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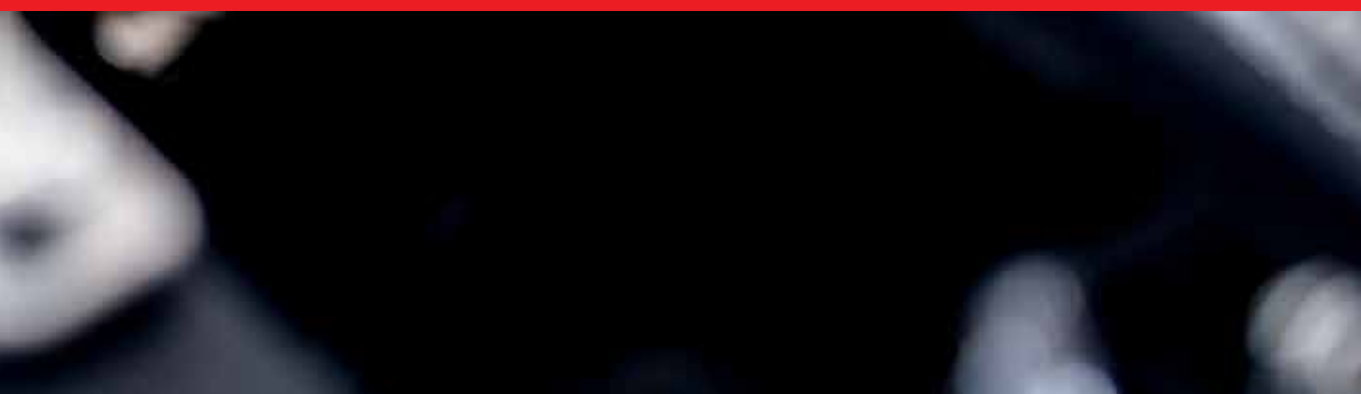

ENDOSCOPY - NOVEL TECHNIQUES AND RECENT ADVANCEMENTS

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Meet the editors

Streba Costin Teodor, MD, PhD, MSc, Associate Professor at the University of Medicine and Pharmacy of Craiova. He is a member of the Research Center of Gastroenterology and Hepatology of Craiova, within the same university. He undertakes research activities in the field of liver and pancreatic disease diagnostics and has received extensive training in histological image analysis. He specializes in devising medical-oriented diagnostic systems for gastrointestinal malignancies, which integrate interpretation and computer-aided quantification of various imaging and clinical data. His publication record reflects his dedication to innovative diagnostic techniques in gastroenterology, having had numerous large-scale studies featured in various high-impact publications within this field.

Vere Cristin Constantin, MD, PhD, MSc, Professor of Gastroenterology at the University of Medicine and Pharmacy of Craiova and one of the founding members of the Research Center of Gastroenterology and Hepatology of Craiova. His research interests span from neuroimmune mechanisms of gastrointestinal disease to novel diagnostic techniques in gastroenterology. Pioneering the introduction of wireless videocapsule in Romania, he established a dynamic team of PhD students and full-time scientists specializing in both medical sciences and bioinformatics. His publication record attests to his dedication to innovation in the field of gastroenterology and the complex integrative mechanisms that form the basis for this pathology.

Dan Ionut Gheonea, MD, PhD, MSc, Professor at the University of Medicine and Pharmacy of Craiova, he is an active member of the Research Center of Gastroenterology and Hepatology Craiova (www.umfcv.ro/ccgh) and is involved in the development of most of the laboratories and new techniques implemented there. He initiated and participated in writing more than 30 grant proposals. As team leader of the Elastography and Virtual Intelligence Laboratory, he developed these techniques at a national level, being invited many times as expert to lecture at national specific meetings. He has published and communicated more than 100 papers in Romania and abroad, several of them in high-impact publications.

Contents

Preface

The fields of diagnostic and therapeutic endoscopy are two of the most dynamic fields in today's medical world. Nowadays, minimally invasive endoscopic techniques are routinely used in screening programs for early diagnosis of various pathologies or even to decipher novel cellular features. An important aspect of current endoscopy practice is applying innovative surgical solutions, with minimal discomfort and side effects for the patient.

The use of endoscopic procedures is not restricted to one medical specialty or to one purpose. Direct investigation of lesions or defects is always desirable in all fields of medicine; from neurosurgery to gastroenterology, any endoscopic procedure that makes use of natural orifices and causes minimal damage to anatomic structures can provide essential diagnostic data. Obtaining direct visualization offers the possibility to apply local treatment and can guide further therapeutic endeavors.

We have strived to select, within this book, some of the most interesting and novel approaches to different issues, from a variety of medical fields: gastroenterology, pulmonology, neurosurgery, or otorhinolaryngology. What all chapters have in common is a comprehensive view of their respective niche. With this book, both specialists in each field and also general practitioners or those who are studying medicine can find useful information, in a comprehensive format and with clear images. Tables were used throughout the chapters to summarize the most important information, providing immediate access to key issues.

With all these prospects in mind, we feel that this book project comes at the right time, having authors that present recent breakthroughs, as well as re-establishing core concepts and revising the basic principles. We hope that everyone can find something of interest in this current volume – the goal was to bring together as many views and perspectives as possible, in a coherent, easy to follow, format.

We would like to extend our immense gratitude towards our mentors, close and distant collaborators that offer their invaluable contribution to our daily practice and academic efforts. Also, we would like to thank the authors, their collaborators, as well as the editorial team that made this project possible. A final – and most important – "thank you" goes to our families who give us the motivation to go forward and always offer their unconditional support.

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Introduction

Chapter 1

Introductory Chapter: Endoscopy-Novel Techniques and Recent Advancements

Costin Teodor Streba, Bogdan Silviu Ungureanu,
Dan Ionuț Gheonea and Cristin Constantin Vere

Additional information is available at the end of the chapter

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1. Introduction

Over the years, medicines and the way we approach the patient have evolved from the basic clinical situations and the way we interpret signs and symptoms to imaging technologies that help us provide a faster and more reliable diagnosis. Nonetheless, along with endoscopy appearance in daily practice, patient's survival rate and treatment have improved, and have gradually become the mainstream of current use by introducing screening programs as in colorectal cancer (CRC) [1]. Based on the perceived balance between the necessity and benefits of endoscopy, this technique has prompted its need to be kept in current practice and has become a benchmark for human organs or cavity exploration.

The use of endoscopy within the gastrointestinal tract has been embedded as a welcome development for both diagnosis and therapeutic paths [2]. Continuous research of available technologies has led to a groundbreaking promising foundation to explore new options for patient's condition [3].

A large array of therapeutic alternatives has positioned endoscopy as the cornerstone for most of the diseases of the gastrointestinal tract and gradually has become a technique that may obviate surgery in some situations. From basic tissue harvesting to real-time confocal microscopic assessment [4] or from palliative therapeutic armamentarium to procedures more close tied to surgery procedures, gastrointestinal endoscopy has become more and more popular and along with its advantages or challenges has penetrated the gastroenterology community, becoming the touchstone for this medical specialty [5].

Modern gastroenterology is based on the availability of endoscopy and its secondary features in assessing the gastrointestinal tract. Technological development is a continuous process

in our day-to-day life and has been gradually inserted into endoscopy advances along with high-resolution endoscopes, devices, or accessories. The fact that some organs could have only been accessed by surgical procedures has promoted endoscopy to a level worthy of further appraisal. Among the different steps in endoscopy, the ones that surely changed the way we tend to diagnose or treat patients in daily practice are endoscopic retrograde cholangiopancreatography [6], capsule endoscopy [7], and endoscopic ultrasound [8, 9]. Thus, a new window was opened for both patients and physicians, and allowed the concept of evidence-based medicine to be used in daily practice.

Perhaps the biggest efforts in endoscopy were to improve the diagnosis of gastrointestinal tumors [10]. With various methods which are certified for cancerous gastrointestinal lesions, endoscopy has also become a valuable asset for early-stage diagnosis [10] and is still exploring new therapeutic avenues. Endoscopy screening and treatment of pre-cancerous lesions is part of a growing trend and has been increasing exponentially in many specific lesions due to new technology embedment or transposing current surgical procedures. Thus, a shift has taken place and the use of endoscopic systems has allowed technology to become part of both the physician and patient's life.

2. Diagnostic novelties in gastrointestinal endoscopy

2.1. High-definition endoscopy imaging

Substantial innovations in endoscopy imaging have occurred in the last 30 years, allowing physicians to perform a more personalized therapy for patients. With an increasingly technology-driven field, the current focus is to use high-definition (HD) techniques in a platform that will eliminate all disadvantages and will enhance the gastroenterologist's ability to provide a better diagnosis or therapeutic management [11]. Endoscopy has taken an important leap from basic imaging to digital, high-definition white-light resolution which detects and highlights mucosal changes that were not perceived by the previous techniques.

The use of HD endoscopes and monitors allows substantial image improvements by producing fewer artifacts on rapid movement and when combined with the corresponding processors may reach an image quality of over 2 million pixels [12]. HD magnification endoscopes have the ability of enlarging the image up to 150× with an adjustable focus and to discriminate between lesion's characteristics from 10 to 71 microns in diameter [13, 14]. Topical application of agents such as acetic acid, methylene blue (chromoendoscopy), congo-red, or even hematoxylin has proven beneficial [15].

Narrow band imaging (NBI) was introduced for early detection of lesions. By using a narrow band filter for blue and green, it illuminates tissue at wavelengths absorbed by hemoglobin, showing microvascular patterns (**Figure 1A–E**). This allows better characterization of lesions, which appear darker than the surrounding tissue [16, 17]. A different solution uses algorithms based on mathematical estimations of pixels. This technique has the advantage of generating a large number of wavelength permutations with adjustable settings [18, 19]. The I-scan technology uses three algorithms which may be applied simultaneously or one at a time: surface enhancement, tone enhancement, or contrast enhancement [20, 21].

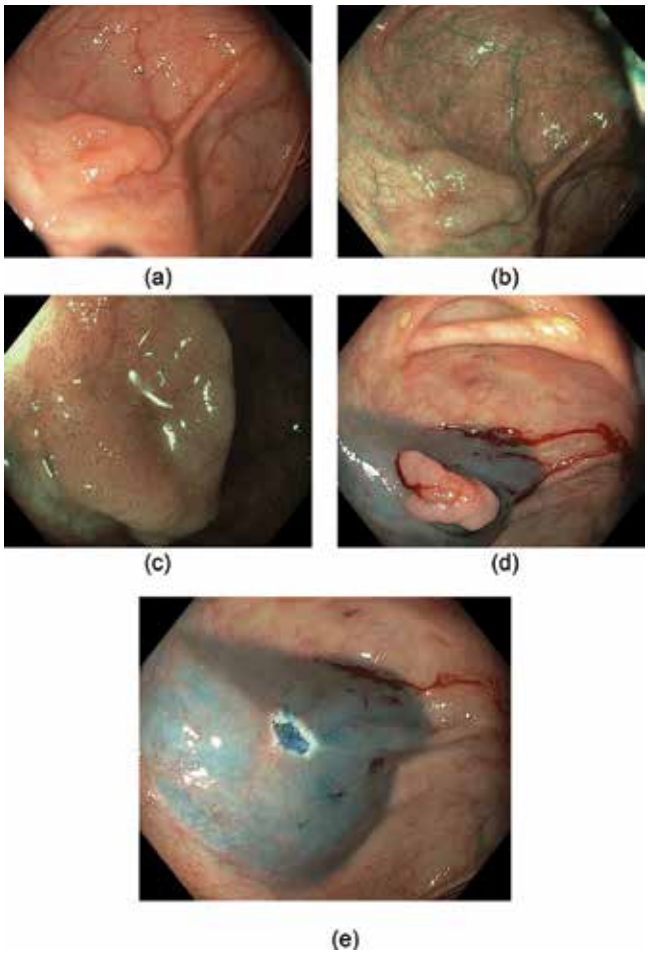

Figure 1. (A) HD endoscopy of a large colonic polyp; (B) NBI view for better characterization of the vessels; (C) HD endoscopy with NBI and magnification for pattern assessment; (D) submucosal injection of methylene blue and epinephrine 1/10,000 for elevation and enhancement in order to perform polipectomy (E).

2.2. Confocal laser endomicroscopy

Confocal laser endomicroscopy (CLE) is a cutting edge technique based on real-time image reconstruction on a subcellular level, in any endoluminal cavity by using flexible endoscopy [22]. The ability to see the microarchitecture in vivo in a non-invasive setting has opened up new windows of opportunity for a faster diagnosis. Thus, providing images of the mucosal layer will not only ensure a rapid assessment of the lesions, but will also have a role in choosing the right therapeutic management [23].

Based on a low-energy light source that enables acquisition of histology-like images, CLE usually requires the use of a dye for a better characterization of morphology or vascular pattern. The most used dye is fluorescein which has a safety profile, and has the ability of highlighting the vessels. However, the direction seems to be toward individualized situations whereas specific antibodies such as CD 31, CD105, and EGFR [24, 25] might be more useful for tissue

architecture description. CLE is considered a valuable tool with great potential that may overcome some of the disadvantages of classic histology such as time waiting or sampling bias, thus facilitating live diagnosis and treatment decisions. Also, its use might also lead to a lower number of biopsies, provide a real-time differential diagnosis in pancreatic tumors or access to the biliary tree, or even reduce the number of noncancerous lesions removed through endoscopic procedures [26, 27].

CLE is available either in an integrated conventional endoscope (Pentax, Tokyo, Japan) or on a probe-based system which is connected to a laser unit (Mauna Kea Technologies, Paris, France). Endoscope-based CLE (eCLE) systems (**Figure 2A, B**) are used for both upper and lower gastrointestinal tract examinations with depth scan images from 0 to 250 μm and scan rate of 1.6 frames/s. However, eCLE is no longer commercially available [28–30]. In contrast, probe-based CLE (pCLE) consists of different confocal miniprobes (Coloflex UHD, GastroFlex UHD, CholangioFlex) which provide images at different depths depending on its use, either for gastric, colonic, or biliary tract lesions. Moreover, a special probe was designed for an endoscopic ultrasound setting through a 19 gauge needle for a real-time assessment of pancreatic tumors. All miniprobes depending on their lesions' objective may be used for a maximum of 10 or 20 investigations.

Various applications have been tested for CLE from early gastric cancer [31], Barrett's esophagus [32], colonic polyps to inflammatory bowel disease (IBD) [33], and biliary strictures [34]. Many clinical settings have confirmed this technique as an evolutionary step and in synergy with histology have led to several atlases for pattern and morphology recognition. Surveillance CLE imaging after polyp resection or IBD therapeutic mucosal assessment has confirmed its success [35]. The advantages of CLE have been recognized by the Federal Drug Administration and it is currently used in some clinical settings and settled by insurance policies [36]. Thus, the field of endomicroscopy, a rather challenging one due to long learning curve and high costs, is on a continuous expansion with multiple methods being tested.

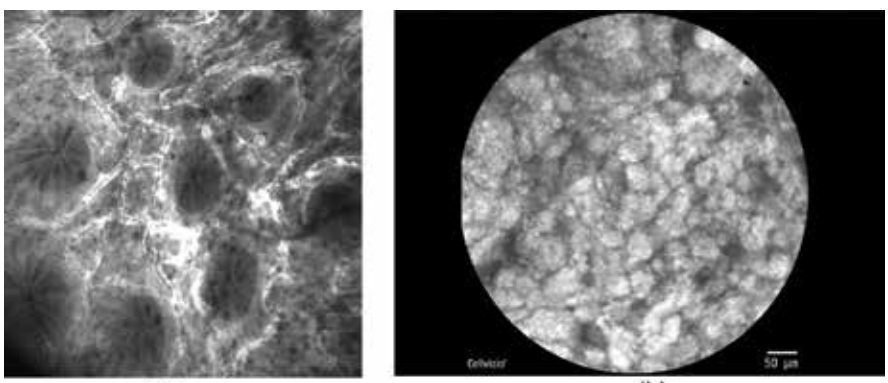

Figure 2. (A) CLE of normal colonic mucosa—the mucosal vessels as honeycomb appearance represented by a network of capillaries circumscribing the mucosal glands. Blood cells can be observed as dark shadows in the lumen; (B) pCLE image of an ex-vivo normal pancreas. Acriflavine staining which emphasize the acini distribution.

2.3. Capsule endoscopy

Video capsule endoscopy (VCE) has revolutionized the way we explore bowel disease, and has become the reference method for small bowel imaging diagnosis. From its commercial release in 2001, VCE surfaced as the most challenging alternative for upper endoscopy or colonoscopy [37]. However, as it turned out, its full potential is directed toward the small bowel, which until then represented an area difficult to explore.

Over the years, as technology evolved, the optical lenses and image resolution have laid grounds for new improved VCE, now reaching an image resolution of 512 × 512 pixels [38]. Moreover, the use of a dedicated analysis software may enhance the picture quality and provide more details that might suggest a more accurate diagnosis. This facilitated the new ways to analyze patterns and lesions, decreasing inter-observer variability [39].

The main indications are obscure gastrointestinal bleedings, with current guidelines available on Crohn's disease initial diagnosis, suspected celiac disease, and hereditary polyposis syndromes [40–42] (**Figure 3A, B**). There are also some dedicated capsules for the esophagus directed to Barrett's esophagus, esophageal varices or gastroesophageal reflux disease, or the colon, successfully used for CRC screening or adenoma detection. Colon CE (CCE) has also proven its efficiency in unsuccessful colonoscopies, or when patients willingly refused to perform a colonoscopy [43].

The major setback in VCE is the lack of biopsies. This has welcomed the implementation of virtual chromoendoscopy, color enhancement, or flexible spectral imaging. Rigorous colon preparation is required, as movements, washing, or aspiration are not possible [44]. While movement is based on bowel peristalsis or segmentation, future directions focus on systems controlled by active locomotion. Several robotic forms of CE have been developed. External magnetic systems have also been studied, either with direct control by the physician or by using external platforms with a console or robotic arm in conjunction with MRI or CT [45, 46].

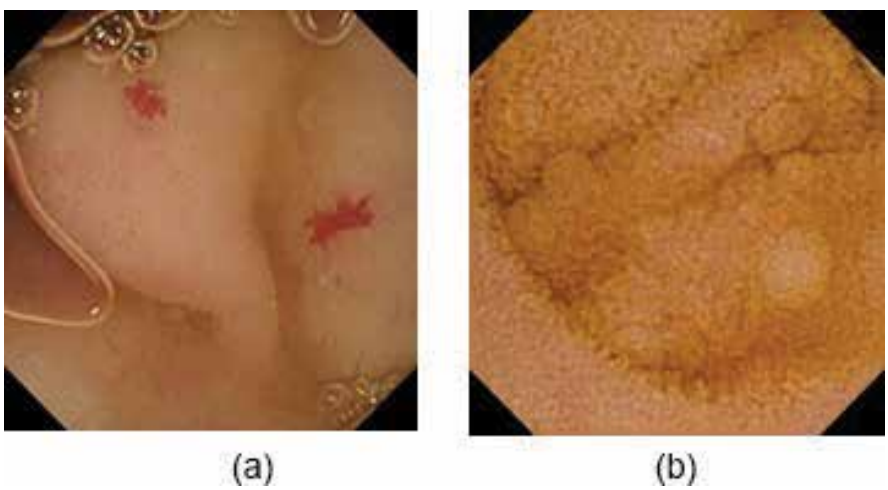

Figure 3. (A) VCE imaging of a telangiectasia and (B) an intestinal polyp.

The future of VCE is directed to remote-controlled tools for both diagnosis and therapy as in drug delivery systems. This will provide a non-invasive and easier management for the patient with potentially less side effects and stress than ordinary procedures.

3. Therapeutic endoscopy

3.1. Endoscopic retrograde cholangiopancreatography (ERCP)

Endoscopic retrograde cholangiopancreatography (ERCP) is the standard method for therapeutic management of biliary disease [47]. Progresses have been met from stone extraction to biliary stenting for both malignant or benign stenosis and even ablation of biliary tumors. On this latter platform, the next step was set to the development of the peroral retrograde cholangioscopy, a technique that can provide direct images of bile and pancreatic duct [48–50]. A single operator device employed through the working channel of the duodenoscope has provided images that changed the way some diseases are managed [51]. It is mostly used for the differential diagnosis of biliary strictures; cholangioscopy decreases perforation and bleeding rates [51–55]. Spyglass digital system technology has stepped into the next generation of devices by providing high-resolution images with a field view of 110 and by eliminating degradation over excessive use [56]. With a friendly-user interface, this technique might solve the so far inaccessible path of biliary irresolute diagnosis (**Figure 4**).

3.2. Endoscopic ultrasound

Endoscopic ultrasound (EUS) development has opened up new horizons for diagnosis and management, especially in pancreatobiliary disease [57]. While on a continuous evolution process, EUS has been introduced as a standard diagnosis technique which provides information

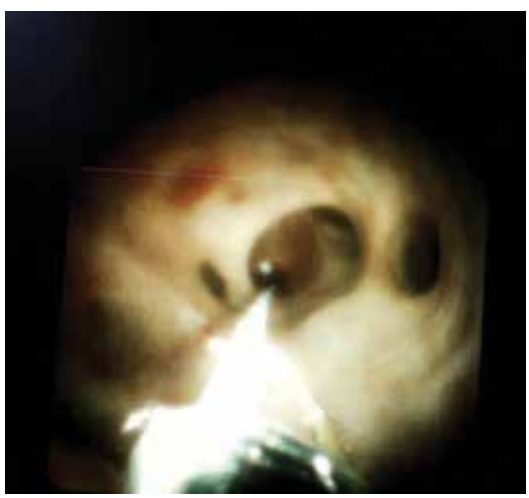

Figure 4. Spyglass endoscopy. Cholangioscopy image with biliary stenosis and dilatation of the biliary tract.

of structures located near the gastrointestinal tract. The arrival of fine-needle aspiration (FNA) has paved the way for various new therapeutic options that may substitute several surgical procedures or provide new options for cancer therapies [58]. EUS-drainage of fluid collections represented the grounds for novel techniques which focus on joining two cavities [59]. Along with the additional growth of the industry of endoscopy supplies, EUS has enabled novel therapeutic alternatives. Lumen-apposing metal stents are highlighting a fine line between the gastroenterology and surgical community [60] (**Figure 5A, B**). EUS-guided gallbladder drainage [61], EUS-choledochoduodenostomy [62], EUS-pancreaticogastrostomy [63], and the most recent EUS-gastrojejunostomy [64] represent some of the challenges that were introduced with focus on minimally invasive therapy.

Cancer-directed therapy has been the EUS objective with several alternatives so far. EUS-guided radiofrequency ablation has been successfully used in pancreatic tumors, along with alcohol injection. However, the most interesting technique seems to be injection of chemotherapeutic agents either directly within the tumor or within the venous system. This setting might provide a larger volume of drugs to the tumor and enhance their effect, while avoiding systemic reactions. Pain therapy has also been a matter of discussion especially in pancreatic cancer with the EUS-guided celiac plexus neurolysis and celiac plexus block after alcohol injection [65–67].

3.3. Submucosal endoscopy

Greater experience in flexible endoscopy and new devices development have gradually introduced the concept of therapeutic endoscopy from endoscopic mucosal resection (EMR) to endoscopic mucosal dissection (ESD) [68, 69]. Recently, the concept of endoscopic full thickness resection (EFTR) has gained attention trying to secure the possible complications [69]. Over-the-scope clips and new suturing endoscopic devices are instruments worthy of appraisal even though it gets us closer to natural orifice transluminal surgery (NOTES) [70]. Currently, peroral endoscopic myotomy (POEM) for the treatment of achalasia represents one of the most advanced NOTES technique performed in gastroenterology, which requires a high level of skill in performing submucosal tunneling, injection, and hemostasis. POEM has prevailed as a new reference method in achalasia treatment [71].

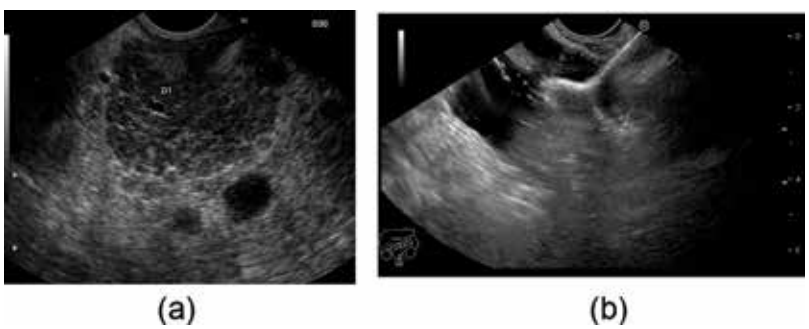

Figure 5. (A) EUS of the pancreas—inhomogeneous tumor with hyperechogenic foci localized at the level of the head of the pancreas; (B) balloon-assisted EUS-gastrojejunostomy in a pig with a hot metal lumen-apposing metal stent.

Conflict of interest

The authors have no conflicts of interest to declare.

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Section 2

Respiratory Tract

Chapter 2

How to Sample the Unreachable: Transbronchial Biopsy

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Abstract

Transbronchial biopsy (TBBx) or bronchoscopic lung biopsy (BLBx) should be a diagnosis tool for focal peripheral lesions and for diffuse lung disease in every bronchoscopic suite around the world. The main advantage of this procedure is that it avoids open lung surgery for peripheral lung biopsy. The procedure is usually safe and can be done in an outpatient setting with moderate sedation, but life-threatening complications can occur, so a proper evaluation of the risk benefits ratio should be carefully analyzed before the intervention. There is no need for guidance in diffuse peripheral lesions, but for localized peripheral lesions, the diagnostic yield of TBBx is significantly higher with fluoroscopic guidance. In this chapter, we assess the utility, indications, and contraindication of this technique, as well as its clinical applications and complications.

Keywords: lung biopsy, transbronchial biopsy (TBBx), bronchoscopic lung biopsy

1. Introduction

Transbronchial biopsy (TBBx) or bronchoscopic lung biopsy (BLBx) should be a diagnosis tool for focal peripheral lesions and for diffuse lung disease in every bronchoscopic suite around the world. The main advantage of this procedure is that it avoids open lung surgery for peripheral lung biopsy. The procedure is usually safe and can be done in an outpatient setting with moderate sedation, but life-threatening complications can occur, so a proper evaluation of

the risk benefits ratio should be carefully analyzed before the intervention. There is no need for guidance in diffuse peripheral lesions, but for localized peripheral lesions, the diagnostic yield of TBBx is significantly higher with fluoroscopic guidance. In this chapter we assess the utility, indications, and contraindication of this technique, as well as its clinical applications and complications.

2. Indications

TBBx is a solution to consider in a large variety of peripheral lung disorders. TBBx can be combined for an increased yield of diagnosis with other bronchoscopic diagnostic procedures, like bronchial and bronchioloalveolar cytology washings, cytology brushes, and peripheral transbronchial needle aspirations.

The main indications for TBBx are malignancies, infections, and diffuse lung diseases.

2.1. Malignancies

In peripheral malignancies, the average diagnostic yield of TBBx is 57% (17–77%). When this procedure is done in combination with peripheral bronchial washing and brushing, it comes with an exclusive diagnosis in up to 19% of the patients [1].

In lymphangitic carcinomatosis, TBBx appears to have a high diagnostic yield, but in metastatic pulmonary tumors, the diagnostic yield is limited (17%).

There is great debate around the number of biopsies necessary in order to have a satisfactory diagnostic yield. Descombes et al. showed a 21% diagnostic yield in the case of 1–3 TBBx biopsies and 78% yield when 6–10 biopsies were taken. Popovich et al. showed an increase of 25% between the first TBBx diagnostic yield (45%) and multiple biopsies (70%). There is a general consensus, based on these studies and many more, that 6–10 biopsies should be taken for an optimum diagnostic yield in lung cancer [2, 3].

