

Geriatric Anesthesia-related Morbidity and Mortality in China: Current Status and Trend

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Abstract

Objective: The population of elderly patients and the amount of geriatric anesthesia have been growing rapidly in China. Thus, understanding the morbidity and mortality associated with geriatric anesthesia in China is critical to the improvement of anesthesia quality and outcome. The aim of the review was to discuss the geriatric anesthesia-related morbidity and mortality in China, as well as to point out the future trend.

Data Sources: Articles in this review were all searched from Wanfang, China National Knowledge Infrastructure (CNKI), VIP, PubMed, and Web of Science databases, based on the reports originated in China from January 2011 to December 2016.

Study Selection: A total of 57 studies were selected for further study, including 12 retrospective studies, 35 prospective studies, 3 meta-analyses, 4 reviews, 1 viewpoint, and 2 case reports. Of the total studies, 42 studies were in Chinese while 15 were in English.

Results: The mortality and morbidity associated with geriatric anesthesia in China are not yet completely reported. Some factors have been recognized, while some are yet to be identified and confirmed. Several studies addressed postoperative cognitive dysfunction and postoperative delirium, whereas only a few studies can be found on renal complications. Thus, a nationwide registry is essential for geriatric anesthesia-associated adverse outcomes. The mortality associated with geriatric anesthesia in China should be reported promptly. In the future, the perspective of geriatric anesthesia needs to be expanded into perioperative geriatric medicine to improve the perioperative management strategy based on the postoperative outcome-directed concept transformation.

Conclusions: Anesthesiologists should evaluate the physiological and medical status and focus on the prevention of potential complications in the perioperative setting with the goal to enhance elderly patients' long-term well-being and survival quality.

Key words: Anesthesia; China; Geriatric; Morbidity; Mortality

INTRODUCTION

The elderly population has been growing rapidly in China, thereby designating it as the country with the largest aged population (≥ 60 years old) in the world, with 185 million at the end of 2011 that might likely reach 200 million by the end of 2020.^[1] The elderly patients are not only those with an extended age but also those with reduced reserves of various physiological functions.^[2] Although some studies have focused on the long-term well-being and survival of elderly patients, the systemic research on the morbidity and mortality associated with geriatric anesthesia in China was incompletely reported. The goal of this review was to discuss the morbidity and mortality associated with geriatric anesthesia based on the reports originated in China in the recent 5 years and point out the future trend

of geriatric anesthesia, to improve the quality of geriatric anesthesia management.

MORBIDITY ASSOCIATED WITH GERIATRIC ANESTHESIA IN CHINA

Respiratory system

The respiratory complications following anesthesia are common and fatal for elderly patients. According to the investigation

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conducted by Nanjing University, the overall incidence of early postoperative pulmonary complications following total knee arthroplasty was 45.9%, and the proportions of pneumonia, pleural effusion, and atelectasis were 14.4%, 38.7%, and 12.6%, respectively.^[3] Factors contributing to the respiratory complications are summarized in Table 1.

Factors that may contribute to respiratory complications

Age is a major risk factor in elderly patients.^[4] Several clinical trials have shown that age >50 years is an independent risk factor for increased postoperative respiratory complications (odds ratio [OR] = 2.389, 95% confidence interval [CI] = 1.641–3.588, $P < 0.05$), and the

