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Notice

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Meet the editor

Dr. Riza Hakan Erbay was an anesthesiologist at the Pamukkale University in 1996. He was an assistant professor in 1997, an associate professor in 2005, and a professor in 2011. He has mainly worked in the field of orthopedic anesthesia, regional anesthesia, and intensive care medicine. He worked as an education coordinator at the Faculty of Medicine during 2007–2009 and served as the vice president at the Department of Surgical Sciences, Faculty of Medicine during 2009–2012. He was an intensivist in 2013 and worked as the head of the Anesthesiology Clinic at the Izmir Tepecik Training and Research Hospital during 2013–2014. He is currently the chairman at the Department of Anesthesiology and Reanimation, Faculty of Medicine, Pamukkale University.

Contents

Preface

Endotracheal intubation is the most important component of airway management and is of vital importance. Airway management is a complicated medical practice in which many medical disciplines are involved. These medical disciplines include anesthesiology, emergency medicine, critical care, pulmonary medicine, and surgery. Various examinations, maneuvers, and positions may also be required for tracheal intubation. In addition, if the tracheal intubation could not be performed, surgical intervention should be implemented and oxygenation should be provided by tracheotomy or cricothyrotomy. Thus, if intubation difficulty is predicted in medical situations where the airway opening should be provided, or if intubation is not possible, a "difficult airway algorithm" should be used for life-saving procedures. In this book, the medical basis of hypoxia and oxygenation, functional airway anatomy and physiology, and difficult airway management are described. I am grateful to the authors for their contributions to this book and hope that this book will be helpful to the readers.

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Section 1

Functional Anatomy and Phsiology of Airway

Chapter 1

Functional Anatomy and Physiology of Airway

Aslı Mete and İlknur Hatice Akbudak

Additional information is available at the end of the chapter

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Abstract

In this chapter, we scope the importance of functional anatomy and physiology of the upper airway. The upper airway has an important role in transporting air to the lungs. Both the anatomical structure of the airways and the functional properties of the mucosa, cartilages, and neural and lymphatic tissues influence the characteristics of the air that is inhaled. The airway changes in size, shape, and position throughout its development from the neonate to the adults. Knowledge of the functional anatomy of the airway in these forms the basis of understanding the pathological conditions that may occur. The upper airway extends from the mouth to the trachea. It includes the mouth, the nose, the palate, the uvula, the pharynx, and the larynx. This section also describes the functional physiology of this airway. Managing the airway of a patient with craniofacial disorders poses many challenges to the anesthesiologist. Anatomical abnormalities may affect only intubation, only airway management, or both. This section also focuses on the abnormal airways in obesity, pregnancy, children and neonate, and patients with abnormal facial defects.

Keywords: anatomy, airway, function, physiology, upper airway

1. Introduction

The upper airway has an important role in conducting air to the lungs. Both the anatomical structure of the airways and the functional properties of the mucosa, cartilages, and neural and lymphatic tissues influence the characteristics of the air that is inhaled [1]. The upper airways begin with the nasal cavity and continue over nasopharynx and oropharynx to the larynx and the extrathoracic part of the trachea. The structure and function of this system have a major influence upon the conduction of the air to the lower airways [1]. Functions of the airway include phonation, olfaction, digestion, humidification, and warming of inspired

air [2]. Clinical application of anatomical and physiological knowledge of respiratory system improves patient's safety during anesthesia [3]. This chapter focuses on airway anatomy and physiology, which form the basis for airway management and endotracheal intubation, and also for anesthesiologists.

2. Functional anatomy and physiology of airway

The knowledge of normal anatomy and anatomic variation is important in guiding anesthesiologists in airway management planning. The airway can be divided into upper airway, which includes the nasal cavity, the oral cavity, the pharynx, and the larynx, and the lower airway, which consists of tracheobronchial tree (**Figure 1**) [4].

2.1. The upper airway

2.1.1. Nasal cavity

The nose originates in the cranial ectoderm and is composed of the external nose and the nasal cavity [2]. The nose is divided into the external nose and the nasal cavity [5]. The external nose is a pyramidal structure, situated in the midface, with its base on the facial skeleton and its apex projecting anteriorly [6]. The external nose is formed by an upper framework of bone, a series of cartilages in the lower part, and a small zone of fibro fatty tissue that forms the lateral margin of the nostril (the ala). The upper framework of bone is made up of the nasal bones, the nasal part of the frontal bones, and the frontal processes of the maxillae [5]. The paired nasal bones form the external nose superiorly and two sets of paired cartilage inferiorly. The upper lateral cartilages provide the shape of the middle third of the nose and support for the underlying nasal valve. The paired nasal bone form consists of two parts, the upper nose and the lower cartilage. The upper lateral cartilage

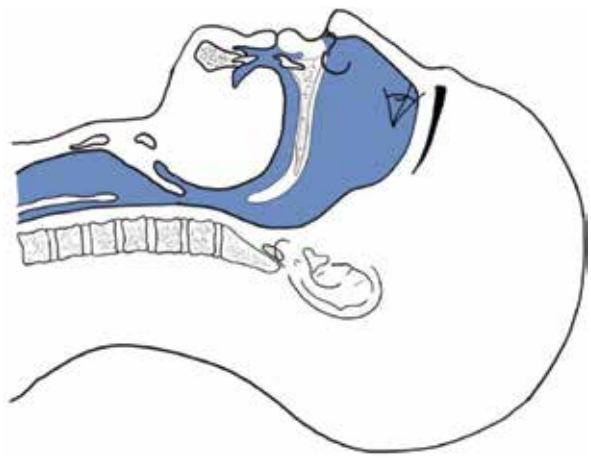

Figure 1. Functional upper airway.

provides protection which is of the shape of the middle third part of the nose and supports the nasal valve. The lower lateral cartilage segments are butterfly shaped and consist of medial and lateral crures. The medial crus forms the columellar, while the lateral crus forms the nasal area. These crures together form the nasal vestibule deficit. Cartilage is supported by nasal septum [6]. The nasal cavity is divided into two compartments by the nasal septum. One of them opens out into the nostrils. The other compartment is the nasopharynx, which opens to the concha or the posterior nasal opening. The vestibule, which includes the nostrils between the small flat nose hairs, is a small aperture [5]. **The nasal septum** divides the nasal cavity into two separate compartments. It consists of an anterior cartilaginous portion, which provides support for the nasal tip, and a posterior bony portion formed by the perpendicular plate of the ethmoid and the vomer (**Figure 2**) [6].

Deviations of the septum are very common; in fact, they are present to some degree in about 75% of the adult population. When the rapid growth in this region, septal cartilage, occurs from an unspecified minor dislocation, the deformity as often as the appearance of the second tooth structure often does not manifest itself. A distribution that supports this traumatic theory is that men are more often affected than women [5]. Due to the possibility of septum deviation, before passing instrumentation, through the nasal passages, the more open side should be determined [4]. The lateral wall of the nasal passages includes **the turbinates (the concha).** These are three, rarely four, scroll-like projections from the lateral nasal wall. The lower two, referred to as the inferior and middle turbinates, are functionally the most significant. Each turbinate consists of a bony frame with the overlying respiratory epithelium (**Figure 3**) [6].

The **inferior meatus**, between the inferior turbinate and the floor of the nasal cavity, is the preferred pathway for the passage of nasal airway devices [4]. The cribriform plate, part of

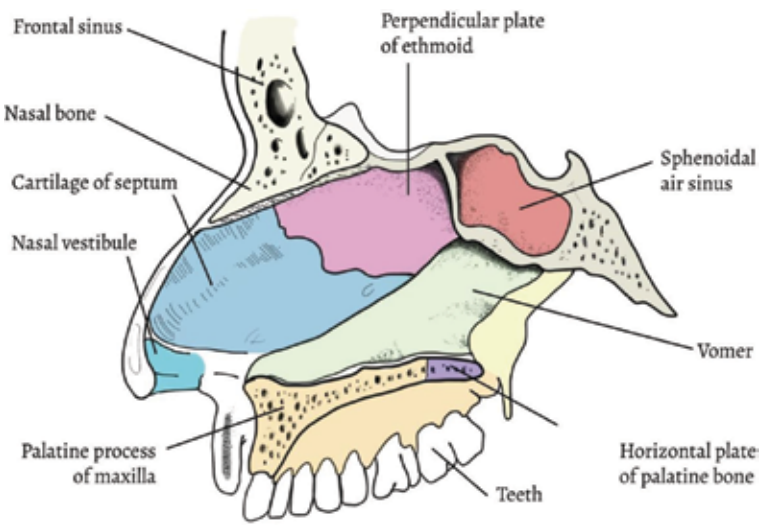

Figure 2. Nasal Sinuses.

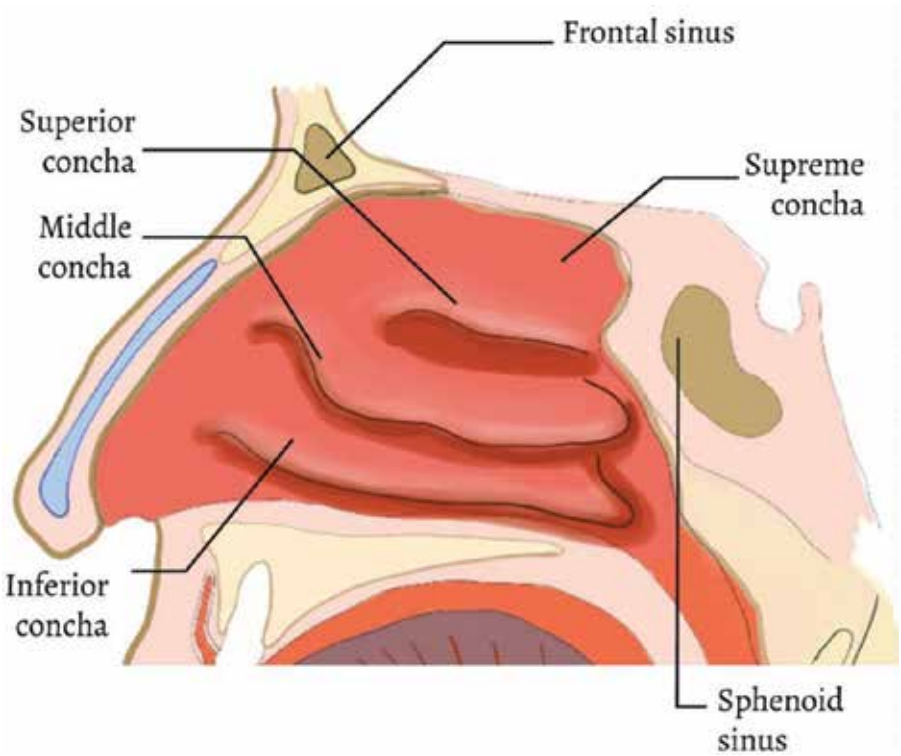

Figure 3. Lateral wall of the nasal cavity.

the ethmoid bone, is a fragile structure of the nasal cavity. This structure is in communication between the nasal and the intracranial cavity. Cerebrospinal fluid may leak when this part fractured [4]. **The paranasal sinuses** consist of the maxillary, sphenoid, frontal, and ethmoidal sinuses. They are outgoing from the lateral wall of the nasal cavity into which they drain. They are rarely symmetrical. There are traces of spines and sphenoid sinuses in the newborn; the remainder being between the ages of 7 and 8 depending on the detonation of the second teeth and the extension of the face. They only develop completely in adolescence [6].

The olfactory nerve (I) innervates the region designated as the nose-specific olfactory area, which covers an area of 2 cm^2 in the uppermost part of the nose and the lateral wall of the nasal cavity. The nerves of common sensation are derived from the nasociliary branch of the first division of the trigeminal nerve (V1) and also from the second, or maxillary division (V2) [4].

Blood supply: the upper part of the nasal cavity provides arterial blood flow from the anterior and posterior ethmoidal branches of the ophthalmic artery and a branch of the internal carotid artery. The sphenopalatine of the maxillary artery feeds the lower part of the cavity. The lower part of the septum is also infused by the septal part of the upper labial branch of the facial artery. This area, also known as the little area, is a region where 90% of the epistaxis develops [6].

The nose is the main portal of air exchange between the inner and the outer environment. The nose creates favorable conditions for approximately 37.8° and 100% relative humidity

of respiratory air required for vital functions, and it plays a role in conjunction with local defense and filtering of particulate matter and gases introduced. There is also a role for the individual in defending and delighting smells. In a healthy adult, the total nasal airway resistance is relatively stable, but the airflow of each nasal cavity changes in a reciprocal manner (as the flow increases in one space, the flow decreases on the other). This change in airflow, known as the nasal cycle, reflects changes in the vascular involvement of the canals and septal tuberculosis. The normal individual is unaware of this return, because the total airway resistance remains constant. During the cycle, the water vapor saturation level of the breathing air is not affected. The warning center for the nasal cycle is located in the hypothalamus [5].

2.1.2. Oral cavity

Oral cavity consists of mouth, palate, teeth, and tongue. The mouth cavity is bounded by the alveolar arch of the maxilla and the mandibula, and teeth in front, the hard and soft palate above, the anterior two-thirds of the tongue and the reflection of its mucosa forwards onto the mandible below, and the oropharyngeal isthmus behind [6]. For a secure intubation, it is important that the anesthesiologist should evaluate the condition of **the teeth** on preoperative evaluation. For a protective strategy, it is important that anesthesiologists have a thorough knowledge of the anatomy of the teeth, supporting structures, dental pathology, and techniques used in dental restoration so that they can properly identify the under-exposed teeth. Adult dentition includes 32 teeth supported by two opposing bones: mandibula and maxilla. The dentitions are divided into four sections each with eight teeth (one central front tooth, one lateral tooth, one dog, two small teeth, and three small teeth). However, the number of teeth of the infant consists of no more than 20 teeth, and each quarter has five teeth (a center cutter, a lateral cutter, a canine, and two molar teeth). The tooth is divided into two parts: the root and the crown. Healthy teeth are very strong and designed to withstand the pressures created during mastication. However, the insertion, manipulation, or removal of any airway device can cause lesions in the oral cavity. Although there is a risk of dental injury during extubation, the risk during intubation is more important. The upper maxillary teeth, especially the upper left central cutter, are the most risky of injury, but the lower and back teeth may also be injured. Patients with difficulty in intubation are 20 times more at risk for dental lesions. During laryngoscopy, the support on the upper jaw and consequently on maxillary incisors improves the line of sight and facilitates the insertion of the endotracheal tube, which explains the high incidence of dental injury during difficult intubation [7]. **The hard palate** is made up of the palatine processes of the maxillae and the horizontal plates of the palatine bones [6]. **The soft palate** hangs the back edge of the hard palate. Its free border bears the **uvula** centrally and blends on either side with the pharyngeal wall (**Figure 3**) [6]. **The tongue** is interwoven with various structures with different muscle structures [4]. Genioglossus muscle is the most clinically relevant to the anesthesiologist, which connects the tongue to the mandible (**Figure 4**) [4].

The epiglottis functionally separates oropharynx and laryngopharynx at the root of tongue. In addition, it prevents aspiration by closing the glottis during swallowing [8]. The jaw-thrust maneuver uses the sliding component of the temporomandibular junction (TMJ) to move the mandible and the attached tongue anteriorly, thereby relieving airway obstruction caused by the posterior displacement of the tongue into the oropharynx [4]. Oral cavity is more

preferred for airway instrumentation due to the narrow nasal passages and the high possibility of bleeding after trauma. Many airway procedures require adequate mouth opening. This is possible with rotation and subluxation of the temporomandibular joint [4]. The hinge movement of the mandible controls mouth opening. A horizontal gliding movement allows for subluxation of the mandible, which allows additional anterior displacement of the tongue during direct laryngoscopy (**Figure 5**) [9].

Mouth opening is an important parameter for intubation, and its definition is the distance between the mandibular and the maxillary central incisor teeth. Temporomandibular joint dysfunction, congenital fusion of the joints, trauma, tissue contracture around the mouth, and trismus may limit mouth opening [9]. The Mallampati score is a scoring scale for estimating the size of the tongue according to the oral cavity, and it can be useful in predicting whether or not the laryngoscope will be easy to move with the laryngoscope blade. In addition, it also assists in whether or not the opening of the mouth to allow intubation [10]. Protrusions of the anterior teeth are among the factors affecting intubation. During laryngoscopy and placement of the intubation tube, the anterior teeth and tongue will affect the imaging on the oral cavity [9]. A small mandibular space may fail to adequately accommodate tongue displacement, thus interfering with visualization of the larynx [9].

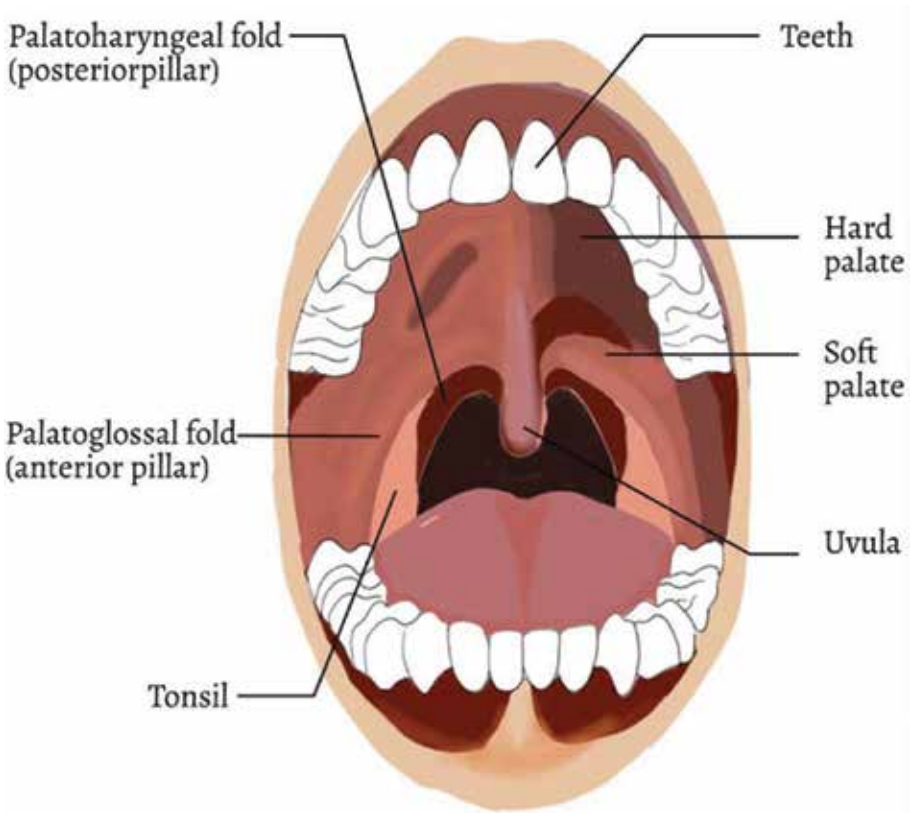

Figure 4. Oral cavity and oropharynx.

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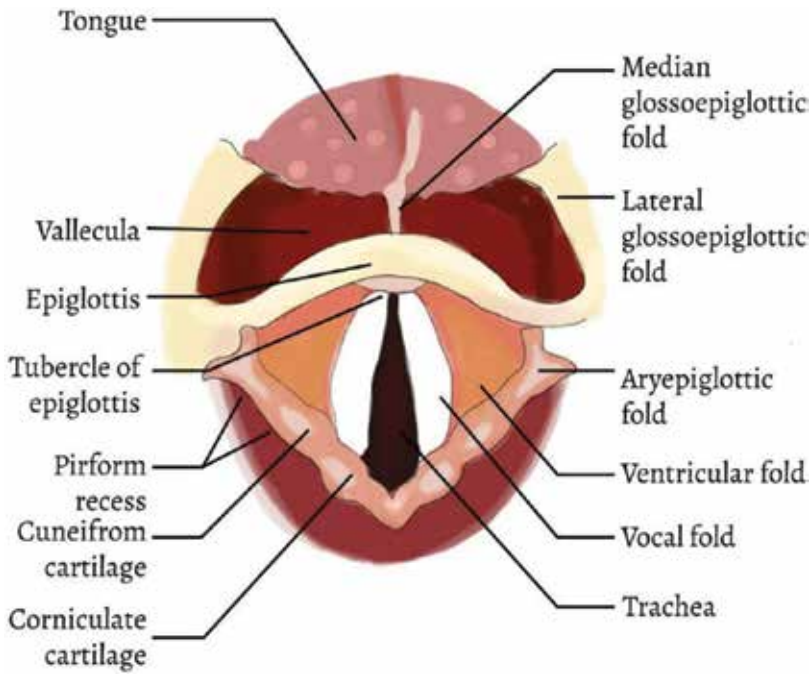

Figure 5. Larynx as visualized from the hypopharynx.

The pharynx is a tube-like passage that connects the posterior nasal and oral cavities to the larynx and esophagus. It is divided into nasopharynx, oropharynx, and laryngopharynx [3]. The pharynx is a muscular tube extending from the base of the skull down to the level of the cricoid cartilage and connecting the nasal and oral cavities to the larynx and esophagus [4]. In order to facilitate the understanding of its functions, the pharynx can be divided into three or four parts (**Figure 6**).

Nasopharynx → between the nares and the hard palate;

Velopharynx or retropalatal oropharynx → between the hard palate and the soft palate;

Oropharynx → from the soft palate to the epiglottis;

Hypopharynx → from the base of the tongue to the larynx (**Figure 7**).

Pharynx is a tube-like passage that connects the posterior nasal and oral cavities to the larynx and the esophagus. It is separated into nasopharynx, oropharynx, and laryngopharynx [3]. The pharynx is a muscle tube extending from the base of the skull to the level of the cricoid cartilage and connecting the nasal and oral cavities to the larynx and the esophagus [4]. To facilitate understanding of its functions, the pharynx can be divided into three or four parts. These four structures form the appropriate route for air passage from the nose to the lung. It also has other physiological functions such as phonation and swallowing. There are 20 or more airway upper muscles surrounding the airway and actively constricting and expanding the upper respiratory tract lumen. These muscles can be divided into four groups: muscles that

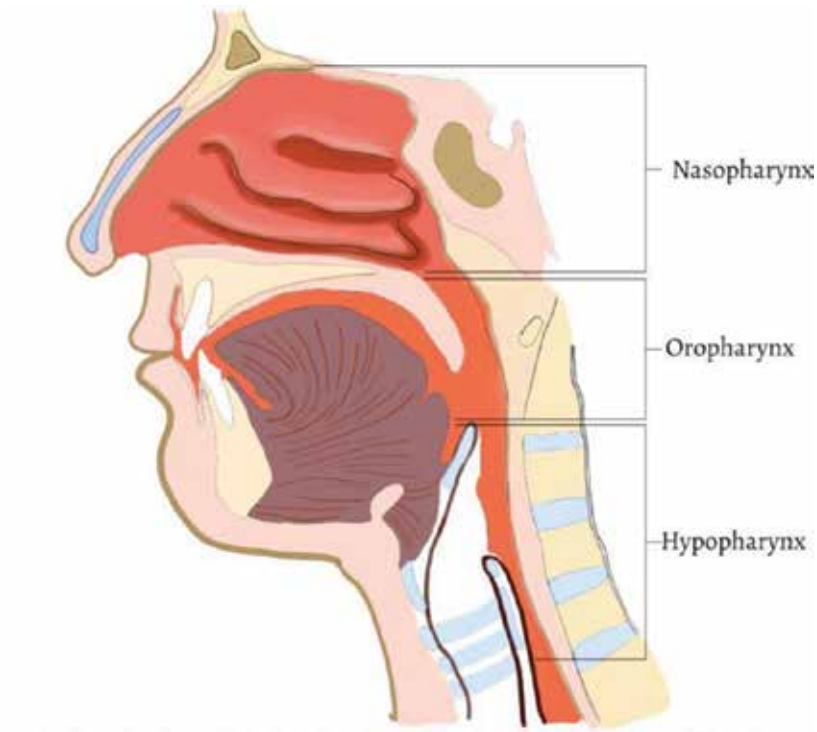

Figure 6. Sagittal section through the head and neck showing the subdivisions of the pharynx.

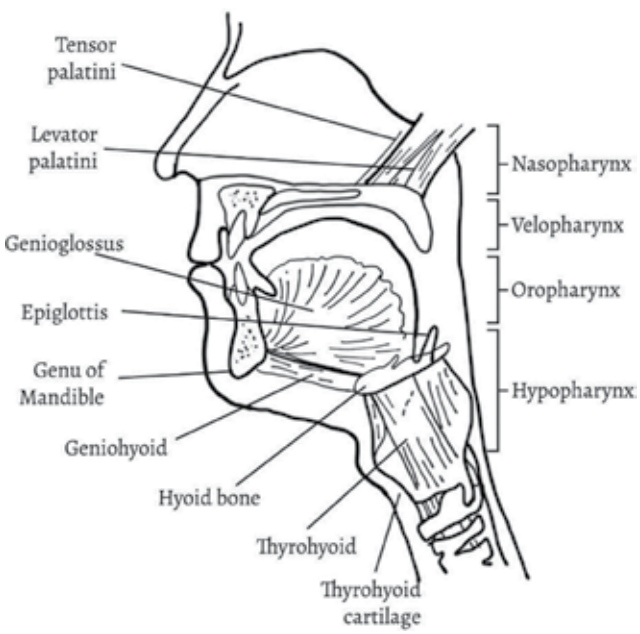

Figure 7. Upper airway lateral view.

regulate the soft palate position (ala nasi, tensor palatini, levator palatini), tongue (genioglossus, geniohyoid, hyoglossus, styloglossus), hyoid device (hyoglossus, genioglossus, digastric, geniohyoid, sternohyoid), and posterolateral pharyngeal walls (palatoglossus) pharyngeal constructors). These muscle groups interact in a complex way to keep the airway open and close. Soft tissue structures form the walls of the upper airway and tonsils including soft palate, uvula, tongue, and lateral pharyngeal walls (**Figure 4**) [11]. The pharyngeal muscle structure seen in the patient who is awake helps to maintain airway patency. However, during anesthesia, the loss of pharyngeal muscle tone is one of the major causes of upper airway obstruction [4]. **The nasopharynx** lies behind the nasal cavity and above the soft palate and communicates with the oropharynx through the pharyngeal isthmus, which becomes closed off during the act of swallowing [6]. Between the superior and the posterior walls of the nasopharynx are adenoid tonsils, which can lead to chronic nasal obstruction and which airway facilities may have difficulty passing. In the soft palate of the nasopharynx, after the end of the ear, it is called velopharynx and is a common area of airway obstruction in patients who are awake or anesthetized [4]. The pharyngeal opening of the pharyngeal tympanic (Eustachian) tube is located in the lateral wall of the nasopharynx, 1 cm behind and just below the inferior nasal convolutions. The posterosuperior side of the nasopharynx is the sphenoid sinus that separates the phalanges from the sella turcica containing the pituitary gland. This sinus is fundamental to the transnasal approach to pituitary surgery [6].

The oral cavity enters the oropharynx via oropharyngeal isthmus, which is limited by palatoglossal arches, soft palate, and lingual dorsum [6]. The oropharynx begins with a soft palate and extends to the epiglottic level. The lateral walls contain, respectively, palatoglossal folds and palatopharyngeal folds, referred to as front- and back-faceted (tonsillar) columns. These layers include palatine tonsils and cause hypertrophy of the tonsils, leading to airway obstruction [4]. The anterior wall of the oropharynx is mainly limited with the soft palate, the tongue, and the lingual tonsils, and the posterior wall is delimited by a muscular wall of the upper, middle, and inferior contraction muscles lying in front of the cervical vertebrae. The minimum diameter of the upper airway during waking, retropalatal oropharynx as a primer, is of interest as a potential localization of collapse during sleep [11].

The laryngopharynx is the last part of the pharynx extending from the edge of the epiglottis to the lower border of the cricoid at the level of C6. Its front faces are the laryngeal entrance first confined to the aryepiglottic folds, then the rear portions of the arytenoids, and finally the cricoid cartilage [6]. The larynx extends toward the center of the laryngeal pharynx and tends to swallow sharp foreign bodies such as chicken-bone bones, leaving a recess on both sides called the piriform fossa [4, 6]. The inner lobe of the superior laryngeal nerve passes into the submucous part of the piriform fossa. Local anesthetic solutions applied to the piriform fossa surface may provide anesthesia for the voice strands. During laryngoscopy procedures, this fossa may be useful as a nerve block supporting oral anesthesia [6].

The larynx is a dynamic, flexible structure composed of a cartilaginous core with interconnecting membranes and associated musculature. The larynx is a midline structure positioned at the interface between the digestive and the respiratory tracts [12]. Larynx is a complex structure of cartilage, muscles, and ligaments that serves as the entrance to the trachea and performs various functions, including phonation and airway protection [4].