The size of the lesion and its relationship with the bronchial tree are also very important to assess the utility of TBBx. Regarding the size of the lesion, studies showed a diagnostic yield of 34% in the case of a lesion smaller than 2 cm and 63% for lesions greater than 2 cm in diameter [4]. Regarding the position of the lesion in relation to the bronchial tree, there are four situations very well described by Tsuboi et al. (**Figure 1**): type I, in which the tumor is at the end of the opened bronchus; type II, when the tumor contains the bronchus; type III, when the bronchus trajectory is modified, and the diameter can also be modified, either compressed or narrowed by the tumor mass, but the bronchial mucosa is normal; and type IV, when the bronchus is narrowed in the proximal part by the submucosal and peribronchial infiltration of the tumor, fibrosis, or enlarged lymph nodes [5].

There is an issue regarding the bronchus sign often seen on thoracic CT, which means that the permeable bronchus is contained in the tumor mass or it ends with the tumor. The significance

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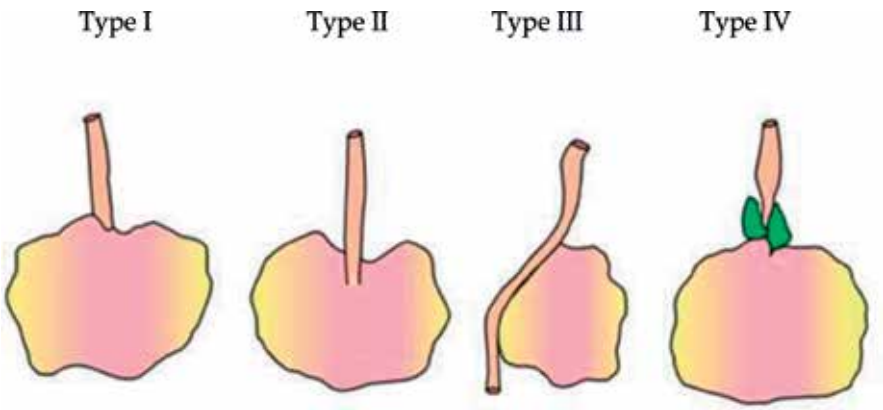

Figure 1. Relationship between tumor mass and tributary bronchus [5].

would be that with the bronchus sign present on thoracic CT, the yield of TBBx is 60–82%, compared with 0–44% when the bronchus sign is absent [6–8].

It is recommended that in the case of a type III or IV lesion, peripheral transbronchial needle aspiration (TBNA) should be used for sampling the tumor instead of TBBx, due to the needle ability to pierce the tumor directly beyond the narrowed and displaced bronchial tree, which is very hard for the TBBx forceps to do.

2.2. Infections

TBBx is used in a variety of pulmonary infections as well. The main indications for TBBx in lung infections are non-resolving pneumonia, *Mycobacterium tuberculosis* or nontuberculous *Mycobacterium* infection, fungal infections, *Pneumocystis carinii* pneumonia, and some viral infections, such as CMV pneumonitis.

2.2.1. Non-resolving pneumonia

The term non-resolving pneumonia, which must be differentiated from non-responding pneumonia and slowly resolving pneumonia, is defined as the persistence of clinical symptoms and signs (cough, sputum production, with or without fever >37.7°C) and failure of resolution of the radiographic features by 50% in 2 weeks or completely in 4 weeks on serial chest X-rays, in spite of antibiotic treatment for at least 10 days. Arancibia et al. reached a diagnosis in non-resolving pneumonia patients who failed antibiotic treatment in 57% of the cases. Nevertheless, TBBx is seldom used for non-resolving pneumonia, because other methods are less invasive and at least as useful, like protected brushing and bronchoalveolar lavage. TBBx is invaluable because it can confirm other pathologies like *Mycobacterium* (tuberculosis or non-tuberculosis) infections, fungal infections, neoplasms (bronchioloalveolar cancer), BOOP, and histiocytosis [9].

2.2.2. Tuberculosis

Tuberculosis has a high morbidity and mortality worldwide. Nowadays, despite the discovery and availability of specific preventive and curative chemotherapy, pulmonary tuberculosis is still a fatal airborne transmitted disease [10]. Fiberoptic bronchoscopy and TBBx are an important bronchoscopic procedure to evaluate patients with negative smears and radiologic and anamnestic suspicion of pulmonary tuberculosis. It can provide immediate histopathology and smear-positive diagnosis, and it can rule out malignancies and fungal infections presenting like pulmonary tuberculosis as differential diagnosis [11].

In the vast majority of patients, adding TBBx to bronchoalveolar lavage is the maximum of procedures that can be undergone to have a confirmation diagnosis. The usual candidates for these methods would be patients with a clinical suspicion of active tuberculosis, with suspected lesions on chest X-ray or thoracic CT and at least three negative acid-fast bacilli sputum exams, or with inability to provide good quality sputum. TBBx provides confirmation diagnosis in 17–60% of active pulmonary tuberculosis cases [12].

TBBx also provides rapid confirmation diagnosis in smear-negative miliary tuberculosis, with a diagnosis yield of 60–80% [13, 14].

2.2.3. Non-tubercular mycobacteria

TBBx should be performed whenever there is a suspicion of non-tubercular pulmonary infection. According to the American Thoracic Society, the diagnosis of non-tubercular pulmonary infection requires one of the following microbiological criteria, in a favorable clinical setting: at least two separate positive sputum cultures *or* at least one positive culture from bronchial lavage *or* transbronchial biopsies with granulomatous inflammation, Ziehl Nielsen acid-fast bacilli with positive non-tubercular bacilli cultures, and at least one sputum exam or bronchial wash culture positive for non-tubercular mycobacteria [15].

2.2.4. Fungal infections

In fungal infections usually there is no need for TBBx, because a confirmation diagnosis is reached with the help of bronchial washings and bronchioloalveolar lavage procedures. There is little improvement in diagnostic yield with this procedure, and so it should not be done at first bronchoscopy except in the case of negative initial tests, with a maintained suspicion of fungal infection [16, 17].

2.3. Diffuse lung diseases

2.3.1. Sarcoidosis

In sarcoidosis, a confirmation diagnosis is established at bronchoscopy with a combination of bronchioloalveolar lavage, endobronchial biopsy, transbronchial biopsy, and transbronchial needle aspiration. As we can see, there are a lot of diagnostic possibilities to choose from when we are looking for a confirmation. It depends, however, on the stage of sarcoidosis to choose

the best, minimum invasive procedure that will provide a confirmation. The stages of sarcoidosis are stage I, when we have lymph node involvement; stage II, when we have lymph node involvement and pulmonary infiltrates; stage III, when granulomas are only present in the lung tissue, expressed radiologically as pulmonary infiltrates; and stage IV, when diffuse scarring is found in the lung tissue, indicating irreversible damage. The diagnostic yield of TBBx varies between 50 and 65% in stage I, 63 and 82% in stage II, and 80 and 85% in stage III. Bronchial mucosa is frequently involved in all stages of sarcoidosis, so an endobronchial biopsy adds an average of 20% over the diagnostic yield of TBBx [18–20].

Of course, one should always look for reaching the most affected areas of the mediastinum and lung parenchyma. For example, in lymph node involvement (stage I and III), one should always puncture the nodes (conventional transbronchial needle aspiration or echo-guided needle aspiration) with or without endobronchial biopsy and TBBx, in the same procedure.

2.3.2. Lymphangitic carcinomatosis

The nonspecific diffuse interstitial pattern of lymphangitic carcinomatosis is a serious differential diagnostic problem, especially in patients without any obvious primary carcinoma, and it is often a cause of delayed diagnosis and postmortem tissue confirmation. In these patients, differential consists of acute or subacute infectious processes, radiation pneumonitis, chemo drug reaction, idiopathic pulmonary fibrosis, or diffuse tumor infiltration [21].

2.3.3. Pulmonary alveolar proteinosis

The worldwide accepted diagnosis for pulmonary alveolar proteinosis (PAP) is still reached by flexible bronchoscopy with bronchoalveolar lavage (BAL). Transbronchial biopsies can be combined with BAL findings when these are done in the affected lung segments, and these are both usually sufficient to establish the etiology. One must be aware of this diagnosis possibility and request PAS staining. Usually, this is the cause of underdiagnosis (low suspicion). PAP can still be diagnosed by requesting Papanicolaou staining from BAL that can show specific green and orange globules. BAL analyzed by electronic microscopy can also reveal specific multilamellar structures.

2.3.4. Pulmonary Langerhans histiocytosis

Clinical features and high-resolution computed tomography usually suggest this diagnostic, but tissue confirmation is still needed. Surgical lung biopsy for confirmation is the golden standard because of being able to sample the affected areas and to provide an appropriate amount of tissue. TBBx can also provide tissue for a confirmation diagnosis in some cases, but the yield varies from 10 to 40%. This low yield is probably due to biopsy site selection error secondary to patchy distribution of the lung infiltrates. In conclusion, a nondiagnostic TBBx procedure should be followed by a surgical biopsy confirmation. One should always look for Langerhans cells staining for CD1a (>5%) and S100 protein on immunocytochemistry, but false-positive results can be found in smokers [22, 23].

2.3.5. Amyloidosis

Without lung biopsies, amyloid lung disease often goes unrecognized. Amyloidosis represents a heterogeneous group of diseases characterized by the deposition of congophilic fibrils in the extracellular matrix of tissues and organs. In an amyloid lung, there can be multiple clinicopathologic forms of lesions. These are diffuse amyloidosis with an alveolar-septal pattern, nodular amyloidosis, and tracheobronchial amyloidosis (less frequent encountered). There is no specific localization or extent of these lesions, but there have been described three types of lesions: proximal, mid, and distal involvement. Flexible bronchoscopy with TBBx is the preferred tool for tracheobronchial amyloidosis diagnosis. Computed tomography usually appreciates the extent of the disease. Severe amyloid deposition in the proximal and mid bronchi can endanger air passage, a situation in which laser or/and forceps recanalization is required. External beam radiation therapy can also be used for endobronchial debridement. The mortality is an important matter in this situation, because recurrence is very common and approximately 30% of these patients eventually die [24].

2.3.6. Lymphangioleiomyomatosis (LAM)

LAM is a rare cystic lung disease that affects women during their reproductive years. LAM is usually difficult to diagnose because of its similarity to other lung diseases and because symptoms are variable from patient to patient. There are a number of tests that a physician can address to in order to confirm or infirm the existence of LAM and to evaluate the extent of lung damage, as well as the spread. High-resolution CT scan (HRCT) is the most accurate and noninvasive test for diagnosing LAM. It can be used in combination with VEGF-D blood test to help distinguish LAM from other cystic lung diseases. Sometimes, an elevated VEGF-D level is enough to confirm diagnosis, though it can be looked at as a replacement for lung biopsy. Nevertheless, lung biopsy is the gold standard for LAM diagnosis, and transbronchial biopsy plays an important role because it is less invasive than surgical lung biopsy. However, the amount of tissue obtained through this procedure may sometimes not be enough for a definitive LAM diagnosis. Also, immunohistochemical studies from the lung biopsies show positive staining of LAM cells for HMB-45 monoclonal antibodies and for estrogen receptors, and they both strongly support LAM diagnosis [25–27]. Some authors found that TBBx has a yield of approximately 60% in patients with LAM. Therefore, they concluded that TBBx is safe and effective for the diagnosis of LAM, avoiding surgery with lung biopsy in more than half of LAM patients [28].

2.3.7. Bronchiolitis obliterans with organizing pneumonia (cryptogenic organizing pneumonia)

The pathologic hallmarks of COP include granulation tissue in the terminal and respiratory bronchioles and alveolar ducts which can be extended and organized into alveoli. Also, chronic inflammatory changes in the surrounding interstitial space can be found. As mentioned before, in some settings TBBx was found to be adequate for diagnosis, but thoracoscopic or surgical lung biopsy has the advantage of larger lung biopsy specimens, and this is needed in order to exclude other conditions that mimic COP. In specialized centers though, TBBx in COP has sensitivity of 64%, specificity of 86%, and positive predictive value of 94% and negative predictive value of

40%. Literature recommends TBBx before referring the patients for more invasive methods. Nevertheless, if diagnosis remains unclear after TBBx and if incomplete response to oral corticosteroids is seen, a surgical approach with lung biopsy must be performed [29–34].

2.3.8. Hypersensitivity pneumonitis (HP)

HP is mostly a clinical diagnosis, and histopathological confirmation is only necessary when diagnosis is uncertain or the clinical outcome is inadequate in spite of treatment. Large biopsy specimens are needed, but in some cases of acute and subacute HP (less in chronic HP), TBBx showed adequate specimens. The histopathological findings in subacute HP consist of cellular bronchiolitis, diffuse interstitial infiltrates of chronic inflammatory cells, and scattered noncaseating granulomas [35–37].

3. Contraindications

There are absolute and relative contraindications for TBBx.

Absolute contraindications:

- Absence of informed consent
- Lack of patient cooperation
- Inadequate facilities for patient resuscitation
- Uncorrected bleeding disorders
- Severe pulmonary hypertension
- Massive hemoptysis
- Refractory hypoxia
- Uncontrolled arrhythmias
- Uncontrolled cough
- Uncontrolled bronchospasm

Relative contraindications:

- Uremia—Because uremic patients have a higher risk of bleeding when TBBx is performed, serum creatinine should be measured in the case renal insufficiency is presumed. Some studies showed increased bleeding when both BUN >30 mg/dl (urea >64.2 mg/dl) and serum creatinine >3.0 mg/dl [38]. However, elevated BUN can also be encountered in other situations, like congestive heart failure, dehydration, gastrointestinal bleeding, some antibiotics, and high-protein diet.
- Thrombocytopenia (when the platelet count is less than 50,000/μL).

- Pulmonary hypertension (although there is little evidence regarding excessive bleeding after TBBx even in severe pulmonary hypertension, it is considered to be a safe procedure when pulmonary hypertension is mild to moderate) [39, 40].
- Anticoagulants and antiaggregants, if not discontinued. Aspirin can be continued, but clopidogrel must be discontinued at least 5 days before TBBx. Warfarin must be discontinued 3 days before the procedure and heparin 6 hours before, whereas enoxaparin given in deep vein thrombosis can be discontinued 12 hours before the procedure (do not administer in the morning of the procedure). Targeted international normalized ratio (INR) must be below 1.5 (some studies showed a better safety profile when INR is below 1.3) [41, 42].
- Mechanical ventilation—In these patients there is an increased risk of tension pneumothorax when TBBx is performed, so benefits should be balanced against the risks and discussed with the patients, for proper management.

4. Complications

There are different percentages of procedure-related complications in the literature, depending of many factors, like patient selection, the pulmonary disorder for which the TBBx was done, the use of sedation, the number of biopsies taken, forceps size, and nevertheless, the bronchoscopist's experience.

The major complications of TBBx are pneumothorax and bleeding.

Pneumothorax is encountered in 1–6% of patients with performed TBBx [2].

A prospective study of 350 cases revealed that chest X-rays are usually not necessary after TBBx, but it is still recommended for safety reasons [43].

The size of the pneumothorax was associated with the symptoms, so it is possible to have an immediate evaluation of the pneumothorax magnitude based on patient's clinical status. Pneumothorax is a rare instance but may be followed by a pigtail catheter insertion for lung re-expansion. Repeated chest radiographs are usually necessary to follow lung re-expansion and to choose the right moment to extract the chest tube.

Failure to control coughing during TBBx increases pneumothorax risk. Patients with positive-pressure ventilation devices are more likely to manifest pneumothorax after TBBx. In patients with bullous emphysema and in those with pneumocystis pneumonia, the pneumothorax risk is higher [44].

Fluoroscopic guidance during TBBx lowers the risk of pneumothorax. Fluoroscopic examination can reveal pneumothorax cases right after TBBx, but sometimes slowly developing pneumothorax is encountered several hours after the procedure [45].

Tension pneumothorax is a rare event. If no symptoms are present 4 hours after the procedure, a pneumothorax with clinical significance is usually not present. Chest X-ray should be

performed after ½–1 hours after TBBx when high-grade suspicion is present despite normal post-bronchoscopy fluoroscopy. The presence of symptoms and the extent of pneumothorax on chest X-ray establish the management of pneumothorax, but oxygen delivery and continuous inpatient observation usually are sufficient. Another method used in patients with moderate symptoms, but with determined significant pneumothorax, is Heimlich's valve placement in the bronchoscopy lab. In these instances, if repeated X-rays show no increased pneumothorax after 4–6 hours, they can be discharged with Heimlich's valve on. In case of lung re-expansion failure or incomplete lung re-expansion using Heimlich's valve, especially when severe symptoms are present, it is mandatory to place a chest tube drainage system. If pneumothorax is encountered in patients mechanically ventilated, it is also mandatory to place a chest tube system without delay [46].

Bleeding after transbronchial biopsy occurs in 0–26% of cases. Important bleeding is encountered in 1–2% of patients after TBBx [47].

Bleeding risk is higher in patients with renal insufficiency and in patients with depressed immune system, and though sporadic reports of deaths caused by bleeding after TBBx have been published, it is thought to be an underreported instance. Usually, bleeding events developed after TBBx can be managed in the bronchoscopy suite. Patients with minor bleeding after TBBx are usually observed with the bronchoscope, waiting for the bleeding to stop. One should not apply suction near the biopsy area because the clot must be allowed to form. This way, the bleeding is mostly self-limited. The main concern in case of bleeding after a TBBx procedure is not the risk of exsanguination but the risk of flooding other lung segments. That is why one must keep the bronchoscope wedged into the tributary bronchus in order to prevent the blood flooding other lung segments and with the purpose of letting the clot to be formed. This technique has been first described by Zavala [48]. In case of significant bleeding despite bronchus blockage, it is important to put the patient in the safety position, with the affected bleeding side inferiorly.

The wedged position of the bronchoscope can be lost during TBBx and when it happens, the bronchoscopist must reposition the bronchoscope in the same wedged position as soon as possible. Sometimes, this maneuver is difficult when there is significant bleeding from the biopsy site, so the bronchoscopist must be able to reposition the bronchoscope without visual help, only by picturing in his mind the bronchial tree and repeating the exact insertion movements of the bronchoscope in order to reach the previous wedged position. Fluoroscopic guidance can help when endoscopic view is lost. Usually, the bronchoscope is wedged for only 5 minutes, and then it can be gently retracted slowly, verifying the withdrawal step by step and assuring that the bleeding is contained. Another way of dealing with bleeding risk is to withdraw the bronchoscope and to apply suction preventing blood from entering other vicinity pulmonary segments. One can also administer 1:20000 epinephrine in total quantity of 20 ml and cold saline bursts on the channel of the bronchoscope, and as final safety solution, one can place an endobronchial blocker that practically blocks the segmental bronchus tributary to the bleeding biopsy site. Few post-TBBx bleeding cases need endotracheal tubes to secure the airways, balloon tamponade, or even contralateral lung selective

intubation. The existing literature recommends that the bronchoscopy suites should be able to sustain a possible rigid bronchoscopy intubation as ultimate safety solution for these special cases, if the bleeding cannot be controlled only with the help of flexible bronchoscope [46].

Rare complications that have been reported include mediastinal and subcutaneous emphysema.

5. Procedure preparation

Each patient should have detailed history taken and thorough physical examination and radiological assessment (chest X-ray and a thoracic computed tomography) before the procedure. A complete blood work is not mandatory but is based on patient's history and clinical evaluation. It should contain complete blood count, coagulation profile, blood chemistry, and arterial blood gas analysis. Spirometry and electrocardiogram are not mandatory before the procedure. These investigations should be reserved for individual clinical relevant findings or in the case of known comorbidities.

Adequate airway examination should precede the transbronchial biopsy. For this to happen in an undisturbed matter and with total patient cooperation, one must control cough with progressive lidocaine instillation, as well as administer sedation with systemic administration of opiates. This way, the patient is calm, with no anxiety or cough that can interfere with the procedure and lead to a higher risk of complications, like pneumothorax.

A proper bronchoscopic and TBBx technique must be mastered, regardless of the degree of sedation and anesthesia used, because it reduces the incidence of complications, also. Fluoroscopy is nevertheless important, when it can be used, because it can increase diagnosis yield and decrease pneumothorax as complication of TBBx. Other factors that can help decrease complication rates are the presence of an intensivist-anesthesiologist and a second interventional pulmonologist. The team must be prepared to intervene in emergency situations like pneumothorax and massive bleeding from the biopsy site. Necessary equipment for complication management, like balloon catheters, endobronchial blockers, chest tubes, or endotracheal intubation tubes must be immediately available [49].

6. Pre-procedure concerns

Chest computed tomography (CT) must be performed before bronchoscopy because it shows the anatomic appearance, vascularization, and nearby reports of the targeted lesions. CT can provide a probability diagnosis corroborated with a proper anamnesis especially in patients with sarcoidosis, usual interstitial pneumonia, Langerhans cell histiocytosis, subacute hypersensitivity pneumonitis, acute eosinophilic pneumonia, or lymphangioleiomyomatosis. In the event of non-diagnosis abnormalities, chest CT still provide a picture of peribronchovascular

and central lesions that can easily be sampled by TBBx, like centrilobular nodules of ground-glass attenuation, for example [37].

7. Equipment

When a TBBx is necessary, one must have an interventional bronchoscopy room equipped with devices for monitoring oxygen saturation, heart rate, blood pressure, respiratory rate, and, if possible, end-tidal CO_2. Of course, one must have available adult-size flexible video bronchoscope, suction device, biopsy forceps, specimen containers, as well as proper cardiopulmonary resuscitation equipment, and mandatory supplemental oxygen. If possible, in case of emergency, the interventional bronchoscopy multidisciplinary team must be able to convert the flexible bronchoscopy into rigid bronchoscopy, for safety reasons. In regard to the TBBx forceps, it can be cupped and toothed with a needle that can anchor the lesion. It is not mandatory but is recommended to have fluoroscopy equipment in the room for better localization of the lesions and to minimize the risk of pneumothorax [46].

8. Patient preparation

Usually, TBBx is performed with the patient in supine position. After positioning, topical anesthesia with lidocaine 2–4% is delivered by spraying or by instilling directly on the nasal and/or oropharyngeal mucosa, depending on the preferred way of inserting the bronchoscope. A good laryngeal anesthesia is then achieved by instilling or aerosolizing lidocaine using a nebulizer.

After a good anesthesia is carried out, the patient can undergo moderate (conscious) sedation using narcotics and benzodiazepines, in incremental doses. This method is safe and increases the yield of TBBx, since the procedure is performed without patient cough or anxiety. Both benzodiazepines and narcotics have different degrees of respiratory depression as side effects, so permanent monitoring is required. The best way of assuring good sampling of the targeted peripheral lung parenchyma remains rigid combined with flexible bronchoscopy, though. In this case, general anesthesia is mandatory [49].

Benzodiazepines are used for their effects of amnesia, anticonvulsant, anxiolytic, muscle relaxant, and behavioral disinhibition.

Usually, midazolam is the best benzodiazepine for short-term moderate sedation because it has the highest lipid solubility (that reassures better nervous system penetration), is one of the fastest onset of action (3–5 minutes), has an incremental dose of 0.5–1 mg (loading dose is around 0.02–0.1 mg/kg), with an average total dose of 1–5 mg that can be administered every 3–5 minutes depending on the degree of sedation needed, and has the shortest effect duration of all intravenous benzodiazepines, of only 0.5–2 hours.

Fentanyl is also used for moderate sedation at a large scale. Its high degree of lipid solubility provides a better penetration in central nervous system structures, as well. Next to morphine, fentanyl has 600 times more lipid solubility and has less hemodynamic effects with the same level of analgesia at a nearly 1/100 of the morphine dose, and the onset of action is faster (1–2 minutes). It has an effect of action 30–60 minutes with a loading dose of 50–100 μg.

Propofol and dexmedetomidine are also used [49].

9. Technique

Radiological and fluoroscopic findings, when available, guide the choice of the biopsy site. One should not attempt TBBx from the both lungs in the same procedure because of an increased risk of bilateral pneumothorax. When we have focal disease, the selection of biopsy site is relatively easy to choose. If diffuse disease is present, the choice of biopsy site requires some things to be taken into consideration. In these cases, literature recommends to take the biopsy from the lower lobes, left or right lung, because of the fact that the bleeding is usually contained in these areas before it spills into the other lobes. Biopsy from the upper lobes is to be avoided because the blood can easily pass into other segments from the inferior lobes, bilaterally, and thus limiting the time to react in order to stop the bleeding.

Once the selected site is chosen, the distal end of the bronchoscope is passed through the specific segmental bronchus until it wedges. Then, the biopsies are performed, with the help of fluoroscopy, if available. The forceps is introduced and advanced through the working channel of the bronchoscope until mild resistance is usually felt. This is due to the mild resistance encountered when passing through the distal end of the flexible bronchoscope, especially when the biopsy is performed from the upper lobes or the upper segments of the lower lobes, when distal end is more bended than usual. One must not push very hard in this situation, because the channel of the flexible bronchoscope can very easily be damaged by the forceps. The solution is to slightly let go of the control lever and gently advance the forceps until it passes the distal end of the flexible bronchoscope. In this manner, there is a possibility to lose the wedged position of the bronchoscope in the specific segmental bronchus. In this case, one can retract the bronchoscope from the wedged position and push the forceps a couple of centimeters beyond the distal end of the bronchoscope into the targeted segmental bronchus and then gently advance the bronchoscope using the forceps as guide. Using the fluoroscopic guidance of the TBBx, one should advance the forceps in the selected pulmonary segment until resistance is met. This is due to the fact that the tip of the forceps is very close to the visceral pleura. The forceps is then pulled out 2–3 cm in which time the patient is instructed to take a deep breath and hold for a little while. In this way, the peripheral airways are dilated, and so the forceps can be opened easily. The patient is asked to breathe out while the opened biopsy forceps is gently advanced under fluoroscopic guidance until resistance is met. This is due to the fact that the larger surface of the opened forceps is blocked in its advancement earlier than the narrower surface of the closed forceps by the bifurcation of the respiratory and terminal bronchioles, meaning that the site of the biopsy has been reached. Then, the assistant is asked

to close the forceps that can be gently retracted afterwards. The lung parenchyma is usually sampled by tearing off the respiratory and terminal bronchioles [46].

In case there is a focal lung cancer, presenting like a solitary mass or nodule, by the same method, the forceps is advanced until the tumor's margin is reached. If fluoroscopy is available, now is the time to rotate the arm of the fluoroscope to be aware of the movement of the biopsy forceps related to the lung lesion. A good positioning of the biopsy forceps can be trusted if both the lesion and the forceps move together with the movement of the fluoroscope. After confirming the correct position, the forceps is then retracted approximately 0.5–1 cm and then opened. The opened forceps is then inserted firmly into the mass, this position being also confirmed by fluoroscopy, then closed in a decisive manner, and pulled back gently or slightly rotated along with the retraction. Somehow different from the TBBx of diffuse interstitial lung disease, TBBx of a lung mass or nodule does not need respiratory maneuvers. Another sign of a good position and biopsy is the fact that when the biopsy is actually taken, the lesion moves along with the forceps. The ideal transbronchial biopsy specimen consists of four to six samples, with at least one sample containing full-thickness bronchial mucosa and some alveolar parenchyma, so this maneuver can be repeated several times from the same area of interest, in the same time keeping as much as possible the bronchoscope in a wedged position. This prevents the blood resulting from the biopsy site to spill into other parts of the lungs and favors the blood clot formation having a tamponade effect over the source of bleeding. The period of time required for an acceptable hemostasis is of at least 4 minutes after all biopsies have been taken. Of course, one should not apply suction at any time to allow the formation of the blood clot [46].