Table 1: Studies focused on respiratory complications

Study	Study type	Surgery	Gender (male/female), <i>n</i>	Interventions	Effects/risk factors identified
Jiao ^[4]	Retrospective study	–	–	–	Age, smoking, surgery time, secretion clearance, postoperative ambulatory, invasive procedure, antibiotics
Liu <i>et al.</i> ^[5]	Retrospective study	–	–	–	Age, preoperative SpO ₂ <90%, anemia, smoking >1 year, ASA III–IV, cough test (+), operative site, respiratory infection, operation duration
Wei <i>et al.</i> ^[6]	Retrospective study	Orthopedic surgery	–	–	Age, in bed >2 days, general anesthesia
Zhang <i>et al.</i> ^[7]	Prospective study	Orthopedic surgery	–	Combined general-epidural anesthesia (S) General anesthesia (C)	Pulmonary infection ↓ (S)
Xu <i>et al.</i> ^[8]	Prospective study	Gynecological surgery	–	Combined general-epidural anesthesia (S) General anesthesia (C)	SpO ₂ ↑, PaCO ₂ ↓, recovery time ↓ (S, end of extubation)
Xu <i>et al.</i> ^[9]	Meta-analysis	–	–	–	Duration of general anesthesia, normal endotracheal tube, deep intubation, unpracticed intubation >2 h, incomplete extubation indication, age >60 years, smoking history, emergent surgery, chronic respiratory disease history, thoracic or craniocerebral surgery
Wang <i>et al.</i> ^[10]	Prospective study	Orthopedic surgery	11/9 (S) 12/8 (C)	Supreme laryngeal mask (S)/tracheal intubation (C)	Pharyngalgia ↓, systolic blood pressure ↓, adrenaline ↓, norepinephrine ↓ (S, extubation)
Lu <i>et al.</i> ^[11]	Prospective study	Thoracic surgery	13/7 (S ₁) 14/6 (S ₂) 15/5 (C)	Ischemic preconditioning-DEX (S ₁) Ischemic preconditioning (S ₂) Nonischemic preconditioning and DEX (C)	PaO ₂ ↑ (S ₁ , end of surgery), pulmonary infection ↓, atelectasis ↓ (S ₁ , 7 days)
Zhang <i>et al.</i> ^[12]	Prospective study	Thoracic surgery	19/21 (S ₁) 22/18 (S ₂) 20/19 (S ₃) 19/18 (C)	DEX-CPAP (S ₁) CPAP (S ₂) DEX (S ₃) Non-DEX and CPAP (C)	Pulmonary infection ↓, atelectasis ↓ (S ₁ , 1 days), pulmonary infection ↓ (S ₁ , 7 days)
Xue <i>et al.</i> ^[13]	Prospective study	Cardiac surgery	22/8 (S) 25/6 (C)	DEX (S) NS (C)	Hypoxemia ↓, atelectasis ↓ (S, 72 h)
Ye <i>et al.</i> ^[14]	Prospective study	General surgery	–	Norepinephrine-restricted fluid therapy (S) Conventional fluid therapy (C)	Pulmonary complications ↓ (S, 14 days)
Zhao <i>et al.</i> ^[15]	Prospective study	General surgery	28/22 (S) 30/20 (C)	GDFT (S) Conventional fluid therapy (C)	Pulmonary complications ↓ (S, 19 days)
Ge <i>et al.</i> ^[16]	Prospective study	Orthopedic surgery	16/14 (S) 14/16 (C)	Protective ventilation (S) Conventional ventilation (C)	Postoperative pulmonary complications ↓ (S, 3 days)
Ji <i>et al.</i> ^[17]	Prospective study	Gynecological surgery	–	Dezocine (S) Sufentanil (C)	Apnea ↓ (S, recovery)

The groups are divided as study groups and control groups, which are abbreviated as letter S (study group) and letter C (control group). If there are more than one study group, they are numbered separately. –: The author did not mention the particular ratio; ↑: Increased; ↓: Decreased. SpO₂: Percutaneous oxygen saturation; PaCO₂: Arterial partial pressure of carbon dioxide; DEX: Dexmedetomidine; ASA: American Society of Anesthesiologists; CPAP: Continuous positive airway pressure; GDFT: Goal-directed fluid therapy; NS: Normal saline.

risk for patients >70 years old is much higher ($OR = 3.968$, $95\% CI = 2.963-4.118$, $P < 0.05$).^[5]

A retrospective study showed that, in comparison to combined spinal-epidural anesthesia, general anesthesia increased the risk of respiratory complications in elderly patients who underwent orthopedic surgery.^[6,7] These findings were corroborated by the results of big data analysis.^[8,9]

Factors that may reduce respiratory complications

The airway management may influence the incidence of respiratory complications.^[9] Compared to endotracheal intubation, the rate of pharyngalgia is significantly decreased, while the lung compliance is slightly enhanced following laryngeal mask airway.^[10]

The administration of dexmedetomidine may reduce the incidence of respiratory system complications.^[11-13] Moreover, dexmedetomidine combined with remote ischemic preconditioning may reduce the incidence of pulmonary infections by 20% ($P < 0.05$) in elderly patients who underwent thoracotomy.^[11] In addition, dexmedetomidine combined with continuous positive airway pressure (2 cm H₂O, 1 cmH₂O = 0.098 kPa) may decrease the rate of postoperative atelectasis and postoperative pulmonary infection in elderly patients who underwent esophageal cancer surgery.^[12] The rate of respiratory infection was reduced by 15% as compared to the control group.

In general surgery, the continuous infusion of norepinephrine at a rate of 0.01–0.03 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, combined with restricted fluid therapy of 5 ml·kg⁻¹·h⁻¹, may reduce the overall pulmonary complications by about 30% and pulmonary infection by about 20%.^[14]

In oncological surgery, it was shown that goal-directed fluid therapy (GDFT) based on FloTrac™/Vigileo system decreased pulmonary complications by approximately 26%.^[15]

In elderly patients undergoing general anesthesia, the method of protective lung mechanical ventilation has been proven to improve the outcome in patients with mild-to-moderate pulmonary dysfunction (restrictive, obstructive or mixed ventilatory dysfunction; clinical pulmonary infection score: 4.9±1.3 vs. 3.2±1.2, $P < 0.05$, 3 days after surgery).^[16]

Elderly patients undergoing hysteroscopic removal of intrauterine device demonstrated a reduced incidence of apnea by about 10% as a result of the application of dezocine as compared to the sufentanil group.^[17]

Furthermore, retrospective studies showed that age, smoking history, general anesthesia, and thoracic surgeries are the common risk factors for postoperative respiratory complications. Smoking may suppress the pulmonary function.^[18] The aging process leads to the decline of both pharyngeal reflex and pulmonary functional reserve, which might explicate the contribution of age as one of the risk factors. The muscle relaxants used in general anesthesia

weaken the respiratory muscles, thereby increasing the risk of aspiration and pneumonia.^[19] The pain associated with thoracic surgery may release the inflammatory factors that might suppress the pulmonary function.^[20] Thus, both laboratory and clinical studies suggested that dexmedetomidine may exert a protective effect on the pulmonary system,^[21,22] leading to a reduced incidence of respiratory complications. The ischemic preconditioning combined with dexmedetomidine might decrease the incidence of postoperative pulmonary complications by alleviating the inflammatory response and oxidation reaction, which are corroborated by the prevention of the surge of interleukin-6 (IL-6) and enhancement of the activation of superoxide dismutase.^[11] However, further studies are essential to elucidate the underlying mechanisms.