The anatomical position, composition, associated musculature, and innervation of the larynx all contribute to this structure's capabilities [12]. The cartilaginous frame of the larynx is made up of different nine cartilages [4]. The arytenoid, corniculate, and cuneiform cartilages are paired, whereas the thyroid, cricoid, and epiglottis are unpaired (**Figure 8**) [13].

They are associated by ligaments, membranes, and synovial joints that are lined by the hyoid bone via the thyrohyoid ligaments and the membrane [4]. The epiglottic, thyroid, and cricoid cartilages make up the three unpaired cartilages and are arranged superior to inferior, respectively. The thyroid cartilage, with the epiglottic cartilage superior, predominates anteriorly and forms the laryngeal prominence (i.e., Adam's apple), while the predominate cartilage dorsally is the cricoid cartilage which sits inferior to the thyroid cartilage [12]. This laryngeal prominence is appreciable from the anterior neck and serves as important landmarks for percutaneous airway techniques and laryngeal nerve blocks [4]. The thyroid cartilage is the largest one and forms a protective shield-like shape in front of the vocal cords [13]. The cricoid cartilage, which lies below the thyroid cartilage and above the entrance to the trachea, is the only complete ring of the laryngeal skeleton. The cricoid cartilage encloses the subglottic region of the larynx. Stenosis may form if the mucosa in this region is injured, as can occur with a prolonged endotracheal tube intubation [13]. The paired arytenoid cartilages are found on the dorsal aspect of the larynx, attached superiorly to the cricoid cartilage. Both arytenoid cartilages give off a lateral extension (muscular process) and anterior extension (vocal process) which aid in supporting the vocal ligaments [12]. The arytenoids are pyramidal-shaped

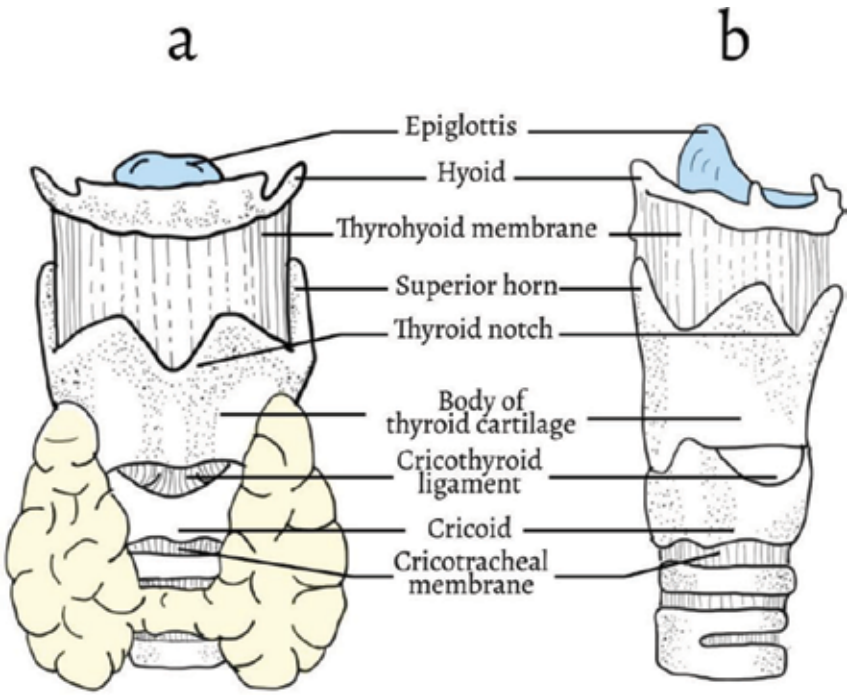

Figure 8. External views of the larynx: (a) anterior aspect; (b) anterolateral aspect with the thyroid gland and cricothyroid ligament removed.

(**Figure 9**) cartilages positioned on the upper border of the posterior cricoid cartilage; these attach at the synovial cricoarytenoid joints. The arytenoids serve as attachment sites for some of the intrinsic muscles of the larynx and allow complex movement and fine adjustment of the vocal cords [13]. In addition, each arytenoid cartilage has an associated corniculate and cuneiform. These two small, paired cartilages border the opening into the laryngeal vestibule both dorsally and laterally cartilage.

The corniculate cartilage can be found at the apex of both arytenoid cartilages. The cuneiform cartilage can be found seated anterior and lateral to both arytenoids. These cartilages form connections via numerous membranes, ligaments, and synovial joints [12].

There are two essential **synovial joints** associated with the larynx. One pair of synovial joints exists between the thyroid and the cricoid cartilages. This joint allows the thyroid cartilage to rotate about the cricoid cartilage and allows the cricoid cartilage to separate from or approximate to the thyroid cartilage anteriorly. The second set of synovial joints exists between the cricoid and the arytenoids (**cricoarytenoid synovial joint**). The cricoarytenoid synovial joint allows the arytenoid cartilages to translate on both an anterior–posterior axis and a lateral-medial axis, as well as rotate about a cranial-caudal axis [12]. Fibrosis or fixation

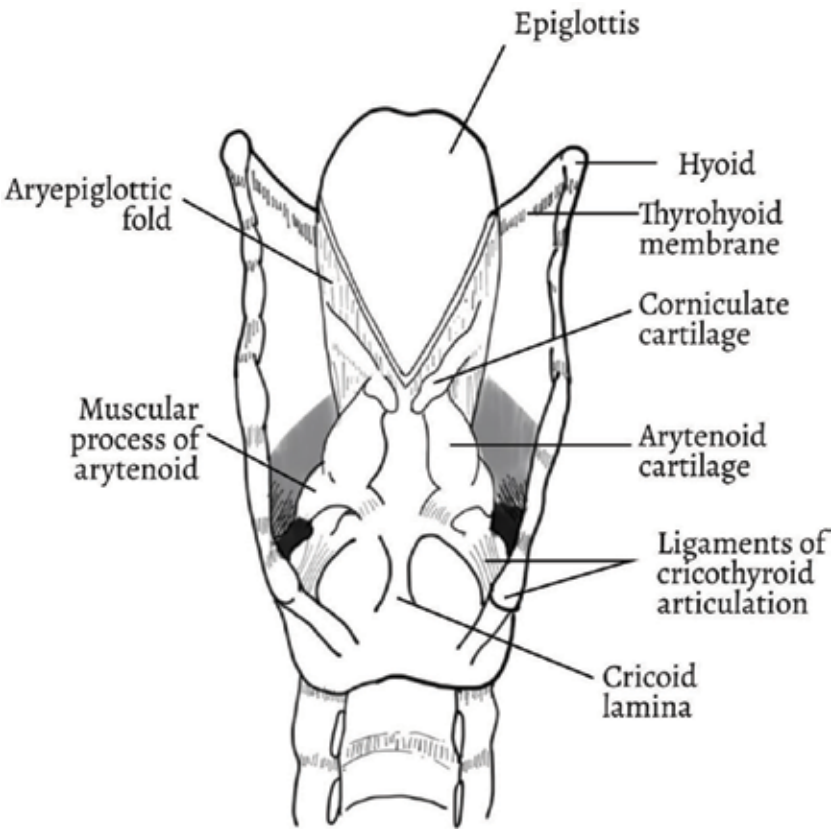

Figure 9. The cartilages and ligaments of the larynx seen posteriorly.

of the cricoarytenoid joint, as can be seen with rheumatoid arthritis or following trauma, can result in vocal fold immobility and respiratory or phonatory impairment [13].

The vocal cords are medial projections of the walls of the larynx that can approximate to each other in the midline to completely obstruct the lumen of the larynx. These vocal folds delineate the plane referred to as the glottis within the vocal cords and there is a muscle known as the vocalis muscle outside the vocal ligament. In addition to the absence of blood vessels on the surface of the folds, the presence of ligaments in this region results in a characteristic white appearance of the vocal cords. This provides visual distinction compared to the pink-appearing vestibular folds. The space found between the vocal folds is termed **the rima glottidis** [12]. **The true vocal cords** are bands of tissue composed of muscle, fibrous ligament, and mucosa extending from the arytenoids posteriorly to the midline thyroid cartilage anteriorly. **The false (or "ventricular") vocal folds** are situated superior to the true vocal cords and are separated from them by a lateral recess termed the laryngeal ventricle. The ventricle contains mucus-producing glands that provide lubrication for the true vocal cords, which are themselves devoid of glandular elements. The false vocal folds are adducted only during effortful closure, as with Valsalva and reflex laryngeal closure due to noxious stimuli. They do not normally approximate during phonation; however, this may be observed in pathologic conditions, such as in patients with incompetent true vocal fold closure due to vocal fold paralysis, mass lesion, or presbyphonia (vocal fold changes due to aging of the larynx) [13].

The larynx is subdivided into three regions: the supraglottis, glottis, and subglottis. The space between the vocal cords is termed the glottis; the portion of the laryngeal cavity above the glottis is known as the supraglottis, and the portion inferior to the vocal cords is known as the subglottis [4]. **The supraglottis** encompasses the area above the true vocal folds and includes the epiglottis, false vocal folds, aryepiglottic folds, and arytenoids. **The glottis** consists of the true vocal folds and the immediate subjacent area extending 1 cm inferiorly. **The subglottis** refers to the region beginning at the inferior edge of the glottis and extending down to the inferior border of the cricoid cartilage [13]. The larynx **during direct laryngoscopy** begins with epiglottis, which is a cartilaginous flap that serves as the anterior border of the laryngeal entrance. Epiglottis functions to divert food away from the larynx during the act of swallowing. This role is not essential to prevent tracheal aspiration [4]. **Laryngeal position**: the anatomical position of the larynx is also dynamic in nature and varies from birth to maturity. Initially, at birth and for the first couple of years of life, the larynx is further superior in the neck than in adults. In infants, this high position results in direct contact between the soft palate and the epiglottis. This allows inspired air to move from the nose to the trachea directly. It is because of this anatomical relationship, an infant is able to swallow liquids and breathe almost simultaneously [12]. By adulthood, the larynx descends inferiorly to its final position. The larynx is the superior portion of the respiratory tract and aligned on its long axis, is vertically adjacent to the trachea, which lies directly inferior to the larynx, and is connected via the cricotracheal ligament [12]. **The muscles of the larynx** are divided into extrinsic and intrinsic muscles. The extrinsic group, including the anterior strap muscles and digastrics, affects the position of the entire larynx in the neck. This is important for laryngeal elevation during swallowing and fixation of the larynx during Valsalva maneuver. The intrinsic muscles are more

delicate and are responsible for the movement of the vocal cords within the larynx as well as subtle tension adjustments related to phonation. The main intrinsic muscles are posterior cricoarytenoid, lateral cricoarytenoid, interarytenoid, thyroarytenoid, and cricothyroid. The thyroarytenoid muscle makes up the bulk of the vocal cord. Movement at the cricoarytenoid joint allows the vocal cords to be adducted during phonation or abducted during inspiration [13]. **Vascular supply for the larynx** is derived from the superior and inferior thyroid arteries. The external carotid artery gives rise to the superior thyroid artery. The thyrocervical artery, which arises from the anterosuperior surface of the subclavian artery, gives rise to the inferior thyroid artery and two other branches. **The venous drainage of the larynx** is via the inferior, middle, and superior thyroid veins. The inferior thyroid veins continue via the subclavian or left brachiocephalic vein. The middle and superior thyroid veins drain into the internal jugular vein. **Lymphatic drainage** of the larynx is accomplished via the deep cervical and paratracheal nodes medially and via the pretracheal and pre-laryngeal nodes medially [12]. **The vagus nerve** innervates the laryngopharynx. The recurrent laryngeal nerves branch from the vagus in the upper chest and reenter the neck in the thoracic inlet. The recurrent laryngeal nerve branches from the vagus in the thorax and loops around the arch of the aorta on the left and the subclavian artery on the right before traveling back up between the esophagus and the trachea [14]. The recurrent laryngeal nerve innervates all intrinsic muscles except for the cricothyroid muscle, which is innervated by the external branch of the superior laryngeal nerve. Motor function of the lower pharynx and the upper esophagus is supplied by direct pharyngeal branches of the vagus and recurrent laryngeal nerve. A mass lesion along the course of these nerves can result in **vocal cord paralysis**. Sensory function above the level of the vocal cords is mediated by the internal branch of the superior laryngeal nerve [12]. Sensory function below the level of the vocal cords is transmitted through the recurrent laryngeal nerve. The vagus nerve receives sensory information from the external auditory canal as well as the hypopharynx. Thus, a reflex cough can be provoked by instrumenting the ear for cleaning, and cancer in the hypopharynx results in ear pain [13].

2.1.3. Lower airway

The tracheobronchial tree: the tracheobronchial airways form a complex series of branching tubes that culminate in the gas exchange area, with the average number of branches approximately (**Figure 10**) [15].

The trachea is a cartilage tissue that can stretch during breathing [14]. The trachea begins at the level of the cricoid cartilage and extends to the carina at the level of the fifth thoracic vertebra (the lower end of the trachea can be seen in oblique radiographs of the chest to extend to the level of the fifth, or in full inspiration the sixth, thoracic vertebra); this length is 10–15 cm in the adult. It consists of 16–20 C-shaped cartilaginous rings that open posteriorly and are joined by fibroelastic tissue; the trachealis muscle forms the posterior wall of the trachea [4, 6, 14]. The cartilage at the tracheal bifurcation is the keel-shaped carina, which is seen as a very obvious sagittal protrusion when the trachea is inspected bronchoscopically [6]. The trachea bifurcates into the right and left main bronchi at the carina. In the adult, the right main bronchus branches out at a more vertical angle than the left main bronchus, as it results in a greater

likelihood of foreign bodies and endotracheal tubes entering the right bronchial lumen [4]. The trachea extends from the neck to the thorax to the midline, but slightly diverges to the right by the aortic arch in the thorax. At the lower part of the neck, the edges of the sternohyoid and sternothyroid muscles are adjacent to the trachea. This region is covered by the inferior thyroid venules with cross-communication between the anterior jugular venules and the lateral side of the thyroid gland which is branched from the aortic arch or brachiocephalic artery. Because of this close association with the brachiocephalic artery, erosion by the tracheal wall of the tracheostomy tube can lead to sudden abdominal bleeding [6]. Laterally, the lateral lobes of the thyroid gland, which are located between the trachea and the carotid sheath [14], the esophagus, and the recurrent laryngeal nerve, lie in the posterior side [6, 14].

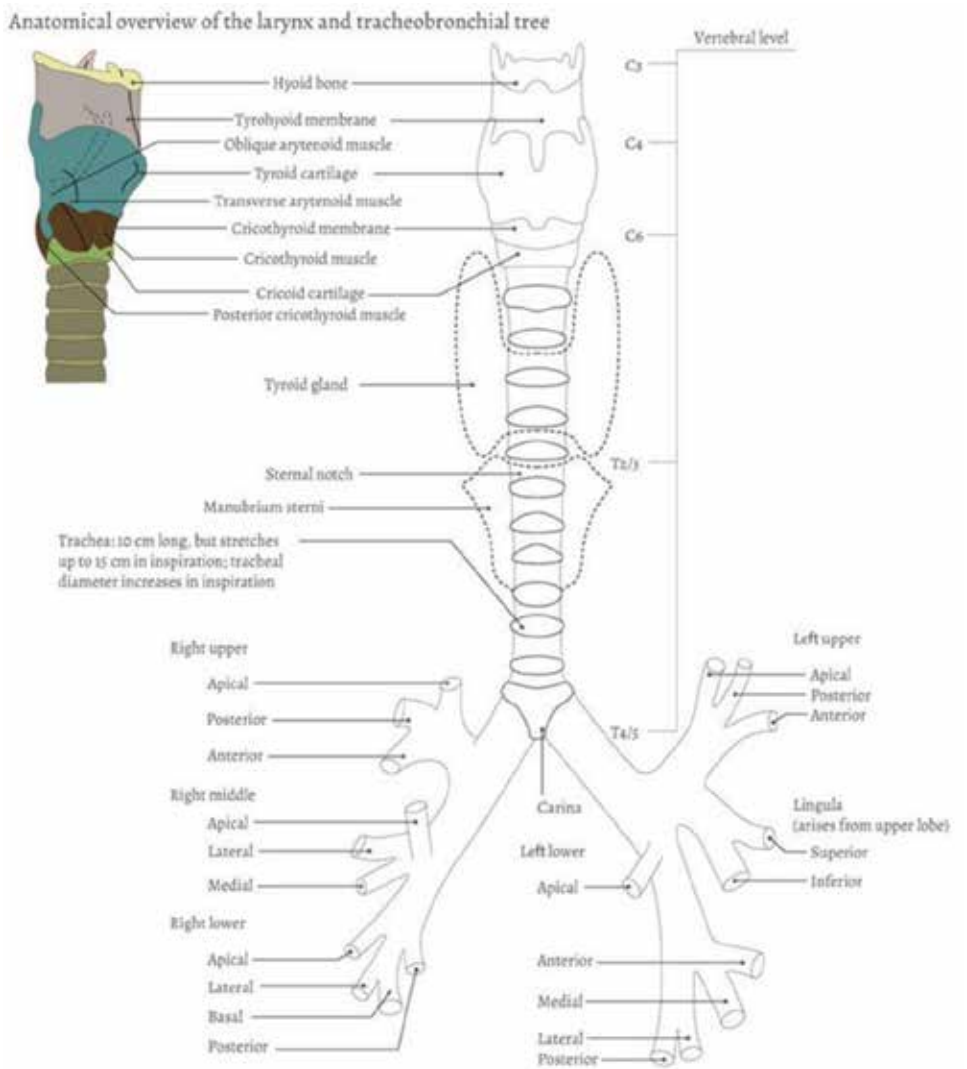

Figure 10. Anatomical overview of the larynx and tracheobronchial tree.

Vascular, lymphatic, and nerve supply: the arterial supply to the trachea is derived from the inferior thyroid arteries, and the venous drainage is via the inferior thyroid veins. Lymphatics pass to the deep cervical, pretracheal, and paratracheal nodes [6]. Nerve supply is from vagus and recurrent laryngeal nerves for pain and secretomotor functions [14] and sympathetic supply from the middle cervical ganglion [6].

2.1.4. The main bronchi

In full inspiration, the bifurcation level is at T6. The right main bronchus is shorter, wider, and more perpendicular than the left bronchus. This situation can be explained by the transformation into a shorter and wider structure because the embryologically will feed larger lungs. In addition, the aortic arc is the reason for the placement to be more perpendicular due to the position (at 25° perpendicular to the 45° left) [6]. This is the result of a greater possibility of foreign bodies and endotracheal tubes entering the right bronchial lumen [4]. The bronchi are supplied by the bronchial arteries from the aorta and drained by the azygos vein on the right and the hemiazygos vein on the left, and also, some drainage by pulmonary veins and the bronchial veins [14].

3. Evaluation of the complex airway

3.1. Pediatric airway differences

The pediatric airway changes significantly from birth to adulthood. These changes affect the development of the skull, oral cavity, throat, and trachea. The head is larger than the body in infants and young children. Due to the absence of paranasal sinuses, the facial skeleton is smaller in neonates compared with neurocranium. Oral cavity is small at birth. It grows in the first year of life due to the significant growth of the mandibles and teeth in the following period. In neonates, the tongue has a flat surface and limited lateral mobility and appears relatively large in the small mouth space. Neonatal laryngeal and tracheal structures are especially important for anesthesiologist. The larynx appears more prominently during direct laryngoscopy, but when compared with adults, the surrounding structure is loosely embedded. External manipulation allows direct laryngoscopic intubation to be easily carried to a position where it is possible. If the epiglottis is not removed by the bladder of the laryngoscope, the glottic appearance on the laryngoscopy is prevented long, narrow, and often U- or V-shaped ("flopping") [16]. Glottis is higher in the newborn (C2/C3) than in the vertebrae, and after 2 years, it falls to the normal position in C5 [17]. In newborn, vocal cords are shorter, and anterior glottis, which normally corresponds to two-thirds in a larger child, constitutes about 50% of the newborn. The newborn larynx is conical, but in a larger child, it is approximately cylindrical. Though the larynx is thought to be widest in the supraglottic region and narrowest in the subglottic region, this suggests that the narrowest portion of the magnetic resonance imaging (MRI) studies may be in glottic. Also, the cricoid ring is the narrowest part of the neonatal airway and is an ellipsoid-shaped mucosa layer which is highly sensitive to trauma. Bypassing the air leak at this level from the untrained tracheal

tube does not guarantee avoidance from the pressure points and the next payment [18]. Intubation tubes with small tracheal internal diameter cause a significant increase in airway resistance and this can lead to an exaggerated mucosal injury. The tracheal length depends on the child's age and height but is not dependent on body weight. During the operation, changes in the head position may lead to a displacement of the tracheal tube and reevaluate the position of the tube with the head's new position. Verification of the position of the tracheal tube clinically (chest movement, auscultation) or by other means (chest radiography, fluoroscopy, ultrasonography, or bronchoscopy) is recommended.

Physiological conditions: in human, the downward movement of the laryngeal structures according to age is the main factor in transaction from nasal breathing to oral breathing. Direct result is the dissociation of the epiglottis and the soft palate. The pediatric airway cannot be assessed in young children without considering very low functional residual capacity. This situation, a high oxygen demand, an increased carbon dioxide production, and an increased closure capacity, is together. And the situation which is in very low tolerance to apnea appears with this result. This rapidly leads to significant hypoxemia and respiratory acidosis. Even the optimal time preoxygenation cannot result in a "safety time" that is long enough to prevent desaturation following short periods of apnea. The smaller the child, the more limited the time is [19, 20]. In human, one of the most strongest reflexes is laryngeal reflexes and it can be thought to prevent pulmonary aspiration. These functional reflexes are undernapped by the inner and outer branches of the larynx, recurrent laryngeal nerve, and superior laryngeal nerves. The afferent innervation of the subglottic part of the larynx and all muscles is also provided by the recurrent laryngeal nerve, except for the cricothyroid scar. The larynx is relatively insensitive to irritant gases that are inhaled but is very sensitive to mechanical or chemical stimuli caused by fluid or solutes.

3.2. Congenital disease

It may produce abnormalities of the head, neck, or upper airway [9]. Cardiovascular, nervous, musculocutaneous, or excretory system disease is more often tabulated with these abnormalities. Crouzon, Goldenhar, Pierre Robin, and Treacher Collins syndromes are known for their abnormal head and neck. The patients with micrognatia, retrognatia, and macroglossia must be remembered for the congenital diseases in childhood [9]. The most significant vascular malformations are vascular rings, usually of aortic arch origin, encircling the trachea. Tracheomalacia, congenital tracheal stenosis, shortened trachea, and bronchogenic cysts can contribute to difficult airway management [21]. Infants with congenital malformation syndromes associated with cardiovascular anomalies and skeletal dysplasia have a shortened trachea significant percentage [21]. Soft tissue changes that cause airway management difficulties are usually divided into two categories as those that disturb the motion of the airway and limit the movements that disturb the airway by mass effects. Soft tissue changes that limit airway motion usually affect mouth opening. Microstomy, a feature of Freeman-Sheldon syndrome, is a condition in which the movement of oral tissues that do not respond to stomach relaxation is limited. Other rare diseases that limit the movement of airway tissue include fibrofacial myositis ossificans and dermatomyositis. The mass effects on the airway due to soft tissue abnormalities may be the result of congenital, end-of-life, or subsequent disease outcomes of surgical interventions [22]. Macroglossia is one of the most common problems appearing with birth, and the tongue expands and fills the oral cavity, making it difficult to

see the larynx. Macroglossia occurs in Beckwith-Wiedemann syndrome, Down syndrome, Sturge-Weber syndrome, and in a variety of dystrophically related syndromes [22].

3.3. Obese patients

Perioperative management in obese patient, including airway management, is an increasing and a worldwide concern for the anesthesiologist. Since obese patients have an increased fatty tissue distributed in a truncal fashion, obesity may have an important and negative impact on the airway patency and respiratory function. Respiratory function and airway patency can be significantly altered by this change in position [23]. Airway assessment of the obese patient should be performed with the patient in both the sitting and supine positions. Respiratory function and airway patency can be significantly altered by this change in position [24]. Body weight may not be as critical as the location of excess weight. Massive weight in the lower abdomen and hip area may be less important than when the weight is in the upper body area. A short, thick, immobile neck caused by cervical spine fat pads will interfere with rigid laryngoscopy. Furthermore, the redundancy of soft tissue structures inside the oropharyngeal and supralaryngeal area may also make visualization of the laryngeal structures difficult. Mask ventilation should be difficult in the obese patient. When a high positive pressure is required to ventilate the patient, the chance of inflating the stomach is increased. Rapidly oxygen desaturation during apnea, secondary to a reduced functional residual capacity, limits intubation time. In the case of a cannot-intubate-cannot-ventilate situation, access to the neck for transtracheal jet ventilation or establishing a surgical airway (emergency tracheostomy or cricothyroidotomy) will also be more complex [9].

3.4. Pregnancy

Maternal, fetal, surgical, and personal factors in pregnancy cause an increase in the incidence of unsuccessful intubation. The mucosa of the upper respiratory tract becomes more vascular and edematous, which increases the risk of bleeding and swelling in the airway [25]. These changes cause the Mallampati score to increase as the pregnancy progresses and during labor. Airway edema may be exacerbated by preeclampsia, oxytocin infusion, intravenous fluids, and Valsalva maneuvers during labor and delivery. A decreased functional residual capacity and increased oxygen requirements accelerate the onset of desaturation during apnea and are further exacerbated in obese patients. Progesterone reduces the lower esophageal sphincter tonus, which results in gastric reflux. Risk of reflux is further increased because of delayed gastric emptying after prolonged painful delivery and opioid administration. Enlarged breasts can make laryngoscopy difficult [26]. Airway anatomy may become distorted during prolonged labor or toxemia, leading to an edematous soft tissue encroachment of the upper airway [27]. At last, in cases of fetal distress or maternal hemorrhage, the emergency nature of the circumstances compounds airway management problems [9].

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Chapter 2

Pathophysiology of Apnea, Hypoxia, and Preoxygenation

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Additional information is available at the end of the chapter

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Abstract

Because intubation becomes a long procedure as potential, arterial oxygen (O_2) desaturation should be taken into account during the intubation. Since oxygen reserves are not always sufficient to meet the duration of intubation, preoxygenation should be routine before anesthetic induction and tracheal intubation. Surveys show that maximal preoxygenation increases oxygen reserves in the body and significantly delays arterial hemoglobin desaturation and hypoxia. In cases of respiratory insufficiency oxygenation can be improved by positive end expiratory pressure (PEEP) or pressure support. Effective technique and FeO_2 monitoring can increase the effectiveness of preoxygenation and thus increase the safety margin. Preoxygenation failures have to be identified and alternative oxygenation methods must be readily available in order to be applied quickly and easily. Although genetic and environmental factors play a role in diseases such as heart attack, stroke and cancer, which have become the cause of the worst death in the twenty-first century, the underlying problem in the development of these pathological conditions is hypoxia. Better understanding of hypoxic areas in ischemic tissues or growing tumors as well as increased knowledge of hypoxia cellular and molecular responses will allow possible applications in the treatment of major diseases associated with tissue hypoxia.

Keywords: apnea, hypoxia, preoxygenation, anesthesia, intubation

1. Introduction

In this chapter, factors affecting the formation of severe hypoxemia during apnea, pathophysiology of oxygen delivery and preoxygenation, pathophysiologic responses to hypoxemia will be discussed.

In an anesthetized patient, oxygen consumption (VO_2) remains fairly constant at 250 mL/min. This is delivered to the tissues by hemoglobin whose oxygen is then replenished, on return to the pulmonary circulation, by the diminishing store of oxygen within the lungs. Alveolar partial oxygen pressure (PAO_2) is constantly reduced not only due to oxygen uptake by the lungs but also due to the severe negative intrathoracic pressure produced by this oxygen uptake, if the airway is occluded at the same time. However, the arterial partial pressure of oxygen (PaO_2) drops directly to PAO_2, while arterial hemoglobin oxygen saturation (SpO_2) remains above 90% as long as hemoglobin can be oxygenated again in the lungs. SpO_2 begins to fall only when the oxygen stores in the lungs are empty and PaO_2 is 6–7 kPa. Their subsequent declines are constant and fast at around 30% per minute. At the beginning of this rapid decline, SpO_2 is still around 90–95%. This bending point can be defined as "critical hypoxia." Since oxymetry detects the fall in SpO_2 before any obvious clinical sign, it has an important place in helping clinical applications to detect and avoid critical situations.

Preservation of oxygenation during intubation is essential because lack of control of O_2 intake can cause life-threatening complications. Anesthesia induction usually leads to apnea. In this case, tissue oxygenation is maintained by the use of oxygen reserve and continuous O_2 administration. In some cases, adequate oxygenation cannot be achieved due to pulmonary disease, inadequate mask ventilation or difficulties in intubation. These critical situations are often predictable and can be avoided by alternative oxygenation methods by following a valid algorithm [1].

