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Brozović, Bernard

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**UNIVERSITY OF ZAGREB
SCHOOL OF MEDICINE**

BERNARD BROZOVIĆ

AIRWAY MANAGEMENT IN OBESE PATIENTS

GRADUATE THESIS

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Graduate thesis, *Airway management in obese patient* is done in Anesthesiology and Reanimatology Department in KBC Rebro, University of Zagreb, School of Medicine, under mentorship of prof.dr.sc. Dinko Tonkovic.

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Head of the Committee: Prof. dr. sc. Slobodan Mihaljević

Second member of the Committee: Doc. dr. sc. Danijela Bandić Pavlović

Mentor: Prof. dr. sc. Dinko Tonković

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Summary

Obesity, a prevalent modern disease, proposes many challenges for the medical profession. There has been substantial research done in order to battle them. Alteration in human anatomy and physiology due to obesity poses additional challenges for anesthesiology and many strategies are being developed to meet all necessary requirements in order to sustain the same quality provided in so-called normal average patients. Airway management underwent a lot of improvements over time and many different techniques have arisen to provide and sustain a patient state of oxygenation and post surgical recovery. Modifications on already existing techniques also have their role in strategies that are getting into protocols used in airway management in obese patient. Such patients come with multiple complications and present a difficulty to have effective preoperative preparation and intraoperative management. To decrease complications and to improve recovery of the obese patients depends on finding a proper plan and the development of new methods for obese patient management.

Key words

Obesity, difficult airway, anesthesia, oxygenation, obstructive sleep apnea, trachea, ventilation, intubation, aspiration, laryngoscopy, supraglottic airway devices.

Sažetak

Pretilost, smatra se modernom bolešću koja donosi mnogo izazova za medicinsku djelatnost danas, no velika količina istraživanja je provedena da bi se došlo do rješenja kad je u pitanju pretilost. Promjene koje se dogode u anatomiji i fiziologiji čovjeka koji je pretio predstavlja veliki izazov za anesteziologiju i velik broj strategija se razvilo da bi se zadovoljili isti uvjeti koji su viđeni kod takozvanih prosječnih normalnih bolesnika. Anatomija mnogih sustava pogotovo dišnog je uvelike pod mehaničkim utjecajem masnog tkiva koje dolazi iz mnogih faktorijskih etiologija i razvija direktnu fiziološku promjenu u pretilih bolesnika. Održavanje dišnih puteva kroz vrijeme se poboljšalo i veliki broj različitih tehnika se razvio kako bi održala razina kisika kod bolesnika i omogućilo oporavak nakon operativnog zahvata. Modifikacije kod već razvijenih tehnika viđenih u radu isto imaju svoj udio u strategijama koje postaju sve više dio protokola rabljenih u održavanje dišnih puteva kod pretilih bolesnika. Postoji veliki broj komplikacija s kojima dolaze pretili bolesnici je također problem koji otežava pripremu bolesnika prije operativnog zahvata a isto tako održavanje bolesnika za vrijeme operativnog zahvata. Naći način na koji dobro proučiti i razviti plan za pretilog bolesnika leži na mnogim promjenama i razvitku novih metoda koje mogu odvesti do smanjenju pojava komplikacija a i poboljšati oporavak bolesnika.

Introduction

Obesity is becoming a major contributor to worldwide health problems and has an increased impact on morbidity and mortality in the global population. It is considered a preventable cause of other comorbidities that occur as a consequence of excessive adipose tissue as metabolic syndrome that can be seen as part of the etiological cause of obesity but also as a consequence of obesity. Considering the types of obesity there is a distinction between central obesity or apple type obese individual and peripheral obesity or pear type obese individual. The importance lies in different reactions and complications seen in these two different types. With obese patient population on the rise, it makes them a special risk population for most of the medical fields specifically due to alternations seen in many levels of functioning from biochemical to macroscopical anatomical level that transfers the problem to other levels and systems in the body. One of these connected issues is seen in respiratory system that presents a large challenge to medical professionals dealing with management of the airways and lung function in the obese patients. Anesthesiological preoperative assessment and preparation is of significant importance in any patient which includes also obese patients in order to identify what are possible difficulties that might present a problem to sustain physiological state of the patient during procedures. Assessment of cardiovascular, respiratory system and overall health state represent the most important pillars that will provide enough information necessary to design an accurate plan for each patient that is facing future surgical procedure. One of the most important managements is the airway management and lung function to sustain normal levels of oxygenation while the patient is in the induced anesthesia. In obese patient reserve and lung function is distorted by obesity presenting difficulties for intubation and securing an airway even before induction of anesthesia. Just having neck circumference >40 cm, together with BMI over

35kg/m² contribute significantly to difficult intubation and additional assessment of the patient state through questions about loud snoring and daytime somnolence that will lead to conclusion of presence of obstructive sleep apnea (OSA) and indication for preoperative treatment in order to optimize an obese patient for the procedure and having better postoperative recovery.

Airway management in obese patient is more demanding since it requires modifications and development of new strategies that might lead to better results in overall outcome. That is why the use of positioning methods and airway manipulations are needed to be able to rapidly secure basal lung function in a patient that will have small results in establishing good oxygen reserve by preoxygenation prior to the intubation. Many other problems develop because of obesity and require changes in anesthetic drug use and dosage, providing different measures that might help in weight reduction. Presentation of obese patients itself is a demanding task due to complexity that arises from interactions of multifactorial etiologies and comorbidities, developing and contributing to overall impact of obesity on all systems. The focus is given to the respiratory system in obesity, from an anesthesiological point of view, protocols of airway management and ensuring a safe environment and due care.

List of aberrations

AHI Apnea/Hypopnea index

BMI Body mass index

COPD Chronic obstructive pulmonary disease

CPAP Continuous positive airway pressure

CTM Cricothyroid membrane

DL Direct laryngoscopy

ETT Endotracheal tube

ERV Expiratory reserve volume

FEV1 Forced expiratory volume in 1st second

FMV Face mask ventilation

FOB Fiberoptic bronchoscopy

FRC Functional residual capacity

FVC Forced vital capacity

HDL high density lipoprotein

LDL Low density lipoprotein

LMA Laryngeal mask airway

LPL Lipoprotein lipase

OSA Obstructive sleep apnea

PFT Pulmonary function test

RV Residual volume

SAP Safe apnea period

SGD Supraglottic airway device

TLC Total lung capacity

VL Video laryngoscope

Respiratory system anatomy

Human respiratory system starts to develop when the embryo is approximately 4 weeks old. The respiratory diverticulum appears as an outgrowth from the ventral wall of the foregut. It then undergoes five different stages of development and maturation to a fully functional respiratory system [1]. Functional anatomy divides the respiratory system into conducting portion and a respiratory portion. The conducting portion, which consists of the nasal cavities, pharynx, larynx, trachea, bronchi, bronchioles and terminal bronchioles. Conducting portion humidifies, warms and cleans the air that does reach the respiratory portion, thus conducting portion is not involved in gas exchange and produces anatomical dead space air. The respiratory portion, where the system's main function of gas exchange occurs, consists of respiratory bronchioles, alveolar ducts, and alveoli but if perfusion of part of alveoli is disrupted that contributes to formation of physiological dead space air. Histological anatomy of the respiratory system is making this system functional for gas exchange and allowing all other systems to be viable because of its physiological functionality. Throughout the airways pseudostratified ciliated columnar epithelium lines the passage of the air and has the ability to move secretions as a functional mucociliary escalator out of the airways. Functional unit in the lungs is made of the respiratory bronchioles, alveolar ducts and alveoli and this triad is referred to as respiratory acinus where actual exchange is occurring [2]. Site where gas exchange actually occurs is referred to as a blood air barrier that is made of endothelium, basement membrane and pneumocytes type 1 that make up 90% of cells in the lungs. Respiratory system is also defined as a lung - chest wall system that relies on skeletal and muscular parts of the thorax that functionally provide the ability to breath. Classification of muscle is established by their function

into inspiratory muscle and expiratory muscles. The lungs can be expanded and contracted in two ways. Diaphragm contraction causes the vertical diameter of the thorax to increase by downward and upward movement of the diaphragm during inspiration and expiration. Second part of breathing is by elevation and depression of the ribs to increase and decrease the anteroposterior diameter of the chest cavity [3]. Normal quiet breathing is accomplished almost entirely by movement of the diaphragm. During inspiration, contraction of the diaphragm pulls the lower surfaces of the lungs downward. Then, during expiration, the diaphragm simply relaxes, and the elastic recoil of the lungs, chest wall, and abdominal structures compresses the lungs and expels the air. During heavy breathing, however, the elastic forces are not powerful enough to cause the necessary rapid expiration, so extra force is achieved mainly by contraction of the abdominal muscles, which pushes the abdominal contents upward against the bottom of the diaphragm, thereby compressing the lungs. The most important muscles that raise the rib cage are the external intercostals muscles, but others that help are the sternocleidomastoid muscles, which lift upward on the sternum, anterior serrati, which lift many of the ribs and scaleni muscles, which lift the first two ribs. The muscles that pull the rib cage downward during expiration are mainly the abdominal recti, which have the powerful effect of pulling downward on the lower ribs at the same time that they and other abdominal muscles also compress the abdominal contents upward against the diaphragm, and the internal intercostals [4]. Respiratory system functions as a unity of both lungs and thoracic musculoskeletal aspects in order to establish necessary conditions in which humans are able to breathe. Breathing is controlled from the centers in the central nervous system (CNS) that determine inspiration and expiration but also the depth and the rhythm of the breathing. Medullary respiratory center is found in reticular formation and has two groups of nuclei that control the breathing. Peripheral chemoreceptors provide information about the level of oxygen,

carbon dioxide and level of acidity to the central system in order to have check on the level of breathing, meaning the depth and frequency to keep physiological body state [5].

