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### Review

## Anaesthesia and the elderly patient, seeking better neurological outcomes<sup>☆</sup>



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#### ABSTRACT

**Introduction:** Elderly patients in need of surgery under anaesthesia present the challenge of maintaining their especially delicate balance under stress conditions.

**Objective:** This review of the literature aims to bring the anaesthesiologist closer to this group of patients, examining some of the physiological changes that occur with ageing, the effects that anaesthesia might have on their postoperative neurological state, the monitoring options, and the most frequent neurological complications.

**Materials and methods:** A search was conducted in the LILACS, MEDLINE and GOOGLE SCHOLAR databases using the terms anaesthesia, elderly, outcomes and neurologic, together with an ambispective snowball search from 2000 until today.

**Conclusion:** Institutions and staff responsible for the care of elderly patients must have the training and knowledge necessary for providing comprehensive treatment to this group of patients, in order to help them maintain their independence and physical and mental health which are so important during the final stage of life.

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### Anestesia y paciente anciano, en busca de mejores desenlaces neurológicos

#### RESUMEN

**Introducción:** El paciente anciano llevado a cirugía y anestesia es un desafío al intentar mantener su delicado equilibrio bajo condiciones de estrés.

**Objetivos:** Esta revisión de la literatura tiene como objetivo aproximar al anesestesiólogo a este grupo de pacientes al examinar algunos de los cambios fisiológicos que se presentan con el envejecimiento, los efectos que la anestesia puede tener sobre el estado neurológico postoperatorio; las opciones de monitorización y las complicaciones neurológicas más frecuentes.

##### Palabras clave:

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**Materiales y Métodos:** Para este artículo se realizó una búsqueda en las bases de datos LILACS, MEDLINE Y GOOGLE SCHOLAR con los siguientes términos anestesia, anciano, desenlaces y neurológico, que se complementó con una búsqueda en bola de nieve ambispectiva a partir del año 2000 hasta la actualidad.

**Conclusión:** Las instituciones y personal a cargo del paciente anciano deben contar con la preparación y conocimiento necesarios para el manejo de este grupo de pacientes, con el fin de mantener la independencia y salud física y mental tan importantes en la etapa final de la vida.

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## Introduction

With improved medical care and health conditions, average life expectancy has increased throughout the world.<sup>1</sup> This increase in longevity results in a growing number of patients over 65 that are taken to surgery.<sup>2,3</sup>

When managing this group of patients it is important to remember that the definitions of ageing and elderly are in constant flux and depend on the environment in which the elderly individual lives. The characteristics used as the basis to define what an elderly individual is may be associated with multiple social factors, including the age at which he or she stops being fully active at work or in society, is forced to change roles, or has lost functional capacities.<sup>3</sup> The definition of the healthy elderly individual must also be considered, including several concepts such as independence for activities of daily living, wellness, social participation and good quality of life.<sup>4</sup> It is generally accepted that an elderly patient is 65 or older.<sup>5</sup>

Elderly patients are complex when it comes to the approach to their management, and it is important to take into account that outcome goals are different than for the rest of the population due to the functional implications that a surgery may have for this group of people.<sup>6</sup> An important percentage of patients over 65 years of age exhibit preclinical stages of Alzheimer's disease, Parkinson's disease, Lewy body dementia or cerebrovascular disease<sup>7</sup>; and this, together with the physiological changes and the effects of surgical stress and anaesthesia, increases the risk of developing postoperative complications when compared with middle aged individuals.<sup>8</sup>

## Methods

For this review, a search was conducted in the LILACS, MEDLINE and GOOGLE SCHOLAR databases, using the terms anaesthesia, elderly, outcomes and neurological, together with an ambispective snowball search between 2000 and today.

