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Anesthetic management of geriatric patients

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NOTES

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Abstract

The number of elderly patients who frequently access health care services is increasing worldwide as well as in Korea. Anesthesiologists are developing the expertise to care for these elderly patients. In this review, we considered concerns when anesthetizing elderly patients. A comprehensive search of major international databases (PubMed, Embase, and Cochrane) and Korean databases (KoreaMed) was conducted. The search was organized and documents were divided conceptually into three domains: preoperative considerations, intraoperative management, and postoperative problems. Preoperative preparation of elderly patients included preoperative functional assessment and immediate preoperative problems, such as cognitive impairment, cardiopulmonary evaluation, depression, frailty, nutrition, polypharmacy, and anticoagulation. Intraoperative management included anesthetic mode and pharmacology, monitoring, intravenous fluid or transfusion management, lung-protective ventilation, and prevention of hypothermia. Postoperative checklists included perioperative analgesia, postoperative delirium, postoperative cognitive dysfunction, and postoperative complication. Older surgical patients require a different level of perioperative care than younger patients because they have multiple chronic diseases and, therefore, are prone to developing postoperative complications, functional decline, loss of independence and other unwanted outcomes. Although the evidence-based perioperative care for elderly patients remains poor so far, to minimize unwanted outcomes after surgery, elderly patients have to be provided optimal perioperative care through close interdisciplinary, interprofessional, and cross-sectional collaboration. Along with adequate anesthetic care, well-planned postoperative care for the elderly should begin in the immediate postoperative period and should extend to discharge transition.

Keywords: Aged; Anesthesia; Frail elderly; Geriatrics; Perioperative care.
Introduction

The WHO’s ‘World Report on Aging and Health’ revealed significant impairments in the elderly population in Europe, and the number of elderly people will double by 2050 [1]. As the population of a country continues to age, the demands for surgical services increases. Elderly patients often require a different level of care than younger patients during the perioperative period. The health care costs of elderly patients are different from younger patients. Strategies should be developed to meet this growing demand, and national strategies should also be developed to meet with the demands for the increasing medical services required by the elderly. As the number of elderly surgical patients expands, optimal anesthesia care to reduce complications and to improve outcomes will be of great value to the individual patients and to the society involved.

This article reviews the perianesthetic considerations for geriatric patients and conceptually divides these considerations into three parts: preoperative considerations, intraoperative management, and postoperative problems. A framework on which the complex issues related to perioperative care of elderly patients will be established.

The authors performed a comprehensive literature review based on major international databases (PubMed, Embase, Cochrane) and Korean databases (KoreaMed) to identify systemic reviews, meta-analyses, practice guidelines, and clinical trials published in the last 10 years (see Appendix 1). The initial search resulted in 1,551 citations and an additional 15 articles were obtained from manual searches of materials that referenced related articles to the initial results. The authors then selected 262 publications for the purposes of review. The authors further narrowed the citations based on strength of evidence, relevance to geriatric patients, and directly related to the perioperative period. The final items included had a total of 172 selected citations.
Preoperative Management

Assessment of functional reserve

Comprehensive geriatric assessment (CGA) in the preoperative period included systemic evaluation of comorbidities, functional status, neurocognitive function, sensory impairment, substance abuse, frailty, nutrition, and medication. Preoperative CGA has a positive impact on postoperative outcomes in older patients undergoing elective surgery [2]. A recent Cochrane review that including 1,583 hip fracture surgeries in subjects ≥ 65 years showed that CGA probably reduces mortality (risk ratio [RR] 0.85, 95% confidence interval [CI] 0.68-1.05) and reduces discharge to an increased level of care (RR 0.71, 95% CI 0.55-0.92) [2]. However, other study argued that CGA may make little or no difference for major postoperative complications and delirium rates [3]. Considering these points, physicians must advocate for their patients to receive all the appropriate preoperative evaluations and interventions to improve patient’s reserved function to ensure that elderly patients can make decision by themselves [4,5]. In this sense, it has been shown that anesthesiologists are strongly encouraged to become involved in national audit projects and outcomes research specifically involving elderly surgical patients [6].

For the estimation of functional status, all patients should be assessed for their ability to perform daily activities (functional status). A short and simple screening test for assessing current baseline functional status in ambulatory patients should be applied first. Then, a more in depth evaluation such as full screening of activities of daily living (ADL) and instrumental ADL should be applied [7,8]. The patient should be evaluated for limitations in gait and mobility using the Time Up and Go (TUG) test [9,10]. Any functional limitation that may require perioperative interventions should be documented. A 2018 prospective cohort study of 131 patients ≥ 65 years old and undergoing elective major surgery for cancer showed that the mortality after 1 year was 28.2%. Patients who were dependent on ADLs and had an impaired TUG test had a significantly higher 1-year mortality (odds
ratio (OR 4.5, 95% CI 1.21-18.25, P = 0.034). As such, functional assessment such as ADL and TUG test as well as mild cognitive impairment are predictors of long-term outcomes in elderly cancer patients [11]. A 2005 prospective study of 120 patients ≥ 60 years old and who underwent thoracic surgery also showed the dependence of ADLs and impaired cognitive conditions as important predictors of postoperative complications [12].

Common diseases of older adults may proceed with aging. Age-associated organ reserve decline, compounded by chronic diseases, has led to high incidence of postoperative complications in the elderly patient. Many types of postoperative complications are neurologic, pulmonary, cardiac, and renal comorbidities. Since definitive studies on the effectiveness of various components of the CGA are lacking, more investigations are needed to derive reliable conclusions. Several of these papers suggest that, first of all, in 2018 meta-analysis showed that comorbidity (Charlson comorbidity Index ≥ 3), polypharmacy (≥ 5 drugs/day), and ADL dependency were predictive factors for postoperative complications in gastrointestinal cancer patients [13,14]. More independent preoperative functional status strongly predicts both better postoperative function and shorter recovery periods after a major abdominal surgery [15]. Using the one million longitudinal health insurance database in Taiwan, another 2017 retrospective study of patients ≥ 65 years old who received anesthesia showed that the leading comorbidity contributing to the postoperative mortality in elderly patients is chronic renal failure (OR = 2.806), acute myocardial infarction (OR = 4.58), and intracranial hemorrhage (OR = 3.758) [16].

Recently published collaborative guidelines from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) and the American Geriatrics Society (AGS) proposed a formal framework for routine multidomain preoperative assessment of geriatric patients. The AGS can also be seen working together to develop the best practices guidelines around optimal perioperative care of the geriatric surgical patient [17,18]. One component of this collaboration
concept is preoperative preparation of patient (prehabilitation), which is best initiated before hospital admission, e.g. correction of deficiency states, optimization of chronic drug treatment, and respiratory training [19].

**Neurocognitive and behavioral assessment**

Dementia is common in elderly people ≥ 65 years old, with a prevalence of 5% to 8%. For individuals over 85 years of age, more than one third may have dementia [20]. As the number of geriatric population grows, the number of people living with dementia is projected to rise dramatically [21]. A 2018 meta-analysis study showed that the mortality of patients with dementia who suffered from a hip fracture was 12%, 32%, 39%, and 45%. Also, dementia increased mortality in patients who underwent a hip fracture surgery by 1.57, 1.97, 1.77, and 1.60-fold after a 30-day, 6-month, 1-year, and > 1-year follow up, respectively [22]. A 2014 retrospective cohort study included a total of 45,602 aged patients who had hip fractures and showed that dementia was associated with an increased risk of long term care admission (hazard ratio [HR] 2.49, 95% CI 2.38-2.61, P < 0.001), higher mortality from community (HR 1.47, 95% CI 1.41-1.52, P < 0.001), and poor prognosis [23]. These large-scale analyses suggest that older people with dementia not only increase their post-op mortality but also increase non-operative mortality.