Respiratory physiology

Pulmonary ventilation relies on expanding of the lungs but in order for air to move in and out of the lungs and provide gas exchange between the air and the blood there must be a gradient between atmospheric air and the alveolar air. The gradient is established by pressure difference between intrapleural and intra-alveolar pressure which is established as a transpulmonary pressure [6]. Ventilation cycle starts from *functional residual capacity* (FRC) which is considering state of rest in terms of ventilation where intrapulmonary pressure is -5 cm of water while intra alveolar being 0 cm of water and no air is being transported into alveoli. Inspiration starts with diaphragm contraction and contraction of other inspiratory muscles and producing more negative pressure in intrapleural pressure to -8 cm of water which will transfer that on intra alveolar pressure to be also negative -1 cm of water that establishes gradient between itself and atmospheric air so that air can flow into the alveoli. This will be reversed by the passive process of expiration but muscles of expiration contraction contribute to reverse the gradient in alveoli to +1 cm of water while intrapleural pressure still stays negative but -5 cm of water to sustain *residual volume* in the lungs which prevents lungs from collapse. Expiration ends by intra alveolar pressure going back to 0 thus returning the whole system into FRC which is the state of inward pull of the lungs being balanced by outward pull of the chest wall and ventilation process continues in this fashion throughout individuals life [7].

In the mechanics of breathing, ie.the lung-chest system, inspiration follows a nonelastic curve while expiration follows the elastic curve of the diagram of hysteresis. The reason behind that is that for the inflation of lungs to occur the work is done to overcome surface tension in the lungs

while expiration is considered to be a passive process that occurs without additional work. Important concept that is necessary to consider in lung physiology is lung compliance that is in direct connection of anatomy and functionality of the lung-chest system since equilibrium between two parts of this system is found at functional residual capacity where lung inward forces are equilibrated with outward forces from the chest wall [8]. Functional residual capacity is starting point when looking at the compliance of the lungs because the compliance is explained as change of volume of the lungs, thus the volume of the air for a change in pressure and changes in the lung - chest system will alter the compliance which we see how easy or hard is to fill a lung with a air at certain pressure. When compliance is high such as seen in emphysema, there is decrease in lung elastance which normal lungs are reciprocal to, consequently the lung recoil is lowered which will result in lung - chest system forces to be recalibrated to a new higher FRC. Opposite to that is lower compliance seen in pulmonary fibrosis or pulmonary edema where lung recoil is increased, which transfers that to lung - chest system being recalibrated to a new lower FRC where the forces are in equilibrium. Importance of understanding of compliance has a direct impact on dealing with ventilation and management of the lungs and airways in obese patient since this aspect is altered by obesity [9]. Beside considering functional anatomy and physiology of ventilation, other important aspect of respiratory physiology is to consider respiratory volumes and flow - volume loops, resistance to airflow in the airways and effects on it and ventilation/perfusion ratio because all of these parameters get altered by the presence of obesity and that consequently produces altered physiology of the respiratory system in obese individuals. Pulmonary function tests (PFTs) measure different lung volumes and other functional metrics of pulmonary function. They can be used to diagnose ventilatory disorders and differentiate between obstructive and restrictive lung diseases where obesity fits in. The most commonly used method is spirometry, which involves a

cooperative patient breathing actively through his or her mouth into an external device. This simple test measures both dynamic and static lung volumes with the exception of *residual volume* (RV) and consequently *total lung capacity* (TLC), as well as airflow rates. Full-body plethysmography is an additional test that relies on Boyle's law and is able to estimate both RV and TLC and is performed with the patient in a closed space of known volume but it has limited clinical use. Importance of this testing relies on changes that are seen in both obstructive lung diseases such as asthma or COPD and restrictive lung disease which can be subdivided into extrapulmonary and intrapulmonary. Intrapulmonary restrictive lung diseases are interstitial diseases such as idiopathic pulmonary fibrosis or any pneumoconiosis, while extrapulmonary restrictive lung diseases are related to disruption of chest wall or neuromuscular parts that are crucial for normal pulmonary functioning thus ventilation [10]. One of the contributions to extrapulmonary restrictive lung disease is seen in obesity that causes restriction in the lung - chest system expansion thus has a restrictive pattern seen in flow - volume loops.

Obesity

Obesity as a disease - etiology

Obesity has a significant impact on the all body systems in terms of anatomical and consequently physiological aspect but its pathogenesis having multifactorial implications leads to extensive determination of its effect as a disease. Association of genetic, endocrinological and environmental etiologies contribute to development of obesity and inducing dysfunctionality at certain levels of physiological systems. Etiology of obesity can be explained by implication of multiple factors that are interconnected and have their share in causing obesity [11]. Age as a etiological factor showed that with higher age there is a change in adipose tissue distribution

which was correlated with an increase in waist-to-hip ratio and studies showed that adipose tissue is more likely to accumulate in the abdominal area rather than in the gluteofemoral area. Gender also plays a role in etiology, where it is seen that men and women differ in distribution of body adipose tissue, where men are more likely to accumulate fat in the upper body, such as the trunk and abdomen while women more in the lower body such as hips and thighs [12]. It is thought that sex hormones have a role in determining this difference in distribution of fat between genders but also that simple adipocyte location difference between gender also provide explanation in this distribution. In men, visceral adipose tissue accumulation generally increases with the amount of total body fat, whereas in women, the volume of visceral adipose tissue is less affected by the amount of total body fat compared with men. Thus comparing genders men are more commonly seen with obesity than women which might be connected to the fact that although premenopausal women have more total body fat than men. They also have lower visceral adipose tissue accumulation and a better metabolic risk profile [13]. The fact is that men do accumulate more fat tissue than women, making them more susceptible to consequences of obesity. Genetics also have a role since family studies showed that there is a connection in obesity appearance and hereditary. Mutation of leptin gene will present with congenital obesity [14]. Appetite regulation is influenced by interplay of ghrelin which is hormone released by the stomach that stimulates lateral area of hypothalamus to increase appetite thus having an orexigenic effect or stimulating hunger. Moreover, endocannabinoids also have a role in increasing the appetite and there are seen to be elevated in obese individuals while satiety hormone leptin released by adipose tissue decreases appetite acting on satiety center in ventromedial area of the hypothalamus seems to be lowered or defective in obesity [15]. Explaining obesity in terms of simple body economy leads to the conclusion that development of obesity sits on positive caloric balance in comparison to caloric expenditure of

that caloric intake which body normally stores as unused energy in a form of fat. On the other hand, what is not seen with this correlation is that this is usually a consequence of social, economical, behavioral, gender, age and genetic factors that tend to tip these habits in favor of developing obesity. Physical inactivity and sedentary lifestyle combined with nutritional factors predispose individuals to have accumulation of adipose tissue and can be considered as a modifiable risk factors since their etiological input comes from inducing energy disbalance that the body does in order to store the energy it is not able to use [16]. Considering epidemiological assessment of the world population it led to the extension of obesity being on rise in the world even though it is not symmetrically spread in the world but there are evidences suggest an increase worldwide. Many syndromes are considered as etiological factors because they have obesity as their component such as Prader-Willi syndrome or Leptin deficiency where regulation on metabolism and metabolic factors gets altered or deficient that produces presentation of obesity because nutrients, hormones and metabolites are not in normal metabolic pathway thus become factors that potentiate unbalanced body energy state [17]. Correlation between endocrinopathy and development obesity is seen in insulin resistance and diabetes mellitus type 2. Metabolic syndrome represents a cluster of physiological and metabolic disturbances that presents an individual with abdominal obesity, glucose intolerance and hyperinsulinemia. This is due to resistance to insulin, dyslipidemia with reduced levels of HDL and elevated triglycerides and presence of hypertension together with some other features that are less common such as endothelial dysfunction, microalbuminuria, polycystic ovary syndrome, hypoandrogenism, nonalcoholic fatty liver disease or hyperuricemia [18]. In the diagnostic protocol for metabolic syndrome weight gain with visceral obesity is considered a major predictor for its determination where waist circumference measurement is preferred in clinical assessment instead of using Body Mass Index (BMI) scaling. BMI has been shown to be insensitive to indicate the risk in

