ANESTESIA NO IDOSO

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Palavras-chave:
- Anestesia:
- Avaliação de Resultados;
- Idoso

Resumo

A tendência para o envelhecimento global tem sido implicada no aumento dramático de algumas doenças crónicas e comorbilidades. Isto levará a uma procura crescente por procedimentos anestésicos e cirúrgicos por parte da população idosa. Este manuscrito pretende abordar a singular fisiologia geriátrica e a avaliação peri-operatória do paciente idoso para ajudar a guiar os cuidados destes pacientes tendo em vista a melhoria destes.

Foi realizada uma pesquisa de literatura, através da base de dados da MEDLINE, por artigos escritos na língua inglesa. Como palavras-chave foram utilizadas "elderly" e "geriatric" combinadas com "anesthesia", "preoperative assessment", "monitorization", "postoperative care" e "postoperative management". Dos resultados obtidos foram escolhidas as publicações que nos pareceram mais pertinentes, incluindo estudos originais, revisões, relatos de casos e cartas ao editor. As suas listas de citações foram também revistas.

No período pré-operatório devem-se avaliar o risco anestésico, cardiovascular, respiratório e renal. Os médicos também devem prestar atenção às doenças endócrinas dos pacientes tal como ao seu estado hematológico, imunológico, mental e à "frailty".

A administração de anestésicos de acordo com o estado patofisiológico do doente é um facto mais importante do que a escolha entre a técnica de anestesia regional e a geral.

A monitorização intra-operatória dá informações importantes à equipa médica acerca do estado geral do paciente cirúrgico.

No que diz respeito aos cuidados pós-operatórios, o controlo da dor e a nutrição têm de ser tidos em conta e os profissionais de saúde devem conjugar esforços em prol da reabilitação do doente.

Compreender a fisiologia e patofisiologia geriátricas é essencial para avaliar e orientar adequadamente os pacientes idosos. Estes indivíduos são caracterizados por declínio funcional progressivo de todos os órgãos, homeostenose e variabilidade interindividual. Mesmo com cuidados peri-operatórios otimizados algumas complicações, como a disfunção cognitiva pós-operatória e o delírio pós-operatório podem ocorrer. Medidas preventivas poderão ser implementadas embora não sejam infalíveis.

A anestesia no idoso pode ser muito desafiante para os médicos. Com a idade surgem várias alterações físicas e psicológicas juntamente com múltiplas doenças. Para que os cuidados de saúde dos idosos sejam otimizados, essas alterações devem ser tidas em conta. Também se deve avaliar o seu risco de complicações futuras para que possam ser implementadas medidas de prevenção.

ANESTHESIA IN THE ELDERLY

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Keywords:
- *Aged;*
- *Anesthesia;*
- *Patient Outcome Assessment*

Abstract

The global ageing tendency has been implicated in the dramatic increase in some chronic diseases and comorbidities. This will lead to a growing demand for surgery and anesthetic procedures by the elderly population. This manuscript intends to approach the singular geriatric physiology and the perioperative assessment of the elderly patient to help guide the care of elderly patients hoping to improve the care of these patients.

A literature search was performed in the MedLine database for articles written in the English language. As keywords, we used "elderly" and "geriatric" combined with "anaesthesia", "preoperative assessment", "monitorization", "postoperative care" and "postoperative management". From the obtained results, we chose the most pertinent publications, including original studies, reviews, case reports and letters to the editor. Their citation lists were also reviewed.

In the preoperative period one should assess the anesthetic, cardiovascular, respiratory and renal risks. Doctors should also pay attention to the patients' endocrine diseases, immunologic and hematologic states as well as their "frailty"

The correct administration of anesthesia according to the pathophysiological status of the patient is more important than the choice between regional or general anesthesia.

Intra-operative monitorization gives the medical team important information about the

global status of the surgical patient.

Regarding postoperative care, pain management and nutrition have to be taken into account and health carers should join forces towards the patients' re-enablement.

Understanding geriatric physiology and pathophysiology is essential to properly evaluate and manage elderly patients. These individuals are mainly characterized by progressive function decline of all organs, homeostenosis and interindividual variability. Even with optimized care some complications, like postoperative cognitive dysfunction and delirium may appear. Preventive measures can be promoted, although these are not infallible.

Anesthesia in the elderly can be very challenging to physicians. With increasing age, several physical and psychological changes emerge along with the co-existence of multiple diseases. In order to optimize the health care of elderly, one should be aware of these changes and properly assess their risk of future complications so preventive attitudes can be implemented.

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INTRODUCTION

Populations all over the world are not only rising in numbers but they're also getting older. In fact, the most recent demographic data are astounding. According to the World Health Organization, the world's population of people 60 years of age and older has doubled since the 80's. They may even reach the 2 billion in 2050. Also, and for the first time ever, people aged 65 or older will outnumber children under 5 in the current year.

This global ageing has its implications. As a matter of fact, ageing, in addition to changes in lifestyle and diet, has been implicated in the dramatic increase in chronic diseases such as cancer, diabetes, hypertension, heart failure and other heart diseases.[1]

Advanced age is not a contraindication to anesthesia or surgery; however, perioperative morbidity and mortality are greater in elderly than in younger surgical patients. Increasing chronic diseases and other comorbidities will lead to a growing demand for surgery. Actually, elderlies already resort to surgery four times more often than the rest of the population and the numbers are expected to increase even more.[2] Also, by 2051, 40% of all anesthetics will be used, exclusively, on people aged over 65.[3] This means not only more physical trauma but also greater exposure to anesthetics and their side-effects.[4]

First, it must be noted that the term "elderly" is a subjective term that refers to an old and ageing person and there is no consensus regarding the age at which an individual is considered to become one. Therefore, and because it meets the general findings in the majority of medical articles, "elderly" shall refer to any person with 65 years old or more. [5-8]

The final objective of perioperative care is to help elderlies return to their pre-morbid sate. For that to happen, clinicians must treat them respectfully, optimise their rehabilitation by preventing complications and always bearing in mind these are particularly frail individuals with multiple comorbidities.[9]

This manuscript will approach the singular geriatric physiology and the perioperative assessment of the elderly patient.