The recent ACS NSQUIP-AGS Guidelines for Optimal Preoperative Assessment of the Geriatric Patient include a routine preoperative neurocognitive assessment to detect deficits before surgery. Preoperative detection is critical for diagnosing new postoperative deficits and anticipating postoperative complications such as postoperative delirium (POD) and postoperative cognitive dysfunction (POCD). Therefore, a preoperative evaluation of cognitive function is essential. For patients without a known history of cognitive impairment, “Mini-Cog” [24] is recommended. The Mini-Cog Assessment is a short, easily applicable, and well-studied tool. Careful documentation of
the patient’s preoperative cognitive status is important because postoperative cognitive dysfunction is common but difficult to quantify without any record of preoperative status. Preexisting cognitive impairment predicts postoperative delirium [25,26]. Postoperative cognitive impairment is associated with longer hospital stay, increased mortality and functional decline. Because explanations may be that patients with impaired cognition were less likely to engage in postoperative aggressive pulmonary toilet and ambulation, causing a high risk of developing postoperative complications such as pneumonia, deep vein thrombosis, stroke and cerebrovascular accident with neurologic deficit.

**Cardiac evaluation**

A reduction in the responsiveness of beta-receptors caused by a beta-blocked state limits the ability to increase cardiac output and to properly respond to blood losses. Baroreceptor dysfunction and reduced responsiveness to angiotensin II further limit the responsiveness to hypovolemia. These factors may be compounded by comorbid myocardial ischemia related to atherosclerosis. Diminished cardiac reserve in many elderly patients may be manifested as exaggerated drops in blood pressure during induction of general anesthesia.

Asking patients about metabolic equivalents (METS) as they related to daily activities is a useful way to assess exercise tolerance of those who may not participate in conventional forms of regular exercise. Geriatric patients should undergo cardiac risk stratification, should have indicated cardiac tests performed, and should have evidence-based optimization strategies applied before surgery [27]. The web-based NSQUIP Risk Calculator is one of the estimating tools recommended by the 2014 American college of Cardiology/ American Heart Association Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery [27]. However, there are still critical gaps in knowledge of informed evidence-based decision making and recommendations targeting older patients. So a 2016 study recommended a critical need for a
multitude of large population-based studies including a broad spectrum of older patients [28]. In a 2002 prospective study of 513 patients ≥ 70 years old undergoing non-cardiac surgery showed that abnormalities on preoperative electrocardiograms (ECGs) are common but are of limited value in predicting postoperative cardiac complications [29]. Because ECG abnormalities in older people are prevalent but nonspecific and less useful than the presence and severity of comorbidities in predicting postoperative cardiac complications. On the other hand, echocardiography can help provide insight into ventricular function and status of valves and should be considered in patients with significant cardiac comorbidities such as history of myocardial infarction (MI), congestive heart failure (CHF), or valvular heart disease.

Older patients are more vulnerable to perioperative cardiac adverse events. In a 2018 retrospective study of 8,441 adult patients who underwent general and vascular surgeries showed that the underlying predictors of cardiac events after surgery included age > 65 years (OR 4.9, 95% CI 3.4-6.9, P < 0.01) [30]. In addition, a 2017 study showed one-year mortality in elderly patients undergoing hip fracture repair to be significantly higher in patients with postoperative atrial fibrillation (AF) and this association did not appear to be attenuated by medical treatment of the AF with anti-arrhythmic therapy [31]. The anesthesia-related cardiac arrest rate is a quality indicator to improve patient safety in the perioperative period. A 2017 systemic review showed that perioperative and anesthesia-related cardiac arrest rates only decreased with a high country’s Human Development Index (HDI) before 1990s or between 1990-2017, and perioperative cardiac arrest between 1990-2017 was 4-fold higher with low-HDI when compared with high-HDI in geriatric patients [32]. Therefore, there is a clear and consistent reduction in anesthesia-related and perioperative cardiac arrest rates in high HDI countries, but not in low HDI countries. Another 2014 study showed that the large majority of cardiac arrests in older patients were caused by factors not anesthesia-related. The major predictors of intraoperative cardiac arrests were poorer physical status based on the American Society of Anesthesiologists (ASA)
and emergency surgery. All anesthesia-related cardiac arrests were medication-related or airway-related, so the preventive strategies for at least these two concerns is important [33].

**Pulmonary evaluation**

Pulmonary function declines with age due to loss of both lung and chest wall compliance, and oxygen diffusion capacity. Also, this decline is more profound in smokers. Age related decline in oxygen capacity and pulmonary changes contribute to decline in both oxygen uptake and oxygen delivery. Age and functional dependence have been identified as the most reliable risk factors for postoperative pulmonary complications (PPC). A 2006 systemic review showed that patient-related risk factors for PPC included advanced age, ASA class 2 or higher, functional dependence, chronic obstructive pulmonary disease, and congestive heart failure. In patients undergoing noncardiac surgery, the rates of PPC are 14% and 15% for ages ≥ 65 years and ≥ 70 years, respectively [34]. A 2017 prospective study for PPC, which included 1,202 patients showed that significant PPC risk factors such as, emergency (OR 4.47, 95% CI 1.59-12.56), surgical site (OR 2.54, 95% CI 1.67-3.89), and age (OR 1.03, 95% CI, 1.02-1.05) were nonmodifiable [35]. In addition, a 2003 prospective study of 517 patients ≥ 70 years old and undergoing noncardiac surgery showed that 31.7% of patients were died from renal complications (HR 6.07, 95% CI 2.23-16.52, P < 0.001), cancer (HR 2.44, 95% CI 1.78-3.38, P < 0.001), and pulmonary complications (HR 2.41, 95% CI 1.30-4.48, P = 0.005). These studies showed that pulmonary complications were an independent predictor of mortality in elderly patients [36].

**Depression**

Senility alone is a high risk factor for depression, and the preoperative psychological burden that patients likely suffer may complicate the situation. ACS NSQUIP-AGS Guidelines strongly
recommend preoperative depression and substance abuse screening using a simple questionnaire [37]. More than 10% of elderly people have depressive symptoms significant enough to warrant clinical intervention [38]. A 2018 prospective cohort study of 1,035 individuals ≥ 70 years old and who underwent transcatheter or surgical aortic valve replacement surgery showed that baseline depression (31.5% of patients screened positive for depression) was found to be associated with mortality at 1 month (OR 2.20, 95% CI 1.18-4.10) and at 12 months (OR 1.532, 95% CI 1.03-2.24). Persistent depression defined as baseline depression that was still present 6 months after the procedure, was associated with a 3 fold increase in mortality at 12 months (OR 2.98, 95% CI 1.08-8.20) [39]. Therefore, active multi-disciplinary collaboration of these patients is needed perioperatively.

Frailty

Frailty is a syndrome of decreased physiologic reserve and resistance to stressors. It is a clinically distinct entity from comorbidity and disability. According to the cohort study (data from the Cardiovascular Health Study), in which 5,317 participants ≥ 65 years old were studied, the overall prevalence of frailty in this community was 6.9%, and it increased with age and was greater in women than men [40]. A prospectively measured of frailty in 594 patients (≥ 65 years old) summarized that preoperative frailty was associated with an increased risk for postoperative complications (intermediately frail: OR 2.06; 95% CI 1.18-3.60; frail: OR 2.54; 95% CI 1.12-5.77), length of stay (intermediately frail: incidence rate ratio 1.49; 95% CI 1.24-1.80; frail: incidence rate ratio 1.69; 95% CI 1.28-2.23), and discharge to a skilled or assisted-living facility after previously living at home (intermediately frail: OR 3.16; 95% CI 1.0-9.99; frail: OR 20.48; 95% CI 5.54-75.68). Frailty has been shown to independently predict higher rates of postoperative complications in elderly patients [41]. In addition, a 2019 prospective cohort study of 326 geriatric patients (≥ 65 years old) who require emergency general surgery showed that a frail status independently contributed to failure to
rescue and increased the odds ratio of failure to rescue 3 times when compared with a nonfrail status [42]. A 2014 study included 275 elderly subjects \( \geq 65 \) years old showed that the multidimensional frailty score based on comprehensive geriatric assessment is more useful than conventional methods like the ASA classification (area under the receiver operating characteristic curve, 0.821 vs. 0.647, \( P = 0.01 \)) for predicting all-cause mortality rates in geriatric patients undergoing surgery [43]. According to a 2017 meta-analysis, sarcopenia and frailty seem to have significant adverse impacts on the occurrence of postoperative outcomes [44]. Another 2018 meta-analysis identified potentially modifiable prognostic factors (i.e., frailty, depressive symptoms, and smoking) associated with developing postoperative complications that can be targeted preoperatively to optimize care [45]. We think these results lend support to the opinion that intensive management of preoperative modifiable factors can prevent postoperative complications.