development of obesity related metabolic conditions but also cardiovascular disease as well. The incidence of metabolic syndrome increases with age where 60 years of age is the usual border value that determines the increased presence of metabolic syndrome and obesity association but also includes that men tend to be more commonly affected than women. Many correlations are seen as the appearance of secondary induced metabolic syndrome. This is because drug use such as corticosteroids, antidepressants and antipsychotics among others, produces secondary metabolic syndrome as a result of insulin resistance. Thus metabolic syndrome increases the risk of developing diabetes mellitus type 2 that is indirectly connected to development of cardiovascular disease specifically atherosclerosis that is in the domain of inducing cardiovascular insult such as coronary heart disease [19]. Obesity being a core feature in metabolic syndrome has association with inflammatory responses in pathogenesis of metabolic syndrome thus having bidirectional connection between each other. It is proposed that adipocytes release proinflammatory cytokines that have a down regulatory effect on insulin signaling which leads to resistance to insulin and as a consequence of that the anti-inflammatory effects of insulin are also decreased and increased oxidative stress gets increased in obesity that promote inflammation even more, all of which contribute to etiology of the metabolic syndrome [20]. Elevated levels of triglycerides, low levels of high-density lipoprotein (HDL) cholesterol and relatively normal level of low-density lipoprotein (LDL) cholesterol seem to be more abundant but dense and smaller than usual are features of abdominal obesity. Low HDL and hypertriglyceridemia are major blood detectable abnormalities in patients with visceral obesity which is considered to be a atherogenic lipoprotein profile. This profile comes as a consequence of dysregulated lipoprotein transport in obese individual because lipid exchanges by cholesteryl ester transfer protein have been shown to be largely driven by the concentration of triglyceride-donor lipoproteins. The presence of hypertriglyceridemia and elevated VLDL

promotes transfer triglycerides to HDL and LDL for exchange of cholesteryl esters. Now HDL and LDL are rich in triglycerides which makes them highly suitable for hepatic lipase enzymes thus can deplete their lipid core and produce dense and small LDL and HDL particles.

Atherogenic lipoprotein profile is associated with development of atherosclerosis. This occurrence seen in obese patient known as atherogenic lipid triad increases the risk of cardiovascular disease development in obesity. This is also why dyslipidemia is correlated as an etiological factor of developing obesity but also the bridge between comorbidities such as cardiovascular insult and obesity [21].

Complex and multifactorial implications in obesity as a disease provide nonspecific and undetermined cause of it but interactions between factors do lead to the conclusion that obesity is a condition that steps out of normal physiological state and induces complications that come with it.

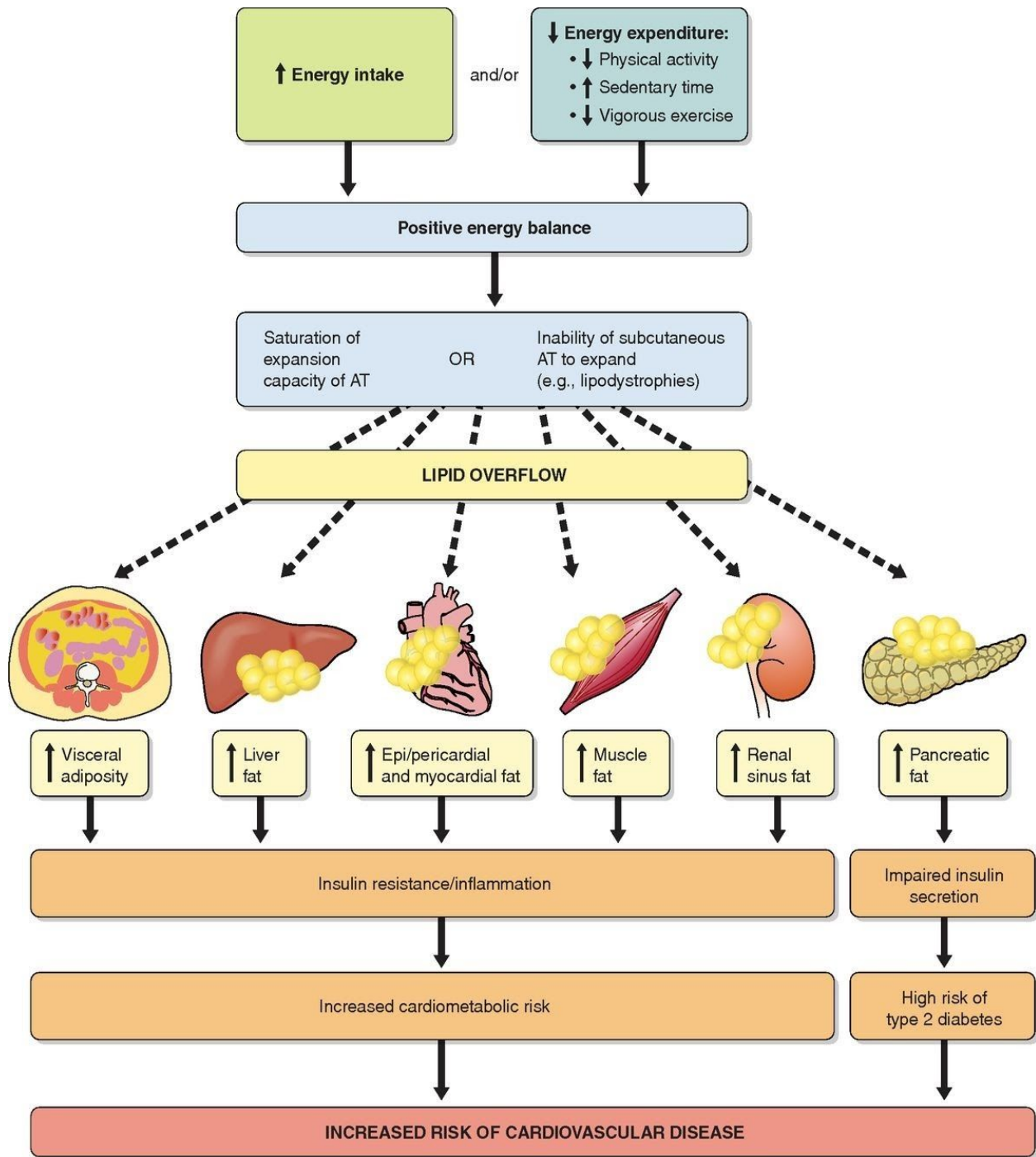


Figure 1
 According to the proposed model excess visceral adiposity (EVA) is correlated to increased cardiometabolic risk. I.e. EVA serves as a possible marker for dysfunctional subcutaneous adipose tissue and its inability to expend in time of energy surplus. This inability leads to a lipid spillover and lipid accumulation in ectopic fat deposition with negative cardiometabolic consequences. *Image by: A. Tchernof & J. P. Despres, Physiology Review, 2013, <https://journals.physiology.org/doi/full/10.1152/physrev.00033.2011>*

Respiratory pathophysiology in obesity

Obesity has a significant influence on the respiratory system, while regional adipose tissue distribution has an impact on obese individuals to develop respiratory alterations and complications. Obesity is responsible for changes in breathing in both normal quiet breathing and breathing during general anesthesia and mechanical breathing. Lung compliance is lowered and can be even very severe, up to two-thirds decrease when we compare it with a non-obese individual. This decrease comes as a consequence of the mechanical impact of adipose tissue that gets accumulated and distributed in the chest area such as around the ribs, the diaphragm and abdominal area [7]. Considering the mechanics of the lung-chest wall system through total respiratory compliance overall it is decreased, but most of the decrease was seen in the lungs themselves while the chest wall was slightly directly affected. Measuring the level of obesity via BMI it is connected to the compliance in an exponential relationship, showing that compliance will decrease with an increase of BMI thus obesity. Decrease in compliance also alters other parameters that depend on it such as causing narrowing and closure of dependent airways. Increasing surface tension in alveoli thus predisposes them to collapsing since the functional residual capacity will decrease and also there will be an increase in the volume of pulmonary blood. Compliance is defined as a change in volume for change in pressure and the starting point was seen as in FRC as where the lung-chest system was in equilibrium with atmospheric pressure. In obesity that point gets altered and volumes thus capacities in the lung consequently change. FRC is made of RV and *expiratory residual volume* (ERV) in obesity gets decreased which correlates with the mechanical impact of adipose tissue on the respiratory function which confirms that obesity is considered as an extrapulmonary restrictive disease that will produce restrictive patterns of airflow [22]. Residual volume does not get sustained as normal or