10. Conclusions

Transbronchial biopsy is a very important tool in the interventional bronchoscopy tools spectrum, mainly due to the fact that surgery can be avoided with a successful TBBx. Patients do not easily accept surgical lung biopsy as diagnosis method because it is more invasive and it requires general anesthesia. TBBx provides an acceptable diagnosis yield in peripheral lung masses, depending on the size of the mass and the presence of bronchus sign, which represent a guarantee that the mass is reachable with the forceps or needle, for that matter. TBBx is also indicated in pulmonary tuberculosis, fungal infections, and other lung infiltrates, when the etiology is unclear. It has an important role in immunocompromised patients and post–lung-transplant patients for the periodic evaluation of the rejection disease, as well as opportunistic infection diagnosis. TBBx has a lower yield, yet important, in the diagnosis of lymphangitis carcinomatosis, sarcoidosis, pulmonary Langerhans' cell histiocytosis, and lymphangioleiomyomatosis. Diagnosis yield is too low to consider in idiopathic pulmonary fibrosis and different types of idiopathic interstitial pneumonia, as well as in lung nodules less than 2–3 cm in diameter. The main complications of this technique are hemoptysis and pneumothorax, encountered in less than 2% of cases. In the event of performing this interventional bronchoscopic procedure, one must be able to efficiently perform the procedure and manage the complications that can follow.

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Digestive Tract

Chapter 3

Applications of Cholangiopancreatoscopy in Pancreaticobiliary Diseases

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Additional information is available at the end of the chapter

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Abstract

Recent advances in imaging technology provide improved direct visualization of the common bile duct (CBD) and pancreatic duct (PD) using small caliber endoscopes and thus allow a wide array of therapeutic interventions. This chapter will review the technique of cholangiopancreatoscopy (CP), indications, effectiveness, and complications as well as the current commercially available options. We will discuss various methods of diagnostic and therapeutic cholangioscopy such as intraductal tissue sampling and biopsy in patients with indeterminate biliary strictures along with its role in the management of difficult bile duct stones. Finally, we will also analyze the role of pancreatoscopy in the evaluation of suspected neoplasms of the pancreas, assessment of pancreatic duct (PD) strictures, and in the treatment of pancreatic duct stones.

Keywords: cholangioscopy, pancreatoscopy, endoscopic retrograde cholangiopancreatography (ERCP), biliary diseases, pancreatic diseases

1. Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) has been largely used as a technique to evaluate and treat diseases of both the biliary tract and the pancreatic duct.

The use of contrast during ERCP only allows for indirect visualization of these structures without direct assessment of disease arising within the ducts and the potential use of a wide array of therapeutic techniques that are now available for gastroenterologists and advanced endoscopists.

Ever since it was described in the early 1940s [1], cholangioscopy has permitted direct visualization of the bile duct and subsequent treatment of bile duct stones when palpation and probing of the bile duct were not efficacious in achieving adequate clearance of common bile duct stones. The use of both small endoscopes and probes used to directly visualize and treat diseases of the biliary tract and the pancreatic duct, eliminating the need for contrast media has been collectively named as cholangiopancreatoscopy (CP).

2. Description of equipment and techniques

Cholangiopancreatoscopy can be performed by either an endoscope-based system or a probe- or catheter-based system.

The endoscope-based systems use the scope itself as the main working tool whereas the catheter-based techniques require the use of the working/accessory channel of an endoscope in order to reach the common bile duct or the pancreatic duct. Cholangioscopy was initially performed by surgeons using a direct surgical approach to the bile duct. The peroral technique of cholangioscopy, using the endoscope-based technique or catheter-based technique was first reported in the 1970s [2].

Finally, there are three other techniques by which CP can be performed, and these include: direct peroral cholangioscopy (DPOC), surgical, and percutaneous cholangioscopy. These are not so widespread since they are technically challenging and are performed by endoscopists, surgeons, and interventional radiologists, respectively.

2.1. Endoscope-based systems

Endoscope-based systems utilize a "mother" duodenoscope and a "daughter or baby" cholangiopancreatoscope. This system requires two separate endoscopic operators to perform the procedure. One of the operators holds the position of the duodenoscope while the other operator performs the diagnostic and therapeutic cholangiopancreatoscopy [3–5].

The currently available instruments for endoscope-based cholangiopancreatoscopy in the United States are the following [6]:

- Olympus Corporation fiberoptic peroral cholangioscope (CHF-BP30) with a distal diameter of 3.1 mm, a working channel of 1.2 mm, and a working length of 187 cm. This endoscope can be passed through a duodenoscope with a minimum 4.2 mm accessory channel and has an angle of view of 90° [7].
- Pentax Corporation fiberoptic peroral cholangioscope (FCP- 9P) with a distal diameter of 3.1 mm, a working channel of 1.2 mm, a field of view of 90°, and a working length of 190 cm. This scope can be used with both the PENTAX Medical ED-3490TK Therapeutic Duodenoscope and the ED-3690TK Large-Channel Therapeutic Duodenoscope [8].

Endoscope-based systems have the following technical difficulties: limited steerability, poor irrigation capabilities, high repair costs, fragility with repeated use, and the need to have two

operators in a large number of cases [6, 9–11]. These limitations along with improved new systems have gradually eliminated the need for endoscope-based systems.

2.2. Probe- or catheter-based systems

Probe- or catheter-based systems do not require the assistance of a separate endoscopist to perform the CP but are rather inserted through the working channel of a therapeutic endoscope or duodenoscope.

The only available catheter-based single-operator system in the United States (US) is the SpyGlass™ Direct Visualization System (Boston Scientific Corporation), which is a disposable probe inserted through the accessory channel of a therapeutic duodenoscope. The SpyGlass™ Direct Visualization System (Boston Scientific Corporation) was designed to overcome the limitations of traditional cholangioscopes, to provide optically-guided therapeutics for targeted bile and pancreatic duct stone therapy, and also to help in the evaluation of pancreaticobiliary ductal strictures [12]. In our experience, the SpyGlass™ Direct Visualization System offers improved ergonomics by being lighter and easy to operate, something that is especially important during longer procedures where hand fatigue could be an issue. This system became first available in 2007 and is now available in two different generations.

- First-generation SpyGlass™ Direct Visualization System became available in 2007. The components of this single-operator cholangioscopy (SOC) system include a SpyScope™ access and delivery 10F catheter which contains a 1.2 mm diameter working channel and two dedicated irrigation channels. This catheter is introduced through a duodenoscope or therapeutic endoscope with a minimum working channel diameter of 4.2 mm. The catheter is capable of tip deflection up to 30° in four directions. Finally, this SOC system contains a reusable SpyGlass™ Fiber Optic Probe which can provide 6000-pixel images [9, 12, 13]. The first prospective clinical study validating the use of single-operator cholangioscopy with the use of the first-generation SpyGlass™ was published by Chen et al. [9] in 2011 with an overall procedure (for both adequate biopsy specimen for histological examination or stone visualization and initiation of fragmentation) success rate of 89%. The first prospective evaluation of SpyGlass™ Direct Visualization System involved 75 patients and was reported by Draganov et al. [14] in 2011. They reported complete stone clearance in 92% of patients with bile duct stones, and in 91% of those patients, this was achieved in the first session. In non-stone-related procedures, this was successful in 98% of patients and, in 20% of patients, new findings—not appreciated in cholangiography—were revealed during the SpyGlass™ Direct Visualization System session.
- Second-generation SpyGlass™ Direct Visualization System was made available in 2015 and has the ability to have an improved setup, ease of use, and image quality [15]. Compared to the first-generation system, this newest system is based on a 10.5 F catheter and delivers enhanced visualization and improved image quality through a digital sensor with 4× more resolution, a 60% wider field of view, automatic light control, and light-emitting diode (LED) illumination. There are dedicated irrigation and aspiration connections to clear the field of view, a redesigned 1.2 mm working channel, and a fixer imager for consistent steering [16, 17].

The following accessories are available or compatible with the SpyGlass™ Direct Visualization Systems:

- SpyScope™ DS Access & Delivery Catheter (**Figures 1–3**), single-use only. This catheter provides dual controls which allow for a 4-way deflection and a locking mechanism that ensures stabilization of direct visualization.
- SpyGlass™ Direct Visualization System's fiberoptic probe is designed to optimize light delivery to the anatomy and to acquire and transmit endoscopic images back to the camera. The probe connector on the proximal end attaches to the light guide and ocular [18]. The SpyGlass™ is inserted through the catheter allowing direct visualization of the pancreaticobiliary anatomy. The fiberoptic probe is reusable up to 10–20 times, although there are reports of its optical resolution deteriorating after 10 uses [19], whereas the rest of the cholangioscope is single use [6].
- Camera, camera head, and ocular. The camera utilizes a ¼ CCD color-image sensor that provides three types of video outputs (RGBs, S-video, or composite). A multi-pin cable connector helps to facilitate the camera connection to the unit, and the ocular makes possible focus and transmission of the image obtained through the SpyGlass Probe™ [18].
- Light source and cable (**Figure 4**). A flexible fiber-optic bundle facilitates the transmission of light provided from a 300 W Xenon source into the SpyGlass Probe™ [18].
- Irrigation footswitch (100–240 V, 50/60 Hz, 25 VA) which provides 0–375 ml/min ±20% using SpyGlass™ Irrigation tube set which allows clearance of debris from the ducts and a better visualization of the anatomic structures.
- SpyGlass Probe™ Trays. This allows storage and protection when the probe is not in use and when it is being disinfected.
- Sony High Resolution 1280 × 1024 video monitor (17.5"W × 15.8"H × 4.75"D).

Figure 1. SpyGlass™ Direct Visualization System Access and Delivery Box (Courtesy of Gulshan Parasher, MD).

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Figure 2. SpyGlass™ Direct Visualization System Access and Delivery Catheter mounted on a therapeutic duodenoscope. The capped white end is the suction port and the uncapped port is the accessory channel (Courtesy of Gulshan Parasher, MD).

Figure 3. SpyGlass™ Direct Visualization System Access and Delivery Catheter mounted on a therapeutic duodenoscope. The capped white end is the suction port and the uncapped port is the accessory channel (Courtesy of Gulshan Parasher, MD).

Figure 4. SpyGlass™ Direct Visualization System Light Source and Cable (Courtesy of Gulshan Parasher, MD).

- Cart (3-Joint Arm and Isolation Transformer). It provides a space for ease of transfers between endoscopy rooms and also for storage of the whole unit. The flexible 3-joint arm allows the endoscopist to place the camera in an optimal position for visualization and comfort. This cart can also include an isolation transformer.
- Power Cable Pack. This pack helps to simplify electrical connections during transfers between rooms.
- SpyBite™ Biopsy Forceps, single-use forceps. This allows direct tissue sampling under direct visualization and is advanced through the therapeutic channel of the SpyScope™ catheter. The specification of the biopsy forceps are as follows: 1 mm outer diameter, 4.1 mm biopsy cup opening at 55°, and a central spike in the specimen cup that aids in securing samples in challenging lesions.

The current set up time for the system is under 5 min (compared to 23 min with the first-generation system) and the equipment is designed to fit on a standard endoscopy cart. The newest version of the system provides an integrated digital sensor along with an automatic white balance and focus feature. Digital single-operator cholangiopancreatoscopy (DSOCP) systems like the SpyGlass™ Direct Visualization Systems have been shown to provide enhanced image quality with shorter procedure times thus limiting radiation exposure when compared to the fiberoptic single-operator cholangiopancreatoscopy (FSOCP) systems [20].

The SpyGlass™ Direct Visualization Systems are compatible with some electrohydraulic lithotripsy (EHL) systems (from Northgate Technologies, Inc.) and with holmium laser probes (from Lumenis) and can be used in conjunction to manage large and impacted biliary and pancreatic ductal stones. The financial feasibility of incorporating cholangiopancreatoscopy into an endoscopy is complex. This can be a profitable venture with large diagnostic and therapeutic CP caseload. Important variables include case volume, purchase cost, and procedure length. The single-use cholangioscope can decrease the potential for contamination, but the initial start-up cost for the system averages at least 50,000.00 USD (United States Dollars) and this has significantly limited the widespread use of this technology in non-tertiary centers.

The two main limitations of the SpyGlass™ Direct Visualization Systems are image quality that is impeded by the use of fiberoptic technology and a relatively small accessory channel providing passage only for dedicated accessories [21, 22].

2.3. Direct peroral cholangioscopy (DPOC)

Direct peroral cholangioscopy (DPOC) is a technically challenging procedure which involves passage of an ultraslim gastroscope capable of providing high-resolution images of the bile duct as well as providing therapeutic interventions [23–26]. Although the use of ultraslim gastroscopes is not approved by the Food and Drug Administration (FDA) for CP, its use has been reviewed by the American Society for Gastrointestinal Endoscopy (ASGE) [27].

The advantages of DPOC are summarized in **Table 1** [28–33]. The use of carbon dioxide (CO_2) and water is highly recommended during DPOC since it decreases the risks of air embolism [6, 34].

Table 2 summarizes the currently available ultraslim endoscopes for use in DPOC in the United States [6, 35–41].

The average price for an ultraslim endoscope is roughly around 30,000.00 USD (United States Dollars).

Two different techniques for DPOC have been described:

- Direct peroral cholangioscopy over a stiff guidewire with or without an overtube: this technique involves the use of a standard ERCP to access the bile duct and the subsequent insertion of a stiff guidewire which will eventually be exchanged by an ultraslim endoscope, which serves as a cholangioscope [6, 42–45]. The use of an overtube helps in overcoming the gastric loop that can be formed with ultraslim gastroscopes [44, 46].
- Direct peroral cholangioscopy using a free-hand technique: this involves the use of ERCP with sphincterotomy and subsequent passage of an ultraslim endoscope without the use of a stiff guidewire. The papilla is difficult to be cannulated directly with an ultraslim endoscope. Therefore, the ultraslim endoscope is advanced to the third portion of the duodenum, and subsequently, a "J maneuver" is used to cannulate the papilla and insertion into the common bile duct [47, 48].
- Direct peroral cholangioscopy using the balloon anchoring method: this method involves the use of a guidewire and a biliary stone extraction balloon in order to help anchor the ultraslim gastroscope. After a standard ERCP, a biliary sphincterotomy is performed, and a guidewire is introduced into the common bile duct along with a balloon that is subsequently inflated and displaced upstream to help straighten the common bile duct and to allow a better navigation with the cholangioscope [6, 49, 50].

2.4. Percutaneous and surgical cholangioscopy

Percutaneous cholangioscopy can be performed by both endoscopists and interventional radiologists. This technique involves the insertion of a cholangioscope through a mature (3–5 weeks) percutaneous fistulous tract [6, 51] from the abdominal wall into the biliary tree. This technique can allow the insertion of the SpyGlass™ Direct Visualization System [52]. A number of diagnostic and therapeutic techniques can be performed, such as percutaneous cholangiography, electrohydraulic and laser lithotripsy, removal of difficult stones, tissue sampling, intraluminal brachytherapy, and stenting of the hepatic and biliary ducts [53, 54].

Advantages of direct peroral cholangioscopy (DPOC)
Single operator
Usage of chromoendoscopy
Utilization of argon plasma coagulation (APC)
Use of photodynamic therapy
Use of confocal laser endomicroscopy
Employment of narrow-band imaging (NBI) to detect fine mucosal structures and tumor vessels
Decreases the costs associated with SpyGlass™ Direct Visualization Systems or other platforms

Table 1. Advantages of direct peroral cholangioscopy (DPOC).

Available ultraslim endoscopes in the United States (U.S.)					
Company	**Working length**	**Outer diameter**	**Angle of view**	**Accessory channel size**	**Other capabilities**
Olympus Corporation					
GIF-XP 190 N/Gastroscope	1100 mm	5.4 mm	140°	2.2 mm	Narrow-band imaging (NBI)
GIF-XP 180 N/Gastroscope	1100 mm	5.5 mm	120°	2.0 mm	Narrow-band imaging (NBI)
GIF-N180/Gastroscope	1100 mm	4.9 mm	120°	2.0 mm	Narrow-band imaging (NBI)
Transnasal Endoscope (PEF-V)	650 mm	5.3 mm	120°	2.0 mm	Used in combination with the VISERA video system to provide high-resolution images
Pentax Corporation					
EG-1690 K	1100 mm	5.4 mm	120°	2.0 mm	i-SCAN digital image processing
Fujinon Corporation					
EG-530 N	1100 mm	5.9 mm	120°	2.0 mm	N/A
Transnasal Endoscope (EG-530 NP Transnasal)	1100 mm	4.9 mm	120°	2.0 mm	Not compatible with high-frequency applications

Table 2. Available ultraslim endoscopes in the United States (U.S.).

In addition, percutaneous cholangioscopy, used in conjunction with DPOC, has been successful in the treatment of intrahepatic and bile duct stones in patients with surgically altered anatomy such as Roux-en-Y hepaticojejunostomy [55–58].

Finally, gastrointestinal surgeons can also perform direct surgical cholangioscopy, which involves the use of a cholangioscope during open abdominal wall surgery or laparoscopic surgery to evaluate and treat biliary pathology when the endoscopic approach fails [59–63].

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3. Indications for cholangioscopy

3.1. Intraductal lithotripsy of common bile duct (CBD) or hepatic duct (HD) stones

Perhaps, the most studied and used indication for cholangioscopy is the evaluation and management of difficult biliary stones that failed with the standard methods of stone extraction such as mechanical lithotripsy and balloon extraction during endoscopic retrograde cholangiopancreatography.

Intraductal lithotripsy during cholangioscopy can be performed using electrohydraulic lithotripsy (EHL) and laser lithotripsy (LL).

Electrohydraulic lithotripsy was first used in the Soviet Union for the fragmentation of minerals, but it was not until the 1970s that this technology was introduced for the management of biliary stones [64, 65]. This method has been traditionally used for the management of difficult biliary stones with some reports of up to 95% of success extraction of gallstones refractory to conventional endoscopic basket extraction [66] although the general stones fragmentation rates are approximately 80% [67–72].

EHL utilizes a bipolar probe which discharges sparks in an aqueous medium with the aid of a generator. The sparks generate high-frequency hydraulic pressure waves that impact the stone resulting in subsequent fragmentation. The EHL equipment is portable, compact, and inexpensive [73, 74].

EHL can be performed under the guidance of fluoroscopy or through a cholangioscope. Fluoroscopy offers only a two-dimensional view of the stone, whereas direct cholangioscopy offers a direct view of the stone and also aids in positioning the probe, minimizing bile duct trauma [73]. During EHL, saline irrigation of the duct is performed as saline provides an aqueous medium for the shock waves to travel as well as it helps in clearance of stone debris [64, 75].

Electrohydraulic lithotripsy is associated with an overall complication rate that has been reported around 7–9% by some authors [73, 76] and its most common reported complications or side effects include hemobilia, cholangitis, common bile duct injury (less than 1%), and delayed common bile duct strictures [64, 73] (**Table 3**).

Laser lithotripsy involves the use of laser probes inserted through the therapeutic or accessory channel of an endoscope that subsequently transmit thermal energy or shock waves in order to fragment and dissolve stones in the common bile duct. The use of LL in humans was first described by Lux et al. in 1986 [77]. There are two main forms in which LL can help fragment stones, one is by using a laser in a continuous fashion with the subsequent generation of heat directed toward a stone [67], whereas the other is by using a laser delivered in a pulsed fashion acting through the shockwave effect in order to fragment and dissolve stones [67, 78–80]. The use of continuous laser has been associated with coagulation and subsequent perforation of the wall of the common bile duct [67, 79]. LL can be used through the cholangioscopic, fluoroscopic, or transhepatic approach [73]. The laser of a wavelength of 504 nm (nm) is absorbed by the pigment consistent of stones [67] and in some studies, pigmented stones have been fragmented using less energy than cholesterol stones [80].

The efficacy of LL in achieving ductal clearance has been reported to be 64–97% [73, 81, 82]. Reports of rare adverse events include pancreatitis, transient hemobilia, cholangitis, and bile duct injury [81] (**Table 3**). As per some authors, laser lithotripsy is not only used as an alternative to electrohydraulic lithotripsy for gallstones that failed clearance by standard techniques such as endoscopic sphincterotomy with balloon/basket extraction and to mechanical lithotripsy (ML), but also is sometimes preferred over EHL since it provides targeted and directed therapy with less potential for injury to the common bile duct [64, 83].

The financial cost of LL, approximately $100,000.00 USD for the initial setup, has limited its use [64]. There a different types of lasers available for LL and they differ in their type of energy, power, wavelength, and pulse width [83]. Nevertheless, short wavelength laser has been the most used in the current therapy of gallstones. Coumarin (504 nm), rhodamine-6G (595 nm), neodymium (Nd):yttrium-aluminum-garnet (YAG) (1064 nm), and alexandrite:YAG (750 nm) are very effective in stone fragmentation with a 80–95% success rate [64] with holmium (Ho):YAG laser (wavelength of 1949 nm) being the most used nowadays. Holmium (Ho):YAG laser has been deemed very safe for lithotripsy since its wavelength is near the optical coefficient of water and its depth of tissue penetration is much shallow than Nd:YAG (0.5, 5 mm, respectively) resulting in minimal injury to the duct wall [64, 83] (**Figure 5**).

3.2. Intraductal assessment of strictures and suspected biliary malignancies

Direct visualization of strictures and suspected biliary malignancies with cholangioscopy has allowed a more careful assessment of them along with the possibility of obtaining targeted biopsies of the suspected tissues. This is certainly a step forward since traditional ERCP offers only a fluoroscopic indirect visualization of the suspected abnormality and brushings do not offer direct tissue sampling.

As described, earlier, the SpyBite™ Biopsy Forceps (Boston Scientific Corporation) allows guided tissue sampling under direct visualization through the therapeutic channel of the SpyScope™ catheter.

A tertiary center prospective study by Draganov et al. [84] in 2011 evaluated the accuracy of cholangioscopy-guided mini-forceps (SpyBite™ Biopsy Forceps) sampling and compared it with standard cytology brushings and forceps biopsies for the tissue diagnosis of indeterminate biliary lesions. This study demonstrated that when comparing the three methods of sampling, mini-forceps biopsy by SpyBite™ provided significantly better sensitivity and overall accuracy compared with standard cytology brushing ($P < 0.0001$) and standard forceps biopsy ($P = 0.0215$). For standard cytology brushings, the sensitivity, accuracy, and negative

Complications of electrohydraulic lithotripsy (EHL) and of laser lithotripsy (LL)
Hemobilia
Cholangitis
Common bile duct (CBD) injury (less than 1%)
Delayed common bile duct strictures
Pancreatitis

Table 3. Complications of electrohydraulic lithotripsy (EHL) and of laser lithotripsy (LL).

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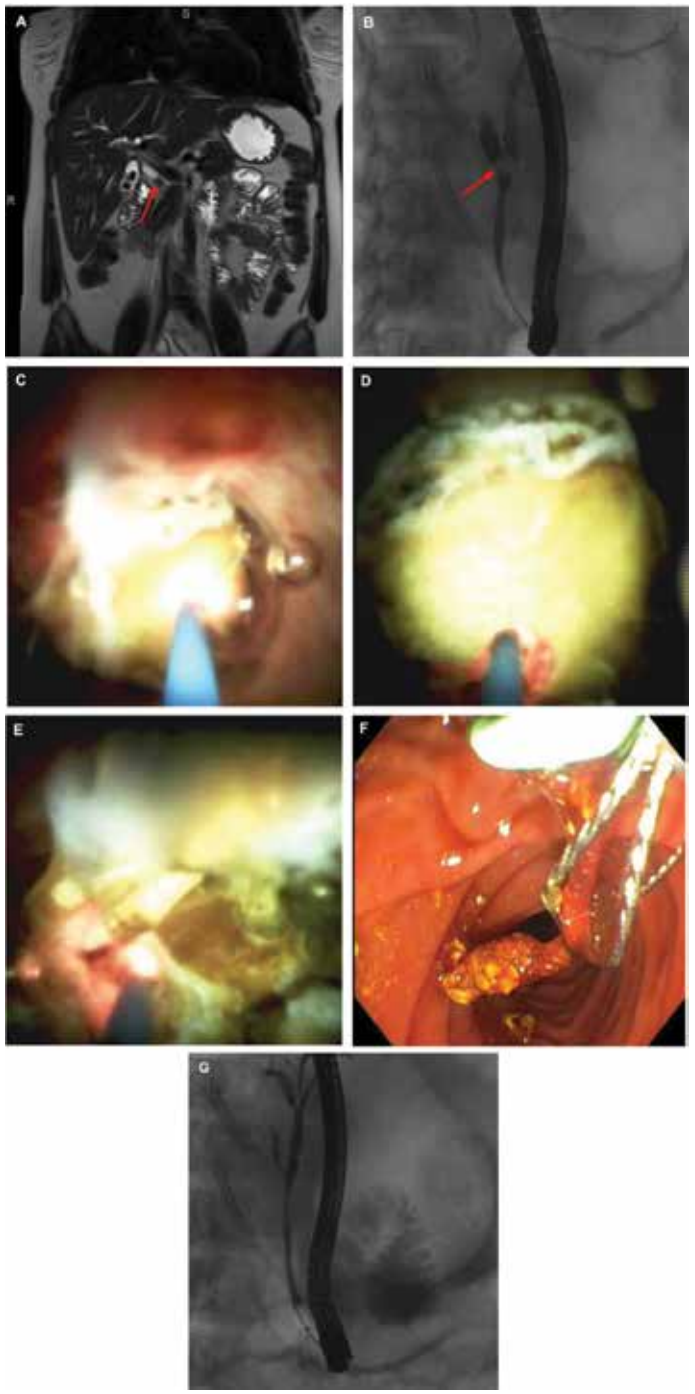

Figure 5. A 36-year-old female presenting with choledocholithiasis. (A) Magnetic resonance cholangiopancreatography (MRCP) showing a stone (arrow) in the common bile duct with (B) subsequent ERCP showing a filling defect in the CBD. This patient underwent (C) ERCP with SpyGlass™ Direct Visualization System showing a CBD stone. (D) Holmium laser lithotripsy (LL) of the CBD stone achieved (E) fragmentation and (F) subsequent successful basket extraction of the stone with (G) fluoroscopy showing adequate clearance of it (Courtesy of Gulshan Parasher, MD and Thomas C. Queen, MD).

predictive value (NPV) reported by them were 5.9, 38.5, and 36%, respectively. For standard forceps, they reported a sensitivity of 29.4%, accuracy of 53.8%, and NPV of 42.8%. Finally, mini-forceps (SpyBite™ Biopsy Forceps) biopsies had the highest sensitivity, accuracy, and NPV when compared to standard cytology brushings and standard biopsies. The values reported by the authors were 76.5, 84.6, and 69.2%, respectively. We as authors believe that indeterminate biliary lesions should always be sampled with the SpyBite™ Biopsy Forceps since they significantly increase the yield for histologic diagnosis.

One systematic review by Navaneethan et al. [85] reported that biopsies with SpyBite™ had a sensitivity of 76.5% compared with brushings (5.8%) and biopsies (29.4%) in the assessment of indeterminate biliary strictures.

The sensitivity and specificity for studies, who have only used direct cholangioscopic visualization for the evaluation of malignancy, have ranged from 88 to 100% and 77 to 92%, respectively [86–94]. Cholangiopancreatoscopy using chromoendoscopy, autofluorescence imaging (AFI), and narrow-band imaging (NBI) has been associated with a higher ability to detect malignancy [95].

In contrast, the overall sensitivity, specificity, and accuracy of cholangioscopy for tissue diagnosis of indeterminate biliary duct strictures using targeted biopsies have been reported to be between 48 and 100%, 55 and 100%, and 70%, respectively [6, 13, 85, 87–92, 94, 96–103]. Although the optimal number of biopsies warrants further study, one study series suggested that a minimum of six biopsies should be taken to prevent inadequate material for histopathological analysis [104]. The use of concomitant endoscopic ultrasound (EUS) with cholangioscopy has been associated with increases in sensitivity and specificity in the detection of pancreaticobiliary neoplasia [105].