2. Pathophysiology of oxygen delivery

Oxygenation during anesthesia mostly depends on three parameters: alveolar ventilation (VA), ventilation-perfusion distribution and VO_2.

2.1. Oxygen reserves

Tissue oxygenation during apnea is usually sustained at the expense of body O_2 reserves that are present in the lungs, plasma, and hemoglobin [2]. When the ambient air is breathing, the lung O_2 reserve is calculated as: 0.21 × 3000 = 630 mL for 3000 mL functional residual capacity (FRC). After full preoxygenation, FAO_2 is close to 0.95 and the reserve increases as follows: 0.95 × 3000 mL = 2850 mL. These theoretical figures are the maximum values; in practice, the rate of ventilation-perfusion is lower than that of FAO_2 because of the heterogeneity. In a subject inhaling ambient air (PaO_2 = 80 mmHg) and a plasma volume of 3 liters, plasma oxygen reserve is calculated as 0.003 × 80 × 3 × 10 = 7 mL. At 500 mmHg PaO_2, this plasma reserve reaches 45 mL. The hemoglobin O_2 reserve is calculated in the ambient air (SpO_2 = 98%) for a hemoglobin concentration of 12 g/100 mL and a total blood volume of 5 L as follows: 1.34 × 0.98 × 12 × 10 × 5 = 788 mL. This value increases to 804 mL for 1 FiO_2 (SpO_2 = 100%). In cases of anemia, hyperoxic ventilation increases the availability of O_2 by replicating solute O_2 [3]. Considering the basic physiological O_2 reserves, while the ambient air is inhaled, the total O_2 reserve is approximately 1450 mL and reaches approximately 3700 mL in the pure O_2 solution.

This increase (approximately 2250 mL) is mainly due to the rice FAO_2 in FRC. Several factors influence O_2 availability: the initial rise in $PaCO_2$ (Haldane effect), FRC, FAO_2, fraction of shunt, VO_2, hemoglobin concentration, and cardiac output. Replacement of nitrogen by O_2 in the lung reservoir during preoxygenation obeys an exponential law [2]. The change in O_2 reserve over time is linear in both blood and tissue compartments.

2.2. O_2 consumption

The VO_2 value of an awake person is about 300 mL/min and falls about 15% in old aged people. After ventilation in ambient air, O_2 reserves allow apnea for up to 3 minutes without serious eff on O_2 transport. This time can be doubled with the correct applied preoxygenation. The duration of apnea tolerated is additionally decreased if O_2 reserves are low due to decreased FRC, low PAO_2 and/or high VO_2 and the O_2 reserves are reduced due to low FRC, PaO_2 and/or high VO_2.

2.2.1. Ventilation/perfusion incompatibility

Preoxygenation leads to an increase in shunt and microatelectasis after induction of anesthesia [4]. The inspired high O_2 fraction (FiO_2) is not the only responsible mechanism; atelectasis was also observed when FiO_2 was used as 0.4 [5]. The use of 0.8 FiO_2 does not inhibit the emergence of microatelectasis and results in a considerable shortening of the time limit before critical desaturation compared to the use of 100% oxygen [6]. Microatelectasis are reversible with alveolar engraftment (>30 cmH_2O tracheal pressure for 15 seconds) and can be prevented by the addition of 10 cmH_2O positive end expiratory pressure (PEEP) [7]. In morbidly obese patients and in parturients, shunt can exceed 20% and even increasing FiO_2 to 1 does not provide correction of the hypoxemia. Implementation of a microatelectasis prevention strategy of alveolar recruitment maneuvers and PEEP limits the extent in elderly and obese patients [8, 9].

2.3. Epidemiology of arterial desaturation during anesthesia induction and intubation

Arterial O_2 desaturation occurs if O_2 reserves are insufficient to support O_2 consumption during apnea. There are three responsible mechanisms: quantitative reduction in the reserve (decline in FRC, deterioration in gas exchange), VO_2 increase (birth, fever), and prolonged apnea.

It is especially important to mention the four high-risk situations:

- Rapid induction sequence in which mask ventilation increases the risk of inhalation of gastric fluid.
- Prediction of difficult ventilation with face mask.
- Anatomical abnormality and prediction of difficult intubation with specific technical assessments (such as double-lumen tube).
- Obesity and pregnancy.

After rapid sequence induction, spontaneous ventilation reinitiation does not occur rapidly after an unsuccessful intubation procedure and saturation falls below 90% in 11% of patients [10]. Administration of succinylcholine (0.56 and 1 mg/kg) after induction with propofol (2 mg/kg) and fentanyl (μg/kg) has increased desaturation risk and apnea duration compared to placebo [11]. In a pharmacodynamic study with succinylcholine (0.3–1 mg/kg), it found that the intubation conditions were excellent at doses above 0.5 mg/kg, but the delay in resumption of spontaneous breathing rose from 4.0 to 6.16 minutes after administration of 0.6 and 1 $mg.kg^{-1}$, respectively [12]. Reversal of deep neuromuscular block (induced by high-dose rocuronium) with sugammadex (16 mg/kg) used for rapid sequence induction is significantly faster than spontaneous recovery of succinylcholine (6.2 ± 1.8 versus 10.9 ± 2.4 minutes) [13]. Reversal with sugammadex following rapid sequence induction with rocuronium allows earlier restoration of spontaneous respiration compared to succinylcholine (216 versus 406 seconds) [14]. Thus, the choice of the rocuronium would increase the margin of safety for a resumption of spontaneous ventilation after a rapid sequence induction.

2.3.1. Desaturation in pediatrics

Desaturation attacks occur frequently in children, with 4–10% during induction and 20% during tracheal intubation [15]. Desaturation occurs faster if the child is younger [16, 17] and apnea duration in predesaturation has a linear relationship with the age of the patient. The low weight of the child increases the frequency of severe arterial desaturation. It is suggested that 95% SpO_2 may be the safe apnea limit during induction of pediatric anesthesia [18]. It was noted that upper respiratory tract infection increased desaturation risk during induction [15]. The number of important factors effect the time from the onset of apnea to the development of critical hypoxemia.

2.3.1.1. Functional residual capacity (FRC)

FRC is the most important oxygen storage in the body. The larger the FRC, the longer apnea times can be preceded before the critical hypoxia develops. Alveolar oxygen fraction (FAO_2) is around 13% in air breathing. For an adult with normal FRC and VO_2, the oxygen content of the lungs (290 mL) will be consumed within 1 minute. This explains why you can expect a critical hypoxia after 1-minute apnea. Reduced FRC patients (lung disease, kyphoscoliosis, pregnancy, and obesity) reach critical hypoxia much faster.

2.3.1.2. Preoxygenation

Preoxygenation using a high FiO_2 before anesthesia induction and tracheal intubation is particularly recommended in patients at risk for apneic arterial oxyhemoglobin desaturation. The success of preoxygenation to delay the onset of desaturation has been known for many years [19–21]. Preoxygenation during anesthesia induction is highly recommended in cases of desaturation prior to airway safety with endotracheal intubation. In situations where manual ventilation is not desired, such as patients with aspiration risk, preoxygenation has become

an integral component during rapid sequence induction/intubation [22–25]. It is also important when difficulties associated with preoxygenation, ventilation, or tracheal intubation are predicted and the patient's O_2 reserves are limited [26, 27].

Guidelines developed by the Difficult Airway Society in the United Kingdom for unforeseen difficult intubation management in 2015 suggest that all patients must undergo preoxygenation prior to induction of general anesthesia [28]. Residual effects of anesthetics or inadequate reversal of muscle relaxants can complicate emergence from anesthesia. These effects may result in decreased functional activity of the pharyngeal muscles, upper airway obstruction, effective cough insufficiency, a fivefold increase in aspiration risk, and hypoxic weakness controlled by peripheral chemoreceptors [29, 30]. Hypoventilation, hypoxemia and loss of airway may follow these changes. Preoxygenation can also minimize neostigmine-induced cardiac arrhythmias [31]. Considering the potential for airway and ventilation problems, "routine" preoxygenation is recommended before reversing neuromuscular blockage and before tracheal extubation [32]. The recommended guidelines for the management of tracheal extubation in 2012 by the Difficult Airway Society in the United Kingdom state that preoxygenation must be performed before extubation due to various perioperative anatomical and physiological changes that may put gas exchange in jeopardy [33]. Preoxygenation is also recommended before any ventilation interruption, such as open tracheobronchial aspiration.

3. Physiological basis, efficiency, and productivity

Preoxygenation increases the body O_2 stores, the main increase occurring in the functional residual capacity. Accurate quantification of the increases in the O_2 volume in various body tissues is difficult, but the estimated increases are notable when assuming that the partition coefficient for gases approximates the gas-water coefficients (**Table 1**, **Figure 1**) [2, 34].

The effectivity of preoxygenation is assessed by efficacy and efficiency. Efficacy indices include FAO_2 increase, decreases in alveolar nitrogen fraction (FAN_2), and increase in PaO_2 [35–42]. The efficiency of preoxygenation is assessed by the decrease in oxyhemoglobin desaturation (SpO_2) during apnea [10, 43, 44]. Preoxygenation increases FAO_2 and decreases FAN_2 (**Figure 2**) [45].

The key to achieve maximum preoxygenation is the excretion of alveolar nitrogen (N_2). The terms preoxygenation and denitrogenation have been used synonymously to describe the

Body store	Room air	100% O_2
Lungs	450	3000
Blood	850	950
Dissolved in tissue fluids	50	100
Combined with myoglobin	200	200
Total	1550	4250

Table 1. Body O_2 stores (in mL) during room air and 100% O_2 breathing [34].

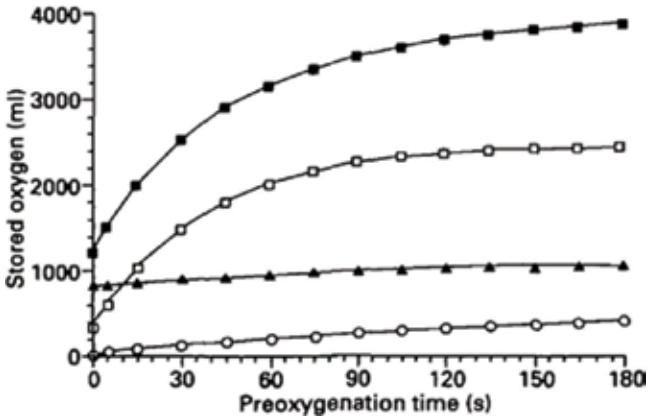

Figure 1. Variation in the volume of O_2 stored in the functional residual capacity (□), blood (▲), tissue (○), and whole body (■) with the duration of preoxygenation [2].

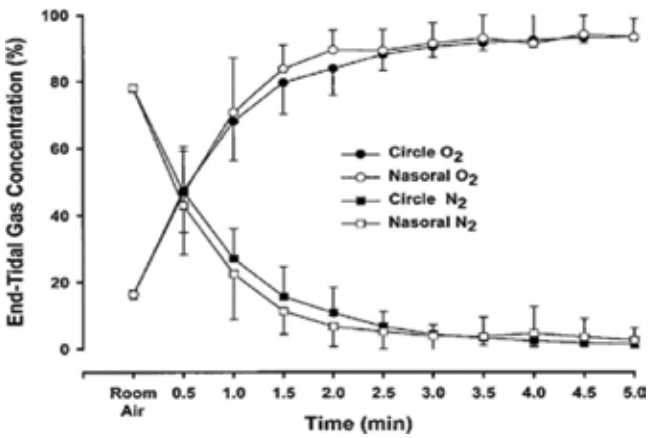

Figure 2. Comparison of mean end-tidal O_2 and N_2 concentration obtained at 30 second intervals during 5-minute period of spontaneous tidal volume oxygenation using the circle absorber and Nasoral systems in 20 volunteers. Data are mean ± SD [45].

same process. In a normal lung function case, filling with O_2 and discharging of N_2 are exponential functions and are controlled by the time constant (t) of the exponential curves. This constant is proportional to the ratio of alveolar ventilation to functional residual capacity. Since preoxygenation prior to anesthetic induction is typically carried out using a semiclosed circular absorber cycle, the washout of the circuit must also be considered using the time constant of the circuit, which is the time required for flow through a container (volume) to equal its capacity. Thus, there are two stages of preoxygenation (**Table 2**) [32]: washing the vessel with O_2 flow and washing FRC by alveolar ventilation.

After 1 t, O_2 at functional residual capacity is 63%; 2 t, then 86%; 3 t, then 95%; and after 4 t, an increase of about 98% is observed. The endpoints of maximum preoxygenation and denitrogenation were defined as an end-tidal O_2 concentration (EtO_2) of about 90% and an

Stage	Description	Determinant of *t*	Recommendation
1	Washout of anesthesia circuit by O_2 flow	Size of circuit/O_2 flow rate	Washout of circuit by high O_2 flow before placing face mask
2	Washout of FRC by VA	FRC/VA	Use of O_2 flow rate that eliminates rebreathing

FRC, functional residual capacity; t, time required for flow through a container (volume) to equal its capacity; and VA, alveolar ventilation [32].

Table 2. Stages of preoxygenation.

after-tidal N_2 concentration of 5% (EtN_2) [2, 35]. In an adult subject with a normal functional residual capacity and oxygen consumption (VO_2), an $EtO_2 > 90\%$ implies that the lungs contain >2000 mL of O_2, which is 8–10 times the VO_2 [26, 46]. Due to the presence of carbon dioxide (CO_2) and water vapor in the alveolar air, it is thought that $EtO_2 > 94\%$ cannot be obtained easily. Many factors affect efficacy and efficiency (**Table 3**).

Factors affecting the efficacy of preoxygenation are FiO_2, duration of preoxygenation, and alveolar ventilation/functional residual capacity ratio. Failure to achieve a FiO_2 of close to 1.0 depends on the height of the ozone beneath the face mask, the rebreathing of exhalation gases, and the high O_2 dispersion of resuscitation bubbles [45, 48, 49]. FiO_2 may also be affected by the duration of the aeration, the breathing technique, and the amount of fresh gas flow [50]. Bearded patients, toothless patients, elderly patients with sagging cheeks, facial mask use at the wrong size, and presence of gastric tubes (nasogastric) are common factors that cause air entrapment and a lower FiO_2. The lack of a normal capnography wave and expected lower end-tidal CO_2 concentration ($EtCO_2$) and EtO_2 should warn of the presence of leaks in the anesthetic cycle [26]. With a FiO_2 close to 1.0, most healthy adults with tidal volume respiration can achieve an $EtO_2 > 90\%$ target level within 3–5 minutes. The half-time for the exponential change in the FAO_2 fraction following each unit change in FiO_2 is given by the following equation:

$$FAO_2 = 0.693 \times \text{Functional residual capacity/Volume of alveolar ventilation.}$$

Efficacy
• Inspired oxygen concentration
• Presence of leak anesthetic system used level of FGF
• Type of breathing (tidal volume or deep breathing) and duration of breathing
• VA/FRC ratio
Efficiency
• Oxygen volume in lungs (alveolar oxygen tension, FRC)
• Systemic oxygen supply versus demand balance (arterial oxygen content, cardiac output, whole body oxygen consumption)

FGF, fresh gas flow; FRC, functional residual capacity; and VA, alveolar ventilation [32].

Table 3. Factors affecting the efficacy and efficiency of preoxygenation.

With a functional residual capacity of 2.5 L, the half-times are 26 seconds when alveolar ventilation = 4 L/minutes and 13 seconds when alveolar ventilation = 8 L/minutes [26]. These findings indicate that hyperventilation can reduce the time required to increase the O_2 stores in the lungs, which provides the basis for using deep breathing as an alternative to tidal volume breathing [41, 42, 51, 52].

3.1. Preoxygenation techniques

Equipment especially face mask should be adapted and it should fit the patient. Mask and stylistic mismatch between the patient's face (mask improper length, beards, or mustaches asset) can prevent the complete closure and lead to failure [35]. The mask must be applied securely on the face of the patient; 20% dilution of O_2 by ambient air occurs when the mask is not tightly applied and 40% dilution occurs when it is held close to the face. The mask should be applied firmly to the patient's face; when the mask is not fully seated, dilution of up to 20% with ambient air in O_2 and 40% dilution when held close to the face appear [53]. The circle system with fresh gas flow (5 L/minutes) is used as the standard for comparison in anesthesia studies evaluating the effectiveness of different circuits because it allows higher inspiratory flow rates. Some open circuit systems (Bain or Magill) have been shown to be much less efficient [54]. Before preoxygenation, the circuit and reservoir must be filled with O_2. Three preoxygenation techniques are used: spontaneous breathing at FiO_2 of 1 for 2–5 minutes, the "four vital capacities" method, and deep breaths.

3.1.1. Spontaneous breathing at FiO_2 of 1

This preoxygenation technique, first proposed by Hamilton in 1955, is still the reference standard: 3 -minute spontaneous breathing at FiO_2 of 1 level. In patients with normal lung function, this leads to denitrogenation with FAO_2 approaching 95%. Denitrogenation is effective from the first minute of preoxygenation; however, delay these effects with a rapid decline in the fugitive FiO_2 on the run [55]. Although pure O_2 breathing for longer than 1 minute seems it may have little SpO_2 or denitrogenation benefit, it has positive effect on apnea duration before desaturation [51]. In experiments with healthy subjects, the duration of the apnea can be as long as 10 minutes after the 3-minute classic preoxygenation. The apnea time can be increased by an additional 2 minutes by application of positive pressure during the preoxygenation and by ventilation to the mask after induction [56].

3.1.2. Vital capacity maneuvers

The four vital capacity method is used in cases where the patient cannot cooperate, and the duration of apnea without desaturation is shorter after four capacity maneuvers than with spontaneous breathing. Technical requirements are responsible for the limitations of this technic: bag capacity, inspiratory flow, and room gas inspiration. These problems are partially solved with an additional 2-liter bag and a non-rebreathing ambu valve. Vital capacity maneuver begins with forced expiration to optimize FeO_2 increase [57]. To be fully effective, the inspiratory O_2 flow should be greater than the peak inspiratory flow, which is attained by

activating the O_2 system "by-pass" during inspiration; 4 or 5 forced breaths of pure O_2 were found to be as efficient as conventional preoxygenation assessed on the FeO_2 [58]. However, these results were not verified when using PaO_2 for comparison. After four vital capacity maneuvers, it is observed that PaO_2 (293 ± 86 mmHg) is lower compared to after spontaneous ventilation in pure oxygen (397 ± 48 mmHg) [59].

3.1.3. Deep breathing method

Eight deep breaths at a constant oxygen flow of 10 mL/min in a 60-second period create a simple method for preoxygenation. This technique results in an average arterial oxygen pressure of 369 ± 69 mmHg, which is not significantly different from the value achieved by 3 minutes of tidal volume breathing at an oxygen flow of 5 L per minute [42]. It has been argued that the voluntary hyperventilation technique (1 minute in FiO_2 followed by voluntary hyperventilation for 2 minutes) prevents postapneic hypercapnia. Postintubation $PaCO_2$ was similar when preinduction hyperventilation was used as preoxygenation technique or normal respiration was used for 3 minutes [60].

3.1.4. Pressure-assisted ventilation (PSV)

In healthy volunteers, PSV has been shown to improve preoxygenation quality by two mechanisms: accelerate nitrogen excretion and provide better contact between mask and face. In a study of healthy volunteers, the mean expired fraction of O_2 (FeO_2) after 3 minutes of preoxygenation was higher ($p < 0.001$) with 4 cmH_2O (94 ± 3%) PSV/PEEP and 6 cmH_2O PSV/PEEP (94 ± 4%) [61]. Increasing fresh gas flow (FGF) between 5 and 10 L during deep breathing does not provide a significant increase in FiO_2 value during tidal volume breathing [50]. Due to the breathing properties of the circulator system, the minute ventilation during deep breathing can exceed the FGF, causing a reincrease in N_2 in the exhalation gases and therefore lower FiO_2. However, regeneration of N_2 in exhalation gases during tidal volume breathing is insignificant, and thus increasing FGF by 5–10 L has minimal effect on FiO_2 [50].

All investigations have demonstrated that preoxygenation markedly delays arterial oxyhemoglobin desaturation during apnea. [26, 36, 38, 43]. The extent of this delay in desaturation depends on the efficacy of preoxygenation, the capacity for O_2 loading, and the VO_2 [47]. Patients with a decreased capacity for O_2 transport (decreased functional residual capacity, PaO_2, arterial O_2 content, or cardiac output) or those with an increased VO_2 develop oxyhemoglobin desaturation more rapidly during apnea than healthy patients [26, 43].

Farmery and Roe developed and validated a computer model describing the rate of oxyhemoglobin desaturation during apnea [62]. The model is particularly useful for analyzing oxyhemoglobin desaturation values below 90%. These values are dangerous to allow in human subjects because below 90%, there will be a steep decline of PaO_2 due to the sigmoid shape of oxyhemoglobin dissociation curve. In a healthy 70 kg patient, when FaO_2 is progressively decreased from 0.87 (FiO_2 of 1.0) to 0.13 (air), the apnea time to 60% SaO_2 is decreased from 9.9 to 2.8 minutes (**Figure 3**) [43].

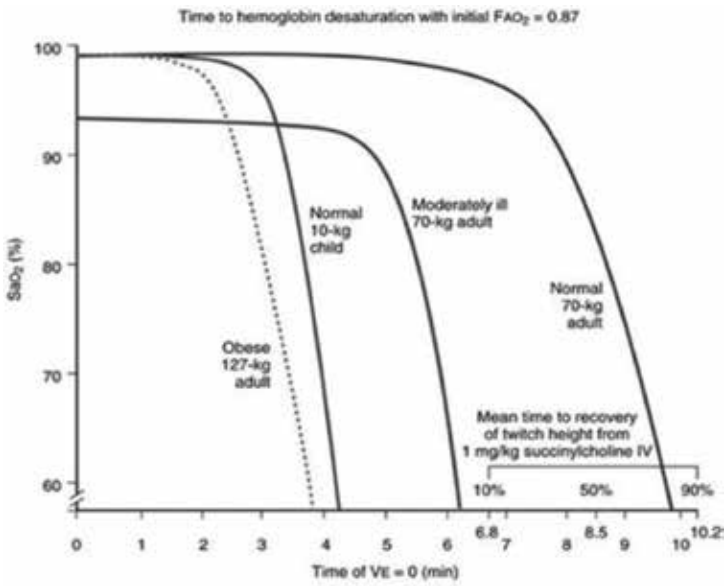

Figure 3. Arterial oxyhemoglobin saturation (SpO_2) versus time of apnea in an obese adult, a 10 kg child with low functional residual capacity and high ventilation, and a moderately ill adult compared with a healthy adult. FaO_2 indicates fractional alveolar oxygen concentration; VE, expired volume [43].

Regardless of the technique used, the goal is to reach the end of maximal preoxygenation, which can easily be measured by most anesthesia monitors.

3.2. Preoxygenation for high-risk patient population

3.2.1. Pregnant patients

Rapid sequence induction/intubation is often used in pregnancies given general anesthesia and preoxygenation is important in these patients. Maximum preoxygenation can be achieved faster in pregnant women than in nonpregnant women due to higher alveolar ventilation and lower functional residual capacity [37, 63]. However, oxyhemoglobin desaturation in pregnant women during apnea develops more rapidly because they are associated with a limited O_2 volume and increased VO_2 in their less functional residual capacities. During the apnea, the time required for SaO_2 to fall to 95% was 173 seconds for pregnant women and 243 seconds for women who were not pregnant in the supine position [64].

Using the 45° head up position causes an increase in the desaturation duration in nonpregnant women, but it is not seen in pregnant women. The size of the uterus may prevent the descent of the diaphragm and may not allow the expected increase in functional residual capacity in the head-up position [64]. Four deep breathing techniques in pregnant women are below the 3-minute tidal volume breathing technique and should not be used except in emergencies [65]. Increased minute ventilation in pregnant women requires the use of an O_2 flow of 10 L/minutes during preoxygenation [66].

3.2.2. Morbid obesity patients

Studies have demonstrated that following preoxygenation with tidal volume breathing for 3 minutes, the time required for SaO_2 to fall to 90% during apnea is markedly reduced in morbidly obese patients (BMI > 40 kg/m^2) compared with nonobese patients [67, 68]. During apnea after preoxygenation, the mean time to reach 90% of SaO_2 in normal body weight patients was 6 minutes, while in morbid obese patients it was 2.7 minutes [69]. Rapid oxyhemoglobin desaturation during apnea in morbidly obese patients was attributed to an increased VO_2 and a markedly reduced FRC.

Spontaneous respiration and effectiveness of eight deep breaths as preoxygenation method are similar in obese patients with previous apnea before reaching 95% of FeO_2 and SpO_2 [70]. Continuous positive airway pressure (CPAP) (7.5 cmH_2O versus Mapleson circuit) during spontaneous ventilation in pure O_2 was observed not to improve the duration of apnea (240 and 203 seconds CPAP versus zero end expiratory pressure, respectively) [71]. PaO_2 improved significantly after intubation when PEEP and PSV applied together after CPAP [72]. PSV improves preoxygenation quality, possibly by increasing alveolar circulation in obese patients [73]. Compared to 5 minutes of spontaneous ventilation with FiO_2 of 1, PSV results in increased FeO_2 (96.9 ± 1.3% versus 94.1 ± 2.0%) and acceleration of nitrogen elimination (185.3 ± 46.1 versus 221 ± 41.5 s) [74]. When combined with recruitment maneuvers, PSV activity has statistical significance in terms of arterial oxygenation [75]. In morbidly obese patients, preoxygenation resulted in better oxygenation compared to 5 cmH_2O CPAP neutral pressure breathing combined with 5 cmH_2O PSV and prevented desaturation episodes [76]. Postintubation PaO_2 was significantly higher in the CPAP/PSV group (32.2 ± 4.1 kPa) than in the control group (23.8 ± 8.8 kPa) ($p < 0.001$). Lower oxygen saturation was lower in the control group (median 98%, range, 83–99%) than the CPAP/PSV group.

The supine position reduces the functional residual capacity due to the upward displacement of the diaphragm. It has been shown that placement of severe obese patients in the 25° up position during preoxygenation prolongs the desaturation time [77]. Some anesthetists may prefer awake fiberoptic intubation instead of rapid sequence induction/intubation in morbid and super morbid obese patients (BMI > 50 kg/m^2), especially when they have associated problems [78].

3.2.3. Pediatric patients

Respiratory physiology of young children is age-specific. The inhibition of intercostal tone with general anesthesia is responsible for the reduction in FRC. Hypoxia occurs more rapidly in children due to higher VA/FRC ratio, higher O_2 consumption and lower O_2 reserves. Children exhibit a delay of approximately 80–90 seconds before reaching FeO_2 values close to 90% when breathing at FiO_2 of 1 level [79]. After a period of at least 2 minutes breathing at FiO_2 of 1 and after muscle paralysis, the duration of apnea before the SpO_2 reaches 90% is found to be 96.5 seconds in children less than 6 months of age, 160.4 seconds in 2–5 year olds, and 382.4 seconds in 11–18 year olds [80]. In children younger than 6 months, even shorter apnea time limits, on the order of 70–90 seconds have been reported [16]. The duration of apnea required to reach a SpO_2 of 98, 95, or 90% is significantly increased when the preoxygenation is extended for 1–2 minutes, but no benefit was found by extension past 3 minutes [18].

Studies have shown that maximal preoxygenation (EtO_2 = 90%) can be achieved in children faster than in adults [79, 81]. With tidal volume respiration, almost all children can reach 90% EtO_2 within 100 seconds, whereas it can be reached within 30 seconds by deep breathing [79, 81]. However, since children have a lower functional residual capacity and a higher VO_2 than adults, they may be at a greater risk of developing hypoxia when interruption of O_2 transport occurs, such as during apnea or airway obstruction [82–84]. In a comparison of three groups of children who breathed O_2 (FlO_2 = 1.0) with tidal volume breathing for 1, 2, and 3 minutes before apnea, the time needed for SaO_2 to decrease from 100 to 95% and then to 90% during apnea was least in those who breathed O_2 for 1 minute and there was no difference between those who breathed O_2 for 2 and 3 minutes [85]. Based on these findings, 2 minutes of preoxygenation with tidal volume respiration seems to be sufficient to provide a maximum benefit and a safe apnea period [85]. The advantage of preoxygenation is greater in a larger child than in a baby. For example, in an 8-year-old child, the duration of the apnea-safe period may be extended to 5 minutes or longer with preoxygenation, whereas the duration is 0.47 minutes without preoxygenation [86]. The smaller the child, the faster the start of desaturation [80, 83, 84]. After the onset of apnea, most infants reach 90% SpO_2 within 70–90 seconds (despite preoxygenation) and this time may be shorter in the presence of upper respiratory tract infection [16, 87]. Pediatric anesthesiologists expressed concern about the use of the "adult" version of the rapid sequence induction/intubation technique in children [88]. Concerns include the safe duration of apnea and the potential for airway obstruction induced by cricoid compression. A modified version of the rapid sequence induction/intubation technique appears to be more appropriate for children with emphasis on full muscle relaxation and gentle manual ventilation using high O_2 concentration with adequate anesthesia depth without cricoid pressure before intubation [89].