increased that is why the RV-to-TLC stays normal or also increased but the ERV gets strongly decreased with increase of BMI. The reason behind that exponential decrease of ERV comes from diaphragm displacement into the thorax pushed by excess of the adipose tissue and its weight but also restricting diaphragmatic movement and increased mass of adipose tissue pushing onto the chest wall thus on the lungs [23]. Following the restrictive pattern of flow-volume loop VC and TLC decrease linearly even though this decrease is not as prominent as in ERV so TLC is still sustained within the limits of considered normal. Using spirometry and testing most of the volumes except for RV, expiratory flow will show profound decrease in FVC but only small decrease in FEV1. This will produce FEV1/FVC ratio being normal but also increased which can be explained by air trapping and peripheral airway narrowing and closure which directly decreases vital capacity (VC). Tidal volume is also decreased in severe obesity which transfers that restrictive pattern of breathing which is rapid and shallow. [24]. That pattern of breathing can be connected with anatomical deficiency of breathing muscles and their work deficiency. Thus is further correlated with measurement of respiratory muscle endurance which show a decrease in obese individuals and even greater decrease in people with *obesity hypoventilation syndrome* (OHS). OHS demonstrated an inability to have normal maximal inspiratory and expiratory pressures at all lung volumes but having those pressures decreased [25,26]. This can all be related to metabolic level where muscle function is decreased due to adipocytes accumulate in muscles interfering further with normal contractile function. It does so by disrupting mitochondrial metabolism which is necessary for oxidative metabolism to supply ATP that is crucial for normal reaction between myosin and actin by producing reactive oxygen species. Reactive oxygen species damage the membranes including mitochondrial and disrupt the enzyme function in oxidative metabolism, lowering the usage of metabolites such as fatty acids that normally undergo beta oxidation in the mitochondria. This is indirectly observed on

obese individuals to have lowered metabolism of fatty acids and correlated with decreased endurance and strength of respiratory muscles. All the elements seem to get back to normal and regaining normal pulmonary compliance, volumes and ventilation patterns in individuals that have lost weight after being obese [27]. Airway resistance can be assessed by Poiseuille law where resistance of the airway major determinant is the radius to the power of 4 and considering obese individual it conclusion comes that the resistance is increased in such person because of compression on the airway which is not the case. Rather, the resistance increase and airway narrowing come as a consequence of lowered lung volumes, not from obstruction but because at lowered lung volumes there is decreased traction on the airways and thus decreased caliber and more prone to collapse [28,29]. Work of breathing in obesity requires several fold higher oxygen consumption than in non-obese individuals because elastic work that needs to be done and restrictive nature of obesity on the work of ventilation muscles produces higher workload that naturally requires more oxygen. This setup makes obese patients having a certain respiratory insufficiency that results in a limited ventilatory reserve predisposing them to respiratory failure in the settings of acute or systemic illnesses [30]. The increase in breathing work that requires higher levels of oxygen consumption and higher basal metabolic requirement can be related to FRC that can be looked as a reserve volume of air to have extra oxygen in case of hypoventilation or even apneic state to avoid fast hypoxemia. Since FRC is decreased in obesity that reserve is very scarce and because of that obese individuals will desaturate their oxygen level quite fast [31,32]. Obesity affects the respiratory system more than any other system and produces many changes in physiology of the body that is transferred as an important and significant impact on clinical practice.

Comorbidities in obesity

Beside the respiratory system being affected the most in obesity, there are many influences that are translated onto other systems stemming from obesity, being both multifactorial and multisystemic. There is no one direct cause or mechanism in which obesity induces a pathological state in the cardiovascular system [33]. One of the examples is development of atherosclerosis that is correlated with obesity, ie. it is more likely to occur in the presence of excess adiposity where many mechanisms interplay in its pathogenesis that is induced by obesity [34]. Proposed obesity-induced mechanism in development of atherosclerosis lies in pathophysiology of obesity that contains altered adipose metabolism and induction of oxidative stress, e.g. in blood vessels, causing the damage and inflammation at the vessels that is seen as endothelial dysfunction prone to accumulation of inflammatory cells and lipids [35]. Thus many actions that come from different pathways contribute to the development of atherosclerotic vascular disease. Similar approach is developed in explaining the fundamental cause of obesity in any cardiovascular disease. To illustrate, such is the case in development of obesity-induced hypertension where both adipose size in abdominal subcutaneous and visceral compartments were related to development of hypertension due to connection of size of adipose cells and their adverse changes in their metabolism. Important metabolic concept demonstrates that hydrolysis of triglyceride-rich lipoproteins catalyzed by LPL and triglyceride synthesis are major determinants of the fatty acid flux and triglyceride storage in a given fat compartment. Furthermore, that is also a determinant of the size of adipocytes which reflects the balance between storage and lipolysis and because of that determines the rate of lipid accumulation in the compartment [36,37]. How this is related to development of hypertension comes from the conclusion that the waist circumference measurement is the strongest

independent predictor of blood pressure. Connection of altered adipose metabolism and insulin resistance come all the way from metabolic syndrome. Independent mechanisms of insulin resistance are also proposed, where excess adipose tissue in obesity alters the structural function of the kidney, translating it into an altered function of Renin-Angiotensin system that lies in the pathophysiology of hypertension. Hypertension is a risk factor to many other diseases of the cardiovascular system and it provides an indirect link to developing other negative consequences to the system due to obesity [38,39]. Other important comorbidities are *obstructive sleep apnea* (OSA) syndrome and *obstructive sleep hypopnea* (OSH) syndrome due to disruption of normal pulmonary function. However, from anesthesiological point of view it presents risk in difficulty intubating and stabilizing the airway in obese patient. Repeated episodes of cessation of breathing longer than 10 seconds during sleep is due to the upper airway collapse. Obstruction which increases the resistance to airflow will disrupt the sleep cycle and as a consequence the individual can have daytime somnolence that tends to be a characteristic presentation in someone with sleep apnea. It can also be a development of other consequences such as systemic/pulmonary hypertension, arrhythmias (AFib, AF), cognitive impairment or even death, all induced by nocturnal hypoxia. OSH syndrome is similar to OSA but different in that it has partial airway narrowing or obstruction in which the patency is decreased for 50% of the normal lumen occurring 15 or more times during each hour of sleep and as well lasting 10 or more seconds per episode [40,41]. What is seen in both of these syndromes is there is going to be a nocturnal hypoxia because ventilation is disrupted and causes lack of adequate gas exchange. This further leads to the lowering of the partial pressure of oxygen in arterial blood and its saturation decreases as well for at least 4% of its normal saturation. Carbon dioxide gets retained in the blood so its partial pressure is elevated [42]. Diagnosis of both lies on polysomnography, or a sleep study, during which the patient's

electroencephalogram, electrocardiogram, electrooculogram, capnogram, nasal or oral airflow, esophageal pressure, arterial blood pressure, pharyngeal and extremity electromyograms, pulse oximetry, and room noise are typically monitored and recorded [43,44]. To report the severity of either of these syndromes there is an established index, i.e. apnea/hypopnea index or AHI, providing information based on the number of apneas and hypopneas divided with a total sleep time. AHI severity scale provides that for mild disease, the parameters are 5 to 15 on the AHI events per hour, then for moderate disease - the AHI is of 15 to 30 events per hour and in severe disease - the AHI is of greater than 30 events per hour [45]. Obesity represents the biggest risk factor for presence of OSA and around 70% patients who are obese have concomitant obstructive sleep apnea/hypopnea syndrome with predominance in males than in females. Importance in diagnosis of OSA is that it provides benefits for the patient if it is found prior to surgery, facilitating a better response to analgesics and anesthetics, decreased postoperative sleep deprivation and better normalization of cardiovascular disturbances [46]. In the etiology of OSA it is seen that there is anatomical and neuromuscular implication in its development. Anatomical impact comes from the presence of obesity that excess of weight causes mechanical compression on the airways and possible excess of parapharyngeal tissue in the adults or adenotonsillar hypertrophy in children. The neuromuscular impact comes from neuromuscular weakness in a sense of upper airway dilator muscles relaxation in transition from wake to sleep state which leads to airway narrowing. It consequently leads to a collapse that may come from decreased vagal nerve influence during sleep. This will produce a decrease in tone of smooth muscle thus increasing the tendency of the airways to collapse. Based on this concept of causation of OSA, a therapeutic approach was developed that is focused on stimulation of hypoglossal nerve via implantable nerve stimulator. This stimulates an innervation of hypoglossal nerve on the tongue more efficiently during sleep that will consequently cause

enough forward push of the tongue during sleep thus increasing anteroposterior diameter of the upper airway path and decreasing occurrence of OSA [47]. Association of OSA and obesity with metabolic syndrome is also seen as a part of the cycle of events that involve both arousal from rapid eye movement (REM) sleep, oxyhemoglobin desaturation, cycles of hypoxia and reoxygenation. All the aforementioned change the inflammatory profile of the patient with elevated inflammatory cytokines that are seen in etiology of metabolic syndrome and in atherosclerosis pathogenesis [48]. Many other systems are affected by obesity and present a diagnostic challenge for finding a proper way in management.

