Multidisciplinary modulation of perioperative brain status is pivotal to perioperative brain health in elderly patients

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[Abstract] Preservation of perioperative brain health in elderly patients indicates maintaining the postoperative geriatric brain function at the preoperative basal level or even improve it through preoperative screening, diagnosis and optimization of treatment, intraoperative systematic surveillance, management and preventive measures, as well as postoperative active prevention, early recognition and timely intervention of complications. Therefore, perioperative management of geriatric brain status requires the participation of multidisciplinary experts to form a new medical model and clinical management pathway, including: (1) Establishing a perioperative geriatric multidisciplinary assessment center for screening neuropsychiatric diseases and sleep disorders that may impact their perioperative brain health; (2) Building geriatric comorbidity ward in which multidisciplinary experts participate in optimizing the geriatric brain health status before operation; (3) Systematically designing perioperative management program and clinical pathway to reduce the impact of intraoperative factors deleterious to the brain; (4) Closely monitoring the neuropsychiatric and sleep status after operation, and taking preventive, early detection and treatment measures; (5) Following up after discharge to ensure the postoperative brain function of elderly patients works well in family and the society.
[Key words] Elderly patients; Perioperative period; Brain; Interdisciplinary Communication
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Elderly patients often have multiple comorbidities, including neuropsychiatric diseases and sleep disorders, and their brains are more fragile. They are prone to various complications (including neuropsychiatric complications) and even death after undertaking anesthesia and surgery [1-2]. Preservation of perioperative brain health in elderly patients indicates maintaining the geriatric brain function at the preoperative baseline level or even improving it by preoperative screening, diagnosis and optimization of treatment, intraoperative systematic surveillance, management and preventive measures, as well as active postoperative prevention, early detection and timely intervention of the complications. The goal is to enable the elderly to maintain their brain function which meets the needs to return home and society after undergoing surgical treatment [3].

The diagnosis, prevention and treatment of neuropsychiatric diseases and sleep disorders for elderly patients require multidisciplinary involvement. Similarly, to achieve the goal of perioperative brain health in elderly patients also requires the participation of multidisciplinary experts. Thus, the traditional medical model and clinical pathway should be changed into the new ones with the following aspects.

1. A perioperative multidisciplinary assessment center for elderly patients should be established for screening neuropsychiatric diseases and sleep disorders that may impact their perioperative brain health. The elderly patients with surgical indications confirmed by the surgeon, should be transferred to the center to receive a systematic and comprehensive assessment for general conditions other than surgical diseases, including cognitive function, neuropsychiatric diseases and other concomitant diseases, present treatment, nutritional status, fragility, independency and sleep quality[4-5]. For example, the coexistence of preoperative depression, anxiety, and sleep disorders can be identified through psychological screening. The coexistence of cerebrovascular diseases, Alzheimer's disease, Parkinson's disease, cognitive impairment and peripheral neurological diseases can be confirmed through neurological system screening. If the diagnosis of neuropsychiatric disorders and/or sleep disorders is confirmed and the disorder is well controlled, perioperative clinical management plan should be made to guide perioperative management am reduce related complications [6].

If neuropsychiatric disorder is newly diagnosed after screening or it is not well controlled, the patient should be transferred to comorbidity ward for further diagnosis and treatment. By introducing a perioperative research platform with full data link and assistant decision-making system, the geriatric perioperative multidisciplinary assessment center can offer the perioperative multidisciplinary physicians and related teams more relevant clinical management guidance.

2. By establishing geriatric comorbidity ward, multi-disciplinary experts can participate in optimizing the brain health status for elderly patients before operation. Evidence from previous studies indicated [7-8] that for elderly patients with pre-existing neuropsychiatric diseases and sleep disorders, if preoperative diagnosis and optimization of treatment were not made, the incidence of postoperative neuropsychiatric complications and mortality would be significantly increased, and their long-term postoperative brain health status and ability to return to society and family will be also impaired. Therefore, patients confirmed by preoperative multidisciplinary expert evaluation with uncontrolled neuropsychiatric diseases or sleep disorders should be admitted to a geriatric comorbidity ward firstly. After receiving further diagnosis and optimized treatment by the specialists of neurology, taking psychiatry or sleep medicine, and getting re-evaluation and confirmation of improved brain health status, they can be transferred to a surgical ward for surgical treatment [9]. For elderly patients receiving preexisting medication or medical device treatment, the therapy should be maintained or optimized as necessary.

3. The perioperative management plan and clinical pathway should be designed systematically to reduce the impact of intraoperative factors deleterious to the brain. After being notified of the patient's coexisting neuropsychiatric and sleep disorders and existing treatment, anesthesiologists should communicate with the surgeon and educate the patients and their families adequately, and develop corresponding surgical plan pertinent to the risk of their potential postoperative complications.

The nursing team should make corresponding nursing plan according to the preoperative neuropsychiatric diseases and sleep status. Special attention should be paid to continuing or withholding previous medication. When planning for restarting the drug therapy postoperatively, the patient's cognitive condition and implementation ability should be considered to ensure the drug will be taken with the proper dose and at the right time. For the patients with preoperative depression or mental disorders, the preoperative and postoperative safety measures must be taken. For the patients with preoperative sleep disorders, special attention should be paid to their sleeping environments.

During preoperative visits, the anesthesiologists should examine the patient's preoperative neuropsychiatric diseases and sleep disorders thoroughly, and communicate fully with the patients. Many intraoperative factors may exacerbate postoperative neurological, mental, psychological and sleep disorders. For the high-risk patients with definitive diagnosis and treatment, adequate monitoring, early warning and systematic management measures should be taken based on the perioperative decision-making suggestions from the multidisciplinary experts, so as to reduce the harmful stress to the brain during surgery and to reduce the incidence and severity of cerebral complications after surgery. For patients taking neuropsychiatric drugs preoperatively, special attention should be paid to the possible effects during emergence period from anesthesia, and consultation to the specialists on intraoperative management should be made if necessary.The key to maintain brain function during operation depends on the anesthesiologist's effort to protect the brain from the harmful intraoperative stimulations. To enable postoperative recovery of the geriatric brain function as soon as possible, the following efforts should be made, including avoiding the neurotoxicity of anesthetics, controlling pain effectively, prevention of hypoperfusion caused by anesthesia and surgery and suppression of the neuroinflammation from excessive systemic inflammatory reaction [10].

4. After operation, the neuropsychiatric and sleep status should be monitored closely. Preventive, as well as early detection and treatment measures should be taken. 48-72 hours after surgery is the high-risk period for the development of neuropsychiatric, psychological and sleep complications in the elderly. During this period, close monitoring by PACU, ICU and ward nurses is very important. The surgeons and specialist should be informed of the early signs and symptoms as soon as possible, so that prompt diagnosis and treatment can be made. Noisy ward environment, painful stimuli, activity restrictions due to various catheters, sleep disorder and delayed food and drink intake may provoke deterioration of preexisting disease [11-12]. Prevention, control and elimination of these predisposing factors as early as possible are critical to reduce the incidence of postoperative mental, neurological, psychological and sleep disorders. Preoperative neuropsychiatric medications should be resumed as soon as possible after surgery to avoid the delay of postoperative recovery by the preexisting diseases. Special nursing care should be given to the high-risk elderly patients with neuropsychiatric or sleep disorders. If possible, they should be accommodated into an independent room accompanied with family members or long-term care worker, to reduce their psychological stress and accelerate the postoperative recovery process.

5. After discharge, the patients should be followed up to ensure that their postoperative brain function works well in family and social life. Surgical treatment mainly aims at specific disease while maintaining perioperative brain health is a prerequisite to ensure long-term healthy life for elderly patients after surgery. Therefore, multiple postoperative follow-up approaches including hospital visit, APP, telephone follow-up and family communication should be established to assess the long-term postoperative brain health status of the patients. This step is crucial for improving the clinical management of perioperative brain health. The ultimate goal is to ensure that the geriatric brain function is superior to their preoperative status and meets the needs to return to family and society after undergoing anesthesia surgical stress.

We believe that the release of the Chinese Multidisciplinary Expert Consensus on Perioperative Brain Health in Elderly Patients will play an important role in improving postoperative long-term brain health and quality of life for Chinese elderly patients.

Conflict of interest All authors declare that there is no conflict of interest.

Reference

[1] Manku K, Bacchetti P, Leung JM. Prognostic significance of postoperative in-hospital complications in elderly patients. I. Long-term survival [J]. Anesth Analg, 2003, 96(2): 583-589, table of contents.DOI:10.1213/00000539-200302000-00051.

[2] Oresanya LB, Lyons WL, Finlayson E. Preoperative assessment of the older patient: a narrative review[J]. Jama, 2014, 311(20): 2110-2120.DOI:10.1001/jama.2014.4573.

[3] Gorelick PB, Furie KL, Iadecola C, et al. Defining optimal brain health in adults: a presidential advisory from the American Heart Association/American Stroke Association[J]. Stroke, 2017, 48(10): e284-e303.DOI:10.1161/str.0000000000000148.

[4] Chinese Medical Association Geriatrics Branch, Department of Geriatrics, PLA General Hospital. Chinese expert suggestion on preoperative evaluation of elderly patients (2015) [J]. Chinese Journal of Geriatrics, 2015, 34(11): 1273-1280. DOI: 10.3760/cma.j.issn.0254-9026.2015.11.033.

[5] Mohanty S, Rosenthal RA, Russell MM, et al. Optimal perioperative management of the geriatric patient: a best practices guideline from the American College of Surgeons NSQIP and the American Geriatrics Society[J]. J Am Coll Surg, 2016, 222(5): 930-947. DOI:10.1016/j.jamcollsurg.2015.12.026.