The major limitation of most of the studies is the lack of imaging evidence. The pre- and post-operative X-ray diagnosis of the respiratory system might give a strong evidence supporting the research outcome. Further studies may use the imaging technique as an universal method to help diagnose respiratory complications.

Postoperative cognitive dysfunction

Postoperative cognitive dysfunction (POCD) has a high prevalence in elderly patients after surgery and anesthesia. The overall incidence of POCD cannot be found in the database of Wanfang, China National Knowledge Infrastructure (CNKI), and VIP databases. Comparative studies on the incidence of POCD following spinal anesthesia and nerve block are yet lacking. The factors contributing to POCD are summarized in Table 2.

Factors that may contribute to postoperative cognitive dysfunction

Penicyclidine hydrochloride administration during anesthesia may increase the incidence of POCD in elderly patients in a dose-dependent manner (Mini-Mental State Examination [MMSE] score, 72 h after surgery). The dose of 0.002 mg/kg penicyclidine hydrochloride may have a similar incidence of POCD as compared to scopolamine, while the dose of 0.01 mg/kg may significantly impair the postoperative cognition.^[23]

Cohort studies showed that patients receiving general anesthesia seem to have a higher incidence of POCD compared with epidural anesthesia in patients undergoing orthopedic surgery (39% vs. 4%, $P < 0.001$, 1 month after orthopedic surgery; MMSE score 25.2 ± 2.7 vs. 26.1 ± 2.1, $P < 0.05$, 72 h after surgery).^[24,25]

A retrospective study showed that advanced age is a risk factor with an OR of 1.660 ($P < 0.05$).^[26] Some studies even pointed out that age >70 years is an independent risk factor.^[27] Prolonged anesthesia (more than 5 h) may increase the incidence of POCD in elderly patients undergoing spinal surgery compared to those undergoing spinal surgery at <5 h (relative risk = 2.223, $P < 0.05$, 7 days after surgery) according to the logistic regression.^[27]

Table 2: Studies focused on postoperative cognitive dysfunction

Study	Study type	Surgery	Gender (male/female), n	Interventions	Effects/risk factors identified
Bi <i>et al.</i> ^[23]	Prospective study	Urologic surgery Orthopedic surgery	30/0 (S ₁) 30/0 (S ₂) 30/0 (C)	Penehyclidine hydrochloride Low dose (S ₁) High dose (S ₂) Scopolamine (C)	MMSE ↓ (S ₂ , 72 h), dose dependent
Luo and Deng ^[24]	Prospective study	Orthopedic surgery	26/23 (S) 24/25 (C)	General anesthesia (S) Epidural anesthesia (C)	POCD ↑, MMSE score ↓ (S, 1 month)
Zhang <i>et al.</i> ^[25]	Prospective study	Orthopedic surgery	20/27 (S) 21/25 (C)	General anesthesia (S) Spinal epidural anesthesia (C)	MMSE score ↓ (S, 72 h)
Chen <i>et al.</i> ^[26]	Retrospective study	General surgery	–	–	Age, diabetic mellitus, hypertension
Peng <i>et al.</i> ^[27]	Retrospective study	Orthopedic surgery	–	–	S-100β ↑/age, education, anesthesia duration, intraoperative hypotension
Song <i>et al.</i> ^[28]	Prospective study	Orthopedic surgery	10/38 (S) 10/38 (C)	Second operation (S) First operation (C)	IL-6 ↑, IL-10 ↓, POCD ↑, MMSE score ↓ (S, 5 days)
Sun <i>et al.</i> ^[29]	Prospective study	Orthopedic surgery	23/25 (S) 21/27 (C)	DA (S) NS (C)	MMSE score ↑, POCD ↓ (S, 3 days)
Ge <i>et al.</i> ^[30]	Prospective study	Neurosurgery	14/5 (S) 12/7 (C)	DEX (S) NS (C)	MMSE score ↑ (S, 72 h)
Tan <i>et al.</i> ^[31]	Prospective study	Cardiac surgery	–	DEX (S) NS (C)	MMSE score ↑, POCD ↓ (S, 7 days)
Chen <i>et al.</i> ^[32]	Prospective study	General surgery	59/26 (S) 31/32 (C)	DEX (S) NS (C)	MMSE score ↑ (S, 7 days) No significant differences in MMSE score in 1 month
Lei <i>et al.</i> ^[33]	Prospective study	General surgery	24/21 (S) 20/25 (C)	Location training (S) Nonlocation training (C)	POCD ↓ (S, 7 days)

The groups are divided into study groups and control groups, which are abbreviated as letter S (study group) and letter C (control group). If there are more than one study group, they are numbered separately. –: The author did not mention the particular ratio; ↑: Increased; ↓: Decreased. IL: Interleukin; MMSE: Mini-Mental State Examination; DEX: Dexmedetomidine; NS: Normal saline; DA: Dopamine; POCD: Postoperative cognitive dysfunction; S-100β: S-100β calcium-binding protein.