GERIATRIC PHYSIOLOGY AND PATHOPHYSIOLOGY

It is of common knowledge that aging is followed by a decline in physical capability resulting from a progressive deterioration of all organs. In addition, people become more sedentary with advanced age and, so, the majority of elders have chronic diseases and comorbidities that must be assessed before anesthesia and surgery.[10]

The first two concepts to have in mind are the limited functional reserve and the interindividual variability that define these patients. Limited functional reserve refers to the inability of an organ to maintain its function when experiencing some sort of stress, namely, a surgical procedure. This incapacity to maintain homeostasis is sometimes described in the literature as "homeostenosis". The limited reserve is, in part, responsible for the longer time elderly need in order to be as functional as they were before surgery, when compared to younger patients. In severe cases, or in certain surgeries, they may become totally dependent on others because they stop being able to do simple everyday tasks by themselves.[11]

Interindividual variability emphasizes that elderly patients are not all alike. While some show frail presentations and suffer from quick functional deterioration, others show less signs of organ damage and can be fully independent at very advanced ages. Besides, there is also significant variability within the same individual (intraindividual) since the speed at which each organ or system ages is not the same.[12]

CARDIOVASCULAR SYSTEM

Elders have a reduced arterial elasticity which is a result of fibrosis of the media layer. This will lead to an increased afterload, an elevated systolic blood pressure and finally, to left-ventricle hypertrophy. Diastolic dysfunction follows not only systolic hypertension but is also associated with valvular diseases, coronary artery disease and cardiomyopathy. Diastolic dysfunction, itself, will result in increased telediastolic pressure, rising up the risk of heart failure.[13]

Like the vessels media layer, the myocardium and the cardiac conduction system also become fibrotic and the heart valves are frequently calcified.[13] The compromise of the conduction system and the natural loss of node cells may conduce to arrhythmias, namely, atrial fibrillation and atrial flutter.[12]

Maximal heart rate decreases with age because of an increased vagal tone, on one hand, and less beta receptor sensitivity in the myocardium, on the other. This way, elderly patients will have more difficulty in responding to situations like hypoxia, hypovolemia or hypotension, since elders lack compensatory tachycardia.

Blood also takes more time to complete a circulation cycle, which means there will be a delay in the onset of intravenous drugs and an acceleration of the induction time of inhalatory anesthetics.[12, 14, 15.]

RESPIRATORY SYSTEM

Respiratory deterioration is also typical of this age group. It includes structural and functional changes. Changes on the curvature of the spine, like hyper kyphosis, distort the correct disposition of ventilatory muscles, affecting their efficiency. This is aggravated even more by the age-related loss of function of all muscles[16, 17] and the final result is a reduced respiratory strength and total amplitude.

Aged individuals also have increased difficulty in clearing mucus from the lungs due to reduced cough strength and an impaired mucociliary function.[18, 19] The loss of tissue elasticity plays a major role on respiratory dysfunction and it is connected to the elevated levels of tissue and plasmatic inflammatory cytokines observed in aged subjects. Lack of elasticity produces two immediate consequences: airspace dilation and the collapse of small airways with decreased efficiency of gas exchange. So, in other words, loss of elastic tissue predisposes elderly to hypoxia and, ultimately, the development of chronic obstructive pulmonary disease.[6]

In summary, respiratory deterioration encompasses decreased vital capacity, a decreased expiratory flow, an increased residual volume and increased lung compliance.[10] All these will lead to an increased ventilatory impairment in the recovery room.

RENAL SYSTEM

Glomerular filtration rate, renal mass and renal blood flow also tend to fall with aging, predisposing elders to acute renal failure in the post-operatory period. Although plasma renin activity also falls with age, angiotensin sensitivity and sympathetic tone are increased. These, in addition to the lowered prostaglandin synthesis, contribute to a higher renal vascular resistance. Effective renal plasma flow decreases proportionally more than the glomerular filtration rate and this can explain, in part, the higher filtration fraction in the elderlies.[20, 21]

The ability to maintain and eliminate electrolytes such as sodium or potassium and to concentrate and dilute urine is impaired in the elderly. These can lead to clinically important consequences, namely, dehydration, water intoxication, sodium retention and hypo/hyperkalaemia.[22, 23] The response to antidiuretic hormone and aldosterone is reduced and reabsorbing glucose is more difficult.[12]

LIVER PHYSIOLOGY

Liver mass is reduced by 20% to 40%, in the elderly, and more markedly in women than in men. Advanced age is associated with low plasmatic albumin, alanine aminotransferase and γ-glutamyl transpeptidase and high bilirubin plasma concentration, which suggests liver function is also compromised in the elderly.[24] Another age related fact is that cytochrome P450 activity is 32% lower in subjects above 70 years than in subjects aged 20-29 years.[25]

The hepatic along with the renal changes are responsible for pharmacokinetic and pharmacodynamics alterations that turn drug metabolism and elimination into deficient processes. This will have repercussions on drugs plasma concentration.

