The effect of general anesthesia on geriatric patients’ cognitive function
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Objective
The objective of this study was to review how these effects of general anesthesia affect geriatric patients’ cognitive function and the precautions taken by anesthesiologists to reduce these effects.

Data analysis
A systematic search of MEDLINE (PubMed, Medscape, Science Direct, Journal of Clinical Anesthesia, ASA Publications, The Open Anesthesia Journal) and also of the materials available on the internet was carried out. The search was performed in the electronic databases in the English language only from 2003 to 2019.

Study selection
The initial search presented 150 articles of which 40 met the inclusion criteria. The articles studied the effect of general anesthesia on geriatric patients’ cognitive function.

Data extraction
Articles not reporting on the effect of general anesthesia on geriatric patients’ cognitive function in the title or abstract were not included. Four independent investigators extracted data on methods, health outcomes and traditional protocol.

Data synthesis
Data were synthesized qualitatively, and we did not perform a quantitative data analysis.

Findings
Multiple studies have found that postoperative cognitive disorders including delirium and postoperative cognitive dysfunction are common postanesthesia complications in elderly patients.

Conclusion
As the population ages, the number of geriatric patients undergoing surgery is increasing and, with it, the prevalence of postoperative cognitive disorders. Postoperative cognitive disorders including delirium and postoperative cognitive dysfunction are common postanesthesia complications in elderly patients. Several risk factors for postoperative disorders have been identified, and anesthesiologists usually adapt their practice habits when taking care of elderly patients to try to reduce the effects of the anesthetics on postoperative cognitive functions.

Keywords:
general anesthesia, geriatric patient, postoperative cognitive dysfunction

Introduction
Every day, around the world, lots of patients receive general anesthesia to safely undergo surgical procedures. A high fraction of the patients receiving general anesthesia are elderly, 65 years of age, or older. There are two main different entities of postoperative cognitive disorders that occur in the elderly following general anesthesia and sedation: postoperative cognitive dysfunction (POCD), and delirium [1]. Delirium is an acute change in cognitive function that develops over a brief period of time, often lasting for a few days to a few weeks, having a fluctuating course. It is characterized by inattention, and disorganized thinking and/or altered level of consciousness, while POCD is a persistent cognitive disorder that lasts from a few days to several months. It can range from the simple problem of fact-finding and memory impairment to dementia and Alzheimer-like symptoms. Because the subtler forms of POCD may go undetected without formal neuropsychological testing, the prevalence of this disorder may be greater than currently appreciated [2]. Risk factors for postoperative cognitive disorders include advanced age; pre-existing cerebral, cardiac, or vascular disease; preoperative mild cognitive impairment; low educational level; history of alcohol abuse; marked disturbance of homeostasis; infection; malnutrition; electrolyte imbalance;
dehydration; severe pain and inadequate analgesia; and organ ischemia due to hypoxia or hypoperfusion [3]. Anesthesiologists are well aware that the anesthetic management of older patients requires different approaches from the management of younger patients. The doses of anesthetics required to achieve the same level of general anesthesia in the elderly can range from 10 to 50% less than that required for younger patients [4]. An increase in heart rate and a decrease in blood pressure are more likely with older patients following induction of general anesthesia by bolus administration of a hypnotic, and measures are routinely taken to prevent the untoward consequences of these expected changes [5]. Although the primary sites of intended anesthetic actions are in the brain and central nervous system, less attention has been paid to the brain and how its normal aging may affect the anesthetic requirements of elderly patients. Hence, monitoring anesthetic depth with depth of general anesthesia monitors such as bispectral index (BIS), patient state index, and Narcotrend monitor, which analyzes stages and substages of anesthesia, is important in elderly patients. Therefore, the aim of this work was to review how the effects of general anesthesia affect geriatric patients’ cognitive function and the precautions taken by anesthesiologists to reduce these effects.

Materials and Methods

Data sources
We reviewed papers on the effect of general anesthesia on geriatric patients in several databases such as PubMed, Medscape, and Science Direct, and also International Journal of Anesthetics and Anesthesiology and all materials available on the internet published from 2003 to 2019. We used general anesthesia/geriatric patient/POCD as search terms. In addition, we examined reference lists in relevant publications.