[6] McGory ML, Kao KK, Shekelle PG, et al. Developing quality indicators for elderly surgical patients[J]. Ann Surg, 2009, 250(2): 338-347. DOI:10.1097/SLA.0b013e3181ae575a.

[7] Rudolph JL, Jones RN, Levkoff SE, et al. Derivation and validation of a preoperative prediction rule for delirium after cardiac surgery[J]. Circulation, 2009, 119(2): 229-236. DOI: 10.1161/circulationaha.108.795260.

[8] Ansaloni L, Catena F, Chattat R, et al. Risk factors and incidence of postoperative delirium in elderly patients after elective and emergency surgery[J]. Br J Surg, 2010, 97(2): 273-280.DOI:10.1002/bjs.6843.

[9] Aldecoa C, Bettelli G, Bilotta F, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium[J]. Eur J Anaesthesiol, 2017, 34(4): 192-214.DOI:10.1097/eja.0000000000000594.

[10] Li Y, Zhao L, Fu H, et al. Ulinastatin suppresses lipopolysaccharide induced neuro-inflammation through the downregulation of nuclear factor-κB in SD rat hippocampal astrocyte[J]. Biochem Biophys Res Commun, 2015, 458(4): 763-770.DOI:10.1016/j.bbrc.2015.01.155.

[11] Anesthesiology Group of Elderly, Chinese Society of Anesthesiology, Chinese Medical Association. Guideline on perioperative anesthesia management for elderly patients in China[J]. International Journal of Anesthesiology and Resuscitation, 2014, 35 (10): 870-881, 901. DOI:10.3760/cma.j.issn.1673-4378. 2014.10.002.

[12] Su X, Meng ZT, Wu XH, et al. Dexmedetomidine for prevention of delirium in elderly patients after non-cardiac surgery: a randomised, double-blind, placebo-controlled trial[J]. Lancet, 2016, 388(10054): 1893-1902. DOI: 10.1016 / s0140-6736(16)30580-3.

Chinese Multidisciplinary Expert Consensus of Perioperative Brain Health in Elderly Patients (I)

Overview

I. Background of the Expert Consensus

China has a rapidly aging population. By the end of 2017, the percentage of population aged 60 and over in China has exceed more than 17%, reaching 244 million. The increase in the aging population has posed arising challenge to health care, social security and quality of life[1]. The number of elderly patients with surgical indications has increased dramatically. Their decreased physiological functions as well as multiple chronic diseases lead to higher postoperative morbidity and mortality [2-3]. This poses challenges to perioperative anesthetic management of the elderly and restrains the elderly with surgical indications from surgery. Perioperative cerebral complications are common in the elderly [4-5], which significantly affect the postoperative outcome and long-term quality of life, and increase family and social expenditures. Therefore, it is imperative to implement perioperative brain protection and brain health strategies for elderly patients.

Preservation of perioperative brain health in elderly patients calls for the participation of multiple disciplines. By playing expertise of each discipline and jointly developing corresponding clinical management pathway, the goal of maintaining perioperative brain health and improving the long-term life quality for elderly patients can be achieved. Perioperative brain health management for elderly patients is the manifestation of the evolution from anesthesiology to perioperative medicine and the evolution from geriatric anesthesiology to perioperative geriatrics.

II. The Definition and Scope of Perioperative Brain Health in Elderly Patients
A heath brain means that the structure and function of the brain are in good condition, and the brain is able to adapt and adjust to the changes of internal and external environment. Perioperative brain health strategy for the elderly involves preoperative screening and diagnosis of brain diseases and optimization of brain function, intraoperative monitoring, early warning and management of brain dysfunction, as well as postoperative monitoring brain function and early intervention of complications through the cooperation of multidisciplinary physicians so as to minimize the damage of perioperative factors to the brain. The final goal is maintaining the brain function of the elderly at the preoperative level or even improving it despite of perioperative stress, and enabling them to return to their families and society.

The scope of perioperative brain health in elderly patients includes not only the preoperative concomitant brain diseases, such as ischemic cerebrovascular disease, Parkinson's disease, Alzheimer's disease, but also the common mental and psychological diseases (such as depression and anxiety) and preexisting sleep disorders, but also the new-onset brain complications after anesthesia and surgical stress, such as acute stroke, postoperative delirium, postoperative cognitive dysfunction [6] and postoperative psychiatric problems (such as depression and anxiety) and sleep disturbances. Through preoperative assessment and intervention, intraoperative dynamic monitoring and preservation strategy of brain function, and early postoperative screening and intervention of brain complications and mental disorders, this consensus aims to achieve the final goal of maintaining perioperative brain health in elderly patients.

Ischemic Cerebrovascular Disease

I. Ischemic Cerebrovascular Disease and Its Incidence
Cerebrovascular disease is characterized by high incidence, high recurrence rate (17.7%), high disability rate and high mortality. In the UK, there are 152,000 new cases of stroke and 46,000 transient ischemic attacks (TIAs) annually [7]. In China, cerebrovascular disease is the first leading cause of disability and the third leading cause of death. Due to the increasing aging population, cerebrovascular diseases are the key threats to the health status of the elderly.

According to "Chinese Classification of Cerebrovascular Diseases 2015" of the Chinese Society of Neurology, cerebrovascular diseases are divided into: (1) ischemic cerebrovascular disease, including transient ischemic attack, cerebral infarction (acute ischemic stroke), intracerebral steal phenomenon and chronic cerebral ischemia; (2) hemorrhagic cerebrovascular disease, including subarachnoid hemorrhage, cerebral hemorrhage, and other intracranial hemorrhage; (3) atherosclerosis, stenosis, or occlusion of the head and neck (not resulting in cerebral infarction); (4) hypertensive encephalopathy; (5) intracranial aneurysm; (6) intracranial vascular malformation; (7) cerebral vasculitis; (8) other cerebrovascular diseases; (9) intracranial venous system thrombosis; (10) cerebrovascular disease without acute focal neurological deficit symptoms; (11) sequelae of stroke; (12) vascular cognitive impairment; and (13) post stroke disorder [8]. This consensus focuses on ischemic cerebrovascular disease, the most common cerebrovascular disease in the population [9].

Ischemic stroke was the most common perioperative stroke. According to pathogenesis, about 62% are embolic cerebral infarction, 3% are lacunar infarct, 1% are cerebral thrombosis, and 9% are cerebral hypoperfusion cerebral stroke [10-12]. From 2004 to 2013, the incidence of perioperative acute ischemic stroke increased from 0.52% to 0.77% [13], forming an important risk factor of perioperative morbidity and mortality.

II. Preoperative Management of Patients with Concomitant Ischemic Cerebrovascular Disease

For elderly patients with symptomatic cerebrovascular disease within 6 months before surgery, cerebrovascular disease screening and corresponding treatment can be performed according to the following procedure (Figure 1) [14]. According to the 2014 non-cardiac guidelines of European Society of Cardiology (ESC)/European Society of Anesthesiology (ESA), revascularization is recommended within 12 weeks in patients with symptomatic carotid lesions, and revascularization within the first two weeks after symptom onset is most beneficial.

Before elective non-cardiac surgery, revascularization is recommended within 12 weeks after the onset of symptoms in patients with carotid stenosis greater than 50%. It is unnecessary to preform carotid imaging in patients without neurological symptoms and signs [7, 14–16].

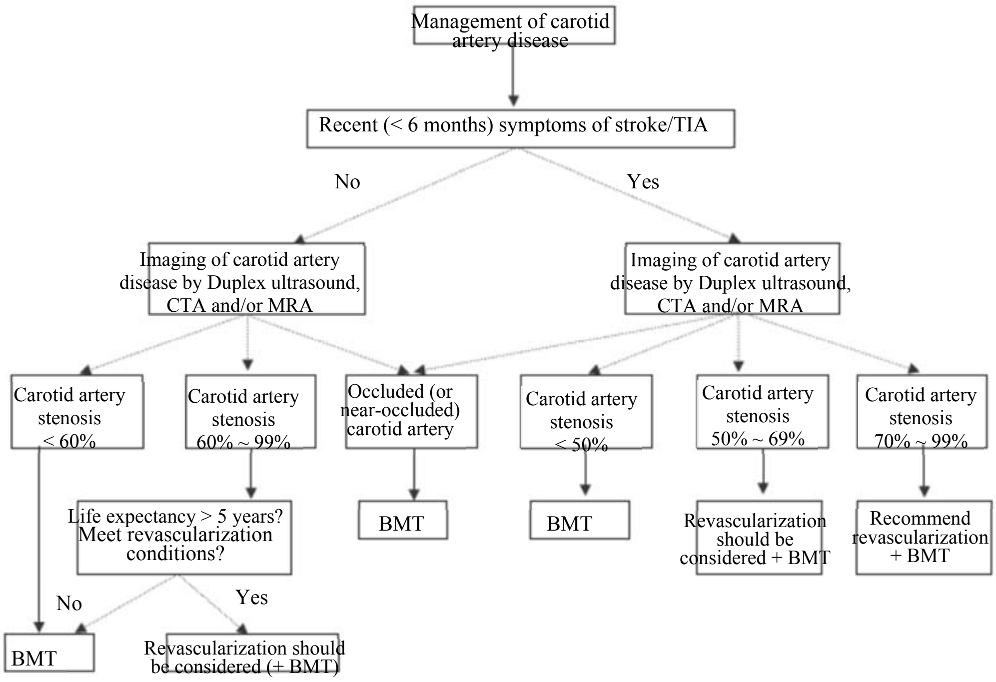
If a hospital can't provide carotid artery revascularization that the patient needs, it is necessary to fully discuss the risk of perioperative acute stroke with the patients and the families preoperatively, initiate secondary prevention such as antiplatelet drugs, anticoagulants, antihypertensive drugs and statins before operation, develop the perioperative antiplatelet and/or anticoagulant therapy strategy, balance the risk of thrombosis and surgical bleeding, and reinforce cardiovascular and cerebral function monitoring preoperatively to maintain stable cerebral perfusion.

