain. A vast body of scientific literature related to this procedure has been developed, thus increasing the indications for this analgesic blockade given the analgesic efficacy and relative ease at the time of reproducing said procedure in different patients, even more so now that a multimodal approach to pain management is performed [31, 32].

The anatomical basis for performing this block is in the paravertebral musculature, in the thoracolumbar fascia on the transverse processes and the muscular group called the erector spinae made up of the spinalis, longissimus thoracis, and iliocostalis muscles, in addition to the transverse-spinal muscles and levatores rostrum. The deposit of local anesthetic at this level generates its diffusion toward the vertebral and epidural space as well as the intercostal space, thus managing to cover the dorsal and ventral branches of the spinal nerves from their emergence at the level of the site of injection as well as a diffusion toward cranial and caudal between three and four levels demonstrated by Chin et al. [33] in cadaveric studies, reason for achieving both somatic analgesia of the posterior and antero-lateral thoracoabdominal wall, as well as visceral [34, 35].

Regarding the technique, it should be considered that since it is an invasive procedure, the patient must be previously monitored in addition to complying with the standard of asepsis and antisepsis of each institution. Once this prerequisite has been carried out, the block can be performed with the patient awake or under general anesthesia if applicable, always guided by ultrasound to achieve greater effectiveness when blocking the area. However, there is a description of the block by means of anatomical references. The positioning of the patient will depend on the patient's state of consciousness, being possible to perform the procedure in a sitting position, lateral decubitus, or prone.

Performing the ESP block by anatomical reference takes as its starting point palpation of the spinous processes of the level to be blocked, for gynecological/obstetric abdominal procedures such as Cesarean section. It is performed at the T9 level, and then, it is displaced 3 cm laterally to try to palpate the transverse processes, the site where we are going to perform the puncture perpendicular to the skin with a G22 needle or a G18 Tuohy needle until the transverse processes are located at an approximate distance of 2–4 cm deep, although this could vary if we take into account the physiological changes that occur in pregnant women [2, 31, 32, 34, 35]. The injection of the local anesthetic is performed prior to negative aspiration to avoid inadvertent intravascular injections, interspersed with boluses of 5 mL of anesthetic solution. Similarly, to carry out this ultrasound-guided procedure, the transducer is placed in an axial direction at the level of the spinal process and later, the transverse processes are traced and we turn the transducer in a longitudinal direction and thus observe the muscular distribution of the erector spine and its deep fascia visualized in a hyperechoic way on the acoustic shadow generated by the transverse process. The administration of the anesthetic solution is carried out in the same way as for anatomy references, injections of 5 mL after negative aspirations until an average volume of between 15 and 20 mL or 0.2 mL/kg per side is completed to visualize how the deep fascia is distended (**Figure 12**) [2, 31, 32, 34, 35].

The indications for performing this block fall into a very wide range since there is a number of bibliographies in which better analgesic control and a decrease in the requirement of opioid analgesics is reported in the postoperative period in various thoracic and abdominal surgeries. However, to date the administration of intrathecal morphine remains the gold standard for analgesic management for

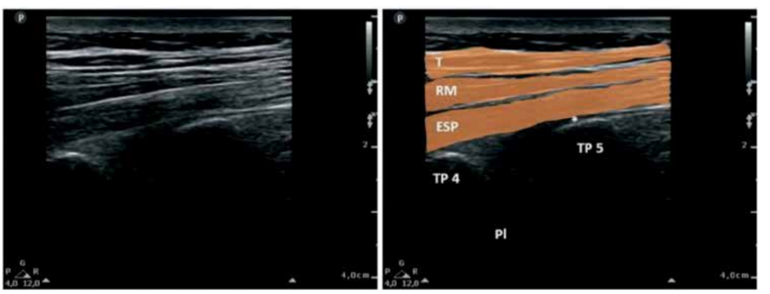

Figure 12.
*Sonoanatomy of ESP Block at the T5 level. TP: transverse processes, T: trapezius muscle, RM: rhomboid major muscle, ESP: erector spinae muscle, Pl: pleura. * Needle point [3, 4].*

elective cesarean sections, as recommended in the PROSPECT study [3], where they place regional blocks as an alternative for cases in which there is a contraindication to approach the neuraxis and consequently, the administration of IT morphine or an IT opioid is not available. Although it is true, most of the references point to a benefit in performing the ESP block for analgesic management. This bibliography is mostly case reports or case series and there are very few studies with a high level of evidence to support the widespread use of regional analgesia in Cesarean sections [2, 36, 37].

Hamed et al. [38] compared IT morphine at a dose of 100 μg with the execution of the ESP block without IT opioid administration, in 140 studied patients no statistically significant difference was found in the perception of pain during the 24 hours after surgery, both at rest and with Valsalva maneuvers (cough), or in reducing the consumption of postoperative opioid analgesics. However, the study reports methodological limitations that could be biasing the result, but the usefulness is emphasized as a multimodal analgesic management in obstetric patients.

In prospective studies in which ESP block was compared with TAP block, such as the one by Malawat et al. [7], as well as by Boules et al. [39], superiority is defined for ESP block for analgesic management and reduction of the requirement postoperative analgesic in series of 60 patients analyzed in each study (ropivacaine 0.2%,2 mL/kg in each puncture). However, there was an important difference in the duration of analgesic effects, reaching around 43 h of analgesia with ESP vs. 12 h with TAP block in the report by Malawat contrasting with that described by Boules, who stated that the ESP block provided 12 h of analgesia compared with 8 h of the TAP block.

Complications or adverse effects with this regional block are rare, especially if it is performed guided by ultrasonography. Despite this, there are reports of unexpected motor blockade of the lower limbs due to the spread to the paravertebral and epidural space, latent risk of pneumothorax due to an inadvertent pulmonary puncture, as well as allergic reactions or cases of poisoning by local anesthetics when administering an excessive dose since a high volume of anesthetic solution is administered or an inadvertent injection into a blood vessel. It is important to perform all these procedures in a place that has the resolution capacity in case of any complication, as well as the personnel trained to carry them out [2, 38, 40].

6. Discussion

Cesarean delivery is one of the oldest and best established surgical procedures in the history of medicine and is currently the most common major surgery performed on humans anywhere in the world. Postoperative pain management after Cesarean section fairly varies from non-obstetric surgeries; women need to recover rapidly to take care of their newborn baby. Ideal pain treatment is mandatory for the success of immediate-term and long-term rehabilitation after Cesarean delivery. There is growing evidence that perioperative pain management has consequences extending well beyond the immediate recovery period. Unalleviated acute postoperative pain is a striking risk factor for the development of chronic post-Cesarean pain.

Undoubtedly, the gold standard has for decades been the use of intrathecal morphine in doses ranging from 50 to 100 mμ. Multimodal analgesia or balanced analgesia has significantly improved the management of acute post-Cesarean pain, being the combination of drugs mandatory to achieve satisfactory and effective pain relief with reduced side effects. Paracetamol, NSAIDs, magnesium sulfate, alpha2 agonists, dexamethasone, and ketamine are some of the non-opioid drugs used in multimodal analgesia.

There are numerous post-Cesarean regional analgesia techniques that have been studied for decades; from epidural analgesia with or without opioids, intrathecal morphine, intraperitoneal instillation, or surgical wound infiltration with local anesthetics have demonstrated analgesic effectiveness. The advent of ultrasound-guided regional blocks has come to revolutionize post-Cesarean analgesia, showing to be a very safe, effective technique with fewer side effects than other analgesia modalities.

The TAP block has been shown to be the most effective block reducing pain, reducing the use of rescue analgesics and increasing the satisfaction of postpartum women [8, 9, 15]. The posterior approach produces better analgesia than the lateral approach. The addition of dexamethasone, clonidine, or dexmedetomidine prolongs the analgesic effect of this block and reduces the doses of rescue analgesics [17, 18]. The addition of alpha2 agonists induced mild sedation. When ilioinguinal and iliohypogastric nerve blocks are combined with TAP blocks, better analgesia is obtained and the need for salvage opioids is reduced [19, 20].

Another alternative is the quadratus lumborum block [27–29]. Although there are very varied results, there are studies that found better analgesia than with TAP block, but it is not superior to epidural analgesia or intrathecal morphine. More research is required comparing this type of analgesic block with the most commonly used blocks.

Erector spinae plane block is another possibility of ultrasound-guided analgesia as it produces satisfactory pain reduction when compared with intraspinal morphine and TAP block [38, 39].

7. Conclusion

At the present review, we show several data about the efficacy of the regional analgesic block alternatives to manage the post-Cesarean section pain. The most studied technique is the TAP block due to ease of replication and its effectiveness. But there has been developed new techniques that require a little more experience to perform them and guarantee a better analgesic outcome like the quadratus lumborum block or the ESP block. Nevertheless, the gold standard for the pain management after Cesarean section still remains the intrathecal morphine, with the use of regional analgesic techniques just as adjuvants or when intrathecal morphine is not available. The most recent studies have lack of statistical power to demonstrate if any of these techniques is superior to intrathecal morphine, so they remain like a powerful tool in the multimodal analgesic regimen.

Regional analgesia is a complementary technique to programs to improve recovery after Cesarean delivery, considerably reducing hospital stay, facilitating the integration of the mother-newborn pairing, and surely reducing the incidence of chronic post-Cesarean pain.

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Chapter 5

Regional Anesthesia for Shoulder and Clavicle Surgery

Ciro Alfonso Rodríguez-Gómez,
José Ramón Saucillo-Osuna and Karen L. Iñiguez-López

Abstract

The shoulder joint and clavicle are innervated by the brachial plexus, the cervical plexus, and nerves to muscles around the joint and clavicle. Regional anesthesia is aimed at producing optimal surgical conditions, prolonging postoperative analgesia, being free of complications, reducing costs, and minimizing hospital stay. Regional upper extremity anesthesia can be achieved by blocking the brachial plexus at different stages along the course of the trunks, divisions, cords, and terminal branches. The gold standard of regional anesthesia for shoulder surgery is interscalene brachial plexus block plus cervical plexus block, but it is associated with a high rate of neurological complications and phrenic nerve block. The interest of the anesthesiologist has been directed towards regional blocks avoiding these complications; techniques that approach nerves more distally than interscalene block have been described. These approaches include supraclavicular nerves, upper trunk, suprascapular nerve by anterior approach, axillary nerve block in the axillary fossa, clavipectoral fascia block. The objective of this chapter is to describe the anatomy, sonoanatomy, technique, and the clinical utility of these accesses.

Keywords: regional anesthesia, shoulder, clavicle, upper trunk, supraclavicular nerves, suprascapular nerve, axillary nerve, clavipectoral fascial, interscalene block

1. Introduction

Shoulder surgery by arthroscopy or open methods has increased in recent years. The choice of anesthetic technique depends on the patient's conditions, the preferences of the surgical group, the position the patient is to be placed, and the experience of the anesthesiologist. General anesthesia (GA) has been considered the ideal technique for this type of surgery, but advances in regional anesthesia have gradually changed this statement. The approaches, interscalene (ISBP) block (C5 C6) or the upper trunk (UT) are the most established options; the supraclavicular approach offers optimal coverage, including the proximal arm. Patients with respiratory compromise may not tolerate hemi diaphragmatic paresis (HDP) associated with proximal approaches. Distal approaches are associated with lower rates of HDP, but coverage of the proximal upper extremity may be incomplete. The use of ultrasound guidance (USG) for nerve blocks has increased success and safety and has allowed access to more peripheral brachial plexus blocks to prevent diaphragmatic paralysis. Regional anesthesia is also an excellent supplement to GA to improve postoperative pain management and decrease the need for opioid use.

Clavicle surgery has even more controversy about the choice of the regional block, since the innervation has not been well described. But in recent years, alternative regional block methods to interscalene brachial plexus block have appeared that are suitable as single anesthesia or combined with sedation or GA.

In this chapter, we pretend to describe the innervation of the shoulder and clavicle based on current knowledge and the sonoanatomy of the neck and armpit as a guide for the performance of regional nerve blocks.

2. Regional anesthesia for shoulder and clavicle surgery

Since shoulder surgeries produce severe postoperative pain, regional anesthesia techniques could effectively control pain at rest and in motion, reduce muscle spasm and facilitate early discharge [1].

2.1 Shoulder innervation

2.1.1 The brachial plexus (BP)

The BP is formed by the fusion of the ventral ramus of the spinal nerves C5, C6, C7, C8, and T1, with the variable contribution of C4 (15-62% of cases) and T2 (16-73% of cases). The roots emerge in the groove between the anterior scalenus and middle scalenus muscles [2]. Shoulder and proximal arm innervation are provided by branches of the BP: suprascapular nerve (SSN) (from posterior division of UT), axillary and subscapular nerves (from posterior cord), lateral pectoral nerve, and medial brachial cutaneous nerve (MBCN)) (from lateral cord), and the intercostobrachial nerve (ICBN) (originating directly from proximal intercostal nerves). SSN may be spared by an infraclavicular approach (**Figure 1**) [3, 4].

2.1.2 Articular branches to the shoulder

The most frequently identified innervation pattern comprises three nerve bridges consisting of articular branches from suprascapular, axillary, and lateral pectoral nerves, connecting trigger points (**Figures 2** and **3**) [5–7].

2.1.3 Nerves and articular branches

2.1.3.1 Suprascapular nerve

Articular branches classified in relation to the spinoglenoid notch:

a. Medial branch (MSAb) originates 1.3 cm proximal to the suprascapular notch, giving branches to the coracoclavicular ligaments and the medial pole of the subacromial bursa, clavicular insertion of the acromioclavicular ligament, and motor branches to the supraspinatus muscle.

b. Lateral branch (LSAb) originates at the level of the suprascapular notch, giving sensory branches to the lateral subacromial pole and acromial insertion of the acromioclavicular ligament. Two subacromial branches provide medial and lateral sensory innervation (bipolar) to the subacromial bursa.

c. The posterior glenohumeral branch (PGHb) originates at 3 cm from the suprascapular notch, and posterior to the spinoglenoid ligament, course inferomedial towards the posterior capsule of the shoulder [8].

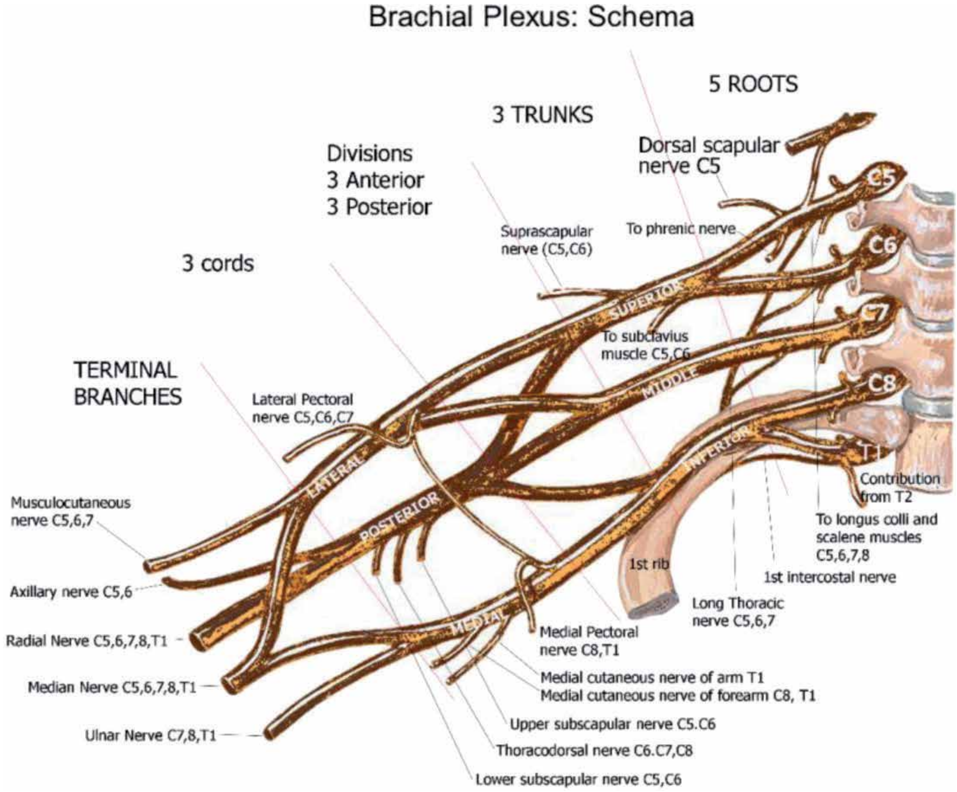

Figure 1.
Brachial plexus. Roots – Start in the spinal cord. Arise from anterior rami C5-T1. Landmark: Pass inferolateral between the anterior and middle scalene muscles. Trunks –the roots merge: Superior/upper (C5/C6); middle (C7); inferior/lower (C8/T1). Landmark – Usually found between scalene muscles and 1st rib. Divisions –the trunks split each one into 3 anterior divisions and posterior divisions. Landmark – Divide around the 1st rib and pass under the clavicle. Cords: 3 cords – Termed according to relation to the axillary artery. Posterior (made up of all 3 trunks posterior divisions - contains all C5-T1 fibers). Lateral (anterior divisions of superior and middle trunks – Contains C5-C7). Medial (anterior division of inferior trunk – Contains C8-T1). Landmark – Runs alongside the axillary artery lateral to the clavicle [2]. The roots C5, C6, C7, and C8 pass behind the vertebral artery and settle in the respective groove of the transverse process, they are directed laterally and inferiorly towards the first rib, where they merge to form trunks. The ventral branch of T1 passes over the first rib and travels higher and laterally to join C8 at the level of the groove that the plexus produces over the first rib. The anterior ramus of spinal nerve C5 contributes to the PN; the anterior ramus of spinal nerve T1 branches to become the first intercostal nerve. These nerves are not considered part of the BP.

2.1.3.2 Axillary nerve (AN)

One or two articular branches of the main trunk travel with the anterior humeral circumflex artery between the tendons of the subscapular and latissimus dorsi muscles branching into medial branch to scapular aspect of the anteroinferior capsule and portions of the axillary recess; lateral branch to humeral portion of the anterior capsule [6]. The posterior division (after leaving the quadrangular space) gives a branch for the teres minor muscle, from which emerge 1 to 4 articular branches, to innervate the posteroinferior capsule. The branch innervating the deltoid muscle gives small multiple articular branches towards the lateral aspect of the humeral head the posterior and lateral supra-lying fascia of the shoulder capsule [6, 9, 10].

2.1.3.3 Lateral pectoral nerve (LPN)

The LPN arises from two branches of the anterior divisions of the upper and middle trunks (33.8% of cases), or as a single root of the lateral cord (23.4%). It

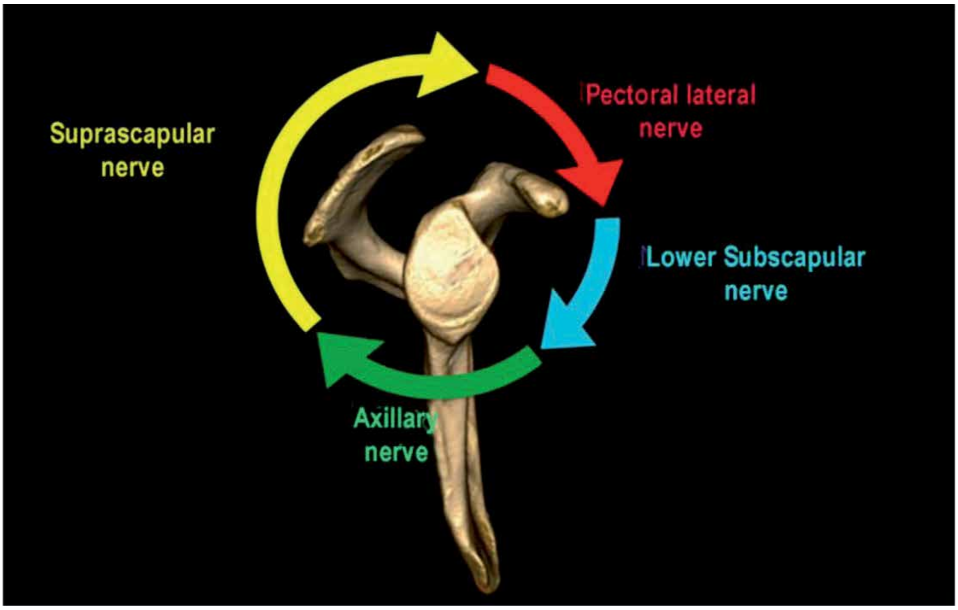

Figure 2.
Distribution of shoulder articular branches. Courtesy of MF Rojas.

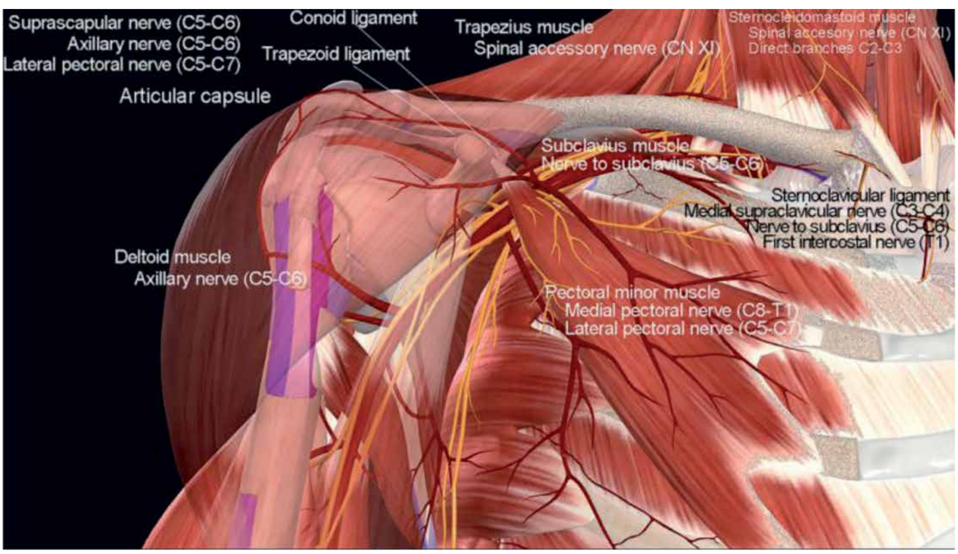

Figure 3.
Shoulder structures and their related innervation.

receives fibers from C5 to C7. Cross the superomedial side of the coracoid process and sends small branches to the coracoclavicular and coracoacromial ligaments, anterior acromioclavicular joint, subacromial bursa and anterosuperior portion of the glenohumeral capsule. It gives branches to the periosteum of the clavicle. Therefore, its blockade produces analgesia for distal clavicle surgery [6, 11]. The muscular branch originates from the articular branch of the LPN and innervates the deltoid muscle and skin over the subacromial region (**Figure 4**) [7, 11].

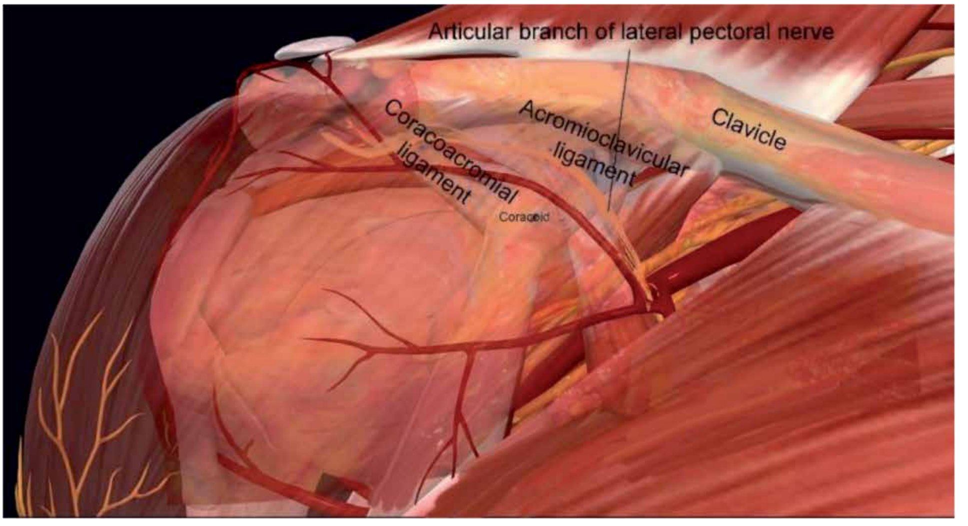

Figure 4.
Lateral pectoral nerve.

2.1.3.4 Inferior subscapular nerve

A glenohumeral articular branch anastomosis with branches of the AN to innervate the long head of the biceps tendon (LHBT) and anterior capsule. The superior subscapular nerve gives 1 or 2 articular branches to innervate the anterosuperior quadrant of the glenohumeral joint [12]. Receives fibers for C5-C6.

The *SSN* is (individually) the largest contributor to global shoulder innervation: posterior glenohumeral capsule, subacromial bursa, coracoacromial and acromioclavicular ligaments. The *AN* innervates portions involving the inferior portion of the anterior and posterior glenohumeral capsule. The anterior face has a more complex innervation pattern: the medial portion is mainly innervated by muscular branches of the inferior subscapular nerve; the lateral face of the capsule is supplied by articular branches originating directly from the AN; the lateral pectoral nerve innervates the anterosuperior quadrant of the shoulder, including the anterior edge of the subacromial bursa, coracoacromial ligament, and glenohumeral capsule. Therefore, nerves other than suprascapular participate in the innervation of most of the joint. See **Figures 1**–**3**.

Mechanoreceptors are more concentrated in the medial and lateral insertions of the anterior capsule. Nociceptors are identified primarily in the upper quadrant of the shoulder, including the subacromial bursa (SAB), glenohumeral ligaments (GHL), coracoacromial (CAL), coracoclavicular ligaments (CCL), the proximal portion of the LHBT, and the transverse humeral ligament (THL). The SAB is the area of densest and tripolar nociceptive innervation. These three nociceptive poles may correspond to the location of the lateral/medial subacromial branches of the SSN (i.e., lateral and middle poles) and the articular branch of the lateral pectoral nerve LPN (anterior pole); Thin articular branches of the AN may also participate in the innervation of the lateral pole of SAB [6].

2.2 Clavicle innervation

The most painful structures in clavicle surgery include the skin over the incision area and the highly innervated periosteum. The supraclavicular nerve originates

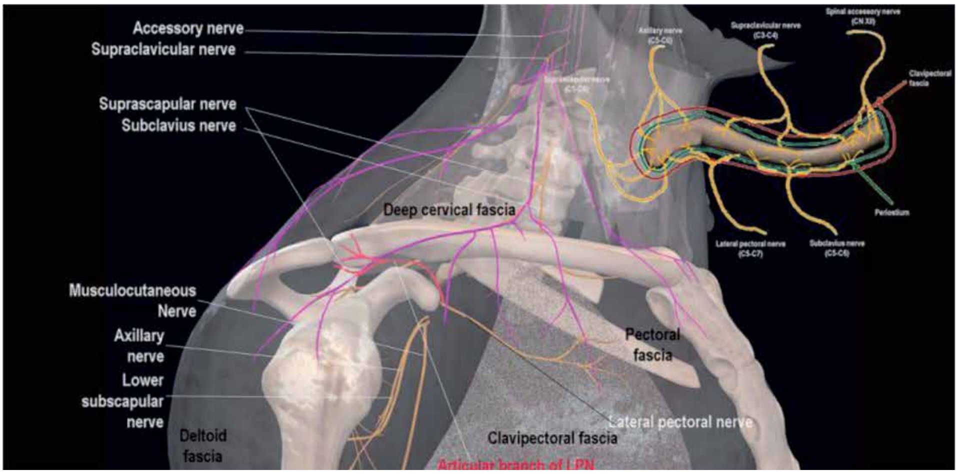

Figure 5.
Nerves involved in clavicular innervation.

as a single trunk from the anterior ramus of cervical nerves C3-C4. It divides into medial (suprasternal), intermediate (supraclavicular), and lateral (supra-acromial) branches. The medial branch supplements the skin over the anterior aspect of the thorax, as far below as the second rib, and the sternoclavicular joint. The intermediate branch pierces the deep cervical fascia just above the clavicle and runs over the pectoralis major and deltoid muscle; supply cutaneous innervation to the skin above

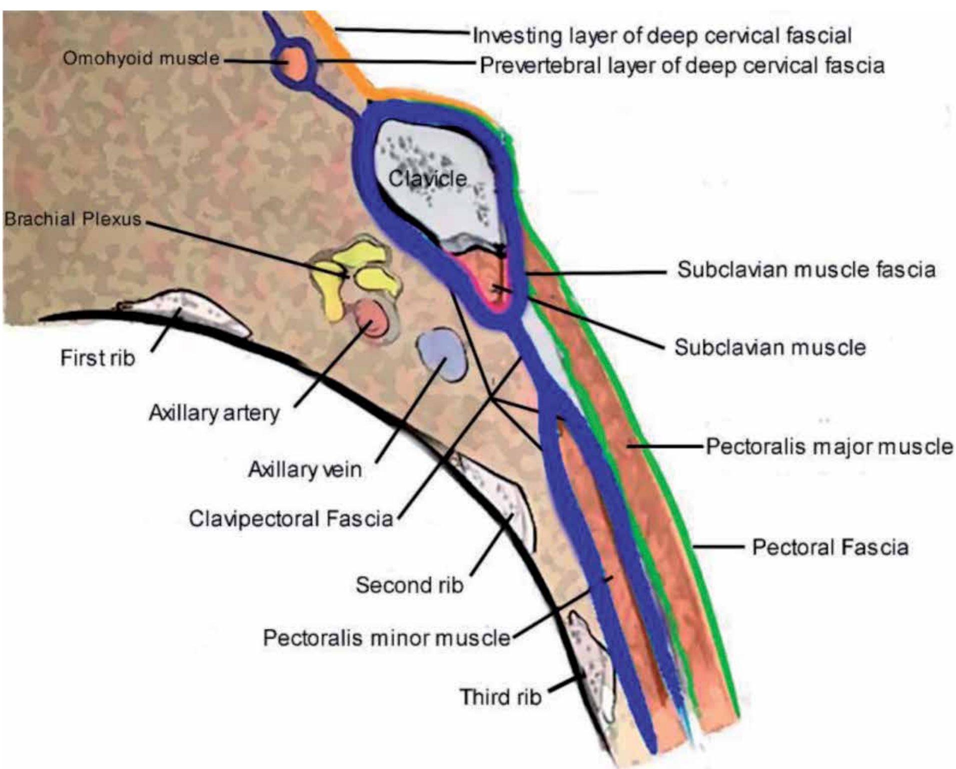

Figure 6.
Clavipectoral fascia.

these muscles, as far below as the second rib. The lateral branch pierces the deep cervical fascia just above the clavicle, passes over the acromial process, to innervate skin of the upper and posterior shoulder regions (**Figure 5**) [13, 14].

Innervation of the clavicle itself is less well described. Different authors attribute contributions from SSN, long thoracic, nerve for the subclavian muscle, and LPN [15].

2.2.1 Fascias related to the clavicle

2.2.1.1 Clavipectoral fascia

Situated posterior to the clavicular part of the pectoralis major muscle. It extends from the clavicle, costochondral joints, and coracoid process. It converges in the axilla and acts as a protective structure over the neurovascular package. The clavicular fascia splits to enclose the subclavius muscle before attaching to the clavicle, the posterior layer fuses with the deep cervical fascia which connects the omohyoid muscle to the clavicle. Medially, it is attached to the first rib before coming together with the fascia over the first two intercostal spaces. Laterally, it is attached to the coracoid process before blending with the coracoclavicular ligament. The fascia often thickens to form the costocoracoid ligament, between the first rib and coracoid process. Inferiorly, the fascia becomes thin, splits around pectoralis minor, and descends to blend with the axillary fascia and laterally with the fascia over the short head of the biceps. It is pierced by CALL [cephalic vein, artery (thoracoacromial), lateral pectoral nerve, lymphatics]. The clavipectoral fascia surrounds the clavicle, and the nerve endings of the clavicle penetrate this fascia (**Figure 6**) [16].

3. Peripheral nerve block for shoulder surgery

Interscalene or supraclavicular block of the BP are considered the standard technique for anesthesia and analgesia in this type of surgery. The most common adverse effect is HDP due to ipsilateral PN block in 100% of patients and a 27% decrease in forced vital capacity and forced expiratory volume at the first second [17]. At the level of the cricoid cartilage (C6 transverse process (TP)) the PN is 0.18 cm prior to the BP, but it diverges at a rate of 3 mm for each centimeter below the cricoid cartilage.

USG has allowed to decrease the anesthetic minimum volume required in 50% of patients (5-7 mL vs. 30-40 mL) using ropivacaine 0.75% or bupivacaine 0.5%, and a decrease of 50% in the incidence of paralysis of the diaphragm when the injection is performed laterally to the C5-C6 roots. If the concentration of the anesthetic is also diluted to a half or third, the HDP rate is reduced to 20% (it is still a contraindication in patients with decreased lung reserve) but carries the risk of not achieving surgical anesthesia and decreasing the duration of the blockade. According to Renes et al., if the injection is done at the C7 root level, the minimum volume required to block C5-C6 in 50% of patients was 2.9 mL (maximum volume of 6 mL), with no PN block (although there is a substantial risk of vascular lesions from punctures at this level). Renes et al. avoided PN block by administering the anesthetic in the "cornet pocket " (intersection of the first rib with the subclavian artery and posterolateral aspect of the BP) and a volume less than 20 ml [18]. Aliste et al. compared ISB with supraclavicular block following the Renes technique, finding equal pain control, but with HDP rate of 9% [19]. Cornish found a 1% of HDP rate by advancing a catheter from the supraclavicular level and locating the tip at the infraclavicular level, inferomedial to the coracoid process [20, 21].

A combination that could be effective would be the association of a SSN block with a BP block at infraclavicular level [22] (addresses the axillary, lateral pectoral, subscapular nerves), although Petrar et al. [23] reported a 3% incidence of HDP during infraclavicular BP block (30 mL ropivacaine 0.5%).

The following paragraphs describe different techniques to achieve a selective block of the nerves supplying the shoulder.

3.1 Upper trunk (UT) approach

It focuses on the anesthetic deposit near the UT, before the take of the SSN. At this level, the phrenic nerve (PN) has diverged from the BP. Compoy et al. [24] found that 5 mL of methylene blue injected around UT stains SSN, lateral pectoral nerve, and roots of C5 and C6, but not of the PN [25]. Kim et al. found analgesic equivalence between UT block and ISB, achieving equivalent surgical anesthesia and HDP incidence of 5% vs. 71% using 15 mL of injectate [26]. Ultrasound (US) examination reveals the plexus in the groove between the anterior and middle scalene muscles, deep to the prevertebral fascia. The sternocleidomastoid muscle (SCM) lies superficially, and the PN can be seen on the anterior surface of the anterior scalene muscle (ASM), crossing it towards the medial side, after the last contribution originating in the C5 root. Sonoanatomy of the transverse processes can be used to identify spinal roots. Serial images reveal the process of confirmation of the UT [27].

The blocking needle is advanced from lateral to medial, under the deep cervical fascia until its tip reaches the UT lateral edge, proximal to the exit of the SSN (it is identified as a rounded hypoechoic structure that separates laterally from the UT and runs deep to the omohyoid muscle). The needle does not pass through the middle scalene muscle (MSM), where the dorsal scapular nerve (DSN) and long thoracic nerve (LTN) are located. The injectate volume is 7 to 12 mL of local anesthetic (LA) (one-half or one-third strength). Here the nerves have a greater amount of perineural tissue, protecting against neurological dysfunction, which has been reported in about 14% of ISBP blocks and can last for up to 10 days (**Figure 7**).

The UT provides anesthesia to nerves from the spinal cord segments C5 and C6 (originating fiber to SSN and AN, inferior subscapular nerve, and partially, to LPN) [25] and decreases the incidence and severity of PN block. HDP was observed in 97.5% in ISB vs. 76.3% of the UT block groups (P = 0.006); paresis was complete in 72.5% vs. 5.3% of the patients, respectively. The decrease in spirometry values from baseline was significantly greater in the ISB block group. UT block provides non inferior analgesia compared to ISBP block [28].

It can be supplemented with blockade of the supraclavicular nerves to anesthetize the skin over the shoulder. The needle is retracted to the space between prevertebral fascia (over the MSM) and superficial (enveloping) layer of the deep cervical fascia, under the SCM, where the supraclavicular nerves are located. A new injection of 2 to 3 mL of LA blocks nerves supplying skin over collarbone and shoulder cap and their sensitive contribution to the acromioclavicular joint.

3.2 Supraclavicular nerve trunk blockade

The supraclavicular nerve trunk (C3 and C4) emerges at the posterior edge of SCM. The superficial cervical plexus (SCP) is localized by placing a transducer on the posterior edge of the SCM at the level of the upper pole of the thyroid cartilage. It can be difficult to identify the individual nerves. The greater auricular nerve (GAN) is a useful reference reliably identified as a small superficial hypoechoic round structure on SCM (**Figure 8**) [29].

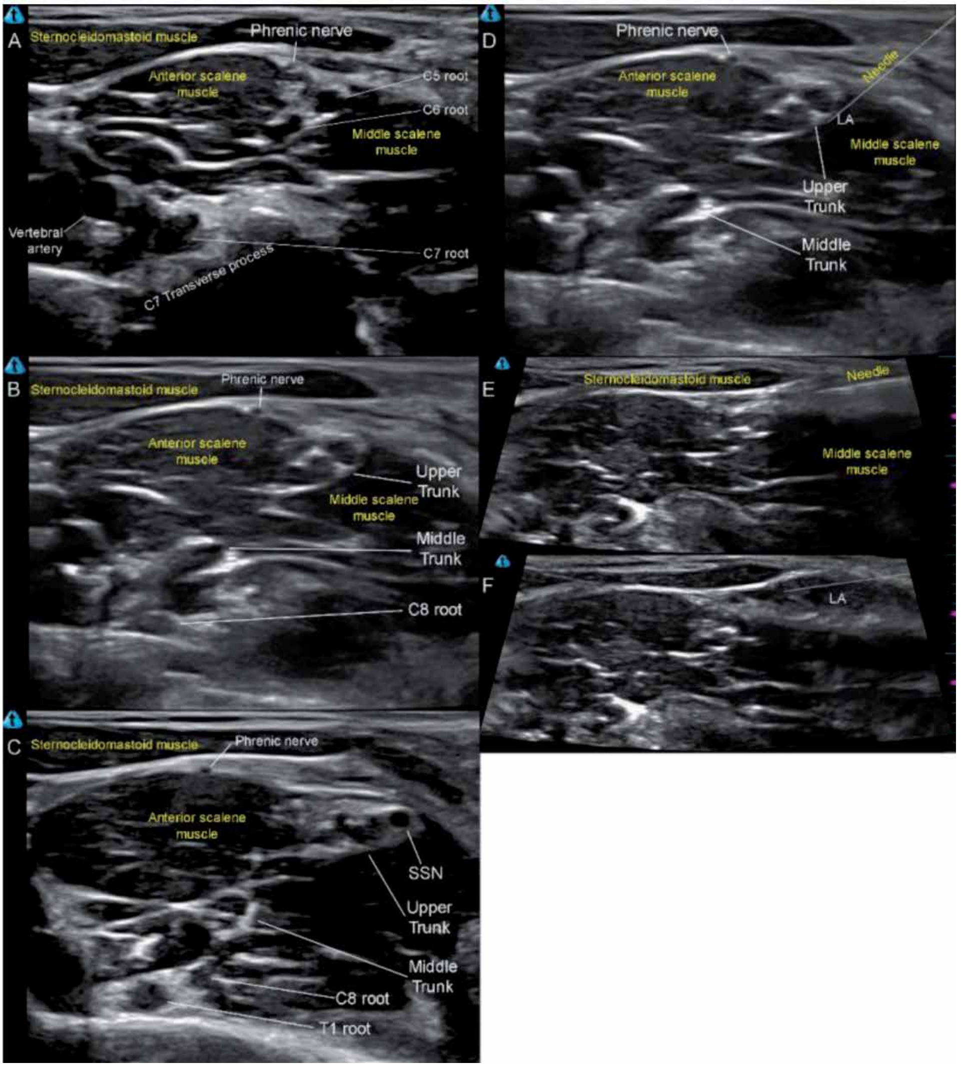

Figure 7.
Upper trunk and supraclavicular nerves blockade. A. C5 and C6 (bifid) roots at interscalene space, near to PN. C7 TP view. B. UT formation (inferior to C7 TP). C. Origin of supraescapular nerve (SSN). D. Back to UT - needle at its posterior surface. Local anesthetic (LA) injection at posterior surface of UT. E. Retreated needle to space between SCM-MSM. LA injected around supraclavicular nerves.