There is increasing evidence that preoperative frailty is associated with increased adverse outcomes after emergent or nonemergent surgeries in elderly patients. Although further studies are still needed in this field, frailty evaluation will be a useful preoperative risk-stratification tool in perioperative geriatrics [46]. With the help of geriatric specialists, not only they be able to make more extensive assessments and implementation of prior rehabilitation measures can be possible. Moreover, anesthesiologists should be aware of their role in patient preparation, maintaining or enhancing patient’s functional reserve to facilitate postoperative rehabilitation and discharge back into the society.

**Nutrition**

A 2015 meta-analysis showed that perioperative oral nutritional supplementation had a positive effect on the serum total protein and led to fewer complications, such as wound infection, respiratory infection, and urinary tract infection, but did not have a positive effect on postoperative mortality [47].
Another clinical trial study showed that perioperative taurine supplementation attenuated postoperative oxidative stress in elderly patients who sustained a hip fracture, but did not improve postoperative morbidity and mortality [48]. However, a 2016 review study which included 41 trials with a total of 3,881 participants showed that oral multinutrient supplements started before or soon after surgery may prevent complications within the first 12 months after a hip fracture, although no clear effects on mortality were seen [49].

Oral nutrition and supplementation counteract the effects of poor appetite and illness. Prolonged preoperative fasting should be avoided (except in cases with an intraabdominal pathology). Yeniay et al. [50] measured the preoperative fasting durations with respect to time of the day and its effect on vital parameters and electrocardiogram in elderly patients undergoing surgery under spinal anesthesia. They showed that the fasting times in their population were far longer than recommended and fasting prolonged over 15 hours was related to a transiently increased cardiac stress and mild hypothermia. Malnutrition is a frequent problem often overlooked in the surgical field.

However, there is still unsolved problem. A number of assessment tools exist to identify malnutrition in patients with colorectal cancer, but different tools have different diagnostic accuracies and lack a standardized method. Therefore, it was recommended that an accurate diagnostic test of nutritional tools based on evidence should be used to further determine the predictive value of nutritional status.

**Polypharmacy**

It was reported that geriatric patients are great consumers of medications (3.9 drugs/day for ages between 65-80 years, 4.4 drugs/day for ages > 80 years) and the most common prescription drugs are cardiovascular medications (65%), followed by those acting on the central nervous system. When compared with younger adults, older people are more likely to have impaired renal function, therefore,
it is critical to adjust dosages to prevent adverse effects. Polypharmacy is the term applied to describe patients taking multiple medications. It is said that the risk of adverse drug reactions increases with the number of drugs taken, leading to more hospital stays [51]. A 2016 analysis of 272 elderly patients with consecutive hip fracture showed that the total number of medications at the time of discharge was predictive of rehospitalization (OR 1.08, 95% CI 1.01-1.17, P = 0.030) but not predictive of mortality [52]. Also a 2018 meta-analysis showed that comorbidity (Charlson comorbidity Index ≥ 3) [13], polypharmacy (≥ 5 drugs/day) and ADL dependency were predictive factors for postoperative complications [14]. The ACS/AGS Best Practices guidelines for the Optimal Preoperative Assessment of the Geriatric Surgical Patients discuss the management of essential and nonessential medications before surgery [17,53]. They recommend that when possible, nonessential medications should be discontinued perioperatively and the addition of new medications should be kept to a minimum.

For patients at risk for postoperative delirium, it is agreed that new benzodiazepines [54] and meperidine should be avoided [55,56]. Antihistamine H1 antagonists and strong anticholinergic effective drugs should be cautiously prescribed [54,57]. According to the American College of Cardiology/American Heart Association (ACC/AHA) a guidelines for perioperative beta blockers, and initiation of statin therapy, beta blockers are indicated for the patients who are already on it or have an immediate risk for vascular surgery with known coronary artery disease [58-60]. They should be started at least days to weeks before elective surgery and titrated to a heart rate of 60 to 80 beats/minute in the absence of hypotension. Preoperative statin should be started as soon as possible before surgery for patients who have known vascular disease. For patients undergoing noncardiac surgery and who are currently taking statins, statins should be continued [60].

Cholinesterase inhibitors (e.g., galantamine, rivastigmine, donepezil), used to slow cognitive decline in older patients, was not associated with an increased risk of postoperative respiratory
complications among older patients (66 years or older) with dementia undergoing hip fracture surgery [61]. The cholinesterase inhibitors may interact with muscle relaxants, prolonging the actions of succinylcholine, and reversing the effects of non-depolarizing neuromuscular blocking agents, and leading to larger doses needed to achieve a proper degree of neuromuscular blockade [61,62].

**Anticoagulation therapy**

A 2016 population-based cohort study of 154,047 hip fracture patients showed that 33% of them used 1 or more antithrombotics on admission. Among the users of antithrombotics, there was a higher proportion of men and with a higher mean age [63]. In the majority of cases, perioperative bridging anticoagulation is no longer recommended when using novel oral anticoaguants and vitamin-K antagonists [64]. However, this recommendation does not apply to patients at high risk for thromboembolism. The use of anticoagulants in the elderly is essentially the same as in younger patients; however, the reduced renal function frequently seen in elderly patient requires consideration.

**Intraoperative Management**

**Anesthesia in elderly patient**

The elderly population is increasing as is the number of surgeries performed in this population. There are many analyses on perioperative outcomes of geriatric surgery. A 2019 meta-analysis showed that postoperative morbidity and mortality increased with age [65]. A 2018 meta-analysis showed that laparoscopic hepatectomy is a feasible and safe alternative to open hepatectomy in elderly patients because of the lower rates of morbidity and favorable postoperative recovery and outcomes [66]. Another 2018 meta-analysis showed that the outcomes of laparoscopic gastrectomy for elderly gastric cancer patients were comparable to those in nonelderly patients. A 2017 study showed that laparoscopic liver resection of colorectal liver metastases in subjects ≥ 70 years of age
is associated with a significant lower morbidity and a shorter stay with comparable oncological outcomes when compared with open liver resection even though the benefits of the laparoscopic approach appear to fade with increasing age [67]. Other recent retrospective studies of patients ≥ 80 years old who underwent transabdominal preperitoneal repair of groin hernia showed that the incidence of postoperative complication is influenced by poor performance status, lower hemoglobin level, and lower albumin level rather than old age [68]. Therefore, age alone should not preclude laparoscopic gastrectomy in elderly patients [69].