III. Preoperative Assessment of Patients with Concomitant Ischemic Cerebrovascular Disease

(I) Risk factors for perioperative stroke

Preoperative risk factors include: (1) patient's own factors that cannot be intervened: such as advanced age (> 70 years), gender (female); (2) intervenable factors (i.e., preoperative comorbidities): including hypertension, diabetes, renal insufficiency [serum creatinine (Cr) > 2 mg/dl or Cr >177 μmol/L], smoking, chronic obstructive pulmonary disease (COPD), peripheral vascular disease, heart disease (coronary heart disease, arrhythmia, heart failure), left ventricular systolic dysfunction (ejection fraction < 40%), history of stroke or TIA, carotid stenosis (especially symptomatic), ascending aortic atherosclerosis (in patients undergoing cardiac surgery), abrupt interruption of antithrombotic drugs before surgery, hypercholesterolemia and hyperlipidemia [17–18].

Intraoperative risk factors include: (1) surgical factors: types of surgery (for example, the risk of perioperative stroke is lower in coronary angioplasty than coronary artery bypass grafting), long duration surgeries, cardiac surgeries with cardiopulmonary bypass and prolonged aortic cross-clamping, and surgeries at the site of aortic atherosclerosis;



Note: TIA: transient ischemic attack; CTA: CT angiography; MRA: magnetic resonance angiography; BMT: best medical therapy

Figure 1 Management Process of Cerebral Artery Disease

(2) Anesthetic factors: Anesthetic methods (regional block has lower incidence of postoperative complications than general anesthesia), intraoperative arrhythmia (such as atrial fibrillation), hyperglycemia (> 10 mmol/L), hypotension and hypertension, etc. Intraoperative hypotension is one of the important factors of perioperative stroke, especially in patients with high risk of stroke, which can lead to cerebral watershed infarction. The acceptable range of intraoperative hypotension is generally more than 80% of the baseline value of mean arterial blood pressure or systolic blood pressure [10, 17, 19–20].

Postoperative risk factors include: heart failure, low ejection fraction, myocardial infarction, arrhythmias (atrial fibrillation), dehydration, blood loss, and hyperglycemia (> 10 mmol/L) [17].
Table 1 listed 10 risk factors for perioperative stroke, accounting for 88.1% of the risk factors of stroke. These 10 risk factors are associated with 90% risks of stroke [21].

Table 1 Risk factors for perioperative cerebral apoplexy [21]

Risk factor	Population attributable risk [% (99% *CI*)]
Hypertension	34.6 (30.4 ~ 39.1)
Smoking	18.9 (15.3 ~ 23.1)
Waist-to-hip ratio	26.5 (18.8 ~ 36.0)
Diet	18.8 (11.2 ~ 29.7)
Physical activity	28.5 (14.5 ~ 48.5)
Diabetic mellitus	5.0 (2.6 ~ 9.5)
Alcohol (> 30 drinks per month) or alcohol abuse	3.8 (0.9 ~ 14.4)
Psychosocial factors and depression	4.6 (2.1 ~ 9.6) and 5.2 (2.7 ~ 9.8)
Cardiac factors	6.7 (4.8 ~ 9.1)
Ratio of apolipoprotein B to apolipoprotein A1	24.9 (15.7 ~ 37.1)

Note: 99% *CI* : 99% confidence interval

(II) Preoperative Assessment Scale

1. Ischemic Stroke Primary Prevention Risk Assessment: The scale for assessing the risk of ischemic

stroke and anticoagulation bleeding in patients with atrial fibrillation (CHADS2 scale) is the most widely used scale (Table 2) for predicting the risk of ischemic stroke in patients with non-valvular atrial fibrillation. It is generally recommended that low-risk patients (CHADS2 score = 0) should not be treated, while higher-risk patients (CHADS2 score ≥2) should take oral anticoagulants (OACs) such as warfarin. For patients with a CHADS2 score of 1, no therapy, aspirin, or OACs is recommended.

2. Ischemic stroke and TIA Secondary Prevention Risk Assessment Tool: The risk of ischemic stroke is significantly increased after the occurrence of TIA. 4% to 20% of patients with TIA will have a stroke within 90 days, and approximately half of these strokes occur within 2 days after TIA. Early identification of high-risk patients could help to initiate secondary stroke prevention strategy as early as possible. Once a focal or global neurological deficit is manifested, the anesthesiologist or surgeon should seek help from a neurologist and brain imaging scan should be performed promptly. Unenhanced CT enables definitive distinction of ischemic stroke, intracranial hemorrhage, and neurological symptoms due to nonvascular causes.

Table 2 The Scale for assessing the risk of Ischemic Cerebral Stroke and Anticoagulation Bleeding in Patients with Atrial Fibrillation

Risk factor	Score
Congestive heart failure	1
Hypertension	1
Age≥ 75 years	1
Diabetic mellitus	1
Prior stroke or TIA	2
Total score	6

The clinical application of the Essen scale to assess long-term recurrence risk in patients with ischemic stroke is recommended (Table 3). In the Essen assessment scale, 0~2 was classified as low risk of recurrent stroke and 3~6 as high risk of recurrent stroke.

Table 3 Essen Assessment Scale

Risk factor	Score
Aged 65 ~ 75 years	1
Age > 75 years	2
Hypertension	1
Diabetic mellitus	1
Previous myocardial infarction	1
Other cardiovascular disease (except myocardial infarction and atrial fibrillation)	1
Peripheral arterial disease	1
Smoking	1
Previous transient ischemic attack or ischemic stroke	1
Total score	9

[Recommendation] CHADS2 score can be used for risk assessment of ischemic stroke versus anticoagulant bleeding in patients with atrial fibrillation as primary prevention; while the Essen score can be used for risk assessment of ischemic stroke and TIA as secondary prevention.

IV. Optimized Preoperative Treatment of Patients with Concomitant Ischemic Cerebrovascular Disease
(I) Risk Factor Control
1. Hypertension Treatment: Hypertension is a major risk factor for stroke and TIA. Antihypertensive treatment is recommended for patients with hypertension combined with a history of ischemic stroke and TIA [22]. Before launching antihypertension therapy, the following should be considered, including advanced age, baseline blood pressure, previous prescriptions and patient tolerance. Generally, the blood pressure target is below 140/90 mmHg (1 mmHg = 0.133 kPa) and ideally ≤ 130/80 mmHg [23–24]. The targets of blood pressure varies according to the etiologies of ischemic stroke or TIA, although the recommendation is lack of solid evidence: (1) For subcortical minor stroke due to small vessel disease, it is recommended to control systolic blood pressure < 130 mmHg [25]; (2) For acute ischemic stroke or TIA due to intracranial or extracranial arteries stenosis induced hypoperfusion, reducing blood pressure too early may aggravate cerebral hypoperfusion and trigger aggravation or recurrence of stroke [26]. Therefor caution should be paid to the reduction of cerebral perfusion due to lowing blood

pressure.
[Recommendation] For ischemic stroke and TIA patients with hypertension, antihypertensive treatment is recommended, with the general goal of ≤ 140/90 mmHg, ideally ≤ 130/80 mmHg. The blood pressure target should be adjusted accordingly to the etiology.

2. Glycemic Control: 60% to 70% of patients with ischemic stroke have abnormal glucose metabolism or diabetes [27]. For young diabetic patients, strict glycemic control from the onset of the disease may reduce the risk of diabetic microvascular complications. Lifestyle modification and/or pharmacological intervention can reduce ischemic stroke or TIA events in patients with diabetes or prediabetes. The recommended target of glycated hemoglobin (HbA1c) is lower than 7%. For patients with short disease duration, average life expectancy and no significant cardiovascular disease, HbA1c can be controlled within the range of 6.0% to 6.5% while avoiding hypoglycemia or other adverse reactions [28]. However, a recent systematic review indicated that there were insufficient data from randomized control trials conforming the benefits of strict glycemic control in elderly patients or patients with macrovascular disease. The targets and treatment goals of glycemic control need to be individualized considering patient age, disease progression, macrovascular disease, as well as lifestyle and disease management capabilities [29].
[Recommendation] In elderly patients, the target of preoperative HbA1c below 7% is recommended.

(II) Antiplatelet Aggregation
Antiplatelet aggregation is an important measure for secondary prevention of ischemic stroke and transient ischemic attack. However, the use of antiplatelet drugs during perioperative period remains controversial. Discontinuation of antiplatelet drugs increases the risk of recurrent cerebral infarction [30], but continuing antiplatelet drugs may increase the risk of surgical bleeding [31]. The 2014 ESC/ESA guidelines and the 2016 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines suggest that the use of perioperative aspirin should be based on comprehensive individual risk-benefits assessment, weighing the risk of bleeding according the type of surgery against the risk of thrombosis [16, 32]. The American College of Chest Physicians recommends using thrombotic and bleeding risk stratification strategies (Tables 4, 5) as well as the HAS-BLED score (Table 6) to assess bleeding risk [7, 33–35]. For patients using dual antiplatelet agents, it is recommended to postpone elective surgery until the completion of dual antiplatelet therapy. If surgery is necessary and the risk of bleeding is high, stop clopidogrel for 5 to 7 days and continue aspirin. For patient with coronary artery disease and a coronary stent, current guidelines recommend (1) deferring elective surgery until the completion of dual antiplatelet therapy and continuing using aspirin in subsequent therapy whenever possible. For patients with stable coronary artery disease, elective surgery should be delayed for a minimum of 4 weeks, and ideally up for 3 months after bare-metal stent implantation. Aspirin should be continued during perioperative period as far as possible weighing the risk of bleeding against the risk of stent thrombosis. Dual antiplatelet therapy was recommended up to 12 months for first-generation drug-eluting stents (DES) and up to 6 months for the second and third-generation DES.
For patients with acute coronary syndrome, dual antiplatelet therapy should be used up to 12 months regardless of the type of stent. (2) For non-elective surgery, either stable coronary heart disease or acute coronary syndrome, dual antiplatelet therapy is recommended up to 4 weeks for patients with bare metal stents and up to 3 months for DES.