CENTRAL NERVOUS SYSTEM (CNS)

The aging brain also undergoes anatomical and physiological alterations. The decline of brain weight begins soon at 45-50 years of age and it does not stop until the age of 86.[26.] However, decreases in brain mass cannot be explained solely by age-related losses. It constitutes a multifactorial process and some comorbidities like hypertension or diabetes can have ominous effects on white matter tracts and on the blood-brain barrier permeability.[27, 28] There are subclinical vascular diseases, frequent in the elderly, that cause changes in cognition such as impaired attention, psychomotor speed and executive function.[29]

Neurogenesis is affected as well, restricting the elders' ability to learn and leading to cognitive decline.[30]

Cognition itself can be defined in two main ways, acquired knowledge and processing speed. Although the first one only declines after the 60s, the second one starts decreasing in the early adulthood. Memory decline occurs in more than 40% of people aged over 60 years.[31, 32]

PREOPERATIVE ASSESSMENT

It is important to screen the presence and evaluate the stability of the patient's medical conditions and treatments through a preoperative consultation. It is the physician's task to identify diseases prone to cause disturbances in the normal functioning of vital organ systems like coronary disease or diabetes so they can be optimized preoperatively. It is also crucial to understand the true organic functional reserve of the patient. An adequate medical history and a methodical physical examination are the keys for preoperative assessment.[33, 34]

ANESTHESIA RISK ASSESSMENT

There have been multiple scales and scoring systems to help physicians estimate the operational risk. The American Society of Anesthesiologists (ASA) Physical Status classification system was initially created in 1941.[35] The purpose of the grading system is simply to assess the degree of a patient's "sickness" or "physical state" prior to selecting the anesthetic or prior to performing surgery. This is the most commonly used scale nowadays and consists of 6 classes allowing an overview of the patient's health. Besides, the letter "E" can be added to the class if the procedure at issue has an urgent nature.[15, 36] Describing patients' preoperative physical status is used for recordkeeping,

for communicating between colleagues, and to create a uniform system for statistical analysis. The grading system is not intended for use as a measure to predict operative risk but various studies found a correlation between the ASA classification and mortality.[37, 38] Despite being very versatile and simple to use it lacks on reproducibility as different anesthetists often come to different conclusions when assessing the same patient.[39] Besides, ASA criteria do not take into account patients age neither the complexity of the surgery and there is no differentiation between a systemic disease leading to a procedure and one that is an incidental chronic finding.[40]

Measures of outcome are needed in order to allow monitoring the quality of healthcare service. One way to achieve those measures of outcome is by using score systems. The POSSUM score was created by Copeland *et al*[41] so it could be easily used across the multiple types of surgery and whose main utility would be during a surgical audit. This score is, basically, the sum of a physiological score (twelve variables) and an operative severity score (six variables). The result provides an indicator of the risk of morbidity and mortality in the general surgical patient and, thus, measuring the quality of healthcare delivery. Since its creation, back in 1991, some variations of the POSSUM score have emerged. As an example, after some literature references to the tendency of the POSSUM score to over predict mortality in low-risk patient groups, the P-POSSUM score was developed later on.[42, 43] This last score uses the same information as the original but a different risk predicting equation. In 2004, in order to better estimate the mortality of colorectal cancer patients, another modified version, the Cr-POSSUM was created.[44] More recently, the Elderly (E) POSSUM score was constructed to predict the mortality of elderly patients undergoing major colorectal cancer procedures.[45]

CARDIOVASCULAR RISK ASSESSMENT

According to the most recent European guidelines[46] on assessment and management of non-cardiac surgery, cardiovascular risk evaluation should focus, basically, on four elements: the surgical risk for cardiac events after the procedure, functional capacity, risk indices and non-invasive testing.

Surgical Risk for Cardiac Events after the Procedure

Patient-related risk factors, the type of the surgery and its clinical context may be responsible for cardiac complications after non-cardiac surgery.[46] Regarding surgical specific factors; urgency, invasiveness, type and duration of the operation, changes in body temperature, blood loss and fluid shifts seem to be the most relevant.[47]

Risk Indices

They represent the relationship between the clinical history and the risk of perioperative mortality and morbidity. The European guidelines[46] emphasize two of them: "the Lee index"[48] and the NSQIP/MICA model.[49] The Lee index was designed for predicting post-operative myocardial infarction, pulmonary oedema, ventricular fibrillation or cardiac arrest and complete heart block. This index includes six independent predictors for developing postoperative cardiac complications: high-risk type of surgery, ischemic heart disease (IHD), history of heart failure, history of cerebrovascular disease, preoperative treatment with insulin and preoperative creatinine level >170 mmol/L (>2 mg/dL). The more predictors the patient has, the greater the likelihood of future complications: the risk of postoperative cardiac complications for 0, 1, 2 or more risk factors is, approximately, 0.4%, 1%, 7% or 11%, respectively.[48, 50] The NSQUIP/MICA model was developed to evaluate the risk of intra or post-operative myocardial infarction or cardiac arrest and it uses the American College of Surgeons National Surgical Quality Improvement Program database.

The NSQUIP/MICA model predicts death better than the Lee index but, on the other hand, it lacks an estimation of the risk of perioperative pulmonary oedema and of complete heart block. So, the two indices may give physicians' complementary information and using them both could help doctors to make safer decisions.[46]

Functional Capacity

Preoperative determination of functional capacity is fundamental. It is measured by metabolic equivalents (METs). This feature may be objectively assessed by exercise testing but more commonly it is estimated from the ability to perform certain activities of daily living. If patients are unable to climb two flights of stairs it means their functional capacity is less than 4 METs and this condition is associated with an increased risk of perioperative cardiac events with increased mortality in case of thoracic surgery. When the functional capacity is high, the prognosis is excellent. On the other hand, if it is poor or unknown, preoperative risk stratification and perioperative management should be determined based on the presence and number of risk factors in relation to the risk of the surgery.

Non-invasive tests

Non-invasive cardiac testing investigates left ventricular (LV) dysfunction, myocardial ischemia and valve abnormalities. All these three can be assessed by stress echocardiography, recommended in asymptomatic individuals before high-risk surgery in patients with more than two clinical risk factors and poor functional capacity (<4 METs).