3.2.4. Elderly patients

Old age is associated with significant structural and physiological changes in the respiratory system [90, 91]. The changes also include a reduction in elastic recoil with weakened respiratory muscles and parenchymal changes in the lungs. Lung volumes are reduced by increased closure volume, which causes ventilation-perfusion mismatch, reduced pulmonary reserve, and impaired oxygen uptake in the lung. While basal VO_2 declines with aging, impaired O_2 intake creates a faster desaturation during apnea under anesthesia [91]. In elderly patients, tidal volume breathing of 3 minutes or longer has been shown to be more effective than four deep breathing techniques [92, 93].

3.2.5. Patients with lung diseases

Severe pulmonary disease is associated with decreased FRC, increased ventilation-perfusion incompatibility, and increased VO_2, which can reduce the safety margin. Anesthesia has been shown to cause further deterioration of gas exchange in patients with chronic obstructive pulmonary disease [94]. As well as in aspiration, even short ventilation interruptions can cause desaturation. Besides, atelectasis is not a consequence, presumably the chronic hyperinflation of the lungs resists volume decline and collapse [95]. For maximum preoxygenation in these patients, 5 minutes or more may be needed with tidal volume breathing [96].

3.2.6. Patients in high altitude

High altitude does not shift inhaled O_2 concentration but reduced barometric pressure causes in a decrease partial alveolar pressure and arterial PO_2 [97]. As altitude increases, PaO_2 decreases exponentially. Patients at high altitudes may need longer lasting preoxygenation.

3.3. Techniques to improve preoxygenation

3.3.1. Apneic diffusion oxygenation

Following preoxygenation, "apneic diffusion oxygenation" is an effective maneuver that prolongs the safe duration of apnea [32, 98–102]. The physiological basis of this maneuver is: In adults, VO_2 averages are 230 mL/min during apnea, whereas CO_2 delivery to alveoles is only 21 mL/min [32]. The remaining 90% (or more) of CO_2 is buffered in body tissues. As a result, O_2 enters the lung by diffusion, provided that the lung volume initially decreases by 209 mL/min and forms a pressure gradient between the upper airway and the alveoli, and the airway is not obstructed. If CO_2 cannot be excreted, $PaCO_2$ increases to 8–16 mmHg for the first minute of apnea followed by a linear increase of about 3 mmHg/min [103]. The advantage of apneic diffusion oxygenation depends on reaching the maximum preoxygenation before apnea, remaining open in the respiratory tract, and is on the presence of high FRC relative to body weight. Although the drop in PaO_2 is directly related to PaO_2, SpO_2 remains greater than 90% as long as the hemoglobin is oxygenated again in the lungs [46, 99, 100, 104]. SpO_2 decreases only after the O_2 stores in the lungs are exhausted, and PaO_2 falls below 60 mmHg. When SpO_2 becomes <80%, the saturation reduction rate is approximately 30%/min. In the presence of an airway obstruction, the volume of gas in the lungs decreases rapidly and the intrathoracic pressure decreases with respect to lung compliance and VO_2. When airway obstruction is relieved, a rapid O_2 flow begins in the lungs and preoxygenation with high FiO_2 improves [46]. Some studies have shown that through an open air pathway, apneic diffusion oxygenation can keep the SpO_2 value above 90% for up to 100 minutes [99, 100]. When FiO_2 is at a high level, a small increase can cause a fairly disproportionate delay in hemoglobin desaturation. The delay in hemoglobin desaturation obtained by FiO_2's raising from 0.9 to 1.0 was above that obtained by FiO_2's raising from 0.21 to 0.9 (**Figure 4**) [105].

Apneic diffusion oxygenation can be achieved with maximum face mask preoxygenation following O_2 insufflation to 15 L/minutes via a nasopharyngeal or an oropharyngeal cannula or a needle inserted into the cricothyroid membrane. In healthy patients with a healthy airway, this technique can provide adequate oxygenation for at least 10 minutes. Although oxygenation can be maintained for a longer period of time, a limiting factor of apneic oxygenation is the gradual rise of $PaCO_2$ during apnea [103].

3.3.2. Continuous positive airway pressure (CPAP) and positive expiratory pressure (PEEP)

The CPAP usage in the preoxygenation delayed the desaturation period by mechanical ventilation using positive end expiratory pressure (PEEP) for 5 minutes before removing the mask and securing the airway [106, 107].

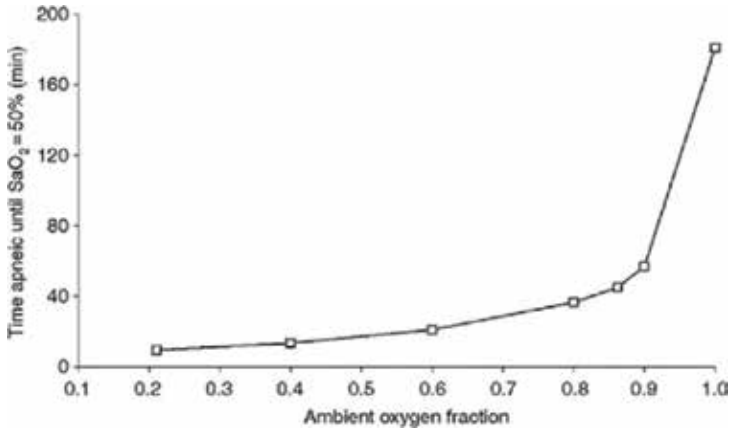

Figure 4. The time (duration of apnea) required to reach 50% SaO_2 with an open airway exposed to various ambient O_2 fractions [105].

3.3.3. Noninvasive bilevel positive airway pressure (BİPAP)

BiPAP combines pressure-assisted ventilation (PSV) and CPAP advantages and keeps the lungs open during the respiratory cycle. BiPAP has been used during preoxygenation to decrease intrapulmonary shunting and to increase the margin of safety during apnea in morbidly obese patients [108]. This technique is also used to reduce postoperative pulmonary dysfunction and to treat patients with respiratory insufficiency from various etiologies [109].

3.3.4. Transnasal humidified rapid insufflation ventilatory exchange (THRIVE)

THRIVE is a new technique that is available for use in critically ill patients and in patients with difficult airways. The technique combines the benefits of apneic oxygenation and CPAP with a reduction in CO_2 levels through gaseous mixing and flushing of the dead space [110]. THRIVE is used as standard with a nasal, high flow oxygen delivery system, as sold in the market. The THRIVE technique has been shown to significantly prolong the period of apnea safety while avoiding CO_2 increase [111].

3.4. Potential risks of the preoxygenation

- Delay in the diagnosis of the esophageal intubation.
- Absorption atelectasis.
- Production of reactive oxygen radicals.
- Cardio-cerebrovascular responses.

It causes a decrease in heart rate and cardiac output. Systemic vascular resistance and arterial blood pressure increase [112–114]. These changes are detected by chemoreceptors or baroreceptors. Direct coronary vasoconstrictor effect of hyperoxia is due to oxidative inactivation of nitric oxide and other vasodilators released by vasculature [115–117]; it reaches up to collapse

of the endothelin and K^+ channels sensitive to ATP [118, 119]. It is well known that high O_2 inhalation may reduce cerebral blood flow due to vasoconstriction [120–123]. It has been proposed that this effect may be because, at least in part, of the associated decrease in $PaCO_2$ that accompanies high O_2 breathing rather than to a direct effect of O_2 [121]. The decline mechanism in the $PaCO_2$ is that: When PaO_2 is increased by 100% O_2 inhalation, the CO_2 dissociation curve for blood changes (Christiansen-Douglas-Haldane effect), thus CO_2 affinity for blood is reduced. This causes an increase in the cerebral tissue PCO_2 and hydrogen ion concentration, which stimulate respiration that causes cerebral vasoconstriction with a decrease in $PaCO_2$ [122, 123]. Researchers assessed the effect of hyperoxia on cerebral oxygen consumption using a functional magnetic resonance technique and found that hyperoxia caused a reduction of about 20% in cerebral O_2 consumption and decreased neuronal activity [122]. The reduction in cerebral O_2 consumption is thought to be due to the fact that reactive oxygen radicals damage lipids and proteins and reduce enzyme activity in the oxidative metabolic pathways. Studies in animal models have shown that hyperoxia causes vasoconstriction and causes a decrease in blood circulation in the peripheral vascular beds, including the kidney and gastrointestinal tract [120, 124, 125]. However, it is doubtful that changes in peripheral vascular beds will have any significant clinical effect during preoxygenation. So far, cardiovascular findings do not provide any justification for limiting the use of preoxygenation.

4. Maintenance of a patent airway

There is a dynamical balance between O_2 and CO_2 during breathing. The volume of CO_2 passing from the pulmonary circulation to the alveolar space is 80% of the oxygen volume moving in the reverse direction. This changes radically at the onset of apnea. During apnea, the rate of oxygen extraction from the alveoli remains at 250 mL/min without being affected. The amount of CO_2 entering the alveoli is very low. The reason is that CO_2 is more water soluble than oxygen. For this reason, only 10% of the CO_2 produced per minute (about 20 mL) reaches the alveolar space. The remaining 90% remain molten in the textures. Therefore, the volume of gas in the lungs decreases rapidly during apnea, and if the airway becomes clogged, intrathoracic pressure decreases due to oxygen consumption and thoracic compliance. The closed airway apex begins with an intrathoracic pressure equal to or slightly greater than the ambient pressure. Oxygen uptake causes by an almost subatmospheric intrathoracic pressure. During long-standing apnea, the intrathoracic pressure may be much lower than the environmental pressure, and the alveolar partial pressure of oxygen is significantly dangerously reduced. An open airway will allow oxygen to spread to the apneic lung. Providing an open airway and exposing 100% oxygen creates "apneic mass movement oxygenation," which has been shown to provide oxygen saturation for up to 100 minutes in animal and simulated human studies. If the denitrogenesis of the alveolar space is as complete as possible and a tight compliance mask is used, this passive diffusion of oxygen is more effective. It is important to provide a very high oxygen fraction FiO_2 in order to extend the safety time of the apnea; increasing the oxygen fraction applied to the respiratory tract from 90 to 100% doubles critical hypoxia time with open air [126]. Increasing the FiO_2 applied to the airway from 21 to 90% has a much greater effect on the critical hypoxia time. In a patient with an apnea, 100% oxygen administration to the patent airway will delay the onset of critical hypoxia, but this approach will not reverse the

hypoxemia that is currently developing. Moreover, after a while, it does not prevent continuous development of hypercapnia, which is life threatening and acidosis related to hypercapnia.

5. Reoxygenation

When airway obstruction is relieved during apnea, there is a flow of gas through the pressureless thorax. Securing a high FiO_2 during this one passive inhalation saves time to save the airway. Securing a high FiO_2 during this one-time passive inhalation may lead to a significant prolongation of the duration of the apnea. If airway obstruction is relieved with 100% oxygen, the patient is likely to have a temporary improvement in hemoglobin oxygen desaturation, even though the tidal volume is not maintained and inspired oxygen volume is small.

6. Hemoglobin concentration

The prominence of hemoglobin is not that it is an oxygen storage but it is an efficient oxygen transport from the lungs to the tissues. Anemia causes a small decrease in the time of critical hypoxia; however, this effect will also be more pronounced in patients with reduced FRC.

7. Metabolic rate

Metabolic rate has a simple and predictable effect on the rate of oxygen uptake and hence the duration of critical hypoxia. Increasing the oxygen consumption from 250 to 400 mL/min reduces the time for SpO_2 to increase from 40 to 50% [126].

8. Physiological shunt and dead space

The venous shunt reduces the PaO_2 and SpO_2 foreseeably, but severe hypoxemia develops when the accessible oxygen stores are exhausted. However, many patients with venous shunts also have a reduced FRC (e.g., pulmonary edema), which will accelerate the onset of hypoxia.

8.1. Physiopathological responses to hypoxia

Heart attacks, stroke, and cancer have become the most common causes of death in the twenty-first century, as the average age in many countries around the world is constantly increasing. The causes of these diseases are many and varied; it indicates genetic predisposition and environmental effects. But limited oxygen is a common feature that is contributing to the development of these pathological conditions all around. However, cells and organisms can trigger adaptive responses aimed at helping them cope with these threats to hypoxic conditions. Under this heading, the role of hypoxin in three pathological conditions consisting of myocardial, cerebral ischemia, and tumorigenesis will be briefly explained. The ability to

sustain oxygen homeostasis is crucial for survival of all vertebrate species. For the O_2 presentation, correct forming of complex platform such as entry (lungs), transport vehicles (erythrocytes), motorways and secondary roads (vasculature), and repulsive force (heart) during development and regulations in organism entry form the basis for oxygen homeostasis.

8.2. Physiological responses to hypoxia

8.2.1. Systemic responses

Hypoxia and hyperoxia are detected by specialized chemoreceptor cells. In cases where the use of O_2 is impaired, chemoreceptor systems rapidly change blood circulation as well as pulmonary ventilation and perfusion to optimize O_2 delivery to tissues. This process is based on the direct response of the neuroepithelial bodies present in the airway to the specialized chemoreceptor cells, such as arterial circulation carotid bodies, and the hypoxia of vascular smooth muscle cells.

8.2.2. Vascular smooth muscle cells

While the peripheral vein are enlarged in response to low oxygen, the veins in the pulmonary vein narrows in order to achieve ventilation-perfusion matching by removing blood from areas where ventilation is worse [127]. Hypoxic pulmonary vasoconstriction is a rapid response in the pulmonary arteries and venules. It is abundant in small resistance arteries. Pulmonary vein is an intrinsic feature of the vein smooth muscles and begins with the inhibition of one or several of the various K^+ channels that regulate the membrane potential [128]. The resulting depolarization activates voltage-gated Ca^{+2} channels, and activation of the channels increases the systolic calcium level and leads to myocyte constriction (**Figure 5A**). While K^+ channels are the effects of hypoxic pulmonary vasoconstriction, it does not known that whether they are intrinsically O_2-sensitive or under the control of an actual O_2 receptor. Hypoxic vasodilatation is another rapid response that increases blood perfusion in O_2-deprived tissues. This is especially indicated in coronary and cerebral vessels. Hypoxic vasodilation is mediated in part by K-ATP channels opened in response to hypoxia-induced ATP reduction in vascular smooth muscle cells (**Figure 5B**) [129].

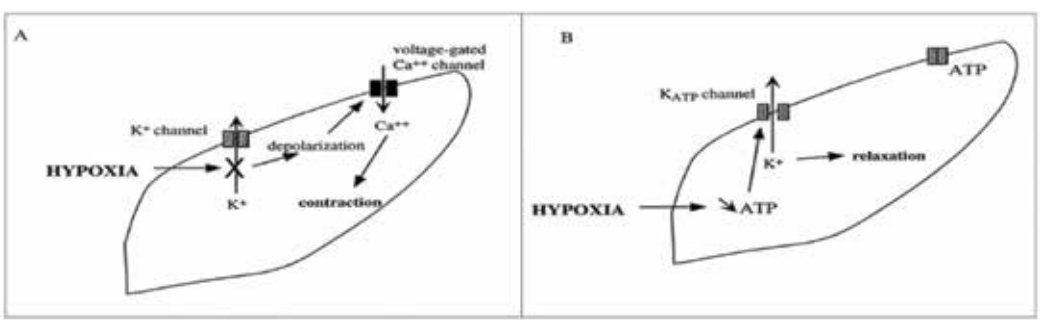

Figure 5. Schematic representation of the response of vascular smooth muscle cells to hypoxia. (A) Pulmonary smooth muscle cells and (B) peripheral smooth muscle cells [129].

However, there are other O_2-sensitive mechanisms that most likely function by regulating the entry of Ca^{+2} into the cell.

8.2.3. Carotid and neuroepithelial bodies

Airway neuroepithelial bodies perceive changes in oxygen inspired, while carotid objects perceive arterial oxygen levels. Both of them respond to low O_2 presentation by initiating activity in efferent chemosensory fibers to form cardiorespiratory regimens in the event of low O_2 [130, 131].

The induction activity of chemoreceptor cells by hypoxia/hypoxemia is dependent on the presence of membrane K^+ channels inhibited by low O_2. As a result, increased cytosolic calcium concentration causes activation of neurotransmitter release and efferent sensory fibers.

8.2.4. Regulation of the cellular metabolism

One of the most essential parameters that healthy cells have to maintain is high ATP content. Cell death occurs when the ATP production does not meet the energy required to sustain the ionic and osmotic balance. When ATP levels fall, ion-motivated ATPase regeneration occurs, leading to membrane depolarization, Ca^{+2} flow into the cell from voltage-gated Ca^{+2} channels, and subsequent activation of calcium-dependent phospholipases and proteases. These events result in uncontrolled cell swelling, hydrolysis of the major cell components, and eventual cell necrosis (**Figure 6**) [132].

8.2.5. Effects of hypoxia on mitochondria

Oxygen deprivation is generally considered mitochondrial respiratory failure in the case of hypoxia or ischemia. In fact, mitochondria are the main source of molecules with high-energy

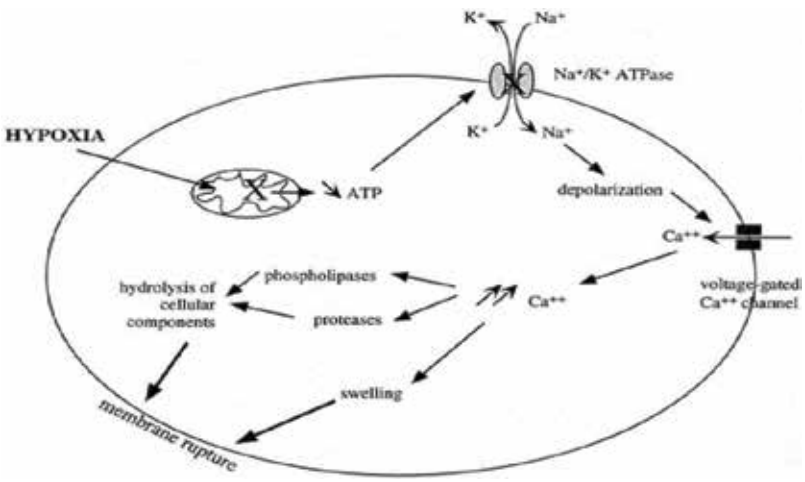

Figure 6. Schematic representation of the cascade leading to cell death when cells are exposed to severe hypoxia [132].

phosphate bonds in normal cells. Electron transport into O_2 in the oxidation of NADH and $FADH_2$ is tightly bound by ATP synthesis. Electron transport is carried out via protein-bound redox centers to complex III then (Co-enzyme Q-cytochrome c reductase) and complex IV from complex I (NADH-coenzyme Q reductase) or II (succinate-coenzyme Q reductase) and forms an electrochemical H + gradient in the inner membrane of the mitochondria. This gradient is used for ATP synthesis by complex V (ATP synthase) after electrochemical gradient: this process is known as oxidative phosphorylation.

Studies on isolated mitochondria have shown that the basic effect of decreasing O_2 on mitochondrial respiration is inhibition in the respiratory chain and increase in proton leakiness while phosphorylation is less affected [133, 134].

8.2.6. Adaptation to hypoxia

Hypoxia adaptation at the cellular level is accomplished by increasing the efficiency of the energy-producing pathways in a basically increased anaerobic glycolysis activity, while reducing energy consuming processes [135]. Ion-motive ATPase and protein synthesis are predominant processes in energy consumption in cells at standard metabolic rate, producing over 90% of ATP consumption in mouse skeleton and 66% in mouse thyocytes [136]. Hepatocyte studies have shown that protein synthesis is largely inhibited in response to hypoxia [137]. Buttgereit and Brand [138] have shown that ATP-consuming processes are in fact organized in a hierarchy, protein synthesis and RNA/DNA synthesis are the first inhibitory processes when energy becomes limited, and Na/K pump and Ca cycle have the highest priority. This phenomenon, also known as oxygen adaptation, involves very precise regulatory mechanisms at the level of translation initiation [139].

Hypoxic cells turn to glycolysis to meet energy needs. Oxygen-dependent mitochondrial respiration from two pathways of ATP production lowers oxygenation than oxidative phosphorylation in oxygen-independent glycolytic ATP production. In the presence of sufficient glucose, glycolysis may continue to produce ATP, depending on the increased activity of glycolytic enzymes. Phosphofructokinase is the major regulator that controls carbon flux by glycolysis. It is allosterically activated by ADP and AMP and inhibited by ATP; in this way, the rate of glycolysis is regulated according to the energy requirement. However, the most potent allosteric activator is fructose-2, 6-biphosphate [140]. The synthesis and degradation of the fructose-2, 6-biphosphatase are dependent on a single enzyme (6-phosphofluoro-2-kinase/fructose-2, 6-biphosphate [PFK-2]). This enzyme is regulated within minutes by phosphorylation via AMP-activated protein kinase (AMPK) [141], but the expression is also enhanced by transcriptional activation via hypoxia-induced factor-1 (HIF-1) [142]. AMPK phosphorylates PFK-2 in a single site resulting in an increase in the Vmax of kinase activity, thus the allosteric activation of phosphofructokinase enhances.

The active kinase opens the ATP-producing catabolic pathways and closes the ATP-consuming anabolic pathways [143, 144]. This acute direct phosphorylation is chronically provided by gene expression. Phosphorylation of PFK-2 is an example of this. AMPK activation has been reported to transport glucose-transporter Glut-4 to the plasma membrane, resulting in glucose uptake. Glut-4 increases the expression of mitochondrial enzymes that play a role in the

long-term hexokinase and tricarboxylic acid cycle and in the respiratory chain. On the other hand, AMPK directly inhibits the expression of fatty acid, triglyceride, and sterol synthase and the expression of fatty acid synthase and gluconeogenesis enzymes [145].

8.2.7. Regulation of the gene expression

When faced with hypoxic difficulties, various responses are developed by cells and tissues:

- Increased ventilation and heart rate
- Return from aerobic metabolism to anaerobic metabolism
- Promotion of increased vascularization
- Strengthening the O_2 transport capacity of blood.

Most of these processes take place very early with the onset of hypoxia and are caused by the activation of existing proteins; but in the long run, all of these responses are mediated by the upregulation of genes encoding key actors, for example:

- Tyrosine hydroxylase, which plays a role in dopamine synthesis in carotid body type I cells.
- Glycolytic enzymes phosphoglycerate kinase 1, pyruvate kinase m, phosphofructokinase, aldolase A, glyceraldehyde 3-phosphate dehydrogenase enolase 1, and glucose carriers Glut-1 and Glut-4.
- VEGF and PDGF to induce angiogenesis and NO synthase that increases vasodilatation
- Transferrin receptors supporting erythrocyte production [146]. The transcriptional side is largely mediated by the HIF-1 activity.

HIF-1 is a heterodimeric factor consisting of HIF-1α and HIF-1β/ARNT. Both subunits belong to the Per-ARNT/Ahr-Sim family of bHLH transcription factors. While the HLH and PAS motifs play a role in dimerization, the main coil is the DNA-binding site. The HIF-1 [alpha] protein contains two transactivation regions at the C-terminus. ARNT is structurally expressed and is located in the nucleus. On the other hand, hypoxia accumulates when HIF-1α mRNA levels are constant in normoxia and hypoxia, and normoxide protein is rapidly destroyed. Normoxide targets the HIF-1α polyubiquitin and destroys the protozoa. In addition to the reduction of hypoxic synthesis of all proteins, ARNT and HIF-1α proteins are translocated efficiently due to the presence of the internal ribosome entry in the mRNA corresponding to the normoxia and hypoxia and normoxside [147].

HIF-1α contains an oxygen-dependent degradation site in which a highly conserved binding site for the tumor suppressor von Hippel Lindau protein (pVHL) is present. The pVHL targets a HIF-1α degradation to form a complex that activates the E3 ubiquitin ligase that ubiquitinates HIF-1α. Inactivation of pVHL is associated with von Hippel Lindau cancer syndrome. It prevents the binding of pVHL mutations to HIF-1α, leading to structural expression of this transcription factor and target genes. Such mutations probably increase angiogenesis potential

by continuous VEGF synthesis. The interaction between HIF-1α and pVHL is regulated via the hydroxylation of two proline residues of HIF-1α with the prolyl hydroxylase enzyme. In the absence of oxygen, this enzyme is no longer active: unmodified prolyl-HIF-1α does not interact with pVHL and accumulates [148, 149]. The absolute oxygen requirement of this prolyl hydroxylase suggests that this enzyme may function as a direct oxygen sensor. Other pathways indicate that HIF-1α stabilization and/or synthesis is also dependent on the PI-3 kinase/Akt pathway in the case of hypoxia. The usage of PI-3 K inhibitors prevents accumulation of HIF-1 [150]. The increase in HIF-1α synthesis is also dependent on the PI-3 K/Akt pathway [151].

HIF-1α stabilization is the first step in HIF-1 activation: For complete transcriptional activity, sufficient redox conditions, separation from chaperone HSP90, phosphorylation as well as coactivators such as CBP/p300 or SRC-1 are required [152, 153]. Hypoxia directly regulates the association of HIF-1α with the coactivator CBP/p300. Similarly to prolyl hydroxylase, it hydroxylates the HIF-1α carboxy-terminal transactivation site on Asn 803 of asparagyl hydroxylase, whose activity is tightly bound to the oxygen. This modification prevents the association with CBP/p300 in the case of normoxia [154].

HIF-1α is not only essential for a variety of physiological responses in chronic hypoxia but also for embryonic survival and cardiac and vascular development. Hif1a$^{-/-}$ mice are not viable: development of Hif1a$^{-/-}$ embryos arrests by day E9.0 and mice die by E10.5 [155, 156]. There is a marked regression of blood vessels in the cephalic region and replacement by a smaller number of enlarged vascular structures. Loss of pericyte support of the endothelium leading to vascular regression is probably responsible for these defects. Massive cell death in cephalic mesothelium was observed concurrent with the deterioration of the vessel development. Heart development in HIF-1$\alpha^{-/-}$ embryos is also abnormal. In ARNT$^{-/-}$ mice, embryonic death probably occurs due to insufficiency of the embryonic component required for vascularization of placenta [157]. Observation of similar vascular abnormalities in HIF-1α and VGEF-deficient embryos suggests hypoxia-induced overexpression in VEGF for the development of the vascular system.

8.2.8. Pathological responses to hypoxia

Hypoxia due to deteriorated blood flow has detrimental effect on organ structure and function. This is especially true in prolapse (cerebral ischemia) and heart infarction (myocardial ischemia). Hypoxia also plays an important role in the regulation of tumor growth and metastasis. Here, we describe the role of hypoxin in these three pathological conditions.

8.2.9. Cerebral ischemia

High energy requirements compared to low energy reserves make the brain particularly susceptible to hypoxic conditions. Although the brain produces a small fraction of total body weight (2%), it proportionally accounts for a large percentage of O_2 consumption. The increased O_2 requirement in physiological conditions is met by a rapid and satisfactory increase in cerebral blood flow. However, hypoxemia and ischemia in children suffering from severe asphyxia and in prolapse sufferers result in brain damage. Longer periods of

hypoxia/ischemia lead to greater effects in the brain. The most sensitive areas appear to be the brain stem, hippocampus, and cerebral cortex. If the damage processes and eventually oxygenation is not restored, it becomes irreversible. Acute cell death is primarily caused by necrosis, but hypoxia also causes by late apoptosis. Although it is the only way to protect tissue, it should be noted that mainly reactive oxygen species reperfusion induces cell death through production and inflammatory cell infiltration. If the decrease in pO_2 is not too severe, it suppresses some of the cell functions; for example, proton synthesis and spontaneous electrical activity are suppressed and this condition is called penumbra, which is characterized with return when O_2 is provided [158, 159].

8.2.10. Myocardial ischemia

Acute coronary syndromes resulting from occlusion of one of the coronaries expose heart to ischemic conditions. If reperfusion is achieved after short ischemic periods (<20 minutes), it is reversible and not associated with necrosis development, but results in stunning phenomena. If the coronary occlusion duration goes beyond this point, a necrosis wave propagates from the subendocardium towards the subepicardium. After a few hours, reperfusion does not diminish the size of myocardial infarction.