4. Indications for pancreatoscopy

Many of the same devices (i.e., SpyGlass™ Direct Visualization Systems) used for cholangioscopy can be used for the visual assessment and lithotripsy of pancreatic duct stones, sampling of PD strictures, and to evaluate suspected pancreatic malignancies. Currently, SpyGlass™ Direct Visualization Systems is the only system approved by the FDA for its use in pancreatoscopy [6].

4.1. Intraductal lithotripsy for pancreatic duct (PD) stones

Although the number of studies evaluating the use of pancreatoscopy for clearance of pancreatic duct stones is limited, the use of EHL sometimes along in combination with extracorporeal shockwave lithotripsy (ECSWL) has been reported to be effective in complete clearance of PD stones in approximately in 59–100% of cases [6, 106–110]. As per Komanduri et al., this data for complete clearance is hard to interpret since electrohydraulic lithotripsy was combined with decompressive surgery or ECSWL [6, 111].

Most recent studies have included the use of laser lithotripsy combined with electrohydraulic lithotripsy with an overall success rate of 74–79% in the management of main pancreatic duct stones [112, 113].

Furthermore, the use of intraductal lithotripsy for PD stones might help not only to decrease the pain and opioid/narcotic dependence in patients with chronic calcific pancreatitis but can

also decrease the risk associated with the more invasive surgical approaches like the lateral pancreaticojejunostomy (LPJ) [112–114].

4.2. Intraductal assessment of pancreatic duct (PD) strictures and suspected pancreatic malignancies

Evaluation and direct visualization with narrow-band imaging (NBI) of intraductal papillary mucinous neoplasms (IPMNs) and pancreatic duct strictures have been one of the most well-studied indications for peroral pancreatoscopy (POPS) with one study reporting the ability of POPS to visualize and diagnose up to 63% of pancreatic cancers, 80% of benign strictures, and 95% of IPMNs [115]. In this study, neoplasia assessment was based on the presence of coarse-friable mucosa, papillary projections, and tumor. As per the authors, tumor vessels and papillary projections/tumor were observed when pancreatic cancer was less than 2 cm, but not when the tumor was larger than 2 cm. Other studies like the one from Arnelo et al. [116] have reported the correct identification of main duct (MD-IPMN) and branch duct (BD-IPMN) in up to 76 and 78% of cases, respectively.

Table 4 summarizes the endoscopic findings that have been correlated with malignant pancreatic lesions with a sensitivity and specificity of 68 and 87%, with some authors reporting a lower sensitivity for BD-IPMN compared to MD-IPMN [6, 117, 118] (**Figures 6–9**).

Pancreatoscopy findings suspicious for intraductal papillary mucinous neoplasms (IPMNs)
Coarse-friable mucosa
Tumor vessels
Papillary projections
Fish egg-like, villous, and prominent mucosal protrusions
Tumor

Table 4. Pancreatoscopy findings suspicious for Intraductal papillary mucinous neoplasms (IPMNs).

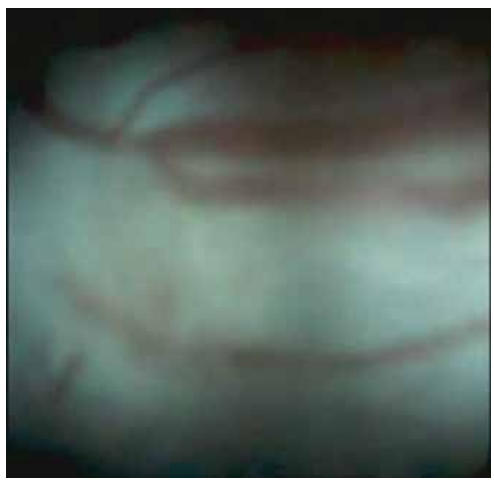

Figure 6. SpyGlass™ Direct Visualization System showing tumor vessels characteristic of an IMPN. (Courtesy of Gulshan Parasher, MD).

Peroral pancreatoscopy can be used along with intraductal ultrasonography (IDUS) to differentiate between benign and malignant intraductal papillary-mucinous tumors (IPMTs) [117], and also it has been described as a tool to obtain pancreatic juice cytology and aid in the diagnosis of IPMNs [119]. Narrow-band imaging offers a better detection of vascular patterns and protrusions and should be used whenever possible during POPS [120].

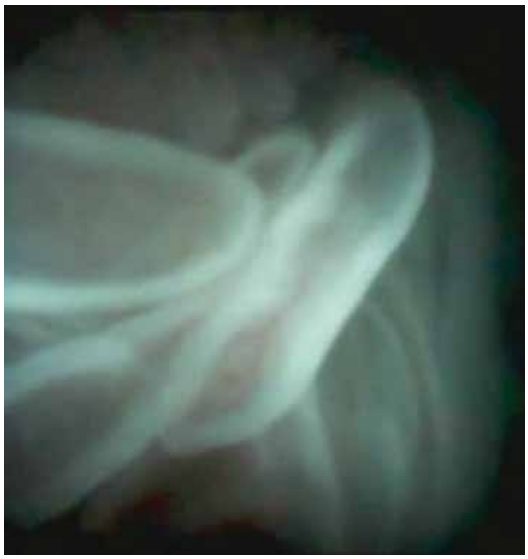

Figure 7. SpyGlass™ Direct Visualization System showing papillary projections characteristic of an IPMN (Courtesy of Gulshan Parasher, MD).

Figure 8. SpyGlass™ Direct Visualization System showing "egg-like protrusions" characteristic of an IPMN (Courtesy of Gulshan Parasher, MD).

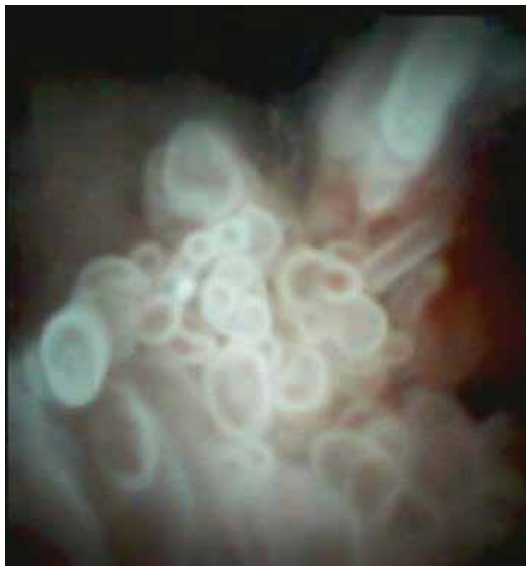

Figure 9. SpyGlass™ Direct Visualization System showing "egg-like protrusions" characteristic of an IPMN (Courtesy of Gulshan Parasher, MD).

Intraoperative pancreatoscopy of the main PD combined with intraductal biopsies plays a significant role in the surgical management of patients with IPMNs and should be considered in all patients presenting with a sufficiently dilated main PD since it can alter the initial operative planning up to approximately 20% of cases [6, 121]. Post-endoscopic ERCP pancreatitis is a well-known side effect of POPS and has been reported to happen in up to 17% of cases [116].

5. Unusual indications of cholangiopancreatoscopy (CP)

Some uncommon indications for the use of cholangiopancreatoscopy include selective guidewire placement, assessing unexplained hemobilia or intraductal biliary ablation therapy such as radiofrequency ablation of tumor ingrowth, photodynamic therapy for cholangiocarcinoma, and retrieval of migrated pancreatic and biliary stents [122].

Finally, successful endoscopic transpapillary gallbladder drainage and stenting using the SpyGlass™ Direct Visualization System has also been reported [123].

6. Efficacy and safety of cholangiopancreatoscopy (CP)

Although there are numerous studies evaluating the safety and efficacy of cholangiopancreatoscopy in the assessment and treatment of biliary and pancreatic stones, indeterminate biliary strictures, and suspected pancreatic malignancies, the authors have selected the ones with the highest and most relevant impact on our practice as gastroenterologists and endoscopists, and these are presented as follows.

Arya et al. [76] evaluated the safety and success of patients who underwent peroral endoscopic fragmentation of bile duct stones with electrohydraulic lithotripsy under direct cholangioscopic control using a "mother-baby" endoscopic systems and showed that of the 94 patients, successful fragmentation (61 complete, 28 partial) was achieved in 89 of 93 patients (96%) (one patient was excluded from analysis due to a broken endoscope) in difficult choledocholithiasis and intrahepatic stones. In those with successful EHL, fragmentation balloon or basket extraction was used to remove the remaining fragments. One EHL session was needed in 76% of patients, whereas two or more sessions were needed in 24% of patients. The complications reported by the authors included: cholangitis and/or jaundice (13 patients); mild hemobilia (1 patient); mild post-ERCP pancreatitis (1 patient); biliary leak (1 patient); and bradycardia (1 patient). There were no deaths related to EHL.

The first study evaluating the success rate of single-operator cholangioscopy was published by Chen et al. in 2011 [9]. This was a multicenter prospective clinical cohort study involving 15 endoscopy referral centers in the United States and Europe, and 297 patients requiring an evaluation of bile duct disease or biliary stone therapy. Procedural success was defined as either visualization of lesions and collection of biopsy specimens if indicated, or visualization of stones and its subsequent fragmentation. The overall procedure success rate for the aforementioned procedures was 89% (95% CI, 84–92%). Eighty-eight percent of patients who underwent biopsies had adequate tissue for diagnosis with biopsies associated with a sensitivity of 49% for diagnosing malignancy, whereas visual impression from SOC had a sensitivity of 78% for the same purpose. Sensitivity was higher for intrinsic bile duct malignancies. Procedure success for SOC-directed stone therapy, defined as visualization of biliary stones and initiation of stone fragmentation and removal, was achieved in 92% of 66 patients with stones and complete stone clearance during the study SOC session was achieved in 71% of cases. The incidence of serious procedure-related adverse events was 7.5% for diagnostic SOC (17 patients; early cholangitis in 7, bacteremia in 2, transient hypotension in 2, abdominal pain/distention in 2, pancreatitis in 1, elevation on amylase/lipase with no clinical pancreatitis in 1, ERCP-related nausea with emesis, abdominal pain, gas, and cramping, and radiculopathy in 1) and 6.1% for SOC-directed stone therapy (five events in 4 patients; cholangitis in 2 patients, 1 patient with ERCP-related duodenal perforation and SOC-related desaturation secondary to aspiration, and bile duct perforation in one patient).

A retrospective, single tertiary center, study by Aljebreen et al. [124] evaluated the efficacy and safety of Spyglass™-guided electrohydraulic lithotripsy for difficult common bile duct stones not amenable to conventional endoscopic therapy. In this cohort, all patients who underwent Spyglass™-guided EHL were compared with a historical cohort who had extracorporeal shockwave lithotripsy. Of a total number of 13 patients who underwent Spyglass™-guided EHL, bile duct clearance was achieved in all of the cases with 76% of patients requiring one ERCP session to clear the CBD and 23.1% requiring two or more sessions for the same purpose. Eleven percent of patients experienced cholangitis and 4.4% had pancreatitis as adverse effects. Although the study enrolled a small number of patients (13 in total), it showed that cholangioscopic-guided EHL was an effective therapy for difficult bile duct stones and a higher a CBD clearance rate compared to ESWL (100 versus 64.4%).

The largest, multi-center prospective, clinical study evaluating the technical success and safety of single-operator cholangioscopy-Ho:YAG laser-guided lithotripsy for the management

of difficult bile duct stones was published by Patel et al. [83]. This study was performed in patients with refractory bile duct stones who failed endoscopic retrograde cholangiopancreatography. Cholangioscopic-guided Holmium laser lithotripsy resulted in complete removal of bile duct stones in 97% of patients. In 74% of patients, biliary clearance was accomplished in one endoscopic session. The average stone size in patients with a single stone was 20.2 mm (range, 10–36 mm). Successful extraction of stones in this group of patients occurred in 46 of 47 patients (98%) and was similar to that of the other patients (21/22, 95%). To facilitate the removal of fragmented stones, endoscopic papillary balloon dilation (12–18 mm) and mechanical lithotripsy were performed in conjunction with laser lithotripsy in 7 and 17%, respectively. Laser lithotripsy failed in two patients who ultimately required biliary surgery. One patient had multiple large cystic duct stones, and the other failure occurred in a patient in which the stone (21 mm) was embedded in the common bile duct. The study reported an overall adverse event rate of 4.1%, with 2 patients experiencing minor bleeding of bile duct wall and 1 patient with mild post-ERCP pancreatitis.

A systematic review by Navaneethan et al. [85] published in 2015 evaluated the utility of SpyGlass™ Direct Visualization System peroral cholangioscopy and targeted biopsies for malignant strictures and cholangiocarcinoma (CCA) involving 456 patients showed that for cholangioscopy-guided biopsies, the sensitivity was 60.1% and the specificity was 98.0% in regards to malignant biliary strictures. The same author has reported in a previous metanalysis that fluorescence in situ hybridization (FISH) increases the specificity for the diagnosis of CCA in patients with primary sclerosing cholangitis (PSC) [125].

A recent 10-year single center experience by Attwell et al. [112] evaluated the safety and efficacy of endoscopic retrograde cholangiopancreatography with peroral pancreatoscopy (POP) with electrohydraulic lithotripsy/laser lithotripsy for 46 patients with chronic calcific pancreatitis using a 10F cholangioscope (POP-Endo, 31 patients) and catheter-based system (POP-Cath, 15 patients) in which EHL/LL was performed. Stone extraction without EHL or LL was performed in 7 (15%) of 46 patients. Technical success for POP-Endo versus POP-Cath was 27 (87%) of 31 versus 15 (100%) of 15 patients (P = 0.29). Complete clearance of pancreatic duct stones was achieved in 21 (68%) of 31 versus 11 (73%) of 15 patients, respectively (P = 0.519). The authors reported peroral pancreatoscopy-related complications in 9 patients (10%). Six patients developed mild post-ERCP pancreatitis (3 in POP-Endo and 3 in POP-Cath). Two patients developed exacerbations of abdominal pain requiring overnight observation or emergency department evaluation after post-procedure discharge, and one patient developed perforation during combined EUS-guided pancreatography and POP. This was managed conservatively.

Peroral pancreatoscopy has been used sporadically for diagnosis of a number of pancreatic neoplasms, especially intraductal papillary mucinous neoplasm of the main pancreatic duct, besides ductal adenocarcinoma. The role of peroral pancreatoscopy in the evaluation of 79 patients with indeterminate pancreatic duct strictures, dilations, or with suspected or known main duct IPMN was published by El Hajj et al. [126] in 2014. The technical success of POP was achieved in 97% of cases. In the PD neoplasia group (33 patients), the final diagnosis was based on index confirmatory POP-guided tissue sampling in 29 patients (88%). The authors showed that tissue sampling has a higher sensitivity (91 versus 87%), specificity (95 versus 86%), positive predictive value (PPV) (94 versus 83%), negative predictive value (NPV) (93

versus 91%), and accuracy (94 versus 87%) when compared to visual impression only. Among 102 POPs, the adverse event rate was of 12% (seen in 12 patients) with 7 patients (7%) experiencing a flare-up of baseline abdominal pain that required admission for more than 24 h, and with 5 patients (5%) having serious adverse events (4 patients with post-procedure acute pancreatitis and 1 patient with moderate post-sphincterotomy bleeding requiring hospitalization, endotherapy, and blood transfusion).

Peroral pancreatoscopy with ductal visualization for the diagnosis of main duct IPMN lesions has a sensitivity of 67–100% compared with computed tomography (CT) (16–32%), intraductal ultrasound (56–100%), and endoscopic ultrasound (55–92%) [6, 117, 127].

Finally, a multicenter retrospective study by Adler et al. [128] evaluating the frequency and severity of adverse events with single-operator cholangiopancreatoscopy in 222 patients undergoing single cholangioscopy and pancreatoscopy included post-ERCP pancreatitis (N. = 11, 3.9%, all mild), post-ERCP cholangitis (N. = 4, 1.4%), bleeding (N. = 3, 1%), and perforation (N. = 2, 0.7%). In addition, his study showed that vigorous irrigation of the bile ducts was not associated with increased rates of post-procedure cholangitis although some authors recommend that antibiotic prophylaxis for all patients undergoing cholangioscopy should be considered [129], given some studies reporting increased rates of cholangitis when ERCP is performed with cholangiopancreatoscopy [130].

Overall cholangiopancreatoscopy appears to be a safe and effective technique with acceptable morbidity. The applications of cholangiopancreatoscopy are similar through the world as they are in the United States.

7. Future directions of cholangiopancreatoscopy (CP)

Cholangiopancreatoscopy continues to be an effective and evolving technique. The current cholangioscopes have improved significantly as far as digital imaging is concerned and availability of disposable devices continues to have a great impact on future development in this field.

The future cholangioscope would see continued improvement in digital imaging resulting in higher resolution high definition (HD) scopes along with narrow-band imaging capabilities. This may help to address some of the limitations in visibility that occur at times with the existing digital systems.

Minimizing the electronics and increasing the size of the accessory channel may improve therapeutic capabilities as well as the yield of tissue sampling. The use of near infra-red (NIR) fluorescence cholangiopancreatoscopy in the detecting of pancreaticobiliary malignancies is also a promising field which will warrant more study in the near future [131].

8. Summary

Substantial advances in cholangiopancreatoscopy have resulted in the widespread adoption of this procedure into advanced endoscopy practice in many centers worldwide.

Recent advancement in the field of cholangiopancreatoscopy have provided gastroenterologists and endoscopists with invaluable tools that not only significantly aided in the evaluation and treatment of suspected biliary and pancreatic diseases (difficult biliary stones, indeterminate biliary strictures, pancreatic duct stones, pancreatic duct strictures, and suspected pancreatic neoplasms) but most importantly also have reduced the morbidity and mortality associated with the more aggressive and invasive surgical procedures used to evaluate and treat these type of disorders in the past.

Newer cholangioscopes are continuously developed by different manufacturers utilizing improved optics and technology to further increase the efficacy and safety of the technique of cholangiopancreatoscopy.

Finally, it is very important to note that the best outcomes from these procedures occur when they are performed by well-trained and experienced endoscopists in tertiary centers. Whenever possible, these patients, especially patients with previously failed procedures and the elderly, should be referred to these centers for further evaluation and treatment.

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Chapter 4

Endoscopy for the Diagnosis of Inflammatory Bowel Disease

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Additional information is available at the end of the chapter

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Abstract

The diagnosis of inflammatory bowel disease (IBD) and the differentiation between Crohn's disease and ulcerative colitis can be challenging. Colonoscopy with ileoscopy is the useful diagnostic test for patients with suspected inflammatory bowel disease. Esophagogastroduodenoscopy, enteroscopy, and capsule endoscopy all have complementary roles to ileocolonoscopy. Endoscopy not only allows for the visualization of inflammation due to IBD but also for histological analysis, both of which can aid the in proper diagnosis and to exclude other causes of enteritis and colitis. This chapter will describe the use of endoscopy for the diagnosis of IBD.

Keywords: inflammatory bowel disease, Crohn's disease, ulcerative colitis, colonoscopy, diagnosis

1. Introduction

Colonoscopy is the most essential diagnostic tool for patients with suspected inflammatory bowel disease (IBD). Ileoscopy at the time of colonoscopy is critical to both diagnose IBD, differentiate between ulcerative colitis (UC) and Crohn's disease (CD), and to determine the extent and distribution of inflammation as this will affect prognosis and treatment. Other endoscopic modalities including esophagogastroduodenoscopy (EGD), capsule endoscopy, and enteroscopy all have a role in the diagnosis of IBD in select situations. It is critical to understand the endoscopic features and perform the endoscopy appropriately to improve the diagnostic yield and differentiate between IBD and other causes that might mimic IBD as well as differentiating CD and UC as the medical and surgical treatments can be different. This chapter will focus on the practical approach of using endoscopy to diagnose IBD.

2. Ileocolonoscopy

Colonoscopy with ileoscopy is the gold standard for the diagnosis of IBD. It allows for both direct visualization of the most commonly affected areas of bowel in patients with IBD and tissue sampling for histologic analysis. While the inflammation seen in UC is mainly limited to the colon, CD may present with inflammation anywhere from the mouth to anus. Therefore, any colonoscopy done to evaluate symptoms concerning for IBD, or less commonly if a patient is incidentally found to have colonic inflammation during colonoscopy, intubation of the terminal ileum should be attempted. If ileoscopy is successful, taking biopsies of the ileum and colon are also critical aspects of the diagnostic evaluation as this is more sensitive than visual evaluation of the mucosa to find evidence of inflammation.

2.1. Crohn's disease

Crohn's disease was initially described as regional ileitis in 1932 in which a new entity was described as being similar to UC but affecting the small intestine and leading to luminal stenosis [1]. Since then, the endoscopic features and distribution of CD has been extensively elucidated. CD can affect any part of the alimentary tract from the mouth to the anus, but the terminal ileum and colon are most commonly affected. About 29% of patients with CD have involvement of both the ileum and colon, 35% have isolated ileitis, 36% of patients have colitis, and 4% have upper gastrointestinal tract involvement at the time of diagnosis. This distribution can evolve over time during a patient's disease course and so these proportions may not stay static in a population with CD over time [2].

Findings on index ileocolonoscopy at the time of CD diagnosis vary depending on the severity of inflammation, but the distribution and pattern can be helpful in diagnosing CD. Skip lesions, areas of inflamed mucosa separated by normal appearing mucosa, is characteristic of CD [3, 4]. Rectal sparing occurs in at least 50% of patients. The inflammation is patchy and circumferential inflammation is uncommon [5, 6].

Mild inflammation presents endoscopically with erythema, granularity, altered vascular pattern, friability, and small discrete superficial and aphthous ulcers. As the inflammation progresses, deep, serpiginous, and linear ulcerations and cobblestoning develop (**Figure 1**). About one-third of patients with CD will develop a fistula over their lifetime. In perianal disease fistulas may be apparent on physical exam, and perianal fistulas are more commonly seen in patients with rectal inflammation. Endoscopically, fistula openings may be visible as small openings in the colon or ileal mucosa [7]. Strictures, perianal disease, and isolated ileitis are also indicative of but not 100% specific for CD [6, 8]. Because of the discontinuous inflammation in CD, the area immediately surrounding inflammatory patches or ulcers are more likely to have an intact vascular pattern and absent or minimal inflammation on biopsy [9].

2.2. Ulcerative colitis

The inflammation seen in ulcerative colitis begins at the anal verge and extends proximally. Ulcerative colitis always involves the rectum, but if treatment has been started prior to

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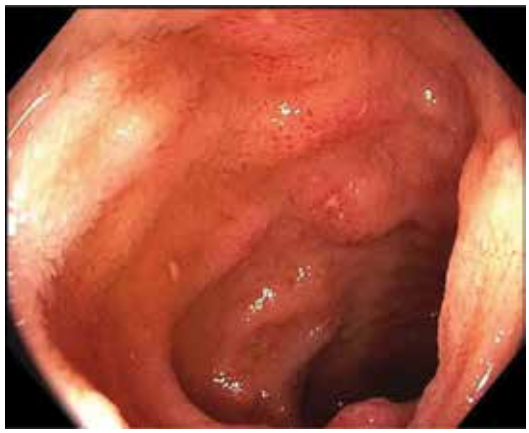

Figure 1. Terminal ileitis due to Crohn's disease.

colonoscopy the rectum may be spared or there may be patchy rectal inflammation [10]. The proximal extent of inflammation varies—about 46% of patients with UC have proctosigmoiditis, 37% have left sided colitis, and 17% have pancolitis [11].

On colonoscopy the inflammation in UC is circumferential and continuous. The features vary depending on severity. Early and mild inflammation appears as erythema, edema, and abnormal vascularity. Moderate UC has a "wet sand-paper" appearance due to changes in light reflection, erosions, superficial ulcers, and friability. As the severity of inflammation progresses the ulcerations become confluent, friability worsens, and spontaneous bleeding may develop [12–14] (**Figure 2a** and **2b**). Because the inflammation is continuous, the mucosa surrounding ulcerations will usually at a minimum have a diminished vascular pattern but more commonly will show more obvious signs of inflammation [9].

Pseudopolyps are also often seen in UC and develop as a result of regenerating epithelium but can be seen in CD as well [15]. They develop in patients with more severe and extensive periods of inflammation. While pseudopolyps themselves are not at risk of malignant transformation, UC patients with pseudopolyps may have a higher incidence of colorectal cancer as a result of more severe inflammation that predisposes to pseudopolyp formation [15, 16]. Pseudopolyps do not need to be resected, but there can be difficulty in distinguishing between pseudopolyps and adenomatous tissue, in which case biopsies or resection should be performed [12].

Patients with UC may have two unique areas of inflammation that may that may be confused as representing CD. In patients without inflammation in the right colon, there may be a "cecal patch", or localized inflammation around the appendiceal orifice (**Figure 3**). The prevalence of peri-appendiceal inflammation in UC is 5%. The significance of the cecal patch is uncertain, but its presence does not signify a more aggressive disease phenotype or higher colectomy rates [17]. Additionally, 10–25% of patients with pan-colonic UC have "backwash ileitis" which can be confused as representing CD. Backwash ileitis usually presents as localized, continuous, and short segment erythema in the terminal ileum without discrete ulcerations

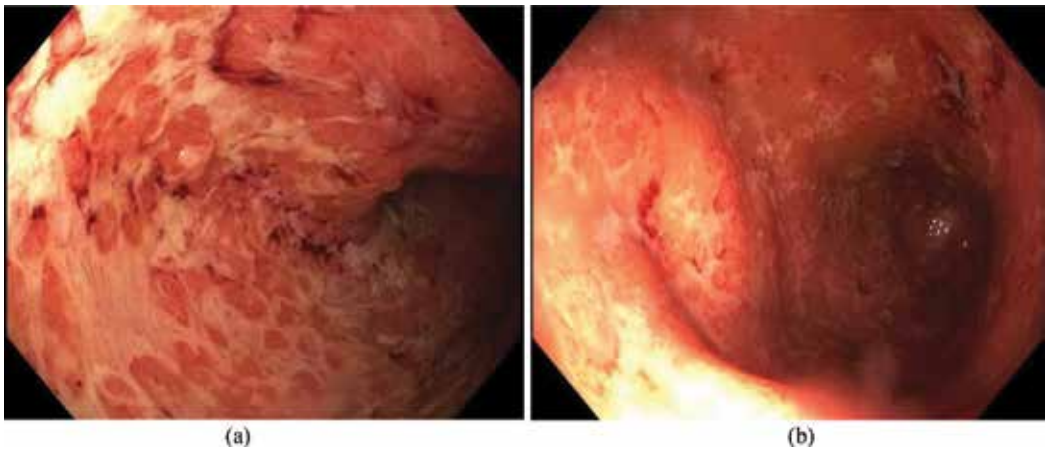

Figure 2. Severe ulcerative colitis.

or strictures and always occurs in the setting of pancolitis [18–20]. In contrast to peri-appendiceal inflammation, backwash ileitis represents a more severe disease course and increased risk for colectomy [21]. It should be noted that these observations are based on observational findings and one should not use these findings as definitive findings for distinguishing CD from UC. These findings further do not necessarily alter the medical management of IBD.

2.3. Biopsy collection

Biopsies should be obtained from both normal and abnormal appearing mucosa. A minimum of two biopsies should be taken from at least five sites throughout the colon including the rectum and terminal ileum. The biopsies should be labeled appropriately and separated so that the site of biopsy can be correlated with histology [13, 22, 23]. A full set of colonoscopic biopsies improves the diagnostic yield by histology for both CD and UC. Full biopsies may also reveal inflammation not seen well endoscopically that can affect prognosis and need for dysplasia surveillance [22]. Granulomas are present in patients with CD in at most 25% of patients at initial presentation and therefore cannot be used to differentiate between CD and UC when absent [24]. However, biopsies taken from micro-ulcers <5 mm in size and ulcer edges are more likely to demonstrate granulomas [25]. Terminal ileal biopsies are also vital in distinguishing UC from CD and for ruling out IBD mimickers.