A preoperative electrocardiography is commonly performed. It is very important for patients with ischemic heart disease and it is "recommended for patients who have risk factor(s) and are scheduled for intermediate- or high-risk surgery". When the goal is to assess the LV function, then echocardiography is the most available and user-friendly tool. Although its routinely use is not recommended by the European guidelines for preoperative assessment, it may be useful in asymptomatic patients with high surgical risk.[46] As it has already been said, the diastolic dysfunction is a pathological situation that can be a consequence of multiple clinical conditions and, ultimately, can lead to heart failure. This situation is more incident in the elderlies and is mainly caused by a loss of left ventricular compliance. This limits the heart's ability to relax and results in increased telediastolic pressure. This is the reason why atrial contribution to the ventricular filling is so important in the elderly. When telediastolic pressure is

too high, blood may flow retrograde to the pulmonary circulation with resulting pulmonary venous congestion and oedema. Some patients are asymptomatic while others present with exercise intolerance, cough, dyspnea or fatigue. The clinical picture may also appear similar to left ventricular systolic failure. It is very important to make the correct diagnosis because some therapeutic measures such as diuretics or inotropic stimulation, useful in systolic failure, may aggravate diastolic dysfunction. Echocardiography is the preferred method to assess diastolic dysfunction. Typically, if the patient presents this dysfunction, echocardiography will show a preserved or hyperdynamic left ventricular systolic function and a ratio of greater than 15 between the peak early mitral inflow velocity (E) and the peak early diastolic mitral annular velocity (e'), through Doppler measurement.[51-53]

RESPIRATORY RISK ASSESSMENT

As a part of a preoperative consultation, medical history should focus on smoking, occupational exposures, respiratory symptoms, restricted exercising capability and history of pre-existing infections and lung diseases. [33]

Back in 2006, the American College of Physicians (ACP) elaborated a guideline on "Risk Assessment for and Strategies To Reduce Perioperative Pulmonary Complications for Patients Undergoing Noncardiothoracic Surgery",[54] based on a previous 2-part systematic review conducted by ACP itself.[55] This guideline defined patient and procedure-related risk factors for postoperative complications. The first ones include age older than 60 years, cigarette use, chronic obstructive pulmonary disease (COPD), congestive heart failure, functional dependence and ASA scale class II or higher.

Respecting procedure risk factors, the site of surgery must not be forgotten, according to this guideline, because interventions in some anatomical regions are more prone to cause complications than others. Abdominal, thoracic, neurological, head, neck and vascular surgeries are particularly associated with an increased risk of postoperative respiratory complications.

Regarding laboratory testing, serum albumin below 35 g/L and blood urea nitrogen (BUN) higher than 21 mg/dL were proved to be predictors of mortality.[54, 56] Preoperative spirometry and chest radiography should not be used routinely for predicting pulmonary complications but they can be useful to identify patients who are not likely to survive after pulmonary resection and in patients with previous COPD or asthma.[33, 54, 57]

More recently, in 2010, Canet *et al*[58] developed a predictive index for postoperative respiratory complications using a population-based cohort. This index uses seven variables: age (≤50, 51-80 or >80 years-old), preoperative SpO_2% (≥96, 91-95, ≤91), respiratory infection in the last month, preoperative anemia (≤10 g/dL), the surgical incision location (peripheral, upper abdominal or intrathoracic), the duration of surgery (≤2, >2 to 3 or >3) and if it is an emergency procedure. Using the sum of each B-logistic regression coefficient and multiplying it by 10, after rounding off its value, the index categorizes subjects into low (<26 points), intermediate (26-44 points) and high-risk (≥45 points) patients.

Despite using only seven variables, this index had good discriminative capacity and calibration value. According to the authors this tool is suited for clinical practice since age, SpO_2 and hemoglobin "are easily quantifiable and verifiable, and the three surgical risk factors can be anticipated" [58]

PREOPERATIVE RENAL RISK ASSESSMENT

Acute kidney injury (AKI) is very common, especially, during the perioperative period and in the intensive care unit. 1 to 5% of all hospitalized patients develops AKI and elderly, in particular, seem to be more and more affected by it. This condition is related to higher morbidity and mortality along with longer hospital stays. The postoperative risk of acute renal failure varies from 1.1 to 17% depending on the used definition of acute renal failure.[59]

In order to define and to stratify AKI for severity, two sets of criteria were created: the risk–injury–failure–loss–endstage renal disease (RIFLE)[60] and the Acute Kidney Injury Network (AKIN).[61].

The first one to emerge was RIFLE. These criteria are based on two variables: plasma creatinine/glomerular filtration rate and urinary output. According to the criteria the patient can be classified as being at risk, the least severe category, followed by injury, and failure is the most severe category. RIFLE criteria can also describe changes in AKI severity over time and foresee outcomes. If a patient shows a complete loss of renal function he/she may be categorized as loss or as having end-stage renal disease (ESRD).[62]

AKIN came later, it was also based on creatinine levels and the urinary output but it brought four major changes in the AKI classification. First, instead of the risk, injury and failure RIFLE categories, AKIN defines stages 1, 2 and 3, respectively. Stage 1 of AKIN is also defined by an absolute increase in creatinine of at least 0.3 mg/dL which is not the case of the risk category in RIFLE criteria. Also, patients who receive renal replacement therapy are automatically classified as Stage 3, independently of their creatinine and urinary output values. Finally, the outcome categories (Loss and ESRD) are not part of AKIN.[62]

Postoperative AKI is known to increase in-hospital mortality, length of stay, and hospital costs after surgery so it is important to assess the risk of developing it preoperatively. [63] For that purpose several score systems have been created.

Kheterpal *et al*[64] for instance, defined a list of independent preoperative predictors of postoperative AKI and stratified them into five classes based on the number of risk factors. That list encompasses age equal or superior to 56 years old, male sex, active congestive heart failure, ascites, hypertension, the emergence character of the procedure, intraperitoneal surgery, mild or moderate renal insufficiency and diabetes mellitus.

Regarding laboratory testing, an accurate assessment of the renal function in elder patients is necessary, according to the National Kidney Foundation. However, despite the growing investigation on this area, no single equation has been recommended for evaluating the GFR in the elderly population so far.