Table 4 Type of Surgery and Risk of Bleeding [7, 33]

Moderate to high risk	Low risk
Neurosurgery	Minor dermatological surgery such as skin biopsy
Spinal/epidural surgical procedures	Cataract or glaucoma surgery
Urologic surgery	Dental procedures such as simple extractions
Vascular surgery	Laparoscopic cholecystectomy
Gastrointestinal - major intra-abdominal surgery	Biopsy of a compressible site
Breast surgery	Joint aspiration/injection
Thoracic surgery	
Invasive ophthalmic surgery	
Reconstructive plastic surgery	
Pacemaker or ICD implantation	
Biopsy of liver tissue	

Note: ICD: implantable cardioverter defibrillator

There are few clinical studies on perioperative use of clopidogrel or dipyridamole, but it is generally believed that clopidogrel should be discontinued 7 days before non-cardiac surgery and dipyridamole should be discontinued 7 to 10 days before surgery. In patients with high perioperative thrombotic risk, bridging therapy with low-molecular-weight heparin may be used after discontinuation of antiplatelet therapy.

[Recommendation] For patients taking antiplatelet drugs for a long time before surgery, discontinue plan and alternative therapy should be determined according to the surgical site, severity of trauma and perioperative bleeding/thrombosis risk, so as to minimize the risk.

(III) Oral Anticoagulant Therapy

There is no optimal management strategy for patients with stroke who take anticoagulation preoperatively. Caution should be taken in balancing the risk of thrombosis against bleeding. Warfarin may be continued in patients with less bleeding risk [36-37]. If the risk of surgical bleeding and trauma is high, it is recommended to discontinue the drug for 5-7 days before surgery [38-40], and bridge with low-molecular-weight heparin to reduce the relative risk of thromboembolism by 66% to 80% [41-42]. New oral anticoagulants, such as dabigatran and rivaroxaban, with short half-life [43-44] can be discontinued within 24 ~ 96 h before surgery depending on patient's preoperative renal function and the risk of surgical bleeding. Table 7 shows the withdraw time of different anticoagulants. For the patients with normal renal function, it is not necessary to undergo preoperative bridging therapy [7].

Table 5 Thromboembolic Risk Stratification [7, 33]

Disease Type	High risk [a]	Moderate risk	Low risk
Mechanical heart valve	Any mechanical mitral valve; Older mechanical valve model aortic valve (caged ball/tilting disc); stroke or transient ischemic attack within the last 6 months	Bi-leaflet aortic valve implantation with 1 or more of the following risk factors: Atrial fibrillation, previous stroke or TIA, hypertension, diabetes mellitus, congestive heart failure, age > 75 years	Bi-leaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke
Atrial fibrillation	Rheumatic heart valve disease; stroke or TIA within the last 3 months; CHADS2 score: 5-6 points	CHADS2 score 3 ~ 4 points	CHADS2 score 0 ~ 2 points (presumed no previous stroke or TIA)
Venous thromboembolism	Venous thromboembolism within 3 months; Severe thrombophilia (protein C, S, or antithrombin deficiency or antiphospholipid antibodies; multiple abnormalities)	Venous thromboembolism 3-12 months ago; Recurrent venous thromboembolism; nonsevere thrombophilia (e.g., heterozygous V Leiden mutation or prothrombin gene mutation); cancer (within 6 months or palliative treatment)	Venous thrombosis 12 months ago or no other risk factors

Note: CHADS2 score includes the following risk factors: (1) congestive heart failure; (2) hypertension; (3) diabetes mellitus; (4) age > 75 years; (5) history of cerebral apoplexy or TIA, thromboembolism, each scored as 1 point, and cerebral apoplexy or TIA onset or thromboembolism history scored as 2 points; High-risk patients also include cerebral apoplexy or TIA 3 months before elective surgery, patients with CHADS2 score < 5 and thromboembolism formation during interruption of vitamin K antagonists, and those who are undergoing certain types of surgeries that increase the risk of cerebral apoplexy or other thromboembolism (e.g., heart valve replacement, carotid endarterectomy, major vascular surgery)

Table 6 Clinical Characteristics Composing the HAS-BLED Bleeding Risk Score [34]

Letter	Clinical Characteristic	Points Awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1/2
S	Stroke	1

B	Bleeding	1
L	Labile INRs	1
E	Aged (> 65 years)	1
D	Drugs or alcohol (1 point each)	1/2

Note: HAS-BLED is an acronym for hypertension (uncontrolled >160mmHg systolic), abnormal renal/liver function, stroke, bleeding history or predisposition (anemia), labile international normalized ratio (INR) (i.e., therapeutic time in range <60%), elderly (>65 years), drugs/alcohol concomitantly (antiplatelet agents, nonsteroidal anti-inflammatory drug).
Major bleeding: any bleeding requiring hospitalization and/or causing a decrease in hemoglobin level of >2 g/L and/or requiring blood transfusion that was not a hemorrhagic stroke. Hemorrhagic stroke: focal neurologic deficit of sudden onset, diagnosed by a neurologist, lasting >24h and caused by bleeding. Abnormal renal function: chronic renal dialysis or renal transplantation, serum creatinine ≥ 200 μmol/L. Abnormal liver function: chronic hepatic disease (e.g., cirrhosis) or biochemical evidence of significant hepatic derangement (e.g., bilirubin >2×upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase >3×upper limit of normal, and so forth). Caution should be exercised in patients at high risk of bleeding regardless of warfarin or aspirin therapy, and regular review and management of correctable bleeding risk factors should be initiated after antithrombotic therapy.

[Recommendation] For patients receiving preoperative oral warfarin, if severe trauma and heavy bleeding is expected, it is recommended to stop warfarin 5~7 days before surgery and bridge with low molecular weight heparin. Bridging therapy is not required for patients receiving short-acting anticoagulants. The short-acting anticoagulant can be discontinued within 24~96h before surgery depending on renal function and the risk of surgical bleeding.

It is not necessary to withdraw warfarin before surgery in patients with small risk of bleeding.

Table 7 Preoperative Withdrawal Time of New Oral Anticoagulants

Creatinine clearance (ml/min)	Risk of bleeding	Withdrawal time (h)	
		Rivaroxaban	Dabigatran
≥ 80	Low	≥ 24	≥ 24
	High	≥ 48	≥ 48
50 ~ 79	Low	≥ 24	≥ 36
	High	≥ 48	≥ 72
30 ~ 49	Low	≥ 24	≥ 48
	High	≥ 48	≥ 96
15 ~ 29	Low	≥ 36	Not indicated
	High	≥ 48	Not indicated
< 15	Cannot be used		

(IV) Use of β-blockers

In the POISE study, perioperative extended-release metoprolol was associated with a reduction of the incidence of acute myocardial infarction and cardiovascular mortality, but the incidence of postoperative stroke and overall mortality was higher in patients undergoing non-cardiac surgery [45]. However, in observational studies, long-term administration (≥ 30 days) of β-blockers before surgery did not increase the risk of perioperative stroke[46]. ACC/AHA 2014 guidelines recommend that when considering the perioperative use of Beta-blockers, the risk of major adverse cardiovascular events (MACE) should be weighed against the risk of perioperative stroke [47]. Continuation of β-blockers is recommended for patients taking them long time prior to surgery.

[Recommendation] If patient is already on β-blockers for a long time before surgery, it should be continued until the morning of surgery. When determining perioperative use of β-blockers, the risk of cardiovascular events should be weighed against the risk of acute stroke.

(V) Statin Use

Statins can reduce the incidence of atrial fibrillation and other potential risk factors of stroke. Interruption of statin therapy may impair vascular function. Current evidence suggests that statins should be continued in patients with a history of stroke if they have taken them for a long time [48]. In clinical practice, LDL-C level remains an important criterion for clinicians to assess the efficacy and compliance of statin therapy. LDL-C should be lowered to less than 2.5 mmol/L (100 mg/dl) with an optimal level of less than 1.8 mmol/L (70 mg/dl) [14, 22].

[Recommendation] Statins should be continued during perioperative period in those already on statin therapy for a long term.

V. Timing of Surgery Based on the Assessment of Perioperative Stroke Risk and Postoperative Outcome

The incidence of cardiovascular events after non-cardiac surgery was higher in patients with recent stroke, especially stroke within 3 months prior to surgery (OR = 14.23, 95% CI: 11.61 ~ 17.45), and the mortality with 30 days of surgery was also increased (OR = 3.07, 95% CI: 2.30 ~ 4.09) [49]. Therefore, for patients with recent stroke or TIA, it is safer to postpone elective surgery at least 3 months after the event [50]. In non-elective surgeries, perioperative blood pressure should be maintained within 120% of baseline, and maintain cerebral blood perfusion with goal-directed fluid therapy and prophylactic vasoconstrictors under continuous arterial pressure monitoring [51]. If possible, anesthesia depth and non-invasive cerebral oxygen saturation should be monitored to implement individualized brain protection strategy.

[Recommendation] For patients with recent stroke or TIA, it is recommended to be postponed elective surgery 1 to 3 months after the event. For patients undergoing non-elective surgery, after balancing the risks and benefits, perioperative blood pressure should be maintained within 120% of baseline, and maintain cerebral blood perfusion with goal-directed fluid therapy and prophylactic vasoconstrictors under continuous arterial pressure monitoring. If possible, anesthesia depth and non-invasive cerebral oxygen saturation should be monitored to implement individualized brain protection strategy.