Reportedly, the cognitive dysfunction in elderly patients may be increased on day 5 (10.4% vs. 2.1%, $P < 0.05$) after the second operation.^[28]

Factors that may reduce postoperative cognitive dysfunction

Compared to general anesthesia, epidural anesthesia led to an increased MMSE score in elderly patients following orthopedic surgery (26.1 ± 2.1 vs. 25.2 ± 2.7 , $P < 0.05$, 72 h after surgery).^[25]

A cohort study reported that the continuous infusion of dopamine at a rate of $5-9 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ during spinal anesthesia might reduce the incidence of POCD 7 days after orthopedic surgery as compared to those receiving normal saline (MMSE score: 25.2 ± 2.7 vs. 27.4 ± 2.0 , $P < 0.05$, 72 h after surgery).^[29]

Dexmedetomidine was shown to reduce the incidence of POCD after general, cardiac, and neurological surgeries (MMSE score: 27.6 ± 1.2 vs. 25.7 ± 1.5 , $P < 0.01$, 1 week after general surgery; 26.6 ± 1.3 vs. 25.6 ± 1.3 , $P < 0.05$, 7 days after cardiac surgery; 26.6 ± 0.8 vs. 27.2 ± 0.7 , $P < 0.05$, 72 h after neurosurgery).^[30-32]

Preoperative memory training may lower the incidence of POCD by about 20% in elderly patients (16% vs. 36%, $P < 0.05$, 1 week after surgery).^[33]

The advantage of spinal-epidural anesthesia on POCD may occur due to the influence of anesthetic agents on the central cholinergic system in addition to the decreased stress response caused by the spinal-epidural anesthesia.^[25] Some clinical studies indicated that aging and general anesthesia may be correlated with apoptotic neurodegeneration^[34] and decrease of gray matter.^[35] A previous study suggested that dexmedetomidine may prevent the expression of lipopolysaccharide-induced micro-RNA, which is associated with neuroinflammation and cognitive impairment, in adult rat brain,^[36] which supports the use of dexmedetomidine to reduce the incidence of POCD. However, these results necessitate further validation by human studies. Some cytokines may contribute to POCD: increase the concentration of IL-6 and decrease the concentration of IL-10.^[29] The dexmedetomidine may suppress the inflammation mediated by stress modulation^[37] and decrease the concentration of some cytokines, thereby further decreasing the incidence of POCD.

Present studies on POCD also have limitations. The first is that most of the studies used the MMSE score to judge whether the patient developed POCD. However, various standards for the MMSE score decrease were adopted in different studies, which makes the overall incidence of POCD not as accurate as reported. Another limitation is that the data-collecting time points differ widely among each group, which may also influence the results. Most of the studies focused on the cognitive function 72 h after surgery, a few studies focused on cognitive function 1 week or 1 month after surgery. Further studies need a universal standard to help identify patients develop POCD.

Postoperative delirium

Postoperative delirium (POD) is an acute postoperative brain dysfunction characterized by a change in cognition that cannot be optimally accounted for by a preexisting or evolving dementia time. The overall incidence of POD is about 9–87% based on the worldwide studies except China.^[38] A total of 404 cases of POD were thoroughly reported in China by the end of December 2013 according to the database of Wanfang, CNKI, and VIP databases.^[39] The rate of incidence is approximately 21.0% in Chinese patients over 65 years old undergoing total hip arthroplasty.^[40] The factors that might contribute to POD are summarized in Table 3.

Factors that may contribute to postoperative delirium

According to a logistic analysis based on the domestic studies, education ≤ 9 years ($OR = 1.83$, $95\% CI = 1.18-4.61$, $P < 0.05$), American Society of Anesthesiologists (ASA) physical status $\geq III$ ($OR = 3.68$, $95\% CI = 1.32-7.65$,

$P = 0.01$), preoperative MMSE score < 23 ($OR = 7.59$, $95\% CI = 2.77-14.32$, $P < 0.01$), and intraoperative blood transfusion > 500 ml ($OR = 1.96$, $95\% CI = 1.73-5.36$, $P < 0.05$) are independent factors associated with an increased incidence of POD in elderly patients.^[49]

A meta-analysis stated that pulmonary infection and pain might contribute to the increased incidence of POD.^[39]

Age is an independent risk factor for POD.^[39,41] Age ≥ 80 years ($OR = 1.75$, $95\% CI = 1.23-2.67$, $P < 0.05$) may significantly increase the incidence of POD.^[49]

The administration of midazolam has a high potential of causing POD than dexmedetomidine in elderly patients.^[42]

The intraoperative blood pressure fluctuation, instead of the absolute or relative hypotension, is associated with a high incidence of POD 48 h after surgery ($P > 0.05$, 2 days after surgery).^[43]