In 2010, van Pottelbergh *et al*[65] concluded that the determination of serum creatinine alone was not a good marker of kidney function. That finding can be explained by the influence of some nonrenal factors such as total muscle mass, age, sex, diet and race.[66] They also analyzed, among others, the performance of both modification of diet in renal disease (MDRD) and the Cokroft

- Gault formulas but they could not certify which one of these was better for assessing the renal function in people aged 65 years and older.[65]

In 2013, Koppe L *et al* states that the recently developed BIS – 1 (Berlin Initiative Study) formula was the most reliable one in terms of evaluating the renal function of elderlies, particularly, in those with chronic kidney disease (CKD) stages 1-3. However, one year earlier, Schaeffner et al elected the BIS – 2 equation over the BIS – 1 as the first choice formula to determine the renal function in persons over 70 with normal or mild to moderately reduced kidney function.[67, 68]

PREOPERATIVE ENDOCRINE DISEASES

The classical definition of metabolic syndrome identifies central obesity, insulin resistance, hyperinsulinemia, glucose intolerance, dyslipidemia and hypertension as its main features.[69] This syndrome can lead to pro-thrombotic and pro-inflammatory states, hepatic steatosis and obstructive sleep apnea disease. It also increases the risk of cardiovascular disease by 2-fold and the risk of type 2 diabetes mellitus by 5-fold.[70] Metabolic syndrome is a very common medical condition, especially in the elderly, reaching 44% of the population between 60 and 69 years old and 42% of people with 70 years and older.[71]

Nowadays, there are multiple definitions of metabolic syndrome and diagnostic criteria vary. The most commonly used definitions were developed by the National Cholesterol Education Program Adult Treatment Panel (NCEP/ATP) and by the International Diabetes Federation (IDF). While de classical definition of Reaven *et al*[69] emphasized the insulin resistance as mandatory for the diagnosis, these most recent criteria[72] give more attention to the central obesity measured by waist circumference.[73] Unfortunately, none of the current available definitions consider the effects of aging on the diagnostic variables and that's why they have a lesser predictive value when applied in elderly populations.[74]

The number of obese elderlies is growing. However, it has been difficult to establish the correct way to approach them namely because some relative health risks actually decline with increasing body mass index (BMI) in older adults. For example, there is an association between obesity and increased bone mineral density and decreased osteoporosis. This, along with the larger trochanteric fat pads, provides protection against hip fractures in both men and women. Also, the effectiveness of the obesity treatment is uncertain in the majority of cases, in this population, and losing weight may cause harmful effects on both muscle and bone mass.[75] BMI consists in a simple formula used to classify patients into weight categories. However, in the elderly, the relationship between the BMI value and the percentage of total body fat is distorted. This happens because of the combined effects of progressive, age-related, loss of height as a result of the compression of vertebral bodies and the increase in total fat mass along with the decrease of total muscle mass.[74] That is why, on this population, it is preferable to determine central obesity through measuring the waist circumference rather than calculating BMI.

Abnormally high glucose states are very common among the elderly. It is estimated that one-third of people above 65 years old have diabetes and 75% of them have pre-diabetes or diabetes. Despite these astonishing data, however, half of older individuals with this disease are still undiagnosed.[76] This is a disease affecting multiple organ systems and known to cause, if uncontrolled, dehydration, electrolyte imbalances and an increased risk of wound infection in the perioperative period.[77]

The preoperative assessment should concentrate on diabetes stability and sensitivity to the usual hypoglycemic therapy, cardiovascular and cognitive fallouts and neuropathy. It is also crucial to have in mind that a clinical entity described as older-onset diabetes rarely presents with the classical triad: polyphagia, polydipsia and polyuria. [33]

HEMATOLOGIC AND IMMUNOLOGIC SYSTEM

More than 10% of people older than 65 years old have anemia, according to the WHO definition (hemoglobin < 12 g/dL in women and < 13 g/dL in men).[78] Also, after 50 years old this clinical condition increases with advancing age reaching 20% of elderlies older than [85.79]

In elder populations, most cases of anemia are mild, well tolerated and with low clinical significance.[80] Nevertheless, anemia can be responsible for multiple adverse outcomes impairing the quality of life, the cognitive and physical function. It can also influence other clinical conditions such as cardiovascular diseases and frailty, contribute to longer hospital stays[81] and may even increase the risk of death, including perioperative mortality.[82, 83]

The exact cause for the anemia in the elderlies may be difficult to be determined since this population has several comorbidities, disorders and take various medications. In the majority (80%) of cases,[84] however, physicians are able to identify the reason for the hemoglobin drop. Basically, the causes of anemia, in the elderly, are divided in 4 different groups: nutrient-deficient anemia, anemia of chronic inflammation, anemia related to chronic kidney disease and unexplained anemia. The anemia's severity is not correlated with the underlying cause. This is a concept that should not be overlooked.[84] If a patient scheduled for elective surgery was found to have anemia and he/she is expected to lose great amounts of blood during the procedure, that should constitute an indication for rescheduling the surgery until the proper evaluation and management.[85]

The term "immunosenescence" comprises all the dysfunctional changes to the immunologic system that progressively emerge with aging.[86] It seems T-cells are particularly affected by the aging process. The number of naïve T-cells is reduced through the years while CD8+ memory T-cells increase. But changes are not restricted to the adaptative immune system since they extend to natural-killer cells, dendritic cells and other effectors of the innate immune system.[87]

Systemic immunity impairment can lead to an increase prevalence of neoplastic, chronic inflammatory and autoimmune diseases in older patients. Also, vaccines will work less effectively making these patients more susceptible to common pathogens such as *influenza*.[87]

FRAILTY

The term "frailty" has been increasingly used to indicate people at high risk of adverse outcomes such as onset of disability, morbidity, institutionalization or mortality and those who are not

able to respond adequately to a certain stress. Disability is not the cause but rather a consequence of frailty. Doctors are usually capable of noticing a frail patient who is more often, although not always, elderly but its assessment remains a problem.