VI. Intraoperative Management of Patients with Cerebrovascular Diseases

(I) Intraoperative monitoring based on risk stratification

Continuous noninvasive blood pressure or arterial pressure should be monitored for high-risk patients or high-risk surgery. In order to track the cardiogenic sources of emboli, optimize cardiac function and maintain systemic oxygen delivery, functional hemodynamic monitoring or transesophageal echocardiography may be performed according to the duration of surgical procedures, the severity of trauma, the amount of blood loss and cardiac function. The limits of acceptable blood pressure is determined by the adequacy of vital organ perfusion. Maintaining arterial blood pressure within 120% of baseline can effectively prevent perioperative stroke [52].

If available, noninvasive cerebral monitoring techniques such as transcranial doppler (TCD) and regional cerebral oxygen saturation (rSO2) monitoring should be applied to provide important intraoperative therapeutic information. A reduction in middle cerebral artery blood flow velocity >50% by TCD indicates cerebral hypoperfusion.

Prolonged hypoperfusion may cause cerebral ischemia or even infarction in the ipsilateral area [53]. TCD also helps to detect micro-embolic as an indicator for a higher risk of stroke. The presence of emboli can be the sign of a proximal arterial dissection, partially occlusive thrombus, or cardiac source of embolism [54]. Near infrared spectroscopy (NIRS) is another noninvasive technology that enables real-time monitoring of regional cerebral oxygen saturation. An absolute rSO2 value <50%, a 20% reduction below baseline or a 20% left–right difference usually imply brain ischemia [55-56]. Persistent desaturation may increase the incidence of stroke [52]. Interventions including correction of hypotension, hypocapnia, hypoxia, anemia, hypoglycemia and hyperglycemia to correct desaturations and hypoperfusion may reduce the incidence of perioperative stroke. Induced hypothermia, vascular bypass or selective cerebral perfusion may be beneficial to reduce the risk of cerebral ischemic damage during certain surgical procedures.

[Recommendation] It is strongly recommended to implement continuous noninvasive or arterial pressure monitoring for high-risk patients and high-risk surgery. The choice of implementing goal-directed fluid management under functional hemodynamic monitoring should be decided upon surgery duration, traumatic severity, blood loss and cardiac function. If available, non-invasive brain monitoring technology such as TCD or rSO2 should be used to improve postoperative neurologic outcomes.

(II) Intraoperative strategies to prevent acute stroke

As mentioned previously, there are many intraoperative risk factors for perioperative stroke. However, the intraoperative onset of stroke (indicating intraoperative etiology) is relatively infrequent [57-58]. Intraoperative management may lower the incidence of perioperative stroke.

1. Anesthetic technique and agents: The choice of anesthetic techniques mainly depend on the surgical procedures and surgical sites. Regional anesthesia including neuraxial anesthesia and peripheral nerve

block is recommended whenever possible. A study from a large database focusing on knee and hip arthroplasty found that general anesthesia was an independent risk factor for postoperative stroke (OR = 3.54, 95% CI: 1.01~12.39) [59]. Compared to combined neuraxial/general anesthesia and general anesthesia, 30-day mortality was significantly reduced under neuraxial anesthesia [60]. Regional anesthesia is recommended for patients undergoing extremity surgery [58], while more evidence are needed to show the benefits of regional anesthetic in other types of surgery.
Whether anesthetics agents would influence the incidence of perioperative stroke is still controversial. The risk of cerebral ischemia is increased in certain types of surgeries, including carotid endarterectomy, cerebral aneurysm and surgeries involving deep hypothermic extracorporeal circulation. However, data supporting neuroprotective effects of anesthetics is limited even for these procedures [58]. No concrete evidence shows the difference of cerebral protective effect using total intravenous, inhalational or combined intravenous-inhalational anesthesia [61]. Anesthetics do not increase the risk of perioperative stroke as long as cerebral perfusion is maintained [62].
[Recommendation] Regional anesthesia is recommended for patients undergoing extremity surgery to reduce the risk of perioperative stroke.

2. Intraoperative use of β-blockers: It has been demonstrated that intraoperative metoprolol was associated with perioperative stroke in patients undergoing noncardiac surgery. The study showed that intraoperative hypotension was associated with perioperative ischemic stroke, but there is no co-linearity between intraoperative hypotension and preoperative metoprolol use. Intraoperative use of esmolol or labetalol had no association with stroke [57]. Therefore, if required, β-blockers with a short duration of action such as esmolol is recommended for intraoperative use.
[Recommendation] Short-acting β-blockers such as esmolol are recommended during surgery.

3. Perioperative blood pressure management: Hypotension is common intraoperatively and has been identified as a cause of postoperative stroke. As the risk of stroke increases with the prolonged duration of hypotension [57, 63], intraoperative blood pressure management is crucial for preventing perioperative stroke. Maintaining intraoperative blood pressure within 100% to 120% of baseline is associated with reduced the incidence of stroke and mortality.
GTD combined with vasoconstrictors helps to maintain hemodynamic stability. Key parameters of GTD for mechanically ventilated patients include stroke volume variation (SVV), pulse pressure variation (PPV) and perfusion variation index (PVI). SVV or PPV > 13% indicates insufficient cardiac preload and rapid fluid resuscitation should be administered. A fluid challenge can be used to predict fluid responsiveness and to guide fluid therapy in non-mechanically ventilated patients. A fluid challenge is the rapid administration of a bolus of fluid given over a short amount of time, i.e., rapid infusion of 3 mL/kg (standard body weight) of crystalloid or colloid fluid within 5min. A dynamic positive fluid responder may be defined by stroke volume increase (ΔSV) >10% after a fluid challenge. Fluid challenge can be repeated until ΔSV is <10%. Excessive fluid infusion in anesthetized hypotensive patients to increase blood pressure may cause fluid overload. Vasoconstrictors can be infused to restore blood pressure [64].
Cerebral perfusion decreases in the beach chair position [65]. Consideration should be given to the blood pressure gradient between the brachial artery and brain. It is suggested that the arterial pressure transducer should be placed at the level of the external auditory meatus [66].
[Recommendation] Combined vasoconstrictors with GTD is recommended for patients with fragile brain to maintain intraoperative blood pressure within 100% to 120% of baseline. Continuous arterial pressure should be monitored with transducer placed at the level of the external auditory in the beach-chair position.

4. Intraoperative bleeding and blood transfusion: A number of clinical studies have associated acute anemia and massive bleeding with cerebral injury in perioperative patients, especially during cardiac surgery [67–68]. The results of the Peri-Operative Ischemic Evaluation (POISE) study found that hemoglobin <90 g/L in the setting of β-blockade increased the risk of stroke [69]. Therefore, for non-cardiac, non-neurosurgical patients who have taken β-blockers, hemoglobin should be maintained ≥ 90 g/L to minimize cerebral injury and stroke [58].
For patients at high risks for cardiovascular diseases, a restrictive transfusion strategy (transfusion when hemoglobin < 80 g/L) does not increase the risk of postoperative stroke in noncardiac, non-neurosurgical patients [70]. Hemoglobin should be maintained above 70 g/L during surgery [71].
[Recommendation] Hemoglobin should be maintained >70 g/L for patients with cardiovascular disease, and >90 g/L for non-cardiac, non-neurosurgical patients already taking β-blockers.

5. Intraoperative ventilation strategy: Currently there is limited evidence on the interaction of intraoperative $PaCO_2$ or $EtCO_2$ and stroke. Intraoperative hyperventilation has multiple deleterious effects including reduced lung compliance and decreased oxygenation (due to ventilation/flow mismatch and increased shunt), increased myocardial oxygen demand and decreased blood supply (coronary vasoconstriction), increased risk of arrhythmias, and decreased cerebral blood flow [58]. In the nonsurgical setting, stroke patients with hypocapnia have a poor prognosis compared with normocapnic patients [72]. Thus, hypocapnia should be avoided in patients with risk factors for stroke [58]. Currently, whether there are ventilation strategies that can reduce the risk of postoperative stroke remains to be explored.

[Recommendation] Hypocapnia should be avoided in patients with high risk of stroke.

6. Intraoperative blood glucose management: Hyperglycemia (> 11.1 mmol/L) has been associated with increased postoperative stroke incidence after specific surgeries during which cerebral ischemia is predictable, including cardiac surgery and carotid endarterectomy. However, intensive intraoperative insulin therapy (glucose goal of 4.4 ~ 5.6 mmol/L) is also associated with an increased risk of postoperative stroke and mortality [75]. There is no evidence for the optimal level of intraoperative glucose. Glucose levels should be monitored frequently, with a target range of 7.8~10.0 mmol/L in high-risk patients [52].

[Recommendation] In patients at high risk for perioperative stroke undergoing surgery, glucose monitoring is recommended with a target range of 7.8~10.0 mmol/L.

VII. Postoperative Management of Patients with Cerebrovascular Diseases

(I) Prevention of Acute Stroke after Surgery

1. Timing of anticoagulant/antiplatelet therapy: Perioperative use of anticoagulants or antiplatelet drugs are effective for primary prevention of stroke in patients with atrial fibrillation, cardiovascular and cerebrovascular disease [76]. For patients that require anticoagulation cessation in preparation for an invasive procedure, the timing of resuming anticoagulation therapy should be individualized after carefully balancing the risk of thromboembolism against major periprocedural bleeding. With vitamin K antagonist (VKA), it may take longer for elderly patients to achieve the desired INR. Thus, bridging anticoagulation therapy should considered for patients at high thrombotic risk. If deemed safe by the operating surgeon, VKA can be resumed within 24h after surgery. Otherwise, VKA resumption should be delayed [77].