Within seconds of cessation of blood flow energy metabolism shifts from mitochondrial respiration to anaerobic glycolysis. Concurrent active contractions are reduced and then terminated. Accumulation of lactate and protons in cardiomyocytes induces acidosis and osmotic load and subsequent cell edema. In addition, intracellular Ca^{+2} increases, probably due to the combined effect of Na^{+}/Ca^{+2} modulators activated by cellular acidosis. If this happens, it will lead to cell necrosis [160]. To restore aerobic metabolism and to protect ischemic myocytes, it is necessary to restore the arterial flow. However, this situation itself increases the damage. This process is called ischemia-reperfusion injury. In the first few minutes of reperfusion, a large amount of released reactive oxygen radicals is a possible cause of this contractile failure.

8.2.11. Tumor angiogenesis

The onset of new vascularization in many primary tumors is defined as the angiogenic switch. Several key signaling events have been identified that involve immune/inflammatory responses and genetic mutations, but metabolic stress (hypoxia) is probably the most important of these factors [161, 162]. Tumor cells survive in the fluctuations of HIF-1 activation in oxygen tension. Various studies using HIF-1 mutant cells have shown that HIF-1 has profound effects on tumor biology. For example, tumors arising from embryonic stem cells with HIF-1α defect show abnormal vascularity and low growth rate [39]. Furthermore, HIF-1 is upregulated in a wide range of tumors, and there are important links between tumor grade, vascularization, and HIF-1α overexpression [163, 164]. This expression pattern suggests that tumor cells respond to hypoxia caused by HIF-1–mediated angiogenic protein expression. The VEGF is the strongest of these and its expression is regulated by HIF-1. In addition to promoting VEGF secretion, HIF-1 is also important for hypoxia adaptation of tumor cells [165].

8.2.12. Determination of hypoxemia

Tumor hypoxia is the strongest prognostic factor in various cancers. Hypoxic cells contribute to intrinsic radiation resistance. Apoptosis resistance and increased metastasis capacity are other contributing factors to this negative outcome. Therefore, the factors that aim to determine tumor oxygenation have serious clinical safety. A number of studies aim to identify a good hypoxia marker that can be used in immunomicroscopy studies [166]. The use of 2-nitromidazole specifically binding to hypoxic cells has been suggested; pimonidazole and EF5 are the best known of these. Reduction enzymes metabolize these drugs in the presence of oxygen, but when there is no oxygen they are converted to highly reactive free radical molecules that are covalently bound to protein and DNA. Subsequently, drug-protein binding may be detected by specific antibodies. Studies similar to the work of Evans and his colleagues showed the suitability of this method. However, these drugs have the disadvantage that they need to be administered from a tissue sample.

The discovery that HIF-1α specifically undergoes hypoxic upregulation and is rapidly destroyed in the presence of oxygen suggests that this protein may be an endogenous marker of this kind. Several studies examining HIF-1α as an endogenous hypoxia marker have confirmed the spatial association of HIF-1α with EF5 and pimonidazole [167]. It should be noted that the use of HIF-1α as a hypoxia marker is not easy because the level of HIF-1α is also regulated by factors other than hypoxia, such as oncogenic mutations [168].

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Endotracheal Intubation

Chapter 3

Indications for Endotracheal Intubation

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Additional information is available at the end of the chapter

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Abstract

Endotracheal intubation may be required when respiratory distress or airway integrity cannot be achieved or maintained for any reason. It should be considered that intubation may be required when evaluating the patient, and that in the long term, airway protection will be needed or that the problem cannot be solved by noninvasive ventilation via airway aids and devices. Identifying the problem causing the patient's respiratory failure helps in making the decision to intubate. In fact, the clinician must be fast and self-confident when deciding on intubation. It is difficult to decide in some complex situations. It is very important to evaluate the patient, according to clinical status, age, and comorbidity, and to determine urgent intubation need. In non-diagnostic cases, further research is needed to investigate the causes of the condition such as hypoxia/hypercapnia resulting in patient respiratory distress. Different voice tone, swallowing difficulties, coughing attacks, stridor, dyspnea can be a sign of upper airway obstruction. Arterial blood gas analysis will facilitate our decision to make intubation. Noninvasive pulse oximetry and continuous capnography values may also be a guide, but the most important thing is that delayed intubation decision may bring life-threatening situations.

Keywords: intubation, endotracheal, indications, airway problems, rapid sequence intubation, nasotracheal intubation

1. Introduction

Endotracheal intubation is the placement of a tube into the trachea, either orally or nasally for airway management. Endotracheal tube forms an open passage in the upper airways. To be able to ventilate the lungs, the air must be free to enter and exit the lungs. The patient is connected to the mechanical ventilator to provide continuous respiration with an endotracheal

tube. The utilized tube is a flexible plastic tube which is called endotracheal tube placed on the trachea and has a cuff part that can be inflated with air to prevent airway leakage. To facilitate the placement of the endotracheal tube, general anesthesia induction is applied to patients who will be operated and have sufficient fasting time. In emergency cases, endotracheal intubation is performed with various stages and procedures. Sometimes, patients are intubated at the scene or in the emergency room of the hospital. Because the patients' clinical status cannot be fully evaluated during the intubation procedure at the scene, sometimes drugs cannot be given [1, 2]. Deep sedation, rapid sequence intubation (RSI), is performed according to the patient's clinical condition in the hospital and also in patients with Glasgow coma scale (GCS) 4, and, below, the procedures are done without medication. Intubation without medication to trauma patients with high GCS (above 4) is not safe, resulting in intracranial pressure increase, vomiting, esophageal intubation, and aspiration risk. Special procedures are required in pediatric patients and newborns, and their indications for endotracheal intubation can show variability.

Airway management is one of the most important skills of the physician; failure to provide required airflow can cause death or sequelae of the patient, especially in emergency conditions. The control of circulation and intubation, without losing time, in cardiac and respiratory arrest, saves the patient from hypoxia, improving quality of life in the long term [3–6]. If the difficulties in patient airway management are predictable (forced airway, lack of mask ventilation), it is important to take precautions and to ensure that adequate instruments and equipment are available [7]. Studies have shown that the likelihood of the rescue of the patient's life increases if life support is initiated within the first 4–8 minutes [8]. It is known that the treatment of nasal oxygen moistened with high flow prevents hypoxia and desaturation, while intubation is performed under emergency conditions [9, 10]. Its use is becoming widespread in the intensive care unit because of its reliability, ease of use, accessibility, and reduction of complication rate [11]. Although high-flow nasal oxygen therapy is sometimes considered an alternative to intubation, it should be remembered that these patients may need noninvasive ventilation (NIV) and intubation in the long term [12]. Although hypoxemia is a component of respiratory failure, tissue hypoxia and lactic acidosis are frequently encountered as a result of ventilation and perfusion imbalance as well as gas exchange dysfunction. As a result, complex and difficult-to-treat metabolic disorders and sometimes mixed decompensated respiratory and metabolic disorders can develop, bringing the clinical situation of a patient to an irreversible state, resulting often in organ failure [13, 14].

Endotracheal intubation using rapid sequence intubation (RSI) is the cornerstone of emergency airway management. RSI is a safe method in patients with a full stomach but is not beneficial in apneic unconscious patients (GCS <4). A patient suspected of difficult respiratory tract should be approached carefully for RSI. If a difficulty is expected, an awake technique (e.g., fiber optic intubation) is recommended. Alternatively, an anesthesiologist may be called to help secure the airway of a patient having intubation difficulty. It may be beneficial to use evidence-based and scientific techniques when deciding on intubation in emergency situations, but these procedures should be a standard practice in that clinic [6, 15, 16].

It is sometimes difficult to determine the intubation decision and its indications while evaluating a patient. Clinical experience is required to identify signs of respiratory failure and determine

whether it will be reversible in the long term [17, 18]. Before the patient is intubated or until the intubation decision is made, mask ventilation is made, or high-flow nasal oxygen is used [19, 20]. High-flow oxygen therapy helps in difficult airway conditions such as in obesity or in the difficulty of mask ventilation [21, 22].

The fact that the procedure to be performed after the endotracheal intubation decision is invasive, requiring multiple medications and not waking up of the patient due to the sedatives for hours and hypotension risk are the disadvantages of endotracheal intubation [23]. In the opposite case, the patient's clinical condition that can worsen is unpredictable. If tardy for endotracheal intubation, hypercapnia, hypoxia, acidosis, and arrest as a result of circulation collapse in cases where it cannot be compensated take place. For this reason, the patient's clinic, existing diseases, laboratory tests, and blood gas results should be evaluated together, resulting in a better decision. Although evaluation is not possible in case of emergency, the simple imaging methods and ultrasonography can help physicians. In conscious patients with spontaneous breathing and hypoxia without hypercarbia in room air, improvement of saturation after oxygen treatment with 2–4 L/min nasal/mask and reaching a normal value of spontaneous respiration after noninvasive ventilation treatment of 1–2 hours may be the clinical signs that the patient will benefit from noninvasive ventilation. Patients requiring intubation have at least one of the following five indications:

I. Inability to keep airway open (dislocation of the tongue toward the pharynx, obstruction of the upper respiratory tract, obstructive sleep apnea, burns).

II. Failure to protect airway from aspiration (oral and nasal bleeding in trauma patients, secretion, fullness of stomach, gastroesophageal reflux).

III. Ventilation failure (abnormalities in airway anatomy: short neck, wide mandible, the upper jaw being in front, mandible being behind, small mouth, obesity) and difficult mask ventilation may be accompanied with difficult intubation.

IV. Insufficiency in oxygenation (cyanosis, insufficiency of chest wall movements, presence of obstruction findings in lower respiratory tracts in auscultation, gradual decrease of saturation, inadequacy of spirometric and expiratory measurements).

V. Possible conditions that may lead to respiratory failure (hemodynamic changes as a result of progressive hypoxemia and hypercarbia such as tachycardia-hypertension-arrhythmia).

Tracheal intubation is generally used in patients unconscious or with respiratory failure to keep the airway open and to ensure ventilation of the patient. Endotracheal intubation is also performed in cases where general anesthesia will be applied for the operation. Endotracheal intubation is performed in various situations such as failure of noninvasive ventilation in intensive care patients [24, 25].

Acute respiratory failure is one of the most common events in the intensive care unit [26]. Airway management in intensive care unit is often more problematic than in operating theater. In general, the lack of physiological reserves is observed after induction of anesthesia during airway intervention, and some complications are seen after intubation. The person

who manages the difficult airway must recognize the patients who will face the airway problem, must plan to deal with the air, review the algorithms, and use the right agent for induction. Also, the emergency airway kit should be pulled to the bedside, and the end-tidal carbon dioxide values should be monitored for each patient [27, 28]. Although studies have emphasized in recent years that there are changes in the treatment of these patients after high-flow oxygen therapy, most of these patients need invasive mechanical ventilation and tracheal intubation [29]. When planning the treatment of these patients in the long term, the patient comfort should be improved by avoiding complications related to the endotracheal tube by opening percutaneous/surgical tracheostomy without delay [30].

The most common complication of intubation at the bedside is life-threatening hypoxemia [29]. Despite regular preoxygenation, a desaturation can develop. For this reason, various strategies have been developed for the preoxygenation period when the patient is intubated [19]. The intubation stage can be classified into two steps. The first step is the preoxygenation stage, and the second step is the laryngoscopy stage which requires induction [31]. NIV improves preoxygenation and limits desaturation, but its disadvantage is that oxygen flow is separated from the patient during laryngoscopy. In patients with hypoxic respiratory failure, high-flow oxygen is generally used, and uninterrupted oxygen supply is its advantage during intubation [32, 33]. Apneic oxygenation seems to be superior when compared with high-flow oxygen and mask ventilation [34]. It should be noted that in situations where high-flow oxygen is used, the patient's head must be positioned allowing an open airway (jaw thrust), and oxygen up to 60 liters per minute, not less than 15 liters, must be provided. After laryngoscopy, it is necessary to avoid hyperoxia and its complications and decrease oxygen flow [9, 35].

Endotracheal intubation indications can be summarized as follows [6, 24, 28, 29, 36, 37]:

- Airway problems: external pressures on the airway, vocal cord paralysis, tumor, infection, and laryngospasm.
- Respiratory deficiencies: patients with poor general condition, hypoxemic/hypercarbic respiratory insufficiency (respiratory rate less than 8 or more than 30 per minute, PO_2 in blood gas less than 55 mmHg, PCO_2 above 55 mmHg, and non-compensated acidosis-alkalosis).
- Inadequate circulation: cardiac arrest in hypothermic and hypotensive cases.
- Muscle and central nervous system problems and metabolic disorders: diseases of the muscles of respiratory system and auxiliary muscle disorders allowing respiratory failure and central apnea syndromes (Guillain-Barre, amyotrophic lateral sclerosis, myasthenia gravis, muscular dystrophy, acid-maltase insufficiency, phrenic nerve injury, botulism, polymyositis, spinal cord injury, electrolyte imbalance, hypophosphatemia, hypomagnesaemia, hypocalcemia, brainstem infarction, etc.).
- For the purpose of examination and transfer of patients: MRI scan under sedation, interventional radiology, endoscopic procedures.
- If urgent aggressive sedation is required to protect the patient: to avoid postoperative intracranial pressure increase, to provide cerebral protection with controlled hypotension and

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sedation in cerebral blood, to control recurrent attacks of seizures and contractions (status epilepticus and tetanus).

- In head and neck surgery: in case the airway remains in the surgical team site and the mask ventilation is not possible.
- The patient positions that make it difficult to control the airway: in the positions of the face down sit, side down, upside down, and lithotomy.
- Thoracic and abdominal interventions: intrathoracic interventions and abdominal interventions require respiratory control and muscle relaxation. Also, interventions such as cystoscopy and hemorrhoidectomy, which may develop the reflex bradycardia, vasospasm, and laryngospasm through the vagal stimulation.
- Patients at risk of aspiration of the stomach contents, blood, mucus, or secretion.
- Rare cases requiring airway protection such as Stevens-Johnson syndrome and toxic epidermal necrolysis.

2. Indications of endotracheal intubation under emergency conditions

In emergency conditions, equipment, technical skills, and quickness are very important when deciding on intubation indications at the bedside. Endotracheal intubation can be performed under emergency conditions in the following circumstances [6, 7, 25, 28, 29]:

- Apnea, respiratory failure.
- Airway obstruction: variable-level obstruction in the upper and lower airways.
- Inadequate oxygenation (hypoxia), inadequate ventilation (hypercarbia).
- Disruption of the airway reflex.
- In case the patient is hemodynamically unstable.
- The consciousness changes as far as being unable to protect airway (GCS <8).
- Cardiopulmonary resuscitation.
- Flail chest/pulmonary contusion, in case the breathing effort puts the patient's life in danger. In case the treatment of patient is not successful without intubation.

In urgent conditions, nasal, oral, awake, fiber optic, and rigid intubation and, if necessary, intubation through the laryngeal tube can be technically applied, and the choice of method is decided according to the patient's clinic.

When endotracheal intubation is performed under emergency conditions, it may be beneficial to consider the following conditions:

a. Equipment: intravenous (IV) catheter, laryngoscope, and blade, endotracheal tube in appropriate size, injector to inflate cuff, Magill forceps, nasal/oral airway, aspiration catheter, tube changer, guide wire, nasogastric tube, tube fixation.

b. Drugs: atropine, midazolam, lidocaine (1–4%), lidocaine gel, propofol, suxamethonium, thiopental, non-depolarizing muscle relaxants, morphine/fentanyl.

c. Patient history and airway evaluation: difficult airway assessment, risk of aspiration of gastric contents.

d. Aspiration catheter in various sizes should be kept ready.

e. The oxygen source must be switched on and tied; the ambu, anesthesia device, and mechanical ventilator must be in working position, and its circuit must be plugged in.

f. Patient position: the use of a small cushion together with the head extension brings the oral, pharyngeal, and laryngeal axis to the same alignment. If cervical trauma is present, the head is fixed in neutral position, and endotracheal intubation is performed.

Comparison of intubation performed under emergency conditions and intubation performed under elective conditions.

Emergency	Elective
Difficult intubation may not be predictable.	Predict airway difficulty.
There may not be enough time for preparation.	Prepare equipment and assistants for intubation.
It can be difficult to reach experienced personnel.	Confirm availability of help in an emergency.
There may be a risk of full stomach/aspiration.	Safely perform the intubation.
Patient status may not be stable.	Patient is more stable than emergency situations.

Cases where the NIV is contraindicated (coma, postoperative agitation, delirium, noncooperative patients, patients with gastric distention risk) may be in the semi-urgent or urgent category [31, 32]. It is decided according to the deterioration of the clinical course of the patient whose blood gas is followed and having spontaneous respiration.

3. Endotracheal intubation management

After the administration of an induction agent and neuromuscular blocker with rapid effect and high potency to provide adequate mask ventilation, direct laryngoscopy and intubation are performed. Suxamethonium is often preferred because it provides fast and ideal intubation conditions. Non-depolarizing muscle relaxants such as rocuronium, atracurium, and vecuronium can also be used because they provide acceptable intubation conditions. An

important point to consider is that if sufficient mask ventilation is provided, muscle relaxants can be given. Preoxygenation applied to patients gains time for intubation. Patients with a high-risk group (coronary artery disease, cerebral aneurysm) may be given additional pharmacological agents to provide hemodynamic stability. Different techniques, equipment, and agents can be used. Insertion of endotracheal tube into the trachea is essential. Anesthetic agents are not needed in patients under GCS 4 and with cardiac arrest [18, 25].

Generally, Macintosh and Miller blades are used for a direct laryngoscopy. The Macintosh blade is inserted into the gap called vallecula between the tongue base and the pharyngeal surface of the epiglottis. It provides a good passage for minimal epiglottic trauma and endotracheal tube. Miller blade extends to the laryngeal surface area of the epiglottis, making it easier to open the glottis but narrowing the oropharyngeal angle of view. There should be a certain distance between the operator's eye and the patient's airway. A close look at the patient will narrow the angle of vision. The laryngoscope's blade is moved from left to right in the airway by providing adequate mouth opening without damaging the lips and tongue. The blade should never be leaning on the upper jaw and upper incisors, and intubation should not be done by leaning on there. Pressing out of the cricoid cartilage is beneficial for better visualization of the glottis gap [4, 28].

The endotracheal intubation tube is held in the right hand and moved from the right of the patient's mouth toward the vocal cords. If there is a problem of routing the tube, it may be possible to orient the tube anteriorly using a probe. The cuff of the endotracheal tube is fixed after passing the vocal cords and is inflated with an air of 3–4 mL.

3.1. Rapid sequence intubation (RSI) indications

Adequate time and equipment often may not be available for endotracheal intubation. In some cases, it may be decided to intubate very quickly. For example, in various clinical situations that threaten the patient's life, time loss is more dangerous than the risks associated with rapid sequence intubation. In general, rapid sequence intubation is applied in situations indicated below [15, 38]:

a. The presence of all kinds of obstacles blocking the airway:

- Upper respiratory tract edema, as in anaphylaxis or infection
- Face or neck trauma with oropharyngeal bleeding or hematoma
- Obesity, short neck, short jaw, airway deformity

b. Loss of consciousness and airway reflex:

- Failure to protect airway against aspiration
- Loss of consciousness and concomitant vomiting, increased secretion, or risk of blood aspiration

c. Lack of intubation:

- Failure to protect the airway
- Long-term breathing effort resulting in fatigue or failure in respiratory muscles, as in severe chronic obstructive pulmonary disease

d. Failure of oxygenation (pulmonary shunt):

- If the airway is not protected or intubation fails
- Diffuse pulmonary edema, diffuse pneumonia, or emphysema
- Acute respiratory distress syndrome (ARDS), pulmonary embolism
- Cyanide toxicity, carbon monoxide, local anesthetic toxicity, methemoglobinemia

e. Expected clinical course or deterioration (e.g., need for status epilepticus control, except for tests and procedures):

- Patient with a life-threatening injury (such as a chest tube), or with a nonsurgical trauma, who needs urgent computerized tomography
- Hematoma in the enlarged neck region
- Septic shock
- Cerebral hemorrhages requiring close control of blood pressure
- Loss of airway opening as a result of spinal fracture and edema in the cervical region

3.2. General overview of intubation indications

I. The presence of depressive mental disorders:

a. Patients with GCS 8 and lower head trauma, having indications for intubation:

b. Associated with increased intracranial pressure, associated with surgical situation

c. In the presence of hypoxemia and hypercarbia, which increases morbidity and mortality

d. For airway control within 24–48 hours following overdose drug intake

II. Upper airway edema:

a. Inhalation damage: it is among the life-threatening conditions. The inhalation injury without skin burns has a mortality rate of around 10%; if the skin is burned, the mortality is doubled. Fluid resuscitation is needed and the risk of pneumonia is increased. There is an indication of early intubation because the upper airways are precarious [39]. This is because it is difficult to make a clinical decision about inhalation injury. The burn story

in the enclosed area, the carboxyhemoglobin (COHb) value of the patient at the time of admission to hospital, and the presence of coated phlegm are important. The accidents by oxygen therapy that is applied at home in diseases such as chronic obstructive pulmonary may cause inhalation damage, and it can be understood from the story of the patient [40]. Computed tomography (CT) is meaningful to understand the degree of inhalation damage and to see the anatomic changes, and it is valuable to calculate the V/Q (ventilation/perfusion) ratio to evaluate the gas change [41]. Tracheobronchial protease inhibitors in plasma and alveolar fluid have also been investigated in this regard and are valuable in terms of understanding the degree of damage [42]. Although observing the degree of damage in the fiber optic bronchoscope is useful, previous studies have shown that it has no correlation with ARDS [43]. In conclusion, if the inhalational damage is at the upper level of the glottis, the physical findings are more important to decide on intubation (participation of auxiliary breathing muscles to respiration, audible respiratory sounds). But if there is a damage at the lower level of the glottis, it is necessary to assess the thickness of the bronchial wall (BWT) in the COHb level and computed tomography [44, 45]. In cases of shock, inadequate oxygenation, or coma, it is difficult to make an early intubation decision because the intubation tube causes edema around the glottis [39].

b. Ludwig's angina: it is an aggressive cellulitis that affects submandibular and sublingual tissue areas, placed on the mouth base and mylohyoid diaphragm as bilateral. Endotracheal intubation is required because it will be associated with respiratory distress.

c. Epiglottitis: it is a rare but life-threatening case. It is seen in children between 1 and 6 years of age. The cause is *Haemophilus influenzae* type B. Unlike viral croup, there is no cough or very few. Fever is very high and toxic appearance is present. The child sits still to open the airways, the mouth is open and secretions flow. There is a lack of appetite for food because it is difficult to swallow. Oral examination with tongue pushers is very dangerous and can lead to complete obstruction of the respiratory tract and death. Minutes are important even in this disease, and the patient should be taken to the intensive care unit immediately and intubated under general anesthesia.

d. Bacterial tracheitis: it is a rare but dangerous case. Clinically, it resembles heavy viral croup. However, there is a high fever and a toxic appearance. The cause is usually *Staphylococcus aureus* or *Haemophilus influenzae*. In tracheal intubation, dense and viscous secretions are observed.

III. In the case of chronic obstructive pulmonary disease, asthma, restrictive lung disease, tumors, granulomatous diseases, and pulmonary retention of systemic diseases, the patient may need to be intubated, decided as a result of the laboratory evaluation.

IV. Conditions requiring rapid sequence intubation (RSI):

a. Patients with a full stomach: patients are accepted to be full in the case of feeding with clear liquids up to 4 hours before intubation and feeding with solid foods up to 8 hours. In cases where intra-abdominal pressure increases (pregnancy, ascites), gastrointestinal passages out of action (ileus) and the patient's story cannot be reached.

b. Loss of sympathetic stimulation: rapid sequence intubation need may occur in cases where gastric emptying time is prolonged, as in gastric dilation and diabetic patients.

V. Persistent hypotension that needs vasopressor support:

- Cardiac dysfunction, hypovolemia, sepsis

VI. Organ failure:

- Renal failure, hepatic failure

3.3. Deciding on endotracheal intubation in pediatric patients

Inadequate airway management can cause cessation of attempts to save lives and even cause cardiac arrest and death. Various airway equipments have been developed to provide adequate ventilation and oxygenation so far [46]. Although supraglottic airway devices developed for this purpose are available, they should be used cautiously because of the possibility of displacement, not suitability for patients with full stomach, and the possibility of increasing airway edema [33, 47]. If the patient is unable to breathe through the mask, oxygenation is inadequate, or in case of bleeding, edema or big foreign material in the upper airway, the patient should be intubated immediately [46, 48]. As in adult patients, the process of nasal preoxygenation with high flow provides the advantage of reducing inspiratory resistance, filling the nasopharyngeal dead area, reducing the metabolic work caused by gas exchange (conditioning), and supporting respiration through improving airway conductance and clearance. Lower levels of positive airway pressure are applied in children compared to adults. For newborns, 2 l/min is high-flow rate, whereas for older children, 4–6 lt/min is accepted as high [49].

3.3.1. Indications of endotracheal intubation in pediatric patients

If the child trauma patient is awaking, talking, or crying, being able to maintain breathing, he will be treated with supportive therapy as a conservative (oxygen supply with a facial mask or nasal cannula). If intubation is decided, the safest and most appropriate technique is applied according to the condition of the patient (traumatic injury, cord damage, the special anatomy of pediatric patients, and experience of the practitioner) [50]. Studies have shown that respiratory arrest is more likely in adults than in children and usually mediated by extrinsic factors [51]. The need for emergency intubation, number of recurrent interventions, tube diameter, and existing cardiovascular disease brings some complications such as desaturation, hypotension, and bradycardia. If we review intubation indications in general in children [50, 52–54]:

- Traumatic brain injury
- Hemorrhagic shock
- Respiratory failure due to pneumonia
- Muscle and metabolic diseases
- Foreign material in airways, upper airway obstruction
- Elective surgical procedure
- Pulmonary secretion control, therapeutic hyperventilation

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- Seizure
- Cardiac disease
- Drug intoxication, poisoning
- Acute laryngospasm, epiglottitis, inspiratory stridor

3.3.2. Indications of endotracheal intubation in newborns

Considering intubation for the newborn patient group to be difficult, it is also crucial to have full preparation; aspirator and ancillary equipment should be kept ready [55]. Intubation indications of a newborn can be classified as follows:

- Apnea.
- Bradycardia (pulse below 100). The most important cause of bradycardia is hypoxia.
- Stubborn cyanosis. Premature babies can be intubated electively.
- In cases where tracheal aspiration is required (baby painted with meconium).
- Inadequate positive-pressure ventilation applied through airway and mask.
- Extended NIV. Respiratory distress syndrome: lack of surfactant and structurally lower gas exchange area and excessive respiratory activity.
- Need for application of chest pressure (cardiac arrest). Endotracheal drug intake.
- Diaphragm hernia.

3.3.3. Rapid sequence intubation (RSI) protocol in pediatric patients

Rapid sequence intubation (RSI) is a method in which a number of neuromuscular blockers and sedative agents are used to make intubation safer, easier, faster, and less traumatic. It is a safe way for emergency service pediatricians experienced on the advanced airway management and sedative paralytic dosage [51].

RSI has 7 P rule (preparation, preoxygenation, premedication, paralysis with sedation, protection of the airway, passage of the tube and confirmation, and post-intubation management).

The success of the method depends on the following criteria:

1. To eliminate protective airway reflexes and spontaneous respiration with sedation and paralysis.
2. The most important determinant of the choice of sedative and paralytic agent is the response of the patient to the drug and the effects of the drug on the patient. Diseases such as asthma and tendency to hypotension should be questioned in particular.
3. Systematic preparation for the implementation of the method is necessary to make the intubation faster and safer.
4. Preoxygenation with 100% oxygen, two intravenous vascular access.

5. Atropine 0.02 mg/kg IV, lidocaine 1.0 mg/kg IV, etomidate 0.3 mg/kg IV, or thiopental 4.0 mg/kg IV.
6. Sellick's maneuver application: if Sellick's maneuver is performed while the patient is vomiting, there is a risk of esophageal perforation; therefore, the head should be placed down in case of vomiting.
7. Succinylcholine 1.0 mg/kg IV or rocuronium 0.6–1.0 mg/kg IV.
8. Intubation after 1 minute.

In children, especially infants, vagal response to the laryngoscopy and tracheal intubation is much more than in adults [51]. Due to this medication, bradycardia and even an asystole in children who were given succinylcholine were reported in the literature [56].

A common recommendation from the American pediatric association is that rapid sequence intubation is done with atropine in the following situations [57]:

- All children under 1 year old
- Children under the age of 5 who are given succinylcholine
- Patients developing bradycardia during intubation

The use of atropine in rapid sequence intubation is still controversial. Following atropine, sinus tachycardia, mydriasis, xerostomia, a decrease in the amount of urine, and hyperthermia can be seen. In addition to the side effects, when used in premedication, salivation and secretion reduction effect is not fast, so it is important to be careful when using it and to determine its indications well. Atropine makes it difficult for the patient to be evaluated in terms of neurologic and cardiological aspects, and its effect on cardiac muscle may last for several hours. Since small doses have a bradycardia-initiating effect, the smallest dose should be at least 0.1 mg. The recommended dose is 0.02 mg/kg [58, 59]. Succinylcholine is contraindicated in children with muscular dystrophy because it forms the rhabdomyolysis and the hyperkalemia that threatens life. It should be avoided in patients with a risk of malignant hyperthermia, large body burn, multi-trauma, spinal cord injury, intracranial injury, brain tumors, and penetrating eye traumas. Rocuronium is an agent that offers better intubation than succinylcholine. The preferred dose is 1 mg/kg.