Frailty is a dynamic clinical condition and the result of a multisystem deterioration that has nothing to do with the normal aging process. Today, the scientific community sees frailty as a syndrome and, therefore, related impairments like sarcopenia, functional status decline, neuroendocrine dysregulation and immune system deterioration can occur in a combined manner.[88] Frailty turn individuals more vulnerable to stressors (ex. Surgery), complications and is the responsible for increasing hospitalization periods.[89] Recent studies state that quantifying frailty helps clinicians in the way that it improves the precision of preoperative risk assessment.[90] Nevertheless, no method of quantifying frailty, especially in the perioperative period, has yet been put into routine clinical practice despite the variety of measurement tools available.

Currently, there are two ways of approaching frailty: phenotype and accumulated deficit. Some measurement tools face frailty as a true clinical syndrome or phenotype and rely on a group of outcomes to identify and quantify frailty. For instance, the "FRAIL" scale consists basically in 5 domains – Fatigue, Resistance (ability to climb one flight of stairs), Ambulation (ability to walk one block), Illnesses (superior to 5) and Loss of weight (more than 5%).[91] Another tool is the "Easy Prognostic Score "developed by Ravaglia et al using nine different predictors of mortality including age, gender and physical activity.[92]

The most well-known and widely used phenotype, though, was described by Fried *et al*. She and her colleagues proposed a frailty phenotype consisted by 3 or more of the following components:

- Unintentional weight loss of more than 10 pounds in prior year or, at follow-up, of more than 5% of total body weight in prior year
- Weakness, adjusted for gender and body mass index
- Poor endurance and energy as indicated by self-report of exhaustion
- Slowness. Calculated based on the required time to walk 15 feet, adjusting for gender and standing height
- Low physical activity level

The major drawback of this score, however, is that it is essentially "physical" and focusing on sarcopenia as the main pathophysiologic feature but ignoring disorders of cognition and mood.

Another way to approach the frail patient is to pay more attention to the quantity rather than the quality of the patient's deficits, which have been accumulating throughout life. Simply put, the more deficits the patient has, the more likely the patient has frailty. One of the scores that uses this system is the "Frailty Index" that seems to be the most promising of the tools to assess this clinical condition because it is less dependent on physical factors.[93]

Unfortunately, clinicians are still searching for an effective way to reverse frailty but many believe that "prehabilitation", a recently emerged concept, is the key factor to optimize frail patients before surgery. However, solid clinical evidence to support this method is still scarce.

Rehabilitation consists in safe and feasible exercise training in order to increase muscle mass, improve balance and delay cognitive decline, in summary, modify deficit accumulations.

A better education and a consistent nutritional support also take part in optimizing frail patients preoperatively.[89]

PREOPERATIVE MENTAL STATUS EXAMINATION

Speech, consciousness, perception, orientation, coherence, memory, and motor activity can be assessed preoperatively to determine baseline cognitive status and postoperatively to measure change in function using the Mini Mental State Examination (MMSE) which is reliable, easy to conduct, and useful for serial testing modifications in cognition.[94]

Alternatively, the Clock Drawing Test, the Confusion Assessment Method and the 3 Item Recall Test are equally suitable tools for routine preoperative assessment of the cognitive function.[94-96] A complete questionnaire about other delirium risk factors like sensorial impairment (mainly, visual and hearing), alcohol and drug abuse, preoperative depression, previous cerebrovascular accident, anticholinergic medication, and cognitive deterioration should also be considered for all elderly surgical candidates.[8, 33]

If the patient was found to have any kind of cognitive impairment, then a more specialized preoperative evaluation, performed by a geriatrician, should be done. If these patients have any kind of substance abuse they may also benefit from being referred to a specialist for preoperative detoxification. [97]

Major depression is also a serious condition in elderly candidates and the Geriatric Depression Scale can be used to detect it.[33, 98] Furthermore, mental screening is also necessary for the physician to investigate the ability of the patient to perceive all the information and to give a valid informed consent. [33]

INFORMED CONSENT

During the preoperative consultation, an informed consent shall be obtained. This is a mandatory procedure in all cases and not just when dealing with elderly patients although some age-related changes, such as dementia or hearing impairment, can compromise the consent. It is the physician's duty to certify that the patient was able to fully understand and memorize all the information presented before signing the consent. In some severe situations like the already referred dementia it might be necessary the collaboration of a family member when decision making is on the line.[99]

ANESTHETIC TECHNIQUE

Before discussing in more detail the specificities of each one of the anesthetic techniques, it is important to remember that the proper administration of an anesthetic in accordance with the pathophysiological characteristics of one patient is more important than the choice between general or regional anesthesia. Many studies have tried and failed to show significant differences between the two techniques.[100-102] However, this conclusion may be distorted because the outcomes studies usually measure are not directly related to anesthesia.[9]

General Anesthesia

There are several age-related factors that can influence the anesthetic drug consumption. Elderly are depleted of neurotransmitters, neuronal density and innervation of skeleton muscles. These changes justify using lower drug doses in the aged people when compared to young and healthy individuals because, in a simple manner, the same concentration produces a larger response. Additional factors can also lower the threshold of overdose in advanced age patients with particular attention to the reduced cardiac index and baroreflex response. The first one increases induction time and the impaired baroreflex response lowers the compensatory tachycardia.[7]

General anesthesia leads to vasodilation by two complementary ways: through direct effects on microcirculation and, indirectly, by central inhibition of vasoconstriction. [103, 104] This conducts to impaired wound healing since vasoconstriction initiates the "inflammation phase" of the wound healing process, attenuates the blood loss and facilitates blood clotting.[7]

In the specific case of inhalatory anesthesia it is useful to remind that elders have reduced alveolar exchanges. This factor contribute to disparities between tele-expiratory and plasma drug concentrations and may lead to overdose of this kind of agents.[7] There is also a group of age-associated pharmacokinetic and pharmacodynamics changes that can influence anesthetics effect and an additional increase in side-effects.

Regional Anesthesia

With regional anesthesia, the physiologic endocrine stress response to surgery is attenuated,[105] a situation that does not occur when physicians use typical dosages of volatile or IV agents.