The rapid onset of action and predictable half-lives of direct oral anticoagulant (DOACs) makes bridging therapy unnecessary in the perioperative period [77]. Neuraxial anesthesia in patients receiving DOACs carries a relatively small risk of epidural hematoma. DOACs should be discontinued preoperatively and restarted 24 h after surgery when hemostasis is achieved [77]. Antiplatelet therapy is commonly used for the secondary prevention of cardio-cerebrovascular diseases. If interrupted preoperatively, it is recommended that antiplatelet therapy should be resumed as soon as possible within 24 hours if bleeding risk is low. Currently there is not sufficient clinical evidence for other antiplatelet agents, considerations for restarting these agents are similar to aspirin [78].

[Recommendation] The timing of resuming anticoagulation therapy postoperatively should be individualized after balancing the risk of thromboembolism against hemorrhage. VKA can be resumed within 24 h after surgery in most scenarios, and bridging therapy is recommended for patients at high thrombotic risk. In patients after neuraxial anesthesia, DOACs can be restarted 24 h after surgery. Antiplatelet therapy should be resumed as soon as possible within 24 h after surgery.

2. Postoperative circulatory management: A 25% to 35% decrease in blood pressure can be tolerated in healthy adults. However, hypotension may lead to watershed infarction in patients with severe carotid stenosis/occlusion, incomplete circle of Willis, or comprised cerebral autoregulation [52]. In patients with these conditions, a drop in blood pressure should not exceed 20% of the baseline. Hypovolemia and anemia should be corrected to avoid cerebra ischemia. For elderly patients with preoperative ventricular systolic dysfunction, vasoconstrictors and positive inotropes can be used to maintain hemodynamic stability. Patients with preoperative paroxysmal atrial fibrillation are at risks of developing atrial fibrillation episodes postoperatively. The etiology leading to rapid atrial fibrillation should be actively sought and then effectively treated. Esmolol or amiodarone can be used to control heart rate. Patients with lethal hemodynamic instability require immediate electrical defibrillation [52].

[Recommendation] Maintain Postoperative blood pressure in high-risk patients within ±120% of baseline. Hypovolemia, anemia, and arrhythmias should be effectively treated to maintain cerebral perfusion and prevent postoperative stroke.

(II) Early Recognition, Diagnosis and Treatment of Postoperative Acute Stroke

In the event of acute stroke, preventing secondary injury and achieving optimal outcome are based on rapid recognition and intervention [58]. The diagnosis and treatment of postoperative new-onset acute stroke should be consistent with corresponding clinical guidelines. Early initiation of stroke unit has proven to be effective in regaining quality of life and reducing mortality [48, 79]. The concept of comprehensive stroke units is that stroke patients are accepted acutely, and undergo work-up, secondary prevention and rehabilitation. It is staffed by a multidisciplinary team that consists of anesthesiologist, neurologist, radiologist, and interventional neuroradiologist [80].

1. Assessment and diagnosis of postoperative stroke: Various physiologic, pharmacologic and pathologic factors in the postoperative period can mask symptoms of stroke, resulting in delayed identification and treatment. Simple, quick screening tools for stroke that can be used in the perioperative period are gaining popularity. Examples of such tests include Face Arm Speech Time (FAST) [81], Los Angeles Prehospital Stroke Screen (LAPSS) [82], Melbourne Ambulance Stroke Screen (MASS) [83] and Recognition of Stroke in the Emergency Room (ROSIER) [84]. A detailed neurologic examination should include the use of the National Institutes of Health Stroke Scale (NIHSS) to quantify neurologic deficits and facilitate communication with neurologists [48].

Clinical evaluation should also include measurement of blood pressure, oxygen saturation, temperature, blood glucose, serum electrolytes, blood count and coagulation status [48]. Patients with suspected stroke should be immediately inspected with computed tomography (CT) or magnetic resonance imaging (MRI) of the brain to determine whether the stroke is ischemic or hemorrhagic and to correlate neurologic deficit with radiologic findings. CT perfusion imaging or MRI weighted diffusion-perfusion imaging is of great value in determining the need for urgent endovascular intervention [48].

[Recommendation] A stroke rating scale, preferably the NIHSS, is recommended for early identification and assessment of postoperative stroke. Emergency imaging of the brain is recommended for diagnosis before initiating any specific therapy.

2. Treatment of ischemic stroke: Treatment of stroke includes pharmaceutical thrombolysis, endovascular intervention, and surgical treatment. Administration of intravenous recombinant tissue-type plasminogen activator (r-tPA) to appropriate patients remains the mainstay of early treatment of acute ischemic stroke. However, it is contraindicated in a number of situations, especially for intracranial or spinal surgery. Endovascular therapy should be adopted in patients with contraindications or after failed attempts for intravenous r-tPA [48, 85]. Aspirin as an alternative to intravenous fibrinolysis or thrombolytic therapy is not recommended. In patients with non-embolic acute ischemic stroke, antiplatelet therapy helps to prevent new clots from developing and reduces the risk of recurrent stroke and other cardiovascular events. Emergent anticoagulation has no significant effect in improving clinical outcomes for patients with acute ischemic stroke. Intermittent pneumatic compression and other antithrombotic therapy (such as oral aspirin and rehydration therapy) for bedridden patients with recent stroke may be considered for deep vein thrombosis prophylaxis[48].

Maintaining appropriate physiologic stability is critical during acute stroke care [48]. Supplemental oxygen should be used to maintain SpO2 saturation greater than 94%. The airway should be secured in patients with depressed levels of consciousness, bulbar dysfunction, or inability to protect the airway.

Effort such as blood pressure optimizations should be made to preserve cerebral perfusion pressure. For patients eligible for r-tPA therapy, systolic blood pressure is usually treated if greater than 185mmHg, and diastolic pressure is treated if greater than 110 mm Hg. For patients requiring mechanical thrombectomy, maintain blood pressure ≤ 180/105 mmHg during surgeries and within 24 h after treatment. The source of any fever (temperature > 38℃) following stroke should be ascertained, and the fever needs to be treated with antipyretic agents. As hypoglycemia (< 3.3 mmol/L) can be a consequence of a severe stroke, maintaining euglycemia (7.8 ~ 10 mmol/L) during the period of acute stroke is beneficial. After stabilization of the patient’s condition, rehabilitation, measures to prevent long-term complications can be started when appropriate [48].

[Recommendation] Intravenous r-tPA remains the mainstay of early treatment of acute ischemic stroke. Endovascular intervention and surgical treatment should be considered if r-tPA failed or is contraindicated. Antiplatelet agents may help reduce the risk of recurrent stroke and other cardiovascular events. Supplemental oxygen should be provided to maintain oxygen saturation >94%.Maintaing target glucose level between 7.8 and 10.0 mmol/l.

Parkinson's Disease

I. Incidence of Parkinson's Disease

Parkinson's disease (PD) is a common degenerative disease with a prevalence of 1700/100000 population over 65 years of age in China and increases with age. The main pathological manifestations of the disease are loss of dopamine neurons in the substantia nigra and formation of Lewy bodies, and the main biochemical changes are decreased dopamine transmitters in the striatum [86]. Concomitant Parkinson's disease increases the risk of surgical procedures and affects perioperative complication and mortality rates [87].

II. Basic Symptoms and Treatment of Parkinson's Disease

Clinical presentations of Parkinson's disease are divided into motor and non-motor symptoms. Motor symptoms include bradykinesia, muscle rigidity, resting tremor and postural balance disorders, with bradykinesia, muscle rigidity, and resting tremor as core motor symptoms. Non-motor symptoms include anosmia, rapid eye movement sleep behavioural disorders, constipation, and depression. Treatment modalities for Parkinson's disease include medical therapy, surgical treatment and rehabilitation. Levodopa is the most important drug treatment, including dopamine agonists, amantadine, monoamine oxidase B inhibitors (MAO-B), catechol-O-methyltransferase (COMT) inhibitors, and anticholinergics (Table 8). The effect of early drug therapy was obvious. Deep brain stimulation (DBS) may be considered in patients with significant reduction in long-term outcome or those with severe motor fluctuations and dyskinesias.

Table 8 Common Antiparkinsonian Drugs Affecting Anesthesia and Perioperative Management

Drug	Adverse reaction
Monoamine oxidase B inhibitors (e.g., selegiline, rasagiline)	Increase in serotonin activity and predisposition to serotonin syndrome. These drugs include: (1) a subset of opioids: e.g., meperidine tramadol; (2) selective serotonin reuptake inhibitors: e.g., citalopram, fluoxetine; (3) tricyclic antidepressants: e.g., amitriptyline; (4) some antibiotics: e.g., ciprofloxacin, linezolid, fluconazole, etc.
Domperidone Antidepressants	QT prolongation and sudden cardiac death caused by selective serotonin reuptake inhibitors (SSRI); aggravation of orthostatic hypotension by tricyclic antidepressants.
Quetiapine	QT prolongation

III. Perioperative Management of Parkinson's Disease

(I) Preoperative Preparation

1. Rating of Parkinson's disease: The Unified Parkinson's Disease Rating Scale (UPDRS) is a commonly used international scale, including 6 subscales, which are used to evaluate mental behavior and mood, ability of daily living, motor function, treatment complications, disease progression, and ability of daily activities in Parkinson's disease patients. The higher the score, the more severe the symptoms of Parkinson's disease. Preoperative and postoperative assessments were primarily evaluated in Part III (UPDRS III, Table 9).

The Activities of Daily Living Scale (ADL) consists of 14 items, which are divided into two parts: the Basic Activity of Living (BADL) and the Instrumental Activities of Living (IADL). Results can be analyzed by total, subscale, and individual scores, with a total score of < 16 being completely normal and > 16 having varying degrees of functional decline, with a maximum score of 64 (Table 10).