However, whether old age itself is the only criterion for determining the indications of surgery or not remains controversial. A 2017 meta-analysis that included 18 studies of pancreaticoduodenectomy in patients ≥ 80 years old showed a higher 30 day postoperative mortality rate (OR 1.51, 95% CI 1.48-3.31, P < 0.001) and length of hospital stay (OR 2.23, 95% CI 1.36-3.10, P < 0.001) in this group of patients when compared with younger patients. The overall postoperative complication rate was high (OR 1.51, 95% CI 1.25-1.83, P < 0.001) in aged patients [70]. Another recent prospective study including 165 patients who had pancreaticoduodenectomy showed that the 90-day mortality rate (5.9% in those ≥ 80 years old vs. 2% in the younger group, P = 0.335) and the postoperative complication rates (64.7% in the elderly vs. 62.8% in the younger group, P = 0.83) were similar, although the older patients were far more likely to be discharged to a rehabilitation facility than younger patients (47.1% vs. 12.8%, P < 0.001) [71]. Careful selection of elderly patients and optimal perioperative care, rather than age, should be used to determine whether surgical intervention is indicated in this age group. Therefore, the question arises as to whether surgery is actually associated with a definitely better outcome for the elderly patient when compared with conservative treatment. Ideally, individual parameters should be assessed at an interdisciplinary level and across all professional groups, thereby preventing a complication-prone, decision-making process based on the surgical diagnosis. Once the decision to operate has been made, appropriately experienced senior personnel should be available at
all times of the day to anesthetize and operate on the patient as well as to organize appropriate postoperative care.

**Mode of anesthesia**

There is insufficient evidence that supports a single best anesthetic plan for elderly patients. There is no difference in postoperative morbidity, rates of re-hospitalization, in-patient mortality or hospitalization costs in geriatric patients undergoing regional anesthesia (RA) or general anesthesia (GA) for repair of hip fracture repair [72,73]. GA and RA are both useful for older non-cardiac patients, but for some procedures e.g., hip fracture surgery, RA seems to be the technique of choice. The mode of anesthesia may only play a secondary role in mobility, rehabilitation and discharge distension. There are no specific recommendations regarding the preferred type of anesthesia for elderly non-cardiac patients [74]. Another 2014 population-based retrospective cohort study that included 6135 matched old adult pairs with dementia undergoing hip fracture surgery showed that GA and RA are associated with similar rates of most perioperative adverse events (GA, 11.3%; RA, 10.8%, P = 0.44) [75]. The mode of anesthesia, i.e., GA vs. RA, did not have significant effects on perioperative outcomes (myocardial infarction, pulmonary complication, stroke, urinary tract infection and wound infection) after lower extremity amputation in total 3,260 geriatric patients [76]. While anesthesia preparation time, length of surgery, start time of surgery, time to sit, and time to walk were shorter in GA, time to fast-track eligibility, phase 1 recovery time, and discharge time were similar among patients who received spinal anesthesia [77]. Another 2014 retrospective cohort study that included 56,729 patients ≥ 50 years old undergoing hip repair surgery found that RA use was not associated with a lower 30-day mortality when compared with GA use (RA, 5.4%; GA 5.8%, instrumental variable estimate of risk difference, -1.1%, 95% CI -2.8 -0.5, P = 0.20) but was associated with a modestly shorter length of stay. These findings do not support a mortality benefit
for RA use in this setting [78].

However, a recent retrospective study that included 16,695 geriatric patients’ mortality within 90 days post-surgical repair of a hip fracture showed that GA and conversion from RA to GA were associated with a higher risk (HR 1.22, 95% CI 1.11-1.35, P < 0.001) of mortality during in-hospital stay when compared with RA, but this higher risk did not persist after hospital discharge. They also showed that GA was associated with a higher risk of all cause readmission when compared with RA and, thus, they concluded that RA may be preferred [79]. Another 2019 retrospective comparative study included 89 patients ≥ 70 years old undergoing major lumbar surgery showed that there was an association between those who receive epidural anesthesia and superior perioperative outcomes, such as episode of hypertension, tachycardia during anesthesia, postoperative delirium, nausea, vomiting and postoperative pain [80]. A 2000 meta-analysis concluded that there were marginal advantages for RA when compared with GA for hip fracture patients in terms of early mortality and risk of deep vein thrombosis [81]. A 2014 review showed that multimodal drug therapy and RA can be effective for perioperative pain management in the elderly, although it did not improve long-term mortality [82].

Taken together, no clear evidence from randomized controlled trials (RCTs) exists to identify the best anesthesia technique for hip surgery in the elderly. However, several large-scale pragmatic trials are ongoing and will provide future guidance [83-85]. No matter which type of anesthesia is chosen, anesthesia should be carried out by experienced anesthesiologists, who are trained to manage perioperative care of geriatric patients [62,86], Therefore, the choice of anesthesia is made by the anesthesiologist and is based on the patient’s preference, comorbidities, potential general postoperative complications, and on the clinical experience of the anesthesiologist. The overall therapeutic approach in geriatric surgical patient should be determined jointly by the surgeon, the geriatrician and the anesthesiologist.

A 2018 study of 392 older patients showed that propofol-based GA might decrease the incidence
of delayed neurocognitive recovery at 1 week after surgery when compared with sevoflurane-based GA (propofol 14%, sevoflurane 23.2%, OR 0.577, 95% CI 0.342-0.975, P = 0.038) [87]. However, another recent study that included 28 RCTs with 4507 participants found low-certainty evidence that maintenance with propofol-based total intravenous anesthesia (TIVA) may reduce POCD. It was uncertain whether maintenance with propofol-based TIVA or with inhalational agents affect the incidences of postoperative delirium, mortality, or length of hospital stay because the evidence was very low [88].

There are some studies on spinal anesthesia for geriatric hip surgery. In elderly patients undergoing hip fracture repair, continuous spinal anesthesia (CSA) provides fewer episodes of hypotension and severe hypotension when compared with a single intrathecal injection of 7.5 mg bupivacaine [89]. A prospective cohort study showed that cardiac output and blood pressure decreased significantly after the onset of SA in elderly patients. This is mainly caused by a decrease in stroke volume and not by a decrease in systemic vascular resistance [90]. A 2014 prospective randomized study of elderly high-risk patients undergoing hip replacement surgery showed that CSA and psoas compartment sciatic nerve block (PCSNB) produced a satisfactory quality of anesthesia. Fewer hemodynamic changes in PCSNB cases when compared with CSA cases were also noticed [91]. A 2015 prospective randomized study comparing midazolam with propofol sedation in hypoalbuminemia (albumin level below 3 g/dl) geriatric patients under spinal anesthesia found that when compared with midazolam, propofol use is associated with more reliable hemodynamic stability, less respiratory depression and faster recovery [92].

Anesthetic pharmacology

Standard anesthetic doses can cause more profound clinical effects in the elderly, because of the differences in pharmacokinetics and pharmacodynamics. Lower doses are required for propofol,
remifentanil, ropivacaine and desflurane [93]. Particular care should be taken with hypnotic agents: the dose required to induce anesthesia is lower, but the onset time is prolonged [94]. Depth of anesthesia monitoring is recommended [95,96]. Anesthesiologists should be familiar with potentially inappropriate medications for use in older patients according to Beers criteria, i.e. elderly people have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase the risk for cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in elderly people [53].

Neuromuscular blocking and reversal agents

The dose of neuromuscular blocking agents (NMBAs) should hardly be reduced for intubation, but their duration of action is often prolonged and difficult to predict along with age-induced changes in pharmacokinetics of long and intermediate-acting NMBAs (especially, aminosteroids including rocuronium and vecuronium), which may cause postoperative residual neuromuscular blockade and associated complications. Therefore, perioperative neuromuscular monitoring including a train-of-four monitoring is strongly recommended [97] .

Benzylisoquinoliniums including atracurium and cisatracurium have more reliable duration of action because they depend less on renal and hepatic function for their elimination and thus, they can be favorably considered for use in the elderly [98]. Neostigmine and pyridostigmine are preferable to edrophonium as NMBA reversal agents because their prolonged duration of action can counterbalance the prolonged duration of action of NMBAs that occur with advancing age, however, neostigmine reversal may be ineffective or prolonged and standard doses of sugammadex are required in the elderly [93,98].

Monitoring
The working party group recommends that anesthesiologists routinely consider use of the following monitoring devices for the elderly, particularly during major or emergency surgery [6]. For the intra-arterial blood pressure monitoring, hemoglobin concentration, blood glucose, arterial blood gas testing and beat-to-beat blood pressure monitoring are recommended. A suitable limit of blood pressure is a fall in systolic blood pressure of more than 20% from pre-induction baseline.