Nonsurgical management of obese patient

Early and persistent management of obesity has multiple benefits for the patient and provides a more promising health state for the future. Nonsurgical management involves lifestyle changes as well as actual treatments when there is a certain pathological condition involved with the obese patient but the approach is to reduce the risk of comorbidities such as cardiovascular diseases and prevention of development of diabetes type 2 and treatment of abnormalities of metabolic syndrome. The most important approach is lifestyle change that focuses on weight loss, physical activity, change in diet habits and reducing or stopping adverse habits such as smoking. Even a small weight loss such as 5 to 10% can have a major impact on improving many metabolic deviations that are the comorbidities of diabetes, dyslipidemia, and hypertension. This is done by lowering total cholesterol and triglyceride levels, raising HDL cholesterol, lowering arterial blood pressure, and lowering blood glucose values while reducing insulin resistance. The best approach to reduce weight is through changes in behavior of the patient that focus on changing the habits, with special emphasis on diet habits. This concept relies on a basic body economy that includes energy input and output through food where an

energy reduced diet will put the individual into a metabolic deficit, allowing the body to reach for the reserves for additional sources that will be transferred as a weight loss [49]. Second important point is physical activity, which can vary from simple walk all the way to more intense exercise programs that are designed to put the body into a higher energy state and thus prone to weight loss if it is constantly applied. An aspect of long-term weight loss and also accelerated and constant way to lose weight is a combination of focused weight loss diet and physical activity through a regular exercise regime, based on standard recommendations of 30 minutes minimum per day of moderate intensity [50]. Behavioral interventions that are most crucial in this therapeutic change requires many programs that are promoting and motivating obese individuals to adhere to proposed new habits or interventions that will lead them to achieving a goal that was set. The key features of typical behavioral programs include self-monitoring, goal setting, nutrition and exercise education, stimulus control, problem solving, cognitive restructuring, and relapse prevention. Even though lifestyle change is therapeutically crucial, many obese patients already have comorbidities or altered values that require pharmacological treatment in order to normalize hypertension or dyslipidemia, to name but a few, as a part of metabolic syndrome presentation. The use of antihypertensive drugs are employed in treating present hypertension in obese patient and in addition to behavioral change, such as proposed restriction of salt in the food, is seen for better achievement of wanted blood pressure value. Even though there is no proposed first line antihypertensive drug, usually there is the need for a polypharmacological approach to be effective in controlling hypertension. Statins are used to maintain normal lipid profile usually when LDL cholesterol is excessive, in order to decrease the risk of cardiovascular disease in someone with diabetes mellitus type 2 and metabolic syndrome. The use of fibrates to increase HDL and decrease triglycerides, Ezetimibe to decrease intestinal cholesterol absorption and the use of nicotinic acid to increase HDL

cholesterol and omega-3 fatty acids to decrease triglycerides and improve sensitivity to insulin are also seen in use to improve lipid profile in dyslipidemic state of obese patient [51,52]. In presence of insulin resistance, hyperglycemia and diabetes mellitus type 2, all quite common set of abnormalities in obese patients, there is use of oral hypoglycemic drugs to address these abnormalities. Many different classes of oral hypoglycemic drugs have been developed over time that address different pathways of controlling glucose levels, e.g. *Metformin*, *Sulfonylurea class*, *Glitazones*, *Meglitinides*, to name a few. Metformin is most commonly used since it is proven that it decreases the risk of developing complications in bariatric surgery, despite reports of the development of lactic acidosis in patients using metformin preoperatively. It is still unclear to which extent this is implicated [49,53].

Obese patients often fail short of reaching expected results considering weight loss through lifestyle and behavioral change. Pharmacological weight loss approach is developed where there are two types of drug class approved for use. They address the weight loss through appetite suppressants and lipase inhibitors. However, only two drugs are available for indication of weight loss, *Phentermine* and *Orlistat*. Phentermine suppresses the appetite which causes decreased food intake which consequently promotes weight loss. This drug works as an adrenergic reuptake inhibitor that increases the adrenergic effects in both CNS and peripheral tissues. On a metabolic level that will be seen as increased resting basal metabolic activity that will use more energy thus use stored energy as a source that will promote loss of weight.

Orlistat on the other hand inhibits lipase enzyme which will lead to decrease of digestion and consequently absorption of certain lipids which will contribute to more effective weight loss.

What is important in use of Orlistat is that it affects lipid soluble vitamin D,E,K,A absorption and can lead to deficiencies, thus additional supplementation of these vitamins is necessary when it is in use [49]. The problem of obesity affected other industries that try to promote their products

as effective such as in the supplementation industry through dietary and herbal products which have not been proven effective or containing certain substances that are effective but dangerous and not approved for the health and treatments such as ephedrine and caffeine [54]. The main idea is that any level of weight loss achieved by obese patient is strongly beneficial and helps to reduce the risks and complications.

Surgical management of obese patient - Bariatric surgery

With the world population getting overweight, seen in an increase in prevalence of both morbid obesity and super obesity, there is a correlation with increased need for bariatric surgery.

Bariatric surgery is a surgical procedure that alters the small intestines or stomach in order to insure weight loss. Importance of the bariatric surgery and consequently weight loss as its main goal, are indirectly correlated with reversing pathophysiological effects in endocrine and cardiovascular systems that are present in obese patient. Bariatric field developed two groups of procedures, *restrictive* and *malabsorptive*. The main goal of the restrictive surgery is to limit the capacity of food intake by the patient that consequently causes less food intake and weight loss that follows [55]. Today most common use procedure is *laparoscopic gastric band* procedure (LGB), a minimally invasive approach, producing a small pouch made from proximal stomach where the band will be set just distal to gastroesophageal junction making a constriction that increases mechanical resistance to solid food decreasing them to pass, but not for fluids. This procedure is also adjustable to determine the patency of the lumen at the constriction and it has an exceptional safety record considering complication and mortality during the procedure [56]. *Malabsorptive procedure* has dual principle which is in combination with a restrictive principle to cause malabsorption of nutrients. Most commonly used malabsorptive procedures today are gastric bypass (GBP), and biliary pancreatic diversion (BPD) procedures but gastric bypass

procedure is more commonly performed than biliary pancreatic diversion since it is considered the safer of the two malabsorption procedures. What is provided by bariatric surgical procedures are two most important beneficial entities when dealing with obesity which are weight loss and resolution of comorbidities. When this approach is compared to nonsurgical approach for obese patient the magnitude of weight loss in surgical approach was significantly larger than in nonsurgical and lead to loss of weight very close to expected [57]. Improvements in obesity-related and metabolic syndrome-related comorbidities have also been evaluated. Diabetes improved in more than 85% of patients and resolved more than 75% overall. Resolution of diabetes following surgery is inversely related to the preoperative duration of the disease and occurs more in those patients whose diabetes is controlled using oral hypoglycemic agents. This finding clearly distinguishes surgical treatment of obesity as an important endocrinologic intervention, especially because the modest improvement in diabetes management that is produced by nonsurgical weight loss is accompanied by relapsing disease in nearly 100% of patients within 5 years [58,59]. Other comorbidities such as dyslipidemia and hypertension were also resolved to a high percentage of patients that undergo any of bariatric procedures. Even though surgical management is more impressive in time and numbers of results the resolution of comorbidities has a similar result in both management's overall [60].

Airway assessment in obese patient

Airway patency in obese patient is of significantly more importance than in non-obese patient since mechanical constriction on the airway decreases its lumen and increases the resistance of the airflow. It furthermore increases a tendency for asthma development, but also promotes collapse of airways causing hypoventilation and ventilation/perfusion mismatch in a form of shunt. All of which may lead to arterial hypoxemia since gas exchange does not occur normally

due to all of the mentioned disturbances [61]. To have an accurate assessment of the airway status it is important to determine the class of the patient's obesity in the patient. This will affect determination of the approach to the airway and this is done through Body Mass Index that is determined by dividing the weight of the individual in kilograms with his height in meters squared. Based on BMI scale there are three classes of obesity in which Class 1 has BMI= 30-35 kg/m², Class 2 having BMI=35-40kg/m² and Class 3 BMI= >40kg/m² that is also called morbid obesity that has a profound effect on the airway patency and cause of rapid oxygen desaturation in the patient when there is ventilation compromise and important relation is seen that in increase in class of obesity there is increase in likelihood of complication or collapse of major airway that may lead to hypoxic damage to organs such as the brain or even being lethal [62].