3.3 SSN blockade

The posterior approach in the suprascapular fossa (in the space between the suprascapular notch and the spinoglenoid notch) where the nerve travels through its floor under the supraspinatus muscle fascia, results in adequate flooding of SSN with minimal propagation to the BP [30] but may spare MSAb. This approach is inferior to ISBP block for pain control, at least in the first 4 hours [31–33]. The UT (C5-C6) is the major contributor to the suprascapular, axillary, and subscapular nerves. Hence, UT blockade can provide adequate control of shoulder pain, but it is still remarkably close to the PN [34, 35].

With ultrasound image, the SSN could be identified as it branches from UT, and runs laterodorsally underneath the omohyoid muscle, in 81% of cases vs. 36% in the supraspinatus fossa, at an average depth of 8 mm vs. 35 mm in the supraspinatus fossa. Peripheral nerve stimulator can help in the identification [35]. Rothe et al.

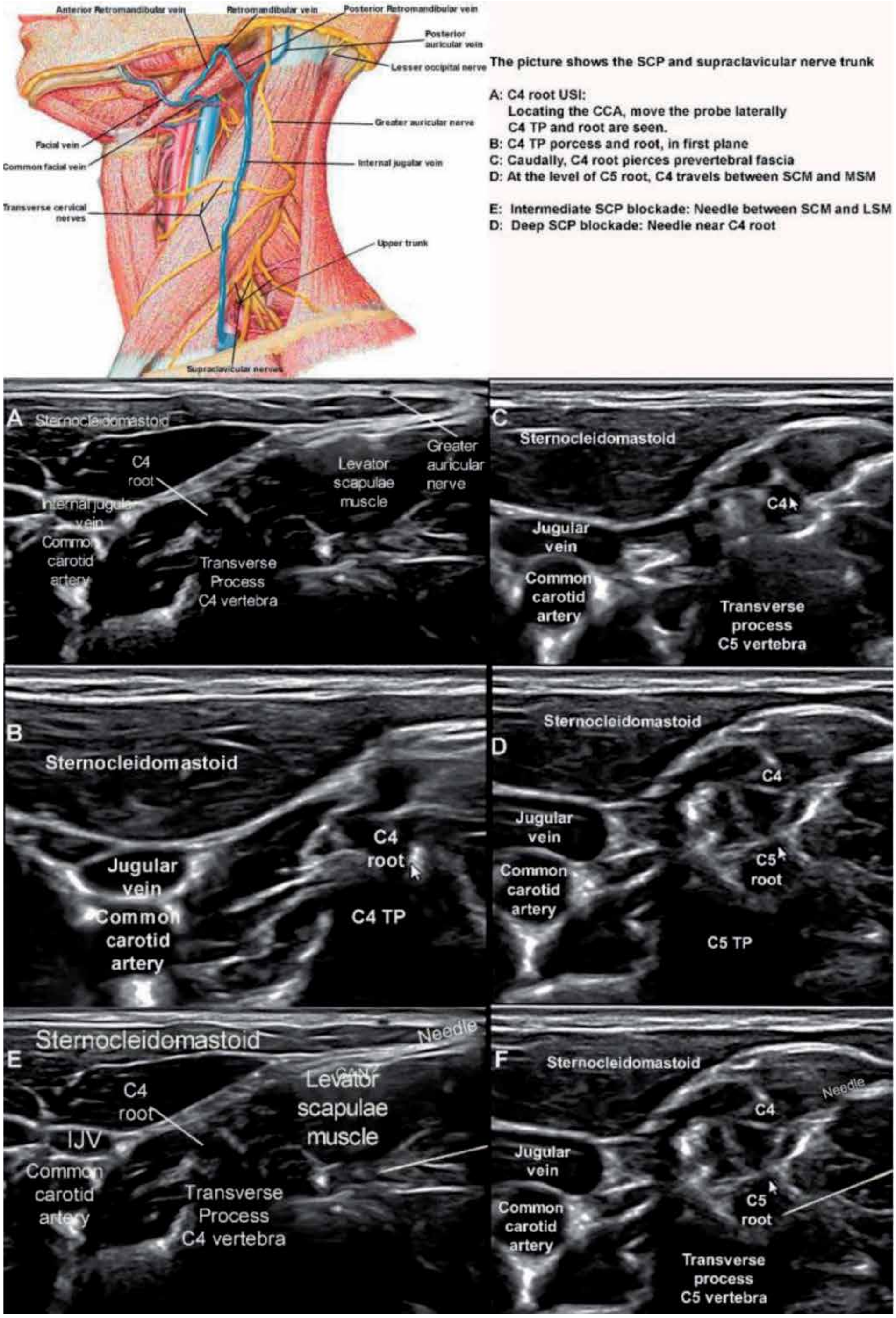

Figure 8.
Supraclavicular nerve trunk and SCP scan process.

studied twelve healthy volunteers; the SSN was followed into the subclavian triangle under the inferior belly of the omohyoid muscle; injecting 1 mL of lidocaine 2%, 10 blocks were performed, 8 demonstrated a reduced manual muscle-testing scale (MMT) of the supra- and infraspinatus muscles at 15 min and 30 min; increasing

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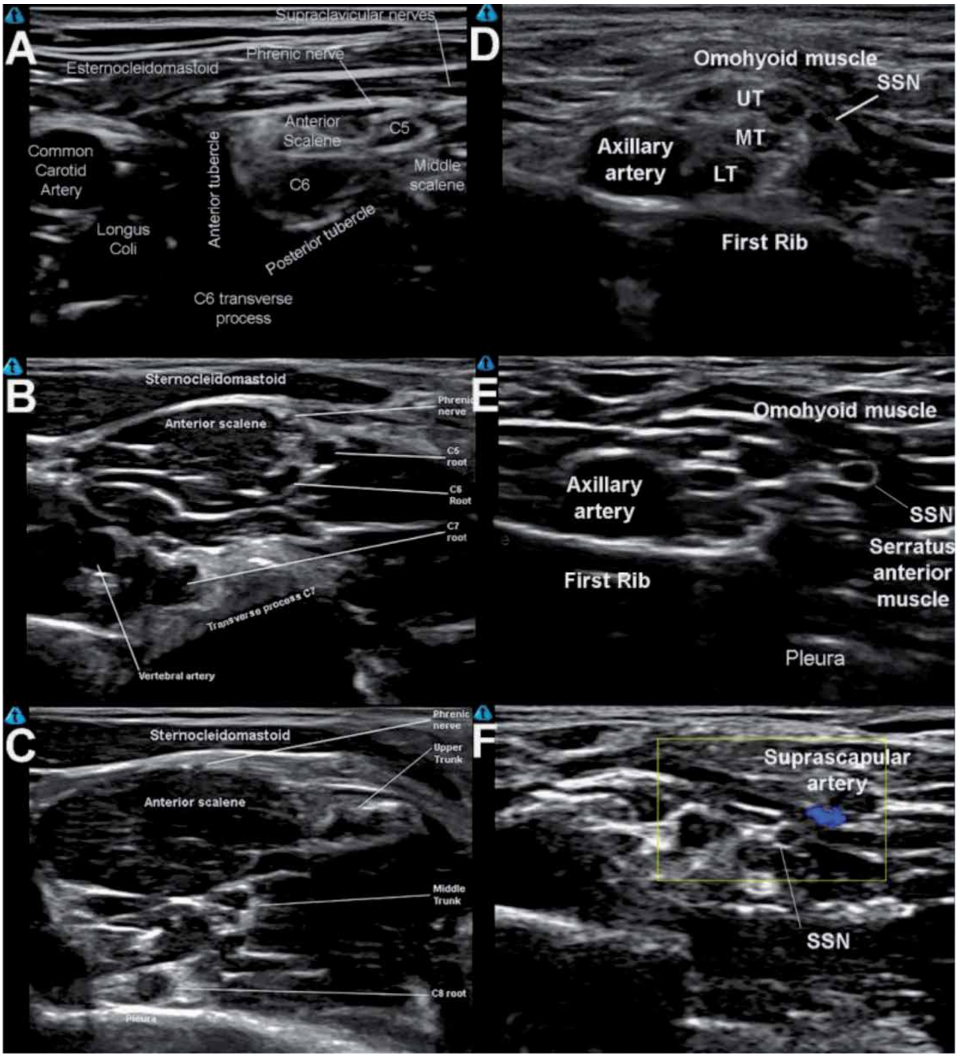

Figure 9.
Scan sequence of the SSN at the supraclavicular fossa. A: Locate the transverse process of C6 vertebral vertebra and C6 and C5 roots. B: Scanning downward, locate the C7 TP and C7 root, which can be seen laterally to vertebral vessels. C: Just below the C7 transverse process, C7 root runs towards the interscalene groove. The PN is diverging from the BP, on the anterior surface ASM. Caudally to the C7 transverse process, UT and MT conformation can be imaged. D: In the supraclavicular fossa. From the UT branches the SSN. E: The SSN travels below the omohyoid muscle. F: The SSN separates from the UT, below omohyoid muscle. The nerve goes along suprascapular artery.

the injected volume, produced musculocutaneous and radial nerves blockade due to cephalic diffusion of the anesthetic (**Figure 9**) [36].

In 14 BP of 7 corpses, the separation between the SSN and the PN was found to be 2.5-6.4 cm, and the injection of 10 mL of solution around the SSN produced staining of the UT of the BP and its branches (SSN, anterior and posterior divisions - 14 cases, 100%), the middle trunk (MT) (13 cases, 93%), the PN (3 cases; 21.4%) [37]. In the cadaveric study by Sehmbi, the SSN and omohyoid muscle were easily identified and, with nerve injections of 5 mL, nerve staining with contrast dye was seen in 90% of dissections. The UT, MT, and LT were stained in 90%, 80% in 20% of dissections, respectively. The PN was mildly stained in 20% of the dissections [38]. **Figure 9** shows the scan sequence of the SSN at the supraclavicular fossa.

3.4 Articular branch of lateral pectoral nerve (LPN)

The articular branch or LPN crosses the superomedial side of the coracoid process [6, 11]. The US probe is placed between the inferior border of the clavicle and the superior border of the coracoid process. Below the deltoid muscle, the acromial branch of the thoracoacromial artery and, along with it, the nerve can be found (**Figure 10**).

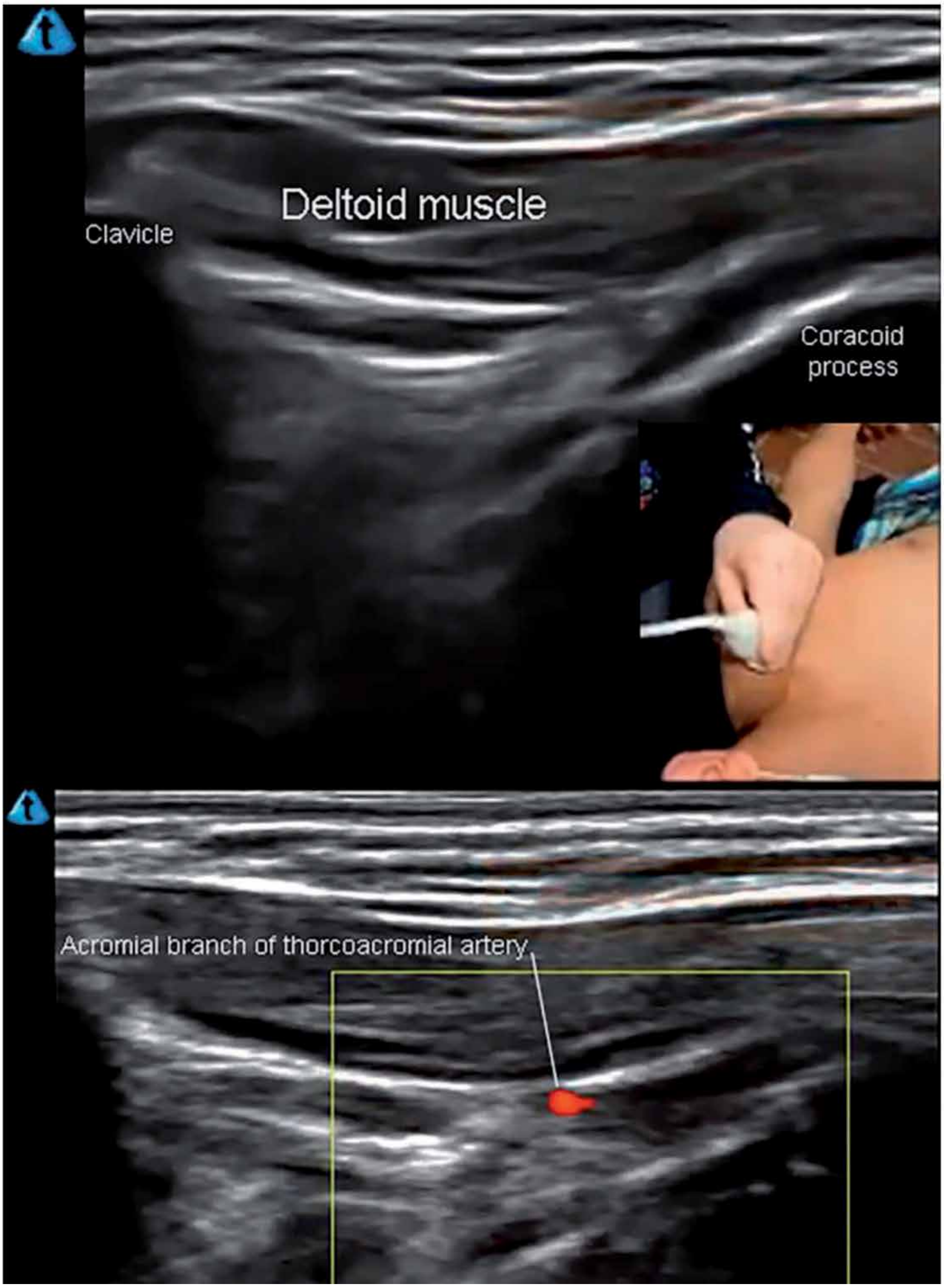

Figure 10.
USG to locate the articular branch of LPN.

3.5 US-guided approach to the AN and ICBN in the axillary fossa

The AN provides motor innervation to subscapular, teres major and minor, and deltoids muscles. The nerve branches before entering the quadrangular space. The anterior division of the AN originates the first articular branch, which ends in the anteroinferior capsule; blocking the nerve by the posterior approach can provide incomplete analgesia.

The sensitive skin supply of the medial aspect of the arm is provided by MBCN, ICBN, and variable branches of the intercostal nerves [39].

The AN run into the inferolateral margin of the subscapular muscle and enters the quadrangular space (QS) (limits: upper, teres minor muscle; inferior, teres major muscle; medial, long head of the triceps muscle; lateral, surgical neck of the humerus; anterior, insertion of the subscapular muscle on the minor tuberosity). The subscapular muscle, the upper edge of the teres major muscle, and the humerus are the sonographic marks that lead to the identification of the AN. The ICBN originates mainly from the second intercostal nerve, with variable contributions from intercostal nerves T1, T3, and T4. It is identified in the axillary subfascial space, along.

with fat, lymph nodes, and other cutaneous branches of the upper intercostal nerves. After crossing the axillary subfascial space, it courses on the surface of the latissimus dorse muscle, covered by the superficial axillary fascia [40].

With the arm abducted 90°, the BP is identified in the armpit (anterior to the teres major and the tendon of the latissimus dorse muscles, seen in short axis) (Position 1, **Figure 11**). The probe moves slightly in a proximal direction (position 2, **Figure 11**) towards the QS, which is identified as soon as the upper edge of the teres major muscle deepens. At this point, the AN appears as an oval honeycomb structure, accompanied by the posterior circumflex artery of the humerus (although it has an inconsistent course and presence). The elevation of the arm from 90 ° to 180 ° brings the nerve closest to the skin by closing the quadrangular space.

3.6 USG anterior approach to AN block

With the arm positioned parallel to the thoracic wall with internal rotation and forearm pronated on the abdomen, a US probe is placed below and parallel to the clavicula identifying the coracoid process and lesser tubercle and intertubercular (bicipital) groove; then the arm is externally rotated, pushing the subscapular muscle rostrally and identifiable under the deep lamina of the deltoid fascia; the first portion of the AN is present between the deep lamina of the deltoid fascia and the superficial lamina of the subscapular muscle, where needle tip is placed. Interfacial position is confirmed after injection of 2 mL of normal saline, then 10 mL of 0.25% bupivacaine is injected. Rotating caudally the medial side of the probe and abducting the limb permits to directly visualize the AN and posterior circumflex humeral artery.

The injection is distributed on the anterior surface of the subscapular muscle and around the proximal insertion of the coracobrachialis and biceps brachial muscles. The sensory block is detected in AN area and areas supplied by the branches of the musculocutaneous nerve, lateral pectoral nerve, lateral supraclavicular nerve, and intercostobrachial nerve.

A complete AN blockade could provide anesthesia to the anteroinferior and lateral edges, and to part of the posterior aspect. of the shoulder joint capsule.

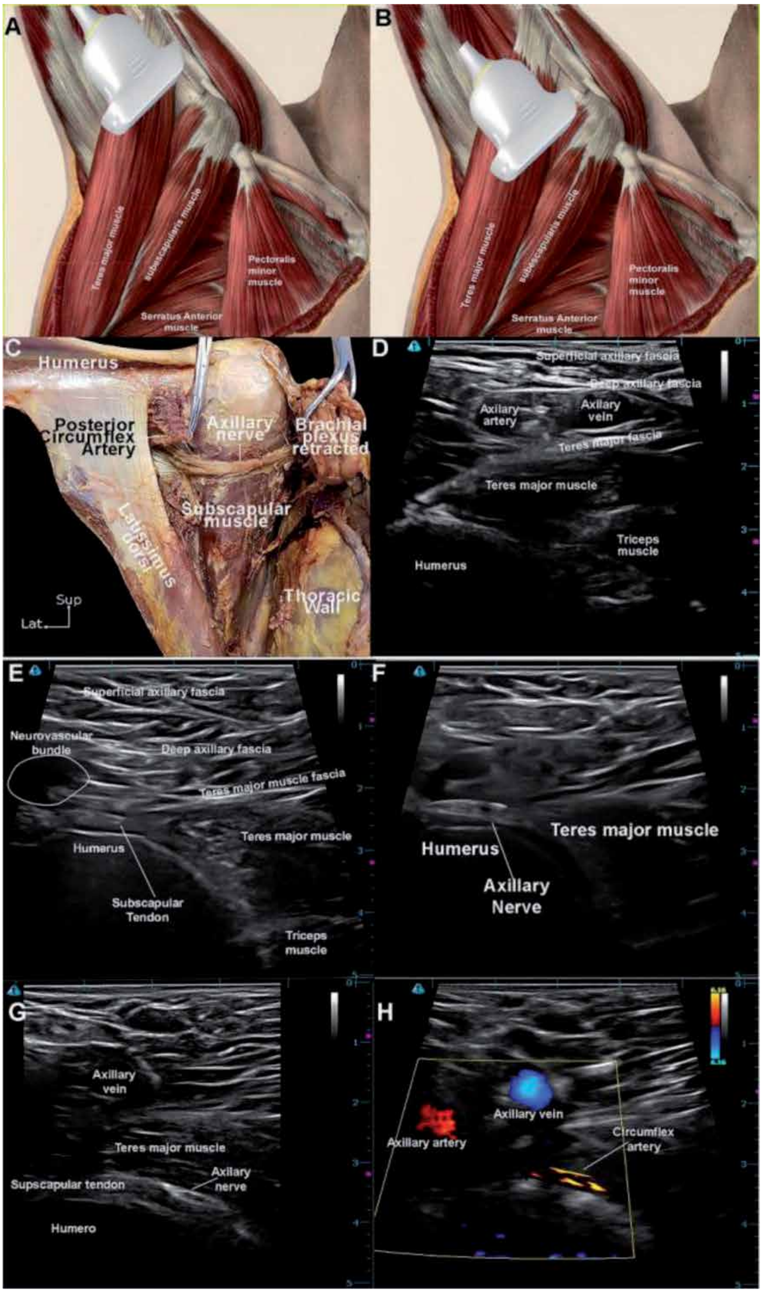

Figure 11.
AN US images at axillary fossa. A. Transducer position 1. The US imagen corresponds to D. B. Transducer position 2. The US imagen corresponds to E. C. Anterior view of axilla showing the quadrangular space; AN emerges posterior to brachial plexus and enters the QS divided in anterior and posterior ramus. D. Scanning starts viewing the brachial plexus at the axillary level, observing the fascia of the teres major muscle. E. Moving proximally the transducer (towards the axillary fossa) shows the teres major muscle fascia deepening and the subscapular muscle tendon; the QS is seen. F. with 180° arm extension, the teres major muscle closes the QS. G and H. the axillary nerve is observed above the subscapular muscle as a hyperechoic image next to the circumflex humeral artery.

The remaining shoulder joint areas are innervated by the SSN, which must be blocked if complete anesthesia of the shoulder is to be achieved. The LPN, or its articular branches, can be blocked by PECS I block or at the space between the coracoid process and clavicle (**Figure 12**) [41, 42].

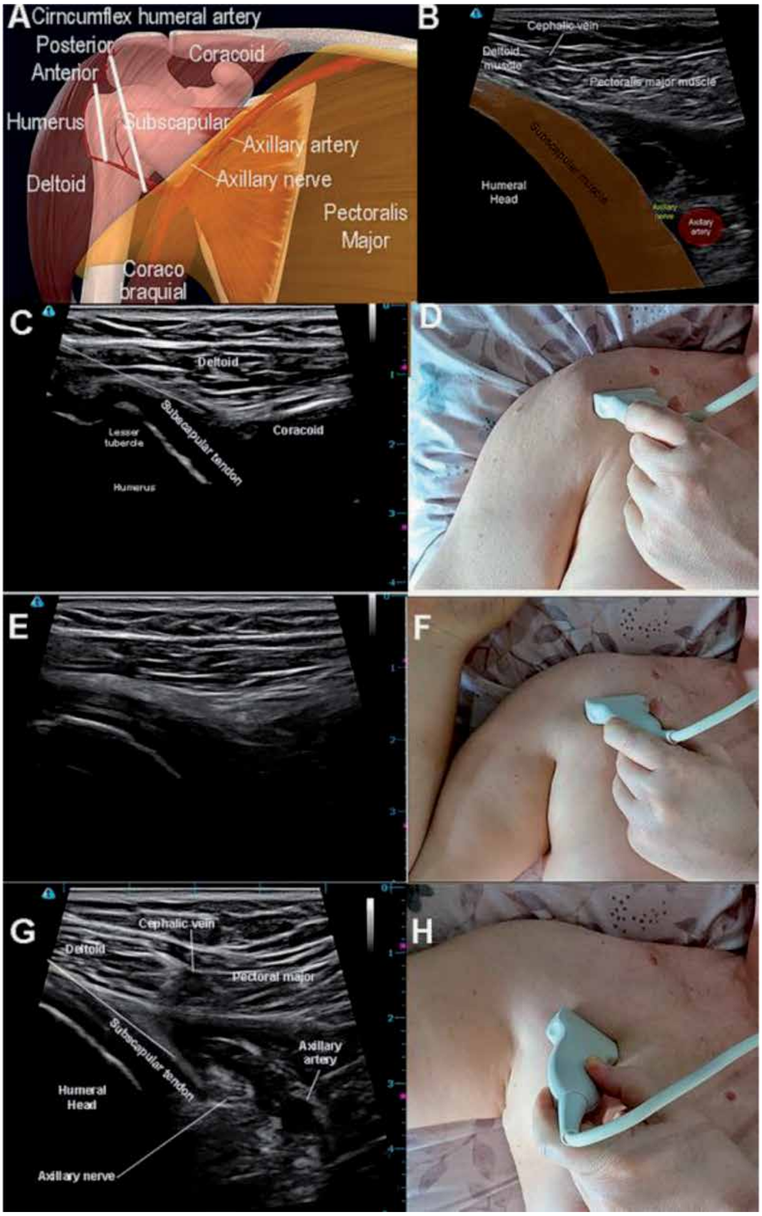

Figure 12.
US-guided anterior approach to AN blockade. A. Axillary nerve and its relations to subscapular, deltoid, and pectoralis muscles, axillary and circumflex humeral arteries, coracoid process, and humerus bone. B. Sagittal oblique ultrasound anatomy of the anterior axilla. C. Ultrasound scan: Transducer between coracoid process (medial) and the lesser tubercle of the humerus. Arm adducted and internal rotation. D. Transducer parallel to the inferior border of the clavicle, ultrasound mark is lateral. E and F. arm rotated externally/no abduction; subscapular muscle appears over humeral head. G and H. full external rotation and abduction of the arm. The medial side of the transducer is rotated inferiorly to obtain a sagittal oblique view of the axilla. The subscapular muscle is pushed rostrally and is identifiable under the deep lamina of the deltoid fascia. The cephalic vein is seen in the groove between deltoid and pectoralis major muscles. The axillary artery appears in the image and laterally to it, the axillary nerve is located. The needle shows the injection around the axillary nerve, on the surface of the subscapular muscle.

4. Surgery involving the collarbone

Clavicle fractures account for 2.6–4% of fractures in adults and 35% of shoulder injuries. The annual incidence is estimated between 29 and 64 per 100,000, and

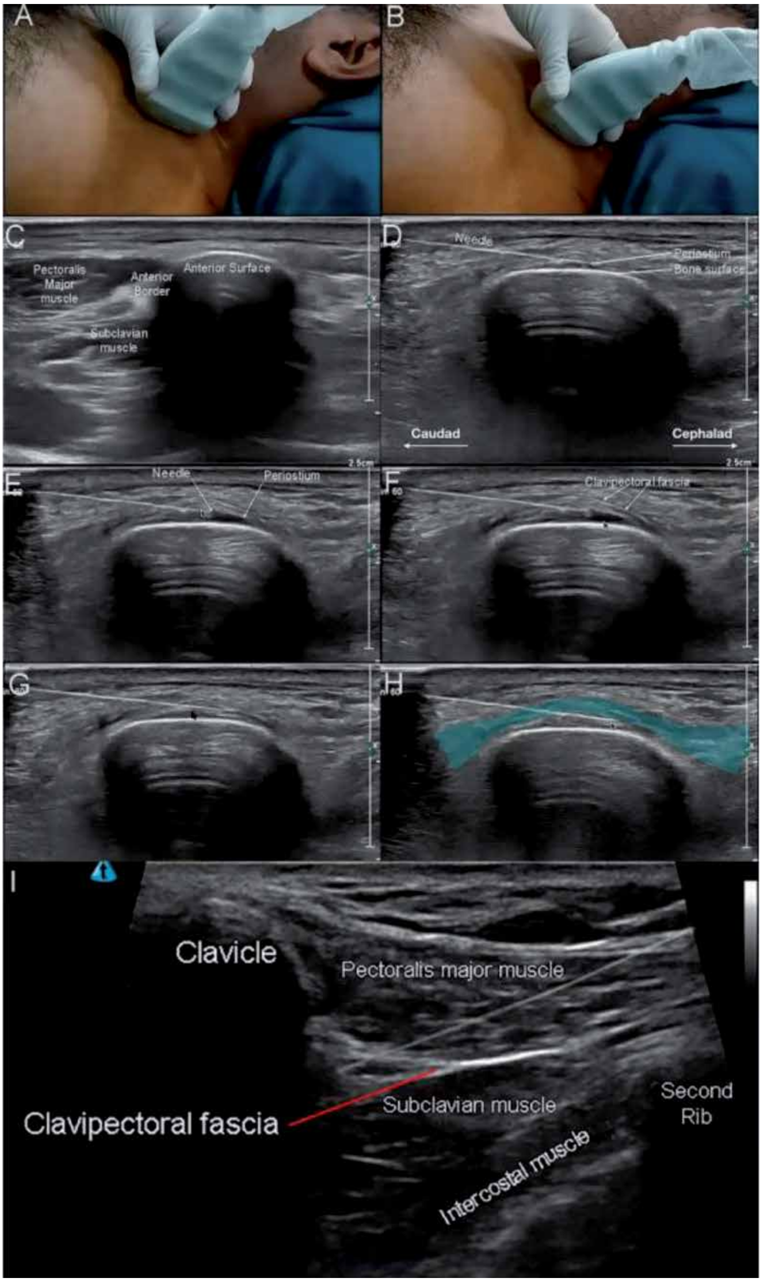

Figure 13.
The peri clavicular fascial plane or clavipectoral planes block (CPB). A: Scan throughout all clavicle surface, identifying the fracture site (proximal segment is displaced upward) B: Initiate the US scan in a sagittal paramedian position C: Tilting the ultrasound probe, is positioned on the upper surface of the clavicle D: Identify the anterior and posterior borders of clavicle E: 25 G needle tip positioned between bony surface and periosteum (if seen: By the fractured site, the periosteum is usually detached F: After 1-2 ml injected, the periosteum is further disengaged G: A second hyperechoic line appears, which correspond to clavipectoral fascia H: Needle tip positioned in the gap between periosteum and clavipectoral fascia I: Initial injection under clavipectoral fascia. Track Injectate spread in caudal and cephalic way along the anterior surface of clavicle I: Alternatively, Clavipectoral fascia scanning and needle in plane insertion from caudal to cephalic over clavipectoral fascia between pectoral major and minor muscles; this plane is the target for injection of local anesthetic.

are distributed as follows: diaphysis 69-82%, lateral end 21-28%, and medial end 2-3%. There is often caudal displacement of the lateral fragment under the shoulder weight and elevation of the medial fragment by traction by the SCM. Infrequently, posterior displacement of the medial end can cause compression of the mediastinum and main vessels requiring urgent intervention. Non-displaced fractures are managed without surgery, while surgical management is preferred in cases of displaced fractures in active adults [43].

Innervation of the skin above the second rib is supplied by the supraclavicular nerves of the SCP. Terminal branches of suprascapular, subclavian, lateral pectoral, and long thoracic nerves pass through the plane between the clavipectoral fascia and the clavicle and, theoretically, contribute to collarbone innervation.

Common approaches in anesthesia for clavicle fracture surgery are GA, regional anesthesia techniques such as ISBP block combined with SCP block. The clavipectoral fascial plane (CPB) block (**Figure 13**) is accomplished by injecting 10 to 15 mL of LA deep to the clavipectoral fascia on the medial and lateral side of the fracture site. A SCP or supraclavicular nerves block should be implemented to provide a sensory block of the skin of the shoulder. This nerve block can potentially involve the PN if the injection is not performed accurately in the proper subcutaneous plane and using low volumes. The block can be used for diaphysis and lateral end interventions, but as isolated block for surgical anesthesia, it only works for diaphysis fractures (**Figure 13**) [44].

For lateral fractures, including acromioclavicular and coracoacromial ligaments, articular branch of lateral pectoral nerve should be blocked. Likewise, if the surgery involves the acromioclavicular joint, the SSN should be blocked. Yamak Altinpulluk states that in the description of Ince et al., the LA was injected between the periosteum of the clavicle and the surrounding fascia (assumed as the clavipectoral fascia), but cadaveric dissections show that the spread is between the clavicle and fascia of the pectoralis major muscle in the upper and anterior aspect of the clavicle, with anesthetic spread under the deep layer of superficial cervical fascia and the superficial layer of pectoralis major fascia. The naming of this block as CPB is misleading and suggests that this block should be named as peri clavicular block (PB) [45]. The publication of a series of cases by Kukreja et al., shows the injection of the LA between the clavipectoral fascia and the pectoralis major muscle, resolving the previous objections described by Yamak Altinpulluk et al. [46].

5. Interscalene brachial plexus (ISBP) block

ISBP block targets the roots and trunks of the BP in the interscalene groove between ASM and MSM, and is directed towards C5-C6 nerve roots or UT. With higher volumes, C7 and even C8 nerve roots may be blocked. The block provides analgesia and anesthesia to the shoulder, lateral two-thirds of the clavicle, proximal humerus, and shoulder joint surgeries. Continuous infusion of 0.15% bupivacaine or ropivacaine (vs GA or intravenous anesthesia) provides adequate pain relief, similar side effects, and high patient satisfaction. ISBP block is associated with a high risk of PN blockade and HDP. Persistent PN palsy after ISBP block has recently gained wider recognition (reported incidence of 1:2000). Phrenic nerve palsy could be due to direct needle trauma or intraneural injection during landmark guided ISB but this complication has not been described with USG ISBP block. More peripheral BP nerve blockades are alternatives in scenarios in which avoiding PN palsy is critical, without clinically meaningful analgesic differences compared with ISBP block, except during recovery room stay [47]. Vocal hoarseness and Horner's syndrome are due to self-limiting temporary blockade of the ipsilateral recurrent laryngeal nerve and stellate ganglion [48]. ISBP block cannot reliably block the C8 and T1 ventral rami [48, 49].

ISBP Blockade relies on the visualization of the relevant anatomy, needle-tip position and LA spread using USG plus peripheral nerve stimulation with or without injection pressure monitoring. USG allows fewer needle passes, lower volumes of LA, and better postoperative analgesia [1].

Figure 14 shows the scan process of interscalene space: At cricoid cartilage level, with transverse scan, identify the carotid artery and move the transducer laterally

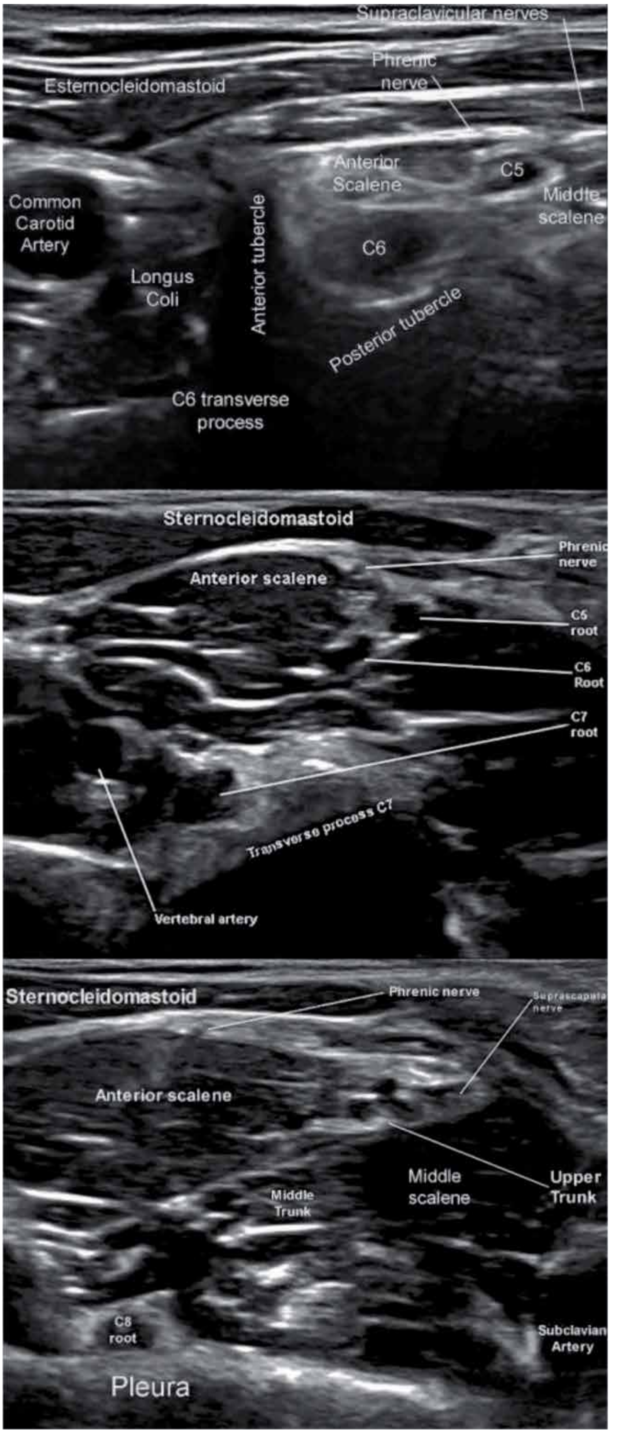

Figure 14.
Interscalene brachial plexus block.

to locate the sonographic image of C5 and C6 TP; C5-C6 nerve roots are seen between the anterior and posterior tubercles and are traced in the groove between ASM and MSM, deep to the prevertebral fascia. The SCM lies superficially, and the PN runs medially over the ASM, away from the C5 root. Below the C6 TP and nerve root, C7 TP appears and the C7 nerve root can be seen anteriorly as hypoechoic round structure, lateral to vertebral vessels (identified by doppler color scan); meanwhile C5 and C6 nerve trunk are merging to conform to the UT; inferiorly to C7 transverse process, C7 nerve root conforms the MT. The dorsal scapular nerve (DSN) arises from the C5 nerve root and is imaged as a hyperechoic structure traversing the MSM, accompanied by LTN. Both must be avoided not needling through MSM. The block is performed positioning the tip deep to the C6 nerve root or UT and seeking the spread of LA anterior and posterior to the nerves, within the interscalene groove, and then repositioning of the needle superficial to the C5 nerve root or UT to obtain a satisfactory spread of LA. Do not needle between C5 and C6. 10-15 mL of LA (ropivacaine 0.75%) produce surgical anesthesia. Supraclavicular nerves blockade is added aimed to provide complete anesthesia to the shoulder cap.

The PN diverges at a rate of 0.3 mm per cm below the cricoid cartilage. Its blockade is reported in as 100% with a traditional landmark-based approach using volumes greater than 20 mL, and between 25 and 50% with lower volumes. Forced expiratory volume in 1 s (FEV_1) may be reduced by up to 40%, and patients with comorbidities (obesity and respiratory disease) may develop troublesome dyspnea. ISBP block has been associated with an incidence of temporary neurological dysfunction in up to 14% at 10 days. Hypotension and bradycardic events occur in up to 20% during shoulder surgery, typically in the sitting position, and at around 30 min after the placement of an ISBP block. High circulating catecholamine concentrations and an underfilled, hyper contractile ventricle (induced by venous pooling) stimulates intramyocardial mechanoreceptors resulting in an abrupt reduction in sympathetic tone together with increased vagal tone. Prompt treatment with an antimuscarinic (ideally atropine) with or without sympathomimetic drugs is indicated [1].

Selective trunk block (SeTB) targets injection around individual trunks, with small volumes of LA. Produces anesthesia of the entire upper extremity (C5-T1) except the ICBN innervated area (T2). Is performed as one injection targeting UT and MT at interscalene and another one targeting LT at the corner pocket of the supraclavicular fossa (Up to 25 ml of LA are used). Produces HDP similar to UT approach [49, 50].