## Most frequent postoperative complications in elderly patients

The frequency of complications in elderly patients is very high. In the United States, 30% of the patients living in retirement

homes who were taken to colectomy died within the first three months after surgery, and 40% of those who survived showed significant functional decline<sup>9</sup>; the incidence of complications increases with age, and 20% of patients over 80 years of age taken to surgery had a complication, and the presence of a complication increased mortality, with a range between 4% and 26%.<sup>10</sup>

The above implies that, in the elderly, the healthcare team is mandated to have a very clear indication for surgery and to give priority to the patient's decision regarding his/her disease and the management options, over those of the family. Close to three-fourths of critically ill patients living in the United States prefer not to undergo any intervention that may entail the risk of decline or loss of their ability to function.<sup>9</sup>

Two of the most frequent postoperative neurological complications with a greater impact on patient outcome are delirium and cognitive dysfunction.

Postoperative delirium is defined as an acute disturbance of consciousness with signs of inattention, disorientation and memory abnormalities that fluctuate over time.<sup>11</sup> It is independently associated with increased mortality, length of stay, functional decline, and overall costs for the institutions. It usually manifests between the first and third postoperative days, with an incidence ranging between 5% and 15%, and may be as high as 33–62% in some groups such as that of hip fractures. The exact cause of this syndrome is yet unknown but it appears to be influenced by several combined factors such as the use of benzodiazepines, opioids or steroid medications, the level of schooling, the type of surgery, the depth of anaesthesia, and comorbidities such as terminal kidney disease or diabetes.<sup>12–14</sup>

Postoperative cognitive dysfunction is a term used to describe a syndrome characterized by consciousness, attention, perception, thinking, memory, behaviour and emotional disturbances that manifest after surgery. This complication appears within days or weeks, as early as within the first 7 days or as late as within the first 3 months. Incidence is highly variable and it is highly significant in cardiac surgery, ranging between 30% and 80%, and in major non-cardiac surgery, ranging between 25% for early stage and 9.9% for late stage. The causes of postoperative cognitive dysfunction are not clear and it appears to be the result of a combination of factors.<sup>15,16</sup> In their study, Monk et al. found age to be an independent risk variable for postoperative cognitive dysfunction and also found a correlation between mortality within the first year after surgery and postoperative cognitive dysfunction. The

presence of late cognitive dysfunction is an important predictor of mortality.<sup>17</sup>

There are various tests that can be used easily and quickly during the consultation and after surgery in order to identify these two syndromes<sup>18</sup>; unfortunately, the staff responsible for the patients are not adequately trained to make the assessment, and reports on the frequency of missed delirium range between 33% and 66%.<sup>19</sup>

### Pathophysiology of neurologic complications

In elderly patients, depending on their preoperative reserve and comorbidities, normal response to surgical stress may be altered, leading to dysfunction of haemodynamic, endocrine and immune responses.<sup>20</sup> Because of changes in their physiology, elderly patients are more prone to neurological complications. These changes include reduced cortical thickness of the brain, in particular in the prefrontal and parietal areas which are critical for memory and orientation, reduced synaptic junctions and dendritic trees in the pyramidal cells of the prefrontal area which is apparently the area with the highest cortical integration with thalamic nuclei; reduced number of neurotransmitters and neuroreceptors, which has been shown to be a risk factor for depression and neurodegenerative diseases like Alzheimer's; and increased susceptibility to the effects of oxidative stress and to the side effects of inflammatory processes.<sup>21</sup>

There is a relationship between ageing and the development of chronic diseases such as Type 2 diabetes, cancer, heart and renal diseases, all of them associated with postoperative complications.<sup>22</sup> In elderly and middle-aged patients with diabetes and arterial hypertension, there is a deterioration of the periventricular and frontal white matter.<sup>23</sup>

Associated with these changes are social factors such as abandonment and isolation, which have a powerful impact on the overall surgical outcome. These factors may mean that an important percentage of elderly individuals may present with malnutrition, inadequate disease management, and cognitive alterations.<sup>24,25</sup>

### Frailty

The effect of frailty must be considered in elderly patients. Frailty is defined as a state of diminished physiological reserve and vulnerability to the effects of stress; when frail patients are exposed to stressful events, they exhibit disproportionate decompensation. A frail patient taken to surgery has increased postoperative adverse effects, prolonged hospital stay, functional decline, disability and increased mortality.<sup>26</sup>