Factors that may reduce postoperative delirium

Multimodal analgesia can reduce the risk of POD as compared to monomodal analgesia (local anesthetic infiltration anesthesia combined with patient-controlled intravenous analgesia [PCIA] vs. PCIA, 30.6% vs. 11.9%, $P < 0.05$), and the emergent treatment of pain may help to alleviate POD.^[44]

Dexmedetomidine may help decrease the incidence of POD by approximately 4–10% as compared to the control group following general surgery (the confusion assessment method [CAM], 8.6% vs. 28.1%, $P < 0.05$, 12 h after surgery),^[45] orthopedic (CAM, 10% vs. 25%, $P < 0.05$,

Table 3: Studies focused on postoperative delirium

Study	Study type	Surgery	Gender (male/female), n	Interventions	Effects/risk factors identified
Yuan <i>et al.</i> ^[39]	Meta-analysis	–	–	–	Hypoxia, hypertension, pain, lung infection, age
Guo <i>et al.</i> ^[40]	Retrospective study	Orthopedic surgery	–	–	Age, albumin, blood glucose, smoking history, TBIL, CRP, surgery duration, RBC transfusion
Zhou <i>et al.</i> ^[41]	Prospective study	Gynecologic surgery	–	DEX (S) NS (C)	POD ↓ (D, 6 h)/age
Zhou <i>et al.</i> ^[42]	Meta-analysis	–	–	–	Midazolam
Ji <i>et al.</i> ^[43]	Prospective study	Laparoscopic surgery	–	–	Intraoperative blood pressure fluctuation
Li <i>et al.</i> ^[44]	Prospective study	Orthopedic surgery	25/34 (S) 22/27 (C)	Multimodal analgesia (S) Conventional analgesia (C)	POD ↓, VAS ↓ (S, 3 days)
Ma ^[45]	Prospective study	General surgery	–	DEX (S) NS (C)	POD ↓ (S, 12 h)
Zhang <i>et al.</i> ^[46]	Prospective study	Orthopedic surgery	39/41 (D) 37/43 (C)	DEX (S) Non-DEX (C)	POD ↓ (S, 24 h)
Chen and Lin ^[47]	Prospective study	Urologic surgery	–	DEX (S) Non-DEX (C)	POD ↓ (S, 3 days)
Xia <i>et al.</i> ^[48]	Prospective study	Orthopedic surgery	–	DEX (S ₁) DEX (S ₂) NS (C)	POD ↓, Glu ↓, Cor ↓, IL-6 ↓ (S ₁ , S ₂ , 48 h)

The groups are divided into study groups and control groups, which are abbreviated as letter S (study group) and letter C (control group). If there are more than one study group, they are numbered separately. –: The author did not mention the particular ratio; ↑: Increased; ↓: Decreased. TBIL: Total bilirubin; RBC: Red blood cell; POD: Postoperative delirium; CRP: C-reactive protein; VAS: Visual analog scale; Cor: Cortisol; Glu: Serum glucose; IL: Interleukin; DEX: Dexmedetomidine; NS: Normal saline.

24 h after surgery),^[46] gynecological (CAM, 3% vs. 30%, $P < 0.05$, 6 h after surgery),^[41] and urologic surgery (CAM, 0% vs. 6.7%, 3 days after surgery)^[47] while the effect is dose dependent (CAM, low dosage vs. high dosage, 5% vs. 20%, $P < 0.05$).^[48]

The aging process may influence the central nervous system,^[50,51] leading to different reactions to anesthetic agents in elderly patients,^[52] which might affect the incidence of POD. The risks posed by the loss of the central cholinergic neurons^[53] and the disruption of a wide variety of neurotransmitter systems including melatonin, norepinephrine, and lymphokines, in addition to the increased age, may synergistically contribute to the high incidence of POD in elderly patients.^[54] The analgesic treatment can relieve the undesired sympathetic reaction that might decrease the incidence of neurotransmitter dysfunction. The dexmedetomidine is a highly selective α_2 agonist, activating the nucleus coeruleus in the spinal cord, which in turn might suppress the release of norepinephrine and cease the transmission of pain signals and relieve the anxiety.^[55] This phenomenon might reduce the incidence of central nervous system dysfunction, including POD.

Compared with POCD, all the data on POD were collected within 3 days after surgery, making the overall incidence

of POD as accurate as possible. However, present studies on POD also have limitations. First, most of them are retrospective studies and few prospective studies could be found. Another limitation is that the education background of the patients was not controlled strictly in different studies. Further studies need to set up a universal standard to help to identify the mental status of POD.

Cardiovascular system

The cardiovascular complications are major morbidities adversely affecting the postoperative outcome in elderly patients. Hypertension, coronary artery disease, carotid artery stenosis, heart valve disease, and cardiac arrhythmia are common co-existing diseases in elderly patients. The overall rate of cardiovascular complications during the perioperative period in China has not been reported in the database of Wanfang, CNKI, and VIP. The factors contributing to cardiovascular complications are summarized in Table 4.