For the central venous monitoring, central venous catheterization may provide an additional route of venous access after complex surgery when vasoactive drug support is necessary, but should be balanced against the possible complication of procedure. For the cardiac output monitoring, there is still limited evidence in the elderly. Because elderly patients have poorly compliant aortas, cardiac output monitoring using Doppler directed at the aorta may provide less accurate information.

For the cerebral oxygen saturation, an episode of cerebral oxygen desaturation more than 15% is indicative of cerebral ischemia. Ružman et al. [99] evaluated the changes of regional cerebral saturation (rSO2) measured by near-infrared spectroscopy during elective laparoscopic cholecystectomy under TIVA and the association between patient's characteristics and critical decline of rSO2. They found that the rSO2 was significantly lower in patients older than 65 years and suggested that monitoring of cerebral oxygenation could be an important part of perioperative care to prevent cerebral hypoxia in older patients. In addition, although further research is needed to strengthen, monitoring of cerebral oxygen desaturation and early intervention may reduce POD or POCD [100].

For the depth of anesthesia monitoring, a processed electroencephalogram (EEG) neuromonitoring including bispectral index or entropy monitor is recommended to avoid excessive depth of anesthesia, thereby preventing the development of POD [95,96] or POCD [100] in elderly patients. Lastly, perioperative neuromuscular monitoring is strongly recommended to keep the proper degree of neuromuscular blockade and its safe reversal [97,101].
Fluid management and blood transfusion

Intraoperative fluid optimization may be associated with benefit in geriatric hip fracture patients. A 2015 systemic review showed that goal directed fluid therapy during hip fracture repair under spinal anesthesia does not result in a significant reduction in length of stay or postoperative complications. Discharge time was similar in anesthetist-directed fluid therapy group and a pulse-contour-guided fluid optimization strategy group, as was total length of stay. A meta-analysis of 355 patients found non-significant reduction in early mortality (relative risk [RR] 0.66, 95% CI 0.24-1.79) and in-hospital complications (RR 0.80, 95% CI 0.61-1.05) when goal-directed intervention fluid therapy was implemented. However, it was also suggested that goal directed fluid therapy has a possible mortality reduction benefit, although further studies are needed to support such a hypothesis [102]. A 2014 systemic review included 734 high-risk patients aged 50 years or older found that the use of a cardiac output-guided hemodynamic therapy algorithm when compared with the usual care did not reduce a composite outcome of complications and 30-day mortality [103].

In high-risk surgical patients, several studies have demonstrated that goal-directed hemodynamic therapy (GDHT) significantly reduced postoperative mortality and morbidity [104,105]. However, several studies on GDHT in elderly patients found that cardiac performance was not improved and there was a statistically uncertain risk reduction of postoperative complications in the GDHT group [102,106]. Subsequently, a 2016 RCT in patients aged ≥ 70 years old undergoing hip-fracture surgery also indicated that the main GDHT component, the stroke volume maximization by fluid challenges, and traditional pre-anesthesia fluid loading are of questionable value in the elderly [107]. Therefore, we should pay attention to a multicenter RCT using a stepped wedge cluster design to assess the effectiveness of an optimization strategy involving GDHT, lung-protective ventilation and depth of anesthesia monitoring for general anesthesia on postoperative morbidity and
mortality in high-risk elderly patients undergoing high-risk surgeries (the OPTI-AGED study) [108].

Consequently, the RCT involving 807 patients ≥ 75 years old concluded that in those patients, the strategies of anesthesia optimization are not in accordance with eligible guidelines. That is, there is a considerable gap between clinical practice and guidelines concerning anesthetic optimization in high-risk elderly patients, and implementation of these strategies varies independently of factors related to the population or type of surgery, and thus the benefit of such multimodal optimization strategy has to be addressed in elderly patients [109].

It is still controversial whether red blood cell (RBC) transfusions might increase the risk of infections after hip fracture surgery in geriatric patients. The Transfusion Requirements In Frail Elderly (TRIFE) randomized study including 284 elderly patients showed that a more liberal RBC transfusion strategy was not associated with higher infection risk of in subjects undergoing hip fracture surgery. Rates of infection were 72% of the restrictive RBC strategy group (hemoglobin [Hb] < 9.7 g/dL; 6 mmol/L) when compared with 66% for the liberal group (Hb < 11.3 g/dL; 7 mmol/L) (RR 1.08, 95% CI 0.93-1.27, P = 0.29) [110]. A 2015 Cochrane review of 2,722 participants ranged from 81 to 87 years old undergoing hip fracture surgery showed low quality evidence of no difference in mortality, functional recovery or postoperative morbidity between the liberal strategy (maintain a Hb level usually around 10 g/dL) vs. the restrictive strategy (based on symptoms of anemia or a lower Hb concentration usually around 8 g/dL) thresholds for RBC transfusion. The currently available evidence does not support the use of liberal RBC transfusion thresholds based on a 10 g/dL Hb trigger in preference to more restrictive transfusion thresholds based on lower Hb levels or symptoms of anemia [111]. Another 2015 sub-research in Transfusion Requirements After Cardiac Surgery (TRACS) randomized controlled trial analysis showed no difference between the two groups of liberal and restrictive transfusion strategy inpatients < or > 60 years old when an analysis of the 30-day all-cause mortality and severe morbidity was done. However, there was an increased rate of
cardiogenic shock in the elderly patients in the restrictive transfusion strategy group [112]. To evaluate controversial issues, a multicenter randomized study has been planned. A 2019 prospective, randomized, multicenter, controlled trial randomizing 2,470 elderly (≥ 70 years) patients undergoing non-cardiac surgery will evaluate whether a liberal transfusion strategy (transfusion of a single RBC unit when Hb is < 9 g/dL with a target range for the post-transfusion Hb level between 9-10.5 g/dL) reduces the major adverse events after non-cardiac surgery compared to a restrictive strategy (transfusion of a single RBC unit when Hb < 7.5 g/dL with a target range for the post-transfusion Hb level between 7.5-9 g/dL) within 90 days after surgery [113]. Such a large scale pragmatic trials will provide evidence for future guidance.

A 2019 RCT showed that salvaged autologous blood leukocyte filtration could improve ventilation, promote oxygenation and gas exchange, and inhibit lung inflammatory and oxidative stress reactions in elderly patients undergoing lumbar spinal surgery [114].

**Lung-protective ventilation**

The ACS NSQIP Best Practice guidelines: prevention of postoperative pulmonary complications shows risk factors of postoperative pulmonary complications and strategies to prevent the complications. A 2018 expert survey included 362 respondents and the design of the Delphi consensus suggested a care bundle composed of factors before surgery, i.e., supervised exercise programs and inspiratory muscle training, factors during surgery, i.e., low tidal volume ventilation (6–8 mL/kg) with individualized positive end-expiratory pressure (PEEP) of 5–8 cmH₂O, and repeated recruitment maneuvers, use of routine monitoring to avoid hyperoxia and efforts made to limit neuromuscular blockade, and factors post-operatively, i.e., deep breathing exercises and elevation of the head of the bed [115].
Prevention of hypothermia

Elderly patients are vulnerable to perioperative hypothermia, leading to increased morbidity. Especially, during transurethral resection of the prostate (TURP) or bladder tumor (TURB) under spinal or general anesthesia, or arthroscopic shoulder surgery under general anesthesia, it is important to maintain a normal range of body temperature throughout the whole perioperative period, and so many studies have been performed to investigate the effects of various active or passive warming devices and methods including a forced-air warming blanket or heated humidifier/circuit on perioperative hypothermia or shivering in elderly patients undergoing TURP or TURB under spinal or general anesthesia or arthroscopic or open urologic surgeries under general anesthesia [116-119]. Jo et al. [116] suggested that a brief period of preoperative forced-air warming did not significantly reduce the incidence of intraoperative hypothermia, but it could significantly reduce its severity in elderly male patients undergoing TURP under spinal anesthesia. Also, Zhang et al. [120] reported that use of a forced-air warming system combined with an electric blanket was a more effective method for maintaining body temperature compared to each individual device group in elderly TURP patients.