Study selection
All the studies were independently assessed for inclusion. They were included if they fulfilled the following criteria:
(1) Published in the English language
(2) Published in peer-reviewed journals
(3) Discussed the clinical management of general anesthesia in geriatric patients
(4) If a study had several publications on certain aspects, we used the latest publication giving the most relevant data.

Data extraction
If the articles did not fulfill the above criteria, they were excluded. Surveys about symptoms and health without exposure assessment, report without peer-review, not within the national research program, letters/comments/editorials/news and studies not focused on effects of general anesthesia on geriatric patients’ cognitive function were excluded.

The analyzed publications were evaluated according to evidence-based medicine criteria using the classification of the US Preventive Services Task Force and UK National Health Service protocol for evidence-based medicine in addition to the Evidence Pyramid [6].

US Preventive Services Task Force [5] were as follows:
(1) Level I: evidence obtained from at least one properly designed randomized-controlled trial
(2) Level II-1: evidence obtained from well-designed controlled trials without randomization
(3) Level II-2: evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group
(4) Level II-3: evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.

Level III: opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Study quality assessment
The quality of all the studies was assessed. Important factors included study design, ethical approval, calculation of evidence power, specified eligibility criteria, appropriate controls, and adequate information and specified assessment measures. It was expected that confounding factors would be reported and controlled for and appropriate data analysis made in addition to an explanation of missing data.

Data synthesis
Data were synthesized qualitatively, and we did not perform a quantitative data analysis. This work lasted from December 2018 to October 2019.

Results

Study selection and characteristics
In total, 150 potentially relevant publications were identified, and 110 articles were excluded, as they did not fulfill our inclusion criteria. A total of 40 studies were included in the review, as they met the inclusion criteria. Most of the studies examined the effects of general anesthesia on elderly patients and focused on postoperative conative function. With regard
to these studies, the observed incidence of postoperative delirium (POD) ranges from 10 to 45%, which increases with age and surgery complexity/risk, and POCD was reported to affect 26% patients over 60 years of age in the first postoperative week, and the incidence falls to 10% in the following 3 months. However, clinical evidence attributing POCD to surgery and anesthesia exposure is inconclusive, as a long-term follow-up study found only 1% of elderly patients suffering from persistent POCD 1–2 years onwards, with preoperative cognitive performance (e.g., mild cognitive decline, possible/probable Alzheimer’s disease) being a better predictor of postoperative cognitive trajectory (Table 1).

Discussion

Anesthesia for the elderly has to take into account the specific physiology of the aging that develops naturally during the course of life. Therefore, all physiological changes of aging should not be considered as pathological issues, because they may be completely compensated for in normal life, and their potentially pathological character is revealed only in extreme conditions. To adjust anesthetic management for old patients with regard to individual pathological and physiological changes related to aging, it is necessary to examine patients with regard to the specific organ systems that are of special relevance for the anesthetist and may directly change the individual anesthetic approach to care safely for the old patients [12]. The elderly population may present conditions known as factors of increased surgical risk, such as polypathology, polymedication, and disorders at the cellular level. Moreover, progress in medical sciences in recent years has helped a large number of elderly patients to survive illnesses. These improvements have consistently increased the number of vulnerable and frail patients presenting for surgery and have caused debates about surgical decisions in many cases. Although many surgical procedures can enhance the quality and duration of life, even in the very old patients, the balance between the expected benefits and the risks (such as cardiac complications, cognitive disorders, or infection) determining undesirable outcomes remains a key issue [8]. Preoperative consultations should occur several days before surgery to allow further investigations if needed. A full history and clinical assessment is required, especially for older and more compromised patients. Clear medical information about the surgical plan is essential. The collection of clinical history may be difficult due to patient sensorial impairment or cognitive deterioration. The presence of a relative or caregiver may be helpful in these cases. Laboratory investigation is indicated by related conditions and the surgical procedure involved; age by itself does not justify extensive testing [7]. Generally, old patients are more sensitive to anesthetic exposure to anesthesia to the aged brain can be a risk of the long-lasting impairments in neuronal communication and faulty formation of neuronal circuitries. Neuroapoptosis, whereby an early exposure to anesthesia causes long-lasting consequences.