Core hypothermia, adverse to the wound healing process, is equally probable either under general or epidural anesthesia.[106] The role of local anesthetics in the wound healing process is still uncertain due to some contradictory data. Reducing pain and the stress response can work positively in terms of healing but local anesthetics also prolong collagen synthesis and inhibit mesenchymal cells proliferation.[107-109].

Spinal anesthesia is one of the most used forms of regional anesthesia and, due to spinal blocking plus age-related comorbidities, can produce severe hypotension and bradicardia especially if the patient has an already low cardiac reserve, as is the case of elderlies. When used on these patients, spinal anesthetics suffer a larger diffusion and produce wider effects than planned, due to some age-related changes in cerebrospinal fluid. Besides, the loss in nervous fibers cause neuronal block to extend through a larger area than desired.[7]

INTRA-OPERATIVE MONITORIZATION

Monitoring is essential in modern surgery. It not also detects the consequences of human errors but it also warns the medical team if the patient's clinical condition is deteriorating for some reason. Thus, intraoperative monitoring helps reducing the risk of accidents.[110-112]

Some of the variables physicians can use to correctly monitorize patients are the following:

Intra-arterial blood pressure: Hypotension can follow the induction of anesthesia and can be particularly severe in the elderly patient. Before the drug administration, intra-arterial cannulation and transduction should be made in order to prevent this condition. Another method that could be used to avoid hypotensive episodes is the "beat-to-beat" monitoring.[9]

Central venous pressure: Central venous catheterization provides an additional route for venous access when vasoactive drug support or parenteral nutrition is necessary. However, this procedure is far from being risk-free since insertion trauma and infection may occur.

Cerebral oxygen saturation: There is evidence supporting that detection of episodes of cerebral ischemia through the determination of cerebral oxygen saturation may help reducing the prevalence of POD/POCD if early intervention is carried out.[113] Nevertheless, this still lacks further investigation to be confirmed.[9]

Bispectral index monitors (BIS) and entropy monitors: Both are useful to evaluate the depth of anesthesia in order to prevent overdose, hypotension and POCD/POD.[9, 114] If these methods are not available the Association of Anaesthetists of Great Britain and Ireland recommend the use of the Lerou normogram to calculate the proper dose on inhalational anesthesia taking into account the lower minimum alveolar concentration (MAC) values of elderly people.[9] Saager *et al* identified a condition called "triple low", consisting of BIS lower than 45, mean arterial pressure under 75mmHg and MAC under 0.7. Individuals with this triple combination were found to be more sensitive to anesthesia with increased risk of brain hypoperfusion and mortality.[12]

Peripheral nerve stimulation: It has already been said that typical pharmacodynamic and pharmacokinetic changes affect elderly individuals and these can unpredictably modify the anesthetics' effect. Neuromuscular blockade may, thus, become longer than expected justifying the routinely use of neuromuscular function monitoring in patient subject to these type of drugs.[9, 115]

POSTOPERATIVE CARE

Anesthetists routinely assess patients towards the end of the surgical procedure in order to decide the intensity of postoperative care. Patients with stable body temperature and blood pressure, proper anesthesia and analgesia will recover more easily, requiring a lighter postoperative care and a shorter hospitalization period. However, in some particularly severe conditions, patients may demand critical care after surgery, despite optimal intraoperative conditions. Analgesia, fluid therapy, blood pressure maintenance and conservation of body temperature should make part of postoperative care to allow the re-enabling of patients and to reduce the risk of potential complications

Pain Management

Pain management is a fundamental part of postoperative because pain may, not only, result in longer hospital stays but also contribute to complications such as postoperative delirium (POD) or postoperative cognitive dysfunction (POCD) POD/POCD, difficulty in mobilization and cardiorespiratory problems.[116, 117]

Assessment is the first thing to do in order to achieve optimal postoperative pain management. Some features like localization, aggravating/alleviating factors, timing, severity and associated symptoms shall be described. Some of these features can be obtain by applying pain scales. Various scales have been studied in the elderly population but, unfortunately, the majority was not capable of accurately report the analgesia needs of elderlies. In general, however, the verbal measures performed better than the non-verbal ones. Unusual behaviors, mobilization difficulties and lack of appetite may also constitute clues to help health carers assessing pain.[118] Of course to correctly evaluate postoperative pain, physicians need to know the pain baseline of the patient, asking about it preoperatively. This is important because surgery may alter some pre-existing conditions such as rheumatic pathologies and, thus, the pain may result from an exacerbation of this conditions rather than post-surgery pain per se.[119]

Opioids, mainly morphine, are considered the basis of postoperative analgesia. Nevertheless, this drug class may cause some adverse effects and health carers should try to prevent these unfortunate events. Mobility, appropriate hydration and co-administration of stimulating laxatives and stool softeners are some of the strategies to avoid or mitigate constipation. Nausea and vomiting may be prevented by giving traditional neuroleptic antiemetics before taking the opioid.[119]

Currently, anesthesiologist usually make use of multimodal analgesia techniques that consist not only in drug administration's but also in some non-pharmacologic strategies like postural support, pressure care and ice to prevent swelling.[9]

Non-steroidal anti-inflammatory medications have to be carefully used because they're associated with increased risk of toxicity, namely renal. Therefore, these drugs should be excluded for any patient with a renal function lower than 50 mL/min. They also can conduce to gastric damage and peptic ulcers. Paracetamol is considered safe and eligible for use in the elderly.[9, 119]

POSTOPERATIVE DELIRIUM AND POSTOPERATIVE COGNITIVE DYSFUNCTION

POD consists of an acute syndrome, occurring in the first few days (24-72h) after surgery with a fluctuating course.[120] It is not a rare situation since 10% of elderly surgical patients may suffer from it and this incidence is variable depending on the type of surgery.[114]