2.4. Complications and contraindications

The complications seen in patients undergoing diagnostic ileocolonoscopy are similar to the general population. Complications include bleeding, perforation, and respiratory failure due to over sedation. It is not clear if IBD patients have an increased risk of perforation, with some studies finding no increased risk and others showing a higher rate of perforation, particularly in hospitalized IBD patients undergoing colonoscopy [26–29]. Full colonoscopy should be undertaken with caution in patients with severe inflammation, in those unable to undergo full bowel

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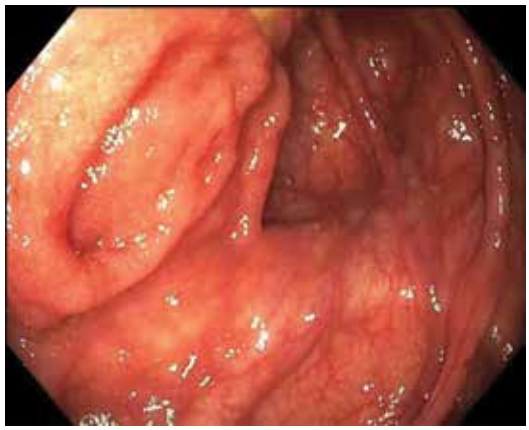

Figure 3. Peri-appendiceal inflammation.

prep because of severe symptoms, and definitely avoided in patients with toxic megacolon. In patients with severe disease and inflammation flexible sigmoidoscopy can be used for diagnosis and ruling out some infections, but sigmoidoscopy may not allow for differentiation between UC and CD. Despite these concerns, the overall rate of perforation is still very low. However, if perforation does occur it can require surgery and cause significant morbidity and even mortality and therefore caution should be taken in the presence of considerable inflammation.

3. Esophagogastroduodenoscopy

Although CD can involve any area from the mouth the anus, upper gastrointestinal (GI) tract involvement is less common than ileal or colonic inflammation. Because upper GI inflammation is often seen in patients without IBD, the prevalence is difficult to accurately determine but has been described in 13–55% of patients with IBD [30]. In terms of the distribution of upper GI tract involvement, one study found upper GI inflammation attributable to CD in the esophagus in 6.5%, upper-middle stomach in 47.8%, lower stomach in 24.6%, duodenal bulb in 31.9%, and second portion of the duodenum in 18.1% [31]. EGD is not necessary for all adult patients with suspected IBD but should be done for those with upper GI symptoms such nausea, vomiting, and early satiety. Endoscopic evaluation of the upper GI tract can also be useful when the diagnosis is uncertain.

EGD is recommended for pediatric patients with suspected IBD at the time of initial colonoscopy. There is a significantly higher proportion of pediatric patients with indeterminate colitis compared to adults, and EGD can help distinguish between CD and UC. There can also be inflammation with granulomas on biopsy even without colonic or ileal inflammation. Additionally, children can frequently present with non-specific symptoms such as weight loss or anemia for which an EGD is warranted to evaluate for IBD as well as other causes such as celiac disease [13, 32, 33].

3.1. Mucosal appearance and distribution

Esophageal Crohn's disease can appear as scattered erosions and aphthous ulcers with mild-moderate disease. More severe esophageal inflammation due to CD appears as longitudinal ulcers and can even have a cobblestone appearance. Stricturing and fistulization of the esophagus is rare but does occur in 20 and 5%, respectively, of patients with esophageal CD [34]. Importantly, esophageal CD must be differentiated from other causes of esophageal inflammation including reflux disease, eosinophilic esophagitis, and infectious esophagitis as the medical and surgical treatment for each condition varies. Granulomas are detected in less than 25% of cases of esophageal CD and therefore the absence of granulomas cannot be used to exclude esophageal CD [31].

Gastric CD is the most commonly observed site of involvement in the upper GI tract. The endoscopic findings are relatively non-specific for CD and include erythema, aphthous or linear ulcers, and granularity most commonly in the antrum. Bamboo-joint-like appearance in the stomach, typically in the cardia and upper body, is more specific finding for CD. The bamboo-joint-like finding appears as edematous folds with fissures or linear furrows arranged transversely [35]. Notably, gastritis without ulceration is often seen in patients with UC and cannot be used to differentiate CD from UC [19].

Mucosal features of duodenal CD can also be frustratingly non-specific. Findings include erythema, edema, aphthous and longitudinal erosions and ulcerations. Duodenal CD may have protruding lesions in the second portion of the duodenum that arrange longitudinally or a notch-like appearance in the second portion of the duodenum that may a more reliable marker of inflammation due to CD [31, 35].

3.2. Biopsy collection

A minimum of two biopsies should be taken from the esophagus, stomach, and duodenum for patients undergoing EGD for suspected IBD. Biopsies should also be taken from the stomach to rule out Helicobacter pylori infection depending on the patient's symptoms and endoscopic findings. More than two biopsies should be obtained from the esophagus and duodenum if there is concern for other diseases such as celiac disease or eosinophilic esophagitis to improve the diagnostic yield of the procedure and directed biopsies should be taken of any visible lesions.

4. Endoscopic evaluation of the small intestine

Evaluation of the small bowel in patients with suspected CD can be useful when the diagnosis is uncertain after ileocolonoscopy or upper endoscopy. Enteroscopy is also valuable for therapeutic benefit in the setting of small bowel strictures at the time of diagnosis and is typically guided by radiographic imaging findings. There are multiple modalities for small bowel evaluation—capsule endoscopy (CE), push enteroscopy, and antegrade (via mouth)

or retrograde (via anus) device assisted enteroscopy. The benefit of push or device assisted enteroscopy is the ability to sample tissue for histology and for therapy in the case of stricturing CD. For all afore mentioned modalities, they should be undertaken if the findings would change medical or surgical management of the patient and are not required prior to starting medical therapy.

4.1. Capsule endoscopy

Capsule endoscopy is important when the diagnosis of IBD is uncertain after EGD and colonoscopy with ileoscopy or in cases of indeterminate colitis. Capsule endoscopy is less invasive compared to standard endoscopy and allows for imaging of the entire small bowel that may not be easily reached even by device assisted enteroscopy. Additionally, CE has a similar or higher sensitivity compared to other small bowel imaging modalities such as small bowel follow through, magnetic resonance enterography (MRE), or computed tomography enterography (CTE). The main limitation of CE is the inability to obtain biopsies for histologic analysis, which can lead to diagnostic challenges as small bowel findings on CE may not be specific to IBD. An advantage of CE over small bowel imaging modalities is the ability to detect subtle inflammation that may not be seen on CTE or MRE [13, 36]. Another disadvantage of CE is that it can become retained in up to 5% of CD patients and may require enteroscopy or surgery for retrieval.

Small bowel inflammation due to IBD has a similar appearance to IBD elsewhere in the GI tract. This includes more subtle features such as erythema, granularity, loss of villi, and edema, to more prominent findings such as ulceration of varying sizes, strictures, and fistula openings [37, 38].

The main complication of capsule endoscopy is capsule retention. Because of the stricturing nature of CD, there is estimated to be a slightly higher risk of capsule retention compared to patients without CD. In patients with known or suspected strictures or with obstructive symptoms, assessment with patency capsule or alternative small bowel imaging modality (CTE or MRE) beforehand is imperative [39]. The risk of capsule retention in patients undergoing evaluation for suspected CD is lower than in patients with established CD but still occurs in about 1–2% of patients [40]. In cases of retention for longer than 2 weeks, the capsule should be retrieved. Occasionally, if a capsule is retained due to a small bowel stricture that is due at least in part to active inflammation, the capsule will eventually traverse a stricture if effective medical therapy is initiated. If unsuccessful, retrieval can be accomplished by balloon or push enteroscopy, but in some cases surgical intervention is required.

4.2. Enteroscopy

The advantage of enteroscopy over CE is the ability to obtain tissue when the etiology of small bowel inflammation is uncertain. Additionally, enteroscopy can allow for dilation of small bowel strictures that may not be reached by standard colonoscopy with ileoscopy or EGD. Push enteroscopy is a technique in which a colonoscope, typically pediatric, is advanced

to the proximal jejunum. Double and single balloon enteroscopy is more technically challenging than push enteroscopy but can be advanced past the reach of push enteroscopy. Single or double balloon enteroscopy can be done antegrade (via the mouth) or retrograde (via the anus) depending on the site of suspected disease. Double balloon enteroscopy can be effective for the diagnosis and staging of suspected small bowel CD in 30–48% of cases but is not the preferred initial test [41, 42]. Findings on enteroscopy are the same as CE, namely erythema, edema, loss of villi, ulcerations, and possibly strictures and fistula openings. The major complication rate of balloon enteroscopy is 0.72% and includes perforation, pancreatitis, aspiration, and bleeding [43]. Complication rates of push enteroscopy are similar to balloon enteroscopy [44]. It should also be noted that enteroscopy whether antegrade or retrograde may not visualize the entirety of the small intestine and typically requires general anesthesia to complete.

5. Indeterminate colitis and differentiating UC and CD

The most important aspect of ileocolonoscopy for suspected IBD is making the correct diagnosis and staging the disease as this will affect prognosis and treatment. Ileocolonoscopy can differentiate UC from CD nearly 90% of the time. Indeterminate colitis is used for a small subset of patients with colitis cannot be easily classified into UC or CD by endoscopic findings or histology [45].

The pattern and distribution of inflammation is critical for distinguishing CD and UC. UC presents with continuous inflammation and in untreated UC always involves the rectum. In CD, rectal sparing is often present and the inflammation is patchy with intervening areas of normal mucosa. However, the presence of rectal inflammation can be seen in up to 50% of patients with CD is therefore not diagnostic of UC [8]. Additionally, because of the continuous nature of the inflammation in UC, the mucosa immediately surrounding ulceration will be abnormal. This is apparent as erythema or decreased vascular pattern around ulcers in UC. In CD, the mucosa around ulcers shows a normal vascular pattern and absence of inflammation [3, 4, 19]. Central to discriminating CD from UC is ileoscopy. While backwash ileitis can be present in up to 25% of UC patients with pancolitis, the inflammation in this setting is usually mild, continuous, and shorter. It should be noted that the definition of backwash ileitis is controversial and the term was initially created prior to the era of ileo-colonoscopy and was used to describe a finding on barium enema. The presence of ulcers in the terminal ileum in a patient without right colon inflammation is specific for CD compared to UC. However, it is important to remember that there are other causes of terminal ileitis, including infection, vasculitis, malignancy, or NSAID induced inflammation [46]. Inflammation, particularly ulceration, stricturing, or fistulization of the upper GI tract or small bowel, is virtually diagnostic of CD over UC, although mild gastritis or duodenitis without ulceration can be present in patients with UC. Granulomas, if present, are also consistent with Crohn's disease, and biopsies of the ulcer edge increase the chance of finding a granuloma [25].

When a diagnosis of CD or UC cannot be made based on endoscopy, histology, and radiography, the term indeterminate colitis or IBD-unclassified is used. About 7–10% of adult patients with IBD will have indeterminate colitis. An even higher proportion of children, nearly 30%, have indeterminate colitis [32, 45]. Some of these patients will be reclassified as CD or UC as the disease evolves and defining characteristics of UC or CD develop. EGD and CE may be helpful in establishing the correct diagnosis by revealing small bowel inflammation consistent with CD in about 15% of patients with indeterminate colitis. However, a normal EGD or CE study does not rule out CD [47]. If a patient is classified as indeterminate colitis, this should not affect therapy choices or present or future endoscopic evaluation.

6. Differentiating IBD from IBD mimickers based on endoscopy

The diagnosis of IBD relies on a combination of symptoms, laboratory analysis, imaging, endoscopy, and histology. However, the endoscopic inflammation in IBD can be non-specific and due to causes other than IBD. In addition to differentiating between CD and UC and staging the extent of disease, other causes of bowel inflammation should be ruled out. This is particularly important as the treatment for IBD may lead to worsening of other conditions, particularly infection.

6.1. Infection

Infection is an important mimicker of IBD on endoscopy. Common infections such as Clostridium difficile and *Escherichia coli* should be ruled out with stool testing prior to colonoscopy. *Yersinia* spp. can often lead to right lower quadrant abdominal pain and fever with imaging showing ileitis and an appearance suggestive of acute appendicitis. *Salmonella, Actinomyces,* and *E. coli* infections can also lead to enteritis and particularly ileitis that may look like IBD [48]. Intestinal tuberculosis can lead to ulceration, nodularity, and stricturing of the terminal ileum and ileocecal valve [49].

Cytomegalovirus (CMV) infection can lead to inflammation and ulceration in any part of the gastrointestinal tract. The ulcers in CMV enteritis or colitis have been described has having a "punched-out" appearance. Biopsies can help differentiate CMV from IBD. However, many patients with IBD will have coexisting CMV and endoscopy is important to rule out concomitant CMV infection that is contributing to bowel inflammation. However, it can be sometimes challenging to determine whether CMV is an innocent bystander or an active participant in inflammation in IBD patients [50].

6.2. Vasculitis

Rarely, vasculitis can affect the bowel, typically the small intestine. Systemic lupus erythematosis, polyarteritis nodosa, Henoch-Schönlein purpura, and Behçet's disease may all be confused with IBD. Polyarteritis nodosa frequently affects the gastrointestinal tract in up to 65%

of patients and may lead to symptoms of bowel ischemia [51]. Behçet's disease in particular can lead to discrete ulcers in the small and large bowel with normal intervening mucosa that can be confused for CD. However, the ulcers in Behçet's disease are usually fewer in number, larger, deeper, and rounder than seen in IBD [52].

6.3. Ischemia

Ischemia can lead to edema, erythema, erosions and ulcerations that can look similar to IBD. Severe ischemic colitis can lead to a dusky and even black appearance with necrosis. The inflammation is usually segmental with a sharp demarcation affected and unaffected mucosa depending on the vascular supply. The left colon is most commonly affected. An accurate history and acuity of symptoms can also help distinguish IBD from ischemic colitis [53, 54].

6.4. Segmental colitis associated diverticulosis syndrome

Segmental colitis associated diverticulosis (SCAD) can be especially difficult to distinguish from IBD. SCAD is associated with diverticulosis and most commonly affects the sigmoid colon. The rectum and right colon are typically spared. The endoscopic features of SCAD include edema, erythema, erosions, and ulcers, often with sparing of the diverticular orifices [55]. Because endoscopic and histologic features overlap with IBD, the diagnosis can be challenging but SCAD is more often found in older patients and often responds to mesalamine [56].

6.5. NSAID enteropathy

NSAIDs are the most common medication that can lead to bowel inflammation. NSAIDs can lead to "diaphragm disease" or pinhole openings due to 2–3 mm thin walled septae with normal mucosa between diaphragms. NSAIDs can also lead to erosions and ulcers not just in the stomach and duodenum but small bowel as well [48].

7. Novel techniques and future directions

This section will discuss techniques that are available or being developed but not widely utilized or have not been evaluated sufficiently to recommend that these techniques be used as standard of care.

7.1. Endoscopic ultrasound

Although still being studied, endoscopic ultrasound (EUS) is emerging as technique that can be valuable for the diagnosis of IBD and differentiation between CD and UC. In one study comparing EUS in IBD patients to healthy controls, patients with active IBD undergoing EUS had increased total wall thickness of the sigmoid colon compared to healthy controls.

Furthermore, patients with UC had increased wall thickness of the mucosa with normal submucosa and muscularis propria, whereas CD patients had increased submucosa thickness with normal mucosa thickness [57]. In addition to being used to assess bowel inflammation, EUS has a recognized role in the diagnosis and evaluation of CD related perianal disease. EUS can determine fistula anatomy with accuracy that is slightly higher than MRI (91% vs. 87%). EUS can also assess for adjacent abscesses and the degree of active inflammation which can in turn guide management [58, 59].

7.2. Endocytoscopy and endomicroscopy

Endopathology, which includes both endocytoscopy (EC) and confocal laser endomicroscopy (CLE), allows for magnification of the mucosal surface and real-time histologic assessment at the time of endoscopy. EC and CLE can be performed with stand-alone probes that are advanced through an endoscope or via probes integrated into the distal end of an endoscope. Endocytoscopy typically requires *N*-acetylcysteine for mucolysis followed by topical application of a staining agent. CLE allows for tissue magnification by illumination with a low power laser light that is reflected through a pinhole and requires either a topical agent or an intravenous fluorescence agent, usually fluorescein sodium, for adequate visualization [60, 61]. Magnification assessment by EC allows for the detection of mucosal inflammatory cells, crypt assessment, and nucleus-cytoplasm ratio, whereas CLE can assess crypt architecture, inflammatory cell infiltrate, and vessel architecture but fluorescein does not allow for nuclear visualization and assessment. Both EC and CLE have excellent correlation with histology in IBD and can diagnose inflammatory and architectural changes even if the mucosa appears normal endoscopically [62, 63]. Both EC and CLE may allow for identification of microscopic changes that can predict relapse in established IBD patients in remission, but their role in diagnosis at this time is unclear. EC and CLE are areas undergoing active investigation and do not yet have widespread applicability.

7.3. Spectroscopy

Elastic scattering spectroscopy, reflectance spectroscopy, and fluorescence spectroscopy have shown promise for the diagnosis of IBD. In addition to aiding in the diagnosis of IBD, Raman spectroscopy has evidence that shows promise for the differentiation of CD and UC. Spectroscopy in general provides a unique tissue signature that is based on the makeup of the tissue and its interaction with light and is different in normal compared to inflamed tissue. Scattering spectroscopy provides information based on the microscopic structure, whereas Raman spectroscopy and fluorescence spectroscopy provide data based on the biochemical makeup of the tissue [64–66]. Spectroscopy in general shows promise for the diagnosis of IBD but needs further evaluation.

7.4. Optical coherence tomography

Optical coherence tomography (OCT) generates a cross-sectional image of the internal microstructure by measuring back-reflected light. OCT can evaluate tissue to a depth of at the least

the muscularis propria in most patients and provides information on transmural inflammation by identifying disruption of the layered stricture of the bowel wall. Such disruption on OCT can therefore help differentiate CD from UC [67, 68]. OCT also requires further study before clinical application.

8. Conclusion

The most important test for the diagnosis of IBD is colonoscopy with ileoscopy being a critical component in initial testing. Capsule endoscopy can be a useful tool when the diagnosis is uncertain and certainly in patients with disease on radiographic studies out of reach of standard ileo-colonoscopy. In addition CE has a similar or higher sensitivity compared to small bowel imaging modalities. In terms of mucosal appearance, continuous inflammation from the anal verge proximally is consistent with UC whereas discontinuous inflammation with ileitis, upper GI or other small inflammation and the presence of stricturing or fistulizing disease is diagnostic for CD over UC. However, the mucosal appearance of the inflammation is not 100% specific for either disease. Appropriate attention should be made to obtaining biopsies to increase the diagnostic yield of the procedure. At least two biopsies should be taken from five sites during ileocolonoscopy including the ileum and rectum and normal and abnormal appearing mucosa. The diagnosis of IBD relies upon a combination of history, radiography, laboratory, and endoscopic features, with ileocolonoscopy providing the most accurate and useful data.

Conflict of interest

Jeffrey Jacobs—none.

Scott Lee—none.

Notes/Thanks/Other declarations

None.

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Chapter 5

Advances in the Treatment of Postsurgical Benign Colorectal Strictures

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Additional information is available at the end of the chapter

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Abstract

Postsurgical benign colorectal strictures occur in up to 20% of patients who undergo colon or rectal resection. Traditionally, treatment has been surgical, but recent decades have seen the growing importance of an endoscopic approach, particularly balloon dilatation, which is now considered the first-line treatment for these benign strictures. However, balloon dilatation is associated with a recurrence of the stricture in up to 25% of cases. When this arises, one can opt for surgery aimed at performing a reanastomosis; a new intestinal anastomosis may be technically complex or even impossible, which would result in the patient requiring a permanent colostomy, with its consequent negative impact on quality of life. Accordingly, different endoscopic approaches have been evaluated for strictures refractory to balloon dilatation, such as the implant of self-expanding metallic stents, biodegradable stents, or incisional therapy, with variable results in efficacy.

Keywords: benign colorectal strictures, postsurgical strictures, self-expanding metallic stents, biodegradable stents, incisional endoscopic therapy

1. Introduction

Acute obstruction of colorectal transit is an emergency, the initial management of which is surgery. In most cases, the obstruction is caused by a malignant condition [1], although multiple other benign causes also exist, like surgical anastomosis, postradiotherapy complications,

Benign colorectal strictures
1. Postsurgical
2. Inflammatory bowel disease
3. Diverticular disease
4. Postradiotherapy
5. Ischaemic
6. Iatrogenic due to chronic use of NSAIDs
7. Treatment of prior lesions by endoscopic submucosal resection

Table 1. Aetiology of benign colorectal strictures.

diverticulitis, inflammatory bowel disease, ischaemia, chronic treatment with NSAIDs (**Table 1**). Endoscopic treatment with submucosal resection of large lesions has been postulated as another common cause in the not too distant future [2].

The most common cause of benign colorectal strictures is currently postsurgical stenosis [3]. This occurs in 5–20% of all surgeries [4], especially affecting anastomoses in the distal extraperitoneal rectum. The factors leading to the appearance of these strictures are not completely clear although certain related factors have been identified, such as the presence of anastomotic leaks, radiotherapy before surgery, relative ischaemia due to excessive tension in the anastomosis, and recently a relation has been found between its increased incidence and the use of mechanical intestinal sutures [5]. The incidence of stenosis is greater with the use of circular endostaplers.

Most studies define postsurgical strictures as those that cannot be traversed by a standard calibre colonoscope. This definition, however, is hardly homogenous as there can exist small but substantial technical differences between the various endoscopes. Truong et al. [6], in a study of 36 patients who underwent endoscopic treatment, defined three degrees of stenosis according to its diameter, which were related with the presence of obstructive intestinal symptoms, in particular Grade 3 or less than 5 mm diameter. Most appear during the first year after surgery, though in some cases they may appear and become symptomatic several years after surgery.

2. Treatment of postsurgical colorectal strictures

Treatment of all postsurgical strictures is recommended when they are symptomatic or when a diagnostic or therapeutic procedure proximal to the stricture is required. Special attention must be given to patients who have undergone surgery for a malignant colorectal cancer in order to be able to undertake an endoscopic follow-up due to the risk of metachronous cancer [7].

Postsurgical strictures have traditionally been managed surgically with dissection and reanastomosis. This, however, does not rule out the possibility of stenosis in the newly created anastomosis nor is it always possible, due to inflammatory phenomena and fibrosis that can appear in the surrounding tissues, particularly in anastomosis of the inferior rectum, where

reintervention is technically more demanding. In some cases, this may lead to the creation of a definitive stoma, with the corresponding reduction in quality of life for the patient. As a result, various minimally invasive strategies have been studied aimed at the treatment of postsurgical strictures.

2.1. Dilatation

Since the first balloon dilatation of a benign rectal stricture in 1984, this technique has become the treatment of choice for this condition, especially when the stricture is postsurgical and related with inflammatory bowel disease [3, 7].

Multiple dilatation techniques have been described, whether guided by radioscopy or by endoscopy. Initially, Savary-Gilliard wire guides were used, but with these only the most distal strictures were accessible. Later there appeared dilatation balloons, OTW (over the wire or achalasia balloon dilation) or TTS (through the scope). The balloons only exert radial force on the stenosis and therefore present a lower risk of perforation, improving the clinical results of the dilatation as compared with guide wires. Generally, the technique requires various sessions with a progressive increase in balloon diameter until the stricture is definitively solved.

Several factors of the stricture can be correlated with the results of balloon dilatation [8] as factors predicting success: a stricture calibre around 10 mm, a length of the stenotic segment less than 4 cm and the postsurgical aetiology of the stricture. Factors predicting failure of the dilatation include malignancy of the stricture, presence of more than one stricture, association of fistulas, complete obstruction of the lumen, active inflammation or marked angulation of the stenotic segment.

The initial success rate of balloon dilatation of postsurgical strictures is 91–100%, depending on the series [7, 9]. Long-term follow-up studies show its effectiveness is maintained, avoiding the need for surgery in 75% of strictures [9, 10], with a low rate of complications, around 15%, mostly minor (such as mild bleeding) that can generally be managed conservatively. A recent review of 850 procedures [11] estimated the overall rate of perforation with this technique at 1.1%.

Recurrence of the stricture does not appear to be clearly related with the number of sessions needed to achieve the cure.

2.2. Self-expanding metal stents (SEMS)

A metal stent is just a cylindrical metal mesh that, when released by its holding device, tends to recover its original shape until it reaches its maximum diameter. They can be made of various different materials, such as stainless steel, elgiloy (alloy of cobalt and nickel) or nitinol (alloy of nickel and titanium). This latter is currently the most widely used and is characterised by its flexibility, which thus enables the stent to be placed in areas with marked angles.

There exists a great range of lengths and diameters among stents, and their designs usually involve larger cups at the ends to prevent migration. Covered stents (either fully or partially) have a silicone membrane covering the openings of the metal mesh (see **Figure 1**).

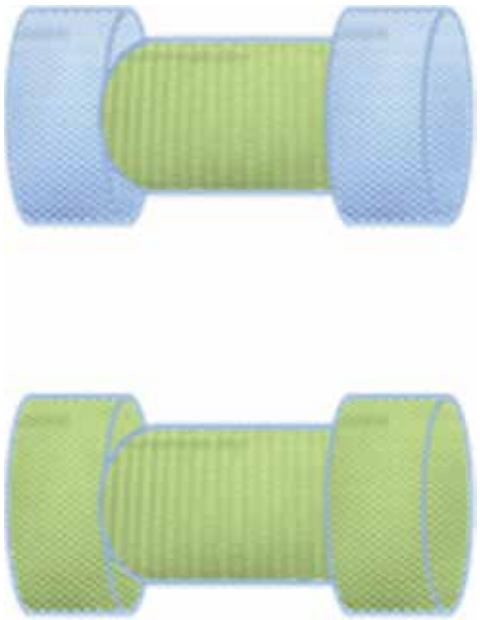

Figure 1. Types of stent.

Table 2 shows the different types of stents used for the treatment of postsurgical colon strictures, explained here and below.

In the context of malignant neoplastic strictures, self-expanding metal stents, or SEMS, have clearly proven their usefulness, both as palliative definite treatment and as bridge therapy to elective surgery. However, their role is not so clear in cases of benign colorectal strictures [12].

The results of studies about benign strictures are difficult to interpret, as most studies involved a low number of patients and a wide variability in the type of stent implanted (uncovered, partially covered or fully covered) as well as the aetiology of the stricture [13–16].

Uncovered stents have a lower risk of migration, but they are difficult to withdraw due to the hyperplastic reaction generated within a few days of implantation. Covered stents, however, are very easy to withdraw but at the expense of a greater risk of migration.

Self-expanding stents
1. Uncovered metal stent
2. Partially covered metal stent
3. Fully covered metal stent
4. Biodegradable stent
5. Lumen-apposing metal stent

Table 2. Types of self-expanding stents used for the treatment of postsurgical strictures.

Studies have evaluated the use of stents as a bridge to surgery (as in malignant diseases) to thereby avoid having to make a stoma in the event of acute colon obstruction of benign origin [13, 14]. The clinical success rate reaches 91%, with major complications in up to 38% of cases. The most frequent complication is stent migration, though this is mostly with effect from 7 days of implantation and in strictures of diverticular or actinic obstruction. A systematic review in 2013 about the use of stents for the management of benign colorectal obstruction [16] that included 122 patients found that a stoma was only avoided in 48% of the patients.