The Parkinson's disease Webster scale divides common symptoms of Parkinson's disease into 10 items, including upper extremity dyskinesia, facial expression, sitting disorder, speech, gait, upper extremity concomitant movements, tremor, self-care ability, muscle rigidity, and posture. The score is between 0 and 72, and the higher the score, the worse the disease (Table 11).

2. Respiratory evaluation in patients with Parkinson's disease: Patients with Parkinson's disease often have obstructive ventilatory dysfunction, dysphagia, decreased cough reflex. During perioperative period, reduced clearance of respiratory secretion and aspiration usually happen, leading to aspiration pneumonia [88]. Therefore, patients with Parkinson's disease should be examined preoperatively, including chest X-ray or CT, pulmonary function tests and arterial blood gas analysis.

3. Cardiovascular evaluation in patients with Parkinson's disease: Patients with Parkinson's disease often have orthostatic hypotension and arrhythmias. Postural hypotension is associated with autonomic

dysfunction, which can be exacerbated by the use of dopaminergic and tricyclic antidepressants in pharmacotherapy. Some drugs commonly used in patients with Parkinson's disease cause prolongation of QT interval [89], including domperidone, quetiapine, selective serotonin-reuptake inhibitors (SSRIs) antidepressants, etc.

Table 9 Unified Parkinson's Disease Rating Scale Part III (UPDRS III) Motor function assessment

3.1 Speech
0 Normal: No problem.
1 Minor: Loss of normal pitch, pronunciation, or volume, but all words are easily understood.
2 Mild: Loss of normal pitch, pronunciation or volume, a few words are not clear, but the overall sentence is still easier to understand.
3 Moderate: The patient's words are difficult to understand. Although not all statements are difficult to understand, at least some are difficult to understand.
4 Severe: Most of the patient's words are difficult to understand.
3.2 Facial expression
0 Normal: Normal facial expression.
1 Minor: Mild mask face, only reduction of blink frequency.
2 Mild: In addition to the reduction in blink frequency, there is also a reduction in expression on the lower face, that is, a decrease in movement around the mouth, such as a decrease in spontaneous smiling, but no separation of the lips.
3 Moderate: There is a mask face, lips sometimes open when the mouth does not move.
4 Severe: There is a mask face, lips open in most of the time when mouth does not move.
3.3 Stiffness
0 Normal: No stiffness.
1 Minor: Stiffness may be noted only on intensive test.
2 Mild: Stiffness may be noted without intensive test, but the range of motion of the joint is not limited and can be easily achieved.
3 Moderate: Stiffness may be noted without intensive test; it takes force for the range of motion of joints not to be limited.
4 Severe: Stiffness may be noted without intensive test and the range of motion of joints is limited.
3.4 Counter finger test
0 Normal: No problem.
1 Minor: Having one of the following conditions: (1) the normal rhythm of the finger tapping movement is interrupted or hesitantly interrupted once or twice; (2) the movement becomes slightly slower; (3) the amplitude of the finger tapping movement decreases near the 10th time.
2 Mild: Having one of the following conditions: (1) pauses 3 to 5 times during finger tapping; (2) the movement becomes slightly slower; (3) the amplitude of finger tapping begins to decrease when the time of tap reaches half.
3 Moderate: Having one of the following conditions: (1) pauses more than 5 times or freezes (catalepsy) at least once for relatively long time during finger tapping; (2) the movement becomes moderately slower; (3) The amplitude of finger tapping gradually decreases from the first time of tapping.
4 Severe: Due to slow movement, interruption or reduced amplitude, the patient cannot or almost cannot complete this action.
3.5 Fist grip test
0 Normal: No problem.
1 Minor: Having one of the following conditions: (1) the normal rhythm of stretching and grasping fist is interrupted or hesitantly interrupted once or twice; (2) the movement becomes slightly slower; and (3) the amplitude of stretching and grasping fist decreases near the 10th time.
2 Mild: Having one of the following conditions: (1) pauses 3 to 5 times in the process of stretching and grasping fist; (2) the movement becomes slightly slower; (3) the amplitude of stretching and grasping fist starts to decrease when the time reaches half.
3 Moderate: Having one of the following conditions: (1) pauses for more than 5 times or freezes (catalepsy) for at least once during stretching and grasping fist; (2) the movement becomes moderately slower; (3) The amplitude of stretching and grasping fist gradually decreases from the first time.
4 Severe: due to slow movement, interruption or reduced amplitude, the patient cannot or almost cannot complete this action.
3.6 Alternate test
Normal: No problem.

1 Minor: Having one of the following conditions: (1) the normal rhythm of the palm-flip is interrupted or hesitantly interrupted once or twice; (2) the movement becomes slightly slower; and (3) the amplitude of the palm-flip decreases near the 10th time.
2 Mild: Having one of the following conditions: (1) pauses for 3 to 5 times in the process of palm-flip; (2) the movement becomes slightly slower; (3) the amplitude of palm-flip begins to decrease when the time reaches half.
3 Moderate: Having one of the following conditions: (1) pauses for more than 5 times or freezes (catalepsy) at least once for relatively long time during the palm-flip; (2) the movement becomes moderately slower; (3) The amplitude of the palm-flip gradually decreases from the first time.
4 Severe: Due to slow movement, interruption or reduced amplitude, the patient cannot or almost cannot complete this action.
3.7 Toe tapping ground
0 Normal: No problem.
1 Minor: Having one of the following conditions: (1) the normal rhythm of the toe tapping ground is interrupted or hesitantly interrupted once or twice; (2) the movement becomes slightly slower; and (3) the amplitude of the toe tapping ground decreases near the 10th time.
2 Mild: Having one of the following conditions: (1) pauses for 3 to 5 times during toe tapping ground; (2) the movement becomes slightly slower; (3) the amplitude of toe tapping ground begins to decrease when the time reaches half.
3 Moderate: Having one of the following conditions: (1) pauses for more than 5 times and freezes (catalepsy) at least once for relatively long time during toe tapping ground; (2) the movement becomes moderately slower; (3) the amplitude of toe tapping ground gradually decreases from the first time.
4 Severe: due to slow movement, interruption or reduced amplitude, the patient cannot or almost cannot complete this action.
3.8 Lower extremity flexibility
0 Normal: No problem.
1 Minor: Having one of the following conditions: (1) the normal rhythm of the foot lift stepping action is interrupted or hesitantly interrupted once or twice; (2) the movement becomes slightly slower; (3) the amplitude of the foot lift stepping decreases near the 10th time.
2 Mild: Having one of the following conditions: (1) pauses for 3 to 5 times during the process of foot lift stepping movement; (2) the movement becomes slightly slower; (3) the amplitude of foot lift stepping started to decrease when the time reaches half.
3 Moderate: Having one of the following conditions: (1) pauses for more than 5 times and freezes (catalepsy) at least once for relatively long time during the foot lift stepping movement; (2) the movement becomes moderately slower; (3) the amplitude of the foot lift stepping movement gradually decreases from the first time.
4 Severe: due to slow movement, interruption or reduced amplitude, the patient cannot or almost cannot complete this action.
3.9 Arising from chair
0 normal: No problem, one can quickly stand up without hesitation.
1 Minor: Stand up slower than normal; or may need more than one attempt; or need to sit forward to stand up. But don't need a handrail.
2 Mild: Hold handrail can easily stand up.
3 Moderate: Need to hold the handrail, but easy to fall back on the chair; or need to try more than once to hold the handrail to stand up, but still do not need help from others.
4 Severe: Unable to arise without help.
3.10 Gait
0 Normal: No problem.
1 Minor: Mild gait impairment but able to walk unaided.
2 Mild: Obvious gait impairment but also able to walk independently.
3 Moderate: Need auxiliary tools to walk safely (cane or walker) but do not need help.
4 Severe: Completely unable to walk or can only walk with help.
3.11 Gait freezing
0 Normal: No gait freezing.
1 Minor: Pause once when first stepping, turning around or passing through the door, but then can walk smoothly in a straight line.
2 Mild: Pause more than once when first stepping, turning around or passing through the door, but then can smoothly walk in a straight line.
3 Moderate: Freeze gait once during straight walking.