Etomidate is an imidazole derivative and acts as a well-known sedative agent. Its effect begins immediately, providing hemodynamic stable intubation. The effect on adrenal cortex and mechanisms of action of myoclonic jerk side effect in induction were investigated. Patients who have undergone a convulsion after etomidate have previously been reported to have convulsion story. The recommended dose is 0.3 mg/kg. Thiopental sodium, an ultrashort acting barbiturate, should be used with caution because of its known systolic blood pressure-lowering effect, although anticonvulsive properties are preferred. Its dosage is 3–5 mg/kg, but not recommended for children. Ketamine is a sedative and hypnotic agent. It is favorable in terms of protecting the upper airway reflexes, but not recommended in cases where it will increase intracranial pressure. It has an anticonvulsive and a bronchodilator effect. The recommended dose is 1–2 mg/kg. Propofol may be preferred in children under 3 years of age,

which may cause hypotension, and the recommended dose is 1.5 mg/kg. The recommended dose of midazolam which has anxiolytic, sedative, and anticonvulsant properties is 0.3 mg/kg. It should not be forgotten that it may cause respiratory depression because it is slightly more than the sedation dose. It is cheap, is easy to access, and is a drug that clinicians are accustomed to [60].

After endotracheal intubation, pediatric patients should be treated with extra caution. A delicate balance should be established in drug selection, dosage adjustment, and mechanical ventilator settings. Children are at risk for acute hypoxemia; although dead-space ventilation is similar to adults, oxygen consumption is much higher [61].

Because preoxygenation is not sufficient during intubation, high-flow oxygen therapy with a nasal cannula, that is, apneic oxygenation, can enable us to pass the apneic period, without hypoxemia [49]. Intubation in one attempt, especially with video laryngoscopes, minimizes the risk of vagal stimulation due to hypoxemia, hypercarbia, and multiple attempts. Univariate analysis of studies has shown that the use of neuromuscular blockage for intubation reduces complications [62].

Intensive care unit and emergency tracheal intubation cases of 3 years, involving 3366 pediatric patients, were investigated; it was observed that fentanyl (64%) and midazolam (58%) as induction agents and rocuronium (64%) and vecuronium (20%) as muscle relaxants had been used, and succinylcholine (0.7%) and etomidate (1.6%) had been less preferred. It was observed that vagolytic agents (51% of infants and 28% of babies over 1 year old) and ketamine (27%) had been preferred in unstability hemodynamic conditions (39%). However, it was found that the use of ketamine was not associated with low prevalence of hypotension [63].

3.4. Intubation indications in intensive care and rapid decision-making

Intensive care patients may be intubated more difficult than those in the operating room. Previous studies have shown that saturations decrease faster in respiratory failure and they remain under the risk of hypoxemia. Intubation timing should be optimal to avoid desaturation. If patients with hypoxic respiratory failure have spontaneous breathing, it is important when to switch to invasive ventilation. On this subject, some of the criteria related to intensive care patients with respiratory complaints were introduced in the study of Florali.

Criteria used in the study of Florali [9]:

1. The presence of evidence for persistent or worsening respiratory failure: respiration at 40 F/min, situations in which respiratory and tracheal secretion increase, and acidosis (below pH 7.35), situations in which saturation does not exceed 90% for 5 minutes despite oxygen therapy
2. Systolic blood pressure under 90 mmHg or mean arterial pressure less than 65 mmHg or the need for vasopressors
3. Deterioration of neurological condition and GCS under 12

Preoxygenation is a common and time-saving approach to prevent desaturation in patients who are treated in intensive care unit when intubation is done. Special protocols have been

developed to standardize the treatment of preoxygenation. The number 10 scalar Montpellier protocol or its modified form, number 8 scalar, is used for preoxygenation [64]. Preoxygenation is known to be used in rapid sequence intubation.

Preoxygenation application routes:

a. Using 10/5 cm H_2O 100% O_2 with nasal intermittent positive-pressure ventilation.

b. Using 40 L/min 100% O_2 with a high-flow nasal cannula.

c. Applying non-rebreather mask (non-accumulating CO_2) over 15 L/min, which permits maximum oxygen flow, also known as flush flow rate.

d. If rapid intravenous administration of 500 ml of fluids per hour is not clinically contraindicated, sedative, hypnotic agent and muscle relaxant medication are followed by intubation. Intubation made by two personnel who are skilled must be reviewed in terms of RSI. Capnography is used for intubation verification [64].

3.5. Indications of nasotracheal intubation

Nasotracheal intubation is technically similar to intubation but difficult to administer. Firstly, a vasoconstrictor is dripped through an open nostril, and then the tube developed for nasal intubation is driven forward. While the tube Magill is seen in the oral cavity in the laryngoscope being directed toward the vocal cords with the help of Magill forceps, an assistant staff helps to drive the tube forward. Since the tube may curl and cause trauma to the nose, it is necessary to use the spiral tube and select the largest suitable tube diameter. Resistance in ventilation, nasal bleeding, pressure necrosis, and adenoid trauma may occur in the respiratory tract depending on the diameter of the selected tube. It is contraindicated in sinusitis, local abscesses, in cranial fractures, and in zygoma fractures.

It is indicated in maxillofacial and dental surgery and in cases where the jaw opening is limited. In the past, difficult intubation was called blind nasal intubation, but nowadays it is not preferred because there is the chance to reach video laryngoscopy, fiber optic intubation, lighted probes, and similar tools and equipment with the developing technology [65–68].

3.6. Indications of retrograde intubation

Retrograde intubation surgery is an alternative technique to cricothyroidotomy. Following preoxygenation, the cricothyroid area is given local anesthesia. Following the arrival of air from the injector entered with the Seldinger technique, the guide wire is moved through the needle and removed with Magill forceps from the mouth. The endotracheal tube is then driven over the wire. The wire is passed through Murphy's eye, and the guide wire is stretched while the tube is driven. The guide wire is drawn back after the procedure [69].

Indications: lack of glottic imaging due to secretion, vomiting or bleeding, and failure in conventional methods, in cases where intubation cannot be performed. Patients with a congenital anomaly, upper airway tumor, acute epiglottitis, severe kyphosis, cervical arthrosis, or trauma.

Contraindications: it is contraindicated in such situations, upper airway obstruction, larynx trauma, large thyroid gland, infection in the area of cricothyroid, and coagulopathy.

3.7. Additional conditions

The experienced practitioner, who can always detect incorrect intubation, and additional personnel facilitate airway management and may help us avoid complications. There is always a need of the presence of aspirator working at the bedside to prevent aspiration risk. Long-acting muscle relaxants are not given in patients who cannot be ventilated with a mask. If the patient is hemodynamically unstable and the induction drugs cannot be applied, if the patient has a difficult airway history, and if severe airway obstruction is detected during examination and/or laryngoscopy, awake intubation can be performed.

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Chapter 4

The Importance of Proper Positioning for Airway Management for Obese Patients

Craig A. Troop

Additional information is available at the end of the chapter

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Abstract

In the practice of anesthesia patient care, airway management is the first and most important consideration when caring for all patients. In particular, when caring for obese patients, airway positioning requires additional special attention. The head-elevated laryngoscopy position (HELP) has been presented as the best starting point to improve patient safety, lower risk, and facilitate a successful first attempt at intubation. HELP has also been described as the ramped position.

Keywords: obese patients, airway management, airway positioning, HELP, patient safety, intubation, ramped position

1. Introduction

The problem of obesity (BMI > 30) and morbid obesity (BMI > 40) is now of global proportions. The term globesity has been described! It is not the intent of this chapter to address the etiology or reasons for this current clinical issue. Rather, what is presented is a review of concepts and studies that support an adjustment in clinical anesthesia practice to more safely care for the airway of obese and morbidly obese patients. A simple yet highly effective method to lower risk, improve patient safety, and facilitate airway management is to place large patients in a ramped position for all surgical/anesthesia cases (regional and general). The objective of this chapter can be stated in one sentence. If you are caring for a large, obese/morbidly obese patient, first pay attention to positioning.

2. Positioning the obese and morbidly obese patient and airway management

Several articles and textbook writings [6, 7, 8, 9, 10] are available that address the numerous medical concerns when caring for obese patients. It is well accepted that these patients present an increased risk for perioperative morbidity. A partial list of these concerns includes cardiovascular disease (increased cardiac workload, arrhythmias), hypertension, obstructive sleep apnea (OSA) [13], restrictive and reactive lung disease (asthma, chronic hypoxemia, and hypercarbia), and abnormal pulmonary mechanics. The functional residual capacity (FRC) (volume of air that remains in the lungs after a normal breath) decreases in proportion to increasing BMI. Total lung capacity (TLC), forced expiratory volume (FEV), forced vital capacity (FVC), and ratio of FEV to FVC decrease with a BMI > 35. Increased intra-abdominal pressures cause a restrictive pattern that is worsened by a supine position. Simple questioning of the obese/morbidly patient will often reveal that the patient (at home) never lies in a fully supine position but rather sleeps on several pillows or in an extreme case sleeps in a recliner chair. Common sense would suggest that placing these patients in a fully supine position prior to the induction of artificial sleep (anesthesia) is not a good practice. Proper positioning of the obese/morbidly obese patient is a patient safety issue. When caring for the airway of normal-size nonobese patients, the concept of aligning the three airway axes in preparation for intubation has been taught at all anesthesia teaching colleges. Simply put, to facilitate placement of the endotracheal tube, one needs to align the oral, the pharyngeal, and the laryngeal axis to improve the "line of site" from the mouth to the trachea.

A small standard foam head cradle (**Figure 1**) placed behind the patient's head will put the cervical spine in a slight amount of flexion and brings the oral and pharyngeal axes into alignment (**Figures 2** and **3**). Following this, simple extension of the patient's head will aid in alignment of all three airway axes in the majority of normal-size patients. Another way to describe this airway axis alignment is to position the patient such that an imaginary line from the patient's ear (external auditory meatus) to the suprasternal notch (top of the breast bone) is approximately parallel to the OR table. **Figure 4** shows the white imaginary line as an acute angle and the airway axes misaligned. In order to align the three airway axes of the obese/morbidly obese

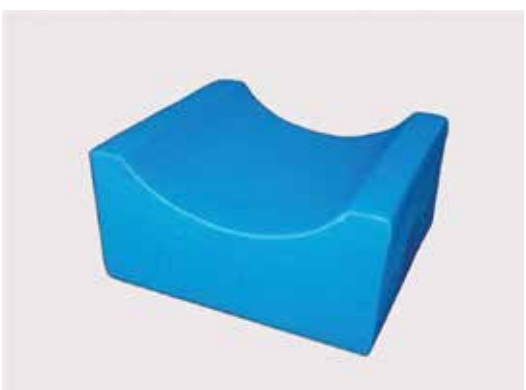

Figure 1. Standard head cradle or head rest.

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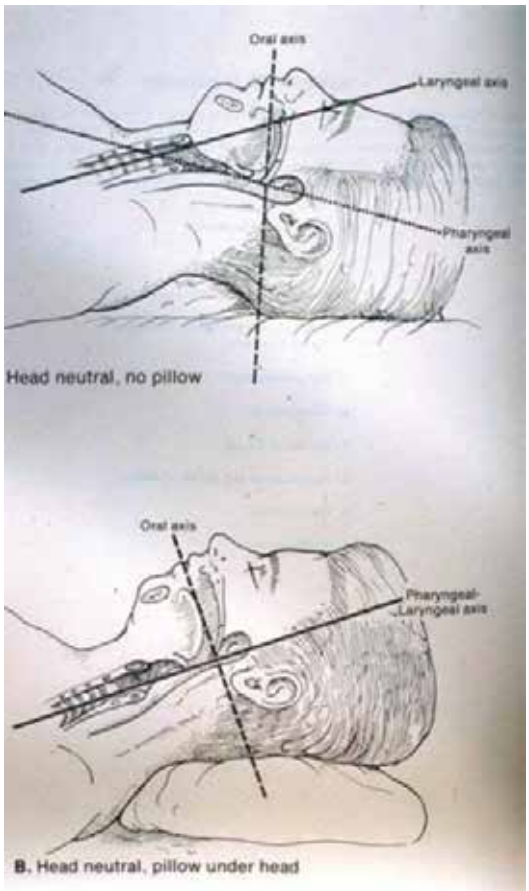

Figure 2. Airway axes.

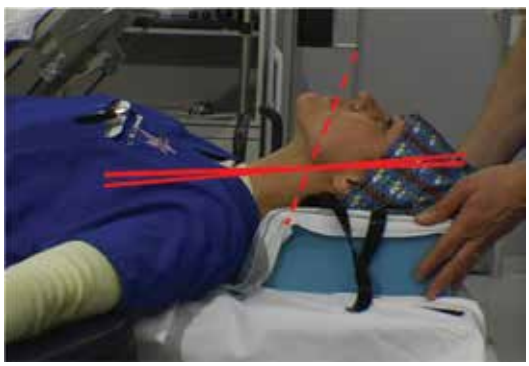

Figure 3. Normal-size person on head cradle with superimposed airway axes.

patient, a standard small head cradle by itself is not sufficient [3] (**Figure 4**). However, simply placing a standard head cradle on a ramp constructed from a stack of blankets "stacking" (**Figure 5**) or the use of a specially sculptured foam ramp (**Figure 6**) will achieve the desired

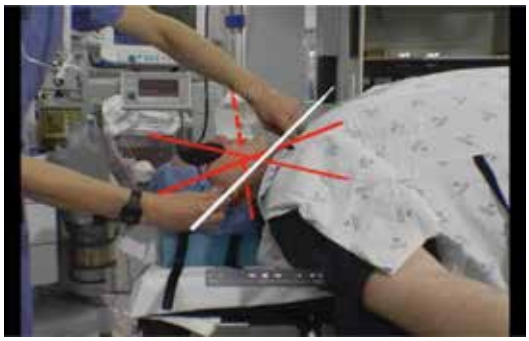

Figure 4. Obese patient. Airway axes misaligned. Lying only on a standard head cradle.

Figure 5. Well positioned on a "stack" of blankets. Obese patient on a ramp of blankets + head cradle.

Figure 6. Troop elevation pillow (TEP) with standard head cradle (note the elevated arm board pads).

result. This stacked position could be described as the "blessing of the blankets" (**Figure 5**) and (Video #1 Supine vs. ramping with blankets).

This simple and easy step or adjustment when caring for the airway of obese and morbidly obese patients has significant clinical benefits (**Table 1**).

Improved ease of breathing = less anxious patient prior to induction of GEA
Better preoxygenation = increased time to desaturation
Easier to mask ventilate the patient and also to rescue ventilate if difficult intubation occurs
Improved line of sight facilitates successful first-pass intubation [direct laryngoscopy (DL) or video laryngoscopy (VL)]
Helps to align the three airway axes (a simple adjustment of the OR table; backup or reverse Trendelenburg does not change airway axis alignment) (see Video # 1 Supine vs. ramping with blankets)

Table 1. Benefits of the ramped position.

This position is perhaps better described by the term head-elevated laryngoscopy position (HELP). This term was described by Levitan [5] in 2003.

Many objective clinical reports support placing the obese patient in a ramped position prior to anesthesia induction. A common subjective remark from the obese patient when placed in a fully supine (flat) position on the OR table is "I cannot breathe like this" (**Figure 7**) (Video #2 Positioning: good for the patient). As previously mentioned, morbidly obese patients (when at home) tend to sleep elevated on several pillows. Such patients understandably are anxious when lying fully supine as the work of breathing increases.

Numerous formal studies also confirm that HELP ramping or stacking the obese patient is of clinical benefit. Two studies are most noteworthy:

1. **Collins et al. Laryngoscopy and morbid obesity** [1]. This study from 2004 demonstrated that the "stacked," "ramped," or "head-elevated laryngoscopy position" (HELP) improves pulmonary compliance, allows easier mask ventilation, and improves conditions for tracheal intubation.

2. **Dixon et al. Preoxygenation is more effective in the 25° headup position than in the supine position in severely obese patients** [2]. This study from 2005 demonstrated a significant increase in the desaturation safety period postanesthesia induction allowing for a greater time for intubation and airway control.

Figure 7. Fully supine obese patient on a standard head cradle only.

To state the obvious, patients are not all the same size and shape. It is well accepted that surgical positioning is adjusted or modified (depending on the type of surgery). Likewise, special attention should be given to airway management for the obese, morbidly obese, or very large patient [14]. Starting from the head-elevated laryngoscopy position (HELP) will aid in better alignment of the three airway axes (**Figures 8** and **10**) and help to isolate the patient's airway above the level of the chest and abdomen. This elevated position is of benefit for the obese patient prior to anesthesia induction as he/she will breathe with greater ease (Video #2 Positioning: good for the patient). The patient will be less anxious but of even more clinical significance is the improvement in pre-oxygenation as mentioned above. An increase in the desaturation safety period is of profound importance. This period is the time from the onset of apnea (not breathing) until the patient's blood oxygen "level" begins to drop. Clinically, the SpO2 monitor (%) value and tone begin to fall precipitously (Video #2 Positioning: good for the Patient). The anesthesia provider must initiate breathing for the patient to avoid a crisis. The anesthesia clinician will benefit as HELP will facilitate easier mask ventilation [17]. Further, the head-elevated position results in a greater incidence of a successful first attempt at intubation [1, 4, 11, 17, 18].

Although proper positioning of the high-risk patient is taught at virtually all anesthesia training programs, many anesthesia providers in a private clinical practice setting do not follow the advice. The reasons for this are varied, but perhaps the two most common reasons for not focusing on good positioning are that building a ramp from a stack of blankets takes too much time and is inherently unstable. Another common remark is "…we have a videoscope; we do not need to ramp our obese patients." This is a misconception as good positioning will facilitate all methods of airway management (mask ventilation, DL, VL, LMA, etc.) [17]. In an effort to encourage today's anesthesia providers to always properly position their obese patients, commercially available foam ramp-shaped positioners have been developed (**Figures 6** and **8**) (Video #3 TEP overview).

This foam positioning device known as the Troop Elevation Pillow (TEP) (**Figure 6**) is **easy** to set up and use. It is very **stable** (unlike a pile of blankets), and the TEP yields a **predictable** result with each use. There are other commercially developed positioners, but the TEP is perhaps the most studied for use in clinical practice [12, 15, 16].

Figure 8. Morbidly obese patients lying on TEP + head cradle/airway axes are beginning to align.

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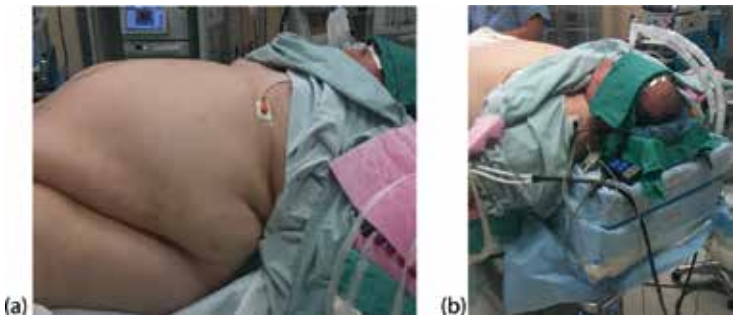

Figure 9. (a) Super morbidly obese patients BMI > 50; (b) well positioned on TEP + addition + head cradle.

Figure 10. Morbidly obese patient, 6 foot 375 pounds: bad vs. good airway positioning.

Super morbidly obese patients (BMI > 50) require additional ramping (**Figure 9(a)** and **(b)**) (Video #4 Super morbidly obese and TEP addition).

3. Conclusion

All obese and especially morbidly obese patients will benefit from the head-elevated laryngoscopy position (HELP) or ramped position. This is applicable for regional anesthesia cases (surgery under spinal, epidural, or local anesthesia with sedation) [16] as the ease of spontaneous ventilation is improved. For general endotracheal anesthesia cases (GEA), the head-elevated laryngoscopy position is a much improved starting "point" for airway care as the position will compliment all methods and techniques of managing the patient's airway. The position facilitates a successful first attempt at intubation. As stated in the introduction, the intent of this chapter is to reveal why proper positioning of the obese/morbidly obese patient is so important. **It is a patient safety issue.** The old saying that a picture tells a thousand words is captured in **Figure 10**, a side-by-side comparison of bad and good positioning. As stated in

the introduction, the objective of this chapter is to convey one simple message: **If you are caring for a large, obese/morbidly obese patient, you should first pay attention to positioning.**

Conflict of interest

The author is the inventor and developer of the troop elevation pillow (TEP). The TEP has been offered by several medical distribution companies around the world since 2005.

Acronyms and abbreviations

BMI	body mass index (a ratio of the patient's weight in kilograms divided by height in meters squared).
DL	direct laryngoscopy.
GEA	general endotracheal anesthesia.
HELP	head-elevated laryngoscopy position.
Induction of anesthesia:	the administration of an anesthetic or causing an anesthetic state.
LMA	laryngeal mask airway.
SpO_2	an indirect noninvasive measurement of the oxygen level (oxygen saturation) of the blood.
Preoxygenation:	prior to the administration of anesthesia, the surgical patient breathes on a mask and circuit of oxygen to increase the O_2 content in the lungs and in the circulation.
VL	video laryngoscopy.

Videos

https://www.intechopen.com/download/index/process/149/authkey/d005b44f07af37019fec01c7788f1ed2

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Chapter 5

Long-Term Complications of Tracheal Intubation

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Additional information is available at the end of the chapter

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Abstract

Endotracheal intubation is an intervention frequently performed in the hospital setting in order to protect the central airway and provide mechanical support of ventilation. Many health care providers are expected to be able to intubate the patients for different indications. As the case in any medical intervention, endotracheal intubation can cause complications. These complications are categorized as early or late according to the time of onset of the presenting symptoms. This chapter will discuss the long term complications of endotracheal intubation that might be encountered by the treating physicians. The chapter will stress on the predisposing factors for these complications and the available methods to avoid and treat them.

Keywords: intubation related complications, obstructive fibrinous tracheal pseudomembranes, post-intubation tracheal stenosis, tracheomalacia, tracheoesophageal fistula

1. Introduction

Intubation is an invasive, however, lifesaving procedure which established its role in the daily management of critically ill patients. Physicians treating patients with endotracheal tubes can encounter complications during or immediately after the procedure. Complication appearance or identification can be delayed for days to weeks. They can be categorized into three categories:

1. Long term complications that occur immediately during endotracheal tube (ETT) insertion
2. Complications of the prolonged intubation
3. Late onset complications

2. Risk assessment and general preventive measures

Risk assessment and preventive measures of the intubation-related complications should be undertaken immediately after the decision for an endotracheal tube (ETT) insertion is taken for the patient's management. These measures can be divided into three main groups:

I. Measures that should be taken *before* intubation:

1. Routine assessment for potentially difficult intubation cases.
2. Choosing the proper sized tube.
3. Using proper technique
4. Choose an experienced, skilled physician to perform the procedure.
5. Preparing alternative plans in cases of unanticipated difficulties. The Difficult Airway Society (DAS) guidelines recommended a four steps plans A–D as the following [1]:
   - **A.** Preparing an initial tracheal intubation plan that includes using the direct laryngoscopy.
   - **B.** Preparing a secondary intubation plan which includes using a dedicated supraglottic airway device such as the classic laryngeal mask airway (LMA) in case of plan A has failed.
   - **C.** When plan B fails; the physician should be prepared to oxygenate and ventilate the patient, postpone the surgery, and awaken the patient.
   - **D.** In cases where physician 'cannot intubate, cannot ventilate' (CICV) rescue techniques such as cannula or surgical cricothyroidotomy should be available at the facility.

II. Measures that applied *during* intubation:

1. Intubating the patients under direct vision.
2. Using intubation assisting devices as the ETT stylet, Eschmann tracheal tube introducer (gum-elastic bougie tube), video laryngoscope or the flexible bronchoscopy in difficult to intubate cases [2].
3. Applying appropriate cuff pressure not to exceed 20 mm H_2O.
4. Stabilization the ETT using fixation tapes or devices.

III. Measures which should be applied *after* intubation:

1. Frequent suctioning of the oral and endotracheal secretions.
2. Application of antiseptics as chlorhexidine to decontaminate the oral cavity.
3. Assessments of skin integrity around lips and adhesive tape at least twice daily.

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3. Complications that occur immediately during endotracheal tube (ETT) insertion

Complications of tracheal intubation might occur at any stage during the intubation with devastating consequences which may last as long as patients survive.

Table 1A lists the chronic complications that usually result from trauma during intubation.

Prolonged voice hoarseness
Arytenoid dislocation
Cervical spine and spinal cord injuries
Traumatic dental injury

Table 1A. Chronic complications that occur immediately at ETT insertion.

3.1. Post intubation prolonged voice hoarseness

Temporary hoarseness is a common complain that occur in one third [3] to half [4] of the intubated patients and usually resolve spontaneously within 1 week; however, the incidence of *prolonged* hoarseness (>7 days) is estimated to be less than 1% [4, 5]. Vocal cord edema or lacerations, epiglottic hematoma and vocal cord paralysis secondary to compression of anterior branch of the recurrent laryngeal nerve are all potential etiologies of prolonged hoarseness [6]. In a prospective study 7 out of 25 cases (28%) of prolonged hoarseness had no identifiable causes [4]. *Permanent* hoarseness is even more rare, and being caused by granuloma of the vocal cord or arytenoid dislocation. The risk factors for this complication found to be longer duration of intubation, older age [4] and female gender [7]. Using a smaller size tube especially for females has been suggested to decrease the incidence of prolonged voice hoarseness [4, 8].

3.2. Arytenoid dislocation

Arytenoid dislocation is a rare cause of vocal cord paralysis with less than 0.1% incidence rate [9]. The commonest mechanism of intubation related vocal cord paralysis is compression of the anterior branch of the recurrent laryngeal nerve as a result of prolonged intubation which will be discussed separately under complication of prolonged intubation subtitle. Risk factors for this complication can either be related to patients or the procedure. Patients related factors include retrognathia, dental malocclusion, a large tongue base, and cricoarytenoid joint involvement by rheumatoid arthritis. While; Procedure related risk factors include traumatic and/or prolonged intubation, protrusion of the endotracheal tube stylet, pressure from the distal curved part of the ETT and inexperience and poor techniques by the performance [10]. The majority of the patients present with dysphagia [11]; prolonged hoarseness, sore throat, and cough are less frequent symptoms. There are two types of dislocation, the posterolateral and the anteromedial dislocation; the latter being the most dangerous as it can compromise the

airway causing acute stridor and acute respiratory distress soon after extubation [12]. **Figure 1** shows example of anteromedial left arytenoid cartilage dislocation [13].

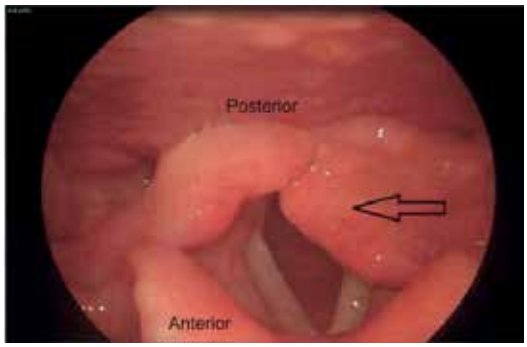

Figure 1. Laryngoscopic image of anteromedial dislocation of left arytenoid cartilage. Courtesy of Oh et al. [13].

Diagnosis can be confirmed by laryngoscopy and/or CT scan [14]. Laryngeal electromyography is sometimes used to differentiate arytenoid dislocation from recurrent laryngeal nerve paralysis. Tracheotomy is required in cases which present with acute airway compromise, other cases may have spontaneous repositioning of arytenoid cartilage thus do not need treatment [15]. Many surgical laryngoscopic techniques have been described as the definitive treatment [16, 17]. Late treatment options include Teflon injection, cricoarytenoid arthrodesis [18] and laryngeal framework procedure [19].