Hong et al. [117] reported that warming blanket application for 10 min before induction of anesthesia reduced the incidence of hypothermia at one hour after induction of anesthesia compared to one-layer cotton blanket application using the same method. A prospective observational study showed a heated humidifier is more effective in preventing intraoperative hypothermia in elderly patients undergoing open urologic surgeries than a heat moisture exchanger [118]. A retrospective study performed in arthroscopic shoulder surgery reported that the incidence of postoperative hypothermia was higher and the associated temperature drop was more prominent in geriatric patients compared to young adult patients and suggested that additional warming methods are needed to prevent perioperative hypothermia in geriatric patients [119]. Despite differences in types and
application periods or methods of warming devices used in the studies, most studies demonstrated various warming strategies could be helpful to keep the body temperature in elderly patients undergoing surgeries under general or regional anesthesia.

**Postoperative Management**

**Postoperative adverse outcomes**

According to the prospective cohort study of 544 patients aged 70 and older undergoing non-cardiac surgery, overall 21% of patients developed adverse outcomes and 3.7% died during the in-hospital postoperative period. Despite the prevalence of preoperative chronic medical conditions, most patients do well postoperatively. The ASA physical classifications, emergency surgery, and intraoperative tachycardia increase the odds of adverse events [121]. Other prospective study of 517 patients ≥ 70 years old and undergoing non-cardiac surgery showed that 31.7% of patients were deceased at the time of follow-up and a history of cancer (HR 2.44, 95% CI 1.78-3.38, P < 0.001), ASA physical status > 2 (HR 2.27, 95% CI 1.61-3.21, P < 0.001), neurologic disease (HR 1.59, 95% CI 1.13-2.24, P = 0.008), age (HR 1.42 per decade, 95% CI 1.11-1.81, P = 0.005), postoperative pulmonary complication (HR 2.41, 95% CI 1.30-4.48, P = 0.005), and renal complication (HR 6.07, 95% CI 2.23-16.52, P < 0.001) were significant independent predictors of decreased long-term survival [122]. Co-morbid conditions, age, and new hospitalization after discharge were important independent predictors of a long-term decrease in quality of life. To improve postoperative long term quality of life of geriatric surgical patients, they should be evaluated and measured their potential pre- and intra-operative risk factors.

**Postoperative transfusion**

A 2016 RCT included 284 frail elderly patients, who underwent surgical hip fracture compared
their outcome and overall quality of life. Their transfusion were treated according to a liberal transfusion strategy with hemoglobin target of 7 mmol/l (11.3 g/dl) or a restrictive transfusion strategy with hemoglobin target of 6 mmol/l (9.7 g/dl). The authors concluded that the liberal hemoglobin target improves survival in the frailest elderly (the nursing home residents) without impairing recovery from physical disabilities and overall quality of life or increasing the risk of infections when compared with the restrictive hemoglobin target. The liberal strategy seems to improve recovery of physical performance within one year after hip fracture surgery which was associated with better overall quality of life [123]. According to the Hb thresholds, recovery from physical disabilities in frail elderly hip fracture patients was similar after a restrictive RBC transfusion strategy (Hb < 9.7 g/dL; < 6 mmol/L) and after a liberal strategy (Hb < 11.3 g/dL; < 7 mmol/L). The 90-day mortality rate was higher for nursing home residents in the restrictive transfusion group (36%) than for those in the liberal group (20%) (HR 2.0, 95% CI 1.1-3.6; P = 0.010). Implementation of a liberal RBC transfusion strategy in nursing home residents has the potential to increase survival [124].

**Perioperative analgesia**

Elderly patients are often undertreated for pain. Acute pain management in the elderly is challenging, with physiological frailty, medical comorbidities and cognitive impairment commonly compounding pain assessment and treatment. A 2003 retrospective cohort study included 8,855 subjects aged 16 years and older to evaluate effect of opioid showed that those aged between 61 and 70 years had 2.8 times the risk of development of respiratory depression (95% CI 1.2-6.6); those aged between 71 and 80 years had 5.4 times the risk (95% CI 2.4-11.8); and those ≥80 years had 8.7 times the risk (95% CI 3.8-20.0) than patients aged between 16 to 45 years old. The risk of respiratory depression increases substantially after 60 years of age [125]. A 2014 review suggested that multimodal drug therapy and perioperative regional analgesia can be very effective for
perioperative pain management in elderly patients [81]. Paracetamol is safe and considered first-line therapy. Nonsteroidal anti-inflammatory drugs should be used with caution and because they can cause gastric and renal damage. Also, although morphine is effective, cautious administration to elderly patients with poor renal or respiratory function, and to the cognitively impaired must be taken into consideration.

Regional anesthesia as part of multimodal perioperative treatment can often reduce postoperative neurological, pulmonary, cardiac, and endocrine complications. Regional anesthesia/analgesia has not been proven to improve long-term morbidity but does benefit immediate postoperative pain control. In addition, multimodal drug therapy utilizes a variety of nonopioid analgesic medications in order to minimize dosages and adverse effects from opioids while maximizing analgesic effect and benefit [81]. A 2018 narrative review showed that comprehensive pain protocols for elderly hip fracture patients are required. Fascia iliaca blocks are a block of choice for these patients [126]. Ultrasound-guided regional anesthesia/analgesia is an important part of the practice of anesthesia for the elderly population, the growth of which will continue to outpace that of the younger population due to improvements in lifespan worldwide [127]. A 2016 RCT compared ultrasound-guided continuous femoral nerve block vs. continuous fascia iliaca compartment block in 60 elderly patients undergoing hip replacement surgery and concluded that both ultrasound-guided blocks provide effective anesthesia and postoperative analgesia for elderly hip replacement patients [128]. Also, a 2014 RCT compared the hemodynamic effects of combined PCSNB with continuous spinal anesthesia in elderly high-risk patients undergoing hip replacement surgery and concluded that PCSNB produced a satisfactory quality of anesthesia in elderly high-risk patients with fewer hemodynamic changes compared with continuous spinal anesthesia [91].

A RCT showed that after a major abdominal surgery in the elderly patient, the patient-controlled analgesia, regardless of the route (epidural or parenteral), was effective and patient-controlled
epidural analgesia using local anesthetics and an opioid provided better pain relief and improved mental status and bowel activity when compared with intravenous patient-controlled analgesia [129].

**Postoperative delirium**

POD is a common serious postoperative complication especially in older people and is associated with increased mortality, morbidity and health costs. The overall prevalence of delirium in older patients after surgery has been estimated to be 10% [130]. In one study in which 144 patients > 50 years were scheduled for an operation requiring a postoperative intensive care unit (ICU) admission showed that 44% of patients developed delirium [131]. Another recent review in which 35 selected articles were reviewed showed that the incidence of POD was up to 50% [132]. A 2015 study included 459 elderly patients found incident POD was not the significantly associated with decreased survival after undergoing hip fracture repair and showed that survival was a function of age at the time of surgery, illness severity based on the ASA physical status, and duration of ICU stay after surgery [133].