Factors that may contribute to cardiovascular complications

A retrospective study listed the history of unstable cardiac angina within 6 months ($OR = 4.943$, $95\% CI = 1.232-19.814$, $P = 0.024$), hematocrit $< 35\%$ before surgery ($OR = 3.292$, $95\% CI = 1.148-9.443$, $P = 0.027$), preoperative

Table 4: Studies focused on cardiovascular complications

Study	Study type	Surgery	Gender (male/female), n	Interventions	Effects/risk factors identified
Liu <i>et al.</i> ^[56]	Retrospective study	–	–	–	Unstable cardiac angina < 6 months, preoperative Hct $< 35\%$, preoperative arrhythmia, ventricular wall motion abnormality
Zhang <i>et al.</i> ^[57]	Prospective study	General surgery	–	ESH/ESC I (S ₁) ESH/ESC II (S ₂) ESH/ESC III (S ₃) Nonrisk factors (C)	Myocardial ischemia \uparrow (S ₁ , S ₂ , S ₃ ; 24 h, 48 h after surgery)
Shan <i>et al.</i> ^[58]	Case report	Cardiac surgery	–	–	Circulation load \uparrow (anxiety emotion)
Lu <i>et al.</i> ^[60]	Prospective study	Orthopedic surgery	6/14 (S ₁) 9/11 (S ₂) 8/12 (C)	DEX (S ₁) DEX (S ₂) NS (C)	Postoperative cardiovascular events \downarrow (S ₁ , S ₂)
Lv <i>et al.</i> ^[61]	Prospective study	General surgery	–	DEX (S) NS (C)	Tachycardia \downarrow , hypertension \downarrow , ST segments depression \downarrow (S)
Li <i>et al.</i> ^[62]	Prospective study	Thoracic surgery	9/6 (S) 8/7 (C)	Cardiac index-stroke volume index-stroke volume variation (S) Central venous pressure (C)	Hypertension \downarrow , arrhythmia \downarrow , myocardial ischemia \downarrow (S)
Zeng <i>et al.</i> ^[63]	Prospective study	General surgery	31/9 (S) 29/11 (C)	GDFT (S) Conventional fluid therapy (C)	Hypotension events \downarrow (S)
Liu <i>et al.</i> ^[64]	Prospective study	–	–	–	Cardiovascular responses \downarrow (lidocaine superficial anesthesia, intubation)
Liu and Zheng ^[65]	Review	–	–	–	Cardiovascular events \downarrow (antihypertensive therapy)

The groups are divided into study groups and control groups, which are abbreviated as letter S (study group) and letter C (control group). If there are more than one study group, they are numbered separately. –: The author did not mention the particular ratio; \uparrow : Increased; \downarrow : Decreased. ESH: European Society of Hypertension; ESC: European Society of Cardiology; Hct: Hematocrit; GDFT: Goal-directed fluid therapy; DEX: Dexmedetomidine; NS: Normal saline.

arrhythmia ($OR = 3.207$, $95\% CI = 1.030-9.963$, $P = 0.044$), and ventricular wall motion abnormality ($OR = 3.907$, $95\% CI = 1.115-13.691$, $P = 0.033$) as risk factors.^[56]

In elderly patients with hypertension, the perioperative rate of myocardial ischemia and arrhythmias was 9.5–40.5% and 28.6–92.9%, respectively, as compared to elderly patients with normal blood pressure.^[57]

Anxiety in elderly patients has been shown to increase the risk of cardiovascular complications.^[58] Anxiety and depression may decrease the levels of adiponectin and aggravate the endothelial dysfunction in patients with coronary artery disease.^[59]

Factors that may reduce cardiovascular complications

Studies showed that the continuous infusion of dexmedetomidine at a rate of 0.25 µg/kg and 0.5 µg/kg for 15 min before anesthesia induction may reduce the incidence of cardiac complications by 45% in orthopedic surgery.^[60] Dexmedetomidine also reduces the incidence of ST-segment depression (≥ 0.05 mV) in patients with coronary artery disease undergoing abdominal surgery.^[61]

Cohort studies have shown that GDFT decreases the rate of cardiovascular complications by at least 18% both in general and thoracic surgeries and shortens the duration of Intensive Care Unit stay by at least 1 day.^[15,62] Another cohort study showed that it provides a more stable perioperative hemodynamic profile in general surgery.^[63]

The intravenous lidocaine was useful for attenuating cardiovascular response to intubation compared to placebo, while the cardiovascular stress responses were blunted by the lidocaine throat superficial anesthesia (1.5 mg/kg).^[64]

For elderly patients with systolic pressure >160 mmHg (1 mmHg = 0.133 kPa), most of the studies demonstrated that antihypertensive therapy may reduce the risk of cardiovascular events according to a review published in the recent years while studies regarding more strict targets yielded mixed findings.^[65]

Patients with preoperative cardiovascular comorbidities could putatively suffer from postoperative cardiovascular complications due to the functional and morphological changes in the heart. The GDFT includes factors of central venous pressure (8–12 cm H₂O), mean arterial pressure (65–90 mmHg), and urinary production (≥ 0.5 ml/kg), focusing on the cardiac index and central venous blood saturation.^[66] Compared with conventional fluid therapy, which only cares about the blood pressure, heart rate, or follows the 4/2/1 rules, the GDFT improves the postoperative outcome and maintains an appropriate volume state via individualized fluid administration mediated by the targeted value to fulfill the altering demand for volume,^[67] which may further decrease the cardiovascular complications.