6. Diaphragm-sparing BP blocks

Shoulder surgery is accompanied by severe acute postoperative pain that continues to be an unresolved problem. The gold standard for analgesia after this surgery is the ISBP. Unfortunately, this block is associated with a high incidence of ipsilateral phrenic nerve block and the consequent HDP, which restricts its use in patients with pre-existing pulmonary involvement, so it is prudent to consider the practical options to avoid or reduce the incidence of this complication. Nerve block techniques without diaphragmatic involvement such as supraclavicular blocks, upper trunk blocks, anterior suprascapular nerve blocks, costoclavicular blocks, and combined infraclavicular-suprascapular blocks are some of the possible alternatives. It has been suggested that costoclavicular blocks could provide postoperative analgesia similar to ISBP along with a 0% incidence of HDP. It is not clear whether costoclavicular blocks could achieve surgical anesthesia for shoulder surgery. The anterior suprascapular nerve blocks have been shown to provide surgical anesthesia and analgesia similar to ISBP. However, the risk of HDP has not been adequately quantified. Of the remaining nerve blocks that preserve diaphragm function, supraclavicular blocks (with injection of posterolateral local anesthetic to the brachial plexus), upper trunk blocks, and combined anterior and infraclavicular suprascapular blocks achieve analgesia similar to ISBP, along with an incidence of HDP <10% [17, 25, 51].

7. Discussion

Orthopedic surgeries are well known to be very painful. General anesthesia or regional anesthesia, or a combination of both, are optimal options for shoulder surgery. Regional nerve blocks are essential for postoperative analgesia and can be used alone or as a complement to GA, therefore the postoperative analgesia could be prolonged for 24 hours or more [49]. Regional anesthesia in the setting of GA has a relative contraindication but, with the use of USG, this statement has been challenged [52].

ISBP blockade is the most common approach and a highly effective technique, but with a high incidence of HDP, that contraindicates it in patients with lung disease or contralateral PN paralysis [25, 51]. Supraclavicular blocks vs. ISBP, result in similar pain control and patient satisfaction, but with an incidence of HDP exceeding 60%, when LA is injected intracluster, vs. 9% depositing LA posterolateral to neural cluster (in this setting, cluster refers to the confluence of trunks and divisions of BP) [25, 28].

UT block targets C5-C6 nerve fibers traveling with SSN and AN, producing analgesia not inferior to ISBP block and a 75% incidence reduction of PN involvement [21–24]. The HDP occurs with an incidence of 5% [25].

AN block (posterior access) plus SSN block (sub supraspinous muscle access) produces a good analgesic effect in minor surgeries, compared to ISBP block, but spares the AN anterior articular branches, the lateral pectoral nerve articular branch, and subscapular nerve [25, 41, 45] and is inferior in terms of analgesia when compared to ISB in major surgeries. SSN block at sub omohyoid level extends to the UT almost always and occasionally to the middle trunk, with almost no PN block [33–35, 37]. It provides surgical anesthesia and similar analgesia to ISB [25]. It remains necessary to formally quantify the incidence of HDP. Both blocks should be accompanied by a supraclavicular nerve block at the lateral edge of the SCM to give analgesia to the skin over the shoulder and its contribution to the acromioclavicular joint [29].

AN block may be performed at the axillary fossa, producing anesthesia/analgesia that includes the anterior and posterior branches, with the advantage that intercostobrachial nerve block may be performed with the same puncture [38]. Access to the AN by anterior route is easy to perform and has the possibility of extending to the musculocutaneous nerve, superior subscapular nerve, lateral pectoral nerve and through the clavipectoral fascia, to the lateral supraclavicular nerve [41]. Clavipectoral fascia and peri clavicular block can provide anesthesia and analgesia for fractures of the middle third of the clavicle, without PN paralysis [44–46].

To date, the strategy that achieves analgesic equivalence with ISB with a 0%-incidence of HDP is the costoclavicular block. In 2019, Aliste et al. [53] compared ISB and costoclavicular block in 44 patients undergoing arthroscopic surgery, finding equivalent analgesia in both groups. Moreover, there is no evidence that this block results in surgical anesthesia [25]. Supraclavicular blocks (with LA injection posterolateral to the BP), UT blocks, and combined infraclavicular-anterior suprascapular blocks have been shown to achieve similar analgesia to ISB [54], coupled with an HDP incidence <10%. Decreasing LA injectate volume could avoid HDP altogether and should also be investigated for the provision of surgical anesthesia [25].

8. Conclusions

The anesthetic challenge imposed by shoulder surgery is considerable. This chapter reviews current options for regional anesthesia in this type of surgery. A regional technique, GA, or a combination of both can be appropriately used. Performing nerve blocks distally to the ISBP approach, PN paralysis can be reduced considerably, although not eliminated, taking care when performing them in patients with lung disease or contralateral HDP.

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Conflict of interest

The authors declare that they have no conflicts of interest.

Acronyms

AN	axillary nerve
ASM	anterior scalene muscle
BP	brachial plexus
CPB	clavipectoral plane block
DSN	dorsal scapular nerve
GA	general analgesia
GAN	great auricular nerve
HDP	hemi diaphragmatic paresis
ICBN	intercostobrachial nerve
ISBP	interscalene brachial plexus
IVA	intravenous analgesia
LA	Local anesthetic
LHBT	Long head biceps tendon
LPN	lateral pectoral nerve
LSAb	lateral suprascapular articular branch
LSM	Levator scapulae muscle
LT	lower trunk
LTN	long thoracic nerve
MBCN	medial brachial cutaneous nerve
MPN	medial pectoral nerve
MSAb	medial suprascapular articular Branch
MSM	middle scalene muscle
MT	middle trunk
PCB	peri clavicular block
PN	phrenic nerve
QS	Quadrangular space
SCM	sternocleidomastoid muscle
SCP	superficial cervical plexus
SSN	suprascapular nerve
SeTB	Selective trunk block

TP	transverse process
US	ultrasound
USG	ultrasound guidance
USI	ultrasound image
UT	upper trunk

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Section 3

Regional Anesthesia by Specialties

Chapter 6

Spinal Anesthesia in Pediatrics

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Abstract

The survival of preterm newborn patients (PNB) depends in a great extent on the anesthetic technique used. Spinal anesthesia (SA) is considered the best-tolerated regional anesthetic method for highly unstable newborn infants (NB) with high risk of complications during the perioperative period. SA has been recommended for children at high risk for postoperative apnea due to general anesthetics or prematurity. Bronchopulmonary dysplasia (BPD) in the newborn is a disease that accompanies the patient to the operating room with a high incidence of mortality. SA in emergency surgery is a well-tolerated anesthetic procedure with proven effectiveness, with less hemodynamic and respiratory repercussions. At the same time, it produces greater protection against surgical stress in the NB weakened by the premature condition. Hemodynamic stability remains constant even in the newborn with heart disease.

Keywords: spinal anesthesia, regional anesthesia, newborn

1. Introduction

The 8% of PNB require surgery to correct an organic birth defect in the first hours or days after birth. BPD in PNB is a serious disease with high mortality rates, which produces significant respiratory fragility with repercussions on the general condition of the patient. General anesthesia (GA) produces cardiovascular and hemodynamic changes that prolong intubation for hours or days after surgery, which complicates the underlying respiratory problem. Inhaled anesthetics, hypnotics, intravenous agents, and muscle relaxants can prolong and worsen the awakening of the NB.

In recent years, a large number of published articles have tried to demonstrate the existence of anesthetic agents that cause brain damage mainly in immature organs of preterm infants. The fundamental premise for the administration of anesthetics is their reversibility, which implies that the brain, spinal cord and peripheral nerves are anatomically and physiologically the same before and after the administration of any anesthetic agent. Therefore, the pediatric anesthesiologist faces the dilemma of which anesthetic agents cause less neurocognitive damage. An alternative to the problem of neurocognitive damage is spinal anesthesia, because local anesthetics (LA) produce a neuroprotective effect on the central nervous system, with minimal physiological changes [1].

The most frequent surgical procedures in the NB are inguinal hernia repair, duodenal atresia, pyloromyotomy, myelomeningocele repair, and imperforate anus repair. In most of these urgent surgical procedures, SA helps us to solve the surgical procedure with proven efficacy and safety. Hemodynamic stability remains constant even in PNB with heart disease, in non-cardiac surgery [2].

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2. Neurocognitive damage

The neurocognitive damage produced by the use of anesthetic agents in immature brains has been well demonstrated in laboratory animal models. The effect of general anesthetics on brain development in children under three years of age can have an impact on the later life of the child. Modifications that have resulted in serious behavioral and memory changes in experimental animals. It is suspected that a similar situation could occur in children who manifest learning disabilities at school age. However, other variables must be taken into account, such as prematurity itself, and concomitant diseases such as seizures, prolonged ventilation in the neonatal intensive care unit, repeated and chronic administration of multiple medications and surgeries. The evidence of such harm in humans, with general anesthetics such as intravenous, hypnotic, and inhaled has been much more difficult to demonstrate. Until today there are two important concepts regarding accelerated apoptosis damage in immature organs; the damage is directly related to the dose and duration of exposure.

The combination of regional anesthesia and general anesthesia makes it possible to reduce the intraoperative exposure of general anesthetics and they are a good alternative for immature NBs. The concept of reversibility of anesthetics is being questioned [1, 3, 4].

3. Benefits of spinal anesthesia

3.1 Cardiorespiratory stability

SA is considered the best-tolerated anesthetic method for cardiovascular unstable NBs. In preterm and ex-preterm with congenital heart disease, SA has shown good stability in systolic, diastolic, and mean arterial pressure, due to the absence of arterial hypotension secondary to sympathetic blockade as observed in adults. The same occurs with the management of respiratory diseases such as BPD. Most NBs show a very low incidence of postoperative complications. Even those weakened NBs are able to maintain spontaneous breathing during surgery, avoiding intubation of the trachea and subsequent mechanical ventilation [5].

3.2 Hemodynamic stability

Spinal anesthesia produces a thoracic and lumbar sympathetic block and therefore vasodilation below the level of the block. However, due to the incomplete sympathetic innervation in children under eight years of age, SA is characterized by excellent hemodynamic stability that does not require prior administration of intravenous fluids or the use of vasopressors. The blood volume in the capacitance vessels of the lower limbs is less. However, when SA is administered with GA, hemodynamic stability is considerably modified due to the pharmacological action of general anesthetics. In the newborn with congenital heart disease, SA is preferred over GA, which produces minimal cardiovascular changes [6].

3.3 Short stay in the post-anesthesia care unit

Respiratory complications in the post-anesthesia care unit (PACU) are more common with the use of inhaled anesthetics, intravenous or opioids, concerning SA, especially in preterm or ex-preterm patients who are susceptible to relatively frequent periods of apnea and respiratory depression. GA and opioids are considered predictors of a longer stay in the PACU. SA has been the most important factor that has reduced the length of stay in the PACU [7].

3.4 Rapid recovery of gastrointestinal function

The restoration of intestinal function after gastrointestinal surgery in the newborn child, with postoperative ileus, has been rapid with SA compared to AG. A situation that is especially important in necrotizing enterocolitis and gastroschisis surgery during the neonatal period. Opioids administered during GA contribute to increased ileus.

Spinal anesthesia facilitates early restoration of intestinal peristalsis. The vasodilator effect of the blockade increases splanchnic perfusion and peristalsis, favoring the rapid restoration of the oral route [8].

3.5 Hypoxia

Most of preterm patients, especially the severely preterm, which is susceptible to a decreased response to hypoxia, and with it, the risk of apnea and perioperative hypoxia. Airway management is complicated in patients with hydrocephalus and Arnold-Chiari syndrome type II, a pathology that occurs in children with lumbosacral myelomeningocele. Other craniofacial syndromes that present with mandibular hypoplasia condition a complicated airway. SA has shown advantages over GA in children with myelomeningocele [9]. SA is particularly important to reduce the risk of postoperative apnea in high-risk NBs and allows a low incidence of respiratory complications [10].

3.6 Response to surgical stress

The degree of stress derived from surgery and anesthesia is directly related to the quality of postoperative analgesia, especially in children with comorbidities. Hormones related to the stress response, such as epinephrine, norepinephrine, cortisol, ACTH, prolactin, and blood glucose levels, are produced in lower amounts after SA due to an interruption in the transmission of pain in the afferent and efferent nerve pathways. These hormone values return to their preoperative baseline values within 24 hours [11].

3.7 Immune response

The immune response is stimulated by LA. It is well known that trauma and surgery favor susceptibility to infection due to immune suppression. Opioids

1.	Cardiorespiratory stability in preterm
2.	Short stay in the neonatal care unit
3.	Quick recovery of gastrointestinal function
4.	Less response to surgical-anesthetic stress
5.	Hemodynamic stability
6.	Accelerates awakening
7.	Postoperative analgesia
8.	Good immune response
9.	Quick onset of action

Table 1.
Benefits of spinal anesthesia.

also stimulate T lymphocyte activity, cell mediation, and antitumor immunity. Therefore, SA favors the immune response, allowing better possibilities of maintaining an adequate immune response to possible perioperative infections (**Table 1**) [12].

4. Anatomy

It is important to remember that the level of termination of the spinal cord depends on the age of the child. In the newborn, the spinal cord ends at L3, lower than in the adult. Therefore, it is prudent to do the lumbar puncture in the disc space between L4-L5 or L5-S1, below the termination of the spinal cord. Using the L4–5 or L5-S1 disc space is safe at this age. The intercrestal line or Tuffier's line can be used to determine the level of puncture since this line passes through these spaces.

During the first year of life, the dural sac regresses at the level of the adult and we find it at S1 and the spinal cord at the level of L1, which is the adult level. At this level, the depth to reach the subarachnoid space is 1 to 1.5 cm from the skin and 10 to 12 mm at one year of age. The volume of spinal fluid is 4 mL/kg, that is, twice that in adults [13]. The flexibility of the spinal column in children and the ease of touching and locating the intervertebral spaces facilitate spinal puncture [13].

Insufficient myelination and a weak layer of the endoneurium in the nerve tracts produce a weak and ineffective barrier for the diffusion of LA, which translates into a rapid onset of action. There are two other important factors to consider; a high cardiac output and a relatively wide vascularization, which help to maintain a short duration of action of SA [14].

5. Spinal anesthesia technique

The most common way to perform SA is to have the child seated with the back flexed. The assistant is responsible for firmly maintaining the sitting position and with the neck extended because flexion of the neck in very young children can cause moderate hypoxia. The child can also be placed in the slightly flexed lateral position. Avoid extreme flexion of the neck as it can also cause airway obstruction and cause hypoxia. A second assistant may be administering oxygen with a face mask. A 45-degree head tilt can help maintain increased CSF pressure, especially in children under one year of age. The depth of insertion of the needle is variable and was described in the anatomy section.

Ultrasound can help decide the puncture site, needle path, and needle depth. Today there are a variety and types of needles for spinal application; however, the most common is the pencil-point needle. The stylet of the needles is necessary to avoid the remote possibility of an epidermoid tumor. Needles 26 and 27 with a pencil point, for pediatric use with a length of no more than 50 mm, produce a low incidence of post-puncture headache [15]. The reflux of the CSF through the needle indicates that the placement of the needle is correct, and the LA should be injected within 20 seconds. Once the needle is withdrawn, the lower extremities should not be elevated because it can result in a high spinal block [14].

6. Clinical monitoring of spinal block

The clinical evaluation of the spinal block is practical during the entire surgical procedure, but especially during the first 10 to 20 minutes of its application, to detect possible complications associated with the technique or the LA used. Most of the immediate complications are due to errors in the dose of LA, generally higher than required. The unwanted effects of LA can be masked by the simultaneous combination of GA. In which case it will be more difficult to notice possible reactions to LA. If the child remains conscious, the side effects of SA can be detected quickly.

Verification of sensory block usually consists of loss of skin sensitivity to cold, gentle pinching or touch. The motor block is also installed progressively and immediately, depending on the type of LA applied. Bupivacaine produces a total motor block. While ropivacaine and levobupivacaine produce a motor block of less intensity. The level of motor block can be verified by gentle puncture of the extremities, hips, and upper abdomen or thorax, being better evaluated using the modified Bromage scale. In sedated children, electrical stimulation is better and a more reproducible method, however, it is not always possible to do [16].

7. Local anesthetics

The most commonly used LA are 0.5% bupivacaine and tetracaine, at doses of 0.3–0.6 mg/kg. Although ropivacaine and levobupivacaine are also safe and effective agents. Ropivacaine 0.5% at doses of 0.5–1 mg/kg, produce a good quality block. With ropivacaine, the motor block is significantly shorter and less intense than with bupivacaine. Levobupivacaine 0.5% at a dose of 0.3–1 mg/kg, is also used clinically with a less intense motor block, similar to ropivacaine.

Bupivacaine, ropivacaine, and levobupivacaine are drugs that are broken down by enzymes in the liver. Therefore, they should be used carefully in PNB because they have a lower capacity to metabolize both anesthetics due to their immaturity [17]. Term NB metabolize LA well, but not preterm infants or patients with other comorbidities.

The duration of action of all spinal LA is one of the great limitations of using this route, since its duration is relatively short, it does not exceed 80 minutes in most of them. Postoperative analgesia is very short. For this reason, many clinicians have used so-called LA adjuvants such as adrenaline, morphine, or fentanyl, to prolong its duration. Most of them manage to extend the duration of action for a time no longer than 30%. However, their safety is questionable due to the possible toxicity of the adjuvants to the development of the spinal cord, which can be vulnerable. Intrathecal medications can allow the development of toxicity by altering the neuronal activity of the spinal cord [18–20].

8. Complications of spinal block

The complications of SA in children are similar to those in adults. However, the evaluation of signs and symptoms is difficult to identify, especially in NB or younger than one year compared to older children. Physiological and behavioral changes rather than verbal ones manifest their conditions.

The main complications of SA may result from the technique used or from the action of the LA itself. In general, the incidence of side effects is low and permanent secondary sequelae have not been reported in most clinical studies. They are shown in **Table 2** [14].

Complications include headache and low back pain, neurological complications, nausea, vomiting, and cardiorespiratory changes. Elevated levels of spinal block, above T4, reduce the expansion movement of the lower rib cage, decreasing intercostal muscle activity and paradoxical respiratory movements may occur.

Kokki 2000	Post-puncture headache
Puncuh 2004	Blockade failure, arterial hypotension, desaturation, airway obstruction, post-puncture headache.
Kokki 2005	Block failure, bradycardia, hypotension, desaturation, post-puncture headache
Imbelloni 2006	Blockade failure, bradycardia, hypotension, bronchospasm, and post-puncture headache
Williams 2006	Blockade failure, bradycardia, desaturation
Kachko 2007	Bradycardia, block failure, high block, apnea.
Ecoffey 2010	High spinal block

Table 2.
Complications of spinal block in children [14].

Monitoring of oxygen saturation and an oxygen source are necessary. Post-puncture headache is the most frequent complication, it has an incidence of 3 to 4%, even with the use of spinal needles 25–27, and the incidence increases with spinal needles number 22. The headache appears in the first 24 hours post-puncture and may be unilateral or bilateral. It worsens with changes in position from lying to sitting and some children may manifest nausea and vomiting, which may be accompanied by blurred vision, vertigo, and tinnitus. These symptoms usually disappear spontaneously in three to five days, and in some children, they can continue for several more days. Caffeine is the pain reliever of choice in children [21].

9. Spinal anesthesia and short-stay surgery

Another reason to prefer SA in the child is the low cost compared to GA, in addition to the rapid recovery from short-stay surgery and early return home. These advantages include a rapid recovery derived from the short duration of SA with rapid recovery of mobility of the lower extremities, and prompt restoration of the oral route, with a low incidence of postoperative nausea and vomiting [22].

10. Sedation

Sedation is often used in the child, for the application of the spinal puncture. The goal of sedation is to produce anxiolysis and to ensure that the child remains motionless during the lumbar puncture. Movement during puncture can cause significant trauma to neurovascular structures. Midazolam, ketamine, propofol, dexmedetomidine, or inhaled sevoflurane can be used. However, any of them can be associated with periods of apnea. The safest are inhaled agents like sevoflurane. Dexmedetomidine produces a natural sleep state and produces anxiolysis and analgesia. Sedatives should be avoided in preterm, weak or high-risk newborns [15].

11. Discussion

SA has been used for a variety of surgical procedures, including inguinal hernia, exploratory laparotomy, omphalocele, and gastroschisis repair, multiple orthopedic procedures mainly of the lower extremities, pylorotomy, and surgery of the anus, bladder, and penis. Epidemiological data show that newborns have a higher risk of complications associated with GA. In multiple studies, the technique that has shown efficacy and safety and that has avoided the use of general anesthesia in the group of preterm, ex-preterm, or high-risk patients has been SA. Most clinicians prefer SA because it is associated with great respiratory and cardiovascular stability, allowing greater survival for newborns. In large study populations on the usefulness of SA, it has been shown that oxygen desaturation of <90% is rarely observed, and < 5% of newborns require supplemental oxygen, although neonates are notoriously susceptible to present hypoxia in response to external stimuli such as surgical stress.

The incidence of apnea in the NB in the first 12 hours postoperatively associated with GA, ranges between 10% and 30%. This seems to be directly related to prematurity and general anesthetics, 70% of apnea is of central origin, 10% obstructive and 20% combined. To the multiple advantages of SA in children, we can add postoperative analgesia with a short hospital stay, a lower cost for the hospital, and a lower incidence of mechanical ventilation after surgery [14, 15, 17, 23].

12. Conclusion

SA in experienced hands has allowed the survival of the preterm or high-risk newborn in a surprising way. The anesthetic technique of choice in children with concomitant diseases is SA, due to the many advantages. Allows for a quick recovery with minimal side effects. LA such as ropivacaine produce fewer motor changes after spinal block. Pencil point needles and ultrasound have greatly improved the side effects of EC.

Conflict of interest

The authors declare that they have no conflicts of interest.

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Chapter 7

Regional Analgesia for Knee Surgeries: Thinking beyond Borders

Kartik Sonawane and Hrudini Dixit

Abstract

Knee surgeries are the most commonly performed joint surgeries in the modern world, which help maintain the quality of life by improving joint functions. These include open trauma, sports injury, or joint replacement surgeries. Among various available regional analgesia options for knee surgeries, the goal is to choose motor-sparing, opioid-sparing, and procedure-specific modalities. Therefore, it is essential to know the complex anatomy of the knee joint, essential steps of various surgical procedures, and innervations of the pain-generating structures for a particular surgery. Background knowledge of all these essentials helps select the most appropriate regional analgesia technique for knee surgeries.

Keywords: Knee joint analgesia, Total knee replacement, Total knee arthroplasty, Procedure-specific anesthesia, Motor sparing analgesia, Opioid sparing analgesia, Subsartorial blocks

1. Introduction

The knee is the biggest and the most complicated joint of the human body. Being a most stressed joint subject to enormous pressure while providing flexible movement, it is vulnerable to injury. During walking and jumping, it is loaded with 7-fold body weight. The attached muscles and ligaments provide stability and flexibility to the knee joint. The most important structure of the knee joint is its cartilage surface which might get damaged due to trauma, overload, and genetic disorders. As a result, the patient experiences pain, inflammation, and a limitation of the range of motion, finally leading to an impaired gait.

Knee surgeries are one of the most commonly performed, life-changing surgical procedures of the modern world, leading to improved health-related quality of life and functional status [1, 2]. Knee surgeries vary from minimally-invasive arthroscopic procedures (in relatively younger populations) to open arthroplasty procedures (in the elderly populations).

Before deciding the analgesia techniques for the postoperative period, knowledge of functional anatomy, surgical steps, pain generation, pain generators, and innervation of the pain generators is essential. A multidisciplinary approach with multimodal analgesia is the demand of time for successful surgical outcomes. Regional analgesia (RA) is an important component of multimodal analgesia to deal with perioperative pain. Among many available RA options, challenges include

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selecting more procedure-specific, motor-sparing, and opioid-sparing options suitable for enhanced recovery after surgeries (ERAS) protocols. A properly planned procedure-specific RA technique provides optimal analgesia without any motor effects, which helps in early mobilization and discharge, reducing opioid consumption and their side effects significantly.

2. Functional anatomy of the knee joint

The knee joint is the largest synovial-type and most-stressed joint in the body. This modified hinge joint is composed of two articulations; the **tibiofemoral** and patellofemoral. The structural and functional stability of the knee joint comes from the muscles and ligaments attached, which also helps to bear considerable biomechanical stress brought upon the joint. Furthermore, the patella acts as an anatomical pulley for the quadricep muscles [3], which enhances knee joint extension by allowing frictionless movements, stabilizes and protects the knee joint. In addition, the joint cartilage and the menisci provide intraarticular flexibility, cushioning, and shock absorption.

2.1 Ligaments of the knee joint

Ligaments provide stability and strength to the knee joint along with bones and cartilage. These include joint capsule, **extracapsular,** and **intracapsular ligaments**.

2.1.1 Joint capsule

It is a thick, fibrous structure mainly formed by muscle tendons and their expansions that wrap around the knee joint. It forms a thick ligamentous sheath around the knee joint. The synovial membrane lying inside the outer fibrous layer lubricates the articular surfaces, reduces friction, and nourishes the joint cartilage. It also has several fluid-filled pouches called bursae that also reduce friction within the knee joint. The folds of the synovium within the joint are called plicae [4].

The synovial fluid in the soaked cartilage (like water in a sponge) squeezes out when the knee bends or bears weight. The osteoarthritic changes in the joint lead to a decrease in synovial fluid that exacerbate joint friction. The anterior capsule has an opening for the attachment to the patella. Similarly, the posterior capsule has an opening for the passage of the popliteus tendon.

2.1.2 Extracapsular ligaments

Extracapsular ligaments include the patellar, popliteal (oblique and arcuate), and collateral (medial and lateral) ligaments.

- **Patellar ligament (Ligamentum patellae)** is a strong, thick fibrous band and a distal continuation of the quadriceps femoris tendon extending from the apex of the patella to the tibial tuberosity. It blends with the medial and lateral patellar retinacula along with the overlying fascia. It stabilizes the patella and prevents its displacement.

- **Popliteal ligaments prevent hyperextension** of the knee joint.

    a. Oblique popliteal ligament (Bourgery ligament) connects the medial tibial condyle with the lateral femoral condyle. It is an expanded portion of the semimembranosus tendon that spans the intercondylar fossa. It reinforces the posterior capsule by blending with it in the central portion.

b. Arcuate popliteal ligament is a thick, fibrous band arising on the posterior aspect of the fibular head. It arches superiorly and medially to attach to the posterior side of the joint capsule of the knee. Thus, it reinforces the posterolateral part of the joint capsule.

- **Collateral ligaments** are two strap-like ligaments providing side-to-side stability of the knee joint and preventing excessive medial or lateral movement.

  a. Medial (tibial) collateral ligament (MCL) is a broad and flat ligament that lies on the medial side of the knee joint. It attaches proximally to the medial femoral epicondyle and distally to the medial tibial condyle. It prevents excessive sideways movement by restricting external and internal rotation of the extended knee.

  b. Lateral (fibular) collateral ligament (LCL) is thin and rounder than MCL that attaches proximally to the lateral femoral epicondyle and distally to the lateral fibular head splitting the biceps femoris tendon. It lies deep to the lateral patellar retinaculum and superficial to the popliteal tendon.

2.1.3 Intracapsular ligaments

Intracapsular ligaments include cruciate (anterior and posterior) ligaments. The paired cruciate ligaments crisscross each other obliquely like a letter “X” within the knee joint. They prevent the femur and tibia from sliding too far forward or backward.

- Anterior cruciate ligament (ACL) arises from the anterior intercondylar area of the tibia and attaches to the posterior part of the lateral femoral condyle (medial surface). It prevents anterior dislocation of the tibia onto the femur by limiting the forward motion of the tibia. It also prevents hyperextension of the knee joint and limits rotation and sideways movement of the knee joint. A newly discovered anterolateral ligament (ALL) works in conjunction with ACL. However, the ACL can get torn by sudden pivoting motions of the knee.

- Posterior cruciate ligament (PCL) arises from the posterior intercondylar area of the tibia and attaches to the anterior part of the medial femoral condyle (lateral surface). It is stronger and more vascular than ACL. It prevents posterior dislocation of the tibia onto the femur by limiting the backward motion of the tibia. It also prevents hyperflexion of the knee joint and limits rotation and sideways movement of the knee joint. However, the PCL can get torn with a forceful landing on the shin.

2.2 Menisci

These are thick pads of fibrocartilaginous crescent-shaped plates found between the articular surfaces of the femur and tibia. By deepening the articular surface, they increase joint stability; and by increasing surface area to dissipate forces further, they act as a shock absorber during weight-bearing and joint movements.

They are highly vascular and thicker in the outer one-third than the inner two-third [5]. The outer one-third contains larger circumferentially arranged bundles whereas, the inner two-thirds contain radially organized collagen bundles. This makes the outer portion of the menisci suitable for resisting tensional forces and the inner portion for adaptation for weight-bearing. The anterior horn of both the menisci attaches to the anterior tibial intercondylar area and blends with ACL. The posterior horn of both the menisci attaches to the posterior tibial intercondylar area. The lateral meniscus is more mobile and smaller than the medial meniscus. The menisci are held in place by other ligaments like transverse ligament, meniscofemoral ligaments, meniscotibial (coronary) ligaments, and patellomeniscal ligament (medial and lateral). All these ligaments indirectly prevent displacement of the knee joint. Surgical removal of the meniscus can lead to osteoarthritic changes in the underlying cartilage.

2.3 Bursae

A bursa is a tiny, slippery, fluid-filled sac located between a bone and soft tissue to reduce friction between them. Arthritis of the knee joint leads to alteration into the joint biomechanics leading to irritation of the bursa. This irritation leads to inflammation called bursitis. Among various types of bursae around the knee, the notable bursae include [6],

- Suprapatellar bursa lies between the quadriceps femoris and the femur
- Prepatellar bursa lies between the apex of the patella and the skin
- Infrapatellar bursa splits into superficial (between the patellar ligament and the skin) and deep (between the tibia and the patellar ligament)
- Semimembranosus bursa lies between the semimembranosus muscle and the medial head of the gastrocnemius

2.4 Muscles around the knee

The muscle groups attached to the knee joint provide strong support and keep the joint stable, well-aligned, and moving. These groups include,

- Quadriceps over the anterior aspect of the thigh
- Hamstrings over the posterior aspect of the thigh
- Adductors over the medial aspect of the thigh
- Lower leg muscles, including the gastrocnemius at the back of the calf

The four movements (**Table 1**) that occur at the knee joint are flexion, extension, lateral and medial rotation. With the flexed knee joint, the lateral and medial rotations occur at the hip joint and vise versa. The hamstrings are responsible for both the hip extension and knee flexion. The knee flexion ranges from 120 degrees to 140 degrees (with the extended hip), increasing 160 degrees with the passive flexion [7, 8].

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Movements	Primary muscles	Secondary muscles
Flexion	Adductors (biceps femoris, semitendinosus, and semimembranosus)	Initiated by popliteus Assisted by gracilis and sartorius
Extension	Quadriceps (rectus femoris, vastus medialis, vastus lateralis, and vastus intermedialis)	Tensor fascia latae
Medial rotation	Popliteus Semimembranosus Semitendinosus	Sartorius Gracilis
Lateral rotation	Biceps femoris	

Table 1.
Muscles responsible for various movements in the knee joint.

2.5 Neurovascular supply

The knee joint has a rich vascularization from the genicular anastomosis around the knee (**Figure 1**) formed by genicular branches from femoral and popliteal arteries [9]. There are approximately ten arteries involved in the formation of genicular anastomosis:

- Descending branches from the femoral artery: Lateral circumflex femoral artery and descending genicular branch.
- Ascending branches from the tibial artery: The posterior tibial artery (circumflex fibular branch) and the anterior tibial artery (anterior and posterior tibial recurrent branches).
- Branches of the popliteal artery: Lateral genicular arteries (superior and inferior), the medial genicular arteries (superior and inferior), and the middle genicular arteries.

The nerve supply of the knee joint follows Hilton's law, as innervations of the muscles which cross joints also innervate the knee joint. The knee joint receives all its

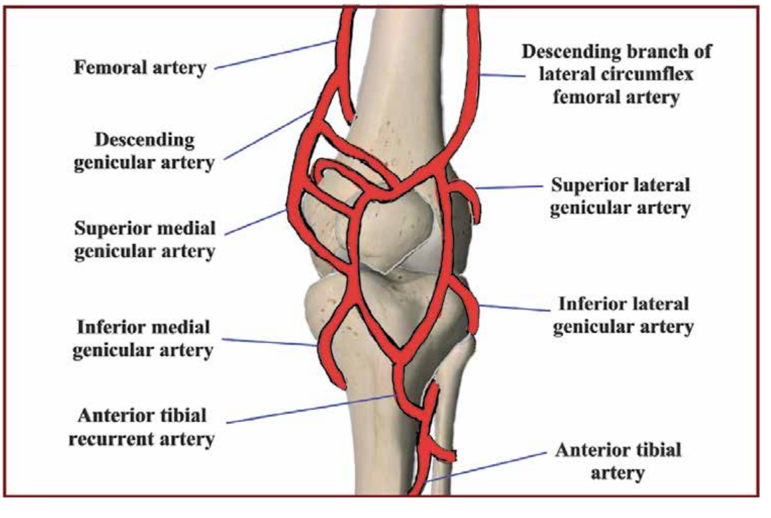

Figure 1.
Genicular anastomosis around the knee joint.

innervation from the branches of the lumbar and sacral plexus. The knee joint innervations need detailed considerations before planning procedure-specific RA techniques.

3. Innervation of the knee joint

A dermatome is an area of skin supplied by the dorsal (sensory) root of the spinal nerve. A myotome is the segmental innervations of skeletal muscle by the ventral (motor) root. An osteotome is the innervation of bone that does not follow a segmental pattern. Various branches (from the lumbar and sacral plexus) innervating the knee joint include the femoral nerve (anterior knee), obturator nerve (posteromedial knee), and sciatic nerve (posterior knee). These nerves have cutaneous branches

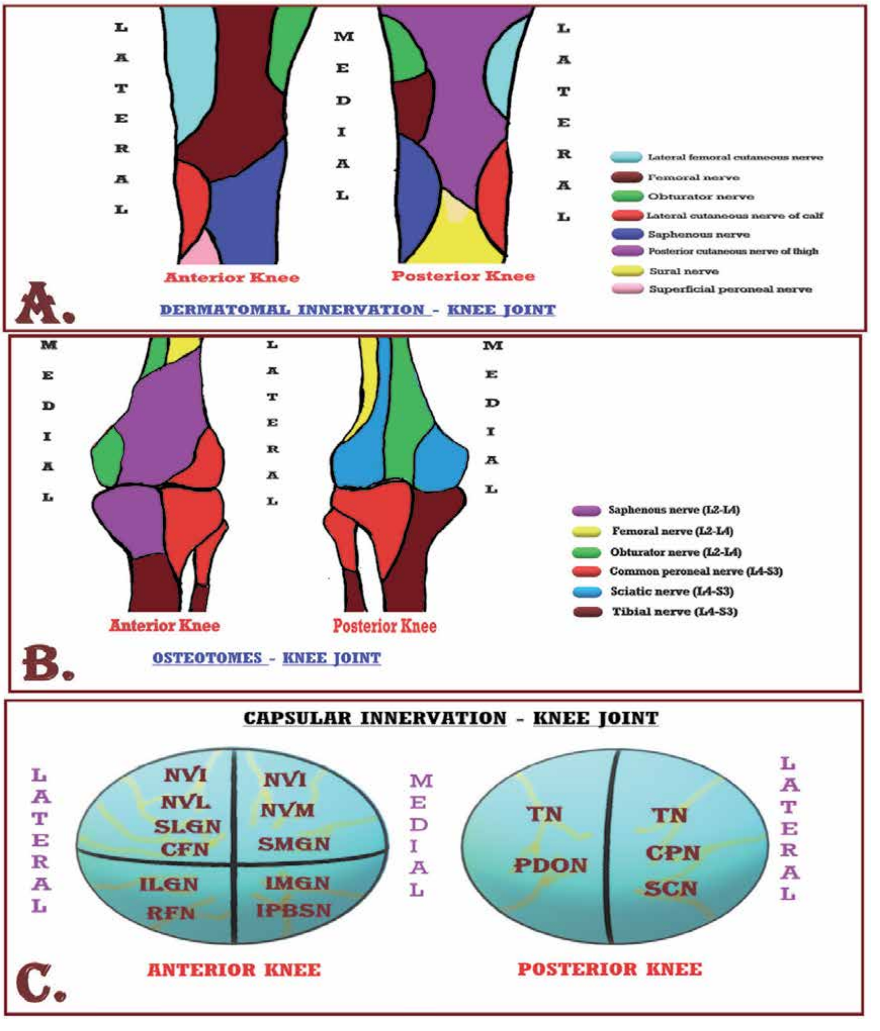

Figure 2.
Dermatomal, osteotomal, and capsular innervation of the knee joint.
***A**: Dermatomal innervations, **B**: Osteotomal innervations, **C**: Capsular innervation.*
*(**NVI**: Nerve to vastus intermedialis, **NVM**: Nerve to vastus medialis, **NVL**: Nerve to vastus lateralis, **SMGN**: Superomedial genicular nerve, **SLGN**: Superolateral genicular nerve, **IMGN**: Inferomedial genicular nerve, **ILGN**: Inferolateral genicular nerve, **IPBSN**: Infrapatellar branch of saphenous nerve, **RFN**: Recurrent fibular nerve, **TN**: Tibial nerve, **CPN**: Common peroneal nerve, **SCN**: Sciatic nerve, **PDOB**: Posterior division of obturator nerve).*

Muscles attached to knee		Innervations
	Anterior knee	
1.	Sartorius	Femoral Nerve (L2-L3)
2.	Quadriceps Femoris Rectus Femoris Vastus Medialis Vastus Intermedialis Vastus Lateralis	Femoral Nerve (L2-L4)
	Medial knee	
3.	Semitendinosus	Tibial Nerve (L5-S2)
4.	Semimembranosus	Tibial Nerve (L5-S2)
5.	Gracilis	Obturator Nerve (L2-L4)
6.	Adductor Magnus	Obturator Nerve (L2-L4) Sciatic Nerve (L4)
	Lateral knee	
7.	Tensor Fasciae Latae	Superior Gluteal Nerve (L4-L5)
	Posterior knee	
8.	Biceps Femoris	Sciatic Nerve (L5-S1)
9.	Gastrocnemius	Tibial Nerve (S1-S2)
10.	Popliteus	Tibial Nerve (L4-S1)

Table 2.
Myotomal innervation of the knee joint.

supplying skin (**Figure 2A**), muscular branches supplying muscles (**Table 2**), and articular or genicular branches supplying knee joint or joint capsule (**Figure 2B** and **C**). Before supplying the knee joint, these nerves contribute to the formation of 3 different plexuses (**Table 3**); Subsartorial plexus, Peripatellar plexus, and Popliteal plexus [10–13].

The anterior capsule [14, 15] of the knee joint is innervated,

- Superomedially by the nerve to vastus medialis (NVM), nerve to vastus intermedialis (NVI), superior medial genicular nerve (SMGN)
- Superolaterally by the nerve to vastus lateralis (NVL), NVI, superior lateral genicular nerve (SLGN), common fibular nerve (CFN)
- Inferomedially by Infrapatellar branch of the saphenous nerve (IPBSN), inferior medial genicular nerve (IMGN)
- Inferolaterally by inferior lateral genicular nerve (ILGN), recurrent fibular nerve (RFN)

The posterior capsule [16] of the knee joint is innervated,

- Medially by tibial nerve (TN) and posterior division of obturator nerve (PDON)
- Laterally by tibial nerve, common peroneal nerve, and sciatic Nerve (SCN)

Plexus	Location	Contributing nerves	Innervations
Subsartorial plexus	Medial knee under the sartorius	• Infrapatellar branch of saphenous nerve • Anterior division of obturator nerve • Medial femoral cutaneous nerve • Nerve to vastus medialis	• Skin over the medial aspect of the knee • Medial retinaculum • Medial collateral ligaments • Anterior capsule of the knee joint
Peripatellar plexus	Around the patella	• Medial femoral cutaneous nerve • Intermediate femoral cutaneous nerve • Lateral femoral cutaneous nerve • Infrapatellar branch of the saphenous nerve • Nerve to vastus medialis (NVM) • Medial retinacular nerve (terminal branch of NVM) • Lateral retinacular nerve (terminal branch of the sciatic nerve)	• Skin over the anterior, superior, inferior, medial, and lateral to the patella • Retinacula • Collateral ligaments • Anterior capsule of the knee joint
Popliteal plexus	Posterior aspect of the knee joint	• Articular branches from the tibial nerve, common peroneal nerve, and sciatic nerve • Posterior division of the obturator nerve	• Posterior capsule of the knee joint • All intraarticular structures • Retinacula • Collateral ligaments

Table 3.
Various plexuses innervating the knee joint.