3.3. Cervical spine and spinal cord injuries

Urgent intubation to ensure protection of the airways is frequently required for poly-trauma patients. Careful manipulation of the neck by an experience health care provider is of crucial importance as such patients potentially have cervical spine injuries. Predictors of spinal injury in poly-trauma cases are accident by motor vehicle collision or fall down. Presence of pelvic fracture or Injury Severity Score (ISS) >15 should alert the physician to a possible cervical spine involvement [20]. Patients with systemic diseases which potentially affect the cervical spine as rheumatoid arthritis or ankylosing spondylitis must be handled as high risk for intubation related cervical spine injuries. Once the health care provider suspects a high risk cervical spine injury, he should maintain the patient's head in a neutral position throughout the intubation procedure. Cervical hyperextension in such cases can traumatize the spinal cord resulting in paraplegia. Manual In-Line Stabilization (MILS) is the recommended method to stabilize the head and neck during high risk intubation. The caveats of this method are: firstly, the need of a second health care provider who stabilizes the patient's occiput and mastoid processes using his **both** hands. Secondly, it decreases the laryngoscopic view by 45% [21]. Application of cervical collar is another important protective measure; available collars include soft collar, hard collar, extrication collar, Philadelphia collar. Again, application of collar significantly limit mouth opening and make intubation harder [22]. Cervical spine can also be stabilized using a bilateral sandbags with 3-inch-wide cloth tape across the forehead. Adding Philadelphia collar to the sand bags further reduced the extension movement [23].

In cases of difficult intubation the available choices are:

1. Video or fiberoptic laryngoscopy intubation.
2. Gum elastic bougie which has been shown in a clinical study to facilitate the intubation while applying MILS [21].

3.4. Traumatic dental injury

The incidence of traumatic dental injury found to be 1:2805 in a large analysis of more than 500 thousand surgeries. The most common tooth to be traumatized is the upper incisors; furthermore, 13% of the cases had multiple teeth involved. Different type of teeth injuries have been described, crown fracture and partial dislocation being the commonest [24]. Difficult intubation is the main risk factor for dental injury, other risk factor include poor dentation and preexisting craniofacial abnormalities [24].

4. Complications of the prolonged intubation

Prolonged intubation is defined as intubation exceeding 7 days [25]. Clinical studies have shown that prolonged intubation is a risk factor for many complications.

Table 1B lists complications of prolonged intubation that present while patient is still on mechanical ventilator or early at extubation.

Pressure ulcer around adhesive tapes
Vocal cord paralysis
Ventilator-associated pneumonia (VAP)
Sinusitis
Tracheomalacia
Laryngotracheal stenosis

Table 1B. Complications of prolonged intubation.

4.1. Mucosal/dermal pressure ulcer

Mucosal/dermal pressure ulcers are caused either by the tube itself or by the securing taps and devices. It can affect the lips, mouth, gums, and tongue. This complication is very common despite it is preventable; its incidence reported to be 20% in mechanically ventilated patients [26]. The identified risks for pressure ulcer are [27, 28]:

1. Hypoalbuminemia, older age, catabolic diseases.
2. Increase pressure, shearing forces and friction over bony prominence.
3. Moisture.

Prevention of ETT related pressure ulcer can be summarized in the following steps [29]:

1. To Proper size of the tube before the insertion.
2. To adequately secure the tube to prevent dislodgment without creating additional pressure.
3. To inspect the skin beneath the tube at least twice daily.
4. To keep the skin under the tube dry and clean as possible.
5. To reposition the ETT to redistribute pressure while make sure that the ETT depth did not change.
6. To remove the tube once it is not absolutely necessary.

Pressure ulcers prevention is crucial as they are painful and their healing process is slow. Generally, removal of the cause of the pressure, cleaning, application of antiseptics and debridement is the available treatment options.

4.2. Vocal cord paralysis

Intubation related vocal cord paralysis is rare with estimated incidence of 0.03%; nevertheless, it constitutes 22.6% of all causes of vocal cord paralysis [30]. It is usually a result of compression of the anterior branch of the recurrent laryngeal nerve between the inflated cuff of the ETT and the thyroid cartilage [31]. Prolonged intubation is the major risk factor for vocal cord paralysis which can be unilateral (left vocal cord is more commonly involved than the right) or bilateral [6]. Unilateral vocal cord paralysis present immediately after extubation with hoarseness of voice and dysphonia; while, bilateral paralysis presented as sever stridor which lead to reintubation. Re-establishment of vocal cord motion is a good prognostic sign of improvement of the voice [32]. In bilateral vocal cord palsy pulmonary function testing shows variable extrathoracic obstruction on flow volume loop [33]. Direct laryngoscopy and/or laryngeal electromyography are the diagnostic test of choice. Intervention is not required for unilateral paralysis as spontaneous resolution usually occurs on average of about 10 weeks [6], however, if no resolution occurs in 12 months then recovery is unlikely [32]. Temporary injection of the affected vocal cord is an option to improve the voice [32]. Unfortunately, tracheostomy is necessary in many cases suffering from bilateral vocal cord paralysis for long term management.

4.3. Ventilator-associated pneumonia (VAP)

Ventilator-associated pneumonia (VAP) is defined in the latest Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) guideline as a pneumonia occurring >48 h after endotracheal intubation [34]. VAP is subsequently divided for practical reasons in to an early onset pneumonia and late-onset pneumonia; the earliest is a pneumonia that develops within the first 4 days of admission in the mechanically ventilated patients [35]. A systematic review has estimated that between 10 and 20% of patients receiving >48 h of mechanical ventilation develop VAP [36]; up to 50% of them develop an early VAP (within the first 4 days after admission) [35]. Interestingly, the VAP hazard is decreasing over days, this has been shown in a prospective multicentre Canadian study where VAP rate was approximately 3% per day in the first week of mechanical ventilation, then the rate dropped to 2%

and 1% per day in the second and the third week respectively [37]. Gastric colonization, oropharyngeal and tracheal colonization, and cross colonization of the patients by contaminated hands of hospital personnel are all risks for VAP. Endotracheal tubes itself appear to be an independent risk factor for VAP [38]. Its presence impairs the host natural defenses against infections; furthermore, bacteria adhere to the plastic tube forming a complete or partial biofilm in 84 and 95% respectively [39]. Intubated patients are having recurrent aspirations of dislodged parts of this biofilm or from the pooled secretions above the tube cuff.

Studies have shown that the bacterial colonization is changed from community to nosocomial pattern after the fourth day of the admission [34]. In early-onset pneumonia the commonest pathogens include, *Streptococcus pneumoniae*, *Haemophilus influenzae* and methicillin sensitive *Staphylococcus aureus* (MSSA); while in the late onset methicillin resistant *Staphylococcus aureus* (MRSA), Gram-negative bacilli such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii* are frequently encountered [40]. Moreover, it is not uncommon for VAP to have polymicrobial infection. VAP diagnosis is achieved by using the following diagnostic criteria [41]:

1. Clinical sign of infection as fever, purulent tracheal secretions, and leucocytosis.
2. Bacteriologic evidence of infection.
3. Radiologic suggestion of infection.

Application of strict prevention measures in the intensive care units is practical approach to deceases the burden of VAP on the patients and the health care system. VAP prevention measures include:

1. *Noninvasive positive-pressure ventilation in selected groups of patients*.
2. *Silver covered tube:* it has been shown in a Cochrane review that silver coated tube decrease the risk of VAP in the first 10 days of mechanical ventilation possibly due to the antimicrobial effect of silver [42].
3. *Mouth hygiene with chlorhexidine as a mouthrinse or a gel:* this has shown in a Cochrane review to reduce the risk of VAP from 24% to about 18% [43].
4. *Positioning the patient in semirecumbent position:* decrease the risk of VAP from 35 to 8% comparing to supine position [44].
5. *Applying an endotracheal tube cuff pressure of 20 cm H_2O to prevent aspiration*.
6. *Continuous aspiration of subglottic secretions (CASS):* it reduce both early and late onset VAP [45].
7. *Discontinuation of mechanical ventilation as early as possible*.

IDSA/ATS updated guideline recommends empirical coverage of both *S. aureus* and *P. aeruginosa* in patients with suspected VAP. They recommended either vancomycin or linezolid to cover MRSA in at risk patients or in patients who are treated in units with high methicillin resistant rate (>10–20%). Single antipseudomonal antibiotic is generally suggested unless the patient is at high risk for antimicrobial resistance or being treated in a unit with high resistant rate for pseudomonas (>10%). A 7-day course is generally recommended [34].

4.4. Sinusitis

Incidence of nosocomial sinusitis is estimated to be 12 cases per 1000 patient-days [46]. Prolonged intubation is the main risk factor as the majority of the infections occur after 7 days of the hospitalization [47]. The rout of intubation either orotracheal or nasotracheal does not alter the nosocomial sinusitis rate as shown in a randomized clinical trial of patients needed intubation for more than 7 days [48]. Other identified risk factor include sedative use, nasoenteric feeding tube, Glasgow Coma Score (GCS) less than 7 and nasal colonization with Gram-negative bacteria [46]. Nosocomial sinusitis usually presents with fever; the disease should be suspected in all intubated patients who have a fever without an obvious source. Most patients have leucocytosis [47]; purulent nasal discharge is a useful clinical sign that raise the suspicion of the sinusitis as a source of the infection. Air-fluid level or opacification are the radiological signs seen on the sinus CT scan images. Microbiological confirmation of the infection can be achieved by culture of sinus fluid in 75 and 90% of the cases using antral tap or endoscopic tissue culture respectively [49]. Infective bacteria that cause nosocomial sinusitis are similar to those of VAP, furthermore, up to 62% of patients with confirmed sinusitis had evidence of concomitant ventilator associated pneumonia (VAP); thus, assessment for VAP is warranted [50]. Nosocomial sinusitis requires 5–7 days of empirical broad spectrum systemic antibiotic that cover the common hospital acquired pathogens until the result of the sinus fluid culture is available [51]. Additional local measures include removal of nasogastric tubes and using nasal decongestants [51]. Surgical drainage of the infected sinuses is indicated if the condition failed to response to the appropriate course of antibiotic therapy within 2–5 days of treatments [51].

5. Late onset complications

In this section we discuss the complications which usually present days to weeks after extubation. Many of the late onset complications are consequences to prolonged intubation. **Table 2** summarizes the late onset complications.

5.1. Obstructive fibrinous tracheal pseudomembrane

Formation of an obstructive fibrinous tracheal pseudomembrane (OFTP) is a rarely reported but potentially fatal complication. OFTP has been reported in 53 patients (39 adult and 15

Obstructive fibrinous tracheal pseudomembrane formation
Post-intubation tracheal stenosis
Laryngeal stenosis
Tracheomalacia
Tracheoesophageal fistula
Tracheoarterial fistula

Table 2. Late onset complications.

pediatric) until September 2016 [52]. The OFTP is not just a thick mucus plug that impact on the tracheal wall; it is a well-formed, well-organized fibrinous membrane.

The exact mechanism of this fibrinous material formation is not completely known. It is hypothesized that OFTP is a consequences of tracheal ischemic injury which lead to mucosal injury. This cause desquamation and necrosis of the tracheal epithelium in addition to polymorphonuclear cells infiltration; and subsequently fibrinous material formation [53, 54]. OFTP has been reported in patients intubated with different types of ETT including cuffed rubber tubes, double lumen tube, and cuffed and uncuffed silicone tubes. Clinical studies have suggested several risk factors such as increase pressure of ETT cuff, usage of large tracheal tubes, traumatic intubation and prolonged intubation [54]. Presence of one or more of the previously mentioned risk factors is not absolutely necessary for OFTP to develop. Patients having OFTP most commonly present with post extubation stridor, cough and/or hoarseness with 74.1%, 13% and 9.3% respectively. Respiratory failure may develop in almost one third of the cases. The median time to onset of symptoms after extubation was 30 h in adult population. Nevertheless, OFTP is still in the differential diagnosis for early extubation failure; it has been presented immediately after extubation in few cases [52]. CT scan can show the intratracheal pseudomembrane, however, the definitive diagnosis is usually obtained by flexible bronchoscopy. Spontaneous expulsion of the fibrinous tracheal pseudomembrane is uncommon (11.1%), and flexible bronchoscopy is a very useful option for removal of the pseudomembrane especially in the pediatric population. Rigid bronchoscopy is another important tool which was reported to be necessary for a successful management in more than 50% of the adult patients [52].

5.2. Post intubation tracheal stenosis (PITS)

The incidence of PITS was previously estimated to occur in 1% of the intubated patients; however, the use of low pressure high volume cuffs has reduced its incidence by 10-fold [55]. The pathogenesis of PITS starts by a mucosal ischemic injury due to excessive ETT cuff pressure (>30 mm Hg) [56]. This compression injury on the tracheal cartilages causes chondritis with subsequent cicatricial fibrosis and progressive stenosis [57]. **Figure 2** shows the ETT cuff related compression injury in a canine module [58].

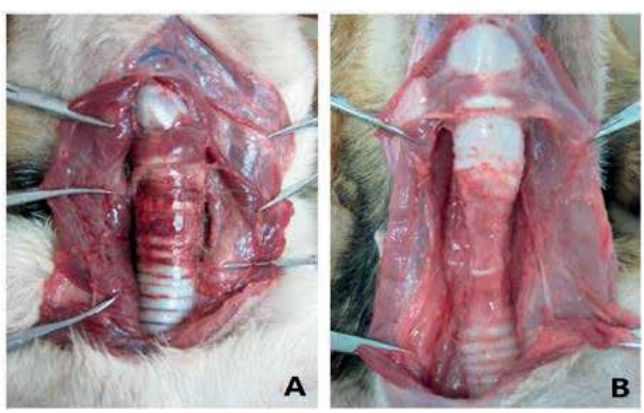

Figure 2. A. Congestion of the external tracheal wall compressed by cuff was observed immediately after extubation. B. Tracheal cartilage underwent necrosis and collapsed at 2 weeks after extubation. Courtesy of Su et al. [58].

PITS is categorized into three types [55]:

1. *Simple (web-like) stenosis* (**Figure 3A** and **D**):
   - The length is less than 1 cm
   - No or minimal damage to tracheal cartilages.
2. *Complex stenosis* (**Figure 3B** and **E**):
   - Longer than 1 cm.
   - Tracheal cartilages are damaged.
   - Usually complicated with tracheomalacia.
3. *Pseudoglottic (A-shaped or tent-shaped) stenosis* (**Figure 3C**) [59]:
   - It is a particular subtype of the complex stenosis that usually follows tracheostomy insertion.
   - The stenosis is due to dislocation or fracture of the tracheal cartilaginous rings with localized tracheomalacia

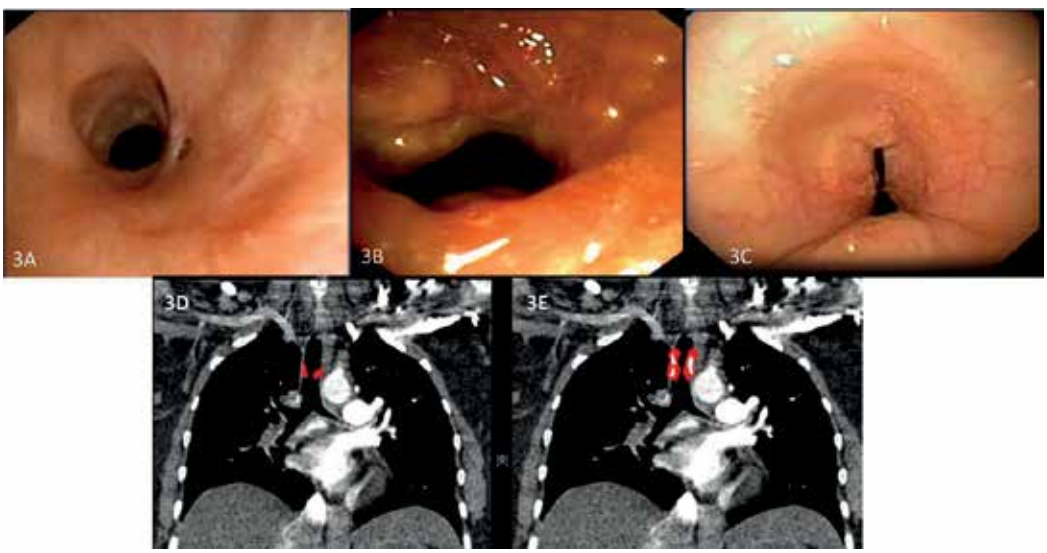

Figure 3. A–C: Bronchoscopic images show the different types of the PITS (G. Stratakos; Intubation/Long-Term Complications of Tracheal Intubation). D and E: Schematic illustration of simple and complex PITS on coronal cut of chest CT (A. Touman; Intubation/Long-Term Complications of Tracheal Intubation).

Increased ETT cuff pressure is considered to be the most important cause of PITS; other proposed risk factors are [60]:

1. *Oversizing the ETT* in comparison to the tracheal lumen.
2. *Prolonged intubation*. It should be noted that a brief intubation does not exclude the diagnosis of PITS as it has been reported to follow intubation of less than 24 h [61].

3. *Hypotension*
4. *Steroid use and local tracheal infection* are potential risk factors.

Patients with PITS usually complain of dyspnea with or without stridor. Expiratory wheeze at exertion is also a feature of PITS which can be easily confused with asthma. Therefore, the diagnosis is not initially suggested in up to 44% of the cases [56]. Furthermore, PITS manifest lately during patients' recovery from the ICU admission; during which patients' physical activity is minimal. Thus dyspnea and stridor may not be clinically evident until the disease reaches an advanced stage i.e. trachea has lost 70% of its diameter [55, 62].

PITS symptoms usually start within the first 3 months after extubation. The stenotic segment can be visualized by the computed tomography or directly during bronchoscopy. If pulmonary function test is requested the characteristic plateaued expiratory curve of the flowvolume loops exhibit only if the tracheal lumen is critically stenosed [55]. Management of PITS requires a multidisciplinary approach including thoracic surgeon and interventional pulmonologist experience in the treatment of such cases. Simple web-like stenoses can be treated by radial incisions at 3 and 9-o'clock positions using neodymium-yttrium aluminum garnet (Nd-YAG) laser, photo-dissection or electro-knife [63]. Circumferential sleeve resection with end to end anastomosis is the treatment of choice if applicable for the Complex stenosis and in cases of multiple relapses of the web like stenoses. In non-operable patients balloon dilatation, Nd-YAG laser, photo-dissection and/or stent placement are alternative options [55].

5.3. Tracheomalacia

Malacia derives from the Greek world "μαλακία" which means softness. Tracheomalacia (TM) describes the condition where the anterolateral wall of the trachea collapses during respiratory cycle due to softening of the cartilaginous rings that maintain the contour of the trachea. If the disease extends to involve the trachea and the main bronchi the term tracheobronchomalacia (TBM) is used. In cases where the posterior membranous part of the trachea excessively displaces anteriorly during expiration as a result of atrophy of the longitudinal elastic fibers of the membranous wall, the condition is described as excessive dynamic airway collapse (EDAC) [64]. TM and EDAC may or may not coexist [65].

The tracheal lumen caliber normally varies during the respiratory cycle; decrease in the cross-sectional area of the trachea by more than 50% is considered abnormal [66]. Tracheomalacia may results from primary (congenital) or secondary (acquired) causes;

The exact incidence of the TM after intubation is unknown; in general the acquired TM is more common than the congenital one [64]. Intubation and tracheostomy are the commonest secondary causes [66]. Risk factors and the pathogenesis of the TM are similar to PITS where the tracheostomy stoma or the excessive and/or prolonged ET tube cuff pressure causes airway ischemia and chondritis which eventually result in necrosis and softening of the tracheal cartilage [66]. Depending on the site of the insult TM can be

intrathoracic or extrathoracic; the intrathoracic (below the thoracic inlet) tracheomalacia being the commonest. In cases of intrathoracic tracheomalacia the trachea collapses during expiration because the intrathoracic pressure exceeds the intraluminal pressure; while in the extrathoracic tracheomalacia the collapse occur during the inspiration because the atmospheric pressure exceed the negative intratracheal pressure [67].

TM might be overseen if the tracheal narrowing is mild; On the contrary, it can be diagnosed early in case of difficulty to wean a patient from mechanical ventilation [6]. Intubation itself can pose diagnostic challenges for diagnosis because the ETT keeps the malacic part of the trachea patent preventing its collapse. Moreover, the positive-pressure ventilation acts as a pneumatic stent [65]. In milder cases, exertional dyspnea, cough, difficulty to clear sputum and hemoptysis are the main symptoms [68]. Barking cough [69] and cough syncope [70] associated with forced cough are also feature of the disease. In severe cases of TM symptoms can progress to hypercapnic (type 2) respiratory failure [71]. Inspiratory and/or expiratory stridor presence depends on the severity of the collapse and the location of the malacic tracheal segment. As was the case with PITS, TM poses diagnostic challenge due to overlap between its symptoms and asthma symptoms. In fact, dyspnea associated with wheeze is present in 51% of TM cases which frequently misdiagnosed as bronchial asthmas. Moreover, physician might confuse the recurrent episodes of bronchitis which result from the retained secretions by asthma exacerbation. History of ET intubation or tracheostomy should alert the treating physician to consider TM especially if the patient condition is refractory to corticosteroids and bronchodilators therapy [65].

Once TM is suspected a dynamic airway CT scan (during inspiratory and expiratory phase) can confirm the diagnosis. The dynamic flexible bronchoscopy preferably performed on spontaneously breathing patients under conscious sedation is considered the gold standard diagnostic method (**Figure 4**) [72]. Cine fluoroscopy and Cine magnetic resonance imaging are alternative methods for diagnosis.

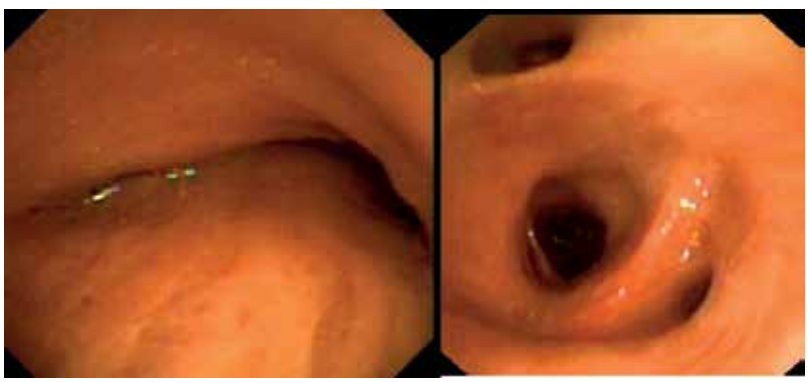

Figure 4. Bronchus intermedius with severe bronchomalacia, before and after establishment of C-PAP non-invasive mechanical ventilation (G. Stratakos; Intubation/Long-Term Complications of Tracheal Intubation).

Different abnormalities on the pulmonary function test can suggest the TM, however, none are characteristic. The reported abnormalities include:

1. The commonest abnormality is an *obstructive lung physiology* with decreased value of forced expiratory volume in 1 s (FEV1); it was reported to occur in approximately 70% of the cases [73].

2. *Flattening of the expiratory limb of the flow volume curve*. This pattern is highly suggestive of TM and it was recorded in 50% of the moderate severity cases [73].

3. *The flow-volume loop shows rapid declines of the maximal expiratory flow following a sharp low peak* [74] **Figure 5**.

4. Rarely, *flow oscillations (saw-tooth appearance)* appear on the flow volume curve (observed in 1.4% of the cases) [75, 76].

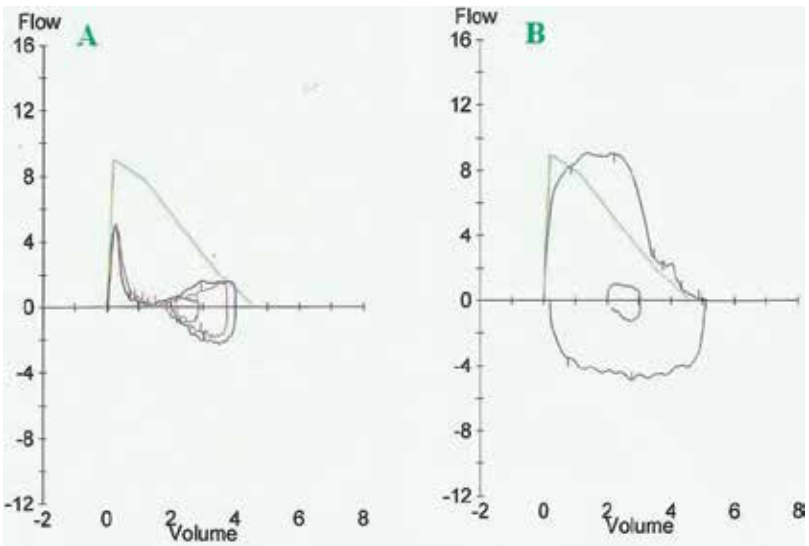

Figure 5. A. The flow volume loop of a post intubation TM patient shows rapid decline in the maximal expiratory flow after a sharp peak. B. Flow volume loop of the same patient after treatment with tracheal silicon stent (G. Stratakos; Intubation/Long-Term Complications of Tracheal Intubation).

Incidental discovery of TM or EDAC during bronchoscopy in asymptomatic patients does not require medical intervention. Available treatments for the symptomatic cases include:

1. *Noninvasive positive-pressure ventilation* (NIPPV) using Continues positive airway pressure (CPAP) which act as pneumatic splint for the malacic collapsing airway [65].

2. *Bronchoscopic interventions and stent placement* are one of the most commonly used treatment options in TM. Silicone stents are preferred because of the dynamic nature of the airway during breathing. Patients should be aware of the need of continues care of the stent to prevent obstruction of the stent by retained mucus [65].

3. *Tracheostomy* which bypasses the malacic segment; if a longer tube used as Montgomery T-tube the tube itself splint the airway open. In cases of long malacic segment it can be combined with the NIPPV [64].

4. *Surgical interventions* such as:

   a. Tracheal resection and end to end anastomosis can be curative in short segment tracheomalacia [77].

   b. Tracheobronchoplasty: different surgical methods have been described to reinforce the wall of the malacic trachea; surgeon used mesh, autologous grafts from fascia, bone or costal cartilage as tracheal splint. Biocompatible ceramic rings and plastic prostheses have also been used [64].

5.4. Tracheoesophageal fistula

Development of a tracheoesophageal fistula (TEF) in an intubated is rare; it is estimated to occur in less than 1% of the intubated patients [78]. High ETT cuff pressure is the major cause of this complication, it cause the tube to erode through the posterior membranous part of the trachea in to the esophagus forming a communicating tract **Figure 6**.

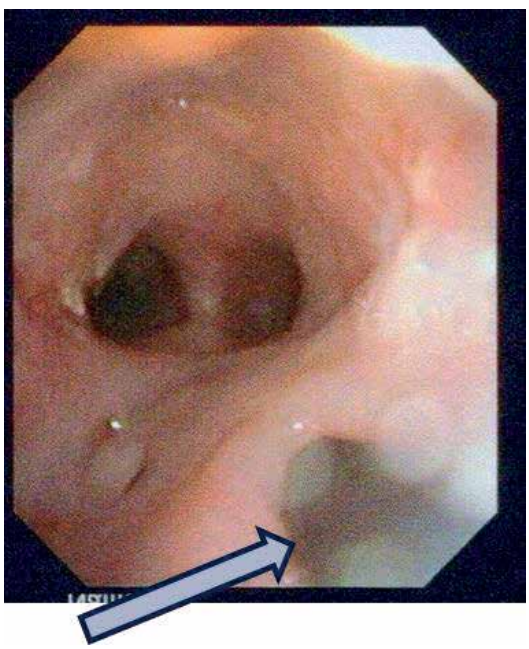

Figure 6. Illustrates a TEF shown during bronchoscopy. Arrow is pointing the orifice of the esophageal fistula (Gr. Stratakos; Intubation/Long-Term Complications of Tracheal Intubation).

Ischemic necrosis starts to appear after as little as 10 h of intubation with ETT cuff pressures of greater than 20–30 cm of water [78]. Other risk factors of TEF include [79]:

1. Prolonged duration of intubation.
2. Excessive repeated ETT manipulations.
3. Use of a rigid nasogastric tube

4. Diabetes, infection and/or steroids use.

TEF presentations are variable and depend in many cases on the size of the fistula and the amount of the gastric contents regurged to the airway. TEF may be discovered by the treating team while the patient on mechanical ventilator in cases the enteral food materials are aspirated from the ETT during suctioning. Physician might also notice that the patient's abdomen is distended with air; positive endotracheal cuff leaks might also be the pointer toward the diagnosis. On the other hand, the patients might present after extubation with choking and coughing with feedings, copious secretions, progressive dyspnea and recurrent episodes of aspiration pneumonia and/or recurrent hypoxemic events [80].

Once the condition is suspected clinically it can be confirmed by imaging. CT scan or esophagograph with barium or gastrografin contrast can be used. The communicating fistulous tract can directly be visualized during Esophagogastroduodenoscopy (EGD) or bronchoscopy. A small or high up fistulas might be missed during bronchoscopy; therefore, bronchoscopist should pull the ETT up and meticulously search the fistula [81]. Bronchoscopic signs of fistula include redness and swollen of the mucosa and/or presence of whitish material in the airway [81].