The high rate of recurrence of postsurgical strictures after balloon dilatation, around 25%, especially in long strictures, with a technique not exempt from complications, has led to multiple studies assessing the role of SEMS [15, 17–20], although all involved just a few patients. Unlike balloon dilatation, stents apply a constant prolonged radial force on the stricture, due to the natural tendency of nitinol to recover its original shape once released. This quality permits definitive remodelling of the stricture, and covered stents also afford the possibility of sealing anastomotic leaks when they are associated with the stricture [17, 18].

The immediate clinical efficacy reported in various studies ranges from 36 to 81% [15, 17, 19–21] and improves with larger diameter stents [19]. However, they are associated with a high rate of complications, mainly migration in 19–63% of cases [17, 19, 21], which, if early, necessitates additional treatment of the stricture, reobstruction due to hyperplastic reaction in the extremes or stool impaction, necrosis due to pressure, bleeding, anal pain or perforation in up to 28% of cases.

Three recent studies of covered metal stents for postsurgical strictures [19–21] report clinical success rates of 100, 100 and 81%, respectively, with long-term results of solving obstruction ranging from 53 to 70% after follow-up periods of 18–21 months.

In 2015, Park et al. [3] compared a group of 43 patients with benign strictures who were divided into two treatment arms (dilatation and SEMS). They found no significant differences in clinical success between the two groups.

The disparity in the results makes it impossible to conclude that metal stents are a suitable option for first-line treatment of strictures in surgical anastomoses, though the results of some studies [19–21] suggest that fully covered metal stents could play a role in those cases that are refractory to treatment with dilatation.

2.3. Biodegradable stents

Recent years have seen the development of stents made from biodegradable materials, used more often in the field of endovascular therapy. They are composed of synthetic biocompatible polymers that gradually dissolve through a process of hydrolysis without generating any harmful products during their degradation. The most used are polylactic acid and polydioxanone. Their rate of degradation depends on the structure and size of the stent, in addition to the temperature, pH and type of tissue with which they are in contact [22]. The most used in the gastrointestinal area are polydioxanone stents (SX-ELLA oesophageal stents), initially designed for the treatment of oesophageal strictures refractory to conventional treatment. They afford the

possibility of maintaining dilatation prolonged over 6–8 weeks, avoiding the need to withdraw the stent, this being their main advantage compared with self-expanding metal stents. They degrade completely after some 11–12 weeks as part of the stent is absorbed and part expelled via the gastrointestinal tract. Their degradation is hastened in media with an acid pH.

A particular feature of these stents is that they require ultrarigid guide wires for placement, with a stricture calibre of at least 9.4 mm to enable passage of the 28 F release system. Thus, prior dilatation of the stricture is often necessary. The release device measures 75 cm, which limits its use in proximal colon strictures [23], though this may be feasible with the use of overtubes.

Potential complications are the same as those for conventional metal stents: perforation, migration, occlusion due to faecal impaction or hyperplastic reaction of the mucus and haemorrhage.

Little evidence exists about the use of biodegradable stents in the treatment of benign post-surgical strictures. Most reports concern clinical cases [24, 25] or series with a low number of patients [23, 26]. The stricture is resolved in up to 45% of cases [26]. The main cause of this poor response is early stent migration, facilitated by the predilatation needed for insertion (minimum calibre 9.4 mm) and intestinal peristalsis exacerbated by the use of laxatives. Their systematic use to avoid faecal impaction in the stent is therefore questioned [27]. Clips and cyanoacrylate have been used to fix the proximal end [23].

A recently published review [27] collects various studies with a total of 36 patients. The technical success ranged from 86 to 100%, the clinical success varied from 45 to 100% and the rate of migration ranged from 0 to 36%.

A specific design of these stents for placement in the colon to reduce early migration as well as the development of adequate fixation systems could possibly improve the long-term results of these stents. The currently available data do not appear to show they are superior to covered metal stents as an alternative in refractory strictures.

2.4. Incisional therapy (EEI: endoscopic electrocautery incision)

An alternative has recently been described for the treatment of benign colorectal anastomotic strictures. Like other treatments for this condition, it has been exported after its use in post-surgical strictures in the upper digestive tract. It is a simple, cheap and accessible technique in most endoscopy units. It consists of performing various radial incisions of the stricture using polypectomy loops, sphincterotomes or an IT knife (insulated tip knife).

Case reports exist of the exclusive performance of radial incisions in the stricture [28], arguing that no additional manoeuvre is needed as the simple passage of stools through the stenotic area will dilate it (**Figure 2**).

Modifications have been made to this technique, withdrawing the tissue from between the radial incisions (RIC: radial incision and cutting) with an IT knife [29, 30] or with argon plasma [31], or else combining balloon dilatation with radial incisions (**Figures 3** and **4**). Other combined treatments give a steroid injection in the incisions to avoid relapse of the stricture.

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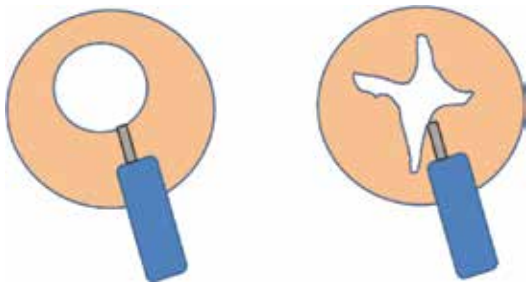

Figure 2. Endoscopic electrocautery incision (EEI).

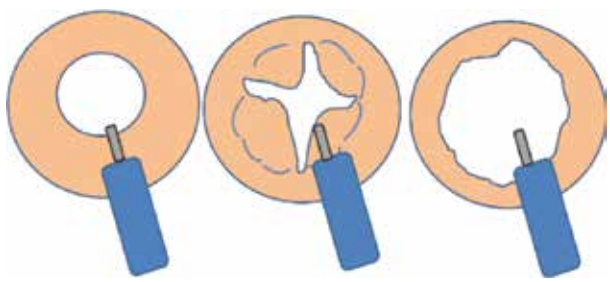

Figure 3. Radial and incisional cutting (RCI).

The following figures show the various steps of the technique combined with dilatation: **Figure 5**, colon stricture; **Figure 6**, making the radial incisions; **Figure 7**, dilatation; **Figure 8**, final result after dilatation and **Figure 9**, endoscopic review after 4 weeks.

In 2016, Bravi et al. [32] reported a series of 60 patients with diaphragm-like strictures no larger than 3 mm. At least 4 radial incisions were made with a needle sphincterotome with no other technique. The stricture was resolved in 100% of the cases, with no complications, in one single session and with a recurrence rate of the strictures of 5% over a follow-up period of 35 months.

In 2017, a meta-analysis [33] of 10 studies involving a total of 186 patients treated with this technique, either alone or in combination with other techniques, found clinical success in

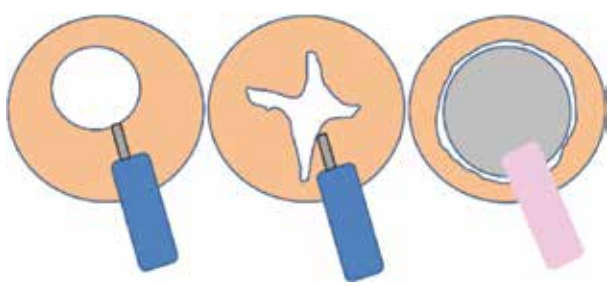

Figure 4. Combined EEI and dilatation.

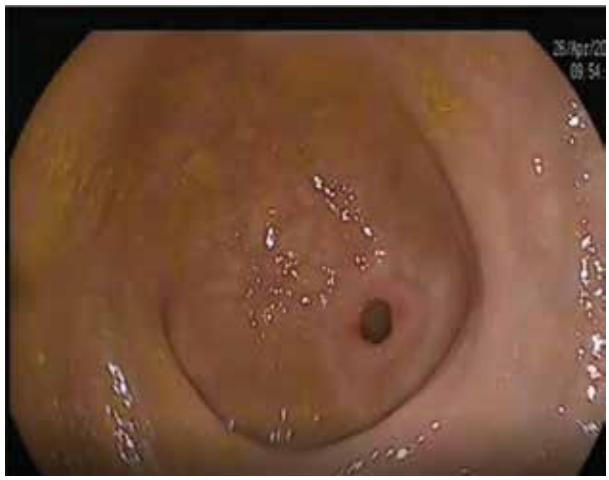

Figure 5. Colon stricture.

95.2% of cases for EEI, 95.8% for RIC and 87.8% for EEI combined with balloon dilatation. The recurrence rate of the strictures was 4.8, 0 and 12.5%, respectively. Complications occurred in 3.8% of cases, consisting of post-procedure abdominal pain. No other complication like bleeding, infection or perforation was noted.

Of note is the greater recurrence when incisions are combined with balloon dilatation. This could be explained by the fact that the dilatation increases the trauma to the stricture, with the corresponding inflammatory changes and retraction.

Accordingly, the results of this last meta-analysis suggest that this technique, either alone or accompanied by others, could be a safe and efficient alternative for short refractory postsurgical strictures or even possibly in naïve patients as it has a lower rate of complications and recurrences than balloon dilatation [34].

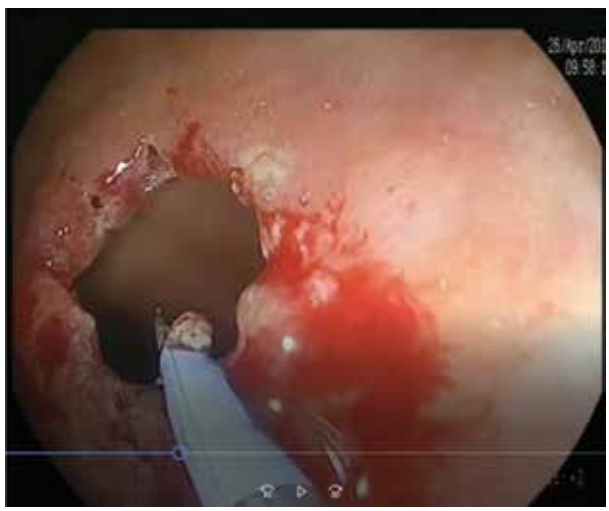

Figure 6. Making the radial incisions.

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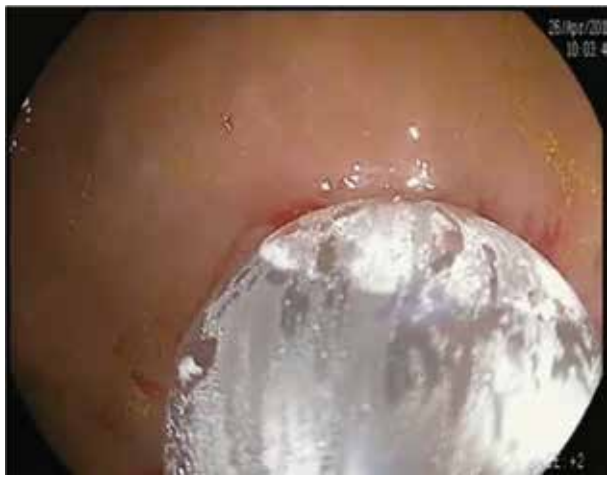

Figure 7. Dilatation.

2.5. Novel treatments: lumen-apposing metal stents

Lumen-apposing metal stents have very recently been incorporated for the treatment of postsurgical benign colon strictures. This stent was designed for the treatment of peripancreatic fluid collections. The ends are shaped like a diabolo, enabling the stent to be anchored by creating an anastomosis between the digestive tract and the fluid to be drained. This reduces the possibility of migration and, as they are fully covered, their later withdrawal is relatively easy (see **Figure 10**).

This characteristic led to its use in the treatment of benign strictures of the digestive tract. Several studies have assessed its usefulness, although with only a few patients and mostly concerning benign strictures of the upper digestive tract; however, some include postsurgical colon strictures [35–38].

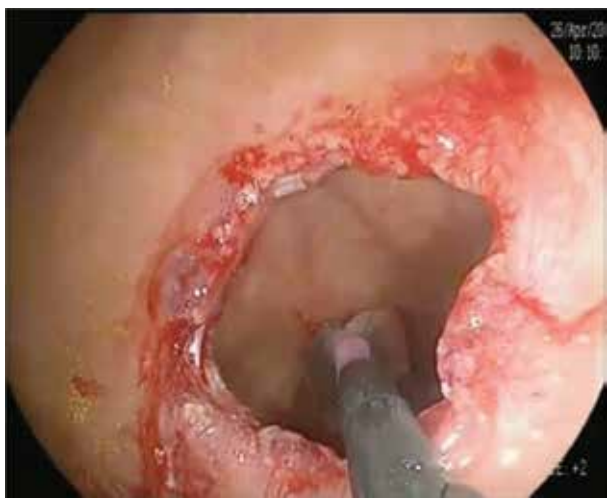

Figure 8. Final result after dilatation.

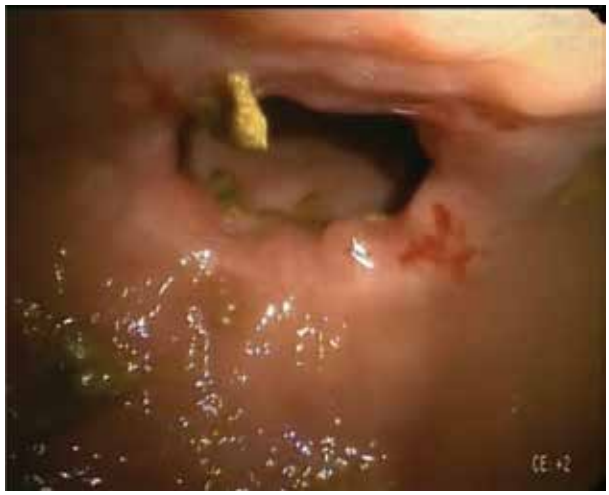

Figure 9. Review after 4 weeks.

Figure 10. Lumen-apposing metal stent.

The clinical success rate improves significantly as compared with the traditional covered metal stents, reducing the rate of stent migration and with a lower complication rate. The study by Irani et al. [35] reports 25 patients, including one case of a colon anastomotic stricture, with a clinical success rate of 60% over a follow-up period of 6 months and a migration rate of just 7%.

Yang et al. [36] presented results for 30 patients, with a clinical success rate of 82.6% after a follow-up period of 100 days. The migration rate was 8%, and complications arose in 13.3% of the patients, only two of which were severe (6.7%). This study included four postsurgical colon strictures, of which three failed to achieve long-term resolution of symptoms.

Other studies, such as those of Bazerbachi et al. [37] or Santos-Fernandez et al. [38], report higher stent migration rates (17.9 and 19%, respectively), at the expense of those implanted for colon strictures. Nonetheless, this complication is considerably less than that observed with conventional metal stents. It should be noted that the former study included seven patients with postsurgical colon strictures and the latter just two patients.

No large series have evaluated the efficacy of lumen-apposing stents in this particular indication; just the patients included in the previously mentioned series or isolated clinical cases [39]. However, they seem to have a promising role if they are able to reduce the complications seen with other types of stent, as seems possible.

Finally, as a novelty, reports exist of the treatment of complete anastomotic strictures in patients with a stoma, approached via distal endoscopic ultrasound-guided rendezvous [39], filling the proximal colon with water to locate by ultrasound the suitable puncture point and then placement of the stent.

3. Conclusions

Although there are no clinical guidelines with established algorithms for the treatment of benign postsurgical strictures, current evidence suggests that the first therapeutic option should be balloon dilation. In cases refractory to this treatment after at least three sessions, one of the following alternatives can be considered: incisional therapy or metal stent, and for the latter, the greatest evidence for safety and efficacy favours fully covered stents. The possible usefulness of lumen-apposing metal stents remains to be established. Biodegradable stents, at least at the present time, have a marginal role with less evidence for their usefulness. Prospective controlled studies are required to determine whether incisional therapy can replace balloon dilatation as first-line therapy.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Section 4

Other Uses of Endoscopic Techniques

Chapter 6

Spine Endoscopy

Álynson Larocca Kulcheski, Xavier Soler I Graells and André Luís Sebben

Additional information is available at the end of the chapter

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Abstract

The evolution of medicine has led to the appearance of increasingly invasive surgeries. Inside the spine area was no different. Currently, there are minimally invasive procedures in the spine, and endoscopic spine surgery has been the peak of these procedures. This procedure was initially described for the treatment of lumbar disc herniations, but with the technical improvement, the materials used are already being made for other pathologies such as lumbar stenosis, thoracic disc hernias, spinal infections, posterior cervical decompression, and cervical herniations. It has a long learning curve, but the benefits of endoscopic surgery are remarkable, such as less postoperative pain, less bleeding, smaller scars, lower infection rate, less injury to the operated tissues, and a return to earlier work activities, among others. In this way, we must follow the evolution of medicine with the learning of these new techniques.

Keywords: spine, intervertebral disc displacement, endoscopy, pain, spinal diseases

1. Introduction

Medicine is always under constant development. All the medical specialties have their progress with new techniques. In spine surgery, it is not different. Degenerative diseases of the spine form part of daily medical practice and their treatment is complicated by medical and socioeconomic problems. Where severe pain or neurologic deficits persist and all conservative treatment options have been exhausted, surgery may be required. Traditional operations of the spine can achieve good results at the expense of great tissue damage, which causes lesions in the coordination and stabilization of the spine. This type of damage occurs even with the use of microsurgery, causing, therefore, the occurrence of cicatricial fibrosis in the epidural space, which influences the postoperative pain syndrome.

One of the most revolutionary progresses in the spine surgery was the recent development of the spine endoscopy for the treatment of various pathologies. Although the field of endoscopic spine surgery is still young and is rapidly evolving, with precise indication, proper diagnosis, and good training, the endoscopic spine surgery can give equally good result as open spine surgeries.

The goal of the endoscopic surgery is to get the same results obtained using standard surgeries, providing effective treatments and not only focused on temporary pain relief, such as in nerve root blocks, but also at the same time avoiding discomfort related with open techniques.

2. History of the spine endoscopy

Minimally invasive spine surgery treatment started with chemonucleolysis in 1963. Lymen Smith described this technique injecting chymopapain intradiscally [1]. After this first step, in 1973, Kambin described an endoscopic posterolateral approach to access the disc space. This was the primordium of the development of the spine endoscopy. In this technique, an inside-out decompression of the disc space was done but without the view of an endoscope. Fifteen years later, in 1988, the same author achieved the first endoscopic views of a herniated nucleus pulposus [2]. After that, the specific instruments have been developed with working-channel rigid endoscopes, high-definition cameras, drills, trephines, and articulated graspers. Kambin, in 1990, after extensive studies on a cadaver, described a triangular safe zone bordered by the exiting root anteriorly, the traversing root medially, and the superior end plate of the lower lumbar vertebra inferiorly [2]. The anatomical description of this safe zone allowed the field of endoscopic spine surgery to outgrow the technique of percutaneous nucleotomy, which was limited by the use of small needle-like instruments. Kambin's triangle was a working corridor that allowed larger instruments and working channels to be introduced in even closer proximity to foraminal pathology without injuring the exiting nerve. Along the years, multichannel endoscopes with larger working channels were introduced by Tsou et al. in 1997 and Ruetten et al. in 2007 [3, 4]. In 1997, Anthony Yeung had designed Yeung Endoscopic Spine System (YESS) endoscope with multichannel fluid integrated working channel rigid endoscope. After that, the modern era of endoscopic disc surgery began. Yeung's technique was based on principle of identification and treatment of pain generators into the foramen and the disc, by freeing exiting and traversing roots, by fragmentectomy, visualization, and clearance of annular tear by ablation and irrigation. This was the Inside-out technique [5, 6]. Choi et al. contributed to the modification of endoscopic technique by access to the far lateral disc herniation, transiliac and interlaminar approach for difficult L5-S1 level disc herniations, approach for up-migrated and down-migrated disc herniations, transpedicular approach for high-grade down-migrated disc herniation, and endoscopic treatment for lumbar spinal canal stenosis [7].

3. Why microendoscopic surgery?

The conventional spine open procedures have their own limitations. They can produce more complications and morbidity to the patients. This has, for many years, led to distrust of patients regarding the acceptance of performing a procedure in the spine.

The minimally invasive surgery, as well as the trend in medicine, has been developing a lot in recent years, whether in anatomical knowledge or in the development of techniques and materials, and this has led to the development of less aggressive surgeries.

Endoscopic spine surgery aims to reduce tissue trauma, prevent iatrogenic problems, and preserve spinal motion and stability. The main benefits are [8–10]:

- smaller incisions and less tissue trauma
- avoid detachment of tendons to the posterior bony elements, especially the multifidus attachments to the spinous process and superior articular processes
- maintain the integrity of the dorsolumbar fascia
- causing lesser soft tissue injury, is less likely to progress to failed back surgery syndrome
- minimal blood loss
- improved illumination and visibility
- earlier return to activities and work
- easier operative approach in obese patients
- easier revision surgery because of less scar tissue in the access portal
- lower complication rates
- lower morbidity in elderly, obese, diabetic, cardiac patients, and smokers
- local or regional anesthesia combined with conscious sedation can be used
- in most cases, less postoperative pain medication is required
- ss a consequence, outpatient procedures are possible
- lower costs due to shorter operating times and shorter inpatient stay

4. Indications of the spine endoscopy

Initially, endoscopic technique was restricted to the lumbar spine. With the popularization of the lumbar surgery, gradually, surgeons started to perform cervical and thoracic disc herniation procedures. Today, expert surgeons can also use the endoscopy for spinal canal stenosis and endoscopic assisted fusion surgeries.

The main indications for spine endoscopy are as follows [11]:

- Endoscopic spine surgery can play an important role in the treatment of adolescent disc herniations, especially for the persons who engage in competitive sports and the athletes where less tissue trauma, cosmesis, and early functional recovery is desirable
- Lumbar, thoracic, and cervical disc herniations with radicular symptoms

- Lateral spinal canal (recess) and foraminal stenosis with radicular symptoms
- Degenerative facet joint cysts with radicular symptoms
- In experienced hands also central spinal canal stenosis with claudication or radicular symptoms
- Some cases of spondylodiscitis (biportal access)

5. Contraindications for spine endoscopy

Although the endoscopic surgical technique is a growing field of study and is valid for many cases, care must be taken not to indicate it indiscriminately. We must follow rigorous criteria of selection of pathologies, as well as patients, in order to be successful with the results. In this way, the future of this access route will be promising. With this in mind, we must always respect the following contraindications of the technique, which are [11]:

- Cauda equina syndrome
- Clinically relevant instabilities, deformities, or back pain that is not due to neural compression are contraindications for endoscopic spine surgery (e.g., spondylolisthesis).
- Very large disc herniations (occupying greater than 50% of the spinal canal) with or without a fresh motor deficit may be contraindications for less experienced endoscopic surgeons
- Calcified herniations
- Nerve root anomalies such as conjugate root

6. Surgical planning

In order to perform the endoscopic surgery in the spine, we must perform, as in any other surgical procedure, rigorous planning. Most cases treated by endoscopic surgery are for the treatment of lumbar disc herniations. In these cases, several parameters such as the height of the patient's iliac crest, the size of the interlaminar window, the location of the herniated disc at the column level, or its positioning—as foraminal or extraforaminal, central or centrolateral—must be evaluated.

In general, foraminal and extraforaminal herniations tend to be treated by the transforaminal or extreme lateral pathway. The central or centrolateral hernias are preferably treated by the interlaminar technique.

At the L5-S1 level, there is a tendency to perform the procedure via the interlaminar pathway, considering that the iliac crest acts as a mechanical barrier for access by the transforaminal pathway. The size of the interlaminar window, which is generally larger at the L5-S1 level, should always be evaluated by radiographs to evaluate the possibility of the interlaminar pathway.

For higher lumbar levels, mainly from L4 to cranial, a coronal evaluation, preferably with magnetic resonance, is mandatory to visualize the positioning of organs in the retroperitoneal space, such as the kidneys, and thus verify if the transforaminal technique is plausible from the point of anatomical view, without causing damages to the organs in the way of access [4, 7, 9].

7. Imaging exams

7.1. Radiography

The radiography of the spine, be it lumbar, thoracic, or cervical, is mandatory for performing the planning of the endoscopic procedure. It must be requested in the incidence front, profile, and dynamic incidence in maximum flexion and extension. Thus, important parameters for surgical planning can be evaluated as: presence of instabilities (which would contraindicate the endoscopic procedure), height of the disc space, and intervertebral foramen (The diameter of the intervertebral foramen decreases in a cranial to caudal direction and additional narrowing may result from degenerative changes), size of the interlaminar window, and deviations of the spine axis (kyphosis, scoliosis, loss of the sagittal balance).

7.2. Computed tomography

Computed tomography of the spine is not the exam of choice for the diagnosis of neural compressions; however, it becomes useful for the diagnosis of calcified disc hernias, which are also contraindication to the endoscopic procedure. This exam helps for planning surgeries in the thoracic spine and in the highest lumbar levels, in in which the study of the thoracoabdominal organs is required.

7.3. Magnetic resonance

Magnetic resonance of the spine is the gold standard examination for the spine. It identifies specifically where and which is the neural compression. This is the best exam for the diagnosis and the best exam for planning the access route for the procedure [11].

8. Anesthesia

8.1. Transforaminal and extreme lateral

For the transforaminal and extreme lateral pathways, a mild sedation and local anesthesia are recommended so that the patient is awake and responsive throughout the procedure. The patient can then provide real-time feedback in case of nerve irritation from instrument pressure or retraction, adding a layer of safety and allowing the surgeon to adjust the instruments accordingly. We use midazolam, fentanyl, and dexmedetomidina for sedation and recommend against using general anesthetics like propofol, which can produce temporary total analgesia,

eliminating the patient's responsiveness to any nerve stimuli. The skin, needle tract, and annulus are anesthetized with lidocaine. This allows anesthesia without motor block of the nerve roots.

8.2. Interlaminar

For the interlaminar procedure, general anesthesia is used. As the surgeon needs to manipulate the neural tissues, the patient would feel pain, and it would be difficult to perform the procedure with safety.

General anesthesia is used for other endoscopic procedures such as spinal stenosis, cervical, and thoracic spine [11].

9. Techniques

The most common techniques for performing the lumbar microendoscopic discectomy are the transforaminal, the extreme lateral technique, and the interlaminar approaches.

There are others less common techniques, which are the thoracic transforaminal and the cervical decompression [12].

9.1. Transforaminal

In the transforaminal technique, the patient is positioned in the ventral decubitus position, prone on a radiolucent table with a pelvic and a thoracic roll. Use of a C-arm is required during the operation. The midline, the inferior, and superior vertebral plates of the desired level are marked, under visualization of the image intensifier, and lateral markings to the midline of 8, 10, and 12 cm which will be the possible entry points. The patient is submitted to a light sedation, and at the point of entry an infiltration with local anesthetic without vasoconstrictor is performed. The sedation should be light, since the patient must be aware so that he can be alert if some nerve root is stimulated during the procedure. After this step, the intervertebral disc is punctured and a discography with methylene blue or indigo carmine, associated with non-ionic contrast, is done. Through the guides, the endoscope is inserted into the intervertebral disc and an indirect decompression of the intervertebral disc is performed (inside-out technique), followed by a thermal nucleoplasty. Reduction of intradiscal volume and pressure can reduce disc-related compression. The entire procedure is performed through the intervertebral foramen between the exiting and traversing nerve roots (Kambin's safety triangle) without need for resection of bony or ligamentous structures [6, 12–15] (**Figure 1**).

In some cases of spondylodiscitis, the possibility of the treatment with a biportal transforaminal technique can be considered. With a biportal, it is possible to achieve decompression, debridement, and biopsy samples for the microbiological diagnosis.

9.2. Extreme lateral

The extreme lateral technique was a modification of the transforaminal technique. It was developed by the German Sebastian Ruetten. First, the location of the incision on the skin is marked.