4. Knee joint injuries

The injuries to the knee joint are not uncommon due to associated biomechanical stress during routine activities. Any unnatural joint movement (twisting, pivoting, sudden change of direction, or a forceful blow) leads to injury to the structures stabilizing the knee joint. Common conditions include:

- **Jumper's knee is** an inflammation of the patellar ligament due to overuse stress on it like sudden impact on the joint during landing after a jump in the sports activity. It is also common in overweight individuals due to significant stress on the joint.

- **Anterior cruciate ligament (ACL) injury** is caused by the hyperextension of the knee joint or by the application of large force over the posterior knee. This injury is common among athletes such as football, occurring due to a sudden change of direction or improper landing after a jump. The ACL injury causes pain, swelling, and instability of the knee joint.

- **Posterior cruciate ligament (PCL) injury** is caused by the hyperextension of the knee joint commonly seen in car dashboard injury that causes posterior displacement of the tibia due to significant force over the flexed knee and shin.

- **Collateral ligament tears** occur most commonly in contact sports due to a blow on the side of the knee. The MCL can be injured by a direct blow to the lateral knee, whereas the LCL can be injured by a direct blow to the medial knee.

- **Terrible/unhappy triad** consists of injury to the cruciate ligament, MCL ligament, and the medial meniscus commonly caused by a lateral blow to the extended knee associated with sports like rugby or football.
- **Housemaid's knee** is inflammation of the prepatellar bursa, causing swelling on the anterior knee caused due to friction between skin and the patella.
- **Clergyman's knee** is inflammation of the infrapatellar bursa caused due to friction between skin and the tibia during kneeling on hard surfaces.

5. Symptoms of the knee joint injury

Knee joint symptoms are variable depending on the injury pattern or disease extent.

- **Pain** over the knee joint can be dull, sharp, constant, or on-and-off type.
- **Unstable knee/Increased range of motion** is due to ligamentous injuries.
- **Decreased range of motion** is due to arthritis changes in the knee joint.
- Immediate **swelling** is usually due to hemarthrosis (bleeding into the joint). Delayed **swelling** or on-and-off swelling is due to the irritation and inflammation of the structures inside the joint, causing excess production of synovial fluid.
- **Locking (or catching)** occurs due to a loose body or a torn meniscus in the knee joint.
- **Giving Way** is due to injuries to ligaments, a loose body, or a torn meniscus.
- **Snaps, crackles, and pops** occur due to osteoarthritis and chondromalacia patella, where the cartilage under the patella starts to wear down.

6. Pain generation and pain generators

Diseases or injuries that affect the knee joint cause biochemical reactions leading to the stimulation of pain receptors present on various structures that contribute to developing significant pain. Nociception is the normal body response to subthreshold noxious stimuli. In comparison, the pain generation process results from the interplay between noxious stimuli, nociceptors, and the central nervous system (CNS). It involves four major processes: transduction, transmission, modulation, and perception [17].

a. **Transduction** is the conversion of suprathreshold noxious stimuli into an electrical signal (action potentials) by the nociceptors - first-order neurons.

b. **Transmission** is the conduction of action potential through nociceptive specific neurons (lamina I, II) and wide dynamic range neurons (lamina III-VI) – second-order neurons.

c. **Modulation** is an augmentation or attenuation of afferent transmission by spinal and supraspinal centers.

d. **Perception** is the subjective awareness produced by integrating inputs in the somatosensory cortex and limbic system – third-order neurons. It is a complex function of several processes, including attenuation, expectation, and interpretation.

6.1 Knee joint nociceptors

Knee joint nociceptors are of two types, slow conducting C-fibers and fast conducting A-delta fibers. They are scattered in the skin, subcutaneous tissue, muscles, joint capsule, intraarticular structures, periosteum of the bone, infrapatellar fat pad, and extra-articular retinacular ligament. The joint cartilages with adjacent cortical and trabecular bone contain no nociceptors.

These nociceptors get activated by mechanical (pressure, pinch), heat, and chemical stimuli. The mechanical and heat stimuli are shorter (fast pain) than the chemical stimuli (slow pain). Chemicals activating or sensitizing primary afferent nociceptors include potassium, histamine, serotonin, bradykinin, prostaglandins, leukotrienes, and substance P [18, 19]. These chemicals are released from damaged tissues and circulating blood cells (migrated to the damaged area). For this reason, the concentration of these chemicals increases in regions of inflammation as well as pain.

6.2 Causes of knee joint pain

The knee joint pain arises due to joint-related and non-joint-related causes [20]. Joint-related causes include infections/inflammation (osteoarthritis), instability (ligament injury or malalignment/loosening of the implant), fractures, femoropatellar problems, and damage to the structures responsible for knee joint stability. Non-joint causes include soft tissue irritation (impingement due to oversize implants and muscle/tendon overuse during aggressive physiotherapy), neurological disease (neuropathies and spine disorders), hip disease (osteoarthritis and hip necrosis), vascular disease (aneurysm and thrombosis), and reflex sympathetic dystrophy.

6.3 Perioperative knee pain

The injury or pathology in the knee joint mainly initiates the pain generation process. Before surgery, the pain usually arises from the damaged or diseased tissues that stimulate free nerve endings and nociceptors. Postsurgical pain is mainly due to surgical insult leading to tissue damage, nerve irritation, microfractures, tendinitis, and inflammation. Postoperative knee pain is of 2 types:

a. **Musculoskeletal pain:** It arises due to damage to the soft tissues and muscles. The nature of this pain is usually aching, dull, and throbbing type. Postoperative tourniquet pain is also a musculoskeletal type of pain that arises after regression of spinal level. This pain arises due to the irritation of nociceptors by various inflammatory mediators released due to muscle ischemia.

b. **Neuropathic pain:** The mechanisms for neuropathic pain are more complex than nociceptive pain. The nature of this pain is usually sharp, electric shooting, and stabbing type. It results from the injury to the nerves involved in

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the pain pathway, leading to an alteration in the pain processing.
The hypersensitivity and hyperexcitability of the neurons result in dysesthesia, allodynia, and hyperalgesia. In addition, psychological factors like stress, fear, and anxiety can influence the experience and extent of pain, known as modulatory influences prolonging the pain episodes in susceptible individuals.

7. The pain management strategies

Pain is "a*n unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage [21].*"

The components of pain assessment include history and physical assessment, functional assessment, psychosocial assessment, and multidimensional assessment. All kinds of pain are associated with stress, which is an essential factor in pain management. Thus, the psychological component of pain is crucial in determining the patient's treatment protocols and promoting active involvement in self pain control. In addition, the pain perceptions may vary among individuals depending upon types of injuries/pathology, duration of pain, and associated psychosocial backgrounds. Therefore, the ABCDE of pain management (**Figure 3**) is essential to deal with any pain [22].

The pain management strategies have been evolving and ever-changing. With the introduction of a new effective protocol every decade, the approach to handle pain has become more comprehensive and target-specific. This evolution in the management strategies resulted in more effective and focused results with reduced complications.

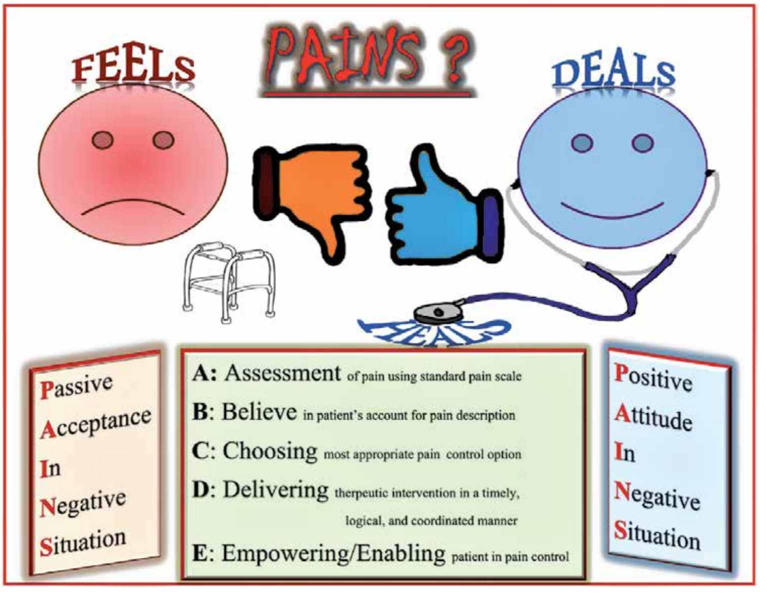

Figure 3.
Perceptions of pain and ABCDE of pain management.

7.1 Evolution of pain management

- **1980**: Pain was underrated and usually treated with intravenous/intramuscular narcotics. Due to fear of the side effects of narcotics (opioid phobia), the pain remained undertreated (oligoanalgesia) in this decade.

- **1990**: The American Pain Society declared pain as the 5th Vital Sign in this decade [23, 24]. Significant efforts by pharmaceutical companies were made in developing new products and aggressive marketing of opioids. In the same decade, Patient Controlled Analgesia (PCA) was also introduced as a mode of delivery of narcotics.

- **2000–2010:** This decade was known as 'The Decade of Pain Control and Research [25].' The concepts of Pre-emptive analgesia and Multimodal Analgesia were introduced to shift focus on reducing narcotic consumption.

- **2010:** Multimodal analgesia became an essential cornerstone of the strategy in this decade. The use of regional techniques (PNB/LIA) was introduced as an essential component of MMA.

- **2020:** Now, the pendulum has begun to swing back from the era of less opioid use, then aggressive use, and now no opioid use. The concept of "Opioid Free Anaesthesia/Analgesia" was introduced. On the same ground, a non-profit organization like the Society of Opioid Free Analgesia (SOFA) was formed to research, promote & educate anesthesia professionals and the general public on opioid-free pain management techniques in Hudson, US.

- **2030 onwards:** Researchers will likely focus more on detailing the innervations and achieving more target-specific blocks. In this decade, new techniques will probably be introduced to replace existing conventional blocks (**Figure 4**).

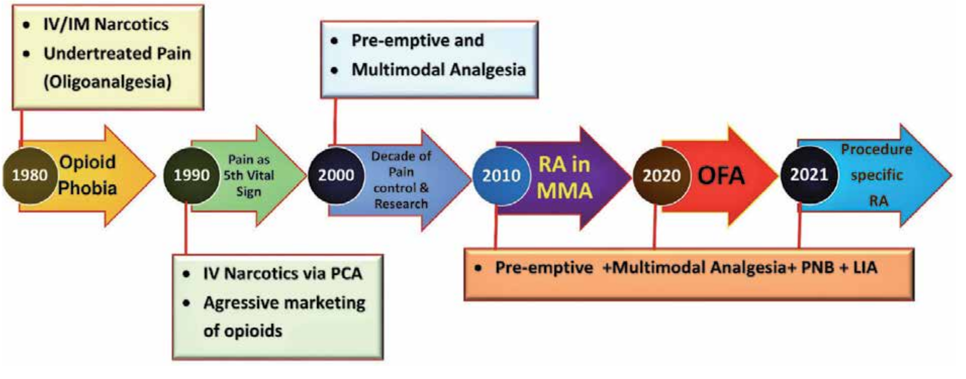

Figure 4.
Evolution of pain.
*(**IV/IM**: Intravenous/intramuscular, **PCA**: Patient-controlled analgesia, **RA**: Regional analgesia/anesthesia, **MMA**: Multimodal analgesia, **OFA**: Opioid-free anesthesia, **PNB**: Peripheral nerve block, **LIA**: Local infiltration analgesia).*

8. Analgesia protocols

The pain generation is a continuous process due to the nonadaptive property of the nociceptors. It depends on transforming the continuous noxious stimuli into the pain signals, transmitting the pain signals through pain pathways, and perceiving actual pain at the central level. Thus, pain treatment protocols should reduce noxious stimuli, interrupt pain pathways, and modify pain perception at the central level. Reduction in noxious stimuli generation is possible by addressing causative factors like inflammations and nerve injuries. Interruption of pain pathways is possible by blocking the transmission using the local anesthetic solution in RA techniques. Finally, modification of pain perception is possible using various analgesic drugs mainly acting on the CNS level. A combination of various pharmacological agents, nonpharmacological techniques, and RA techniques constitutes the concept of multimodal analgesia. The components of MMA act on various levels of pain pathways.

8.1 Multimodal analgesia

Multimodal analgesia (MMA) includes more than one pain-control modality (pharmacological and nonpharmacological)(**Figure 5**) to achieve optimal analgesia [26]. The additive or synergistic effects of these modalities act on various sites of the pain pathways to enhance pain control. It also helps to minimize any side effects that are associated with a single agent. Pharmacological agents include acetaminophen, nonsteroidal anti-inflammatories, steroids, narcotics, N-methyl-D-aspartate (NMDA) receptor antagonists (ketamine or dextromethorphan), and antiseizure medications (gabapentinoids, particularly gabapentin and pregabalin). Nonpharmacological adjuncts include immersive virtual reality, acupuncture, injections (trigger point injections and epidural steroid injections), other neuroexperimental modalities, cryotherapy, transcutaneous electrical nerve stimulation units, and various regional analgesia techniques.

The regional analgesia (RA) techniques play an essential role as an adjunct to MMA by interrupting pain transmission and sensitization (central and peripheral) processes. MMA also includes pre-emptive analgesia, which also plays an essential role in decreasing peripheral and central sensitization. Various studies recommend the MMA as the best approach for any postsurgical pain. Unaddressed postsurgical

Figure 5.
Multimodal analgesia components.

pain initiates several neuroendocrine stress responses - leading to secretion of various hormones [27] like ACTH, catecholamines, and ADH - resulting in an increase in blood pressure, heart rate, prolonged recovery, and infections.

9. Enhanced recovery after surgery (ERAS)

ERAS is one of the leading examples of pathway-based perioperative care (**Figure 6**). It provides a structured mechanism to improve the quality of care, reduce variation in surgical care, minimize complications, and improve outcomes of surgeries [28]. ERAS also controls perioperative physiology to optimize the patient by minimizing the stress response to surgery and anesthesia [29, 30]. The key elements of ERAS protocol include patient education, expectation setting, aggressive optimization of comorbidities, standardized anesthetic and surgical techniques, early mobilization, early oral nutrition, early discharge, and effective pain management using MMA. ERAS decreases postoperative complications and costs, shortens hospital stay, and enhances patient satisfaction [31]. Rapid recovery in knee surgeries is possible because of less invasive surgical procedures, more selective soft tissue balancing, improved patient education, meticulous instrumentation, selecting suitable implant design, and improved analgesia options.

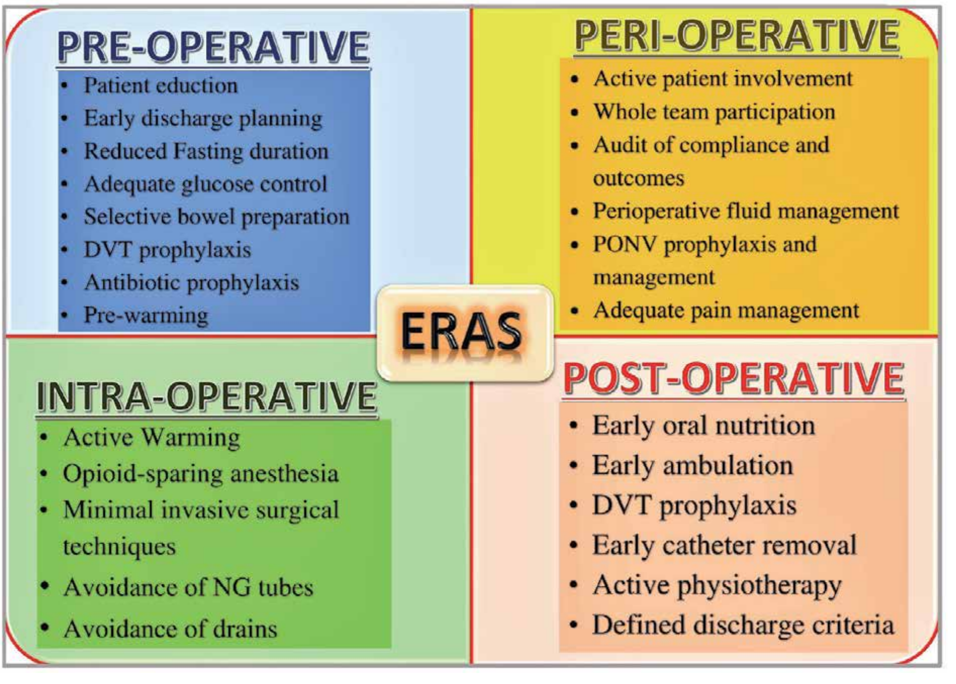

Figure 6.
Enhanced recovery after surgery protocol.
*(**DVT**: Deep venous thrombosis, **PONV**: Postoperative nausea and vomiting, **NG**: Nasogastric).*

10. RA options for knee surgeries

The regional anesthesia or analgesia techniques for knee surgeries have been evolving to improve procedural outcomes, reduce complications and improve patient satisfaction [32]. With the introduction of ultrasound into the RA practice, the perioperative analgesic strategies for knee surgeries have undergone a conceptual revolution in the last decade.

Apart from providing optimal analgesia and intraoperative clear surgical field, RA also helps in the reduction of major postoperative complications like deep venous thrombosis, pulmonary embolism, requirements of blood transfusion, pneumonia, and respiratory depression [33, 34]. RA options available for knee surgeries from center-to-periphery include (**Figure** 7).

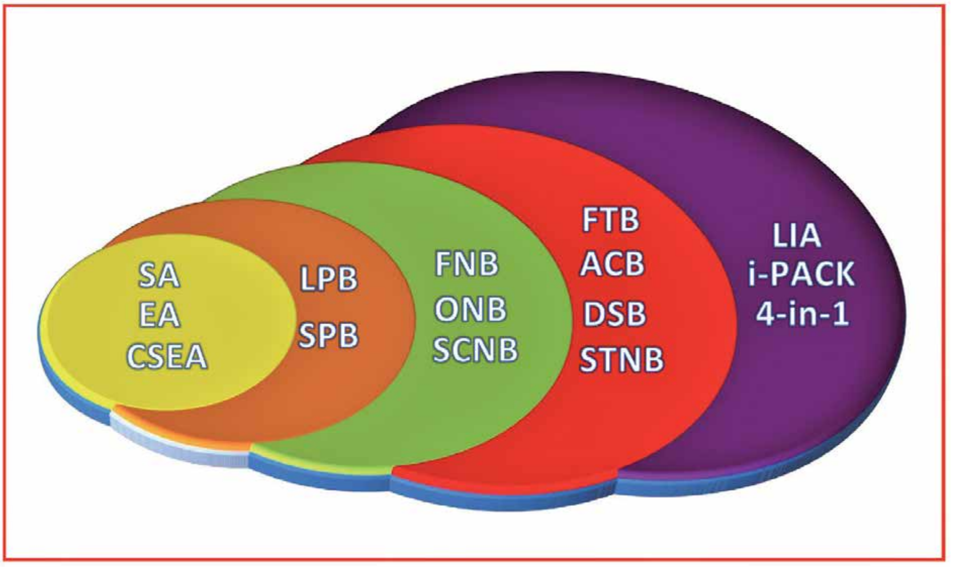

Figure 7.
Regional analgesia options from 'Centre-to-periphery' for knee surgery.
*(**SA**: Spinal analgesia, **EA**: Epidural analgesia, **CSEA**: Combined spinal-epidual analgesia, **LPB**: Lumbar plexus block, **SPB**: Sacral plexus block, **FNB**: Fenoral nerve block, **ONB**: Obturator nerve block, **SCNB**: Sciatic nerve block, **FTB**: Femoral triangle block, **ACB**: Adductor canal block, **DSB**: Dual subsartorial block, **STNB**: Selective tibial nerve block, **LIA**: Local infiltration analgesia, **i-PACK**: Infiltration between popliteal artery and capsule of knee joint).*

A. **Neuraxial blocks**:

- Subarachnoid block (SAB)
- Epidural analgesia (EA)
- Combined spinal + epidural analgesia (CSEA)

B. **Plexus block**:

- Lumbar plexus block (LPB)
- Sacral plexus block (SPB)

C. **Non-motor-sparing peripheral nerve blocks**:

- Femoral + sciatic + obturator nerves block
- Selective tibial nerve block (STNB)

D. **Motor-sparing blocks**:

   I. **Subsartorial blocks**:

      a. Femoral triangle block (FTB)

      b. Adductor canal block (ACB)

      c. Dual subsartorial block (DSB)

   II. **High volume blocks**:

      a. Hi-Volume Proximal Adductor Canal (Hi-PAC) block

      b. 4-in-1 block/modified 4-in-1 block.

      c. Ultrasound-guided Hamstring block

   III. **Infiltrations techniques**:

      a. Infiltration between Popliteal Artery and Capsule of Knee (IPACK) block

      b. Local Infiltration Analgesia (LIA)

      c. Ultrasound-guided LIA or Ring block

A. **Neuraxial blocks**: Neuraxial blocks were considered the gold standard option in providing postoperative analgesia in knee surgeries. However, due to unwanted side effects (like urinary retention, delayed mobility, blocking of other limbs, chances of epidural hematomas in patients on anticoagulants), they lost their popularity [35, 36].

B. **Lumbosacral plexus block**: The lumbar plexus mainly contributes to the anterior knee innervations, whereas the sacral plexus contributes to posterior knee innervations. Thus, both the plexuses need to be blocked to provide complete postoperative analgesia. However, the lumbosacral plexus block remains unsuitable for patients on anticoagulants due to its deeper location and rich vascularity around it. It also results in muscle weakness, causing delayed recovery, mobility, and discharge - Exclusion from the ERAS protocol.

C. **Non-motor-sparing blocks**:

- **Femoral nerve block**: Femoral nerve contributes to the anterior knee innervations. Its blockade provides excellent pain relief, especially over the anterior and medial compartments of the knee. However, due to associated quadriceps muscle weakness, it is not recommended in ERAS protocol.

- **Obturator/Sciatic nerve block**: Due to associated muscle weakness of adductors and hamstrings with obturator and sciatic nerve block, respectively, they are not recommended in ERAS protocol. The sciatic nerve blockade also causes foot drop, which may mask the surgically injured common peroneal nerve in severe valgus deformity.

- **Selective tibial nerve block***: The tibial nerve can be selectively blocked in the popliteal region to avoid unwanted foot drop due to the common peroneal nerve (CPN) blockade. It* presents a viable alternative to sciatic *nerve block.* However, the proximal spread of local anesthetic (LA) showed involvement of CPN, which is unwanted and not solving the purpose. This block is given as an adjunct to the femoral nerve block to provide analgesia for total knee replacement surgeries.

D. **Motor-sparing blocks**:

Due to associated motor weakness with the techniques mentioned above, further leading to the risk of falls, delayed mobility, and delayed discharge, the following alternatives (**Figure 8**) can be considered suitable for ERAS protocols.

Figure 8.
Regional analgesia option for anterior and posterior knee pain.
*(**FTB**: Femoral triangle block, **ACB**: Adductor canal block, **DSB**: Dual subsartorial block, **LIA**: Local infiltration analgesia, **iPACK**: Infiltration between popliteal artery and capsule of knee joint).*

I. **Subsartorial blocks**: For all the blocks in the thigh for knee surgeries, the sartorius muscle is a familiar muscular landmark in the sonoanatomy. The LA solution is deposited below the sartorius muscle during these blocks, hence the name "subsartorial blocks [37, 38]." The subsartorial blocks include femoral triangle block, adductor canal block, and dual subsartorial block (**Figure 9**).

a. **Femoral triangle block**:

The femoral triangle (FT) is a subfascial space in the upper third of the thigh bounded by the inguinal ligament (base), medial

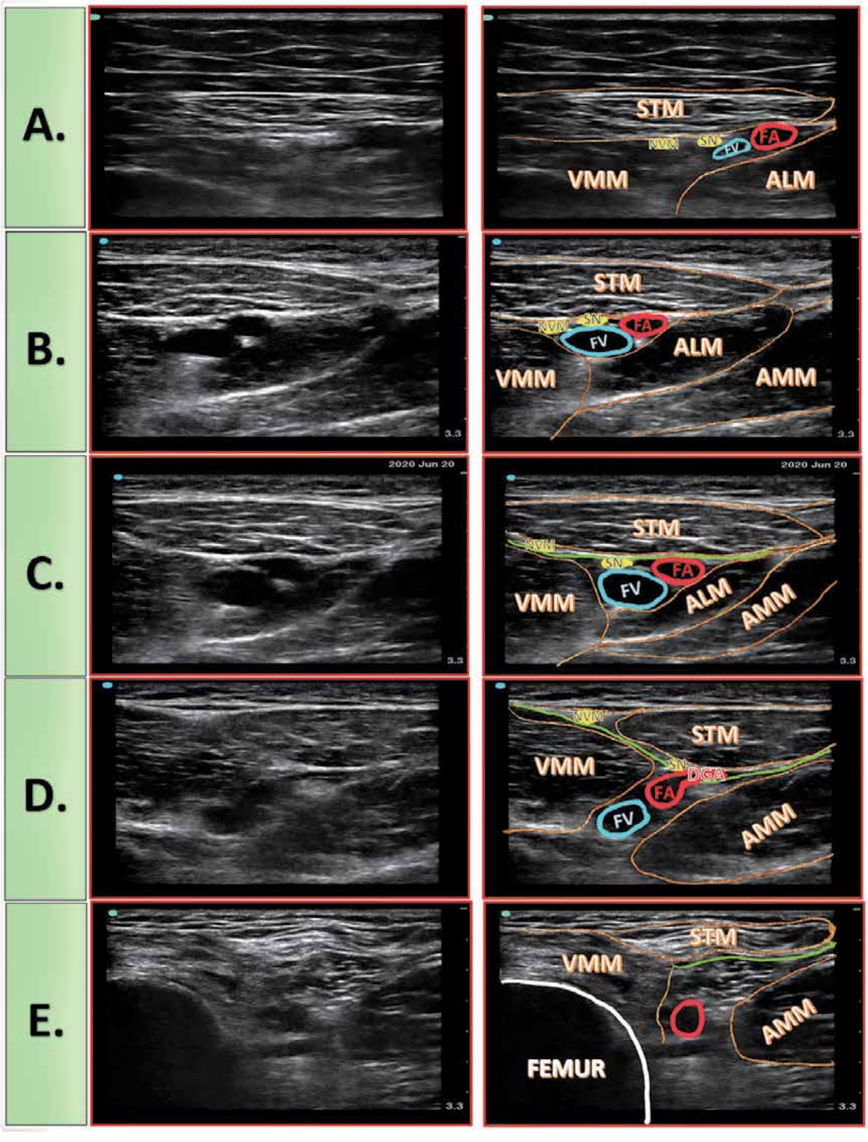

Figure 9.
Sonoanatomy of subsartorial regions.
A*: Distal femoral triangle,* ***B****: Apex of the femoral triangle,* ***C****: Proximal adductor canal,* ***D****: Mid-adductor canal,* ***E****: Distal adductor canal.*
*(****STM****: Sartorius muscle,* ***ALM****: Adductor longus muscle,* ***VMM****: Vastus medialis muscle,* ***AMM****: Adductor magnus muscle,* ***SN****: Saphenous nerve,* ***NVM****: Nerve to vastus medialis,* ***FA****: Femoral artery,* ***FV****: Femoral vein,* ***DGA****: Descending genicular artery,* ***Yellow color****: Nerves,* ***Red color****: Artery,* ***Blue color****: Vein,* ***Brown color****: Muscles).*

border of the adductor longus muscle (medial border), and the medial border of the sartorius muscle (lateral border). Femoral triangle block can be given at the distal-most part of FT, just (1–2 cm) proximal to the apex of FT. Sonoanatomy of this location includes posteromedial adductor longus muscle (ALM), anterolateral vastus medialis muscle (VMM), and medial sartorius muscle (STM). The saphenous nerve (SN) and nerve to vastus medialis (NVM) appear as hyperechoic structure lying lateral to the femoral artery (FA) in the fascial plane between STM and VMM. This analgesic block requires diluted (low concentration) local anesthetic solution with the volume of 10-20 ml. A higher volume (more than 40 ml) or higher concentrated LA may cause proximal spread and include the femoral nerve and its branches, causing unwanted motor weakness. The drug injected into the distal FT spreads distally above and below the vasoadductor membrane (VAM) in the adductor canal region [39, 40]. Due to drug spread between STM and VAM, the subsartorial plexus also gets blocked, providing an additional and required analgesic coverage. The FT block mainly addresses anterior knee pain.

b. **Adductor canal block**:

The adductor canal (AC) is a musculoaponeurotic tunnel extending from the FT apex above to the adductor hiatus below. It is triangular in a cross-section bounded anterolaterally by VMM, posteromedially by ALM proximally and adductor magnus muscle (AMM) distally, and medially by the vasoadductor membrane (VAM). The presence of VAM is the peculiarity of the AC region. Due to VAM, the lower border of the sartorius muscle appears bilayered under ultrasound.

Initially, the adductor canal block (ACB) was considered a saphenous nerve block [41, 42]. Later, various dye studies demonstrated the spread of the dye into the popliteal region when injected in the AC below the VAM. Therefore, the injection at any point distal to the FT apex below VAM can be considered an ACB. However, the involvement of neuronal components will be varied, depending upon the proximal or distal location of ACB. The required LA volume for the ACB is 10–20 ml.

Three critical events occur in the AC [41, 42]:

- Entry of SN along with the femoral vessels from the FT into the AC - in the proximal part of AC
- Exit of SN along with descending genicular artery (a branch from FA) by piercing VAM and leaving AC- in the middle-third part of AC
- Entry of the femoral vessels (with the posterior division of the obturator nerve) into the opening of the AMM (adductor hiatus) - in the distal part of AC.

Due to these events, it is essential to divide ACB into three subdivisions: Proximal, mid, and distal AC. However, in all three locations, a drug injected into the AC below the VAM tracks along with the femoral vessels towards the adductor hiatus (involving the posterior division of the obturator nerve) and enters the backside of the knee (involving the popliteal plexus) [43, 44].

The SN enters the AC in the proximal part but leaves the AC in the middle part, where it lies between STM and AMM above the VAM [41]. Later, it crosses the thigh from the anterior to the medial side and becomes superficial by piercing the deep fascia of the thigh, where it lies between STM and gracilis muscles [41].

So, SN is not the content of mid-to-distal AC. The NVM always lies above the VAM with an additional fascial covering, so not the content of the entire AC [41, 45]. Thus, the analgesic coverage of the AC varies as per the involvement of the neuronal components at different locations.

Proximal adductor canal block is given in the proximal third of AC, just (1–2 cm) distal to the apex of FT. Sonoanatomy includes ALM posteromedially, VMM anterolaterally, VAM medially, and SM above VAM. The hyperechoic SN lies into the adductor canal lateral to the FA.

Mid-adductor canal block is given in the middle third of AC, distal to the proximal AC, where the ALM is replaced by AMM posteromedially.

Distal adductor canal block is given in the lower third of AC, where the femoral vessels enter into the adductor hiatus to become popliteal vessels. Sonoanatomy includes AMM posteromedially, VMM anterolaterally, and VAM (with SM above) medially. No nerves lie in this part of the adductor canal.

c. **Dual subsartorial block (DSB)**:

Dual subsartorial block (DSB) is described as opioid-sparing, motor-sparing, and procedure-specific RA technique for total knee replacement (TKR) surgeries, mainly with medial incisions. It is a hybrid form of subsartorial block combining two subsartorial blocks (distal FT and AC block) to cover all procedure-specific innervations of pain generators involved in TKR surgery [46]. It is given immediately after the surgery with two different injections at two different locations below the sartorius muscle, hence termed a “dual subsartorial block” (**Figure 10**).

The first injection (distal FT block) targets SN and NVM directly and subsartorial plexus indirectly due to the distal spread of the drug under SM but above the VAM [43]. The subsartorial plexus lies between VAM and SM in the AC region. In the second injection (adductor canal block), no nerves are targeted. Simply depositing the drug perivascularly (around FA) under the VAM is sufficient to obtain the desired outcome. A drug injected into the AC below VAM will travel along the femoral vessels and enter the adductor hiatus to reach the posterior aspect of the knee joint [44]. Thus, the second injection indirectly targets the popliteal plexus formed by the articular branches from the posterior division of the obturator nerve, tibial, common peroneal, and sciatic nerve.

Thus, DSB involves blockade of SN, NVM, subsartorial plexus, the medial half of the peripatellar plexus, and the popliteal plexus. It results in sensory blockade over the anteromedial aspect of the knee up to the tibial tuberosity, medial retinacular complex, and intraarticular region (popliteal plexus). It will not cover the skin over the anterolateral (supplied by lateral half of peripatellar plexus) and posterior aspect (supplied by the posterior femoral cutaneous nerve of the thigh) of the knee.

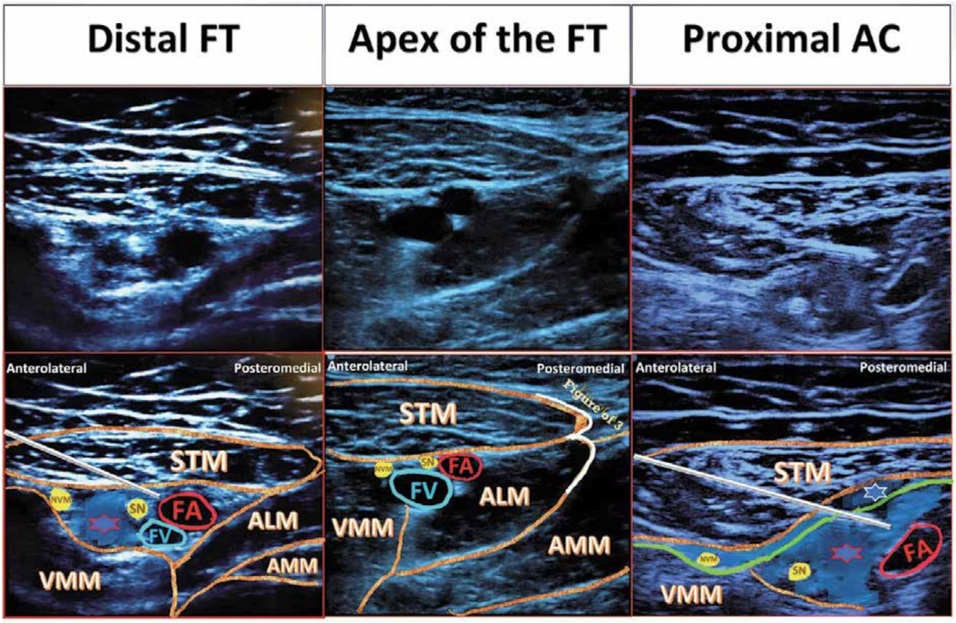

Figure 10.
Sonoanaltomy of dual subsartorial block.
*(**STM**: Sartorius muscle, **ALM**: Adductor longus muscle, **VMM**: Vastus medialis muscle, **AMM**: Adductor magnus muscle, **SN**: Saphenous nerve, **NVM**: Nerve to vastus medialis, **FA**: Femoral artery, **FV**: Femoral vein, **DGA**: Descending genicular artery, **Yellow color**: Nerves, **Red color**: Artery, **Blue color**: Vein, **Brown color**: Muscles, **Green line**: Vasoadductor membrane, **White line**: Needle track, **Blue star with red border**: Drug spread, **Blue star with white border**: Drug spread above vasoadductor membrane).*

These uncovered areas are not included in the total knee replacement surgeries with medial approaches, so the lack of analgesia in the spared region is of little clinical consequence. If given precisely with recommended LA concentration and volumes, the DSB does not cause any motor blockade and involves all target procedure-specific innervations.

II. **High-volume blocks**:

a. **Hi-Volume Proximal Adductor Canal (Hi-PAC) block**:

Hi-PAC block is described recently as an indirect anterior approach of popliteal sciatic nerve block [47]. In this block, high-volume (30–40 ml) and low-concentration LA (0.2% ropivacaine) with an adjuvant (8 mg dexamethasone) is injected in the proximal adductor canal just below the VAM. The probe position and injection technique are the same as the second injection of DSB into the proximal AC, except for higher volume LA in the Hi-PAC block. The analgesic coverage of this block involves territory of the saphenous nerve, posterior division of obturator nerve, popliteal plexus, tibial, common peroneal, and finally popliteal sciatic nerve. Although this block provides analgesic coverage as adductor canal block, it is mainly described for below-knee surgeries due to wide coverage involving all innervations below the knee.

b. **4-in-1 block/ modified 4-in-1 block**: (**Figure 11**)

Unlike the Hi-PAC block (given in proximal AC), the 4-in-1 block [48] is given into the distal AC. The important landmark for this block is descending genicular artery to identify the block site, whereas the landmark for the Hi-PAC block is the apex of the femoral triangle. The volume and type of LA required for this block are 35 ml of 0.2% ropivacaine. It is described to provide analgesia for knee surgeries as well as below-knee surgeries. Due to injection into the distal AC below VAM, there is a possibility of the saphenous nerve and nerve to vastus medialis sparing. The saphenous nerve leaves AC in the mid-adductor canal location and becomes superficial, whereas the NVM always lies above the VAM (thus, not the content of AC). Considering the sparing of NVM, which is an important nerve for knee surgeries, a modified 4-in-1 block was described mainly for knee surgeries.

The modified-4-in-1 block [49] involves two injections: The first injection (5–7 ml of 0.2% ropivacaine) above VAM around the NVM after stimulating it, and the second injection (20–25 ml of 0.2% ropivacaine) below VAM perivascularly. The possibility of the saphenous nerve-sparing remains the same in this block.

Due to the distal spread of injected LA through the adductor hiatus into the popliteal region, both blocks involve posterior division of obturator nerve, tibial, common peroneal, and sciatic nerves.