The reason why different strategies and approaches were developed is because of consequences of lack of recognition and poor planning for potential airway problems as well as difficult mask ventilation, difficult emergency cricothyrotomy especially in obstructive sleep apnea in obese patient and high Mallampati classification. That leads to the conclusion that failure to evaluate the airway and have a proper assessment on the difficulty of the airway are major factors that are causing airway complication and failure since it is more beneficial to have a good strategy on dealing with the airway preoperatively than trying to handle a consequences of airway disaster [61,63]. Thus preoperative airway assessment is extremely important before induction of anesthesia in obese patient in order to achieve adequate management of the patient intraoperatively and to avoid any major and potentially life threatening airway complications. As it is seen that in around 10 - 20% of obese patients present with obstructive sleep apnea (OSA) and usually stays unrecognized all the way to intraoperative stage of management when it may already present with a problem because OSA presents problems of

difficult mask ventilation (FMV), difficult direct laryngoscopy (DL) and has a tendency to obstruct or collapse the upper airway even at minimal sedation. Concurrently with the OSA there is decreased pulmonary reserve so there is expectation of rapid arterial oxygen desaturation at induction or right after the anesthesia but also can continue in postoperative period and if this is sustained will lead to chronic hypoxemia and hypercapnia which proposes a problem because these abnormalities increase sensitivity to residual anesthetic agents and opioids that may induce respiratory arrest in early postoperative period [44,64]. That is why recommendation is established that proposes preoperative screening of any surgical candidate for possible obstructive sleep apnea and if there is a serious one using continuous positive airway pressure (CPAP) in the preoperative stage for treatment. Using sleep study to diagnose it take a lot of implications and it is expensive which make it impractical to do on every patient because of that a useful tool for screening of OSA was developed called STOP-Bang Questionnaire that helps to determine the risk of OSA in a patient and can be combined with some clinical measurements such as pulse oximetry ($SpO_2 = <95\%$), spirometry findings with ERV $<0.5L$ and serum bicarbonate concentration >28 mmol/L give a predictive conclusion of a patient with increased risk for OSA and development of postoperative complications [64,65].

Defined difficult airway is from experiences that in trained anesthesiologists have difficulty with facemask ventilation and tracheal intubation and assessment done by several traditional and already accepted methods such as mouth opening, Mallampati classification and assessment of glottic view by Cormack-Lehane score and in addition to them there are thyromental distance, neck circumference and ability to push jaw forward and teeth position and distance in preoperative examination. When there is inability to sustain oxygen saturation $> 92\%$ during Face Mask Ventilation(FMV) it is considered to be difficult FMV since there is not enough provision of ventilation to the patient which in addition to lower saturation there are also

inadequate seal between face mask and the airway entry as well as airway patency being compromised thus narrowed or obstructed. That is why the obesity and consequent OSA presence are one of the risk factors for having difficult FMV together with Mallampati grade III/IV, neck circumference over 50 cm, having mouth and upper airway malformation or a beard. To have a better education on possible predictors that will lead to difficulty in managing the airway through ventilation or intubation mnemonic STOP-BANG and OBESE was developed to have faster and better responses to risk factors that cause dealing with difficult airway [66,67].

Mnemonics for airway management of the obese patient.

a. Preoperative Evaluation OSA Screening	b. Difficult facemask Ventilation	
STOP-Bang Questionnaire	OBESE	
S Snoring. Do you snore loudly (louder than talking or heard through a closed door)?	O Obese	M Male Gender
T Tired Do you often feel tired, fatigued or sleepy during the daytime? Do you fall asleep in the daytime?	B Beard	M Mask seal which is affected by beard or being edentulous
O Observed Has anyone observed you stop breathing or choking or gasping during your sleep?	E Edentulous	M Mallampati grade 3 or 4
P Blood Pressure Are you hypertensive or do you take medicine for blood pressure?	S Snoring (OSA)	M Mandibular protrusion
B BMI BMI > 35 kg/m ²	E Elderly (>55yr)	A Age
A Age Age > 50 years		S Snoring and obstructive sleep apnoea
N Neck Circumference (measured around Adam's apple) > 43 cm (17 in) for males, > 41 cm (16 in) for females		K Kilograms (weight)
G Gender Male		

TABLE 1

Preoperative screening questionnaire for obstructive sleep apnea patients. *Image by: D. Godoroja et al. / Trends in Anaesthesia and Critical Care 26-27 (2019) 30-37*

Dealing with many changes that make a intubation difficult especially in obese patient, Intubation Difficulty Scale(IDS) was proposed with parameters that will indicate on how the airway is difficult to intubate.

When this scale measurement is equal or above 5 it indicates that airway is difficult to intubate which was tested on both, non obese and obese patient and showed that there is three fold increase in incidence of difficulty in intubation in obese patients than in non obese patients [68].

Intubation difficulty scale (IDS)

Parameter		Score	Rules for calculating
Number of attempts > 1		N ₁	Every additional attempt adds 1 point
Number of Operators > 1		N ₂	Every additional operator adds 1 point
Number of Alternative Techniques		N ₃	Every alternative technique adds 1 point
Cormack Grade = 1		N ₄	Successful blind intubation N ₄₌₀
Lifting forced required	Not Applied	N ₅ = 0	
	Applied	N ₅ = 1	
Laryngeal pressure	Not Applied	N ₆ = 0	Sellick's manoeuvre adds no point
	Applied	N ₆ = 1	
Vocal cord mobility	Abduction	N ₇ = 0	
	Adduction	N ₇ = 1	
Total IDS = sum of scores		N₁ - N₇	

IDS Score >5 = Moderate-Major Difficulty.

TABLE 2

Scale for assessment of intubation difficulty. *Image by: D. Godoroja et al. / Trends in Anaesthesia and Critical Care 26-27 (2019) 30-37*

Preparation for and induction of anesthesia

Strategy

This is approach that focuses on good experienced team abilities and proposed guidelines on dealing with an aspect of patient management, thus strategy relies on preoperative evaluation in order to provide a safe environment for the patient and best possible organization of steps in preoperative, intraoperative and postoperative care. Obese patient makes a challenge in almost every field on patient management such as airway management, anesthetic techniques, anesthetic drugs, pain control, positioning of the patient and monitoring which proposes modifications in approach from standardized steps in all of these areas since alternations are seen in many physiological and anatomical systems of the obese patient [69]. Preoperative evaluation is of profound importance in obese patient because it includes plan in solving comorbidities such as obstructive sleep apnea, hypertension, diabetes and others, optimizing the state of the patient through laboratory findings and applying necessary interventions in order to normalize abnormalities such as hyperglycemia, dyslipidemia, electrolyte disturbances or CPAP appliance for someone with OSA and minimalizing the risk of compromise in airway patency, aspiration and oxygen saturation. Thus strategy in preparation and induction of

anesthesia and intraoperative management of the obese patient just like in non obese patient is approach based on previous experiences and developed guidelines that might have modifications in order to accommodate alteration caused by obesity. In airway management in obese patient strategy is to have airway patency and having upper airway accessible, easier intubation and face mask ventilation, secured airway with low risk of aspiration, applying algorithms for difficult airway if it is encountered and avoiding of sedative anesthetics because of increased sensitivity of obese patient to them and thus increased risk of developing in respiratory depression and possible arrest [70,71].

Positioning

Appropriate positioning has an important role in providing optimal conditions for successful placement of the endotracheal tube under direct vision. Any patient in supine position has increased pressing effect from abdominal content on the diaphragm thus decreasing the compliance of the lungs to expand which affects lung volumes and capacities especially functional residual capacity (FRC) that represents lung reserve for oxygen when there is additional need for it such as in hypopnea or apnea [72]. This alteration is expressed much more in obese patients since they have larger pressing effects from excess of visceral and subcutaneous adipose tissue of the abdomen on the diaphragm but also on the chest wall directly from the outside which transfers that on severely lowering FRC which will produce a rapid desaturation of oxygen in blood in case of ventilation and airway problems such as in apnea. That is why obese patients do not tolerate well states of hypoventilation since they lost most of lung reserve and compromising airway and ventilation will produce rapid lowering of oxygen saturation in the blood which means that their safe apnea period (SAP) that represents a time from the start of the apnea to resulting oxygen saturation being under 90% is shorter than in non

obese patient [72,73]. Based on clinical experiences and previous complications encountered, a simple positioning of obese patient showed to help with reducing of complications with the airway and improving parameters that were previously presenting a potential danger to the patient during surgery such as oxygen blood desaturation and inability to sustain it.

Trendelenburg position is an old positioning technique where the supine patient with elevated feet is above the head for 15-30 degrees that was used in abdominal and urinary system surgeries. In obese patient, the reverse Trendelenburg position is used where the head is elevated for 30 degrees in comparison to feet produced better response to oxygen desaturation thus slowing down the decrease in oxygen content in the blood. This is connected to decrease in pressing effect of the abdominal content and adipose tissue on the respiratory structures and improve respiratory mechanics that consequently causes better lung compliance and oxygen reserve and decreases a probability in airway collapse [74,75].

What is also shown to be beneficial in reverse Trendelenburg position is the intubation and having easier airway view and access but requires modified head position instead of standard sniffing position. In obese patient in reverse Trendelenburg position, the head and shoulders are elevated significantly more in comparison to the chest and the head is in extended position where the sternal notch is in alignment with the ears by using pads, pillows or foam materials under the head, neck and shoulders to achieve this position [76]. This head position provides better view on pharynx and larynx and makes the axis in which the tube needs to follow more prominent and clear. Combining body and head positioning in obese patients provided a better approach and success in managing airway and the state of the obese patient in both, preoperative preparation and intraoperative management.