Among the risk factors for POD, preexisting cognitive impairment and dementia is the strongest predisposing factor [131, 134]. A 2006 study included 333 elderly patients undergoing noncardiac surgery found 46% of patients developed POD. By multivariate logistic regression, age (OR 2.5, 95% CI 1.5-4.2), moderate (OR 2.2, 95% CI 1.2-4.0) and severe (OR3.7, 95% CI 1.5-9.0) preoperative resting pain were important contributing factors [135]. Therefore, adequate opioid-reduced analgesia is of great importance. A 2019 review suggested that a clinical trial on the usefulness of the STOP-BANG questionnaire of obstructive sleep apnea as a preoperative stratification for POD showed no difference between the low risk group and the intermediate-to-high risk groups in POD incidence, duration of delirium, and length of ICU, however, a higher preoperative risk for obstructive sleep apnea is associated with a 3 fold higher risk for POD and coma [136]. A retrospective study that
included 318 elderly patients undergoing total knee arthroplasty also showed that preoperative dementia is the most important risk factor of postoperative delirium, and, thus, suggested that those patients should be thoroughly evaluated and their dementia should be managed preoperatively and adequate management of intraoperative hypotension and preoperative hemoglobin might be helpful in reducing the incidence of POD [137].

A 2018 systematic review which included 104 studies found that there is no evidence to suggest that anesthesia types (GA vs. RA) influence POD [138]. Another 2018 RCT which included 256 patients ≥ 75 years old who received Xenon or sevoflurane anesthesia found that Xenon anesthesia did not reduce the incidence of POD (Xenon; 9.7%, 95% CI 4.5-14.9, sevoflurane; 13.6%, 95% CI 7.8-19.5, P = 0.33) [139]. Meanwhile, a comparison of regional with general anesthesia on POD in elderly patients is underway in the nine clinical trial centers of China and they expected a total of 1,000 patients enrollment [84].

Intraoperative EEG waveform suppression, often suggesting excessive general anesthesia, has been associated with postoperative delirium and thus it had long been in the spotlight to assess whether EEG-guided anesthetic administration decreases the incidence of postoperative delirium. A 2019 systematic review for prevention of POD in elderly patients planned for elective surgery showed multicomponent interventions (comprehensive multidisciplinary care and multimodal interventions), that the use of antipsychotics, bispectral index-guidance, and dexmedetomidine treatment can successfully reduce the incidence of POD in elderly patients undergoing elective, non-cardiac surgery although the included studies were heterogeneous, and high-quality studies were scarce [95]. However, recently, a remarkable large-scale RCT of 1,232 adults aged 60 years and older undergoing major surgery showed that EEG-guided anesthetic administration, compared with standard care, did not decrease the incidence of POD. This finding does not support the use of EEG-guided anesthetic administration for decreasing the incidence of POD [140]. Another 2019 RCT included 200 elderly
patients undergoing hip fracture repair with spinal anesthesia supplemented with propofol sedation found that heavier intraoperative sedation was not associated with significant differences in mortality or return to pre-fracture ambulation up to 1 year after surgery [141]. Therefore, further large-scale and well-designed RCTs are needed to more clearly investigate the association between EEG-guided anesthetic administration or depth of anesthesia and incidence of POD.

A 2012 clinical trial that included 171 elderly subjects with hip fracture found that delirium episodes and cognitive decline during hospitalization were common, but inpatient geriatric consultation teams intervention reduced the incidence of POD (control group 53.2%, intervention group 37.2%, \( P = 0.04, \text{OR} \ 1.92, 95\% \ 1.04-3.54 \)), however, another study found that geriatric consultation had no effect on the severity or duration of POD episodes [142]. Although our results are not conclusive, a close collaboration with the geriatric team approach can be useful [143]. A 2017 meta-analysis that included 1840 elderly patients concluded that comprehensive geriatric care may reduce the incidence of POD (\( \text{OR} \ 0.71, 95\% \ 0.57-0.89, P = 0.003 \)) [144].

A 2019 two systematic reviews using meta-analysis of RCTs showed that in elderly patients undergoing noncardiac surgery, perioperative administration of dexmedetomidine, compared with the use of placebo, reduced the incidence of POD [145,146]. In contrast, a 2019 double-blinded, multi-center, randomized study that included 164 elderly patients undergoing cardiac surgery reported that dexmedetomidine-based general anesthesia resulted in reduced extubation time and postoperative morphine requirements when compared with propofol-based general anesthesia in elderly patients following cardiac surgeries, but no significant difference was observed in incidence of POD [147].

If possible, drugs that precipitate POD such as opioids, antihistamines, atropine, sedative hypnotics and corticosteroids, should, therefore, be avoided in patients at risk, include benzodiazepine [54,148].
Postoperative cognitive dysfunction

POCD is a frequent neurologic complication occurring in geriatric patients. The type of anesthesia or analgesia and the patient's inflammatory response may contribute to POCD. A 2014 clinical trial that included 200 elderly patients with mild cognitive impairment showed that there is no difference in the incidence of POCD at 7 days after radical rectal resection under sevoflurane (33.3%) or propofol-based (29.7%) general anesthesia, but sevoflurane had more severe impact on cognitive function than propofol [149]. However, a 2015 clinical trial that included 90 elderly patients scheduled for resection of an esophageal carcinoma showed the incidence of POCD was higher in sevoflurane than propofol anesthesia using the Mini Mental State Examination (MMSE) score and the Montreal cognitive assessment (MoCA) score. Furthermore, they found elevated plasma concentrations of TNF-α, interleukin (IL)-6, and S-100β protein receiving sevoflurane anesthesia throughout the first postoperative week [150]. However, a 2016 RCT that included 80 elderly patients scheduled for a non-cardiac operation found there is a negative influence sevoflurane anesthesia on the early (48 hours postoperatively) and late (9 months postoperatively) state than propofol anesthesia and there is no difference of inflammatory markers (IL6, IL10, TNF-α) between the two anesthesia groups [151]. A 2018 clinical trial that included 120 elderly scheduled for esophageal carcinoma resection showed that POCD incidence was higher in elderly patient receiving sevoflurane anesthesia and dexmedetomidine could alleviate POCD through decreasing TNF-α and IL-6 [152].

A 2018 RCT compared the effect of general and spinal anesthesia on the occurrence of POCD up to postoperative 30 days in elderly patients undergoing hip fracture surgery and reported that the choice of anesthesia modality did not appear to influence the emergence of PCOD in the elderly patients [153]. Meanwhile, a 2019 RCT investigated the impacts of general and spinal anesthesia on short-term cognitive function and mental status in 80 elderly patients undergoing orthopedic surgery, and concluded that compared with general anesthesia, spinal anesthesia can effectively reduce eye
opening and language presentation times and it also has few negative impacts on the short-term cognitive function and mental status of the elderly patients, along with lower incidence of POCD [154].

A 2017 RCT was performed to observe whether combined general and regional anesthesia affected perioperative cognitive trajectory compared to only general anesthesia in elderly patients with arthroplasty [155]. The postoperative MMSE was significantly higher in the combined anesthesia group and it was significantly improved compared with preoperative MMSE score in both groups. The RCT demonstrated that combined general and regional anesthesia protected perioperative cognitive trajectory, providing evidence supporting use of regional anesthesia along with general anesthesia in elderly orthopedic patients who are vulnerable to POCD.

A 2016 meta-analysis included 13 RCTs of general anesthesia showed that dexmedetomidine significantly reduced the incidence of POCD (RR 0.59, 95% CI 0.45-2.95) and improved the MMSE score (mean difference [MD] 1.74, 95% CI 0.43-3.05) on the first postoperative day; and reduced the incidence of POCD after the first postoperative day (MD 2.73, 95% CI 1.33-4.12) [156]. Other 2019 meta-analysis included 26 RCTs found that perioperative dexmedetomidine treatment significantly reduced the incidence of POCD (pooled ORs 0.59, 95% CI 0.45-2.95) and improved MMSE score (standardized mean difference [SMD] 1.74, 95% CI 0.43-3.05) on the first postoperative day and decreased IL-6 (SMD: –1.31, 95% CI: –1.87—0.75, P < 0.001) and TNF-α (SMD: –2.14, 95% CI: –3.14—1.14, P < 0.001) when compared with saline/comparator treatment [157]. A 2016 clinical trial that included 134 elderly patients undergoing total knee arthroplasty found that parecoxib sodium decreases POCD incidence and plasma IL-1β, IL-6 and TNF-α level. They suggested the parecoxib’s effect on POCD incidence may be explained by the suppression of inflammation and pain [158]. Another clinical trial in 2017 that included 152 elderly patients scheduled for shoulder arthroscopy showed parecoxib sodium pretreatment combined with dexmedetomidine could reduce the incidence
of early POCD and showed higher jugular venous oxygen partial pressure and jugular venous oxygen saturation values at postoperative day one when compared with the control group. They suggested that this effect might be related to the improvement of postoperative analgesia effect and cerebral oxygen metabolism [159].