The pathophysiology of frailty has not been well established but it appears to be related to inflammation, excess oxidative stress and a combination of immune and physiological alterations. Frail patients appear to have dysregulation of the immune, hormonal and endocrine systems, with higher levels of inflammatory cytokines as well as of inflammation biomarkers such as interleukin 6 and C reactive protein.<sup>26,27</sup> These markers have also been associated with the presence of delirium and cognitive dysfunction and are measured more

frequently in elderly and frail patients.<sup>28,29</sup> Leung found a relation between delirium and frailty in elderly patients during the early postoperative period.<sup>30</sup> The incidence of frailty increases with age, and frailty and age have been found to be independent factors associated with postoperative complications.<sup>31</sup> In the population of elderly surgical patients, a significant incidence is found in 41.8–50.3% of cases, highlighting the vulnerability of this population during surgery.<sup>32</sup> For Colombia, there is no accurate figure of the percentage of frail patients taken to surgery. Curcio, in a study conducted in a rural population over 60 years of age, found 15.2% of frail patients, a figure that is quite similar to that found in other studies conducted in Latin America.<sup>33</sup>

Management of frail patients requires the integration of the entire treating team as well as institutional preparedness, including includes information and training on the implications and risks of this syndrome.<sup>34</sup>

### Effects of anaesthesia

A relationship has been found between anaesthetics, surgery and cognitive dysfunction in several *in vitro* and animal studies that have shown effects on neuronal development. It has been found that volatile and intravenous agents used for general anaesthesia appear to have a negative effect on neuronal structures, such as altered axonal growth and formation of neuronal networks, deranged axonal growth, apoptosis, telomere abnormalities, and alterations in critical areas for memory.<sup>35</sup>

The study on late postoperative cognitive dysfunction, ISPOCD1, concluded unequivocally that anaesthesia and surgery produce long-term cognitive decline in elderly patients and that the risk increases with age, although it was unable to explain the pathophysiological causes and the anaesthetic or surgical events that may trigger this complication.<sup>16</sup>

In a review on anaesthesia and neurotoxicity, Lin et al. did not find an age of greater susceptibility to the deleterious neurological effects of anaesthesia, although they did find that the most affected neuronal groups change as age increases.<sup>36</sup> In a study that assessed the effects of desflurane on cognitive performance in rats, Callaway et al. found alterations in memory and in the ability to learn, and observed that those alterations were age- and dose-dependent and manifested in adult rats but not so in young individuals.<sup>37</sup>

On the other hand, a relationship has been found between general anaesthesia administration and Alzheimer's disease. There are two histopathological markers in this disease, namely the extracellular amyloid plaques consisting of the beta amyloid peptide, and neurofibrillary interneuronal tangles made of an aberrant hyperphosphorylated Tau protein. Studies have shown that anaesthesia plays an important role in accelerating the pathogenesis of the Tau protein, which is influenced by hypothermia. Although this is not the definitive factor for the presentation of the aberrant form – equally demonstrated in normothermia – it does produce a marked increase in protein hyperphosphorylation. Although the relationship between hypothermia, increase in aberrant Tau protein and postoperative cognitive dysfunction is not

clear, studies in mice have found memory disorders in animals exposed to hypothermia and general anaesthesia.<sup>38</sup>

## Regional anaesthesia

Several studies on the incidence of postoperative neurological complications in elderly patients have not found differences in terms of the percentage of occurrence or the use of regional or general anaesthesia. Some studies do not even show differences in cardiovascular complications, the use of the intensive care unit, or the overall costs of hospitalization in elderly patients with the use of one or the other type of anaesthesia.<sup>39,40</sup>

In a meta-analysis of 18 randomized studies on delirium and cognitive dysfunction, Bryson did not find significant differences between the use of regional or general anaesthesia, underlining the difficulty of preventing these two events because of the challenge of managing some of the patient-related risk factors.<sup>41</sup>

White, in an observational study of 65,535 patients, did not find any differences in mortality in patients taken to surgery for hip fracture repair under regional or general anaesthesia, and the only difference in outcome was increased mortality within the first 24 h associated with the use of cemented prostheses.<sup>42</sup>