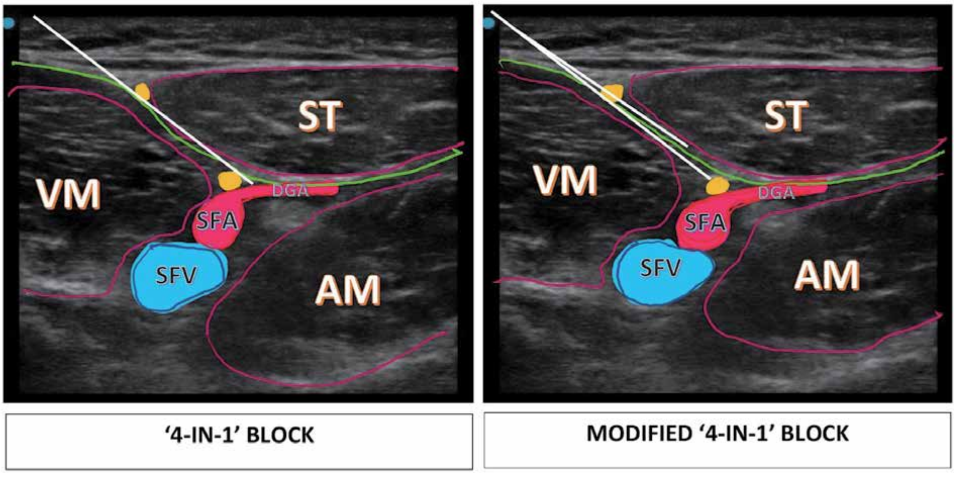

Figure 11.
Sonoanaltomy of 4-in-1 and modified 4-in-1 block.
*(**ST**: Sartorius muscle, **VM**: Vastus medialis muscle, **AM**: Adductor magnus muscle, **SFA**: Superficial femoral artery, **SFV**: Superficial femoral vein, **DGA**: Descending genicular artery, **Yellow dots**: Nerves, **Red color**: Artery, **Blue color**: Vein, **Green line**: Vasoadductor membrane, **White lines**: Needles track).*

c. **Ultrasound-guided Hamstring block** [50, 51]**: (Figure 12)**

- Initially described in 2012 mainly to cover hamstring graft harvesting site
- Reduces pain following hamstring graft harvest for ACL reconstructions

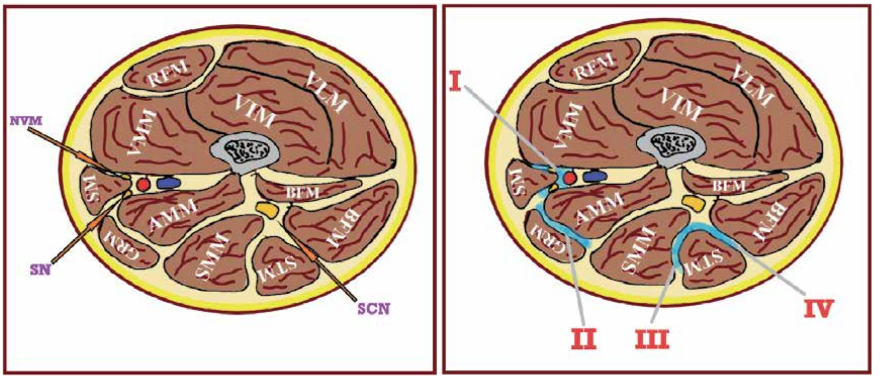

Figure 12.
Hamsting block injection sites.
***I**: First injection under the sartorius muscle in the adductor canal. **II:** Second injection below gracilis muscle. **III & IV:** Third and fourth injections around semotendinosus muscle. (**SM:** Sartorius muscle, **VMM:** Vastus medialis muscle, **AMM:** Adductor magnus muscle, **RFM:** Rectus femoris muscle, **VIM:** Vastus intermedialis muscle, **VLM:** Vastus lateralis muscle, **BFM:** Bicep femoris muscle, **STM:** Semitendinosus muscle, **SMM:** Semimembranosus muscle, **GRM:** Gracilis muscle, **SN:** Saphenous nerve, **NVM:** Nerve to vastus medialis, **SCN:** Sciatic nerve, **Yellow color**: Nerves, **Red color**: Artery, **Blue color**: Vein, **Brown color**: Muscles, **Gray color**: Femoral bone, **Light blue area:** Drug spread).*

- **Needle**: 10–15 cm block needle
- **LA volume:** 30–40 ml

  i. 5–7 ml below the sartorius in the adductor canal

  ii. 10–15 ml below gracilis muscle with probe over the posteromedial aspect of the distal thigh

  iii. 15–20 ml around the semitendinosus muscle (above and below) with probe over the posterior aspect of the distal thigh

III. **Infiltration techniques**:

a. **I-PACK Block**:

The term i-PACK is described as a motor-sparing RA technique that consists of an infiltration of local anesthetic into the interspace between the popliteal artery and the posterior capsule of the knee [52–54]. It can be used as an adjunct to the femoral nerve or adductor canal blocks to cover the posterior knee pain. It creates field block (**Figure 13**), causing blockade of articular branches arising of the tibial, common peroneal, and obturator nerves in the popliteal region. Indications of I-PACK include postop analgesia for TKR surgeries, ACL repairs, and procedures involving the posterior aspect of the knee. The required LA volume for this block is 15–20 ml. This block needs to be given preoperatively due to loss of anatomical landmarks after surgery. It can be given using two approaches: medial approach and popliteal approach, as shown in **Figure 14**.

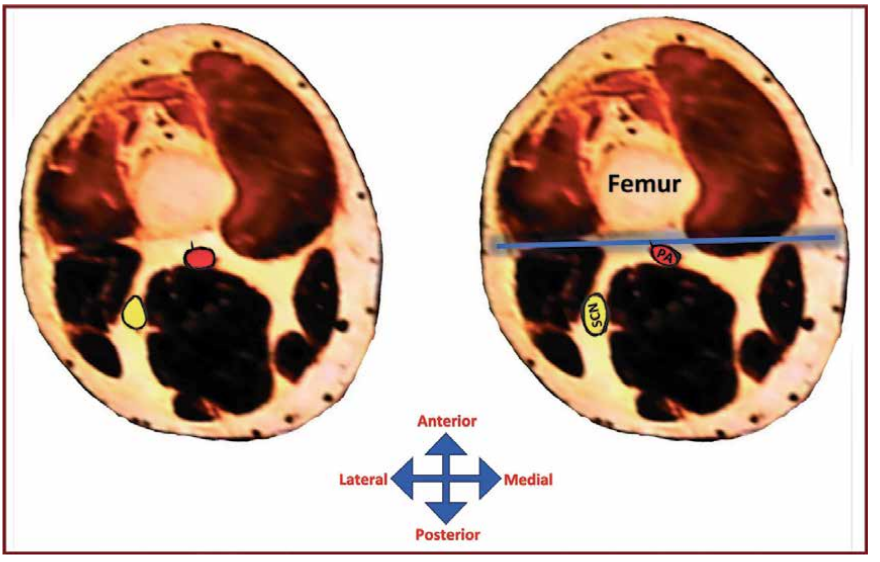

Figure 13.
Needle track and drug spread of i-PACK block.
*(**PA**: Popliteal artery, **SCN**: Sciatic nerve, **Blue color**: Needle track and drug spread between PA and femur).*

b. **Local infiltration analgesia (LIA)**:

Kohan and Kerr repopularized the concept of local infiltration analgesia (LIA) in 2008 for postoperative analgesia for knee surgery [55]. It is mainly given by the operating surgeon during surgery using various drug combinations and volumes.
The cocktail combination used for LIA includes LA (ropivacaine 2 mg/ml or bupivacaine 2.5 mg/kg), NSAIDs (ketorolac 30 mg), adrenaline (10 micrograms/ml), opioids (morphine 5–10 mg), and steroids (dexamethasone 8 mg). The total volume of cocktail combination used for LIA may go up to 100–170 ml. For LIA, the surgeon mainly targets the anterior and posterior capsule of the knee, intercondylar area, collateral ligaments, tissue along the femur and tibia, and subcutaneous tissue.

The analgesic effect of the LIA technique depends on the involved injection sites by the surgeon and used drug combinations. However, the drawbacks of single-shot LIA include its limited duration of analgesia (12–18 hours), chances of infection if sterility is not maintained while loading drugs [56, 57], and chondrotoxicity [58] (due to agents used) that may cause loosening of the implants in the long-term followups. Indwelling LIA catheter is usually avoided due to the fear of infection.

c. **Ultrasound-guided Ring block**:

Ultrasound-guided Ring block is nothing but the LIA technique given by an anesthesiologist under direct vision using ultrasound

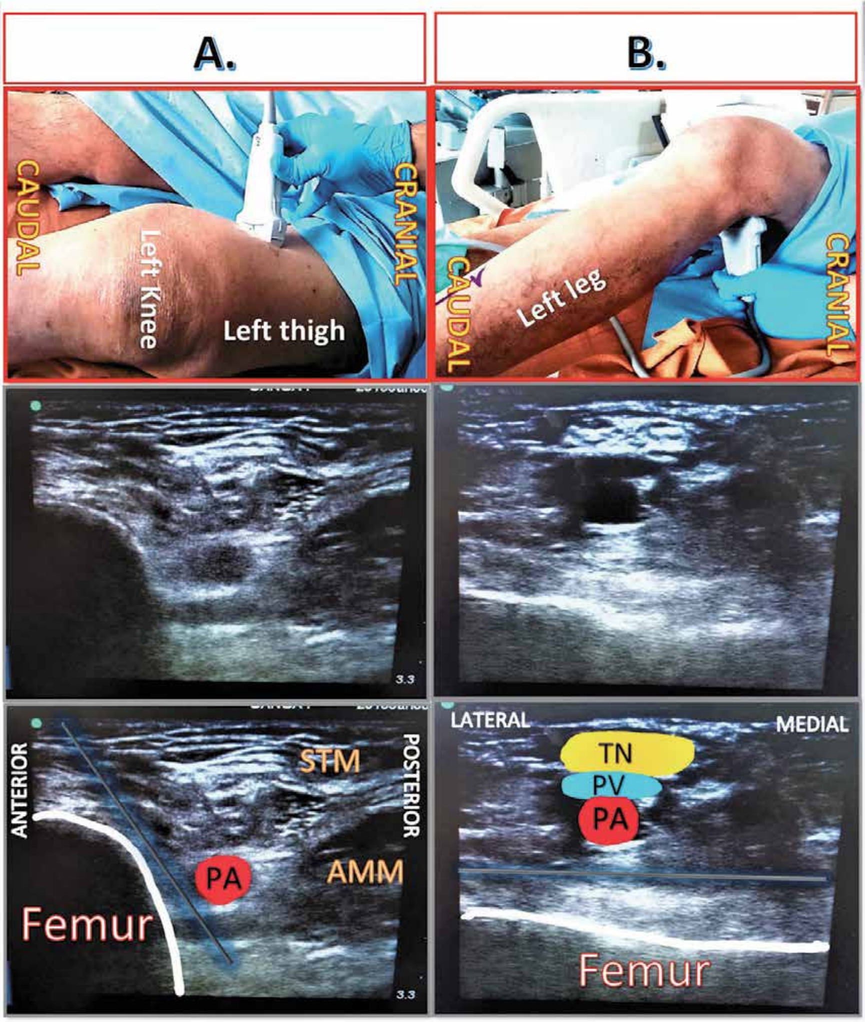

Figure 14.
Probe position and sonoanatomy of various apporaches of i-PACK block.
***A**: Anteromedial approach of i-PACK, **B**: Popliteal approach of i-PACK.*
*(**STM**: Sartorius muscle, **AMM**: Adductor magnus muscle, **PA**: Popliteal artery, **PV**: Popliteal vein, **TN**: Tibial nerve, **Gray line with blue glow**: Needle track and drug spread between PA and femur).*

[59–61]. It targets all innervations responsible for postoperative pain generations. Like conventional LIA, it is also given preoperatively before the beginning of the surgery after the primary mode of anesthesia (neuraxial or GA). This block consists of multiple injections around the knee joint (**Table 4**) except for the lateral spared area of the common peroneal nerve territory (**Figure 15**).

Since this block is given under ultrasound guidance targeting almost all of the innervations of the knee joint, the precision with this block is greater than the LIA given by the surgeon. Surgeons sometimes are reluctant to infiltrate near the popliteal artery in fear of injuring it.

Injections	Probe location	LA volume	Pattern of injection	Target innervations
First	Medial aspect of the mid-thigh	10–20 ml	LA injected into the intermuscular plane between the sartorius and vastus medialis muscles	• Saphenous nerve • Nerve to vastus medialis • Subsartorial plexus
Second	Anterior aspect of the distal thigh	10–20 ml	LA infiltrated into the belly of the vastus intermedialis muscle through multiple passes	• Nerve to vastus intermedialis
Third	Lateral aspect of the distal thigh	10–20 ml	LA infiltrated into the belly of the vastus lateralis muscle through multiple passes	• Nerve to vastus lateralis
Fourth	Posterior aspect of the distal thigh	15–20 ml	LA injected between the popliteal artery and hyperechoic femoral condyle creating a field block	• Popliteal plexus
Fifth	Lateral to the tibial tuberosity in the leg	5–10 ml	LA injected after hitting the bone.	• Inferior lateral genicular nerves
Sixth	Medial to the tibial tuberosity in the leg	5–10 ml	LA injected after hitting the bone.	• Inferior medial genicular nerves

*(**LA**: Local anesthetic)*

Table 4.
Injections sites of ultrasound-guided LIA or Ring block.

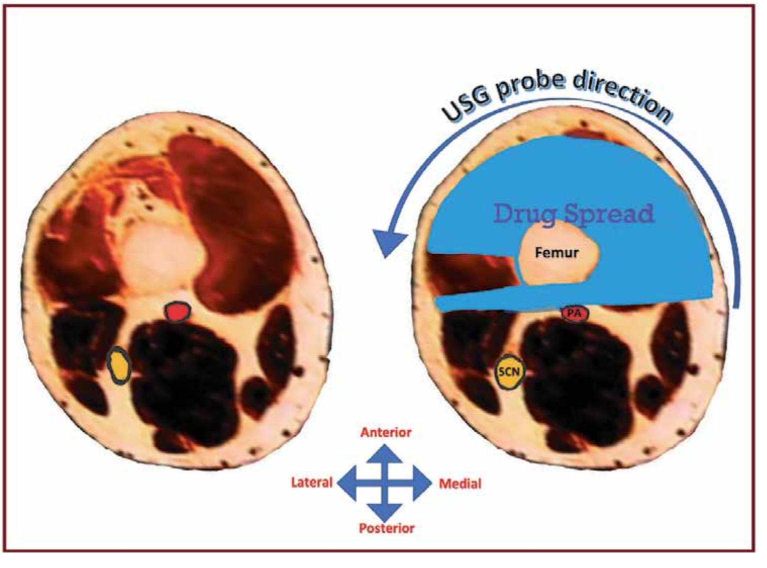

Figure 15.
Field block created by ultrasound-guided LIA or Ring block.
*(**PA**: Popliteal artery, **SCN**: Sciatic nerve, **Blue area**: Field block due to drug spread).*

11. Procedure- specific RA

Sometimes standard regional blocks fail in providing expected analgesia. Block failure may be due to the sparing of some of the innervations of pain-generating structures involved in the surgery. For this reason, understanding surgical steps, innervations of pain-generating structures, and customizing standard RA techniques to make them suitable for the surgery is essential. The standard procedures performed in the knee joint include joint replacement surgery and arthroscopic surgery.

11.1 Knee joint replacement surgery

Knee joint replacement is one of the best treatments available for end-stage osteoarthritis, wherein the damaged cartilages are replaced with an implant, allowing patients to regain joint function. This life-changing procedure improves health-related quality of life and functional status by providing optimal analgesia and near-normal joint function [1, 2].

Depending upon the extent of the disease, joint replacement surgeries can be divided into the following types.

1. Total knee replacement (TKR), where the whole joint (femoral and tibial component with patella) is replaced with implants,

2. Unicondylar knee replacement or patellofemoral replacement where a single component of joint is replaced.

3. Computer-assisted navigation systems (CAS) or robotic surgery allow surgeons to perform many complex procedures with more precision, flexibility, and control than conventional techniques.

Surgical Steps involved in such surgery include,

- **Incision:** TKR can be performed by various approaches (**Figure 16**) like medial parapatellar, lateral parapatellar, Sub-vastus, Mid-vastus, and midline.6Medial parapatellar/longitudinal incision (From 5 cm proximal to

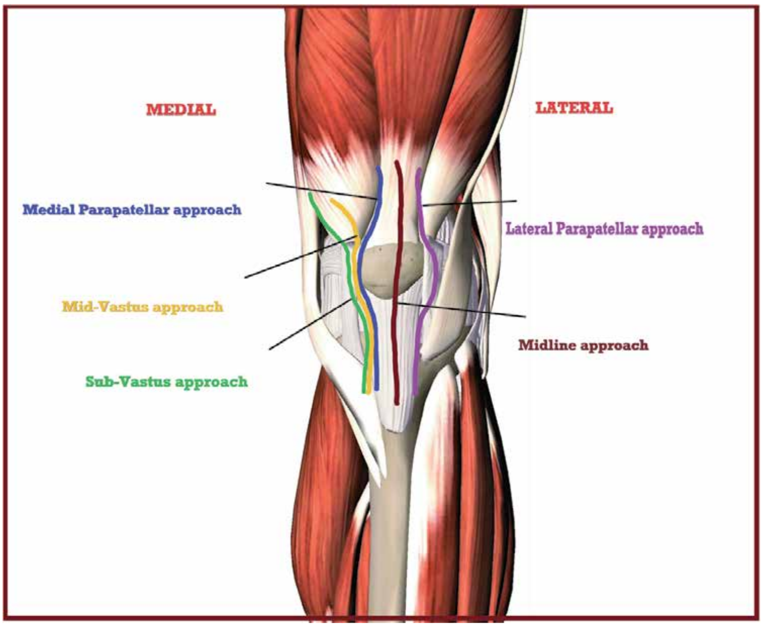

Figure 16.
Various approaches of knee replacement surgeries.
*(**Source**: Images is courtesy of 3D4Medical's essential anatomy).*

the superior pole of the patella to tibial tuberosity) is most commonly performed, especially for varus knees. For this reason, it is called a workhorse of the Varus knee.

- **Dissection** through the medial retinacular complex (Deep fascia + retinacular ligament and fibrous capsule) along the medial border of the quadriceps tendon, patella, and patellar ligament.

- **The knee joint is accessed** by opening synovial membrane to allow removal of menisci, cruciates and transverse ligaments, infrapatellar fat pads, and osteophytes.

- **Resection** of Cartilage of femoral and tibial condyles along with the back of the patella.

- **Shaping** of femoral and tibial bony surfaces to fit metal components of knee prosthesis.

The total duration of surgery is 1–2 hours. The majority of the patients begin physiotherapy within 24 hours of surgery. The patients are usually discharged within 3–5 days post-surgery.

Post-surgery complications include infection, nerve damage, increased risk of fall, bone fractures, persistent/chronic pain, deep venous thrombosis, joint stiffness, prosthesis-related complications (loosening/fracture of prosthesis components, joint instability, and dislocation, component misalignment, and breakdown.

11.1.1 RA options for knee joint replacement surgery

- CSEA: It provides excellent analgesia but is associated with delayed mobility as discussed before, also not recommended for ERAS

- FTB with LIA

- ACB with LIA

- Dual subsartorial block

- Local infiltration analgesia (LIA)

- Ultrasound-guided ring block

11.2 Bilateral TKR

Bilateral TKR, either staged or single-staged (simultaneous), is also a commonly performed joint surgery in relatively younger and healthy patients. Patient selection is very crucial in bilateral TKR as it is associated with advantages as well as disadvantages.

The **advantages** of bilateral TKR surgeries include [62],

- Single event (surgical and anesthesia) with bilateral functional recovery.

- Relatively shorter hospital stay.

- Reduced pain intensity, better functional recovery, and general health due to correction of the pathology of both knees simultaneously.
- The possibility of rehabilitating the patient symmetrically.
- Lower cost as estimated medical care costs savings of 18–26% [63]. An estimated cost of simultaneous TKR is almost half compared to staged bilateral TKR [64–66].
- Reduced risk of mechanical malfunction and periprosthetic joint infection [67–70].

The **disadvantages** of bilateral TKR surgeries include,

- Higher risk of pulmonary embolism (about 80%) in the three months than after a single procedure [71].
- Higher mortality and morbidity risk.
- Higher risk of cardiac complications.
- Associated with relatively more blood loss and need for blood transfusion.
- Increased risk of overall complications (pulmonary embolism, wound infections, and need for the second operation).

11.2.1 RA options for bilateral TKR

- CSEA: It provides excellent analgesia but is associated with delayed mobility as discussed before, also not recommended for ERAS.
- Bilateral FTB with LIA.
- Bilateral ACB with LIA.
- Bilateral dual subsartorial block.
- Bilateral local infiltration analgesia (LIA): Required volume of LA may cross maximum allowable dose.

11.3 Arthroscopic knee surgeries

Knee arthroscopy, also called knee scoping, is a minimally invasive procedure to diagnose and treat joint pathologies or injuries. It is performed using an arthroscope inserted into the knee joint through various portal sites (**Figure 17**).

11.3.1 Type of arthroscopic knee surgeries

- Meniscal repair or removal
- ACL, MCL, or PCL rapair or reconstruction
- Synovectomy

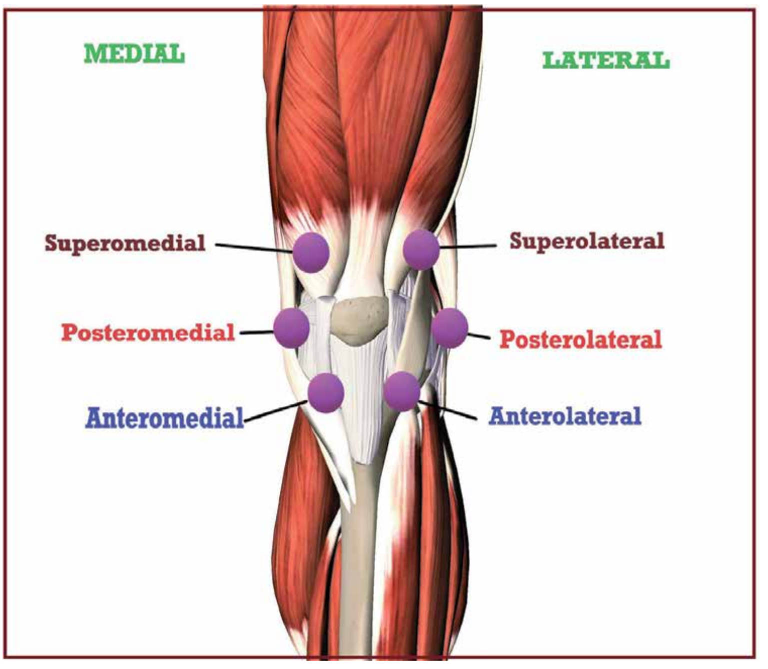

Figure 17.
Various portal sites for arthroscopic knee surgeries.
*(**Source**: Images is courtesy of 3D4Medical's essential anatomy app).*

- Trimming of damaged articular cartilage
- Removal of loose fragments of bone or cartilage
- Treatment of patella (kneecap) problems
- Knee debridement

11.3.2 Arthroscopic portal insertion sites

1. Primary portal sites:
    a. Anterolateral/Anteromedial
    b. Superomedial/Superolateral
2. Secondary portal sites:
    a. Posteromedial/ posterolateral portal
    b. Transpatellar portal
    c. Proximal supoeromedial portal
    d. Far medial or far lateral portal

Duration of surgery is usually <1 hrs (ranging from 30 min to 45 min). Arthroscopic surgeries are minimal-invasive surgeries associated with less severe postoperative pain. The postoperative pain generators include the intraarticular components, portal entry sites, and a hamstring graft-harvesting site in such surgeries. Most of the innervations of the postoperative pain generators involved popliteal plexus and saphenous nerve. So, RA techniques involving these innervations can provide optimal analgesia along with multimodal analgesics.

11.3.3 RA options for arthroscopic knee surgeries

- Adductor canal block as it covers saphenous nerve directly and popliteal plexus indirectly.
- iPACK mainly covers the popliteal plexus.
- Intraarticular administration of LA or morphine or cocktail mixture.
- Ultrasound-guided Hamstrings block

11.4 Postoperative pain generators

The postoperative pain of any surgery depends on the number of pain generators removed and retained after surgery (**Figure 18**). The TKR surgery involves removing many pain generators (like anterior capsule, synovium, meniscus,

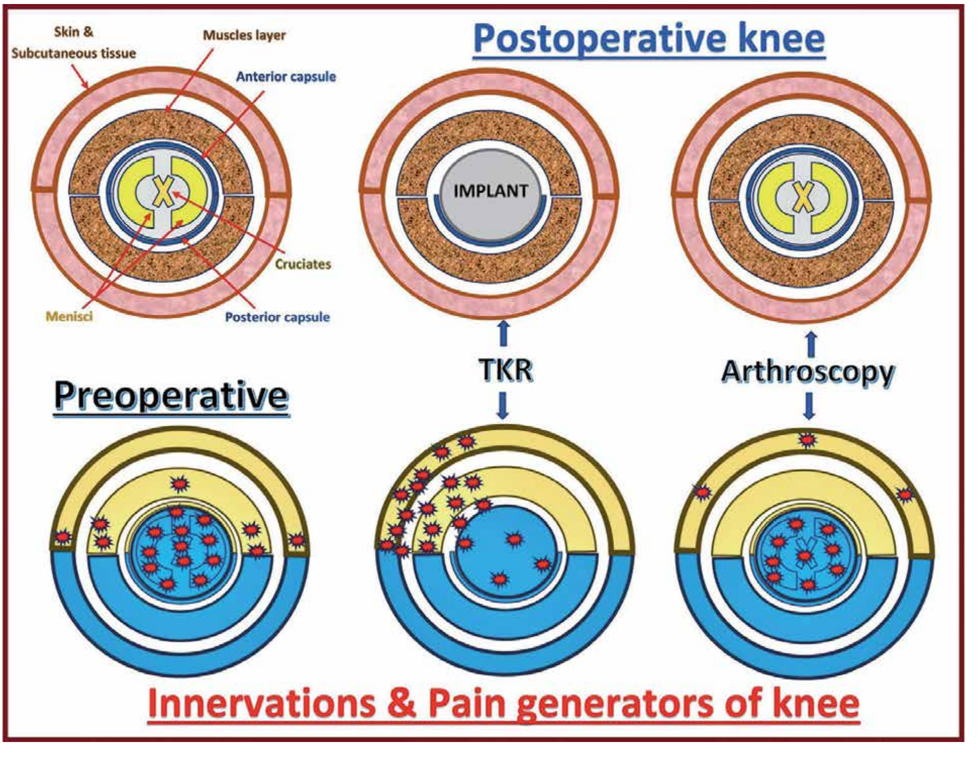

Figure 18.
Preoperative and postoperative pain generating structures of knee surgeries.
***Yellow colored area in circles**: Anterior knee innervations. **Blue colored area in circles**: Posterior knee innervations. **Red star-like dots**: Pain generating area. **TKR**: Total knee replacement.*

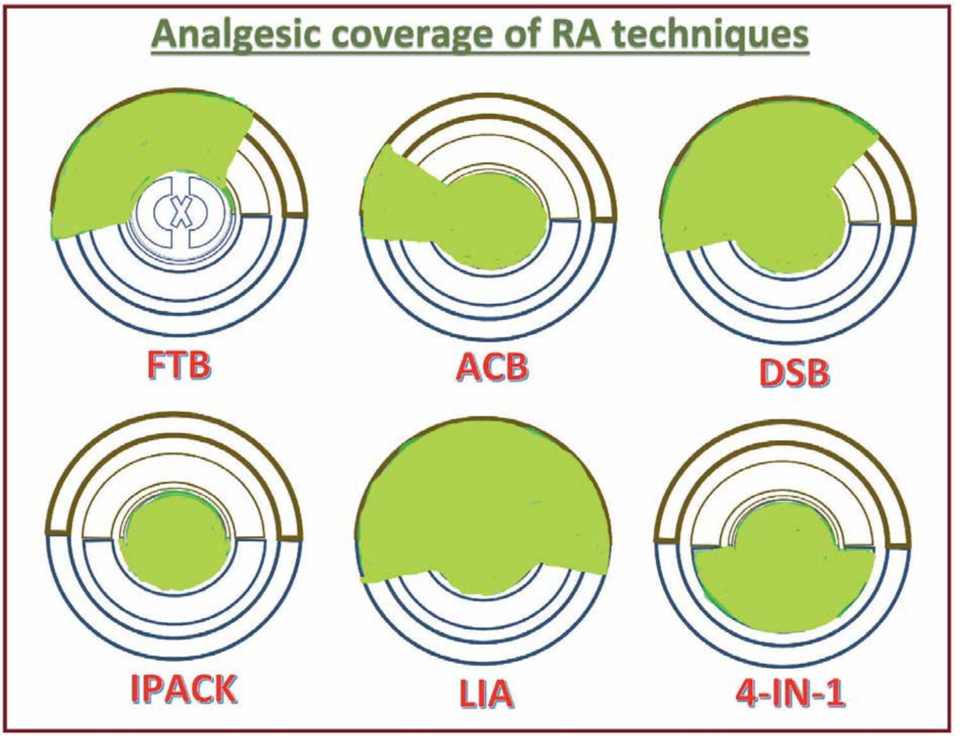

Figure 19.
Analgesic coverage of various regional techniques for knee surgeries.
***Green colored area in circles:** Analgesic covered regions. (**FTB:** Femoral triangle block, **ACB:** Adductor canal block, **DSB:** Dual subsartorial block, **IPACK:** Ilfiltration between popliteal artery and capsule of knee joint, **LIA:** Local infiltration analgesia).*

cruciates, intraarticular ligaments, periosteum of the knee joint, and prepatellar fat pads) [11, 72–77]. The retained pain-generating components responsible for post-TKR pain include skin/subcutaneous tissues over the incision area, medial retinaculum, periosteal rim of the cut bones, remnant of the anterior joint capsule, cut nerves along the surgical dissection area, microfractures, and inflammation. For arthroscopic knee surgery, the pain-generating components are mainly intra-articular. Therefore, the innervations of these retained components are essential targets for any procedure-specific RA techniques.

The analgesic coverage of each RA technique is different, as shown in **Figure 19**. The choice of RA techniques depends on the procedure performed and its associated innervations.

An "identify-select-combine" approach [78, 79] is beneficial to obtain procedure-specific RA techniques for knee surgery (**Table 5**). This approach includes identifying target innervations, selecting target blocks involving most of the target nerves, and combining all target blocks to cover innervations of all the pain generators.

12. Conclusion

Background knowledge of the knee joint and its components is essential to achieve the best surgical and analgesic outcomes. Perioperative pain management of the patient undergoing any knee surgery is a complex and challenging task. Therefore, the holistic approach is required considering the patient's age, comorbid

<table>
<tr><th>Surgical Steps</th><th>Approaches</th><th>Target innervations</th><th>Target blocks</th><th>Procedure-specific RA options</th></tr>
<tr><td rowspan="4">Incision</td><td>Medial</td><td>• Subsartorial plexus</td><td>• Subsartorial blocks</td><td rowspan="12">• Medial approach:
• FTB + ACB
• DSB
• FTB + i-PACK
• LIA
• Lateral approach:
• FNB + ACB infiltration over incision
• FNB + i-PACK + infiltration over incision
• LIA
• Anterior approach:
• FNB + ACB
• FNB + i-PACK
• LIA
• Posterior approach:
• ACB + infiltration over incision site
• Popliteal sciatic nerve block + infiltration over the incision site
• i-PACK + infiltration over incision site</td></tr>
<tr><td>Lateral</td><td>• Peripatellar plexus</td><td>• FNB
• LFCN block
• Lateral cutaneous nerve of calf block</td></tr>
<tr><td>Midline</td><td>• Peripatellar Plexus</td><td>• FNB</td></tr>
<tr><td>Posterior</td><td>• PCNT</td><td>• Infiltration over the incision site</td></tr>
<tr><td rowspan="4">Superficial + Deep dissection</td><td>Medial</td><td>• Subsartorial plexus</td><td>• Subsartorial blocks</td></tr>
<tr><td>Lateral</td><td>• Peripatellar plexus</td><td>• FNB</td></tr>
<tr><td>Midline</td><td>• Peripatellar plexus</td><td>• FNB</td></tr>
<tr><td>Posterior</td><td>• Popliteal plexus
• Sciatic nerve</td><td>• ACB
• i-PACK
• Popliteal SCN block
• LIA</td></tr>
<tr><td rowspan="2">Joint Access</td><td>Anterior capsule</td><td>• Subsartorial plexus
• Peripatellar plexus</td><td>• Subsartorial blocks
• FNB</td></tr>
<tr><td>Posterior capsule</td><td>• Popliteal plexus</td><td>• ACB
• i-PACK
• LIA</td></tr>
<tr><td>Intraarticular dissection</td><td></td><td>• Popliteal plexus</td><td>• ACB
• i-PACK
• LIA</td></tr>
</table>

*(**FNB:** Femoral nerve block, **LFCN:** Lateral femoral cutaneous nerve, **FTB:** Femoral triangle block, **ACB:** Adductor canal block, **DSB:** Dual subsartorial block, **SCN:** Sciatic nerve, **i-PACK:** Ilfiltration between popliteal artery and capsule of knee joint, **LIA:** Local infiltration analgesia)*

Table 5.
Procedure-specific regional analgesia options for knee.

factors, psychological components, complex innervations, multifactorial pain generations, surgery type, and demand for the best analgesic options suitable for ERAS protocol.

Optimum perioperative analgesia reduces the stress response of the surgery or pain. It hastens early mobilization and discharge, reduces hospital stay and associated complications, controls treatment costs, most importantly, improves patient satisfaction. A well-functioning knee joint is essential to improve quality of life and reduce perioperative morbidity and mortality. Multimodal analgesia for multifactorial pain should be the ideal protocol for knee surgeries. The regional analgesia, an essential component of MMA, should be motor-sparing, opioid-sparing, and procedure-specific.

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Conflict of interest

The authors declare no conflict of interest.

Contribution statement

Both the authors contributed equally to design and complete this manuscript.

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Chapter 8

Fast Track Arthroplasty Using Local Infiltration Analgesia

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Abstract

Fast track arthroplasty is a holistic approach to patients who undergo total hip and knee arthroplasty, a journey or care that begins with setting patient's expectation, optimising medical status, using intraoperative local anaesthetic infiltra-tion, decreasing narcotics usage either in spinal or post-operative medication, discouraging usage of patient controlled analgesia or urinary catheters, encouraging day of operation mobilisation and optimising post-operative physiotherapy protocols. The use of local infiltration analgesia (LIA) is a good alternative compared to other traditional pain management techniques. The purpose of adoption of LIA technique is to provide comfort from the trauma associated with hip and knee arthroplasty particularly for the first 36 h post-operatively, during the time of high post-operative pain, to facilitate increased post-operative mobilisation and function. LIA is safe and effective to achieve good outcomes, early mobilisation and decreasing length of stay without jeopardising clinical outcomes. This chapter discusses LIA and its multimodal approach to analgesia, regional anaesthesia and early mobilisation that improves overall patient experience and satisfaction. The chapter discusses LIA techniques, wound catheter placement, and postoperative protocol to achieve fast track hip and knee arthroplasty.

Keywords: local infiltration analgesia, fast track arthroplasty, rapid recovery arthroplasty, enhanced recovery after surgery, total hip arthroplasty, total knee arthroplasty

1. Introduction

Hip and knee joint arthroplasty are effective in reducing pain and improving function and quality of life in patients with osteoarthritis or other destructive joint disease [1, 2]. This brings an increasing demand on healthcare systems to facilitate smooth recovery, not troubled by nausea or the adverse effects of narcotics. Acute pain leads to decreased mobility, increased length of stay, and an increased need for inpatient rehabilitation, chronic pain, subsequently leading to dissatisfied patients and increasing burden on healthcare resources [3–5]. Utilising an optimum analgesic protocol is challenging; outweighing the benefits and risks of each protocol is key in improving clinical outcomes and patient satisfaction.

Rapid recovery following elective hip and knee arthroplasty has been adopted with consistent patient satisfaction without jeopardising clinical outcomes [6–9]. Several modalities for peri-operative analgesia have been used such as patient-controlled analgesia (PCA), systemic opioids, spinal anaesthetic, epidural catheter, and local anaesthetic blocks. These all carry associated risks and benefits which must be weighed.

The use of local infiltration analgesia (LIA) is a technique adopted in lower limb arthroplasty to improve post-operative pain. LIA is a technique described initially in literature by Kerr and Kohan who used a multimodal approach to relieve pain [10]. A cocktail of locally injected anaesthetic and direct acting analgesics create a prolonged analgesic effect post-operatively reduces the requirement of opioid analgesia and thus reducing nausea and increasing mobility.

This chapter discusses LIA and its multimodal approach to analgesia, regional anaesthesia and early mobilisation that improves overall patient experience and satisfaction. The chapter discusses LIA techniques, wound catheter placement, and postoperative protocol to achieve fast track hip and knee arthroplasty.

2. Local infiltration analgesia mixture

The local anaesthetic cocktail usually comprises of multiple active ingredients. The dose and volume of this cocktail is dependent on many factors including body mass index (BMI), renal function and patient's specific comorbidities. Local anaesthetic mixture has been validated in previous studies which showed that LIA is safe and effective in total hip and knee arthroplasty [11–13].

The anaesthetic mixture initially described by Kerr & Kohen in 2008 contained 2.0 mg/mL ropivacaine, 30 mg ketorolac and 10 μg/mL of adrenaline totalling 150–170 mL in knee arthroplasty and 150-200 mL in hip arthroplasty [10]. Ropivacaine was reduced to 250 mg if a patient was less than 55 kg, older than 85 years or had an American Society of Anaesthesiology (ASA) class of 3 or more. In this description, ketorolac was omitted in patients with poor renal function.

According to a study conducted in Ballarat, Victoria in 2020, they used a LIA cocktail derived from Kerr's protocol. Their mixture consisted of 350 mg of ropivacaine, 30 mg ketorolac, 4 mg dexamethasone and 0.5 mg adrenaline [14]. The catheter top-up was injected in the morning post-operative with dose of 20 mL including 100 mg ropivacaine, 4 mg dexamethasone, 30 mg ketorolac, 0.5 mg adrenaline (adrenaline given for total hip arthroplasty (THA) only and not total knee arthroplasty (TKA)) and normal saline. The study showed shorter length of stay, decreased incidence of discharge to rehabilitation, and reduction in healthcare cost without negative impact on patient outcomes when compared to the national average outcomes published in Royal Australasian College of Surgeons Variance Report in 2017. PCA (patient-controlled analgesia) was not used.

In a THR study, Busch et al. used a 100 mL mixture of local anaesthetic comprised of 400 mg of ropivacaine, 30 mg of ketorolac, 5 mg of morphine and 0.6 mL of epinephrine [15]. They found that their patients who received LIA, when compared to those who did not receive, had better pain and satisfaction scores, their PCA use was minimised, and their length of stay (LOS) decreased. Krenzel et al. performed a double-blinded randomised control study for patients with TKA that compared a 20 mL solution of 100 mg ropivacaine against 20 mL of saline placebo [16]. They found that patients received LIA had better pain scores and straight leg raise earlier. The systematic review conducted by Marques et al. used a combination of a local anaesthetic (ropivacaine or bupivacaine), ketorolac and epinephrine [17].

The factors that might impact LIA mixture include surgeon and anaesthetist preferences, low BMI, age, comorbidities, and allergies. Pantoprazole, a proton pump inhibitor, offsets the multiple risks that contribute to gastrointestinal bleeding or peptic ulcer disease in the perioperative period. These factors should be discussed and altered pre-operatively, and still enlist fast track protocol.

2.1 Safety of local anaesthetic

Local anaesthetic agents are toxic at certain levels in systemic circulation. With any use of local anaesthetic, care must be taken to ensure LIA mixture is not injected directly into the patient's circulation. Local anaesthetic will inevitably be transported into circulation at a small concentration. However, it has been shown that the volume of local anaesthetic used in LIA technique is safe, and their levels in blood tests show sub-toxic concentration [18–20].

Fenten et al. took multiple plasma samples after LIA and torniquet release for TKA (at 20, 40, 60, 90, 120, 240, 360 minutes and 24 hours) [18]. The mix comprised of 200 mL 0.2% ropivacaine and 0.75 mg epinephrine 1:1000. Maximum ropivacaine concentration (total and unbound serum concentration) remained well below the assumed toxic threshold at all serum plasma samples. Stringer et al. studied LIA with the use of pain pump infusions for 48 hours post-operatively and measured ropivacaine concentration in THA and TKA patients [20]. The mixture contained 350-400 mg ropivacaine and defined their safe threshold concentration of 1–3 microg/mL intravascularly. Their intra-articular pain pump infusion commenced 12 hours post-operatively. Ropivacaine concentration was below 2 microg/mL with LIA intraoperatively. Once intra-articular pain pump infusion commenced, peak ropivacaine concentration reached 0.65–4.36 microg/mL, however none of their patients experienced clinical signs of toxicity.