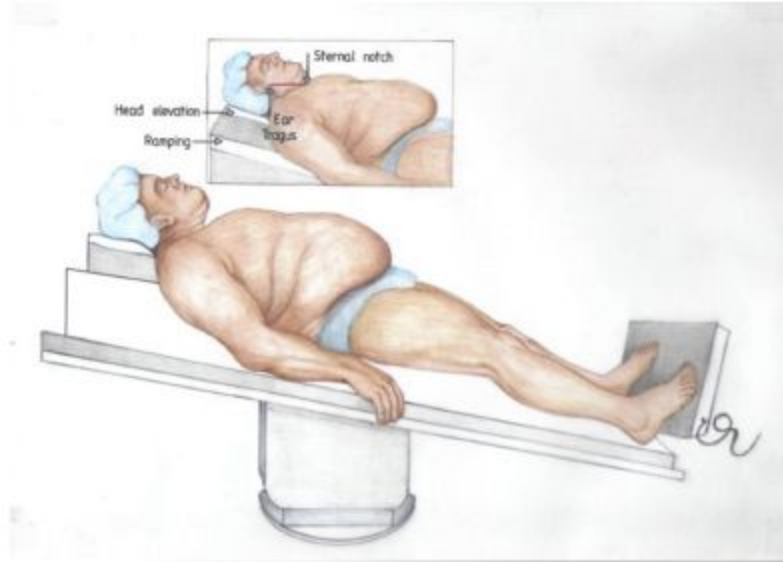


FIGURE 2

Position for Tracheal Intubation in the Obese Patient Ramped Position (Head elevation Laryngoscopy Position) with patient's ear level aligned with sternal notch, and operating table in Reverse Trendelenburg. This increases SAP and improves the view during DL by aligning the oral, pharyngeal, and laryngeal axes. *Image by: D. Godoroja et al. / Trends in Anaesthesia and Critical Care 26-27 (2019) 30-37*

Pre-oxygenation

Breathing of air provides oxygen for exchange between blood and the alveoli, but air consistency is that oxygen is only 21% of inspired air and the rest is nitrogen with very little portion of other gases. The concept in this method is to give a patient via facemask ventilation, the air that is fully oxygen, meaning a 100% oxygen air that when breathing for long enough will replace all of the nitrogen in the alveoli that is a FRC of around 2.5L of lung volume. When there is a healthy patient than this is considered a maximal preoxygenation since there is a full lung reserve present but in obese patient there will be alternation in which the reserve is decreased and because of that there can not be a maximal preoxygenation level reserve [77]. A technique how to be effective in preoxygenation is facemask ventilation of 100% oxygen for 3 minutes will produce around 95% of removed nitrogen in the alveoli by oxygen but also this can be achieved by 8 deep breaths in 60 seconds. Preoxygenation increases safe apnea period for 8 to 10

minutes in non obese patient but only 2 to 3 minutes in obese patient but the idea behind this is to have enough time and oxygen reserve to do correct intubation when the anesthesia is induced. In obese patient preoxygenation is affected by positioning because it was seen that those who had inclined head like explained before had more than 20% better oxygenation thus saturation with oxygen and slower desaturation when they went into anesthesia. Different methods and rates of delivering 100% of oxygen to the patient also have important impact and in some studies it was seen that nasal cannula with delivery of 5 to 15 L/min of 100% oxygen provided better results than the use of continuous positive airway pressure (CPAP) delivery of oxygen regardless of patient being obese or not [78,79]. Besides slowing down the desaturation, the use of continuous positive airway pressure (CPAP) is in use to prevent atelectasis after induction of anesthesia in obese patient but also use of positive end expiratory pressure (PEEP) and mechanical ventilation for the same purpose after induction of anesthesia [80,81,82]. These applications provided decreased atelectasis occurrence and prolongation of non hypoxic apneic period after induction of anesthesia. Preoxygenation management is more complex when dealing with obese patient and requires larger interplay between positioning of the patient and combinations of techniques to achieve best possible level of saturation [83].

Aspiration risk

Patients planned for surgery undergo preoperative instructions in order to have an optimized state for the surgery and to minimize any complications that might occur without these preoperative adjustments [84]. Important directive is non peroral state that requires a patient to restrict oral intake for a period of time prior to surgery which will minimize the risk of aspiration but also even if the aspiration occurs the complications such as pneumonitis, will not be as severe as it would be if there was no peroral instruction. There are different instructions to reach

an optimal level in a non peroral state, but in general for solid food prior to anesthesia is longer than for fluids, thus for an adult should not take solid food around 8 hours prior to anesthesia and 2-4 hours for fluids. Because of secretions in the human gut, the stomach is never actually empty even during longer fasting than 8 hours and the risk of aspiration is increased because induction of anesthesia will decrease the normal laryngeal reflexes that prevent inhalation or aspiration of content from stomach [85]. Regardless of the patient being obese or non obese there is a similar increased risk for aspiration because of this reaction that occurs after induction of anesthesia but securing the airway prevents that if it is done properly after induction of anesthesia which is a more challenging in obese patient. What set an obese patients a part from non obese is that they have comorbidities that tend to have an impact on increasing aspiration risk. One of those is gastro-esophageal reflux disorder that has a weaker tonus of lower esophageal sphincter making stomach content easier to escape into the esophagus and can reach oropharynx and a patient can aspirate. In order to asses the stomach content and the preoperative aspiration risk in obese patient a gastric sonography is in use providing a reliable evaluation [86]. . In today's anesthesiology the most reliable protection from the aspiration in any patient is endotracheal tube placed into trachea passing laryngeal cords via direct laryngoscopy most often, that has a cuff that inflates and secures the tube at determined level in trachea and preventing any content reaching the airways. Conclusion for the risk of aspiration in obese patient does depend on detailed assessment of the obesity and the comorbidities that directly or indirectly increase the risk of aspiration after induction of the anesthesia.

Anesthetic drugs and dosing

Problem of obese patients in anesthetic medications comes as their alterations lead to inducing exacerbations on their comorbidities and metabolic alteration affects the efficacy of the drugs [87]. Use of drugs to induce anesthesia such as propofol but also opioids can induce decrease in pharyngeal tone muscle thus compromise the airway patency and consequently exacerbate obstructive sleep apnea and make an intubation difficult. Another problem in obese patient is that their ventilation and ventilation effort is compromised in a way that they already have lower lung reserve and desaturation can occur very quickly after induction of anesthesia and connection of ventilatory response to rise of carbon dioxide can be considered a possible problem when using volatile anesthetics since they tend to decrease ventilatory response to carbon dioxide. The use of intravenous anesthetic drugs such as fentanyl was seen to be a cause of decrease in spontaneous breathing and leading to more often episodes of apnea which led to possible use of non depressing drugs of ventilation such as alpha 2 agonist such as dexmedetomidine or using short acting drugs to expect faster return of respiratory function to normal level after anesthesia is established [88,89]. Important pharmacological concept of dosing is also important when dealing with obese patient since the sensitivity and metabolism alterations of the anesthetic drugs might be present but also when making a correct dose for a patient it depends on total body weight (TBW) or ideal body weight (IBW) which in obese patient is a major factor that play an important role in determining a dose that is going to be administered. In obese patient a fat solubility of the drugs is also important factor because of excessive quantities of adipose tissue both, visceral and subcutaneous and that consequently changes in the volume of distribution of anesthetic drugs that have lipophilic properties such as benzodiazepines and barbiturates. In determining dosing for any of the drug class and which

class should be used in a obese patient thus depends on properties of the drugs, their main action and the state of the patient in order to establish wanted anesthetic state in obese patient [90,91,92].

Airway techniques

Performing a preoperative airway assessment provides somewhat prediction on how hard it is to deal with the airway and what are possible difficulties that might occur when starting with an intubation and intraoperative management but also helps to design appropriate approach to the airway management. Airway patency can be considered a cardinal point in order to have adequate ventilation and oxygenation intraoperatively that lies on doing detailed history and physical exams. In order to find out any potential risks that might compromise pre-designed plan, such as congenital anomalies, previous surgeries of head and neck or secondary changes that occurred because of some other previous disease such as infection or trauma, all of which might not be a problem on first sight but could manifest in a problematic way proceeding further with the management [93]. The simplest way to ensure patency of the airway in unconscious patients is to use head tilt/chin lift maneuver that causes the tongue to move from the back thus opening a passage to the airway. Another way is a jaw thrust that is used in a patient with a spinal injury in order to avoid moving the neck that was injured and using thumbs to open the jaw while displacing the mandible upward which consequently moves the tongue as well forward. With these maneuvers, using a face mask or laryngeal mask airway (LMA) as well provide support to the airway to keep the patency of the airway but do not secure it which does not protect the airway from aspiration or laryngospasm. Intubation and surgical airway such as cricothyrotomy or tracheostomy are two approaches that support the airway patency and protect

it but other advantages in intubation are ability to provide pharmacological administration, pulmonary toilet and facilitation of positive airway pressure ventilation [94,95].