Table 1 General anesthesia and cognitive function of elderly patients

<table>
<thead>
<tr>
<th>References</th>
<th>Type</th>
<th>Level of EBM</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marcantonio et al. [1]</td>
<td>Case analysis</td>
<td>Comes in the second level with regard to the pyramid of EBM</td>
<td>Delirium (acute confusion) complicates 15-50% of major operations in older adults and is associated with other major postoperative complications, prolonged length of stay, poor functional recovery, institutionalization, dementia, and death</td>
</tr>
<tr>
<td>Monk et al. [2]</td>
<td>Randomized case-control study</td>
<td>Level I or (level A)</td>
<td>Cognitive dysfunction is common in adult patients of all ages at hospital discharge after major noncardiac surgery, but only the elderly (aged 60 years or older) are at significant risk for long-term cognitive problems. Patients with POCD are at an increased risk of death in the first year after surgery</td>
</tr>
<tr>
<td>Zambouri [7]</td>
<td>Case analysis</td>
<td>Comes in the second level with regard to the pyramid of EBM</td>
<td>The preoperative preparation involves procedures that are implemented on the basis of the nature of the expected operation and the findings of the diagnostic workup and the preoperative evaluation</td>
</tr>
<tr>
<td>Yang et al. [8]</td>
<td>A prospective study</td>
<td>Level II-2 or (level B)</td>
<td>Geriatric surgery has become more frequent and requires careful tailoring of the anesthesia technique. The aging process produces physiological, anatomical, and cognitive changes within the major organ systems of the body. Such changes have a significant impact on perioperative outcomes</td>
</tr>
<tr>
<td>Steiner LA [9]</td>
<td>Case analysis</td>
<td>Comes in the second level regarding the pyramid of EBM</td>
<td>As the population ages, frailty will be increasingly seen in surgical patients receiving anesthesia. This study evaluated the instruments that have been developed and validated for measuring frailty in surgical patients and summarizes frailty tools used in 110 studies linking frailty status with adverse outcomes after surgery</td>
</tr>
<tr>
<td>Wu et al. [10]</td>
<td>Randomized case-control study</td>
<td>Level I or (level A)</td>
<td>The developing and aging brain may be vulnerable to anesthesia. An important mechanism for anesthesia-induced developmental neurotoxicity is widespread neuroapoptosis, whereby an early exposure to anesthesia causes long-lasting impairments in neuronal communication and faulty formation of neuronal circuitries. Exposure to anesthesia to the aged brain can be a risk of the long-lasting impairments of cognitive function</td>
</tr>
<tr>
<td>Torrance et al. [11]</td>
<td>Randomized case-control study</td>
<td>Level I or (level A)</td>
<td>For many years, evidence has shown that elderly patients have poorer outcomes and there are specific strategies that hospitals and teams can develop to improve the care received by this vulnerable group. Clinicians need awareness of factors contributing to poor outcome in elderly patients and tools to aid accurate and timely identification and correction of some of these factors to drive up standards</td>
</tr>
</tbody>
</table>