2.2 Adrenaline

The inclusion of adrenaline in LIA cocktail is safe, but it is not well understood whether including it improves outcomes. Adrenaline works as vasoconstrictive agent which prolongs the local anaesthetic effect [21]. However, there is a concern in the recent literature for the usage of adrenaline and its impacts on vasoconstriction and skin necrosis [21, 22].

Van Der Zwaard et al. studied 502 TKA and unicondylar knee replacements, and compared one group of LIA with ropivacaine only with the other group of ropivacaine and epinephrine [23]. They found there was no difference in pain scores between the two groups. The authors of this chapter found the usage of adrenaline in a staged injection technique has benefits. Adrenaline prolongs the effect of local anaesthetic and decrease bleeding which mitigates swelling and haematoma formation, subsequently facilities early mobilisation. We recommend proximal infiltration deep to the deep fascia rather than injecting the skin and subcutaneous in TKR to avoid skin necrosis.

2.3 Corticosteroids

Inclusion of corticosteroids in the local mix is controversial. Periprosthetic infection is a dreaded complication with significant implications for the patient and is of concern with use of corticosteroids given the drug's immunosuppressive properties. Steroids prolong the duration and efficacy of the local mix [24]. A randomised control trial (RCT) showed that adding corticosteroid to the local anaesthetic cocktail improved 24 hour post-operative pain with no increased complications for 12-months, including deep infections [25].

3. Comparative regional anaesthesia options

Several pain management methods are used after TKR and THR such as PCA, narcotics, epidural analgesia, and peripheral nerve block. However, those methods are associated with complications; continuous epidural infiltration and femoral and/or sciatic nerve block improve postoperative pain control and reduce consumption of narcotics but at the expense of other potential problems such as epidural bleeding (with prophylactic anticoagulation therapy), infection, urinary retention, diminished muscle control and nerve damage [26–31]. PCA administration of opioids is often associated with nausea and vomiting, respiratory depression, drowsiness, pruritus, reduced gut motility, and urinary retention. Continuous intra-articular infusion of analgesics is associated with large effusion of surgical wound [15, 26]. Even though those pain management methods have reduced the acute phase of postoperative pain to some extent, they do not address the major concerns of venous thromboembolism (VTE) and hospital-acquired infections.

3.1 Intrathecal morphine

Intrathecal morphine has emerged as an alternative approach to managing post-operative pain following THA and TKA. Intrathecal administration of morphine would manage pain experienced by a patient with lower limb surgery and is commonly used for other procedures such as intra-abdominal and caesarean operations. However, the risks might be respiratory depression, bradycardia and hypotension, seizures, and urinary retention [32].

Both intrathecal morphine and LIA minimise the need for systemic opioid usage and improve patient outcomes. A large meta-analysis performed by Qi et al. compared intrathecal morphine to LIA in patients with THA and TKA [33]. Patients receiving LIA required less systemic opioids (13.52 mg) and had better visual analogue score at rest and mobility at 72 hours, and lower incidence of nausea or vomiting post-operatively.

3.2 Epidural anaesthesia

The epidural catheter is another option for managing pain in THA and TKA patients. Although less commonly used, it is a good way to manage pain and avoid use of oral opioids. While effective, it also carries certain risks including urinary retention, neurological deficits and epidural hematoma, and has a number of contraindications [34]. Berninger et al. in their study found that no difference in pain among different combination of anaesthesia and nerve blocks, however they found that the group that included LIA had higher mobilisation and better muscle strength in the early post-operative phase [35].

3.3 Peripheral nerve block

Peripheral nerve blocks are another widely accepted method for analgesia peri-operatively and post-operatively for THA and TKA. The blocks minimise pain experienced by the patient whilst being more specific than systemic opioids or intrathecal/epidural analgesia. Peripheral nerve blocks however can cause some delays peri-operatively compared to LIA. A sterile field, commonly with ultrasound needs to be prepared and is performed before or after operation, as compared to LIA which is performed intra-operatively.

A large meta-analysis found that pain six hours post-operatively was better when LIA is used compared to peripheral nerve block, but there was no difference between the two for pain later, opioid consumption, length of stay and complications such as deep infection and VTE [36]. Berninger et al. found that the LIA group had better mobility than those who had peripheral nerve blocks, but other parameters were no different [35]. It can be argued that better pain relief acutely and better mobility post-operatively can reduce risk of complications, such as VTE, and would improve patient satisfaction and outcomes [35].

Two common peripheral nerve blocks used for TKA are femoral nerve block and adductor canal block. Kim et al. in their randomised trial, patients underwent TKA received either an adductor canal block or a femoral nerve block, and measured quadricep strength and pain scores at different time frames [37]. They found that the adductor canal group had better quadriceps strength in the 6-to-8-hour post-operative window compared to the patients receiving femoral nerve block, and pain was no different. Quadriceps strength and pain was no different after 24 hours post-operatively. A key fundamental to Fast Track Arthroplasty is early mobilisation and return to function; avoiding motor blockade would assist a patient to functionally progress earlier.

3.4 Complementary patient-controlled analgesia (PCA)

PCA is a commonly used pain management technique that individualises patient need for analgesia and aims to give patients control over their pain management; this helps determine the required oral analgesia. Pandazi et al. performed a randomised controlled trial; two of the included groups were LIA with PCA as rescue versus PCA alone in patients receiving THA [38]. The LIA group was shown to have significantly better pain scores at rest and when mobilising, and had less overall morphine consumption, with no difference in adverse events.

PCA combined with LIA can help manage pain post-operatively for patients with THA and TKA. For some patients however, adding another intravenous line can impede mobility – the enhanced recovery after surgery (ERAS) aims to mobilise patients as soon as possible. A multi-modal approach to analgesia should be utilised, with LIA providing a useful option in a patient's management.

4. Fast track hip and knee arthroplasty is not a new idea

The use of fast track or rapid recovery arthroplasty has been successfully implemented within multiple health systems in many different countries globally over the past 10–15 years [14, 39–43]. To successfully implement fast track arthroplasty, the care pathway involved is complex and multidisciplinary. Goals include ensuring correct indication for surgery and candidate selection, pre-operative optimisation, safe and evidence-based peri-operative management, good functional outcome and high patient satisfaction [44]. According to the Enhanced Recovery After Surgery (ERAS) Society, there are about 20 components of care involved for implementation of effective protocols, which is undertaken in a multidisciplinary fashion including expertise from anaesthetics, surgery, physical therapy, nursing and nutrition [7]. These protocol has been successfully implemented into multiple surgical specialities including gynaecological oncology, urology, vascular and thoracic surgeries [7]. Along with individual studies, systematic reviews and meta-analysis highlighted the benefits of fast-track arthroplasty for lower limb [6, 7, 9].

Malviya et al. implemented a rapid recovery protocol for hip and knee arthroplasty in May 2008 in the United Kingdom. They found the median LOS decreased from

6 days to 3 days and requirement for blood transfusion reduced from 23% to 9.8%, which was statistically significant. Most notably there was a reduction in 30-day mortality from 0.5% to 0.1% along with reduction in 90-day mortality of 0.8% to 0.2% [42].

A retrospective study conducted by Auyong et al. on 252 patients who underwent rapid recovery protocol, showed a reduced length of stay, improved mobility, reduced overall opioid consumption with no difference in readmission rates or complication rates [39].

In Australia, Christelis et al. in their study on 709 patients compared a pre-ERAS and post-ERAS cohort. They found the ERAS group had a reduced LOS with no change in complication rates by 6 weeks post operatively, no increase in hospital readmission along with similar pain scores, and higher patient satisfaction at the 6 weeks post-operative mark [40].

Same day discharge arthroplasty has emerged recently that showed cost-effectiveness without jeopardising clinical outcomes [45]. Basques et al. identified several patient characteristics which favoured same day discharge including decreased age, male, lower ASA class, less obese along with lower rates of respiratory disease and hypertension [46].

5. Author's LIA technique

LIA is an effective method of post-operative pain control in hip and knee arthroplasty [11, 14]. This, combined with low- or no-dose opioid spinal anaesthesia, allows virtually avoids urinary catheters and ensures earlier mobilisation. This multi-modal opioid-sparing approach is central to the rapid recovery model of care, allowing safe early mobilisation with minimal pain. With the use of LIA there is the advantage of having no motor blockade [8], allowing the patient to be mobilised day of surgery.

The purpose of adoption of LIA technique is to provide comfort from the trauma associated with hip and knee arthroplasty particularly for the first 36 h post-operatively, during the time of high post-operative pain, to facilitate increased post-operative mobilisation and function. Further benefits for the use of LIA include no motor blockade also enabling mobilisation, along with reducing the requirement for systemic agents including opioids with associated negative side effects like nausea, vomiting and drowsiness [8, 14]. We have not observed local anaesthetic toxicity, impaired wound healing or increased risk of infection with the use of post-operative pain catheters inserted intra-articularly [8]. Further detail on evidence surround local anaesthetic toxicity is addressed in Section 2 however, nor have other authors found increased infections in hip and knee arthroplasty [13, 19].

The use of bolus injections via 0.22um filter and wound catheter into the joint on the morning after surgery possibly extravasates into surrounding tissues, especially in hip arthroplasty. However, dispersing the injection over a larger area is probably advantageous relative to local anaesthetic infusion, which may be concentrated at the tip of the wound catheter. Furthermore, it avoids "extra baggage" for the patient to carry.

Our LIA technique augments our multimodal therapy approach. Patients routinely receive paracetamol 1 g qid, meloxicam 7.5 mg bd, for more painful operations (TKA, or posterior approach THA) buprenophine 5ug/hr. patch, and tramadol 50 mg 3/24 prn.

5.1 Intra-operative considerations

LIA administration intraoperatively there are four aspects which need consideration; the components of the drug mixture, the injection of the mixture, the catheter placement and, application of compression bandage for TKA [14]. The details of the drug mixture are discussed in Section 2. Before wound closure, a catheter is inserted either intra-articular or periarticular for post-operative continuous or bolus application of LIA mixture.

The commonly used catheter is a 16G Tuohy needle, an 18G epidural catheter, and a 0.22-u high-performance antibacterial flat epidural filter (Portex, Smiths Medical) [10, 14, 19]. The use of a antibacterial filter has laboratory experiments show sustained efficacy of their use for 48 h continuous infusion [47] with efficacy in antimicrobial filtration for up to 60 days with low volume and low injection pressures [48]. To date the use of antibacterial filters have been used in several applications like epidural catheters and within LIA for post-operative delivery of anaesthesia with no reported increase in infections.

5.2 Total hip arthroplasty injection technique

A standard approach can be undertaken to local anaesthesia administration intraoperatively can be adopted regardless of approach used (anterior/posterior/lateral). The primary purpose is to provide anaesthesia to all area affected by the trauma of the surgery. The total volume used intraoperatively of anaesthetic mixture is 150-200 mL where three main stages of administration are involved.

- After skin incision typically 50 mL of mixture is used within the subcutaneous tissue and proximal gluteus maximus (posterior approach) or for 25 ml injected in the region of the lateral femoral cutaneous nerve (anterior approach). Administration is undertaken using a 'moving needle' technique.

- After cup implantation injection of 25 ml infero-medial capsule (where innervated by obturator nerve), and a further 25-50 mL injected through the capsule superiorly and anteriorly (posterior approach) or postero-superiorly (anterior approach) is performed. Once the definitive implantation of femoral components, injection of the periarticular tissue is performed with about 50 mL of mixture. Intra-articular epidural catheter is placed through skin and deep fascia with the use of a Tuohy needle where a small volume is injected to ensure no blockages prior to closing the deep structures. 5-10 cm of the catheter is placed intra-articularly. The exit position of the catheter through the skin within 2 cm of the incision allows it to be secured by the wound dressing. Note that particular care must be made during closure to ensure the catheter does not become inadvertently sutured.

This epidural catheter is then attached to either an antibacterial filter if the intention is post-operative bolus application of anaesthetic mixture or continuous elastomeric pain pump.

5.3 Total knee arthroplasty injection technique

As with hip arthroplasty, in knee arthroplasty the aim is to infiltrate local anaesthetic mixture into areas affected by the surgery. General principals can be broken into four main stages.

- Prior to skin incision, a block 10 cm proximal to the patella, just deep to the deep fascia, injection 25 ml from lateral to medial, and a second 25 ml injection medially in the region deep to sartorius. Administration is undertaken using a 'moving needle' technique.

- After femoral bone cuts are made injection through the posterior capsule of the knee with about 25 mL of mixture each side, aiming proximally, and away from the popliteal artery. Once the definitive implants are inserted structures around medial collateral ligaments, quadriceps, and tibial portion of the iliotibial band. The epidural catheter is placed through the skin, fascia, quadriceps, and joint capsule using a Tuohy needle, then inserting the tip of the wound catheter posterior to the medial femoral condyle. Also, as was mentioned with hip arthroplasty, care must be taken when closing the wound not to catch catheter with sutures which will impede catheter removal.

- The remaining mixture is used for infiltration into the synovium and capsule along with surrounding tissue in layers during closure.

- Compression bandages are then applied once the wound is dressed.

An alternate catheter placement can be within the adductor canal, performed intraoperatively. Adductor canal catheter placement may be performed under direct visualisation on subvastus approach. In recovery, ice pack should be applied hourly for 20-minute intervals for the first four hours to prevent swelling and assist in pain control.

5.4 Post-operative

5.4.1 Continuous infusion vs. bolus in LIA

The evidence favouring continuous, or bolus post-operative catheter regimes is limited. Early development by Kerr & Kohen used a bolus protocol in THA and TKA, along with other published protocols [10, 14, 42, 49]. Ballarat experience in their study published in ANZ Journal of Surgery in 2020 supported that bolus injection demonstrated better outcome. However, there is also evidence to support the use of continuous infusions of anaesthetic mixture delivered by elastomeric pump devices post operatively which has also shown success [50–52]. Typically, the infusion rate of 5 ml per hour for 48 hours if continuous infusion is used.

Our preference is 25 ml LIA cocktail without adrenaline is injected in the morning after surgery as a bolus.

5.4.2 Post-operative bandage

Compressive bandage applied post-operatively prolongs the local anaesthetic within the peri-articular tissues after TKA. An elastic binder compressing a sponge on the hip wound could be used but is not common practice and there is no evidence for efficacy. The bandage should be placed to have enough venous compression but not arterial compression [10].

A compression bandage is applied post operatively over the whole leg, from toes to high thigh, in three layers; one layer of soft padding, one layer of crepe bandage, and outer layer of elastic adhesive bandage as recommended by Kerr and Kohan in 2008 [10]. Another study confirmed the benefits of the compression bandage in TKA and demonstrated the improvement of LIA with compression bandage [53]. The compression dressing is removed 24–48 hours post operatively.

6. Pillars of fast track Arthroplasty

In recent times, many health care systems globally have undergone revision of their hip and knee arthroplasty pathways [40, 54]. The concept of ERAS, 'rapid recovery' or 'fast-tracking' aims to reduce operation-related physiological and psychological stress as well as enhance early mobilisation and reduce recovery time [44]. Implementation of this rapid recovery model has resulted in reduced length of stay with no increase in hospital re-admissions [40, 43]. In recent times, many health care systems globally have undergone revision of their hip and knee arthroplasty pathways [40, 54]. The concept of ERAS, 'rapid recovery' or 'fast-tracking' aims to reduce operation-related physiological and psychological stress as well as enhance early mobilisation and reduce recovery time [44]. Implementation of this rapid recovery model has resulted in reduced length of stay with no increase in hospital re-admissions [40, 43].

Three stages are identified in a patient's journey: pre-operative, peri-operative and post-operative. Pre-operative patient education is a recognised cornerstone in rapid recovery programs [54], with particular attention paid to patient expectation management regarding post-operative pain and LOS. Simultaneously, pre-operative anaesthetic review allows assessment and modification of patient risk factors that have been shown to reduce length of stay in hip and knee arthroplasty patients [55].

6.1 Preoperative

Rapid recovery protocol begins at the pre-admission stage. On presentation to pre-admission clinic, patients require education on appropriate expectations regarding their operation and post-operative course. An assessment tool in assisting prediction on length of stay and discharge destination (i.e. home or rehabilitation facility) is the Risk Assessment and Prediction Tool (RAPT) which has been previously validated [56, 57]. This tool is a score from 0 to 12, the higher the score the better, where points are given based on age, gender, average walking distance, requirement for walking aids, community, and home supports. With RAPT score < 6 the patient will likely require rehabilitation, between 6 and 9 the patient will likely be discharged home and with a score greater than 9 the patient will likely be discharged post-operative day 1 [57].

There is minimal evidence relating to the impact of preoperative patient education where a Cochrane review by McDonald et al. found preoperative education had no measurable impact on preoperative anxiety or surgical outcomes including pain, function and adverse events [58]. McDonald et al. however noted that there was much heterogeneity and low-level evidence within included studies and preoperative education may benefit patients with depression, unrealistic expectations, anxiety or those with limited social support [58]. The authors believe that setting expectations preoperatively is extremely important for patients prior to their day of surgery where they understand arthroplasty will involve pain which cannot be completely removed, they will be mobilised day of operation, and the primary goal will be discharged home once they are deemed safe. Patients should be prepared to go home post-operative day one.

Pre-admission optimisation is another essential factor when preparing for hip and knee arthroplasty. Assessment and optimisation of risk factors including smoking, alcohol consumption, anaemia, nutritional and metabolic status, and low physical activity has been shown to have a positive impact on length of stay and post-operative complications [59]. Smoking has been shown to increase early post-operative complications, however there is level 2 evidence showing that cessation 4 weeks or greater preoperatively can improve post-operative complications especially related to wound healing [8]. Preoperative optimisation within fast-track protocols has also been shown to reduce the number of patients with a delayed recovery [59].

6.2 Perioperative

There are several factors that are considered in fast-track arthroplasty regarding preparation for surgery including fasting duration and carbohydrate loading.

Although now relatively common practice, anaesthetic guidelines no longer recommend prolonged fasting status, rather a 2 hour clear and 6 hour solid fasting status prior to surgery [60]. Although a component of fast-track/ERAS protocol, carbohydrate has mixed evidence on impact of clinical outcomes in hip and knee arthroplasty even though there some studies have shown positive impact on post-operative hunger, pain, glucose metabolism and insulin resistance [8].

Standardised anaesthesia is another component included in ERAS protocols with mixed evidence regarding superiority between neuraxial anaesthesia/regional and general anaesthesia [7, 8, 11]. Several studies showed the benefit of neuraxial/regional anaesthesia including reduced pulmonary compromise, pulmonary embolism, need for transfusion, renal injury, infection, length of stay and 30-day mortality [61, 62]. Alternatively, a systematic review and meta-analysis by Johnston et al. found no difference between neuraxial and general anaesthesia [63]. In general, the aim with fast-track arthroplasty is to reduce systemic opioid use. This avoids associated side effects of opioid analgesia which can inhibit engagement in post-operative recovery by adopting effective multimodal analgesia and anaesthesia.

6.2.1 Tranexamic acid

There is potential for large blood loss with hip and knee arthroplasty which in turn can prolong hospital stay, increase risk of transfusion, renal failure and increase risk of deep infection. The inclusion of tranexamic acid in hip and knee arthroplasty is effective and safe medication which reduces blood loss with no increased risk of thromboembolic events [7, 8].

6.2.2 Post-operative nausea and vomiting

Post-operative nausea and vomiting (PONV) can be extremely distressing for patients which consequently impact their post-operative course. Risk factors include narcotics, inhalational anaesthesia, female sex, non-smoking status, history of motion sickness or previous PONV and predicted requirement for post-operative opioids [7]. Active screening and prophylactic treatment for at risk individuals is recommended, but our experience with Total Intravenous Anaesthesia (TIVA) or at least minimising inhalational anaesthesia suggests nausea and vomiting to be less common than it once was.

6.2.3 Active intraoperative warming

Maintaining normothermia must be a component of anaesthetic care for joint arthroplasty. When normothermia is maintained, it reduces infection, cardiac complications, transfusion requirements and coagulopathy [7]. With joint arthroplasty, aggressive warming has been shown to reduce intraoperative blood loss in total hip arthroplasty and reduce opioid requirements along with improved patient satisfaction in total knee arthroplasty [7]. Several techniques have been described to assist in maintain normothermia including warm IV fluids and irrigation fluid, prewarming and humidification of anaesthetic gases along with forced air-warming blankets and devices [8].

6.2.4 Avoid urinary catheters

With the use of low dose or no opioid spinal anaesthetic, urinary catheters are unnecessary for the majority of patients, avoiding bacteraemia which may increase risk of prosthetic joint infection [64]. A large RCT performed within a hip and knee arthroplasty ERAS program showed that increasing a catheterisation threshold from 500 ml to 800 ml over halved the incidence of catheterisation without increase in urological complications [64]. Routine use of urinary catheters is not recommended as per ERAS consensus statement for hip and knee arthroplasty and if used should be removed within 24 hours of insertion [8]. The catheter adds another line or attachment to the patient which increases risk of fall and does not facilitate early mobilisation. Lines should be removed as soon as possible to improve patients' psychological state and avoid any impediment to mobilisation. This not only pertains to urinary catheters but also applies to PCA and other IV lines unless required.

6.2.5 Surgical factors

Surgical approaches may play a role in ERAS THA and TKA however, the advantages or shortcomings between different approaches in both hip and knee arthroplasty in controversial in the literature. This will not be discussed in details, however, there is no conclusive evidence that surgical approach affect post-operative outcomes [8].

Tourniquet free TKR has recently gained popularity, a systematic review with meta-analysis conducted by Smith and Hing showed tourniquet does reduce intraoperative blood loss however increases rates of haematoma, blisters, superficial wound complications, VTE and pulmonary embolism [65]. Furthermore, the use of knee tourniquet has been shown to negatively affect strength with no impact on range of motion [8]. We do not use a tourniquet. We do not apply but not inflate the tourniquet as this technique often creates a venous tourniquet, making surgery more difficult.

The use of the routine post-operative drain shows no improvement for complications including wound infections, haematomas and healing complications [8] and may increase blood loss and transfusion rate [66]. We do not use drain tubes for primary arthroplasty.

6.3 Post-operative

During the post-operative period, the primary aim is to ensure the patient is at full function as soon as possible. This is assisted by ensuring there is adequate analgesia, and the patient is mobilised at the day of operation. Patients are deemed safe for discharge when satisfy the following criteria.

- Medically stable and well; bladder and bowels working and tolerating food and drink
- Pain controlled
- Safe mobilising which is assessed by physiotherapy
- Safe discharge destination with appropriate support
- Medications arranged
- Appropriate follow-up arranged.

Appropriate education for ongoing rehabilitation is crucial to ensure that they will continue to progress their mobility, strength and range of motion [8].

6.3.1 Block (wound) catheter management

The use of the wound catheter post operatively has varied between different protocols in the literature [11, 12]. The method initially described by Kerr & Kohen was a 50 mL top-up of the anaesthetic mixture used intraoperatively 15–20 hours post operatively with 15 mL injected primarily then the remaining injected as the catheter was removed [10]. Nassar et al. describe a top-up with their anaesthetic mixture 18–24 hours post operatively where 20 mL was injected then the catheter was removed [14].

Alternative protocols which have been used include continuous infusion of 250 mL ropivacaine 0.2% over 48 hrs at which case the catheter is removed. If bolus regimes are used the doses involved the first bolus 12 hours post-operatively and the last (second) bolus at 24 hours post-operatively, each under aseptic technique then removal of the catheter where each injection contains 10 ml of 1% ropivacaine, made up to 20mLs with 0.9% saline.

6.3.2 Mobilisation and function

Early mobilisation is a core component to fast-track arthroplasty protocols. Multiple studies have shown that early (ideally day of operation) mobilisation post-operatively reduced length of stay, thromboembolic risk, and mortality [42, 67]. A systematic review and meta-analysis of 5 RCTs performed by Guerra et al. showed that early mobilisation was associated with reduced length of stay by 1.8 days with no increased incidence of negative events or complications [68]. Consequently, all patients should be mobilised with physiotherapy on the day of their operation and if this is not possible due to a late return to ward, at a minimum they must be transferred to sit out of bed. With the use of LIA there is the advantage of having no motor blockade [8] which further facilitates early mobilisation. In fact, day of surgery mobilisation in TKA has been shown to reduce LOS and improve the likelihood of discharge home rather than to a rehabilitation facility [69]. A haemoglobin level is not required prior to mobilisation, and mobilisation must not be delayed awaiting routine blood results. If there are symptomatic concerns, then an urgent medical review should be requested. To further encourage mobilisation simulating home life is encouraged by having all meals, including the first meal, sitting out of bed along with mobilising to bathroom to open bladder or bowels instead of using bedpans or commodes.

The use of corticosteroids is controversial due to the theoretical risk of infection. As mentioned in Section 2.3 there is no increased risk associated with corticosteroid use of periarticular injection. A systematic review and meta-analysis by Yue et al. showed corticosteroid (dexamethasone 0.1 mg/kg) had reduced PONV and pain within 24 hours post operatively [70]. They also showed systemic steroid use had faster functional rehabilitation with no increased risk of infection however, there was increased rates of high serum glucose levels post-operative [70]. Thus, improved patient well-being and analgesia will encourage early mobilisation and facilitate in early discharge and improved post-operative function.

Early mobilisation does not include sitting. We strongly reinforce to our patients that if not mobilising, it is better to lay down than to sit down. Sitting and using a footstool is not helpful, the wound is too low relative to the heart, the veins are potentially occluded in the groin. We recommend patients minimise sitting to 5-10 minutes at a time - it is better to lay on the bed or lounge suite than allow the leg to become swollen. We use 20 mmHg compression stocking during daylight hours. This approach we expect will diminish the readmisssions after arthroplasty caused by swelling, pain, and potentially thrombosis.

6.3.3 Post-operative analgesia

Multimodal analgesia is a well proven analgesia technique within hip and knee arthroplasty [7, 8, 11, 12]. It targets pain through multiple different mechanisms of action to reduce sensation of pain while also reducing the side effects of any one agent. This has also been shown to limit requirement on opioid analgesia which reduces risk of short term side effects like nausea, vomiting, respiratory depression along with long term addiction and development of chronic pain [8]. This involves the use of paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) along with supplementary opioid analgesia [7, 8], although some of us (DJM) prefer tramadol 50 mg 3/24prn avoiding oxycodone in the vast majority of patients. There has also been evidence for the use of gabapentinoids post operatively that reduce post-operative opioid consumption, pruritus and nausea after joint arthroplasty along with improving sleep however no clear evidence on their role in post-operative pain [8].

6.3.4 VTE prophylaxis

The rate of symptomatic VTE after total hip and knee arthroplasty is approximately 1.9%, with a significant increase of greater than 40% in times where no chemical thromboprophylaxis was used [71, 72]. The National Institute for Health and Care Excellence (NICE) guidelines certifies the use of aspirin, low molecular weight heparin (LMWH), dabigatran, apixaban and rivaroxaban for reducing the incidence of VTE after total knee arthroplasty [73]. In THR, these guidelines support the use of LMWH, dabigatran, apixaban or rivaroxaban [73], with aspirin is not inferior to the other chemical VTE prophylactic agents [74].

Combination of chemical and mechanical thromboprophylaxis is required post-operatively. Ultimately, early mobilisation is significantly influential in reducing the risk of VTE after lower limb total joint arthroplasties, as well as reducing the use of indwelling catheters [75, 76].

We stratify our patients - in easily mobilised patients without other indications for anticoagulants, or past history of thromboembolic disease, we use aspirin 100 mg EC daily, and early mobilisation.

6.3.5 Aim to discharge directly home

Patients will be encouraged to discharge home rather than to inpatient rehabilitation unless indicated by medical issues or limited social supports as per RAPT score. In TKA, home discharge is not inferior to discharge to inpatient rehabilitation which is does not improve functional or patient-reported outcomes [77]. Similarly, inpatient rehabilitation after THA does not reflect any improvement in patient-reported hip pain and function compared to those discharged directly home [78].

7. Keys to success

7.1 Preoperative

- Setting patient expectations
- Use Risk Assessment and Prediction Tool (RAPT) to help predict discharge destination
- Medical optimisation

7.2 Perioperative

- Standardised practice
- Spinal with no (or low) intrathecal morphine
- No blocks that may affect quads, no fascia Iliaca block or femoral block.
- LIA cocktail infiltration
- Wound intra-articular catheter for postoperative cocktail administration

7.3 Post-operative

- Minimal attachments: no urinary catheter or no PCA & all drips and lines out within 24 hrs
- Day of operation mobilisation
- Multimodal opioid sparing analgesia

8. Conclusion

LIA is a good alternative compared to other traditional pain management techniques. LIA is safe and effective to achieve good outcomes, early mobilisation and decreasing length of stay without jeopardising clinical outcomes. Fast track arthroplasty is a holistic approach to patients who undergo total hip and knee arthroplasty, a journey or care that starts with setting patient's mind and expectation, optimising medical status, intraoperative LIA infiltration, decrease the usage of narcotics either in spinal or post-operative medication, discourage usage of PCA or IDC, encourage day of operation mobilisation and optimising post-operative physiotherapy protocols, post-operative exercise protocol.

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Chapter 9

Fan-Shaped Application of Local Abdominal Wall Analgesia in Abdominoplasty Patients: Does the Technique Lead to Better Recovery?

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Abstract

Plastic surgery can be considered an art form, molding and shaping areas of the body to provide enhancement and visual improvements. During this process, anesthesia is a key role player, for both local and general aspects. Proper combinations of local and general anesthesia can provide not only great pain relief and the ability to perform the artwork of plastic surgery, but can also lead to better and faster post-operative recovery of patients. Take a moment to imagine doing our skills without anesthesia, not only would it be barbaric, but also unethical. The method of using fan-shaped anesthesia application will be explored as a technique to improve patient recovery. This, instead of the classic straightforward areal injection application, seems to provide improved anesthetic distribution, penetrates layers better, and offers a swifter and more efficient way of blocking pain receptors. Choosing an appropriate anesthetic from the various ones available today is very important for pain control and postoperative recovery, as well as combining it with other drugs to increase its duration of action. This medley of drug combinations provides patient satisfaction and enhanced recovery.

Keywords: fan-shaped, anesthetic distribution, pain control, enhanced recovery

1. Introduction

The history of local anesthesia starts in 1859 with Niemann's isolation of cocaine. The first drug to be used as a local anesthetic was cocaine by Halstead in 1884. Later, in 1903, Braun used epinephrine as a chemical tourniquet. In 1948, Astra starts to use lidocaine in dentistry. Bupivacaine is discovered in 1957, which is a long-lasting local anesthetic we otherwise prefer. There are many articles detailing local infiltration analgesia used in the abdominal wall. This chapter outlines the use of different long-lasting analgesics in different dosages and compares different analgesics and applications in the rectus sheath, or wounds and nerve blocks. This is the only study that analyzes using this amount of a specific local long-lasting anesthetics (bupivacaine) in all abdominal wall and abdominoplasty wounds. We use general endotracheal anesthesia in abdominoplasty, tumescent infiltration for liposuction in specific dosages, and pure bupivacaine for infiltration of the abdominal wall and wound areas. The underlying reason for this approach is to facilitate easier and faster recovery in patients, and to mobilize patients after surgery in the shortest time possible. Postoperative conditions concerning the abdominal wall and wounds exhibit less pain, quicker mobilization, and activation of patients on the actual day of surgery and patients resume normal activities within a week after surgery. The tumescent solution with local anesthesia provides an analgesic peak after 8–12 h, losing analgesic quality completely after 48 h. With the inclusion of local infiltration analgesia in the rectus abdominis, external oblique muscles, in the inguinal region, and wound area in a section immediately before the closing procedure, wound pains are reduced in the early postoperative setting, but the effect of infiltrated tumescent fluid is not excluded. Our experience in local infiltration analgesia and analysis as well as talking with our patients after each operation provides the evidence that this analgesic infiltration using bupivacaine is useful in reducing pain during the first postoperative days compared to our other patients who in the past did not receive this type of local infiltration analgesia. This is the reason a larger study and more precise analysis should be undertaken as well as more precisely defining the parameters for obtaining scientific evidence that our method is indeed effective.

2. Surgical and analgesic considerations and methods in abdominoplasty

Abdominoplasty is the third most frequent form of body contouring surgery after breast augmentation and liposuction. In 2019, based on the American Society of Plastic Surgery (ASPS) analysis, there were a total of 123,427 cases in the USA. In all, 34 patients underwent abdominoplasty at the Bagatin Polyclinic in 2019. It is one of the most common and demanding procedures requiring significant recovery where patients are absent from work for 2–3 weeks and sometimes even longer. The age of patients varies from 19 all the way to 75 years of age. The oldest female patient who underwent abdominoplasty at our clinic was 75 years of age for a series of procedures that included breast augmentation and thigh tightening around the groin area. Age is not a limit factor in undergoing these procedures, but patient safety is always an important factor, and caution should be taken.

Among all the procedures covering everyday esthetic surgery, liposuction is statistically the most frequent procedure, which is frequently done in combination with abdominoplasty. It has developed through the years and stems from the eternal search for finding ways of achieving the ideal body dimensions, long-term vitality as well as slowing down and delaying the aging process. This surgical method permanently reduces fatty tissue from a specific part of the body which cannot be done or is very difficult using other methods for removing fat and body contouring. Parts of the body where fat accumulates and is difficult to remove through specific exercises are the abdominal part, the segment above the gluteus, thighs, and sections around the knees and upper arm.

The most often myth relating to this surgical procedure is the opinion that it is a method for treating obesity because the disproportionate deposits of fatty tissue are often visible in persons whose body mass index is within normal limits.

Besides removing fatty tissue, this surgical procedure also offers the following positive results:

- contouring parts of the body,
- tightening the skin,
- removing cellulite, with emphasis on parts of the body affected by cellulite which can be painful.

Modern liposuction can also be done under local anesthesia, which in turn enables communicating with the patient throughout the entire surgical procedure and an adequate evaluation of pain. The procedure is ordinarily limited to suctioning up to 3 liters of fat, and the patient is able to quickly return home after the procedure. This form of anesthesia enables abdominoplasty to be performed without plication of the abdominal muscles.

Liposuction has undergone a significant evolution from its beginnings to current mass use. The third generation of ultrasound technology based on VASER® (vibration amplification of sound energy at resonance) [1, 2] offers safer liposuction and satisfactory results, especially when wanting to achieve better definition using surface liposuction (**Figure 1**).

The abdominoplasty procedure ordinarily comprises VASER liposuction [1, 2] of the lower or more often lower and middle section of the back and VASER liposuction of the lower chest area, hips, and abdominal wall, most often plication of the abdominal wall longitudinally and the removal of excess skin in a lateral direction in the area of the lower section of the abdominal wall [3, 4]. It is relatively a significant and long operation often accompanied by intense pain and difficult recovery. This can be most evident in the first days following the operation. Hence, attempts are being directed to devising a specific type of analgesic, which will provide patients with the fastest and least painful recovery, as well as a quick return to daily activities and work.

The abdominoplasty procedure begins with infiltration of the abdominal wall with a tumescent fluid: normal saline solution (0.9% NaCl) containing adrenaline (1 mg), bupivacaine (12,5 ml of 5 mg/ml), and sodium bicarbonate (10 mL of

Figure 1.
VASER device and surgical instrument setup.

8.4% w/v), for each liter used [5]. It is then necessary to wait 10–15 min for the vasoconstriction and fat breakdown to take effect. The VASER used operates on an ultrasound principle which reduces larger segments of fat into smaller pieces, which in turn facilitates its removal. VASER technology provides a more sparing liposuction method that preserves blood vessels, nerves, and connective tissue, and consequently protects vascularization and sensitivity, while, on the other hand, acts specifically on fat and causes bloating and fragmenting of fatty tissue, facilitating the removal of fatty tissue into a less dense form. This reduces mechanical damage to tissue because the fat is more easily taken out using liposuction (**Figure 2**).

After a thorough liposuction, preserving vascularization and innervation of transitional structures and skin, the strengthening of the abdominal wall can commence, most often in terms of plication of the straight abdominal muscles (**Figure 3**).

In addition to the vertical strengthening of the abdominal wall, a horizontal or central plication is performed. This provides contours to the abdominal wall. Indeed, the BMI is always taken into consideration and should ideally be below 30. This is important, given that the internal abdominal content should be as minimally distended, as possible.

In this phase, a long-acting local anesthetic is administered [6, 7] to the plication area, the horizontal incision, and in the oblique radial direction, across the area of the abdominal wall, toward the hips. This is done to reduce pain in the initial phase, after the operation, and to achieve maximum recovery and mobilization. Optimally, this reduces more serious complications, such as deep vein thrombosis and pulmonary embolism, due to faster postoperative mobilization.

The next step is a fixation of the lower horizontal incision. Freeing the umbilicus and removing excess skin and subcutaneous tissue in the lower area of the abdominal wall are performed. Care is always taken to remove a similar amount of tissue on both sides (**Figure 4**).

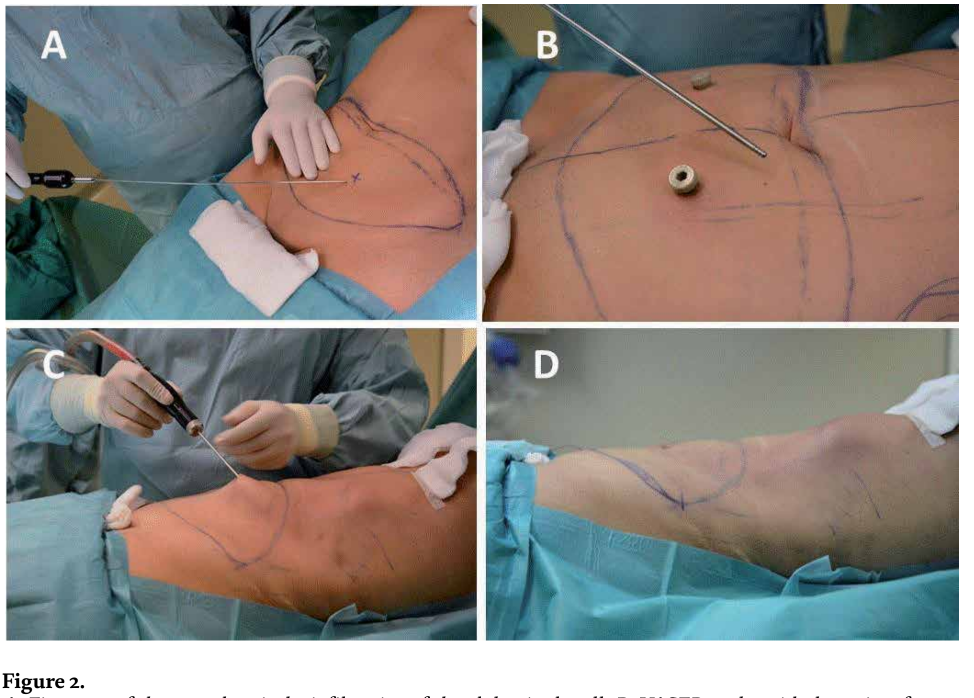

Figure 2.
A: First part of the procedure is the infiltration of the abdominal wall, B: VASER probe with three rings for ultrasound application on the abdominal wall, C: VASER liposuction with VentX cannula, and D: Result immediately after VASER liposuction.