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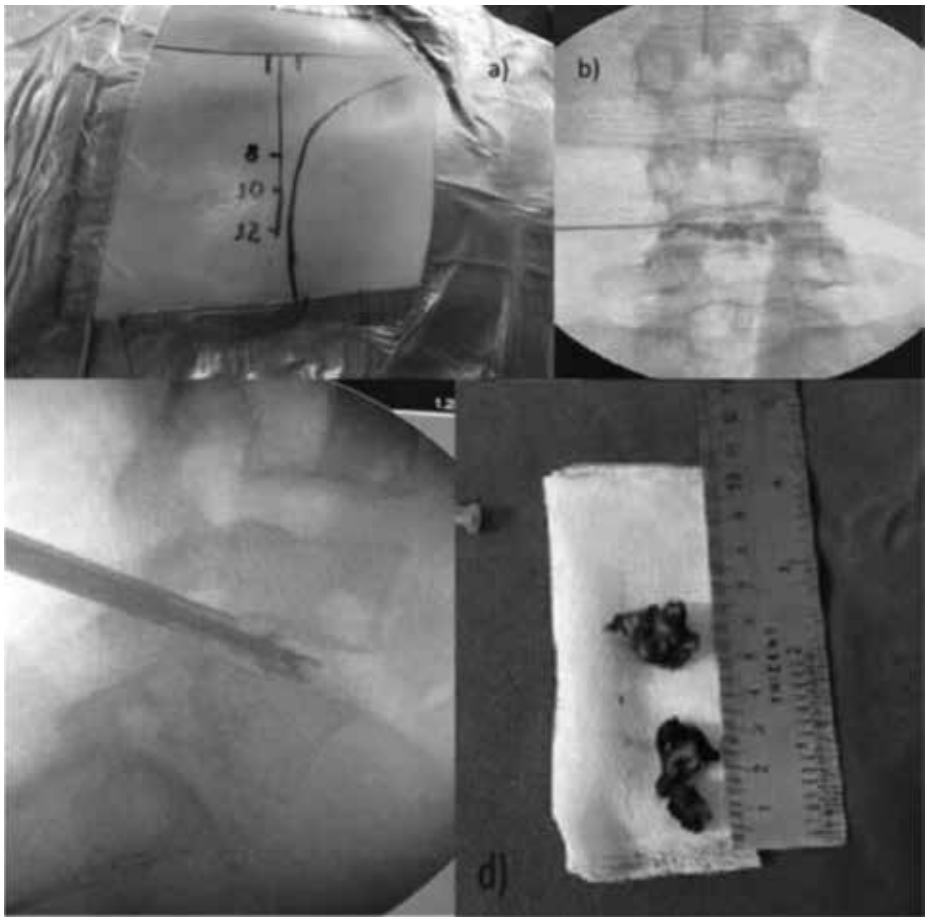

Figure 1. Transforaminal percutaneous endoscopic discectomy. (a) Markings on the skin. (b) Discography in the anterior–posterior view of radioscopy. (c) Imaging in a radioscopy profile with demonstration of the "inside-out" technique of discectomy. (d) Disc material removed.

This depends on the patient's anatomy and the location of the hernia. The smaller the foramen, the more lateral the entrance. The goal is to make the tangential reach to the spinal canal possible. For L3-L4 and L4-L5 levels, the dorsal border of the lower articular process seen in radioscopy is the ventral border of the entry point. At higher levels, such as L1-L2 and L2-L3, due to increased intervertebral foramen, the entry may be less lateral. At these high lumbar and thoracic levels, an axial tomography scan should be performed to evaluate the position of the abdominal and thoracic organs. An initial needle is introduced with an acute angle with the spine, practically parallel to the skin. In profile radioscopy, the needle should remain in the posterior region of the fibrous annulus and in the anteroposterior image remain in the medial pedicular line. Thereafter, a guidewire and, subsequently, a dilator are inserted. Afterwards, the cannula is inserted over the dilator, with the ventral opening, the bevel is rotated 90 degrees, and it remains with the bevel open to the region of the vertebral canal, protecting the emerging root. From this moment, surgical decompression is performed. This is an outside-inside procedure. As in the transforaminal technique, in the extreme lateral, it is not necessary to perform a flavectomy [16].

9.3. Interlaminar

Another technique is the interlaminar endoscopic discectomy. It is preferably used for the lower lumbar levels (L4-L5 and L5-S1) because of the size of the interlaminar window. The patient is positioned in the ventral decubitus position, on a radiolucent table, under general anesthesia. In this technique, general anesthesia is necessary because it is vital to move away from the neural root, which causes discomfort to the patient. The interlaminar window at the desired level is marked on the skin under the aid of the image intensifier and a 1-cm longitudinal access is made near the midline. An initial dilator is positioned in the interlaminar space and the endoscope is inserted. First, the multifidus musculature is dissected to the yellow ligament, which is opened for exposure of the descending root and the perineural fat. The opening of the yellow ligament is a fundamental step during endoscopic surgery by the interlaminar approach, in order to access the nerve structures and the intervertebral disc. This yellowish-colored structure measures 2–6 mm thick and is a protective barrier for the teal sac and nerve structures. The nerve root is removed and protected with a beveled cannula. The intervertebral disc is perforated and decompressed. At the end of the procedure, a thermal nucleoplasty is performed (**Figure 2**). The surgeon needs full anatomical knowledge of structures that are not directly visualized, such as laminae, ligaments, and nerve structures. A complete notion of three dimensionality is required in this type of surgical approach [17–19].

9.4. Lumbar stenosis

Patients with lateral recess stenosis may benefit from the endoscopic procedure. In these cases, through interlaminar access, with burrs and rougeurs, decompression of the lateral recess can be performed.

After the access has been obtained, the bony structures are dissected. It may be useful to start decompression at the caudal end of the descending facet. The medial parts of the descending or ascending facet or of the caudal and cranial lamina can also be resected if needed [20].

9.5. Cervical

The main indications for cervical spine endoscopy are the presence of lateral disc herniations and stenosis with exclusively lateral localization. These are the same indications for posterior foraminotomy.

The operation is performed with the patient lying prone. The cervical spine is delordosated and the head fixed in place with tape. The arms are positioned toward caudal on the body with gentle tension. The line of spinal joints is marked under posterior–anterior X-ray control (about 2-cm lateral from the midline). From this point on, the operation is performed under lateral X-ray control. The procedure comprises determination of the segment, performance of skin incision, and blunt insertion of a dilator onto the facet joint. Insertion of the operation sheath via the dilator beveled opening is made. The dilator is removed. After insertion of the optic, further operation is performed under visual control and continuous irrigation with 0.9% saline solution. The facet joint and the flavum ligament are prepared: start of the

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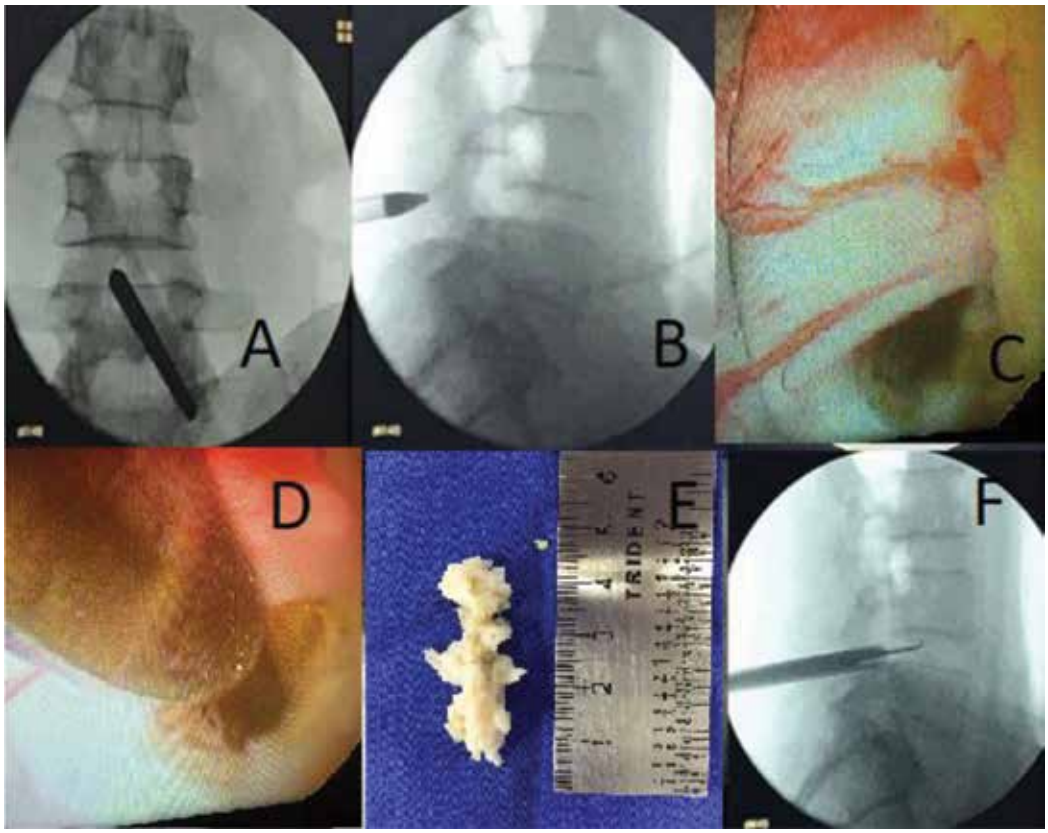

Figure 2. Interlaminar percutaneous endoscopic discectomy. (a) Point of entry into the anteroposterior view of the radioscopy. (b) Multifidus muscle limits in radioscopy profile. (c) Neural root visualized. (d) Probe removing the root after performing the discectomy. (e) Disc material. (f) Probe inside the disc space.

foraminotomy by bone resection at the medial joint segments, resection of the lateral flavum ligament, and identification of the lateral edge of the spinal cord and branching of the spinal nerves. Bipolar radiofrequency coagulation of the venous plexus and dissection spinal nerves. If there is a disc herniation, the nerves should be immobilized and the herniated disc material should be resected. Depending on the pathology in each case, the foraminotomy can be extended toward lateral or craniocaudal. After all instruments are removed, direct closure of the skin is performed [12].

10. Selection of the technique

In general, patients with central and centrolateral disc herniations should be submitted to the interlaminar technique. On the other hand, those who have foraminal and extraforaminal herniation should be submitted to the transforaminal technique. This technique is preferable in the lumbar spine in the levels of L3-L4 and L4-L5. The transforaminal approach is

possible in higher levels, but it is mandatory in the study of the position of the thoracoabdominal organs. Depending on anatomical landmarks, for example, the height of the iliac crest makes the transforaminal technique in the L5-S1 level not possible. In this case, you should consider using the interlaminar technique or the traditional open discectomy. For sequestered and/or migrated disc herniations, it is possible to use the extreme lateral technique in which you have an increased mobility of the endoscope in searching the herniation [17, 19, 21].

11. Surgical equipment for spine endoscopy

The material used for the endoscopic procedures of the spine is highly technological and specialized equipment. (**Figures 3–5**). In general, the equipment consists of an endoscopy tower that is composed of a high-resolution monitor, irrigation pump system, shaver system, radiofrequency system, and lighting system connected to fiber optic cables.

Figure 3. Endoscopy tower.

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Figure 4. Spine endoscopy equipment.

The materials used in the procedure are varied and have particularities specific to each technique but, in general, are the following [4]:

- Working sleeve with bevel
- Dilators
- Probes
- Endoscopes with different working channels

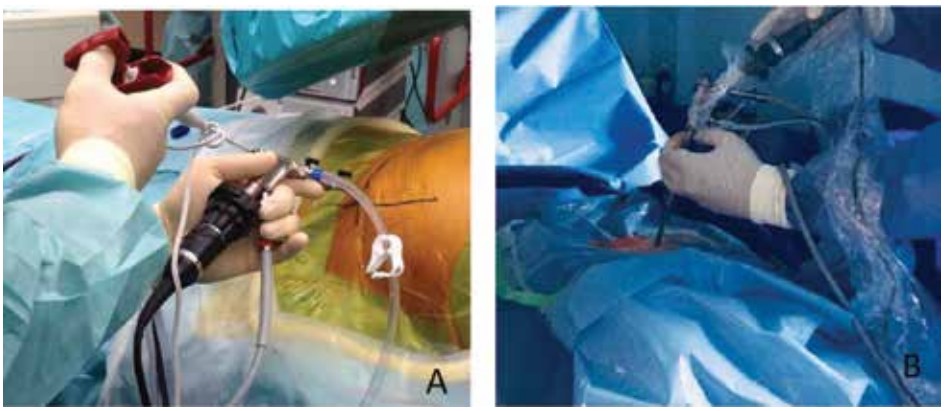

Figure 5. A-extreme lateral endoscopic procedure B-spinal endoscopic procedure- interlaminar approach.

- Optical cannula
- Dissector
- Trigger flex radiofrequency
- Burrs
- Rongeurs
- Mallet
- Guide wires
- Trephines
- Forceps
- Scissors
- Fluid adapters
- Various accessories (hooks, elevators, etc.)

12. Learning curve

It should be taken into account that the endoscopic surgical techniques present greater technical difficulties and challenges than the traditional ones and, consequently, a greater learning curve.

The transforaminal procedure requires less operative learning time than the interlaminar procedure. This approach is recommended for beginning full-endoscopic lumbar discectomy.

Hsu et al. showed that the stabilization of the learning curve for the transforaminal approach occurred around the 10th case based on the operative time, resulting in a steep learning curve, which represents the rapid acquisition of skills and a good thing for a beginner [22, 23].

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Lee et al. observed a significant reduction in the operative time after the 17th patient was treated by percutaneous endoscopic lumbar discectomy [24].

Choi et al. recommended supervision by an experienced surgeon in the initial 10 cases to overcome the learning curve for the interlaminar procedure at L5-S1. Surgeons should gain adequate experience by starting with simple cases first, with small herniations and larger interlaminar windows, in which no serious problems are anticipated from the anatomic conditions [17].

13. Results

The majority of endoscopic spinal procedures are concerned with the surgical treatment of lumbar disc herniations, for which microsurgical intervention using an operating microscope currently is the gold standard when conservative treatment fails or when it is not indicated.

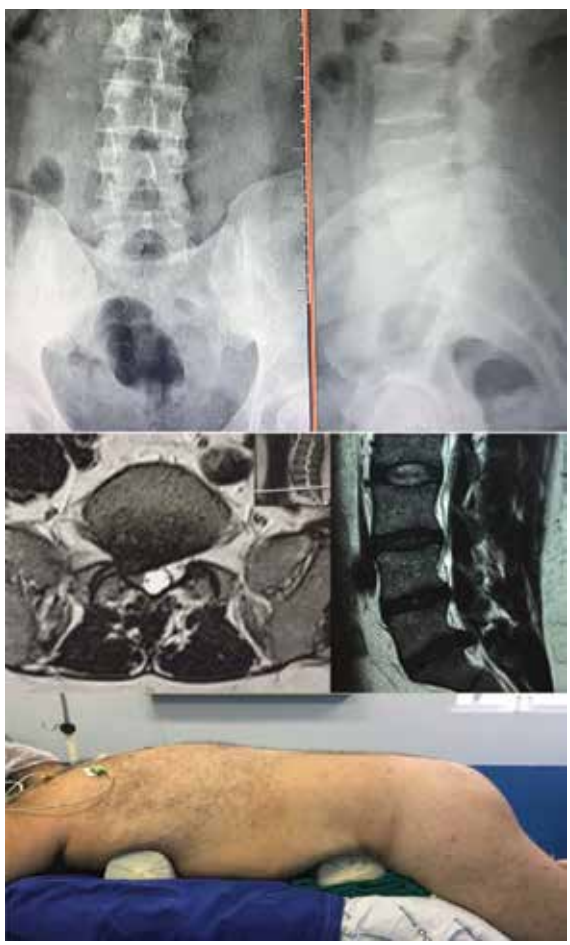

Figure 6. Obese patient positioned for interlaminar spine endoscopy and the MRI images of L5S1 lumbar disc herniation. Note on MRI the extensive subcutaneous tissue.

Microsurgical microscopic disc surgery, also termed "microdiscectomy," therefore has to be the reference to which endoscopic disc surgery is compared [25].

The literature data show that the spine endoscopy yields as good a result as the gold standard.

In a meta-analysis of He et al., that compared the results of microendoscopic discectomy versus open discectomy for lumbar disc herniation, they concluded that the microendoscopic discectomy was associated with similar improvement of symptoms and smaller surgical trauma, but it requires a demanding learning curve [26].

In a prospective study comparing the clinical outcomes of 55 patients with lumbar disc herniation treated with lumbar endoscopic percutaneous discectomy, Sebben el al., showed good results in more than 90% of the patients [27].

The literature evidences that the spinal endoscopy has a special advantage for treating lumbar disc herniation in patients with high body mass index. The endoscopic approach in obese individuals allows a lower surgical risk when compared to conventional open surgery, showing a safe technique with promising results (**Figure 6**) [28].

The results of the spine surgeries, in general, should always be evaluated with scores. Some of the main scores used are: Oswestry 2.0, Visual analogue scale (VAS), SF-36, Roland-Morris Disability Questionnaire, Quebec Back Pain Disability Questionnaire (Neck Disability Index, World Health Organization Quality of Life Assessment, Fear Avoidance The use of questionnaires for evaluation of spine surgery helps to identify factors that may influence surgical results [29].

14. Complications

As any spine surgery, the endoscopic procedures also have its complications. As in open surgery, many complications can occur such as incomplete removal of herniated discs, recurrence of herniations, nerve root injury, dural tear, and nerve root-induced hyperalgesia or burning-like nerve root pain, epidural hematoma, posterior neck pain, or surgical site infection. Unique complications in the endoscopic procedures are passage of the working channel through the spinal canal into the disc space, super-elastic nerve hook caught by exiting nerve root and intraoperative seizure due to high depression of the saline fluid into the spine canal. Most of the dural tears do not need to be repaired because of the small damage of the surrounding tissues [30].

The literature shows that the occurrence of major complications as cardiac events, respiratory complications, pulmonary embolism, stroke and acute renal failure, and in-hospital death are significantly less likely in patients treated with microendoscopic spine surgeries [31].

15. Limitations

Most of the spine surgeons did not have training for the development and application of the minimally invasive technique during their formation, having to learn on their own the technique of endoscopic surgery. There are many steps to this learning, and with proper training and selection of patients, the initial difficulties can be overcome.

The surgeon needs clinical experience and repetitive training to overcome the high technical demand that the approach requires, such as limitation of the surgical field, absence of area and surrounding structures visible and that act as anatomical reference, difficulty in the perception of three dimensionality in a field two-dimensional visual.

In many countries, especially the underdeveloped countries, this technique is not yet part of the routine of spinal surgery, either because of lack of training of the medical team or because of the lack of access to material that is expensive. The high cost becomes a limiting factor to the dissemination of the endoscopic technique, and the procedure is often not covered by the health insurance plans [32, 33].

16. Take-away message

- Spinal endoscopy will probably become the gold standard in the surgical treatment of lumbar disc herniations.
- Less postoperative complications
- Faster return to work
- Still higher costs
- Steep learning curve
- Promising future for this technique

17. Conclusion

The development of new techniques and technologies in medicine has become a constant. However, its transformation into a gold standard is a long and arduous step. In many medical areas, endoscopic treatments are the reference technique. Further dissemination of endoscopic spinal techniques is required with more frequent and easily accessible courses for all spine surgeons. This makes medicine evolve, and professionals become more and more empowered. Thus, it is expected that in the near future, these techniques will become the standard of comparison to others that will emerge.

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We appreciate the opportunity to participate by writing a chapter to such a select and remarkable book. We are also grateful to the Universidade Federal do Paraná and the Hospital do Trabalhador that provided a sophisticated environment with all the necessary technologies and inputs to implant the endoscopic spinal surgery. This equipment is costly and is not accessible to most hospitals in Brazil.

Conflict of interest

The authors have no conflict of interest to declare.

Notes/Thanks/Other declarations

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Chapter 7

Endoscopic Dacryocystorhinostomy

Balwant Singh Gendeh

Additional information is available at the end of the chapter

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Abstract

Epiphora, or abnormal tearing, occurs because of the blockage in the lacrimal drainage system, which impairs normal tearing channeling into the nose. It is essential that with proper history and examination including syringing and probing, a correct diagnosis is made. Syringing and probing are performed only in congenital and acquired nasolacrimal duct obstruction (NLDO). Dacryocystorhinostomy (DCR) is a procedure performed for the treatment of tearing (epiphora) due to blockage of the nasolacrimal drainage system. Endoscopic dacryocystorhinostomy (E-DCR) using telescopes has gained a lot of momentum among otolaryngologists, since the outcomes are comparable to the external approach. Advances in surgical technique and a better understanding of the anatomy have resulted in improvements in outcomes. The anatomy of the lacrimal system will be discussed in detail including the surgical indications and techniques of DCR. The advantages, results, and complications of surgery will be highlighted.

Keywords: epiphora, E-DCR, surgery

1. Introduction

Epiphora or abnormal tearing occurs because of blockage in the lacrimal drainage system. Recurrent infection may also occur as a result of the stagnation. Tears drain into the lacrimal sac located at the upper outer margin of the eye. Between the eye and nose lies the lacrimal sac which funnels tears into the nasal cavity through the nasolacrimal duct (**Figure 1**). Blockage of the nasolacrimal duct is the commonest cause of excessive tearing and be treated by creating a direct opening from the sac into the nasal cavity in a procedure known as endoscopic dacryocystorhinostomy (EDCR). The operative approach to the sac may be external or endoscopic. Toti first described the external approach and West subsequently described the endonasal approach in 1911. The latter approach became unpopular because of difficult visualization

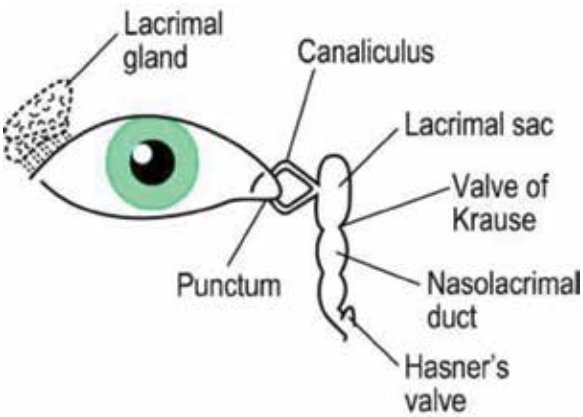

Figure 1. Diagrammatic anatomical picture of the lacrimal gland and nasolacrimal drainage passage way.

Endoscopic DCR	External DCR
No external scar	Cutaneous scar
Less bleeding	More bleeding
Less chances of injury to adjacent structures	More chances of injury to adjacent structures
Less operating time	More operating time
No postoperative morbidity	Significant postoperative morbidity
Better visualization of nose	No visualization of nose
Requires skilled ophthalmologist	Easily performed
Expensive	Less expensive equipment

Table 1. Advantages and disadvantages of endoscopic versus external DCR.

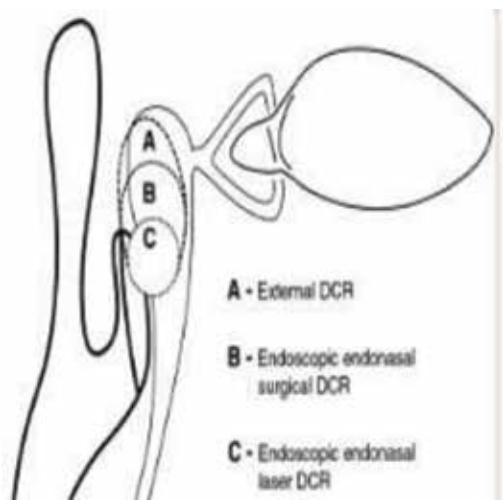

Figure 2. Sites of location of surgical landmarks of external DCR, EDCR, and laser DCR.

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and access to lacrimal sac. However, recently with the advent of newer rigid scopes, these difficulties have been overcome, resulting in the resurgence of the endoscopic approach. The advantages and disadvantages of endonasal versus external DCR are listed in **Table 1**. **Figure 2** highlights the sites of location of surgical landmarks of external DCR, EDCR, and Laser DCR, respectively (**Figure 2**). The evaluation and management of excessive tearing may involve both an ophthalmologist and an otolaryngologist. In this text, the endonasal approach will be discussed using the rigid scopes.

2. Anatomy of lacrimal drainage system

The main lacrimal gland is located in a shallow depression along the superior lateral orbit. The lacrimal glands are exocrine glands, and they produce a serous secretion. The lacrimal system constitutes of the upper and lower puncta, lacrimal canaliculi, lacrimal sac, and nasolacrimal duct [9]. The first 2 mm of canaliculi is perpendicular to the lid margin but the distal 8 mm is parallel to the lid (**Figure 3**). The two canaliculi join to constitute a common canaliculus before entering the lacrimal sac, which is engulfed in an oval-shaped fossa measuring 15 mm in height and 10 mm in width. The fossa is bounded by anterior and posterior lacrimal crests (**Figure 4**). The lacrimal sac opens into the nasolacrimal canal, which is formed by the maxillary, lacrimal, and inferior turbinate bones. The nasolacrimal duct traverses through this osseous canal for approximately 12 mm and turns into a membranous duct for 5 mm before entering the inferior meatus (**Figure 3**) [7]. Hasner's valve at the inferior meatus opening covers the duct orifice to prevent reflux of secretions (**Figure 5**). In some neonates, the nasolacrimal duct outlet is obliterated for about 6 months, and occasional probing may be helpful.

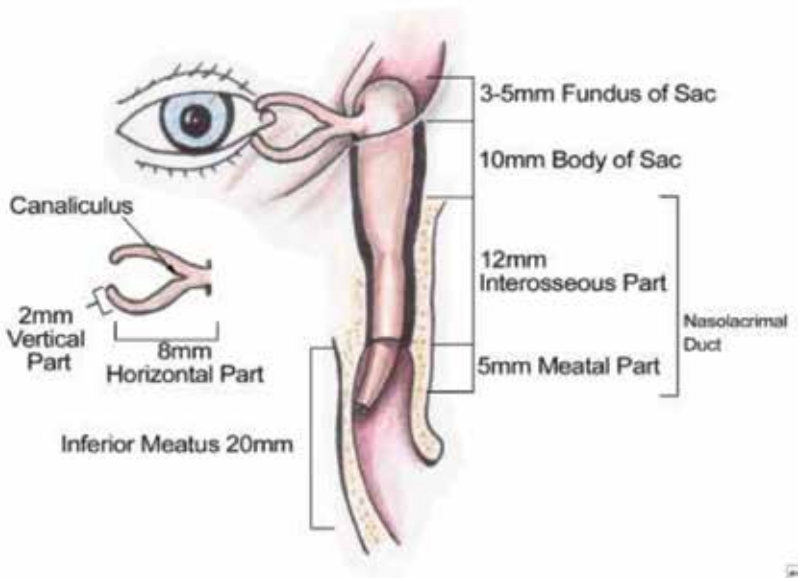

Figure 3. Diagram illustrating the anatomical measurement details of the nasolacrimal drainage pathway.

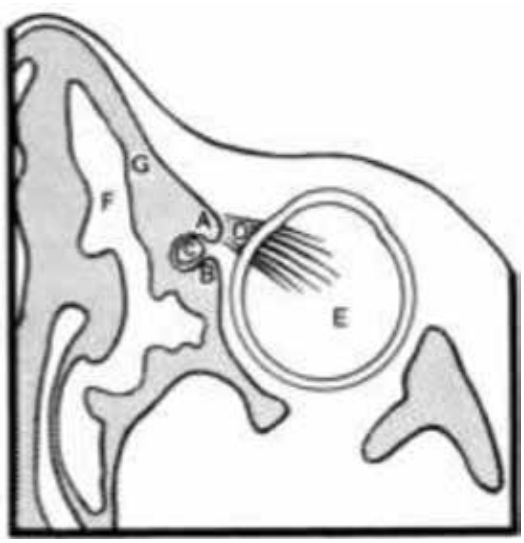

Figure 4. Diagrammatic axial view of lacrimal fossa in relation to anterior and posterior lacrimal crest. (A) Anterior lacrimal crest, (B) Posterior lacrimal crest, (C) Lacrimal sac, (D) Inferior oblique muscle, (E) Orbit, (F) Nasal cavity, (G) Frontal process of maxilla.