In a prospective randomized double-blinded controlled study, the effect of remifentanil and fentanyl on POCD and cytokines level was investigated in elderly patients undergoing major abdominal surgery. Consequently, the two opioid groups were comparable regarding to POCD incidence; however, IL-6 levels were lower in the seventh day after surgery for remifentanil group, which suggested that the use of remifentanil does not reduce POCD compared to fentanyl [160].

Enhanced inflammation response was increasingly reported in association with POCD [161]. Glucocorticoid receptor (GR) signal plays a key role in suppression of inflammation. In a 2010 prospective cohort that included 126 elderly patients undergoing hip fracture surgery with general anesthesia, plasma cortisol levels and the expression levels of GR and FK506 binding protein 51 (FKBP51) in leukocytes were determined at 1 day preoperatively and 7 days. When compared with non-POCD patients, visual analogue scale (VAS) scores at 12 hours after surgery were higher in POCD patients. No significant difference in expression levels of GR was found between the POCD and non-POCD patients, but high expression of FKBP51 in leukocytes and glucocorticoid resistance were associated with POCD in aged patients following hip fracture surgery [162].

A 2017 RCT reported that preoperative oral melatonin supplementation might improve early POCD in elderly patients undergoing hip arthroplasty, suggesting that the restoration of normal circadian function with good sleep quality may be a key factor in preventing or treating POCD [163].

To manage POCD, care bundles and protocols for the perioperative period improves outcomes in the elderly patient. However, there is no clear care bundles and protocols which improves postoperative delirium or postoperative cognitive dysfunction until now. Preventive strategies, early
recognition, and management of perioperative risk factors seems to be the best modality to treat POCD till further progress in therapeutic interventions evolve [164]. Meanwhile, at the southwest of Germany, study protocol for a stepped-wedge cluster randomized trial (PAWEL study) for reduction of delirium risk and POD after elective procedures in adults > 70 years old is now planned and they expect 1,500 patients to enroll. Results of the trial should form the basis of future standards for preventing delirium and POCD in surgical wards [165].

**Prevention of postoperative pulmonary complication**

Pulmonary complications increase the risk of mortality after surgery. Ten multivariable studies showed that age was a significant risk predictor of pulmonary complication and was the second most commonly identified risk factor. The OR was 2.09 (95% CI 1.70-2.58) for patients between 60 to 69 years old and 3.04 (95% CI 2.11-4.39) for those between 70 to 79 years old when compared with younger patients (those < 60 years old). Unadjusted postoperative pulmonary complication estimates for patients > 65 years old ranged from 1% to 34%, with a median postoperative pulmonary complication rate of 14%. For patients > 70 years old, the unadjusted postoperative pulmonary complication estimates ranged from 4% to 45%, with a median postoperative pulmonary complication rate of 15% [34,166]. A large retrospective cohort study that included 8,920 elderly patients with hip fracture repair patients found that cardiac and pulmonary complications were most frequent (8% and 4% of patients, respectively) [167].

Well-documented risk factors for pulmonary complications, include atelectasis, pneumonia, and pulmonary thromboembolism, include advanced age, poor general health status, current infections, pre-existing cardiopulmonary diseases, hypoalbuminemia, and renal dysfunction. Interventions such as lung expansion maneuvers and thromboprophylaxis have been proven to be effective in reducing the risk of pulmonary complications [168]. According to a 2006 systemic review that included 20
RCTs and 11 meta-analyses which were not limited to the elderly patients, good evidence suggests that lung expansion therapy (for example, incentive spirometry, deep breathing exercises, and continuous positive airway pressure) reduces postoperative pulmonary risk after abdominal surgery. Well-designed trials are needed to clarify the magnitude of benefit and the comparative effectiveness of different modalities [169].

A 2019 RCT with 76 elderly patients scheduled for hip joint surgery investigated if pressure-controlled ventilation-volume guaranteed (PCV-VG) may result in better lung ultrasound score (LUS) by reducing atelectasis in the dependent areas of the lung and minimizing respiratory deterioration after surgery in elderly patients, compared with volume-controlled ventilation (VCV), and suggested that PCV-VG showed better LUS results as well as higher dynamic compliance and lower inspiratory peak pressure compared to VCV [170].

**Prevention of urinary tract infection**

A 2019 retrospective cohort study in which 221 female patients (age 85.3 ± 7.0 years) with a history of hip surgery carried out at Toyama Municipal Hospital were recruited. Urinary retention occurred in 34 out of the 221 cases (15.4%) and it showed a significant association of urinary retention with cognitive impairment (OR 4.11, 95% CI 1.53-11.03, P = 0.005), and ADL (OR 2.61, 95% CI 1.11-6.18, P = 0.029), under adjustment with age and body mass index (BMI). This study demonstrated that cognitive function and ADL were the important risk factors for urinary retention, and suggested that the postoperative management of urinary retention is important with taking account of neurofunctional assistance and nursing care in daily living, especially in elderly female patients undergoing surgery after femoral neck and trochanteric fractures [171]. A 2014 clinical study for risk factors of urinary retention included 72 female elderly patients undergoing hip surgery showed that the early removal of the urethral catheter (per 1-day indwelling period increase, OR 0.33,
95% CI 0.11-0.96, P = 0.04), and preoperative dementia and/or delirium (OR 10.4, 95% CI 1.21-89.2, P = 0.03) had significant correlations with postoperative urinary retention. Femoral neck fractures and the surgical procedure used for the hip surgery do not induce damage to the bladder and nerves involved in voiding function, and the voiding function in all of the patients was recovered after short-term intermittent catheterization [172]. Older adults are at particular risk for urinary tract infection. Indwelling urinary catheters should not be used as a substitute for nursing care of patient who is incontinent patient.
Conclusion

The aims of effective perioperative care are to improve the likelihood of the elderly patients returning to their pre-morbid condition and maintaining continuity in the community. Perioperative care of elderly patients requires a multidisciplinary team approach to optimize patient care. This includes risk stratification models, multidisciplinary coordination through the whole perioperative period. However, the aforementioned approaches are time-consuming and remain a challenge in clinical routine because of limited human resources in hospitals and lack of funding from healthcare systems. The evidence based informing perioperative care for the elderly patients remains poor until now. There is no clear evidence in the form of RCTs considering the efficacy of general vs. regional anesthesia for surgery. There is no clear care bundles and protocols which improves POD or POCD. Preventive strategies, early recognition, and management of perioperative risk factors seems to be the best modality till further progress in therapeutic interventions evolve. Anesthetic techniques to manage appropriate hemodynamic status during the perioperative period to avoid ischemic complications are required. Anesthesiologists must participate in discussions about the utility of surgery and resuscitation and are strongly encouraged to become involved in national audit projects and outcomes research especially related to the elderly surgical patients. We hope that daily practitioners will use this information to improve their conduct and additional research to further improved our future.
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Figure Legend

Records identified through database searching (n = 1551)

Additional records identified through other sources (n = 15)

Records after duplicates removed (n = 1152)

Records screened (n = 1152)

Records excluded (n = 890)

Full-text articles assessed for eligibility (n = 262)

Studies included in qualitative synthesis (n = 172)

Full-text articles excluded, which were not relevant to the review (n = 90)

Fig. 1. Flow diagram for article search and studies included in this review.

Appendix 1. Search strategies and items found for each database (attached as a file)