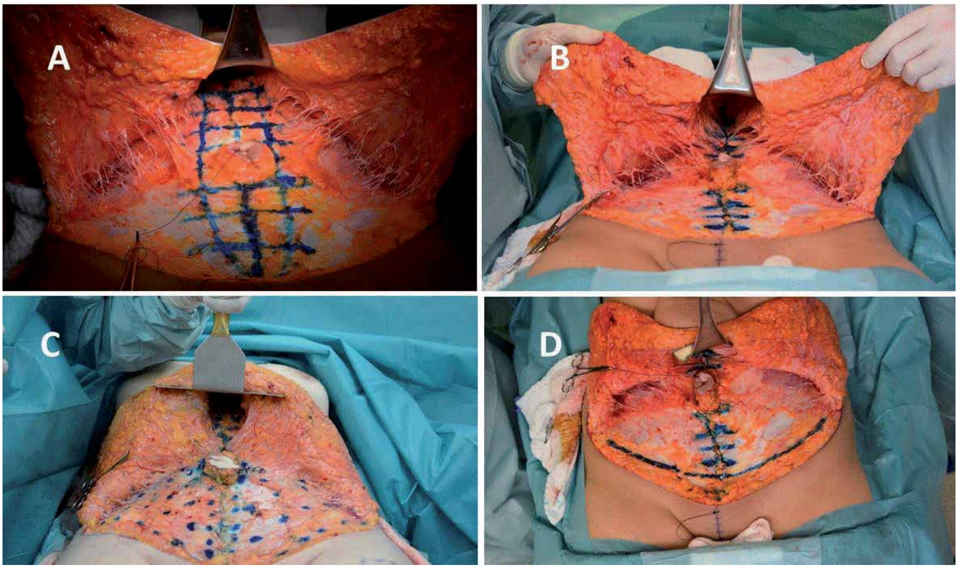

Figure 3.
A: Markings for plication of straight abdominal wall muscles, B: Result after plication of abdominal wall muscles, C: Markings for application of long-lasting infiltration analgesia, and D: Markings for fixation of lower abdominal wall straight scar.

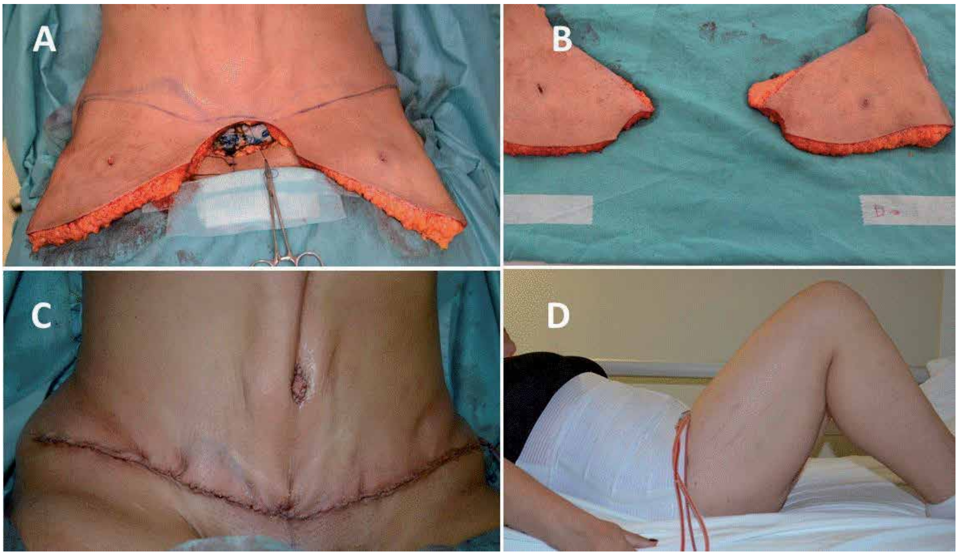

Figure 4.
A. Excess of skin and subcutaneous tissue in abdominoplasty patient. B. Removed tissue in abdominoplasty patient. C. Appearance at the end of abdominal wall surgery (abdominoplasty), and D. position in bed after abdominoplasty.

Within this phase involves the further mobilization of skin and subcutaneous tissue, as required. The fixation of skin and subcutaneous tissue is performed horizontally and if necessary, vertically to a lesser extent, to achieve the desired results. The final phase involves further freeing of the navel, within the mobilized skin and subcutaneous lobe centrally and this is then fixed into a position just above the hips. Pressurized drains are placed to drain excess fluids. All the wounds are closed off in layers. Sterile surgical bandages and compression garments are applied. The bed should be with an elevated head position, the patient lying comfortably on

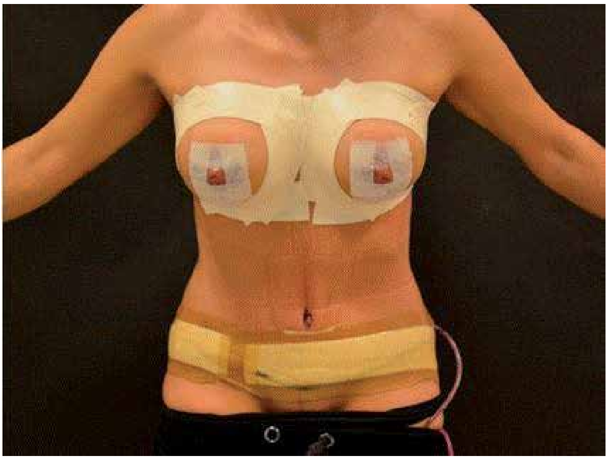

Figure 5.
Final presentation and straight position of the patient day after surgery. This shows that patient can straight up without pain immediately after surgery. This is very important for overall recovery.

their back, legs bent at the knees, to provide support, and careful not to stretch the freshly operated abdominal site (**Figure 5**).

3. Innervation of the abdominal wall

The thoracic ventral rami (intercostal nerves) are allocated mostly in the region of the anterolateral walls of the chest area and abdominal wall. There are 12 of them on each side, but only 11 are intercostal. Twelve pairs are situated under the last ribs and end in the subcoastal area. The upper six pairs of intercostal nerves are limited to supplying the thoracic parietal region, and in addition, a significant number of fibers from the upper two pairs participate in forming the brachial plexus, innervation of the upper extremities. The lower five pairs of intercostal nerves and subcostal nerves supply the parietal region of the chest and abdomen area and provide fibers to the diaphragm [8].

Typically, the lower 7–12 thoracic and intercostal nerves extend longitudinally toward the thoracic abdominal wall under the respective ribs and intercostal veins. Behind, the nerves extend between the pleura and rear intercostal membrane, and then between the internal and most internal (last, rear) intercostal nerves. Each nerve provides collateral branches and lateral cutaneous branches. The last ones separate from the primary ramus only a few centimeters from the spine, lowering downward into the same intercostal layer as the larger nerves, extending longitudinally along the lower boundary of the intercostal area and ending in the front as small cutaneous nerves or as connected to the main ramus. The lateral cutaneous branch follows the main intercostal nerve to the middle axial line before penetrating the intercostal nerve obliquely and is divided into front and rear branches that have a larger cutaneous distribution. Intercostal nerves supply the intercostal, subcostal, and transversal thoracic muscles. The lower five or six intercostal nerves also supply filaments of the peripheral parts of the diaphragm [8].

The five lower intercostal nerves and subcutaneous nerves stem from the lower rib cartilage and enter the abdominal wall to supply oblique, transversal, and horizontal abdominal muscles and end as the anterior abdominal cutaneous branches. The tenth nerve serves as a dermatome at the umbilicus level. The lateral cutaneous branch of the subcostal nerve (T12) penetrates the internal and external oblique muscles and then extends lower over the iliac crest so as to assist in supplying the skin on the lower lateral area of the groin [8].

The ventral primary ramus of the lower spinal nerves (five lumbar, five sacral, and one coccygeal) are divided and connect in a plexiform manner to form the lumbar, sacral, and coccygeal plexuses. They are interconnected as described earlier (rami communicantes) with the sympathetic trunks.

The lumbar plexus is formed with the ventral rami from the first three lumbar nerves and mostly the fourth (and also partly from the subcostal twelfth nerve). It is situated in front of the lumbar transverse vertebral body and sits in the rear section of the psoas major muscle which should be dissected for the plexus to be visible. The most common flow and distribution of plexus components and its relationship with bone structures as well as muscle and aponeurotic layers are shown on the next two pages, but consideration should be given to the fact that variations within the system of the lumbar plexus are frequent [8].

After gaining a branch from the subcoastal nerve, the first lumbar nerve is divided into the upper and smaller lower branches. The last section in the iliohypogastric and ilioinguinal nerve is later connected to the branch of the second lumbar nerve to form the genitofemoral nerve. The remainder of the second lumbar nerve, third and fourth nerve that contribute to this plexus are divided into front and rear sections that in turn are connected to form the obturator and femoral nerves. The accessory obturator nerve, when present, forms from branches in the front section of the third and fourth nerves, whereas the lateral femoral cutaneous nerve appears with the fusion of small parts of the rear sections belonging to the second and third lumbar nerves. The muscle branches from the subcostal and upper four lumbar nerves supply the quadratus lumborum muscle and those from the first and second extend to the psoas major and minor muscles. The psoas major muscle is further innervated with branches from the third and sometimes fourth nerve, which also supplies the muscle iliacus [8].

The iliohypogastric and ilioinguinal nerves are similar to thoracic nerves based on their position and distribution and are analogous to the main trunks and collateral branches of the intercostal nerves. The last nerve provides the lateral branch, which passes over the iliac crest a short distance behind the respective branch of the subcostal nerve, where both nerves then extend to the skin in the upper lateral section of the groin. Extending toward the front branch of the iliohypogastric nerve, it sends filaments toward the transversal and oblique abdominal muscles, passing through the external oblique aponeurosis some 3 cm above the surface inguinal ring and ending with innervation of the skin above the pubis [8].

The ilioinguinal nerve supplies the filaments of the adjacent muscles and after passing through the same muscles, as is the case with the iliohypogastric nerve, it passes under the funiculus spermaticus and through the superficial inguinal ring to supply the upper internal side of the groin area, the root of the penis and front section of the scrotum in men as well as the mons pubis and labia majora in women [8].

After leaving the lumbar plexus, the genitofemoral nerve passes through the psoas major muscle and descends to its anterior surface behind the peritoneum, which is then segmented at the fifth lumbar level into the genital and femoral branches. The last branch enters the inguinal canal through the deep inguinal ring, supplying the cremaster muscle, and provides some branches for the scrotum skin and labia major (external spermatic nerve). The femoral (lumboinguinal) branch passes laterally from the external iliac and femoral artery, passing behind the inguinal ligament and after passing through the anterior layer of the femoral sheath and fascia lata branches into the surface skin and skin of the upper section of the femoral (Scarp's) triangle. The genitofemoral nerve and its branches carry many efferent and afferent fiber to and from the common iliac, external iliac, and femoral arteries [8].

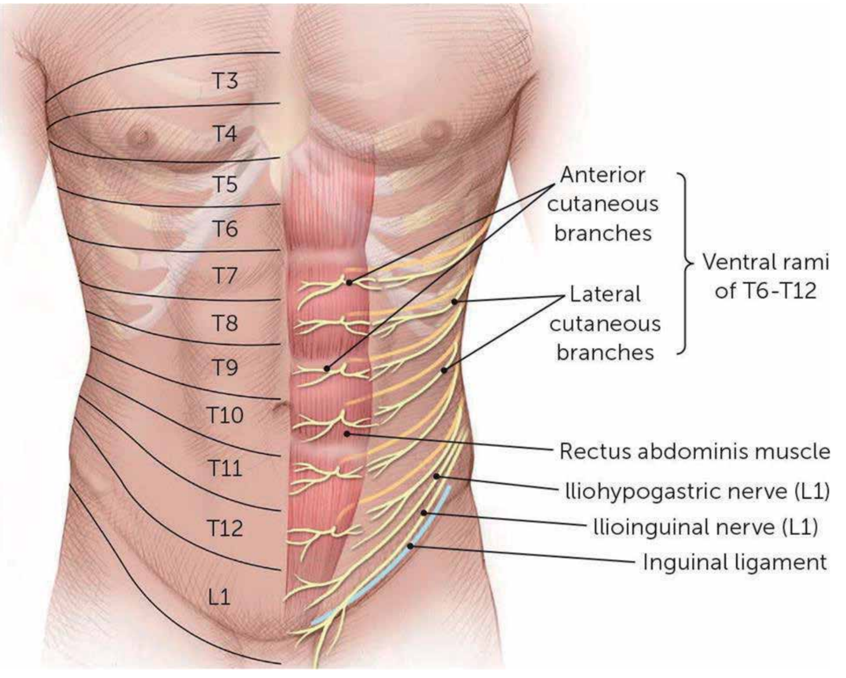

Figure 6.
Innervation of the abdominal wall in the male patients [8].

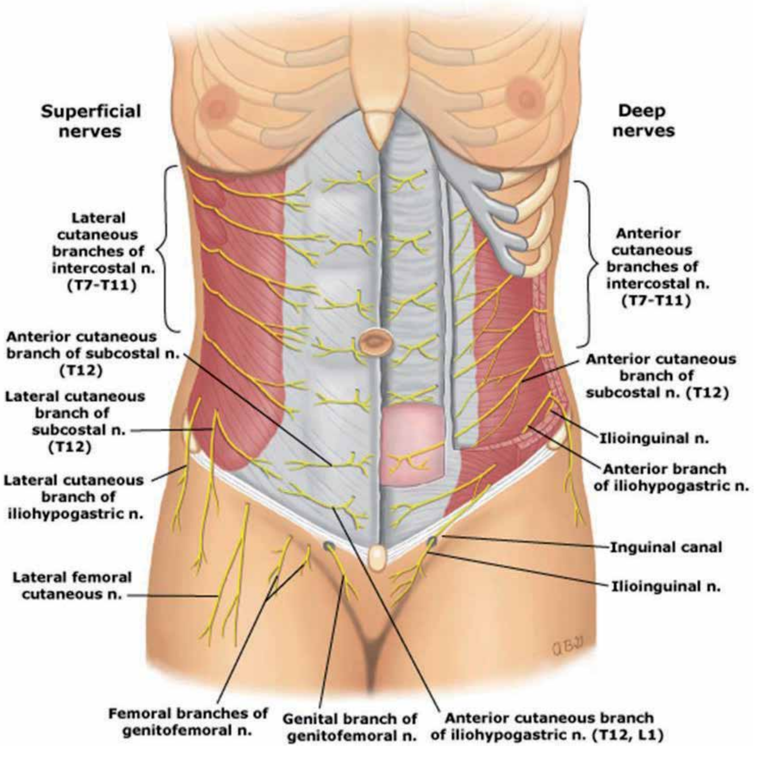

Figure 7.
Innervation of the abdominal wall in the female patients [8].

The other branches of the lumbar plexus (larger branches, femoral nerve) with the exception of the muscular branches for the quadratus lumborum, psoas major, and muscle iliacus are allocated at the lower extremities and that is why they are not discussed here [8] (**Figures 6** and 7).

4. Prophylactic (preemptive) analgesia

This kind of analgesia is a new approach to treating postoperative pain and blocks surgically caused painful sensitivity using regional or systematic anesthesia, prior to its onset. Therapeutic use of the prophylactic analgesia is based on local infiltration anesthesia (LIA) subcutaneous in the area planned for the surgical incision or for instance in the area of the abdominal wall.

LIA implies blocking incoming nerve paths prior to the onset of pain sensitivity due to incision of the skin and subcutaneous tissue, as well as contact with abdominal wall muscles, thereby preventing or reducing the level of pain occurring due to terminating paths of the nervous system between surgically sensitive organs and the brain [9].

The positive effects of a well-planned preemptive analgesia during a surgical procedure can be well utilized for the general well-being, meaning primarily for the patient, and then also for institutions in which the procedures are undertaken, because possible harmful effects can be well supervised and prevented under controlled conditions. Anesthesiologists in collaboration with surgeons determine the most effective preemptive analgesic regime for limiting sensibility of the nervous system throughout the entire perioperative period.

The concept of preemptive analgesia is based on advancements and research in the science of pain, as well as on clinically proven research. It has been shown that a surgical incision is not the only catalyst for central sensitivity of the nervous system, and accordingly, preemptive analgesia is further profiled and developed [10].

Regardless of the results obtained and proven in clinical research on animals, in clinical practice not only in Croatia but throughout the world, controversies do exist in terms of administering preventive analgesia. The reason for this is the general consensus that there is insufficient evidence as to the one-hundred-percent effectiveness of this manner of preventing postoperative pain. The recommendation is, therefore, to expand antinociceptive protection during the postoperative period, which ensures preventing analgesic infiltration, in order to include the most effective possible treatment for the inflammatory phase in the location of the operative area. Some studies on animals have shown that anesthesia techniques that deeply reduce the amount of information on pain reaching the spinal cord and brain may prevent central sensitivity and reduce pain-linked behavior when given prior to the onset of pain [11].

5. Description of analgesia applied to the abdominal wall

As we have previously described in the anatomy section, it is clear that there is a nerve supply in the area of the abdominal wall from T7–11 intercostal nerves and the T12 subcostal nerve, leading to the anterior and lateral segments, as well as the iliohypogastric and ilioinguinal nerves and their branches. Based on the actual procedure and experience, painful stimuli of the abdominal wall are certainly caused by liposuction, plication of the abdominal wall, lower fixation of the lateral scar, and closing of wounds. This is the main reason why, in the earlier stages of general analgesia and liposuction, the decision to administer additional analgesia into the abdominal wall with 40 mL of levobupivacaine or bupivacaine (0.5%) is used. This step is very important, depending on the availability of local long-lasting anesthetics and analgesics [9].

The pattern of administering the local anesthetic is radial, in the form of a fan-shape. It is applied with a G23 needle, administered centrally, toward the sides, and in the region of the horizontal incision, approximately 40 injections on each side, using 40 ml of the solution. Each jab provides 0.5 ml of local anesthetics.

Levobupivacaine, as opposed to lidocaine, is a long-lasting local anesthetic, providing significantly more than 2–3 h of anesthesia (>9 h) and up to 24 h as analgesia [6, 7]. It acts by blocking transmission in sensory and motor nerves through sodium channels on the cell membrane, but also by blocking potassium and calcium channels. It is far less systemically toxic than lidocaine. It is used as an anesthetic in larger surgical procedures, for instance as an epidural during a cesarean section, as well as an anesthetic in smaller surgical procedures, like those done on the eye. It is used as an analgesic for epidural infusion in treating postoperative pain or as an analgesic during labor. It is contraindicated for patients with known sensitivities against levobupivacaine and bupivacaine, or some of the auxiliary substances, as an intravenous regional anesthesia, and in patients with cardiovascular shock due to serious hypotension.

Due to its known interaction with some drugs, an important factor in the proper and quality administering of levobupivacaine is the experience of the operator.

The most often recorded adverse side effects are mostly related to the side effects based on the group of drugs to which it belongs, which includes hypotension, nausea and vomiting, anemia, dizziness, headache, pyrexia, and fetal distress syndrome. Compared to bupivacaine, levobupivacaine has been shown to have a long-lasting effect, less indirect toxicity, reduced cardiac effect in terms of bradycardia, and a weaker depressive effect on the CNS **Figure 8**.

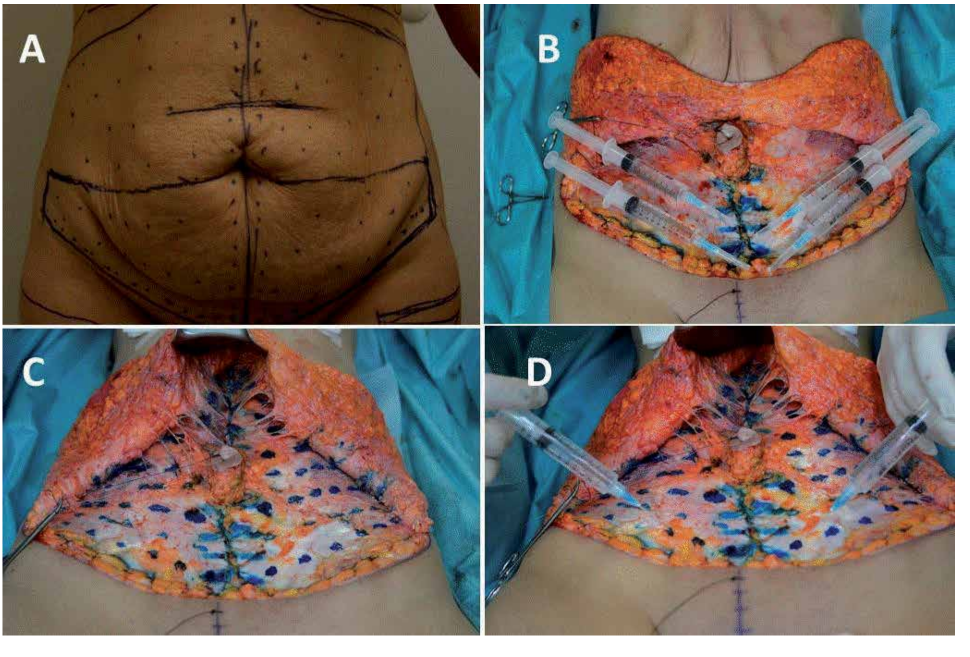

Figure 8.
A. Plan of application of local abdominal wall analgesia on the skin. B. Long-lasting local infiltration prepared for application. C. Plan for application of local infiltration analgesia in the abdominal wall, and D. application of long-lasting local anesthetic in the abdominal wall.

6. Treating acute postoperative pain

In the literature as well as in clinical practice, pain treatment is often addressed in procedures involving modern analgesia, which, in addition to the continual administering of drugs, implies the continual evaluation of pain, with the aim of titrating the administering of analgesics depending on the changes to pain intensity. All available and applied processes, whether it involves techniques for overcoming pain or administering drugs, must satisfy criteria requiring minimal negative effects on patient mobilization, which in turn means preventing the onset of expected complications and their least possible manifestation. Therefore, the basis for solving postoperative pain is preemptive action, which has the following goals:

- Preventing and halting the transmission of painful stimuli to the central nervous system,
- Preventing the onset of excessive oversensitivity to pain, that is, hyperalgesia, as well as preventing allodynia, which is the onset of pain due to non-painful stimuli,
- Thirdly, reducing the sensitivity of the central nervous system.

In patients who have undergone liposuction and abdominoplasty, the expected period of the presence of pain is relatively long. Therefore, a standardized approach is used in pain management, where an important role is given to the medical nurse as part of the team. It is necessary to do the following:

- Inform the patient of the available methods for preventing postoperative pain,
- Encourage the patient to articulate their sense of pain,
- Educate patients on the importance of taking analgesics over an agreed period of time at intervals,
- Show the exceptional importance of regular medical checkups and regular pain evaluation in order to undertake corrections to analgesic therapy.

Administering analgesics mostly implies the use of opioids. Opioid analgesics have quite a wide range of difficulties and complications, and their use requires educated personnel, in order to achieve the best effect with minimal side effects. Opioid doses used to act on acute postoperative pain are very low; hence, the negative effects are minimal to almost unnoticeable, whereas the internal of administering them is varied depending on the evaluation, which in the first hours is measured in intervals for at most one hour.

Doses are repeated until the desired effect is achieved, and the level of pain is reduced to under level 3 on the VAS scale of 10. The prescribed algorithm for administering drugs given estimates based on the VAS scale is as follows:

- Level 1—pain on the VAS scale amounting to 4—non-opioid and adjuvant drugs,
- Level 2—pain on the VAS scale amounting to between 4 and 7—non-opioid, opioid, and adjuvant drugs,

- Level 3—pain on the VAS scale amounting to between 7 and 10—strong opioids, non-opioids, and adjuvant drugs.

According to this model of levels, the principles in administering drugs are as follows:

- Whenever possible per axis,
- Administer in exactly specified intervals,
- Administer according to a level-based schedule.

Among the non-pharmacological techniques in treating postoperative pain, a psychological approach has been proven to be adequate by reducing anxiety and fear as well as preventing sleep disorders, and also contributing to the well psychological condition of the patient.

The psychological approach is achieved through the following:

- Good quality information provided to the patient,
- Relaxation techniques—proper breathing, muscular relaxation,
- Stress management.

7. Our experience with the described technique

We have analyzed a total of the 30 most recent patients (N = 30) on whom the VASER liposuction and abdominoplasty procedures were undertaken at the Bagatin Polyclinic in Zagreb. The patients were analyzed in the 2020/2021 period. About 67% of the patients were women, and 33% were men. The surveyed group of women ranged from 19 to 51 years old, and the men varied from 21 to 61 years of age. The bodyweight of the women ranged from 46 to 110 kg and a body height from 155 to 178 cm. The bodyweight of the men ranged from 63 to 108 kg, and a height from 167 to 190 cm. Of the 30 subjects undergoing VASER liposuction and abdominoplasty, 13 were smokers of which 9 were women and 4 men, and 17 were nonsmokers, that is, 12 women and 5 men. In terms of the ASA score, 17 were categorized into Group 1, 12 into Group 2, and 1 into Group 3. All patients were recommended not to smoke 4–6 weeks prior to the operation and also the period after the procedure. The longest operation lasted 8 h and 30 min, and the shortest was 2 h.

Of the total number of subjects who required analgesics in the postoperative period, 69% receive the drug immediately and 29% in less than 10 min, and 2% had no need for analgesics. In all, 64% of the subjects who received some form of an analgesic did not report any of the examined difficulties such as tenderness and soreness, prolonged loss of sensation, difficulty with breathing, headaches, sleepiness, itchiness, or constipation. In the remaining 36% of subjects, vomiting was present.

On a scale of 1–5, as to the question of assessing satisfaction with hospitalization, 100% of the subjects provided a score of 5. Also, all 100% of subjects received directions on pain treatment immediately while being discharged.

Upon being discharged to home care, 60% of the operated patients continued to take analgesics in the period ranging from 3 to 15 days. **Figure 9** shows the number

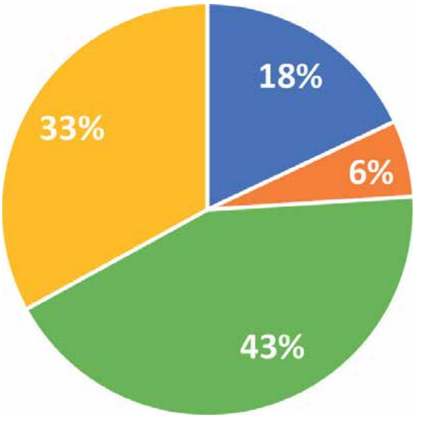

Figure 9.
Percentage of patients taking analgesics at home.

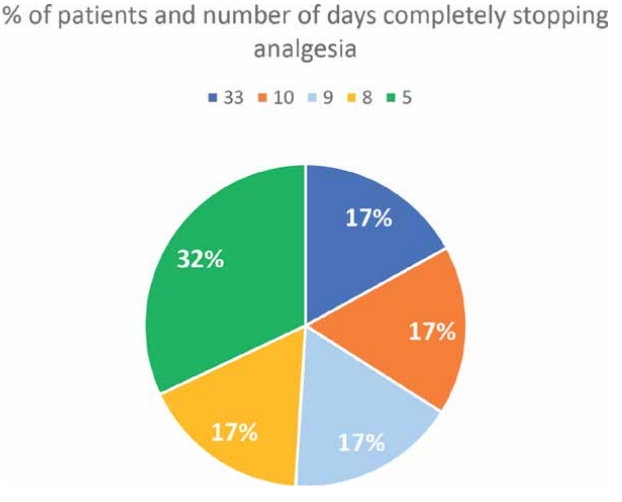

Figure 10.
Percentage of patients and the number of days completely stopping analgesia.

of patients who took analgesics at home, and **Figure 10** shows the number of days after completing ceasing to take analgesics.

Of the total number of operated patients, 7% said that the recommended analgesics were sufficient in overcoming pain, and 93% took medication only temporarily when experiencing stronger pain. In the period covering 10 days of home care, 20% completely ceased taking analgesics. A month after the surgical procedure, the level of pain in the subjects had significantly subsided, whereas the level of pain after three months had almost completely ceased in almost all patients.

8. Discussion

The fan-shaped, local infiltration anesthesia (LIA), this technique provides a more dispersed area of anesthetic coverage. Although this technique can be more expensive due to the cost of longer-lasting local anesthetic drugs, it allows for an increased certainty that all desired areas will have adequate pain relief, with minimal breakthrough or patchiness. As presented in pain scoring and drug requirements for pain relief data, the pain scores were significantly reduced, a shorter duration of analgesia was required, and overall patient satisfaction was increased. The advantages seen with this technique are as follows: a faster, more complete analgesic spread in the operative area, less areas being missed out or untouched, reduced postoperative pain, reduced need for long-term analgesic requirements, and increased patient satisfaction. The ripple effect of these advantages leads to faster mobilization, improved and enhanced healing, a faster convalescent stage, and a return to a preoperative functioning state.

9. Conclusion

Fan-shaped LIA is a preventative procedure in managing acute postoperative pain which is based on the systematic, targeted infiltration of local anesthetics plus adrenaline to the operative area which in this case is the abdominal muscular wall. The fan-shaped LIA technique enables quick mobilization of patients and their early discharge.

Pain symptoms are considered an ideal parameter for assessing the quality of the fan-shaped LIA application, in postoperative patient care, not only in hospital environments but also in outpatient surgical practices. Pain management as part of medicine has undergone vast development in the last two decades. However, the treatment of pain still needs to be addressed adequately, which means establishing a specific series of protocols in order to prevent and not only treat pain. The statement, "better to prevent than treat" states a lot about this aspect.

The modern era has placed before us a great challenge, not only before physicians and other health care experts, but also the entire system of management in every country, in order to identify a better way of organizing work, and allocating work tasks on a daily basis, in order to eliminate obstacles that stand in the way to successful practices in pain management. The effectiveness of treating pain is closely linked to an awareness of consequences stemming from suffering caused by pain, including the psychology of pain, the effects of stressors from the immediate environment, cognitive perceptive abilities of persons, and life attitudes.

Administering long-lasting local anesthetics prior to and after a surgical procedure has a significant effect on reducing the intensity of postoperative pain due to surgical procedures involving VASER liposuction and abdominoplasty, which leads to discharging patients from the polyclinic on the same day as undergoing the surgical procedure, or at most within 48 h after the procedure.

Administering fan-shaped LIA intraoperatively into the abdominal wall provides early mobilization and quicker recovery of patients. The fact that patients feel less soreness within the first 48 h after the surgical procedure, their ability to actively mobilize earlier, and their satisfaction gives confirmation to use this method routinely.

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Chapter 10

Tackling Local Anesthetic Failure in Endodontics

Krishnamachari Janani, Kavalipurapu Venkata Teja, Harini K, Kaligotla Apoorva Vasundhara and Jerry Jose

Abstract

Achieving anesthesia in a hot tooth or tooth with inflamed pulp is challenging, especially during endodontic treatment. In the presence of symptomatic irreversible pulpitis, mainly in mandibular teeth, pose even more challenge to attain profound anesthesia. Tetradoxin resistant channel is a class of sodium channel that is found to be increased in such condition and is found to resist local anesthesia. The pH also determines the success of local anesthesia. In inflammatory conditions, the surrounding area's pH, which eventually decreases the amount of base form of local anesthetic penetration into the nerve membrane, thereby causing anesthetic failure. In such conditions, the excitability threshold is reduced, leading to failure in achieving anesthesia. This chapter highlights and discusses the cause of anesthetic failure and its management in obtaining profound anesthesia during endodontic treatment.

Keywords: Local Anesthesia, Endodontic Treatment, Pain, Irreversible Pulpitis Pulpal Inflammation

1. Introduction

Pain is an unpleasant sensation that can range from slight discomfort to excruciating agony and can be linked to actual or potential tissue damage [1]. It is a multimodal and biopsychosocial event with an individual objective and subjective occurrences, resulting in significantly diverse perceptions of pain between the individuals. One of the most common reasons for a patient to visit an endodontist is dental pain. Managing dental pain and anxiety during and after treatment is still a difficult task, which depends on the clinician's skill and knowledge [2].

2. Pulpal inflammation

In symptomatic pulp tissue diagnosed with irreversible pulpitis, extracellular levels of Substance P are elevated. When comparing pulp tissue diagnosed with irreversible pulpitis to clinically normal pulp tissue, an 8-fold rise in Substance P was found [3]. As a result, irreversible pulpitis is linked to high peptidergic system activation. It is generally known that root canal preparation causes inflammation in the periapical tissues, explaining why root canal therapy causes post-treatment pain (such as symptomatic apical periodontitis). SP is released in the periodontal ligaments as a result of varied canal preparation approaches, which was found to be quite interesting. However, the amount of released SP differs among procedures. Inflammation in the periapical tissues could be triggered by an elevation in SP [4]. This might thus be considered a key mediator of neurogenic inflammation and related hyperalgesia, and hence a prospective target for therapeutics targeted at regulating pain and minimizing the harmful effects of tissue injury [5].

When a carious lesion gets close to the pulp, the pulp's inflammatory alterations get worse. An acute exacerbation of chronic inflammation occurs at this stage, with an influx of neutrophils and the release of inflammatory mediators (prostaglandins and interleukins), proinflammatory neuropeptides and mediators (substance P, Bradykinin, and calcitonin gene related peptide) [6]. These mediators can increase pain perception and neuronal excitability by stimulating peripheral nociceptors within the pulp of the affected tooth. This causes moderate-to-severe discomfort. Conventional procedures may not provide sufficient anesthesia. As a result, endodontists must achieve profound anesthesia in order to alleviate the pain [7].

3. Local anesthetics

The use of local anesthetic agents in pain management plays a vital role. It is the safest and most effective medications to prevent and manage pain during dental treatment [8]. Today's availability of a variety of local anesthetic agents allows dentists to choose an anesthetic with specific properties such as time of onset and duration, hemostatic control, and degree of cardiac side effects that are suited for each individual patient and dental operation [9]. 2 percent lignocaine (Xylotox, Adcock Ingram; Xylesthesin, 3 M) with 1:80000 adrenaline content, 3 percent mepivacaine (Carbocaine) without a vasoconstrictor and 4 percent articaine (Ubistesin 3 M) with either 1:100000 or 1:200000 adrenaline concentration is currently the most commonly used local anesthetic agents in general dentistry [10]. Each local anesthetic has its own maximum recommended dose (MDR) measured in mg/kg body weight. Unfortunately, the literature7 shows that the mg/kg MDR for each drug ranges from 4.4 mg/kg 8 to 6.6 mg/kg [11, 12].

4. Evaluate the anesthesia before treatment

When dealing with a tooth that has been diagnosed with irreversible pulpitis or "Hot" tooth, it's critical to determine whether enough local anesthetic has been attained. Subjective and objective testing has historically been used to validate successive inferior alveolar nerve block (IANB). Signs such as lip numbness, probing the gingiva surrounding the tooth to be treated, and so forth are examples of subjective tests [13]. Patients should not suffer discomfort throughout therapy if they respond favorably to the subjective results. These approaches, however, are not confirmatory test for detecting pulpal anesthesia.

5. Failure of local anesthesia

5.1 Anatomic factors

While it's possible that the operator's inability to deposit anesthetic solution close to the targeted nerve would result in an insufficient blockade in both normal and non-inflamed states, it's also possible that a partial blockade would suffice in neurons that inflammatory mediators did not sensitize. It's crucial to understand the nerve supply to the anesthetized tissue and the anatomy of the injection site and any changes [14].

During a local infiltration at the root apex, however, the cortical bone of the body of the mandible can effectively block the anesthetic. The maxillary cortical bone is often thinner. Anesthetic diffusion is more easily achieved through this bone. Therefore, infiltration anesthesia, which is routinely used in the maxilla, would be less affected by anatomic variance. Block anesthesia is advised in the mandible because it is more predictable. Still, it demands a deeper awareness of the deep anatomy of the jaw and is more technique sensitive, which is why anesthetic failures in the mandible are more common. Inadequate local anesthetic has also been linked to accessory innervation of the mandibular teeth from various sources. The nerve to the mylohyoid muscle, in particular, has been linked to the transport of afferent fibers from the mandibular teeth [14]. The clinician has many alternatives for overcoming accessory innervations from the mylohyoid nerve, including using a blocking technique that deposits anesthetic solution higher in the pterygomandibular space.

5.2 Inflammation and tissue pH

The pH of the anesthetic solution determines the ratio of RN to RNH^+. According to the Henderson–Hasselbalch equation, there are equal amounts of half-charged and half-uncharged molecules when the acid dissociation constant Pka equals the pH of the solution. In a cartridge of local anesthetic solution, both charged (RNH^+) and uncharged (RN) molecules exist in equilibrium. The deionized lipid-soluble (RH) form penetrates the neuronal membrane and takes up H^+. RNH^+ within the nerve, resulting in RNH^+, which enters the sodium channel and blocks conduction. To produce anesthesia, the body buffers the pH-injected anesthetic solution to the physiological pH [15].

This becomes potentially critical since inflammation-induced tissue acidosis can cause local anesthetics to get "ion trapped." According to this theory, the low tissue pH causes a higher proportion of the local anesthetic to be held in the charged acid form of the molecule, preventing it from passing through cell membranes. This theory has been proposed as a primary cause of local anesthetic failures in situations like endodontic pain [16].

5.3 Central sensitization

Local anesthetic failures may be exacerbated by central sensitization. Increased sensitivity may enhance incoming sensory nerve impulses. There is a significant response to peripheral stimuli in central sensitization, and as a result, the IANB may allow adequate signaling to occur, leading to the experience of pain [16].

5.4 Central core theory

According to this hypothesis, the nerves on the exterior of the nerve bundle supply the molar teeth, while the nerves on the inside supply the anterior teeth. Even if the anesthetic solution is placed in the right location, it may not disperse enough into the nerve trunk to reach all nerves and cause a sufficient block. This concept may only apply to the increased failure rates associated with IANB in the anterior teeth, not the posterior teeth [17].

5.5 Tetrodoxin resistant channels (TTXr)

The Tetrodoxin resistant channels (TTXr) family of sodium channels have been demonstrated to be resistant to the effects of local anesthesia. Anesthetic failures in a hot tooth are caused by increased expression of sodium channels in the pulp. The TTXr channels are resistant to lidocaine, resulting in insufficient anesthetic [18]. TTXr channels are expressed on nociceptors, and their activation with Prostaglandin E2 is relatively resistant to lidocaine. Because they are less susceptible to lidocaine, sodium channels that are resistant to TTX. As the concentration of lidocaine rises, the sodium channels get blocked [19].

5.6 Altered membrane excitability of peripheral nociceptors

Inflamed tissue nerves have a lower excitability threshold and an altered resting potential. Lower excitability thresholds are responsible for impulse transmission [20].

5.7 Psychological factors

Anxiety in the patient may also play a role in the local anesthetic failure. Clinicians who have worked with anxious patients know that they have a lower pain threshold and are more likely to complain about an unpleasant dental experience. The sight of a needle and the sound of the dental handpiece are frequently reported as causes of anxiety in patients. Furthermore, patients may be particularly apprehensive about root canal therapy.

5.8 Effect of inflammation on blood flow

Inflammation has several additional consequences on the physiology of local tissues. Inflammatory mediators cause peripheral vasodilation, which increases the rate of systemic absorption, lowering the concentration of local anesthetics. Local anesthetics, in most circumstances, need formulation with vasoconstrictor drugs. Thus, this is a potentially relevant mechanism. Although regional variations in blood flow occur in inflamed dental pulp, little is known regarding inflammation-induced vascular alterations in periradicular tissue [21]. Furthermore, this vasodilation is likely to be confined and not seen at distant injection sites. As a result, compared to nerve block anesthesia, this concept may be more useful in understanding issues with infiltration anesthesia.

5.9 Effect of inflammation on nociceptors

Inflammation alters the production of many proteins in nociceptors, resulting in a rise in neuropeptides such substance P and calcitonin gene-related peptide. These neuropeptides have an essential role to perform have a role in regulating pulpal inflammation. Furthermore, tissue damage can change the composition, distribution, and activity of sodium channels expressed on the nociceptors. Inflammation's effect on these sodium channels might substantially impact local anesthetic failures [22].