In analysing the physiological effects of regional anaesthesia, particularly in elderly patients, it may be that the effect is more severe because of depleted compensatory mechanisms as a result of chronic illnesses like hypertension, atherosclerosis, coronary heart disease, cardiac hypertrophy or dilatation, reduced ejection fraction, besides the physiological changes associated with age *per se*.<sup>7,43,44</sup>

There is also the dose-effect relationship of medications in the central or peripheral nervous system as a result of the deterioration of myelin bridges and reduced amount of cerebrospinal fluid.<sup>45</sup>

## Intraoperative neurological monitoring devices

Devices for measuring the depth of anaesthesia have been developed over the past few years. Based on the measurement of electroencephalographic changes, they include the bispectral index monitor, the entropy module and the narcotrend monitors, which apply Fourier's theorem to transform the electroencephalographic signal into an interpretable numerical readout. Although studies are still needed to confirm some of the advantages attributed to these devices,<sup>46</sup> there is evidence already of the benefits of their use, particularly in patients with neurological or vital risk, as is the case with elderly patients.

From the anaesthetic perspective, these devices allow for a tighter control of the effects of anaesthesia on the brain, as they allow observation of signals that appear to be related with patient outcomes.

Sessler showed an increase in mortality and length of stay in patients with bispectral index values (BIS) under 45, low anaesthetic concentration, low mean alveolar concentration (MAC) and low arterial pressure.<sup>47</sup> In an earlier study, Monk

had already shown an increase in mortality one year following the surgery, finding a correlation between comorbidities, and low BIS and intraoperative blood pressure values.<sup>48</sup> The association between mortality and low BIS values could be secondary to an intrinsic patient sensitivity to the anaesthetic agents, where an "overdose" may occur without adequate dose measurement in the brain, increasing postoperative complications and short-term mortality.<sup>49</sup> BIS monitoring to avoid values under 40 for more than 5 min could be useful for patient management.<sup>50</sup>

Using near-infrared spectroscopy (NIRS), the brain oximeter measures light-wave absorption and release at a specific frequency with a venous/arterial proportion of 70% and 30%, respectively, to determine the content of oxygenated haemoglobin.<sup>51</sup>

Oximetry values are relative as they depend on the patient's basal state, and have to be individualized for each case.

Cerebral oximetry helps recognize the basal level of brain oxygenation and identify changes in brain perfusion resulting from changes in arterial pressure and oxygenation during surgery, thus optimizing potential sources of neurological risk.<sup>52</sup> Hoppenstein analyzed the changes in regional blood flow measured with cerebral oximetry during anaesthesia in patients with femoral neck fractures randomized to general or spinal anaesthesia, and found that desaturation percentages were higher in patients who received spinal anaesthesia compared to those who received general anaesthesia. The author concludes that the observation may depend on the patient's prior pathophysiological state and the ability to respond to changes in regional blood flow.<sup>53</sup> In a study in patients under general anaesthesia, Burkhart observed a lower autoregulation capability in elderly patients compared to younger patients, using cerebral oximetry values as markers of autoregulation effectiveness.<sup>54</sup> In geriatric patients taken to surgery under general anaesthesia for hip fracture repair, Papadopoulos observed a relationship between brain desaturation and increased postoperative cognitive dysfunction.<sup>55</sup> Casati also found a relationship between cerebral desaturation and postoperative cognitive disorders, and also prolonged length of stay.<sup>56</sup> The effect of cerebral desaturation as a measurement of brain autoregulation may influence outcome, reflecting integrated information regarding oxygen supply and consumption in the brain; cerebral oximetry is a promising technology considering that it monitors essential and relevant physiology.<sup>57</sup>

## Conclusions

Elderly patients require a different approach based on the understanding of the physiological, anatomical, social and vital differences that occur with old age, in order to offer better therapeutic options that are sometimes far from science and closer to the form of vital support derived from listening and understanding.

The adequate treatment of elderly patients leads to the reduction of complications that usually result in higher overall costs for the health system and for society.

Programmes focused on elderly patient care, supported by social programmes that promote maintenance of a healthy

and functional life, should be set up at least in high complexity centres.

### Conflict of interest

The author has worked as speaker and consultant for Medtronic.

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The author's own resources.

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