The main symptom of this condition is disturbed attention. Other cognition deficits like disorientation and memory loss may also become part of this syndrome.[114] Delirium can be classified into three different types: hyperactive/hyperalert, hypoactive/hypoalert and mixed. As the name suggests, hyperactive delirium is more exuberant and its signs are easier to detect. Hypoactive delirium, on the contrary, remains undiagnosed more often and can be easily misdiagnosed with dementia or depression.[121] This type of delirium is also associated with pressure ulcers, longer hospital stays and increased risk of short- and long-term mortality.[122]

Another way to categorize delirium is to classify it as psychotic, emotional and mixed. A patient with psychotic delirium can experience hallucinations, paranoia, illusions or delusions while other with emotional delirium is affected more with a depression-like syndrome having a depressed mood, emotional liability and anxiety.[122]

There are multiple risk factors that may increase the risk of POD. Being, roughly, an elderly-related disorder, POD is, unsurprisingly associated with advanced age, cognitive impairment, lower educational level and pre-existing comorbidities. There are also some modifiable risk factors like infection, malnutrition, dehydration and severe pain that should be corrected.[122] POD is believed to be multifactorial. One of the causes may be related to imbalances of CNS melatonin and neurotransmitters such as acetylcholine and dopamine. The stress-induced inflammatory response, caused by surgery, may also be connected with the occurrence of delirium after the intervention.[114]

POCD is a syndrome resulting from the prolonged deterioration of cognitive function that occurs after surgery and anesthesia but, usually, takes more time to get established than POD. It is estimated that 15 up to 25% of geriatric surgery population will present with POCD after the procedure.[120] This condition is defined by memory impairment (both verbal and visual), intellectual limitations and poor executive function that, in most cases, lasts for weeks or months.[109]

The severity of presentation is quite variable. Some patients only have minor symptoms while others suffer from a marked difficulty to focus or to process information, being unable to perform even the easiest of the tasks.[114] Those who are victims of mild variations of this syndrome can pass unnoticed to clinicians. However, POCD has been associated with increased risk of mortality, leaving the labour market prematurely and becoming dependent on socio-economic support, therefore, recognition of this neurocognitive disorder is of utmost importance.[123]

Various researchers have been trying, along the years, to identify the exact cause that could explain POCD but many believe it is multifactorial. The "classical" hypothesis are microemboli, cerebrovascular disease, inflammatory mediation and neurodegeneration. However, there are multiple studies questioning if microemboli really play a role in POCD. Actually, the weight of evidence is against this hypothesis.[124-126] Some risk factors like diabetes, hypertension, obesity, carotid disease, peripheral artery disease and age itself also contribute to POCD. The contribution of a preoperative cognitive deficit due to cerebrovascular disease, although probable, has not been easy to prove.[127]

In order to detect POCD, neuropsychological testing must be executed and it is necessary to obtain base-line tests preoperatively for a comparison purpose. Unfortunately, it is not simple for doctors to interpret the cognitive changes, there is no agreed definition of what constitutes a significant cognitive decline and there isn't a consensual POCD definition.[114]

An important fact is that the incidence, magnitude or clinical pattern do not seem affected by the type of anesthesia, according to recent data.[120, 127]

Prevention of postoperative cognitive dysfunction and delirium

Clinicians should implement measures to minimize the risk of having two of the most feared complications of anesthesia, particularly in the geriatric population. Fulfilling preventive measures of these situations can, not only, reduce prevalence but also improve the outcome in case of a postoperative cognitive problem.

In 2001, a study led by Clegg and Young[128] suggested opioids were associated with a 2-fold increased risk of delirium. Within opioids, pethidine caused the most pronounced risk increment. Benzodiazepines, nifedipine and antihistamine H1 medications were also studied by the same authors and found also to be associated with a higher risk of developing postoperative delirium and, possibly, postoperative cognitive dysfunction. Thus, when dealing with patients with preoperative risk of developing POD/POCD, one should avoid using this sort of drugs.

Another method to fight these threats is by combining a range of "multi-domain interventions"[114] which include an optimal range depth of anesthesia, targeting bispectral index (BIS) levels in between 40 to 60±5. Proper cerebral oxygen saturation monitoring along with blood volume, serum electrolyte and pain management are important actions to prevent POD/POCD as well. Pharmacological intervention is usually not effective against these two entities.[109, 113] Maybe the best manner to prevent POD/POCD is, in some cases, to change the magnitude of the surgery. In other words, by quoting Gibbs,[129] "Perhaps avoiding major surgical procedures in favour of less invasive alternatives, where possible, should be considered".

Nutrition

Postoperative nutritional support reduces the risk of complications, improves clinical outcome and prevents longer hospital stays. Avoiding postoperative nausea permits early enteral nutrition, improving wound healing and recovery. Enteral nutrition seems to have more benefits and, therefore, is preferable to parenteral nutrition.[130] Enteral nutrition is more physiologic, better preventing in functional and morphologic alteration of the gut system and less expensive than parenteral nutrition.[131]

Re-enablement after surgery

Re-enablement consists of a multidisciplinary process through which patients return to their preoperative level of function. Elderly should be assessed in terms of mobilisation and stability and provided with assistance tools, like walkers, to stabilize balance if necessary. Before proceeding to discharge, health carers should also assess the patient's home environment for any inaccessible structures, and formulate a plan to increase muscle strength and improve stability. Stimulating ambulation in well-assessed conditions improves safety and reduces the risk of complications such as deep venous thrombosis and POD. Although "re-enablement" is beyond remobilization and rehabilitation, the recovery of ambulation is a high priority after surgery since only 2 days of hospitalization result in significant functional decline in elderly patients.[9, 119]

CONCLUSION

The number of elderlies undergoing surgery is increasing and this brings new challenges for anesthetists. With advancing age, several physical and psychological changes emerge along with the co-existence of multiple diseases. In order to optimize the health care of elderly, one should be aware of these changes and properly assess their risk of future complications so preventive attitudes can be implemented. Knowledge of the specific pharmacological aspects of the elderly is also needed in order to assure quality of health care.

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