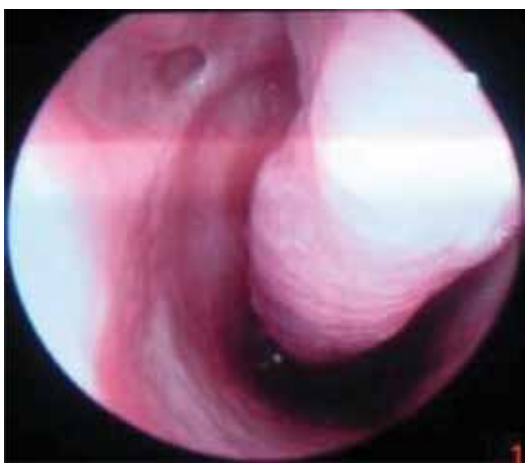

Figure 5. Endoscopic view of the right nasolacrimal duct opening into inferior meatus.

3. Etiology and pathophysiology

The occurrence of symptoms may be related to congenital or acquired causes. Acquired causes include recurrent dacryocystitis, canaliculitis, dacryolithiasis, lacrimal system tumors, nasal pathology obstructing drainage, and iatrogenic trauma. As a result of the obstruction of the nasolacrimal duct, accumulation of tears in the lacrimal sac promotes infection and its accompanying sequelae.

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4. Presentation

Excessive unilateral or bilateral tearing interfering with vision and persistent neglect of the symptom may induce chronic dacryocystitis, resulting in purulent discharge. In acute exacerbation, inflammation of the skin in the region of the medial canthus may occur.

5. Assessment of the patient

5.1. Physical examination

An eye examination is essential in the evaluation of every patient with epiphora. A slit lamp examination can reveal the normal or abnormal tear film over the conjunctiva, and if the film thickness is more than usual, it is a sign of lacrimal system obstruction.

Gentle pressure over the sac produces reflux of mucopurulent material suggestive of lower sac obstruction.

An appropriate lacrimal syringe is gently guided through the inferior lacrimal punctum and 2–5 ml distilled water is injected and if it passes easily into the nose, the drainage system is patent. In complete canalicular obstruction, the irrigation fluid refluxes from the same canaliculus (**Figure 6**).

Nasal endoscopy should be obligatory for every lacrimal obstruction patient. Endoscopy provides a clear diagnostic look for nasal polyps, anatomic variations, tumors, and other pathological conditions such as septal deviation.

5.2. Radiologic evaluation

Radiological tests are performed before EDCR, which include dacryocystography (DCG), nuclear lacrimal scintigraphy (dacryoscintillography), computed tomography (CT), and magnetic resonance imaging (MRI) [6].

An anatomical investigation like dacryocystography is indicated if there is a block on syringing in the lacrimal system.

A functional test like scintigraphy is useful in assessing the site of a delayed tear transit and indicated if the lacrimal system is patent on syringing [8].

For patients with preceded trauma, facial surgery, and tumor or in whom sinus diseases are suspected, both CT and/or MRI is indicated.

5.3. Dacryocystography (DCG)

An injection of the radio-opaque water soluble fluid is instilled into either lower or upper canaliculus, taking magnified images utilizing digital subtraction technique. A DCG better evaluates the lacrimal sac and duct anatomy. It shows intrasac pathology namely dacryoliths

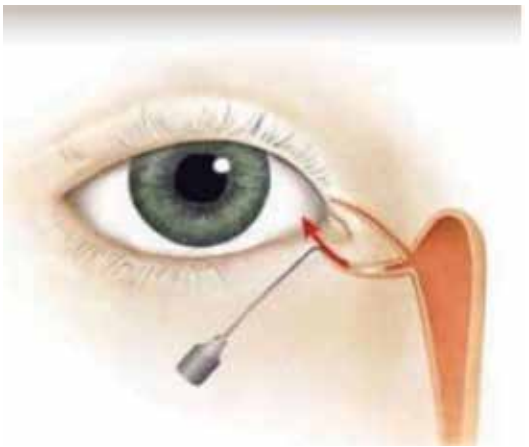

Figure 6. In complete canalicular obstruction, the cannula is advanced with difficulty and irrigation fluid refluxes from the same canaliculus.

or tumor and the sac size (**Figure 7**). It is useful to determine the size of the sac in patients with previous trauma to localize the position of the bone fragments or after previously unsuccessful lacrimal surgery. It helps to determine whether the stenosis is in the common canaliculus or sac and rules out the presence of a lacrimal sac diverticulum. A DCG can often find drainage abnormalities present in patients with "functional obstruction."

5.4. Nuclear lacrimal scintigraphy

It is a simple, noninvasive physiological test that evaluates patency of the lacrimal system using a radiotracer (technetium-99 m pertechnetate). DCG is indicated in complete obstruction,

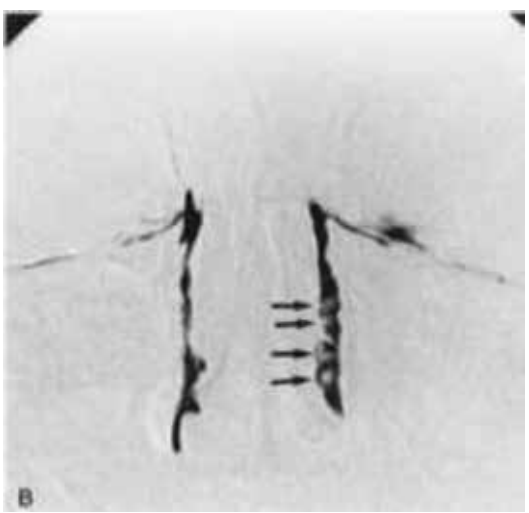

Figure 7. A DCG showing evidence of dacryoliths in the left lacrimal drainage pathway.

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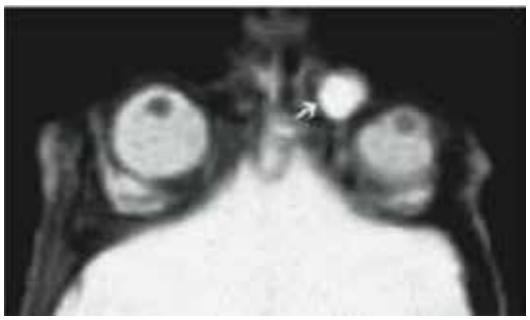

Figure 8. An axial MRI showing a left dacryocystocele.

while scintigraphy for those patients whose lacrimal system is patent to syringing in the presence of constant epiphora. Correlation of anatomical study (DCG) and functional study (scintigraphy) may be necessary in planning surgery. Normal results are considered to be a contraindication to any surgical intervention.

5.5. Computer tomography and MRI

Computed tomography (CT) can be helpful in assessing the structures intimately associated with the nasolacrimal drainage system. The CT scanning is used mainly when an extrinsic disease is suspected and is useful when the lacrimal system is associated with paranasal sinus tumor surgery or facial pathology [2, 9].

MRI is reserved only for cases where differentiation of masses of the lacrimal sac is required (**Figure 8**).

6. Endoscopic dacryocystorhinostomy (EDCR)

EDCR involves creating a bypass from the lacrimal sac to the nose. With a proper history and examination including syringing and probing, a correct diagnosis is achieved. Probing and syringing are indicated in congenital and acquired nasolacrimal duct obstruction (NLDO) and not in acute and chronic dacryocystitis [1].

6.1. Surgical indications

The procedure is performed for NLDO which can be demonstrated clearly on a dacrocystogram (**Figure 9**). EDCR is not indicated for obstruction of a punctum or canaliculus. Distal obstruction may be mixed with numerous degrees of proximal obstruction, and this needs to be explained to the patient. For defining the site of obstruction, syringing and probing are helpful (**Table 2**).

A dacrocystogram is performed if there is evidence of mass within the sac and scintigraphy to define a functional problem. Malignancy of the sac can present with symptoms of bloody discharge from the punctum which will need further investigations. A dacryocystocele can present with epiphora, swelling, or recurrent dacryocystitis (**Figure 10A** and **B**) [4]. Wegener

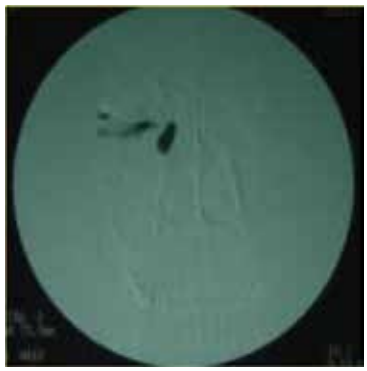

Figure 9. A dacrocystogram showing distal obstruction of right nasolacrimal pathway on failure of penetration of dye into the inferior meatus in a patient with unresolving tearing.

1. Primary acquired NLDO
2. Secondary acquired NLDO
a. Secondary acquired lacrimal duct obstruction due to infection
b. Secondary lacrimal obstruction due to inflammation
c. Lacrimal obstruction due to neoplastic causes
d. Lacrimal obstruction due to traumatic causes
e. Lacrimal obstruction due to mechanical causes

Table 2. Indications for EDCR.

Figure 10. A preoperative (A) and postoperative picture (B) of a patient with large left dacryocystocele presenting with recurrent dacryocystitis.

1. Known or suspected lacrimal system neoplasm
2. Large lateral lacrimal sac diverticulum
3. Common canalicular stenosis
4. Lacrimal system stones
5. Extensive midfacial trauma

Table 3. Contraindications for EDCR.

granulomatosis and sarcoidosis are rare causative factor. Middle-third facial fractures can present with NLDO. Usage of Stammberger Rhinoforce Antrum Punch (Storz, Germany) in endoscopic sinus surgery if placed too far forward to remove uncinate process can result in injury and ultimately NLDO.

6.2. Contraindications

The contraindications for EDCR are listed in the table above (**Table 3**).

7. Highlights of EDCR

- Provides a better esthetic result with no external scar.
- Allows one-stage procedure to also correct associated nasal pathology.
- Avoids injury to medial canthus.
- Preserves the pumping mechanism of orbicularis oculi muscle.
- Is superior to external approach in revision surgery.
- Can be performed during active infection of the lacrimal system.

8. Relevant anatomy

The lacrimal sac which lies in the lacrimal fossa is formed by the thick frontal process of the maxilla anteriorly and the thin uncinate bone posteriorly (**Figure 11**). Inferiorly, the sac forms the nasolacrimal duct, which drains into the inferior meatus about 1 cm posterior to the anterior end of the inferior turbinate (**Figure 4**). The inferior meatal opening is protected by several variable folds of mucous membrane that acts as valves preventing retrograde air aspiration. The anterior lacrimal crest, unlike its anterior margin, is made of very dense bone. In rare instances, an anterior ethmoidal air cell may lie medial to the lacrimal fossa in which instance it needs to be removed before a rhinostomy is created.

The reflex act of blinking is triggered by the contraction of the palpebral fibers of orbicularis oculi muscle. When the muscle relaxes, tears are sucked up through the canaliculi when the

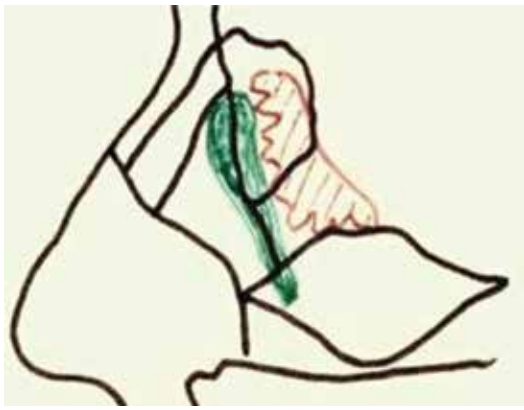

Figure 11. A diagrammatic sagittal section showing the anatomy of the lacrimal sac in relation the frontal process of the maxilla anteriorly and the uncinate process posteriorly.

sac is drawn open. The lacrimal sac then contracts to its original volume, and the tears are pushed down the nasolacrimal duct.

9. Preoperative assessment

Topical local anesthetic drops are placed in the eye followed by dilatation of the upper and lower puncta with punctum dilator followed by passage of Bowman probe through the dilated punctum and angled medially (**Figure 12**). A slight resistance may be felt as a "soft stop" when the probe enters the common canaliculus, and there is a "hard stop" when it touches the medial wall of the sac. Subsequently, the probe is angled vertically down to feel whether there is any sac pathology or distal obstruction. Fine obstructing membranes causing proximal obstruction can be found at the medial aspect of the upper and lower canaliculi when viewed with rigid

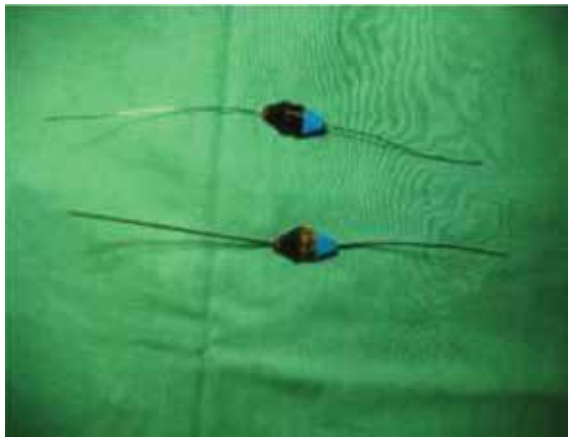

Figure 12. Picture of Bowman probes.

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Figure 13. Picture showing a fiber-optic endoilluminator being introduced via the left inferior canaliculus to illuminate the nasolacrimal sac (A) and a zero degree endoscopic view intranasal identifying the location of the illuminated lacrimal sac in the same patient (B).

0.7-mm dacryocystoscopes [15, 16]. EDCR is not indicated if this is the site of the obstruction. For surgeons becoming familiar with intranasal anatomy, it is helpful to introduce a 20-gauge fiber optic endoilluminator (Storz, Germany) through the superior or inferior canaliculus and advanced gently until a hard stop signifying the lacrimal bone is identified [14]. The location of the lacrimal sac may then be visualized endoscopically by transillumination (**Figure 13A** and **B**).

Distal obstruction is diagnosed by probing and then syringing, and if it refluxes through the other punctum, it indicates that there is distal obstruction. If there is reflux through the same punctum, then there is canalicular or common canalicular stenosis which can be confirmed by gentle probing. Where the sac becomes the duct, is the site most common for distal obstruction. EDCR may be offered to patients with a functional blockage where there is free flow on syringing but a nonfunctioning pump system on scintigraphy. Lester-Jones Pyrex tube is required only in extensive bi-canalicular obstruction on failure of forced probing and silicone intubation.

10. Surgical technique

Nasal decongestion is performed with neuropatties and infiltration with lidocaine and adrenaline, and then, a 15 scalpel blade is used for mucosal incisions horizontally 1 cm superior, commencing 3 mm posterior to axilla of the middle turbinate and moving forward 1 cm onto the frontal process of maxilla. The blade is then turned vertically and incision is made about two thirds of the vertical height of middle turbinate, stopping above the insertion of inferior turbinate into lateral nasal wall. The blade is then turned horizontally, and the inferior insertion commenced at the insertion of the uncinate process and brought anteriorly to meet the vertical incision (**Figure 14**).

The mucosal flap is elevated using a Freer's dissector suction (Storz, Germany) to expose and identify the junction hard frontal process of maxilla and the soft lacrimal bone. The thin

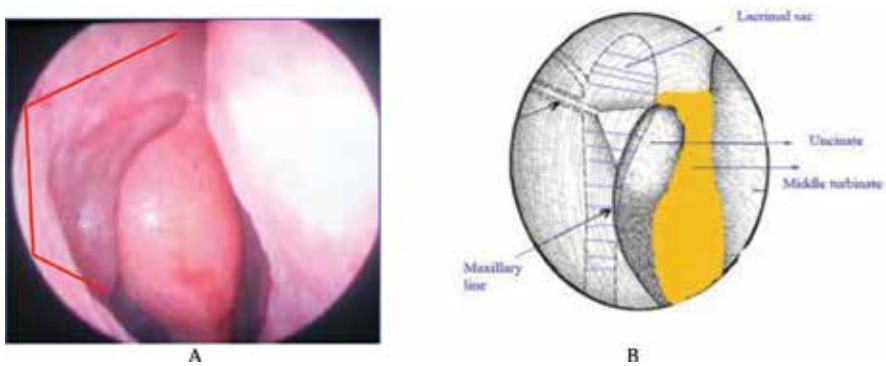

Figure 14. A zero degree endoscopic view of the left lateral nasal wall showing the maxillary line and uncinate process (A) and a diagrammatic illustration (B) showing the anatomical relationship of lacrimal sac to the maxillary line, uncinate process, and middle turbinate.

lacrimal bone is 2 to 5 mm wide anterior to the insertion of the uncinate process where the dissection ends. The soft lacrimal bone is elevated and removed away from the posteroinferior region of the sac using a round knife (Storz, Germany) [11].

The lower portion of the frontal process of the maxilla is removed using a forward-biting Hajek Kofler punch (Storz, Germany; **Figure 15**). During the removal of the hard lacrimal bone, the tip of the punch is used carefully to push the lacrimal sac away from it to expose the anteroinferior portion of the lacrimal sac. Bony removal is performed as far superiorly as possible until it becomes too thick for the punch to engage. The rest of the thick bone up to the superior mucosal incision is removed using a 15-degree curved 2.9 mm rough diamond burr (Medtronic Xomed, Jacksonville, Florida, USA) attached to the micro-debrider (Jones, 1998). Eventually as the sac is followed superiorly above the axilla of the middle turbinate, an agger nasi cell is approached and the frontal recess is exposed on removing it. Damage to the lacrimal sac wall is

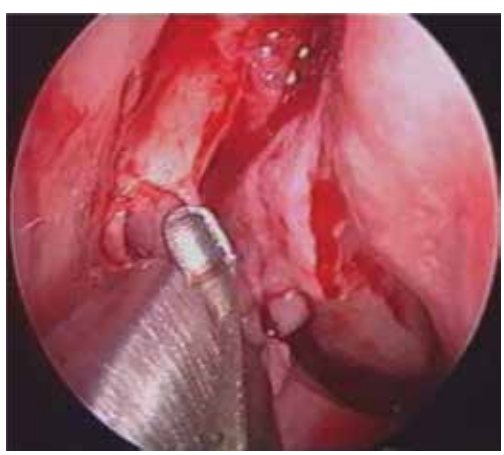

Figure 15. Intraoperative endoscopic view showing right DCR with initial removal of the thin frontal process of maxilla with Hajek Kofler sphenoid punch and subsequently the superior hard bone with a microdrill.

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avoided by using a diamond burr that may cause light contact with it as compared to a cutting burr that will remove the bone faster but with significant damage to the wall.

Next, the inferior punctum is dilated with a punctum dilator, and a Bowman's canalicular probe is passed into the sac (**Figure 16**). If the tip of the probe is not seen to move behind the thin sac wall, the probe is not in the lumen. For complete marsupialization of the sac, it is exposed and incised vertically with a DCR mini-sickle knife (Medtronic Xomed, USA) and eventually an upper and lower releasing incisions made with Bellucci scissor (Storz, Germany) on the posterior flap which is rolled out flat on the lateral nasal wall. To avoid secondary intention healing and reduce the formation of granulation tissue and scarring,

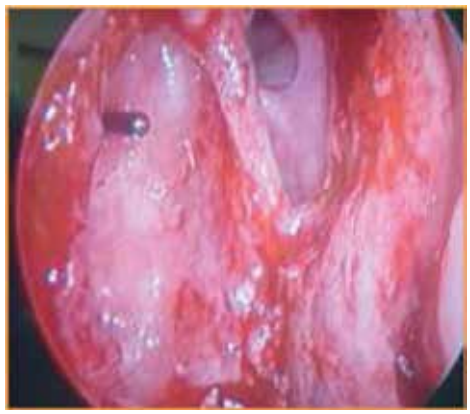

Figure 16. Intraoperative endoscopic view showing a right dacryocystorhinostomy and wide exposure of the nasolacrimal sac with visible end of Bowman's canalicular probe with removal of agger nasi cell exposing the frontal recess.

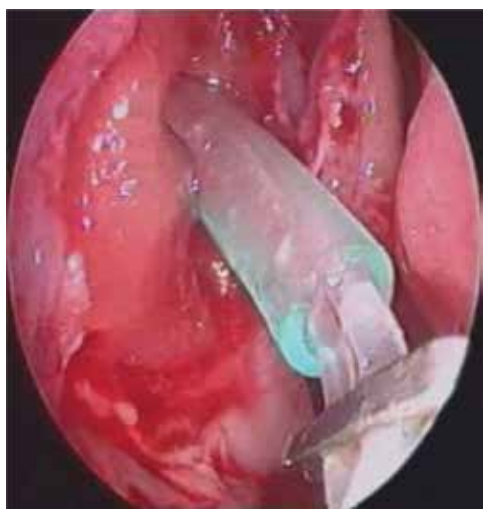

Figure 17. Intraoperative endoscopic view showing right dacryocystorhinostomy with stent and ligar clips in situ in an adult patient presenting with unresolving tearing.

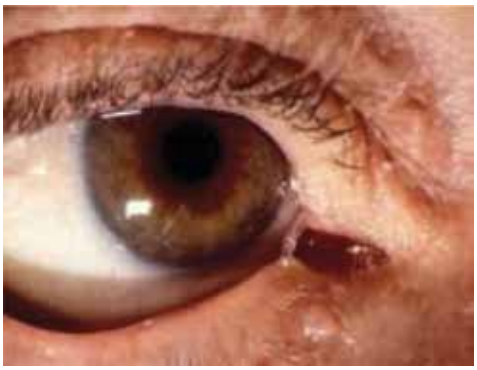

Figure 18. Picture showing looping of the O'Donoghue tubing placed through the upper and lower puncta and retrieved endonasally.

the lacrimal sac lining and nasal mucosa are approximated well. Silastic lacrimal intubation tubes (O'Donoghue tubes) are placed through the upper and lower puncta and retrieved endonasally and secured with ligar clips (**Figure 17**) [3]. A loop of tubing is pulled in the medial canthus of the eye to ensure that the tubes are not tight before placing the ligar clips (**Figure 18**). Tight tubing loops at the medial canthus can cheese-wire through the punctum [5]. To hold the flaps in position intranasally, a square of Gelfoam (Pharmacia NSW, Sydney, Australia) or Merogel (Medtronic Xomed) is slid up the tubing and placed over the flaps [12].

Saline irrigation is commenced within 3 to 4 hours postsurgery, and broad spectrum antibiotics started for 5 days and eye drops for 3 weeks. Removal of the O'Donoghue tubes is performed in clinic at about 4 weeks postsurgery. Stents can be used for small fibrotic lacrimal sacs to make sure that the neo-ostium remains patent. The patient is reviewed for a further 18 months before discharge.

11. Laser-assisted DCR

Laser was used exclusively in the early part of 1990s, and the site for osteotomy was the thinnest bone in the inferoposterior parts of the lacrimal fossa, corresponding to the brightest area in the nasal cavity by the transilluminator. Laser-assisted DCR success rate was around 78%, which was well lower than that of conventional technique. In late 1990s, osteotomy was performed with either a drill or a punch or both, and subsequently with time, the site moved to the level of medial canthus, which was anterior and superior to that of previous surgeries (**Figure 2**). When completed, the common internal punctum was visible on endoscopy, and the success rate improved to 92% [10].

In 65 patients with a mean follow-up of 74 months, it was reported that the success rate of endoscopic laser-assisted DCR has gradually declined over the years to 56%. Umapathy et al., in 2006, did not encourage the use of laser in endonasal DCR with epiphora [13].

12. Revision EDCR

Since the bone along the lateral nasal wall has already been removed in primary DCR, revision EDCR is therefore much easier procedure to perform. The size of the lacrimal duct is of importance in revision EDCR. For a normal sized sac, the success rate is high (89%) compared to low rates in scared condition where limited amount of lacrimal mucosa can be marsupialized. The agger nasi mucosa can be utilized as free graft functional mucosa to surround the common canaliculus-sac junction in severe lacrimal sac stenosis and scarring.

13. Postoperative care

The nasal spacer is removed the following morning. Patients must irrigate their nose with saline at least twice a day, and clinic visit was scheduled 1 week later and intranasal debris was removed then. The silastic tubing is removed in about 4 weeks postsurgery. Exposed tubing at the medial canthus is cut with scissors and the stent is withdrawn through the nose. In revision cases with scarring, the stent can be left in place even longer.

During surgery, sufficient opening from the lacrimal sac into the nose is made but the final size of the healed surgical ostium is 1 to 2 mm in diameter on average (**Figure 19**).

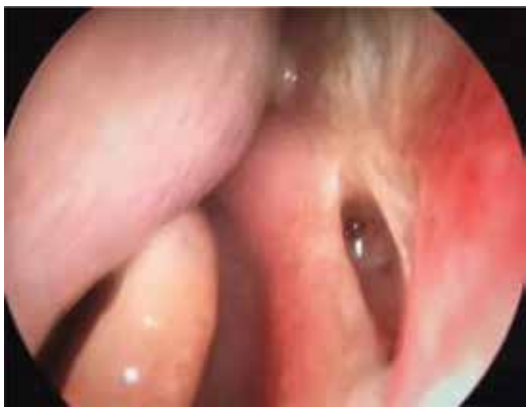

Figure 19. Endoscopic view of a patent left DCR at 6 months postsurgery.

14. Outcome of surgery

14.1. Complications

Complications of EDCR can be divided into intraoperative and early or late postoperative. Early postoperative (up to 1 month) complications include hemorrhage, crusting, perirhinostomy granuloma, transnasal synechia, and periorbital emphysema (**Figure 20**). Most of the

Figure 20. Left periorbital emphysema postpowered endoscopic sinus surgery which resolved spontaneously.

later complications occur between 1 and 3 months of surgery and include surgical failure from impacted tubes, rhinostomy scarring, granuloma, synechia, and cheese wiring.

In inexperienced hands, the rate of complications from EDCR is greater and similar to those of endoscopic sinus surgery (ESS). Poor visualization during surgery due to excessive bleeding can result in major intraoperative complications namely blindness and CSF leak. In such circumstances, it is better to convert to an open technique. A branch of the sphenopalatine artery supplying the remnant of a partially resected middle turbinate can cause bleeding within 1 week of surgery.

Sometimes during bone removal to expose the lacrimal sac, orbital fat may be exposed, and in such situations, the orbital fat should be left alone to avoid injury to orbital contents namely blood vessels, nerves, and medial rectus muscle. Nasal or orbital infection following DCR is rare, and perioperative antibiotics are administered to avoid this complication.

The most common causes of surgical failure for EDCR are postoperative adhesions, which can result in obstruction of new ostium. Surgical insult to the middle turbinate mucosa should be avoided, and the anterior end of the turbinate resected to avoid it from nearing to the ostium. Postoperative adhesions are reduced by prior septal corrections.

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Endoscopic techniques are widely used for screening, diagnostic and therapeutic maneuvers in all groups of patients and for a large spectrum of complaints. The availability of basic iterations of endoscopic techniques made screening programs for various diseases viable in most parts of the world, while the advent of modern techniques opens new perspectives for rapid and correct diagnosis.

Going beyond normal human vision, innovative techniques opened the prospect of in-situ pathology. Endoscopic ultrasound has made incredible progress in recent years. Reaching the smaller orifices by endoscopy was a major step forward in the surveillance of previously inaccessible lesions.

Investigatory techniques were complemented by advances in therapy, with novel applications in many major areas of medicine.

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