Spontaneous closure of the fistula is rare; therefore, once a TEF has been identified a prompt medical intervention should be undertaken as a bridge until the patient general condition improves to allow for definitive surgical interventions. The following management's steps are absolutely necessary [82]:

1. Prompt diagnosis and treatment of the aspiration pneumonia, using broad spectrum antibiotics which cover Gram positive and negative pathogens as well as the anaerobes.
2. A tracheostomy tube should be inserted so that its cuff to be below the fistula. If this is not possible, the ETT cuff to be placed distal to the fistula; its cuff should be inflated with minimal pressure.
3. Insertion of a jejunostomy tube for feeding or using total parenteral nutritions (TBN).
4. Gastrostomy tube insertion to reduce gastric contents reflux to the airway.

Surgical repair is the definitive treatment for most cases of intubation induced TEF. The TEF repair surgeries are high risk surgeries with a mortality rate of 10.9%; the recurrent rate of the fistulas is 7.9% and post-operative delayed tracheal stenosis has been reported to occur on 2.6% [82]. Endoscopic closure of small fistula, or inoperable ones using fibrin glue [81], cardiac septal defect occluders [83] or silicon rings [84] have been reported in few case reports. Single or dual esophageal and/or tracheal stent placement has been used for palliation in cases where TEF is resulted from malignant underlying diseases [81].

5.5. Tracheoarterial fistula

The term tracheoarterial fistula describes an abnormal communication between the tracheobronchial tree and blood vessels. The innominate artery is the most affected vascular structure (72% of the reported cases) due to its close anatomical proximity to the trachea (**Figure 7**). The

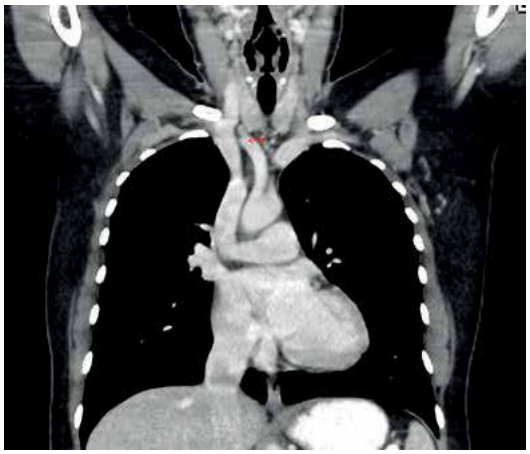

Figure 7. Coronal CT with intravenous contrast shows the innominate artery lies adjacent to the trachea (A. Touman; Intubation/Long-Term Complications of Tracheal Intubation).

incidence of trachea-innominate fistula has been reported to be 0.7% of patient underwent tracheostomy [85]. Fistulas were also reported to occur between the trachea and the carotid arteries in 4.3% and between the trachea and the superior and inferior thyroid artery in 0.9 and 2.6% of the cases respectively [86]. It was also reported with aortic aneurysm (1.8%), or even with a venous structure as the right innominate vein <3.5% [86].

Low lying tracheostomy tube insertion is the major risk for this devastating complication [86]. Tracheoinnominate fistula can also be caused by ETT due to high cuff pressure [87]. Tracheal mucosa erosion can occur with cuff pressure as low as 25 mm Hg and as early as 24–48 h after tube placement [88, 89]. Other possible risk factors along with high cuff pressure are:

1. *Inappropriate cuff size* [87].
2. *Neuromuscular disorders* as (cerebral palsy, myoclonus epilepsy, agenesis of the corpus callosum, cerebral contusion, muscular dystrophy and spinal deformities) because the need of long-term mechanical ventilation and tracheostomy, as well as the presence of atypical head and neck positions of the patient [87, 90, 91].
3. *Tracheal ring fracture* during tracheostomy tube insertion; the tracheal ring fragment can cause continues mechanical irritation and eventually erode through the wall of innominate artery [92].

The full-blown presentation of tracheoarterial fistula might be proceeded by warning symptoms, such as aspiration of blood during suctioning, bleeding beside the tracheal cannula, or pulsation of the cannula.

Bronchoscopy, catheter angiography or CT angiography are the investigational tools to localize the fistula. Nonetheless, a small size fistula can poses diagnostic challenges. In view of almost certain grave outcome in non-operated patients, non-diagnostic results of the investigations in presence of high clinical suspicion should not delay the surgical exploration and repair [93]. **Figure 8** shows catheter angiography picture of tracheoinnominate fistula.

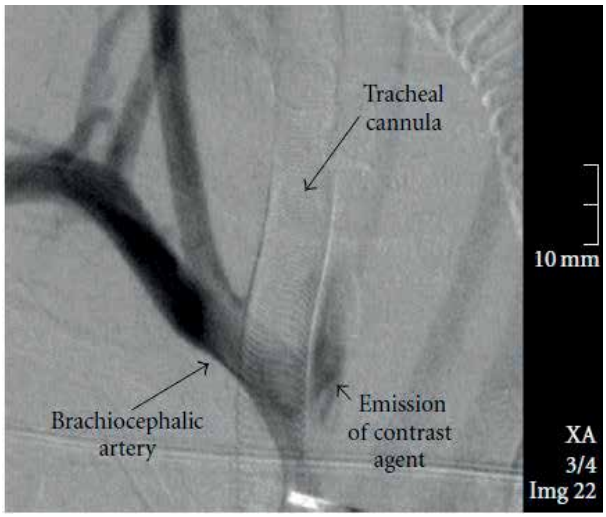

Figure 8. Angiographic scan of a free contrast agent beside the innominate artery and beside left lateral side of the tracheal cannula. Courtesy of Richter et al. [92].

Warning signs such as sentinel bleeding or pulsating tracheostomy tube are described in literature and should be checked and reported despite they are frequently absent. Tracheoarterial fistula presentation is of massive bleeding. The majority of the cases (72%) bleed in the first 3 weeks [86], however, bleeding might occur as late as after 20 years [84]. In cases with massive bleeding hemostasis should be insured before pursuing investigations or definitive treatment. Hemostasis can be achieved by over inflating the tracheostomy/Endotracheal tube cuff until the bleeding stop [90]. The aspirated blood should be suctioned as asphyxiation is more likely to cause death than blood exsanguination. Supportive measures such as intravenous volume replacement to correct hypovolemia, or blood transfusion to replace the blood loss and optimize oxygen delivery should be given as necessary. The definitive treatment is surgical; with various techniques that have been described in the literature. There is always concern while dissecting the innominate artery to cause arterial insufficiency to the cerebral circulation. Neurological deficit reported to occur in 4.5% of fistula repair survivor [91]; therefore, cerebral blood flow monitoring during the surgery is of utmost important [90].

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Difficult Airway Intubation

Chapter 6

Intubation: Difficult Airway

Vaninder K. Dhillon

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.75512

Abstract

This chapter focuses on the difficult airway algorithm during the intubation process. The current published recommendations will address the definition of the difficult airway, steps by which to secure the airway, and when to employ a surgical airway in the form of tracheotomy or cricothyrodotomy. Finally, the role of the Otolaryngologist-Head and Neck Surgeon will be highlighted in the difficult airway team which should be multidisciplinary when handling airway concerns in a hospital. Overall, the goals of this chapter are to educate the reader on how to critically analyze and decide on the means to adopt a difficult airway algorithm in their own institution(s).

Keywords: difficult airway guidelines, tracheotomy, cricothyroidotomy, surgical airway

1. Introduction

Intubation is the mechanism to artificially secure the airway. When assessment of the airway yields concerns of poor oxygenation and ventilation through traditional technique, then a difficult airway algorithm should be considered. The difficult airway algorithm is described in multiple practice guidelines, amongst many specialties [1, 2]. This chapter reviews the definition of a difficult airway, anatomical and physiological considerations of a difficult airway, and the tools that are utilized when attempting a difficult airway intubation. Lastly, from a head and neck surgical perspective, the chapter will discuss the options for surgical airway, when to consider placement of a surgical airway, and what is required from a multidisciplinary approach when left with placing a surgical airway.

2. Definition of a difficult airway

The definition of a difficult airway has been described multiple ways in the literature. There is no single definition of a difficult airway. According to the 2003 revised American Anesthesiology Task Force guidelines, a difficult airway is when a trained anesthesiologist experiences difficulty with face mask ventilation of the upper airway, difficulty with tracheal intubation, or both [2, 3]. Other definitions incorporate a broader definition whereby there is problematic ventilation using a facemask, incomplete laryngoscopic visualization, or as a difficult intubation with standard airway equipment [4]. Difficult ventilation is the inability to deliver the necessary tidal volume via the facemask even when using an oral or nasal airway and necessitating another device such as the laryngeal mask airway. Difficult laryngoscopy is impaired visualization of the true vocal cords despite elaborate external laryngeal repositioning. Difficult intubation requires external laryngeal manipulation, difficult laryngoscopy requiring greater than three attempts at intubation, intubation requiring nonstandard equipment or approaches, or the inability to intubate using all available methods [5].

The importance of identifying a difficult airway is not in a single definition—it is in the recognition by a team in charge of the airway to institute an algorithm to secure the airway appropriately, in order to prevent morbidity and mortality. The incidence of difficult intubation in the operating room ranges between 1.15 and 3.80% [6], with failed attempts in 0.05–0.35% of cases [7, 8]. In the emergency department, difficult intubation occurs in 3.0–5.3% [7, 8] of cases with failure rates ranging from 0.5 to 1.1% [7, 8]. The most common complication related to a difficult airway is mistakes in the algorithm, mainly caused by unpreparedness [4]. This chapter aims to describe ways to prepare and secure the difficult airway.

2.1. Early clinical considerations of a difficult airway

In order to prepare and implement a difficult airway algorithm, it is important to assess the clinical scenarios or patient factors that can help determine the airway plan. Both the environment and patient stability dictate the scope of evaluation and management. The pace at which the assessment, approach and intervention is made is vital to securing the airway.

The initial history and physical examination are crucial in the assessment of the airway. The history is most accessible in an elective scenario or controlled setting where the patient is stable. Patient's age, mental status and cooperativeness is also important [5]. Pertinent history includes prior history difficult intubation, obstructive sleep apnea (OSA), head and neck irradiation, obesity, congenital malformations, cervical spine disability, and thyroid goiters [4]. Each of these factors can be important when deciding electively to secure a potentially difficult airway. In an emergency situation when a patient is not stable, having a history of difficult intubations can be the most important. Lundstrom et al. found that 24% of the patients with a documented history of difficult prior intubation subsequently experienced a difficult tracheal intubation. Amongst the patients with no history of difficult intubation, 95% of them subsequently underwent an intubation with no difficulty [9].

Other important clinical considerations include obstructing upper airway disorders. Amongst these clinical diagnoses include a more progressive process like a glottis or supraglottic tumor, subglottic stenosis, history of longstanding vocal fold paralyzes either unilateral or bilateral [4]. The presentation of patients with significant obstructing airway disorders is variable depending on the cause of the obstruction as well as the acuity or long-term progression. With a gathered history in a stable patient, what is important is the decision to consider a fiberoptic laryngoscopy prior to intubation. Flexible laryngoscopy and bronchoscopy is advisable before airway management [10]. Flexible laryngoscopy is necessary to indicate the extent, location, and nature of the obstructing disorder, and can lead to a more informed and successful airway management communication and plan. Bronchoscopy is good for visualization distal to the vocal folds in cases of subglottic or tracheal stenosis that would impede intubation.

What is important in any difficult airway is the adoption of an algorithm that begins with tracheal intubation. When tracheal intubation is not successful, an algorithm can direct the next steps to securing the airway. The risk of repeated unsuccessful trachea intubations leads to increased morbidity and mortality [11]. As soon as one method is deemed impracticable, practitioners must quickly advance through the algorithm rather than persist in futile attempts.

2.2. Difficult airway algorithm

The difficult airway algorithm is published annually by the American Society of Anesthesiologists (ASA) (**Figure 1**) to reinforce the guidelines and be utilized by anesthesiologists nationwide [2, 3]. It standardizes how to secure a difficult airway. The initiation of the airway algorithm is dependent upon assessing the likelihood and clinical impact of basic management problems such (1) difficult ventilation, (2) difficult intubation, (3) uncooperative patient, (4) difficult tracheotomy. It then proceeds to break down the algorithm into different basic management choices such as awake intubation, non-invasive techniques and spontaneous ventilation compared to intubation after general anesthesia delivery and invasive methods for intubation. Within the branched algorithm, each method is described in a step-wise fashion, and the algorithm offers steps depending on success or failure of each method. Conservative non-invasive methods only become invasive and/or require help and surgical expertise when ventilation is not successful. Caveats for invasive airway techniques are listed at the bottom of the diagram in footnote fashion.

The importance of a multidisciplinary team, the presence of an acting lead in securing the difficult airway, and the timing and number of intubation attempts are all critical components of a difficult airway algorithm.

2.3. Tools to secure the difficult airway

As described in the difficult airway algorithm, alternative approaches to intubation are only possible if the toolbox available has both the basic and the alternative instrumentation for securing the airway. The difficult airway 'cart' should be established and secure in an area in any hospital setting, whether it be in the operating room, the emergency room and/or a

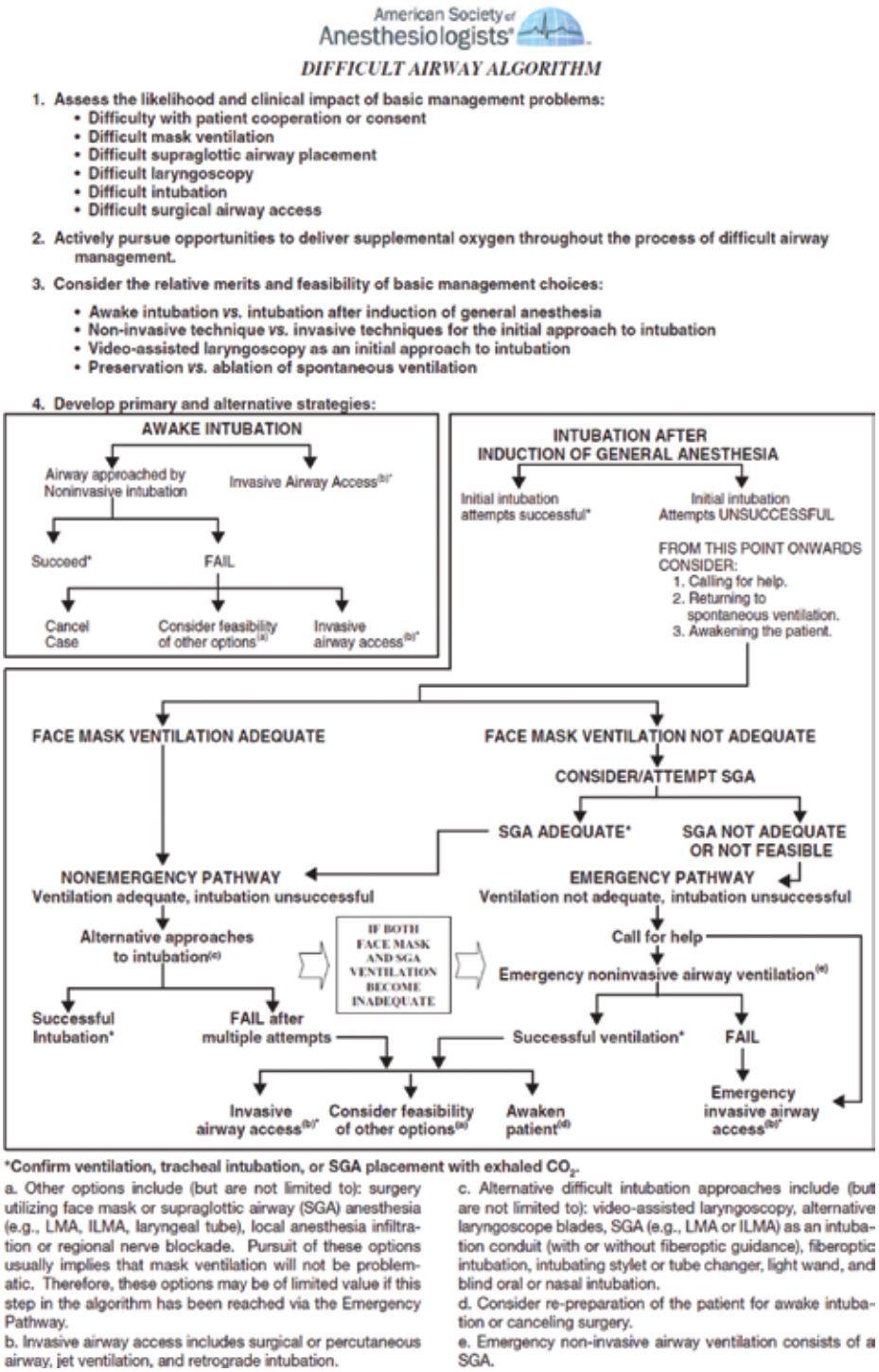

Figure 1. Difficult airway algorithm by the American Society of Anesthesiologist Task Force (2003).

designated area where it can be accessed by anyone who needs it [6, 12]. The tools for a difficult airway can be multiple.

One of the most pertinent tools in any intubation is the laryngoscope. Direct laryngoscopy is the paradigm of tracheal intubation, and has been a part of the armatarium of any provider securing the airway. The role of videolaryngoscopy over direct laryngoscopy has been a topic of discussion and published research, in regards to providing improved benefit over the traditional direct laryngoscopic approach. The authors of a large meta-analysis of five randomized controlled studies with 1301 patients found no difference in first time success in endotracheal intubation between using videolaryngoscopy over direct laryngoscopy [13]. The caveat to this meta-analysis was that most endotracheal intubations were done in an ICU setting. Other reviews and case series demonstrate an improvement in first time intubations in an emergency room setting using videolaryngoscopy over direct laryngoscopy, although there is no large randomized control study that verifies this [14–17].

In the predicted difficult airway, when a patient is able to maintain spontaneous breathing, an awake intubation is an option. The tools for an awake intubation can be either non-invasive or invasive. LMA, supraglottic airways, and nasal-rays are examples of non-invasive tools. Fiberoptic laryngoscopy allowing for placement of a nasal-ray can be done awake. Invasive techniques include a surgical airway under local sedation- open versus percutaneous tracheostomy, or retrograde intubation [1].

Other tools that can be used for awake intubation include a fiberoptic bronchoscope. Apfelbaum et al. described bronchoscope success in 88–100% of these patients, although other tools such as intubation through supraglottic devices, glidescope, and other tools are also successful [3]. The fiberoptic bronchoscope is successful if someone with proficiency is able to perform it [3].

Other tools are also important in placement of endotracheal intubation. Intubating stylets or tube changers are also an option and can be used successfully for difficult intubations. Mild mucosal bleeding and sore throat are complications associated with stylets, and lung laceration and gastric perforation are associated with exchange catheters [3, 18]. This is a blind technique.

Supraglottic airways such as the LMA have shown to be rescue devices in patients who cannot be intubated or mask ventilated. The LMA can be used with a fiberoptic bronchoscope for intubation, and can maintain or restore ventilation in the difficult airway patient [5, 6, 18].

2.4. Surgical airway

In the algorithm of the difficulty airway, the surgical airway is the definitive step in securing the airway. The placement of a surgical airway does not necessitate it being the last step in the algorithm, when non-invasive methods are unsuccessful. It may be the first step in securing the airway dependent upon the clinical context and stability of the patient. A surgical airway may be planned such as an awake tracheostomy in a patient where intubation through the glottis is not possible, or it may be an emergency when a trauma patient initial assessment

is bypassed by airway compromise and a surgical airway is the most appropriate next step for airway security. An awake tracheostomy tube is performed with no sedation and local anesthesia is used. The patient maintains spontaneous ventilation while the tracheostomy is being performed. Plain lidocaine (1%) is injected into the trachea before entering the airway to minimize coughing. After return of CO_2 is confirmed, generalized anesthesia is immediately administered [4]. Difficulties with awake tracheostomy start with inability for the patient to be fully cooperative. Physical factors include fixed cervical spine flexion deformity, obesity and increased neck circumference that decreases ability to palpate laryngeal landmarks. Large thyroid goiters can also be a limitation. History of head and neck radiation also results in distorted anatomy and loss of palpable laryngeal structures that make it hard to complete an awake tracheostomy [4].

In the case of an airway emergency or acute destabilization of a patient requiring immediate airway protection, a surgical airway can take place in two forms: a cricothyroidotomy or a tracheostomy. The pros and cons of each approach are discussed in the next section.

The steps of the emergent surgical airway are:

1. Identifying surgical landmarks, including the laryngeal skeleton and midline trachea
2. Assessment of the patient's body habitus and any potential obstructions to entering the airway (such as obesity, enlarged thyroid goiter, neck irradiation)
3. Topical anesthetic to the skin for local anesthetic and less patient discomfort (if there is time)
4. Taking a large gauge needle and syringe and placing it directly into the airway, with confirmation of aspirated air back
5. Vertical incision with a 15 blade into the overlying soft tissue and through the trachea or a vertical stab incision into the cricothyroid membrane. Placement of an endotracheal tube into the lumen is important with end tidal CO_2 confirmation.
6. Securing the airway is important which may require transportation to an operating room setting if in the emergency department, with revision to a traditional tracheostomy, neckties and achievement of hemostasis.

2.5. Pros and cons of tracheotomy versus cricothyroidotomy

The American Society of Anesthesiologists difficult airway algorithm identifies two acceptable emergency surgical airways in the 'cannot intubate, cannot ventilate' scenario: cricothyrotomy and tracheotomy [2].

According to the guidelines of the American Trauma Life Support developed by the American College of Surgeons, cricothyrotomy is recommended in an emergent setting [19]. Cricothyroidotomy is perceived to be easier to perform as it is safer theoretically, has less bleeding, and requires less surgical time [20, 21]. The difference between a cricothyroidotomy and a tracheostomy is that a cricothyroidotomy is a temporizing measure only [20].

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Furthermore, a needle cricothyroidotomy compared to a surgical cricothyroidotomy limits the time for ventilation before a more secure airway is designated [22]. A cricothyroidotomy should eventually be converted to tracheostomy as it is a more secure airway [23].

In a retrospective chart review conducted by Dillon et al. over a 6-year period at a level-one trauma center, there were 34 surgical airways, of which 10 were cricothyrotomies, whereas the remaining were emergent tracheotomies [24]. The authors concluded that the paucity of cricothyrotomies could not be accounted for and only that at their institution, tracheostomy was preferred in an emergent situation. Other studies have also found that the use of tracheotomy in the setting when intubation is not possible is considered a safe alternative [21, 25]. These studies suggested that although cricothyrotomies are the surgical airway of choice in an emergent setting, emergent tracheotomies are safe and maybe more commonly performed. Both can be performed on the field or an in hospital setting.

There are a few limitations for cricothyrotomy as demonstrated below in the table (**Figure 2**). Cricothyrotomy should not be performed in children less than 12 years of age, as the cricothyroid membrane is quite narrow resulting in an increased risk of permanent laryngeal injury [24]. Furthermore, patients with suspected laryngotracheal trauma should not undergo cricothyroidotomy [25].

Tracheostomy is a secure, permanent surgical airway. The indications and timing of placement has been reviewed extensively [26]. The complications associated with tracheostomy placement can be divided into early and late complications. Hemorrhage is the most common early complication. Any major bleeding, especially from an arterial source, may require operative exploration. Pneumothorax and/or subcutaneous emphysema are less common. Mucous plugging or obstruction due to blood clots can occur postoperatively and can be managed with the use of humidified air and regular gentle suctioning [25].

The part of a tracheostomy tube is important in patient teaching, for long-term use. Most tracheotomy tubes used commonly have an inner cannula which can be removed and cleaned on a routine basis, thus minimizing obstruction. In the early postoperative course, inadvertent displacement of the tracheotomy tube may result in a false passage, as the tract is not mature. Most of the later complications are secondary to constant pressure/irritation applied to the surrounding tracheal mucosa. This includes formation of granulomas, tracheal stenosis, and formation of fistulas in either the esophagus or the innominate artery [25]. An uncommon but

Indications	Facial fractures
	Blood or vomitus in airway
	Clenched teeth
	Traumatic airway obstruction
	Inability to maintain >90% oxygen saturation between intubation attempts or after 3 attempts
	Inability to ventilate the patient with a bag-valve-mask device between intubation attempts or after 3 attempts
	Multiple failed attempts at endotracheal intubation
Relative contraindications	Tracheal transection, fracture, or obstruction below the cricothyroid membrane
	Age <5 to 12 years, due to anatomic considerations (depending on reference)

Figure 2. Indications and contraindications for cricothyroidotomy according to the American College of Surgeons (2008).

life-threatening complication is a tracheo-innominate fistula. These are linked to low-placed tubes and patients with excessive movement of the head. This complication has a 25% mortality rate [27]. If it does occur, manual pressure over the tract or over inflation of the cuff when it is seated in this tract can help tamponade the bleed until the patient can be taken back to the operating room for further exploration.

Tracheostomy placement in the form of an open versus percutaneous approach has been evaluated in many studies, to see if there is an advantage of one approach over the other. A Cochrane analysis of all randomized control and quasi-randomized control studies, evaluated approximately 20 trials that compared percutaneous to open technique [28]. The goal was to evaluate whether there was a higher complication profile amongst one technique over the other. The review looked at studies completed in an ICU over an emergency room setting. Overall, the systematic showed some benefits in terms of effectiveness and safety of the use of percutaneous techniques for tracheostomy, especially in regards to rates of late non-life threatening complications. However there is overall low quality evidence to suggest a difference in postoperative mortality or total mortality from life threatening complications like bleeding, between the two techniques. Generalizability of one technique over the other was not possible according to the Cochrane review [28].

The review concluded that open tracheostomy may still be indicated for selected patients, despite the continuing broader indications for use of percutaneous technique [28]. Again, this review did not evaluate studies that looked at the use of percutaneous tracheostomy in an emergent, difficult airway setting.

2.6. The role of the otolaryngologist-head and neck surgeon

The role of the otolaryngologist-head and neck surgeon is to be an important counterpart to the team involved in a difficult airway. O'dell describes the role of the otolaryngologist as involved in the preoperative evaluation of a difficult airway and the comprehensive algorithm in identifying and evaluating the airway prior or during induction of general anesthesia [4]. The fiberoptic laryngoscopy, used in evaluating the airway, is the trademark tool of the otolaryngologist. The technical expertise and familiarity with the upper airway and larynx allows an otolaryngologist to screen a difficult airway [5], as well as provide therapeutic means to fiberoptically intubate at the same time if needed. Nasotracheal intubations done with the use of a fiberoptic laryngoscope is a common practice, and can be done with the patient spontaneously breathing. The availability and expertise with certain equipment allows the otolaryngologist a more invasive approach to the airway, with determination of what branch of the difficult airway algorithm should be taken next based upon findings.

An otolaryngologist is also equipped to handle the placement of a surgical airway whether it is an awake tracheostomy in a controlled setting for a patient with known upper airway obstruction and difficult intubation [4, 26]. An otolaryngologist is also able to assist in placement of an emergency surgical airway, with most otolaryngologists placing an emergent tracheostomy over a cricothyroidotomy [23, 26].

Overall, the role of an otolaryngologist is both a consultant, and a surgeon. Ultimately, in any difficult airway scenario, the otolaryngologist is a member of a multi-disciplinary team that is involved in securement of the airway with an interdependent and algorithmic approach [2, 4, 5].

3. Conclusion

In conclusion, the definition of a difficult airway is not rigid, nor is it an over-arching diagnosis. A difficult airway can come in all shapes and sizes, keeping in mind that an airway is never stable without ability to oxygenate or ventilate. The importance of a difficult airway algorithm is crucial in organization of steps involved in securing the airway. A difficult airway does not necessarily have to be an emergency, but it does take require a team approach to initiate the appropriate steps in saving a life. Resources such as equipment available to secure a difficult airway, the steps involved in performing a surgical airway, and the pros and cons of a tracheostomy over a cricothyroidotomy, were summarized in this chapter. The goal of this chapter is to allow readers to identify the difficult airway and have a broad understanding of how to provide the appropriate care for these patients. For the otolaryngologist, this chapter aims to serve as a guideline by which to address the airway with the tools and resources available, both in a controlled and emergency situation.

Conflict of interest

Vaninder K. Dhillon declares no conflict of interest in the publication of this manuscript.

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Endotracheal intubation is a mandatory practice in the anesthesiologic management of surgical procedures, cardiopulmonary resuscitation, life-saving procedures in the emergency department, and medical procedures, and it involves many medical issues such as anesthesiology, surgery, and pulmonary diseases. This book deals with the basic principles of hypoxia and oxygenation in terms of functional airway anatomy and intubation requirements as well as difficult airway algorithms.

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