However, a major limitation is that, the definition of cardiac events varied widely among online studies. ST-segment was used as the indicator of cardiovascular events in some studies^[56,61]

while some studies used the hemodynamic parameters as the indicators for cardiovascular complications,^[62,63] which may cause different outcomes. Another limitation is that the physical status of the patients varied widely in different studies, which may make the overall incidence hard to report. Further studies need to set up a universal standard to help identify cardiovascular complications.

Renal system

The complications of renal system include urinary tract infection and acute kidney injury (AKI). Reportedly, the overall incidences of renal complications are absent from the database of Wanfang, CNKI, and VIP databases. However, studies focusing on cardiac surgery revealed that the incidence of AKI in elderly patients undergoing cardiac surgery was approximately 61.5–63.8%.^[68,69]

Factors that might contribute to renal complications

Furosemide is widely used by anesthesiologists when intraoperative oliguria is encountered; mannitol is commonly used in neurosurgical patients. However, both diuretic agents have been reported to possess renotoxicity.^[70,71]

Factors that might reduce the renal complications

In diabetic patients undergoing hepatic cancer resection, the anesthesia maintained with sevoflurane might lead to a decreased level of serum cystatin C at 24 h and 72 h and urinary microalbuminuria at 24 h following surgery as compared to propofol. This phenomenon suggested that combined intravenous-inhalational anesthesia with sevoflurane may reduce the risk of AKI in diabetic patients undergoing liver cancer resection.^[72] In liver transplantation, serum concentrations of creatinine, blood urea nitrogen, and β_2 -microglobulin were significantly decreased at the end of surgery in the combination of intravenous-inhalational anesthesia with sevoflurane, suggesting that the severity of kidney injury was reduced compared to propofol-sulfentanil anesthesia.^[73]

In elderly patients undergoing cardiac surgery, the early postoperative usage of angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker or diuretics is associated with a lower incidence of AKI as compared to the control group (46.1% vs. 66.2%, $P < 0.001$; 57.0% vs. 89.8%, $P < 0.001$, respectively) following cardiac surgery with extracorporeal circulation.^[68]

Nevertheless, only a few studies could be found in the online database focusing on postoperative renal function in elderly patients. Considering the potential kidney injury, diuretics should be used only when the other approaches have failed, when oliguria occurs during the anesthesia period.

MORTALITY ASSOCIATED WITH GERIATRIC ANESTHESIA

The annual mortality associated with anesthesia was reported as 1/50,000–1/30,000 in China, with some tertiary referral hospitals up to 1/200,000.^[74] However, nationwide reports for geriatric anesthesia-associated mortality are yet lacking. The factors that potentially contribute to perioperative mortality are summarized in Table 5.

Some retrospective studies in orthopedic surgery showed that the 1-year postoperative mortality in elderly Chinese population is 16.0–24.8%,^[75-78] while the difference in anesthesia methods (regional anesthesia vs. general anesthesia, $P < 0.05$) may have impacted the mortality.^[76] Another retrospective study revealed that patients undergoing ovarian serous adenocarcinoma surgery with general anesthesia had a lower survival rate at 1, 3, and 5 years as compared to those administered epidural anesthesia (78% vs. 96%, 58% vs. 78%, and 49% vs. 61%, general anesthesia vs. epidural anesthesia, respectively).^[79] The senior age and high ASA physical status score refer to a poor physical condition, especially in elderly patients, which might contribute to the increased mortality.

Several studies claimed that the ASA physical status might influence the mortality in elderly patients, and a higher ASA physical status score (ASA III–IV) might contribute to a higher mortality than a lower ASA physical status score.^[76,80]

Furthermore, a retrospective study showed that patients with higher preoperative systolic pressure (>120 mmHg) and postoperative systolic pressure (>120 mmHg) were predisposed toward a low 3-year disease-free survival (67.2 vs. 82.1%, $P < 0.05$) and cancer-specific survival (81.9 vs. 94.8%, $P < 0.01$) in both patients ≥ 60 years old and <60 years old.^[81]

The major limitation is that, although there are studies focused on the risk factors of long-term survival, the overall

survival rate might not simply depend on the anesthesia method, but also influenced by the disease and the physical status of the patients. In cancer resection surgeries, some studies indicated that the surgical outcome can be affected by multiple factors, so it is difficult to draw a conclusion for all cancer types, and there is no obvious evidence showing that simple alternation in the anesthesia technique would have a remarkable positive effect on postoperative survival of patients with cancer.^[82] The mortality of anesthesia should be further investigated.

FUTURE TREND OF GERIATRIC ANESTHESIA IN CHINA

The aging of the population in China is predominant. According to the precision medicine concept, modern anesthesia needs to be individualized instead of stereotyped, especially in the field of geriatric medicine. Elderly patients might survive from anesthesia and surgical process, yet the short- and long-term complications are high due to various postoperative complications, thereby mandating the anesthesiologists to focus not only on the surgical process but also on the perioperative care.^[83,84] Based on the background of perioperative medicine, the following trends of geriatric anesthesia are summarized in Table 6.