EBM, evidence-based medicine; POCD, postoperative cognitive dysfunction.
drugs. Much lower doses of anesthetic medications are usually required to achieve a desired clinical effect, and the drug effect is often prolonged. Most evidence suggests little difference in outcome between general and regional anesthesia in elderly patients. These results have been reported in many types of surgery, including major vascular and orthopedic procedures [10]. During maintenance of anesthesia, the anesthesiologist should closely monitor these old frail patients with respect to a tight, balanced anesthetic management plan as follows: patients should be properly positioned to avoid nerve injuries and pressure manifestations, and avoid premedication with anticholinergic drugs due to their sedative side effects leading to delayed recovery, urinary retention and increase incidence of postoperative cognitive decline, especially delirium. Close monitoring of vitals, hemodynamics and cardiac output is necessary, as these elderly patients are prone to hemodynamic instability from the hypotensive effects of most of the anesthetic agents, to be able to tailor a tight fluid balance [13]. The depth of anesthesia monitoring by the BIS, patient state index, and Narcotrend monitor would be very beneficial to adjust the dose of anesthetic agents and avoid the deleterious effects of awareness, ranging from hypertension to intraoperative myocardial infarction and cerebrovascular accidents; moreover, monitoring cerebral oxygen saturation by intraoperative near-infrared spectroscopy is very important to improve postoperative cognitive outcomes [14]. Skeletal muscle power monitoring is pertinent to the anesthetic management plan, especially in geriatric anesthesia, due to the decreased pharmacokinetic reserve of the frail patients, which increases the incidence of delayed recovery and recurarization, which is why long-acting nondepolarizing muscle relaxants such as pancuronium should be avoided [15]. Geriatric surgical patients are very susceptible to hypothermia; hence, temperature monitoring and warming the patients is very important, as hypothermia leads to acidosis, delaying recovery even further [16]. Balanced anesthesia should be tailored according to the patients’ general condition and functional status rather than age. Elderly patients tend to have limited neck extension, small mouth opening and are usually edentulous; therefore, anesthetists should always keep difficult intubation in mind [17]. On emergence from anesthesia, all patients should be extubated after full return of muscle power, fully monitored in a well-equipped postanesthetic care unit with available mechanical ventilation. One should assess muscle power, consciousness level, hemodynamics, and pain levels. This helps avoid the usual complications of the immediate postoperative period, including aspiration, desaturation, agitation, emergence delirium and recurarization [18]. Analgesics and antiemetics can be administered to treat postoperative pain and postoperative nausea and vomiting. However, it is best to decrease the doses of opioid analgesics to half the normal adult doses [19]. Elderly patients have a higher rate of postoperative complications. In contrast, younger patients had complication rates that were much less than that found in geriatric patients. Geriatric patients are similar to other patients in terms of the ‘typical’ postoperative complications that can occur with an operation, such as bleeding, infection, or technical errors. However, elderly patients are at risk for a group of unique complications owing to the physiologic changes of aging and the stress of the perioperative period; on top of the list comes the postoperative cognitive impairment in the form of delirium acutely and the delayed POCD, cardiovascular complications, acute renal failure, and the postoperative pulmonary complications, namely aspiration pneumonia [11]. Prevention of POD and POCD is directed toward the correction of contributing factors, such as reducing the use of opioids, benzodiazepines, dihydropyridines, and histamine H1-receptor antagonists in elderly patients. The multifactorial etiology of POD and POCD seems amenable to improvement by using multidomain interventions, including BIS-guided depth of anesthesia monitoring combined with cerebral oxygen saturation monitoring [9]. Pharmacological intervention is rarely of benefit in treating POD/POCD. Haloperidol can be used in cases of severe agitation, and it may decrease the incidence of delirium. Perioperative dexmedetomidine infusion may be useful in reducing the prevalence of POD if patients require intensive care postoperatively [9]. Because of the increased incidence of postoperative complications, these patients require postoperative care by trained clinicians and specialized geriatric nurses, as all these complications have atypical presentations in the frail elderly. Furthermore, early detection of such complications is very crucial to the management plan to decrease morbidity, health care cost, and hospital length of stay, to enhance rapid recovery and return to normal activities of daily living, and to decrease the need for help, dependence, and need for institutionalization, hospitalization, and mortality [20].

**Conclusion**

As the population ages, the number of geriatric patients undergoing surgery is increasing and with it the prevalence of postoperative cognitive disorders. Postoperative cognitive disorders including delirium and POCD are the common postanesthesia complications in elderly patients. Several risk factors for postoperative disorders have been identified, and anesthesiologists usually adapt their practice habits when taking care of elderly patients to try to reduce the effects of the anesthetics on postoperative cognitive...
functions. These practices are acceptable; yet, they are not well supported by an understanding of the aging of the brain and the specifics of how the effects of the anesthetic on the brain change with age. Through electrophysiological studies and functional imaging, much is being learned about the neurophysiology and the neuroanatomical changes of normal aging.

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**Conflicts of interest**
There are no conflicts of interest.

**References**