5.10 Tachyphylaxis

Tachyphylaxis is a condition in which a receptor agonist medication causes a reduction in responsiveness to a subsequent dose of the drug. Because local anesthetics are frequently used in conjunction with vasoconstrictors, the medication may remain in the tissue long enough to trigger tachyphylaxis at the sodium channel. This has been suggested as a factor in decreased anesthetic efficacy, particularly after many administrations [21].

6. Factors influence the efficiency of local anesthesia

6.1 Anesthetic agent

Contrary to popular belief, most moderate-duration anesthetics are equally efficient in inducing deep pulpal anesthetic for root canal treatment. Understanding the anatomical, local, and psychological aspects of each patient against the type of anesthetic utilized is critical to success. Most dentists prefer to employ a combination of anesthetics and a vasoconstrictor. When some types of anesthetic drugs are used, it is possible that the patients would experience more pain. Because of the acidic nature of local anesthetics, lower pH values are considered to produce a burning sensation during injection [23].

6.2 Site of injection

The injection location might influence injection discomfort. According to one study, maxillary buccal injections with plain 2% lidocaine Was found to be considerably less discomfort than 2% lidocaine with 1:80000 epinephrine. However, using the same anesthetic drugs, no difference in injection discomfort was recorded at the palatal location [12]. The type of anesthetic solution has little effect on injection discomfort when a location with less connective tissue (such as the palatal site in the maxilla) is injected. Faster injection speed leads to increased drug distribution. It has been proposed that a speed of injection exposes a larger portion of a nerve to the anesthetic solution, resulting in a higher rate of local anesthesia success. The rapid injections, on the other hand, produced more pain and discomfort during the procedure [23–25].

6.3 Preoperative pain

In individuals with symptomatic irreversible pulpitis, the degree of preoperative pain might impact anesthetic success. The activation of nociceptors during inflammation might be one reason for the lower success rate of inflamed pulp. The peripheral and central pain pathways are altered and modulated by the barrage of painful stimuli, as well as tissue destruction. Another reason for failure is that nerves from inflamed tissue have reduced excitability thresholds and altered resting potentials [26].

6.4 Pre emptive medication

Inflamed pulps may have more tetrodotoxin-resistant sodium channels, which are resistant to local anesthetics. Prostaglandins, which can influence tetrodotoxin-resistant receptors and reduce nerve responses to anesthetic drugs, have also risen considerably in inflamed pulps [27]. As a result, premedication with nonsteroidal anti-inflammatory medicines (NSAIDs) and corticosteroids to increase anesthetic success appear to be a viable option. However, the findings of such research do not agree on the effectiveness of premedication on anesthetic success [28, 29]. However, if the patient does not have spontaneous pain, pre-treatment with particular types of NSAIDs may improve the effectiveness of anesthesia when treating irreversible pulpitis [30]. Premedication with corticosteroids before anesthesia with an inferior alveolar nerve block (IANB) injection resulted in a considerably better success rate.

6.5 Gender and genetic factor

Genetics may play a role in predisposing specific individuals to problems such as discomfort, delayed healing, and abscess development. A range of genetic variations influences pain perception and behavior. Pain becomes significantly more common in women, and various explanations have been proposed, including hormonal and genetically driven sex variations in brain neurochemistry [27].

7. Pain management

7.1 Supplementary anesthesia

7.1.1 Intraligamentary anesthesia

Intraligamentary anesthesia is a technique wherein local anesthetic solution administered via the periodontal ligament to reach the pulpal nerve supply. The use of conventional or customized syringes can be used for this technique. At the mesiobuccal aspect, the needle is placed as deeply between the root surface and alveolar bone at a 30° angle to the long axis of the tooth. The needle can be placed with the bevel pointing in either direction, and 0.2 ml of the solution should be injected per root using back pressure. For 5 to 10 seconds, the needle is held in place [31]. The anesthetic action begins almost immediately and lasts for around 15–20 minutes [32].

In comparison to other anesthetic techniques, Intraligamentary anesthesia allows for a substantial reduction in the overall volume of anesthetic solution and vasoconstrictor supplement. At the same time, the unintentional intravascular application is avoided [33]. Furthermore, the effectiveness of Intraligamentary anesthesia is limited in cases of severe marginal periodontitis or teeth with a sclerotic periodontal gap, and alternate anesthetic methods such as inferior alveolar nerve block can be advised [32].

7.1.2 Intraosseous anesthesia

Intraosseous Anesthesia is more invasive and necessitates the use of specialist equipment, such as a perforator (e.g., Stabident, X-Tip). The gingiva must first be sedated for the perforator to penetrate without discomfort. A slow-speed handpiece is used to move the perforator into the anesthetic gingiva and bone until the cancellous bone is felt like a sharp dip. The perforator is then withdrawn, and a small 27-gauge needle is introduced through the perforation, injecting approximately 1 mL of solution over 2 minutes. It's one of the most effective supplemental methods available [34]. The intraosseous injection permits the local anesthetic solution to be injected directly into the cancellous bone adjacent to the tooth that has to be sedated [35]. The intraosseous anesthetic onset of anesthesia is immediate and lasts for around 15 to 30 minutes, and was found to be more efficient than intraligamentary anesthesia [36].

7.1.3 Buccal infiltration

After a failed IANB, buccal infiltration has been utilized as a supplemental anesthetic for anesthetizing mandibular molar teeth, especially in symptomatic irreversible pulpitis. A mandibular buccal infiltration injection of 4% articaine with 1:100,000 epinephrine as an additional injection to improve the effectiveness of the IANB injection has recently been investigated. The usage of the articaine solution was shown to be better than the lidocaine solution in asymptomatic individuals (88 percent vs. 71 percent, respectively) [37]. Only 58% anesthesia was achievable with buccal infiltration injection when used as a supplement to the IANB in case of symptomatic irreversible pulpitis [38].

7.1.4 Intrapulpal anesthesia

Intrapulpal anesthesia is one of the supplementary anesthesia that is beneficial, especially in a hot tooth. The most crucial aspect of this technique is to pump the fluid into the pulp forcefully. If the physician does not feel pressure or resistance to injection, the solution is not reaching the pulp and is most likely running out of the pulp chamber and back into the access cavity [39]. However, this type of anesthesia is excruciating and should only be used as the last option during endodontic therapy. Intrapulpal anesthesia has the drawback of having a limited duration of effect. As a result, it's critical to remove the pulp from all of the root canals as soon as possible after injection to avoid repeated injection [40]. It is necessary that the patient should be informed that the type of anesthesia will cause moderate to severe discomfort in the beginning.

7.2 Buffered anesthesia

Buffered local anesthesia technique to one of the techniques to improve the efficiency of the local anesthetics. Alkalinization accelerates the dissociation of the LA molecule, increasing in the uncharged base form that penetrates the nerve membrane and acts in the intraneuronal location. The addition of sodium bicarbonate is the most frequent technique for buffering LAs. The addition of sodium bicarbonate to local anesthetics reacts to form sodium chloride water and carbon dioxide. Alkalinization with sodium bicarbonate raise the pH of the solution. Carbon dioxide produces an independent anesthetic effect by changing the local anesthetic inside the nerve direct depressant effect of carbon dioxide on the nerve axon [41]. 50 mEq is the maximum dose of sodium bicarbonate. 20 ml of 1 or 2% lignocaine is recommended to be added with 2 ml of 8.4 percent sodium bicarbonate. The ratio of lignocaine to bicarbonate should be between 5:1 and 10:1 for best effects. If the bicarbonate level exceeds this ratio, precipitation may occur. In individuals with metabolic acidosis and hypocalcemia, this method is contraindicated [15].

8. Conclusion

Pain being the most common symptom, every effort should be made to manage it during and after root canal treatment and should be informed priorly the type of anesthesia administered to the patient. Although various anesthetic agents and techniques are available, the choice of them is specific and customized to each patient and their preoperative status and clinical condition. So, ultimately, the clinician should critically decide on a specific agent or a technique for the clinical condition of the patient. It is necessary to provide appropriate pulpal anesthesia when treating teeth with irreversible pulpitis.

Conflicts of interest

The authors declare no conflict of interest.

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Section 4

Regional Anesthesia and Pain

Chapter 11

Regional Anesthesia in the Prevention of Chronic Postoperative Pain

Brenda O. Lezcano Velazquez
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Abstract

Chronic postsurgical pain (CPSP) develops after a surgical procedure but increases its intensity and persists beyond the healing process without another cause to explain it. The incidence ranges from 5–85%, according to the type of surgery. Patients who develop CPSP may have a protracted ambulation, cardiac and pulmonary complications and increased morbidity and mortality. Several risk factors have been found related to the development of CPSP: female gender, young age, genetic predisposition, and psychosocial problems, hence prevention, early identification and treatment of these factors is essential. Several guidelines recommend the use of multimodal analgesia to treat postoperative pain, and the perioperative management seems to have a preventive role in the development of CPSP. Regional anesthesia (RA) either neuraxial or peripheral nerve blocks, by modulating signaling created by a surgical incision, play a key role in the prevention of CPSP. Local anesthetics have anti-inflammatory properties which decrease sensitization, reduce ectopic firing of neurons, cytokines expression and decrease neutrophil priming. RA reduces pain signals to the spinal cord and supraspinal and cortical nociceptive centers. RA along with other pharmacologic interventions can improve the CPSP as well as the physical and social functionality.

Keywords: acute pain, chronic pain, multimodal, regional analgesia, ultrasound

1. Introduction

Pain is a universal experience but unique for every individual. Any surgical intervention is a common pain source, that results from a planned incision at a specified point in time, often approached and managed sub optimally or without proper prevention, for this reason it should be prevented or controlled. However, there are many factors that contribute to the development and persistence of Chronic Postsurgical pain [CPSP], and only some of these are related to the surgery. As with nonsurgical chronic pain, psychological and social factors have an important influence [1].

Poor pain management will contribute to a worse experience of the disease for the patient, lower satisfaction, delayed ambulation, increased incidence of cardiac and pulmonary complications, and increased morbidity and mortality. It also has

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a negative impact on the health system by having short-term and long-term consequences such as late discharge and slow recovery and late rehabilitation [2].

All clinicians should have some knowledge on CPSP and how to manage established cases, which can persist for months or years after the procedure. As with many other chronic conditions, early intervention is likely to improve outcomes, so identifying patients at risk is crucial. The incidence of chronic postoperative pain varies according to the type of surgery and may be severe and disabling. Chronic pain is difficult to treat and is often permanent. For this reason, efforts to prevent its development after surgery are especially important [3].

An accurate clinical history and physical examination are essential to identify known risk factors leading to postoperative acute and chronic pain. The outcome improves with pharmacological and non-pharmacological multimodal analgesia, peripheral regional anesthesia or neuraxial techniques are some current tools that may reduce the incidence and severity of CPSP.

2. Postoperative pain

The International Association for the Study of Pain (IASP) describes pain as an unpleasant sensory and emotional experience associated with an actual or potential injury or described in terms of such injury [4].

Acute postoperative pain is a result of noxious stimulation of skin, subcutaneous tissues, viscera and neural structures. The 11th revision of the International Classification of Diseases defines CPSP as pain developing or increasing in intensity after a surgical procedure, in the area of the surgery, persisting beyond the healing process (at least 3 months) and not better explained by another cause such as infection, malignancy, or a pre-existing pain condition [5].

The prevention of CPSP is an important goal, for this reason the IASP named 2017 as the Global Year Against Pain After Surgery [6, 7]. Substantial rates of chronic postoperative pain after a variety of surgical procedures, have revealed important demographic, genetic and psychosocial risk factors, which allow us in cases of elective surgery, to investigate or and prevent some of them that may influence pain chronicity. While traumatic injury is clearly not predictable [8].

2.1 Incidence

CPSP has been reported after almost all types of surgery with a high prevalence >20%, the incidence of CPSP varies depending on the surgical procedure ranging from a low of 5% to a high of 85% [9]. Some studies following limb amputation have reported incidences ranging from 50–85%, following mastectomy 11–57%, after thoracotomy 5–65%, and 5–63% following hernia repair [10, 11].

The high prevalence after these procedures may be attributed to the increased risk of nerve injury and central sensitization on this type of surgeries; but also, there could be other explanations, including persistence of a pre-existing pain in the operated area [12].

2.2 Risk factors for chronic postsurgical pain

Several studies have attempted to identify specific surgical factors that increase the risk of developing chronic postoperative pain. The surgical location, duration, and extent, as well as the experience of the surgical team, have been implicated [13, 14]. There are predictors for developing persistent pain, which are divided into preoperative, perioperative, or immediate postoperative and late postoperative.

Among the predictors in the preoperative period are patient factors including female gender, being a young adult, genetic predisposition, and psychosocial factors like depression tendency to catastrophize, preexisting patient conditions, for example, pain present preoperatively, and any preexisting painful conditions [15, 16].

Perioperative factors include duration and type of surgery, extent of nerve damage intraoperatively, longer duration and an open vs. laparoscopic approach [15, 16]. Modifying surgical technique to minimize nerve damage and using minimally invasive approaches may decrease chronic postoperative pain risk [13].

In the postoperative period, the predictors will be related to the analgesic treatment, psycho-social factors, or patient factors such as chemotherapy or radiotherapy treatments, because they could be related to other states of hyperalgesia [17].

The time-point of chronic postoperative pain assessment, ranging from months to several years after surgery, may impact incidence estimates, with longer follow-up times corresponding to lower incidence rates [18].

2.3 Transition from acute to chronic pain

The intensity of acute pain is one of the strongest predictors of chronic postoperative pain, likely because acute pain itself is a product of biopsychosocial variables [19]. Pain is not only a sensation to protect the body from harm, but also a process where nociceptive information is transformed into a complex, subjective, unpleasant, sensory, and emotional experience with different factors that define it [20]. Acute pain responds to tissue damage, a certain pathology or abnormal function of a muscle or viscera. It is protective, adaptive and self-limited, its evolutionary function is to restrict behaviors that increase the risk of inadequate tissue recovery [21]. Nociception is a protective process that helps prevent further tissue damage by triggering reflex withdrawal responses and modification of behavior to avoid injury [22].

Tissue damage triggers profound changes in peripheral and predominantly central somatosensory circuits. Chronic pain does not have a specific function, it is related to inadequate and aberrant adaptation that can include some states of neuroplasticity [23].

Neuropathic pain is defined by the IASP as pain caused directly by an injury or disease that affects the somatosensory nervous system, it is characterized by spontaneous pain with abnormal sensory symptoms [24].

Persistent pain following surgery can have neuropathic characteristics, and many of the surgeries associated with persistent pain, such as thoracotomy, breast surgery and amputation, involve major nerves in the surgical field [13]. Following nerve injury, nociceptive neurons fire rapidly leading to changes in N-methyl-D-aspartate receptors NMDAR composition and activation. NMDARs are highly permeable to calcium, whose influx triggers neuron- specific cascades that underlie synaptic plasticity and, in extreme cases, cause excitotoxicity and neuronal death. In a neuropathic pain model, the conditional deletion of spinal NMDARs prevents calcium-dependent neuronal death and the transition from acute to persistent pain-like behaviors. This shows that glutamate, NMDARs, and calcium influx play an essential role in the development of chronic pan [25].

However, intra-operative nerve transection does not inevitably result in neuropathic pain and avoiding nerve transection does not necessarily prevent chronic pain [26]. Risk factors for persistent postoperative pain, other than nerve injury and ongoing inflammation, include pre-operative pain, younger age, female sex, genetic factors, and psychological vulnerability [13].

The pathophysiological mechanism is considered mostly neuropathic when finding an important association between persistent postoperative pain and sensory abnormalities, the evidence indicates that there are other components involved such as inflammatory processes, central sensitization, damage to nerves or somatic/visceral structures, or a combination of the above [27].

3. Multimodal analgesia

Some risk factors for postoperative chronic pain can be modifiable especially if surgery is elective, like body-mass index, preoperative pain, and some comorbidities, whereas others like demographics, genetics, and pain sensitivity are not. The site, timing and intensity of surgical damage are predictable. An analgesic regimen can be designed to anticipate, prevent, or modify the nociceptive barrage, thereby preventing central sensitization [28].

Multimodal analgesia has become an important concept in the field of modern pain management. The use of multimodal analgesia is highly recommended for postoperative pain management. It is defined as the use of a variety of drugs and combined techniques, with different mechanisms of action at the central and/or peripheral nervous system level and may have an additive effect or synergism. Some of these agents include $alpha_2$ agonists, NMDA receptor antagonists, gabapentinoids, dexamethasone, NSAIDs, acetaminophen, and duloxetine [29].

Advantages include superior analgesia secondary to the synergistic effects of multiple agents acting via different pain pathways, the ability to limit parenteral opioid administration, and minimizing opioid-related side effects [28].

The site, timing and intensity of surgical damage are predictable. An analgesic regimen can be designed to anticipate, prevent, or modify the nociceptive barrage, thereby preventing central sensitization. Pain management plays a fundamental role in enhanced recovery after surgery (ERAS) pathways. The concept of multimodal analgesia in providing a balanced and effective approach to perioperative pain management is widely accepted and practiced, with regional anesthesia playing a main role [30].

There are evidence-based guidelines for the management of postoperative pain, like the American Society for pain management, the European guidelines PROSPECT (Procedure Specific Postoperative Management) and ERAS guidelines (Enhanced Recovery After Surgery), all of them have similar objectives; an early mobilization, a reduction in hospital stay times, a decrease in morbidity and mortality, an increase in patient satisfaction and the use of multimodal analgesia, specially regional anesthesia [30–32]. A multidisciplinary team-based approach for defining the goals is essential, based on each patient's needs, and incorporating patient, surgical, and social factors.

4. Regional anesthesia

The guidelines on postoperative pain management created by multiple societies advocate for the use of site-specific regional anesthetic techniques as part of a multimodal analgesic regimen, which is effective in several surgical procedures including thoracotomy, joint replacement surgery, and cesarean sections. Central neuraxial blocks alone or in combination with catheter techniques are performed in order to decrease stress surgically induced and inflammation, and they could improve pulmonary functions, and reduce the period of hospitalization with better pain control [30].

Effective regional anesthesia may prevent central sensitization by blocking nociceptive input into the spinal cord. Epidural anesthesia and paravertebral blocks reduce the risk of persistent pain after open thoracotomy and breast cancer surgery, respectively [33]. These findings are interesting also in view of the apparent beneficial effect of regional anesthesia in reducing tumor recurrence [34]. Regional anesthesia has been advocated in oncological surgery to reduce the risk of cancer recurrence, based on some evidence by the inhibition of tumor cell seeding and growth by various pathways. These include effective suppression of the adrenergic and inflammatory response to surgery, preservation of immune function and direct action of systemic local anesthetics on tumor cell apoptosis, and indirectly through reduction in the use of opioids which may have their own pro-metastatic effects [35].

Improvement in ultrasound technology may increase clinical applications not only for epidural and paravertebral blocks but also for peripheral nerve and truncal blocks. The use of real time of ultrasound while performing the block may reduce the complications, performance time, and local anesthetic requirements. The rate of success may increase with clinical experience. Peripheral nerve blocks seem to lack systemic side effect related to sympathetic blockade and lesser incidence of minor complications including urinary retention when compared with central neuraxial blocks or catheter applications. For what they seem to be safer than either central neuraxial blocks or general anesthesia, especially in patients with severe coexisting disease [36].

The potential beneficial effect of local anesthesia on inflammation and immune function has long been suggested [37]. Local anesthetics have anti-inflammatory properties which may also decrease sensitization. The clinical anti-inflammatory effect of intravenous lidocaine is today reasonably well documented. The exact mechanisms of action are not clear but seem to involve a reversible interaction with membrane proteins and lipids, thus regulating cell metabolic activity, migration, exocytosis, and phagocytosis [38].

The shift toward peripheral and regional anesthetic techniques has largely been driven by the advent of ultrasound-guided regional anesthesia, it provides real-time visualization and targeting of major nerves that were previously located with landmark-based "blind" techniques, therefore, it has made regional anesthesia safer, more efficient, and more accessible to general anesthesiologists [39]. There is a growing interest in the potential preventative impact of regional anesthesia on chronic postoperative pain, especially with ongoing development of new techniques.

5. Conclusions

The role of regional anesthesia in peri-operative care and acute pain management is more important now than it has ever been. Postoperative pain management continues to be a challenge for the health professional, due to the combination of factors that produce it. If not treated correctly, postoperative pain may become chronic which can cause functional limitation and psychological distress to patients. We should identify the risk factors in a patient undergoing surgery and institute appropriate preventive measures.

When seeking satisfaction in the patient, it must be understood that suboptimal pain management may be due to the lack of an updated and multidisciplinary approach. The use of regional techniques in the pre, intra and postoperative period, based on the recommendations of the multimodal therapy guidelines, implemented according to the setting and the availability of the health center, hence it can make a difference in terms of acute postoperative pain and long-term preventable consequences.

The ability of regional anesthesia to target many areas of the surgically induced pain pathways makes it a powerful tool in reducing neural activation from surgical injury, making it the centerpiece of a well-rounded multimodal approach. Several ongoing studies addressing innovative blocks will likely continue to inform preventative treatment options. Successful approaches to decrease chronic postoperative pain incidence should start at the time of pre-operative planning and extend into the recovery period.

Adoption of ultrasound guidance as the gold standard has been key to this; recently new techniques have been developed. Fascial plane blocks have been an important step in increasing the reach of regional anesthesia, although more research is needed to clarify their role in peri-operative pain management, reason why is particularly important to continue investing into regional anesthesia education. Advances in technology, technique development and pharmacology over the last decade have significantly improved efficacy and safety of regional anesthesia.

Conflict of interest

The authors do not have any potential conflict of interest related to this chapter.

Abbreviations

CPSP	Chronic Postsurgical pain
RA	Regional anesthesia
IASP	International Association for the Study of Pain
NMDARs	N-methyl-D- aspartate receptors
PROSPECT	Procedure Specific Postoperative Management
ERAS	Enhanced Recovery After Surgery

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Chapter 12

Gabapentinoids in Preventive Analgesia: Pharmacological and Clinical Aspects

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Abstract

Optimal postoperative pain management presents a challenge for healthcare providers across all surgical specialties, since it is estimated that many patients submitted to major surgeries do not receive an adequate analgesic treatment, increasing the risk of complications, length-of-stay and costs for health assistance. The development of new agents for postoperative pain control creates possibilities for better combinations in preventive and multimodal analgesia. Recently, the use of gabapentinoids (gabapentin and pregabalin) in the perioperative period has become more popular. Several clinical studies and meta-analyses reveal that perioperative gabapentinoids may evoke a significant opioid-sparing effect and probably decrease the postoperative pain score. Gabapentinoids may be a good strategy for preventive and multimodal analgesia in major surgeries, particularly pregabalin, considering its pharmacokinetics profile. Situations where there are limitations of regional anesthesia techniques or in cases where there is an intention to reduce the use of opioids or anti-inflammatory drugs at the trans-operatory period are certainly good opportunities for their use. However, gabapentinoids are associated with several adverse effects, including sedation, dizziness, and peripheral edema. Therefore, further studies are needed to evaluate the real cost-effectiveness of this approach. Additionally, specific attention should be paid to minor and ambulatory surgeries as well as for the elderly patients to which gabapentinoids are clearly not beneficial and potentially harmful.

Keywords: Gabapentinoids, Preventive analgesia, Pain, Anesthesia, Gabapentin, Pregabalin

1. Introduction

Pain is one of the most common and significant postoperative events experienced by many surgical patients. Optimal postoperative pain management presents a challenge for healthcare providers across all surgical specialties.

Immediate postsurgical pain affects four out of five patients [1]. In a national US survey of adults who had undergone surgery within the previous 5 years, 86% of overall patients experienced postsurgical pain, and 75% of those who reported pain described its severity as moderate–extreme during the immediate postoperative period [2].

The implications of poorly controlled postoperative pain are substantial, including cardiopulmonary complications, opioid-related side effects, unplanned hospital admissions, prolonged hospital stay, increase in health services costs and the subsequent development of chronic pain or opioid addiction [3]. Additionally, it is noteworthy that when surgeons prescribe more doses of opioids or potent opioids when other non-opioid analgesics may be able to control postoperative pain, they are contributing to the opioid epidemic [4].

Recent evidence has raised the importance of preventive analgesia [5, 6] which may be defined as the occasion where the pharmacological intervention is initiated earlier than the painful stimulus to inhibit nociceptive input before it is triggered. It has been demonstrated that preventive multimodal pain therapy has been successfully implemented for numerous surgical procedures, often resulting in decreased opioid consumption and a shorter hospital stay [7, 8]. Medications to achieve opioid-sparing preventive analgesia include non-steroid anti-inflammatory drugs, magnesium, lidocaine, N-Methyl-D-Aspartate (NMDA) receptor antagonists, glucocorticoids, and alpha2-agonists and some anticonvulsant drugs [9].

Moreover, the prescription of the gabapentinoids (gabapentin and pregabalin) in the perioperative period has become increasingly common and they have become ubiquitous components of protocols for early recovery after surgery and preventive and multimodal analgesia.

Despite the existence of several studies comparing the use of these drugs as preoperative medication for the most diverse surgeries, there are conflicting results and no consensus on what the better choice and ideal dose could be [10]. It is generally accepted that the gabapentinoids are effective in reducing immediate postoperative pain and opioid consumption. However, it is noteworthy that the patients' safety has emerged as a broader gabapentinoids concern once these drugs have significant adverse effects as well.

Further definition of uncommon side effects, the optimal preoperative and postoperative doses, treatment duration, and dosage schedule are needed before perioperative gabapentinoids can be broadly recommended as the standard of care for all patients.

Therefore, this book chapter will present a systematic review of literature regarding the pharmacological and relevant clinical features about gabapentinoids for preventive analgesia, including the used drugs with their respective doses, routes of administration, tolerability, and safety profile as well as procedure-related complications and patients' satisfaction.

2. Pain control

The International Association for the Study of Pain (IASP) has stated in 1979 that pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive, and social components [11, 12]. Therefore, it is known that the painful experience involves the interpretation of the biological aspects of pain, but also its interaction with the social and cultural characteristics of everyone [13].

Pain plays an important role in biological signaling as a necessary condition for our survival, evoking autonomic, pathological, and psychological responses to prevent tissue damage and it can be classified as acute or chronic pain [14].

The acute condition has a burden beginning, limited duration and it is associated with a local well-established and self-limited cause, with a time course usually lower than 3 months. On the other hand, the chronic pain may be considered a disease state, since it may be understood as the pain that outlasts the normal time of healing (higher than 3 months) and it may arise from psychological states, it serves no biological purpose, and has no recognizable endpoint [15].

Considering its pathophysiology, pain may be classified as nociceptive, neuropathic, or mixed pain. The neuropathic pain is associated with damage to the somatosensory nervous system. On the other hand, the most common is the nociceptive or inflammatory pain which comes from any tissue other than the neurological one. It happens after different types of stimuli, such as physical, mechanical, chemical, infectious and others, which promotes pain and regeneration of the injured tissue. The post-operative pain as well as those related to trauma and ischemic conditions are known as nociceptive pain [16].

The human body has a physiological protection system that acts as a neural network for the perception of harmful stimuli [17]. Briefly, pain processing starts with the information transduction that occurs when peripheral nociceptors are activated and detect a damage or harmful stimulation from the environment, transforming it into an action potential to inform the central nervous system (CNS) of homeostasis alteration. After that, information transmission by free and specialized nerve endings (known as A-delta and C fibers) occurs and the stimulus is carried out to the CNS through afferent pathways crossing the spinal medulla, arriving at the cerebral cortex where pain perception occurs.

Fortunately, the human body has a descending inhibitory system for acting on pain modulation. Central structures located at the brain, hypothalamus, brainstem, and dorsal horn of the spinal cord release mediators such as serotonin, norepinephrine, gamma aminobutyric acid (GABA) and acetylcholine to inhibit the algic stimuli [14].

Pain is a classic problem related to major surgeries, and its inadequate control occurs in a significant number of patients predisposing dissatisfaction and failure to ambulate, resulting in a longer hospitalization, with higher risk of morbidity and mortality [18]. Therefore, the knowledge of pain physiology is essential to understand the mood of action of many medications used in anaesthesiology, including preventive and multimodal analgesia.

3. Gabapentinoids

Gabapentinoids, a class of drugs including gabapentin and pregabalin, were originally marketed in the 1990s for use as antiepileptics but they have anxiolytic effects and subsequently they were approved to treat neuropathic pain conditions [19, 20]. In Anaesthesiology, these drugs have received increased attention in recent years particularly for preventive analgesia while, on the other hand, the prescription of opioids tended to decrease once they were related to adverse events and suboptimal patient outcomes.

Gabapentinoids were designed as GABA analogues although they do not have any effect on GABA receptors directly [21]. These drugs bind to voltage-gated calcium channels, reducing calcium influx inside the presynaptic terminals [21].

The voltage-gated calcium channels are composed of multiple subunits, but the α-2-δ component has a great association with pain processing. Some studies suggest that increased levels of these subunits may lead to neuropathic pain, even without nerve damage [22]. When the nociceptors are sensitized and activated by a minimal stimulation, the action potential transmitted to the dorsal horn allows the activation of voltage-gated calcium channels and a calcium influx and glutamate release, evoking primary hyperalgesia. In other words, at the site of inflammation and in the dorsal horn, an excitatory signal is produced, increasing postsynaptic nociceptive activation [6, 22]. On the other hand, gabapentinoids can soften the release of excitatory neurotransmitters and reduce the hyperexcitability of dorsal horn neurons induced by tissue injury, explaining their effectiveness on neuropathic pain [22].

Other sites of action involved in the gabapentinoids' analgesic effect have been described with limited evidence, such as sodium channels, NMDA receptors and others. Briefly, a more accurate description of their mechanism is the depression of presynaptic excitatory input onto dorsal horn neurons through interactions with α-2-δ subunit of the voltage-gated calcium channels that are upregulated after injury. Moreover, they inhibit forward trafficking from the dorsal root ganglion, their recycling from endosomal compartments and stimulate glutamate uptake. Additional mechanisms not directly related to neurotransmitter release at dorsal horn include inhibition of descending serotoninergic facilitation, stimulation of descending inhibition, anti-inflammatory actions and influence on the affective component of pain [23]. Indeed, a meta-analysis concluded that gabapentinoids can reduce pain scores in the first 24 hours as well as they may decrease the cumulative consumption of morphine and side-effects, such as nausea, vomiting and itching after spinal surgery [24].

In pharmacological aspects, gabapentinoids have only oral presentations and are easily tolerable by the patients. The most common side effects reported are sedation, dizziness or headache, peripheral edema, and visual disturbances [25].

Although gabapentin and pregabalin have similar structure and mood of action, pregabalin presents higher affinity to the calcium channels subunit site which may evoke not just an increased efficacy but also a risk for side effects in situations that require higher doses [23].

The main differences between these two drugs arise not from different modes of action but rather from different bioavailability. Although both drugs are absorbed by amino acid carriers, gabapentin absorption is limited to a relatively small part of the duodenum, whereas pregabalin is absorbed throughout the small intestine [26]. Therefore, gabapentin presents a plasmatic peak concentration in three hours, in opposition with pregabalin which is rapidly absorbed and demonstrates a peak of plasmatic levels in just one hour associated with a more linear pharmacokinetic profile and less variable bioavailability [21].

Gabapentinoids have a low rate of binding with plasma proteins, their metabolism is not dependent on the liver, and they are excreted unchanged in the urine. Also, the elimination half-life ranges of gabapentin and pregabalin are 4.8–8.7 h and 5.5–6.3 h, respectively [22]. On these terms, patients with kidney failure must have a medication dose adjustment [27, 28]. Similarly, these agents should be used with caution, or the dose should be decreased in elderly [29].

4. Gabapentin

Gabapentin was first approved by the Food and Drug Administration in 1993 and it was initially meant to treat seizures, but as time goes by, it started to be used for chronic pain [30]. Gabapentin consists of a GABA molecule covalently bound to a lipophilic cyclohexane ring. Considering its lipophilic profile, it can cross the blood–brain barrier and it can become an active GABA agonist. As an anticonvulsant drug, it can inhibit tonic hindlimb extension in the electroshock seizure model, as well as clonic seizures [30].

Although gabapentin is approved to treat chronic pain with regular doses ranging from 900 to 1200 mg per day, it is also used as antiepileptic medication (900 to

1800 mg daily) usually requiring a second anticonvulsant drug. However, it is not approved by the FDA for treating or preventing surgical pain, despite its off-label use increase worldwide as well as its recommendation for larger doses and longer treatment duration [31–33].

Gabapentin began to be used as a co-analgesic in the preoperative, as the studies showed no risk of intake, besides the fact that it substantially reduces pain during movement and decreases morphine consumption, making it a very promising medication in the opioid sparing or multimodal strategy. Even though the FDA has not approved it for this use, preoperative gabapentinoids have been widely used. The most common side effects associated with gabapentin use were: sedation, dizziness and peripheral edema [34].

Several clinical studies and meta-analyses reveal that perioperative gabapentin helps to evoke a markedly opioid-sparing effect and a decrease in postoperative pain score [35, 36]. In contrast, Verret et al. reported no clinically significant analgesic effect for the perioperative use of gabapentinoids and a greater risk of adverse events [20].

The use of 150 to 1200 mg of gabapentin prior to the surgery, and in the day after is the most common strategy for decreasing narcotics consumption in a multimodal strategy [21]. The use may initiate preoperatively, intra-operatively, or postoperatively. Despite little evidence, some studies recommend: Gabapentin 1200 mg 1-2 h before incision, Gabapentin 600 mg three times a day for 5 days and Gabapentin 600 mg for up to 14 days [21].

However, patients may show some level of sedation and, therefore, it is recommended to avoid its use in ambulatorial patients as well as caution use in elderly and in patients with cognitive impairment. On the other hand, there are almost no studies using gabapentin and regional anesthesia, so more data should be gathered in order to develop a safe protocol for larger and more routine use, considering risk and benefits.

5. Pregabalin

The pregabalin is an antiepileptic drug whose effectiveness to treat neuropathic pain was discovered in 1965 [37]. It was originally used in the 1990s as an anticonvulsant drug [20] and in 2004 it was approved by FDA for neuropathic pain, then fibromyalgia in 2007 and spinal cord injury neuropathic pain in 2012 [30]. Over the last decade, pregabalin has acquired a new use, for preventing postoperative acute pain and as an opioid spare strategy, and its use became widespread and routine in some countries [20].

Pregabalin has no activity at GABA receptors, but it acts on binding to the α-2δ subunit of voltage-gated P/Q-type calcium channels [21]. The α-2δ receptor has 4 isoforms. The α-2δ-1 isoform mediates the effects of gabapentinoids, and it is found in the brain, skeletal, cardiac, and smooth muscle. The α-2δ-2 and α-2δ-3 isoforms are present in non-neuronal tissues as well, and the α-2δ-4 subunit is expressed in retinal neurons and other non-neuronal tissues [23].

The binding to the α-2δ may inhibit or modulate the process of calcium influx through these channels, on the synaptic bulb of presynaptic neurons, thus inhibiting the release of glutamate and substance P. Additionally, the analgesic effect may occur due to activation on the descending inhibitory noradrenergic pathways [21, 37] and due to inhibition of ascending pain transmission [21, 30].

The bioavailability of pregabalin is approximately 90% and its half-life is about 6–7 hours which allows its use twice a day. Its binding to proteins is minimal and the drug is renally excreted [21, 38].

In comparison to gabapentin, pregabalin has an affinity for the type N voltage dependent calcium-channel six times higher [38]. Because of the expression of α-2δ in cerebellum and hippocampus, pregabalin can cause dizziness, balance disorders, ataxia, visual disturbances, sedation, somnolence, and cognitive impairment [30]. Pregabalin has an antiemetic potential, and it showed significant results for post-operative nausea and vomiting (PONV) reduction, but the primary outcome was never the PONV occurrence [39].

Currently, pregabalin is part of the multimodal anesthetic approach as well as opioid-spare strategy [9, 30]. In addition, although FDA has not approved, pregabalin is used to prevent acute postoperative pain [30].

A 2017 meta-analysis evaluating the use of gabapentinoids for the treatment of acute postoperative pain following spinal surgery showed reduced pain scores compared with placebo. However, the heterogeneity caused by different dosing protocols reduced the level of evidence [24]. In addition, pregabalin seems to be more effective in conditions associated with chronic pain [24]. On the other hand, in an editorial of Anesthesiology published in 2020, the evidence of risk of perioperative gabapentinoids was described to increase, while the benefit has diminished [30].

A 2019 review article showed the limited analgesic benefit of gabapentinoids. In addition, they were shown to increase sedation and dizziness. These drugs increase the potential of opioid-induced respiratory depression and sedation, and they are not part of strategy in enhanced recovery [39].

Finally, in a recent meta-analysis it was reported that the perioperative use of gabapentinoids failed to demonstrate differences in postoperative acute, subacute and chronic pain and the adverse effects caused are underreported [20].

Regarding pregabalin use in the context of regional anesthesia, there are few studies published. The use of pregabalin could not reduce the pain scores at rest or with movement with regional anesthesia. The only positive results were the pooled results of both general and regional anesthesia that showed a 24 h opioid consumption reduction. However, there are several limitations of this study, such as heterogeneity and the risk of bias in individual studies [40].

As the use of pregabalin for the management of postoperative pain is *off label*, there are no dosing guidelines for this indication, neither the ideal dose [40] nor the treatment duration are established [21]. Additionally, it is very unlikely that the use of gabapentinoids could provide additional analgesia benefits in the context of regional anesthesia. Only in selected groups there might be some benefits, and these groups are not known. Therefore, this drug, if recommended, should be used cautiously. Further studies are needed to evaluate the real cost-effectiveness of this approach.

The use may initiate preoperatively, intra-operatively, or postoperatively. Despite scarce evidence, some studies recommend: Pregabalin 75–300 mg 1-2 h before incision, Pregabalin 150–300 mg twice a day, with use for 5 days and Pregabalin 150 mg twice a day for 14 days [21].

Patients in hemodialysis demand extra care, because of its renal excretion [39]. Therefore, the maximum daily dose of pregabalin (in mg) and its correlation with creatinine clearance (in ml/min) is: 600 mg if the clearance is higher than 60 ml/min; 300 mg if the clearance range is from 30 to 60 ml/min; 150 mg if the clearance range is from 15 to 30 ml/min; and 75 mg if the creatinine clearance is lower than 15 ml/min [21].

6. Conclusion

Despite the inconsistencies between the reported results, gabapentinoids may be a strategy for preventive and multimodal analgesia in major surgeries, particularly pregabalin, considering its pharmacokinetics profile. Situations where there are limitations of regional anesthesia techniques or in cases where there is an intention to reduce the use of opioids or anti-inflammatory drugs at the trans-operatory period are good opportunities for their use. However, further studies are needed to evaluate the real cost-effectiveness of this approach. Additionally, specific attention should be paid to minor and ambulatory surgeries as well as for the elderly patients to which gabapentinoids are clearly not beneficial and potentially harmful.

Conflict of interest

The authors declare no conflict of interest.

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Regional anesthesia has progressively evolved and currently occupies a predominant place in our daily practice. The development of skills for the safe practice of regional anesthesia requires in-depth knowledge of anatomy, physiology, pharmacology, and the pathology of each patient candidate to receive some type of regional block, as well as special and prolonged training beyond residence, particularly in this era of the COVID-19 pandemic, during which the training of thousands of anesthesiology residents has been impaired. Undoubtedly, the benefits of regional anesthesia techniques are enormous, as are their complications. Countless guidelines for regional anesthesia have been described based on the classic anatomical recommendations, the search for paresthesias, neurostimulation, and medical images. The introduction of ultrasound guidance and the rational use of local anesthetics and their adjuvants have favorably revolutionized regional anesthesia, making it safer and more effective. This book addresses several contemporary topics in regional anesthesia in a variety of interesting clinical settings with practical importance.

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