Laryngoscopy - direct and video

This procedure is used to view larynx and its vocal cords in order to have a better sense of the space and axis that can be taken in intubation and to see possible difficulties that might arise during intubation. Indirect laryngoscopy is used mostly in cases of having mild problems with breathing or swallowing, having constant ear pain, foreign body stuck in a throat or assessment for any mass growth and it mostly done in outpatient clinics and not for intubation or a major airway management. Direct laryngoscopy (DL) is done using a laryngoscope in order to see vocal cords directly and having a guide to allow you to properly intubate a patient but in morbid obese patient this presents an additional challenge that with direct laryngoscopy there is an need to have additional manipulation of the neck, head position and external laryngeal maneuvers in order to find a path to correct intubation but also laryngoscope may be of different features as well that is modified for a obese patient [96,97]. In advancement in technologies a videolaryngoscopy (VL) was developed that was seen to have a better application in obese patient population by making a view on the vocal cords better that consequently increases better chances to intubate with less intubation attempts. Even though videolaryngoscopy is somewhat superior to the direct laryngoscopy in obese patients, in better view of the larynx, having less time and attempts to make a successful intubation and subsequently leading to avoid complications such as fast desaturation of the obese patient and developing hypoxemia and having less external impact on the airway such as damaging it, DL is still most commonly used technique to intubate an obese patient. VL was compared to the DL by looking at failed intubations using both approaches and it showed that failing in intubation was reduced in VL

technique than in DL because of providing a decrease in difficulty in intubation and having easier teamwork between the operator doing the intubation and the assistant. In airway management guidelines it is suggested that the use of videolaryngoscopy should be available but used in case when there is failure to successfully intubate via direct laryngoscopy but it may be used as a first approach in case of already concluded difficult airway and in morbid obese patient having very limited lung reserve and thus high risk of developing hypoxemia rapidly after induction of anesthesia [98,99,100].

Supraglottic airway devices (SGD)

The use of supraglottic devices as a default airway in the obese patient is still outside of actual guidelines which establishes endotracheal tube as a cardinal airway in all patients, even though there has been use of SGDs in minor elective procedures in patients with increased BMI [101]. To use SGD as an airway falls under many influences such as patient state, body weight and anatomical factors of head positioning and airway assessment level, what procedure is being performed and risk of developing complications such as aspiration since there is lower protection of airway than in ETT which was proven to be a method that fully protects the airway from aspiration when placed correctly. Promotion of use of SGDs as an airway, a new generation of these devices have been developed that contain a gastric channels and better sealing ability in order to lower the risk of aspiration and providing a delivery of higher inspiratory pressures for an obese patient [102]. The problem is that even if they deliver increased inspiratory pressure it still not enough in comparison to ETT delivery since the endotracheal tube is directly placed into the major airway leading to the lungs and if there is a leak in the seal between the device and the airway ventilation will not be beneficial. This is directly correlated to respiratory pathophysiology in obese patient because there is a restrictive

pattern of lungs and in order to ventilate them there must be a higher pressure delivery to be successful and having fully secured and patent airway by ETT comes as a major advantage over SGDs. For now supraglottic airway devices are considered as an alternative to bag-mask ventilation prior to intubation and as a rescue device if ventilation and intubation failed in both obese and non obese patients [103].

Awake tracheal intubation

Obese patient having rapid desaturation and short safe apnea period (SPA) after induction of anesthesia lead to alternative to intubation done in conscious or slightly sedated obese patient that breaths spontaneously. Another reason of using this approach is that in obesity produces higher sensitivity to sedative medications which put these patients in higher risk of developing respiratory arrest after induction of anesthesia but using topical anesthesia is crucial when doing awake intubation in order to numb the upper airways but sometimes nerve blockage around the pharynx and larynx can be considered as well because of manipulation done during intubation. [104]. Awake tracheal intubation can be performed in different patient position, either sitting or ramped supine that is determined by level of obesity and comorbidities where oxygen delivery comes via nasal cannula and view of larynx by videolaryngoscopy (VL) or fiberoptic bronchoscopy (FOB). These two techniques are preferred in awake obese patients since they make intubation more easier, even though of excessive fat tissue and possible difficult airway can be more challenging but these techniques can be seen as a first line since many obese patients are high-risk patients. Intubation is easier done in obese patient with peripheral obesity or pear type in comparison to the one with central obesity or apple type obese individual and consequently more common complications in sustaining the airway and the ventilation. Based

on that is not just that a patient is obese but predominance of the obesity contributes on likelihood of problems and complications [105,106].

The unanticipated difficult airway

Dealing with an obese patient and airway management depends on guidelines but these guidelines tend to be insufficient since many obese patients have unanticipated airway problem that is out of the domain of the training which leads to serious problems in case if this is an emergency situation [107]. That is why this kind of airway management lies on experience of anesthesiologist and available equipment but the problems do rise from gaps in training for obese patients and delays in decision making when sudden compromise of the management starts. In case of out patient case of obese patient that requires oxygen delivery which is done using laryngeal mask airway intubation but if that fails then attempts of oxygenation might be successful with supraglottic airway device or face mask ventilation. Even if those attempts fail then a surgical airway is indicated such as cricothyroidotomy but here a major problem comes with inability to accurately localize cricothyroid membrane (CTM) and having exact landmarks because of excessive adipose tissue to ensure better chances of success. Another challenge is also difficulty with positioning patients head and neck manipulation for both intubation and surgical airway that lead to often failures in both [108]. What is proposed in this situation is a surgical scalpel-finger-bougie technique, with a 10 cm skin incision and blunt dissection of the tissues to reach the cricothyroid membrane (CTM). In an obese patient that can be preoperatively assessed in more detail because of the time and situation, ultrasonography and frequent examination to reach all necessary landmarks helped in better success in airway management in these kind of cases.

In conclusion difficulty with laryngoscopy and intubation usually results from an obese patient's short, thick neck especially in circumference over 40 cm, large tongue, and significant redundant pharyngeal soft tissue [109].

Post-anesthesia management of obese patient

Postoperative care is as important as preoperative and intraoperative management and requires well developed protocols that will reduce the probability of postoperative complications such as poorly controlled pain, nausea and vomiting, altered mental status, hypotension or hypertension or respiratory complications. This refers to both non obese and obese patients but obese patients have a higher chance to present with some of these complications. Once the obese patient is stabilized and awake, conscious and co-operative and has a spontaneous breathing pattern where a tidal volume will maintain normal end tidal carbon dioxide and oxygen levels, extubation may be performed. Performing an extubation in obese patient is done head up position which is sitting position because improves respiratory function and reduces the risk of developing respiratory complications such as airway obstruction, laryngospasm or hypoventilation [110]. The possibility of respiratory complications requires that a extubation procedure is an emergency reintubation strategy in case that a patient goes into respiratory complications. Airway obstruction in postoperative obese patient at extubation can come from reduced muscle tone in the airways caused by residual anesthetic state but also excess of tissue or pooled secretion are also a possibility that is why it is indicated to avoid the use of neuromuscular blockage and have available reversing agents in case of the airway compromise. Other important measures in recovering obese patient is to keep the patient in more upright position in the bed especially head position being at 45 degrees and oxygen supplementation is preferred to keep the level of oxygenation at optimal levels because it was seen that obese

patients tend to have frequent desaturations in first 24 hours after the surgery. Some times obese patient requires a higher care of the respiratory system such as the need for chest physiotherapy or continuous positive airway pressure ventilation (CPAP) in order to keep oxygenation with continuous monitoring of all relevant respiratory and cardiovascular function parameters that have the ability to warn a staff in case of emergent reintubation or other needed interventions [111,112].

Conclusion

Being an obese patient is already a risk factor for having increased probability of dealing with airway difficulty and its management and in addition to this having certain comorbidities or complications due to obesity just contribute to challenging management. Presence of obstructive sleep apnea, having excessive upper body adipose tissue accumulation and assessment airway that lead to conclusion of having Mallampati grade of III/IV will make problems to have effective ventilation or intubation because of inability to see laryngeal cords or narrowing of the upper airway that obscure the axis for intubation and decrease oxygen delivery. When compared to non obese patients, obese patients have very little lung reserve and consequently very short safe apnea period that represents a time reserve for intubation before developing hypoxemia after the induction of anesthesia. Introduction of preoxygenation with 100% oxygen prior to induction of anesthesia leads to replacement of all nitrogen with oxygen that makes enough reserve which will prolong safe apnea period. Even after the preoxygenation, obese patients have significantly lower reserve and the best strategy to be successful is to intubate fast and with as lower attempts as possible, thus the first attempt should be the best one. Obese patients represent a special population that require modification of non obese patient algorithms and development of new approaches to find optimal way in

management of obese patients. Alternations that are seen in obese patients require position strategy for better intubation, drug monitoring and changes in dosing administration such as avoiding or minimising use of depressant agents and developing of low opioid analgesia protocols. As populations is growing in obesity worldwide it is necessary that these measures are established since it will lead to effective care and recovery of obese patient population.

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