1. Pushing the transformation from geriatric anesthesia to perioperative geriatric medicine: The perioperative anesthetic management should focus on the reduction of morbidity and mortality in elderly patients. The future key points should include preoperative evaluation of

Table 5: Studies focused on postoperative mortality in elderly patients

Study	Study type	Disease	Gender (male/female), <i>n</i>	Mortality	Risk factors identified
Sun <i>et al.</i> ^[75]	Retrospective study	Intertrochanteric fracture	94/203	1 year, 16.0%	Age, gender, comorbidities, ASA physical status, duration from trauma to surgery, length of hospital stay
Li <i>et al.</i> ^[76]	Retrospective study	Hip fracture	18/12	1 year, 16.3%	Age, gender, fracture location, ASA physical status, comorbidities, preinjury mobility, COPD, stroke sequelae, anesthesia methods, complications
Li <i>et al.</i> ^[77]	Retrospective study	Hip fracture	18/22	1 year, 16.3%	Age, gender, fracture type, ASA physical status, comorbidities, preinjury mobility, COPD, anesthesia methods, complications
Feng and Shen ^[78]	Retrospective study	Hip fracture with poststroke hemiplegia	20/5	1 year, 24.8%	Gender, ASA physical status, comorbidities, ambulatory status before fracture, cognitive ability, chronic respiratory disease
Lin <i>et al.</i> ^[79]	Retrospective study	Ovarian serous Adenocarcinoma	–	1 year, 4% (E) 22% (G) 5 years, 39% (E) 51% (G)	Anesthesia methods, preoperative CA125 status, histological grade, residual macroscopic tumor, lymphatic metastasis
Liu <i>et al.</i> ^[80]	Prospective study	Femoral neck fracture	14/18	30 days, 21.2% (male) 11.9% (female) 1 year, 23.5%	Age ≥ 85 years, ICU admission, gender, preoperative comorbidities, postoperative complications, ASA physical status
Yu <i>et al.</i> ^[81]	Prospective study	Rectal cancer	–	3 years, 32.8% (high SBP) 17.9% (low SBP)	Age, comorbidities, preoperative blood pressure (mmHg)

The gender ratio refers to patients who did not survive. –: The author did not mention the particular ratio. E: Epidural anesthesia; G: General anesthesia; ASA: American Society of Anesthesiologists; SBP: Systolic blood pressure; COPD: Chronic obstructive pulmonary disease; CA125: Carcino-embryonic antigen 125; ICU: Intensive Care Unit.

Table 6: Specific suggestions on the future trend of the geriatric anesthesia

Study	Study type	Current status	Future trend	Suggestions
Liu and Xiong ^[83]	Viewpoint	Geriatric anesthesia	Perioperative geriatric medicine	Preoperative evaluation
Grocott and Mythen ^[84]	Review	Geriatric anesthesia	Perioperative geriatric medicine	ERAS-oriented cooperation
Wang and Wang ^[85]	Review	Geriatric anesthesia	Perioperative geriatric medicine	Rational drugs application Multiorgan protection Practical closed loop administration system
Gu <i>et al.</i> ^[86]	Case report	Traditional practice	Visualized practice	Video-assisted laryngoscope
Yu <i>et al.</i> ^[87]	Prospective study	Traditional practice	Visualized practice	Ultrasound
Zhang and Xu ^[88]	Review	Independent AIMS	Information sharing	Improve present independent AIMS

ERAS: Enhanced recovery after surgery; AIMS: Anesthesia information management system.

elderly patients, multi-department cooperation based on the principle of enhanced recovery after surgery, perioperative safe drug application, and multiorgan protection strategies^[85]

- Transforming from traditional anesthesia practice to visualized clinical practice: The application of ultrasound and video laryngoscope rendered a visualization of the conventional anesthesia process, especially in the management of difficult airways^[86] and regional anesthesia.^[87] The success rates of various procedures have been remarkably enhanced. To generalize the skill of anesthesiologists, the local medical association should set up an education center for visualization of regional anesthesia, as well as highlight the training course at the local hospitals
- The anesthesia information management system in each hospital is largely independent, thereby rendering difficulty in data integration.^[88] Thus, with the background of perioperative medicine, the large national database for perigeriatric anesthesia is essential. In 2015, the geriatric anesthesia group of the Chinese Society of Anesthesiologists had already set up the north and south centers for the large database of perioperative period of elderly patients. Therefore, the national medical information would be integrated to provide evidence for improving the short- and long-term survival in elderly patients.

CONCLUSIONS

Anesthesiologists should carefully evaluate the physiological and medical status, as well as focus on the prevention of potential complications in the perioperative setting. The complications in POCD and POD were largely reported, while only a few studies addressed the complications of renal system. Clinical studies are essential to systemically investigate the outcome of geriatric anesthesia in China to guide the practice and transform it into perioperative geriatric medicine in the future. Thus, a large database is needed to improve the short- and long-term survival of elderly patients by enhancing their long-term well-being and improving the quality of survival.

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Conflicts of interest

There are no conflicts of interest.

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