4 Severe: Freeze gait for multiple times during straight walking.
3.12 Postural stability
0 Normal: No Problem, resume standing after backing a step or two.
1 Minor: Resume standing after backing 3 to 5 steps, but do not need help to resume standing.
2 Mild: Resume standing after backing more than 5 steps, but still do not need help to resume standing.
3 Moderate: Can stand safely, but lack postural balance reflexes; will fall if scorer does not catch.
4 Severe: Posture is very unstable, tend to lose balance spontaneously or a slight touch on the shoulder can fall.
3.13 Posture
0 Normal: No problem.
1 Minor: Not very straight, but may be normal for the elderly.
2 Mild: Forward lean is definite, scoliosis or inclination to one side, but the patient can correct the posture back after the reminder.
3 Moderate: Hunched back, scoliosis or inclination to one side, and cannot be corrected back by the patient.
4 Severe: body flexion, scoliosis or inclination to one side leading to severe postural abnormalities.
3.14 Spontaneous movements of the whole body
0 Normal: No problem.
1 Minor: Minor slowing or reduction of generalized activity and spontaneous movement.
2 Mild: Mild slowing or reduction of generalized activity and spontaneous movement.
3 Moderate: Moderate slowing or reduction of generalized activity and spontaneous movement.
4 Severe: Severe slowing or reduction of generalized activity and spontaneous movement.
3.15 Postural tremor
0 Normal: No tremor.
1 Minor: Tremor, but the amplitude of tremor is not more than 1 cm.
2 Mild: The amplitude of tremor is at least 1 cm but not more than 3 cm.
3 Moderate: The amplitude of tremor is at least 3 cm, but not more than 10 cm.
4 Severe: The amplitude of tremor is at least 10 cm.
3.16 Action tremor (hand)
0 Normal: No tremor.
1 Minor: Tremor, but the amplitude of tremor is not more than 1 cm.
2 Mild: The amplitude of tremor is at least 1 cm but not more than 3 cm.
3 Moderate: The amplitude of tremor is at least 3 cm, but not more than 10 cm.
4 Severe: The amplitude of tremor is at least 10 cm.
3.17 Resting tremor
Extremity score
0 Normal: No tremor.
1 Minor: Tremor, but the amplitude of tremor is not more than 1 cm.
2 Mild: The amplitude of tremor is at least 1 cm but not more than 3 cm.
3 Moderate: The amplitude of tremor is at least 3 cm, but not more than 10 cm.
4 Severe: The amplitude of tremor is at least 10 cm.
Lip/jaw score
0 Normal: No tremor.
1 Minor: Tremor, but the amplitude of tremor is not more than 1 cm.
2 Mild: Tremor, the amplitude of tremor is at least 1 cm but not more than 2 cm.
3 Moderate: Tremor, the amplitude of tremor is at least 2 cm, but not more than 3 cm.
4 Severe: Tremor, the amplitude of tremor is at least 3 cm.
3.18 Persistence of resting tremor
0 Normal: No tremor.
1 Minor: Resting tremor appeared for less than 25% of the whole time during examination.
2 Mild: Resting tremor appeared for 26% and 50% of the whole time during examination.
3 Moderate: Resting tremor appeared for 51% and 75% of the whole time during examination.
4 Severe: Resting tremor appeared for more than 75% of the whole time during examination.

Prolonged QT interval leads to increased risk of cardiovascular death and stroke. Prior to the operation, the occurrence of orthostatic hypotension should be assessed, and cardiac examinations such as electrocardiograms and echocardiograms should be performed.

4. Preoperative medication adjustment: Patients should take the medicine strictly according to the

normal rules of medication during the hospitalization. Do not adjust the medicine at will. Parkinsonian hyperthermia can occur when antiparkinsonism (e.g., levodopa, dopamine agonists [90], amantadine [91], etc.), especially levodopa, is abruptly reduced or discontinued. This syndrome is similar to neuroleptic malignant syndrome (NMS), manifesting as altered consciousness, rigidity, tremor, hyperpyrexia, autonomic dysfunction, etc., often complicated by acute renal failure, disseminated intravascular coagulation (DIC), etc., with a high rate of disability and lethality, to which sufficient attention needs to be paid [92]. As the half-life of levodopa is only 1 to 2 hours, to reduce adverse effects after discontinuation, such patients are placed at the forefront of the surgical bulletin sheet as far as possible [93].

Monoamine oxidase B (MAO-B) inhibitors (e.g., selegiline, rasagiline) selectively and irreversibly inhibit dopamine metabolizing enzymes and increase the concentration of dopamine in the synaptic cleft. In patients treated with monoamine oxidase B inhibitors, severe adverse effects may occur when concomitant use of drugs that increase serotonin activity, primarily serotonin syndrome, manifesting as altered psychosocial behavior (e.g., dysphoria, anxiety), muscle rigidity, hyperreflexia, and extremely active autonomic function (e.g., increased blood pressure, sweating, tachycardia, etc.), and a 1 to 2-week suspension of use is recommended before surgery [94]. Use of drugs that increase serotonin activity, such as some opioids (pethidine, tramadol), is contraindicated in patients using monoamine oxidase B inhibitors [95]. In addition, selective serotonin reuptake inhibitors (SSRIs such as citalopram, fluoxetine), tricyclic antidepressants, and some antibiotics (ciprofloxacin, linezolid, fluconazole, etc.) can induce serotonin syndrome, which should also be used with caution in these patients [96] (Table 12).

Table 10 Activities of Daily Living Scale

Scale	Project	Score			
Activities of Daily Living Scale (ADL)	1. Cooking	1 ☐	2 ☐	3 ☐	4 ☐
	2. Dressing and undressing	1 ☐	2 ☐	3 ☐	4 ☐
	3. Washing	1 ☐	2 ☐	3 ☐	4 ☐
	4. Getting in and out of bed, sitting or standing up	1 ☐	2 ☐	3 ☐	4 ☐
	5. Walking indoor	1 ☐	2 ☐	3 ☐	4 ☐
	6. Going to the toilet	1 ☐	2 ☐	3 ☐	4 ☐
	7. Control of urination and defecation	1 ☐	2 ☐	3 ☐	4 ☐
	8. Bathing	1 ☐	2 ☐	3 ☐	4 ☐
				Score: () points	
Instrumental Activities of Daily Living Scale (IADL)	1. Taking the bus by oneself (knowing which bus to take and can go alone)	1 ☐	2 ☐	3 ☐	4 ☐
	2. Walking near residence	1 ☐	2 ☐	3 ☐	4 ☐
	3. Cooking (including washing, cutting, lighting/burning, cooking, etc.)	1 ☐	2 ☐	3 ☐	4 ☐
	4. Taking medicine (remembering to take medicine on time and take the right medicine)	1 ☐	2 ☐	3 ☐	4 ☐
	5. Doing general light housework (sweeping, wiping the table)	1 ☐	2 ☐	3 ☐	4 ☐
	6. Doing heavier housework (wiping floors and windows, moving things, etc.)	1 ☐	2 ☐	3 ☐	4 ☐
	7. Washing clothes	1 ☐	2 ☐	3 ☐	4 ☐
	8. Cutting toenails	1 ☐	2 ☐	3 ☐	4 ☐
	9. Shopping	1 ☐	2 ☐	3 ☐	4 ☐
	10. Using the phone (being able to dial)	1 ☐	2 ☐	3 ☐	4 ☐

	11. Managing personal money (meaning that one can buy things, find change, calculate money, etc.)	1 ☐	2 ☐	3 ☐	4 ☐
	12. Staying at home alone (being able to stay home alone for 1 day)	1 ☐	2 ☐	3 ☐	4 ☐
				Score: () points	

Note: Subjects were rated according to their level of intelligence on the following functions, such as "Can you cook? Can you cook by yourself? Can you cook if someone else helps you? "
Scoring criteria: 1 = you can do it; 2 = have some difficulty, but you can still do it; 3 = you need help; 4 = you can't do it at all. A score of 1 was assigned when the patient never did it but was competent; a score of 2 was assigned when he or she never did it but did it with difficulty and did not require assistance; a score of 3 was assigned when he or she never did it but did it with assistance; and a score of 4 was assigned when he or she never did it and was unable to do it. Scores range from 20 to 80, with > 23 being cognitive impairment.

[Recommendation] Patients with Parkinson's disease should be evaluated for basic conditions before surgery, and respiratory and cardiovascular functions should be assessed as well. During the perioperative period, drugs should be taken strictly according to the regular rules, and medication habits should not be adjusted at will. Certain opioids (pethidine and tramadol) and selective serotonin reuptake inhibitors should be contraindicated in patients using monoamine oxidase B (MAO-B) inhibitors to avoid inducting serotonin syndrome.

(II) Intraoperative Medication and Management

1. Choice of anesthetic mode: Compared with general anesthesia, the postoperative complication and mortality rate were lower in regional anesthesia (including intraspinal anesthesia and peripheral nerve block, etc.); In addition, regional anesthesia is performed to facilitate observation of symptoms in patients with Parkinson's disease, and oral anti-Parkinson drugs may be administered temporarily during operation if necessary [90]. However, the choice of anesthetic modality needs to be considered. General anesthesia may be more appropriate in patients with severe dyskinesia, as these patients have laryngeal muscle dysfunction and are prone to laryngeal spasm during surgery. In addition, some patients may have increased oral secretion due to swallowing problems, and endotracheal intubation is safer in this case.

2. Choice of anesthetic drugs: Propofol is often used for induction and maintenance of general anesthesia. Propofol induces dyskinesia in patients with Parkinson's disease. Propofol can potentially activate GABA transmitters. Autopsy findings of increased GABA receptor concentrations in globus pallidus cerebri in patients with Parkinson's disease suggest that these patients are more sensitive to the effects of GABA drugs [96].

Halothane in volatile inhalation anesthetics increases the sensitivity of the heart to catecholamines, and the use of halothane in patients taking levodopa increases the risk of arrhythmias [97]. Isoflurane, sevoflurane, and enflurane are safer than halothane, and no significant adverse effects have been observed in patients with Parkinson's disease.

3. Anti-parkinsonian pharmacotherapy: Patients who develop worsening of parkinsonism during surgery due to drug discontinuation or prolonged operative time can be given anti-parkinsonian medications via nasogastric tube at the original time and dose, to reduce the risk of rigidity and anesthesia [98]. In patients with intestinal malabsorption due to abdominal surgery, morphine can be given subcutaneously in combination with domperidone, but the drug is relatively difficult to obtain and adverse effects such as hallucinations and hypotension could occur. Rotigotine transdermal patches are currently recommended as a temporary alternative to the usual dopaminergic medications.

Table 11 Webster Rating Scale for Parkinson's Disease

I. Bradykinesia of upper extremities
0: None;
1: Difficulty in doing fine activities;
2: Significant difficulties in various activities;
3: Severe slowing, unable to write or perform fine movements.
II. Muscle rigidity
1: Neck muscles appear, muscles in extremities are not obvious;
2: Moderate neck muscle rigidity, which can be relieved by drugs;
3: Severe rigidity of neck and extremity muscles, which could not be relieved by drugs.
III. Posture

0: Normal;
1: Head forward inclination up to 12 cm;
2: Head forward inclination exceeds 15 cm;
3: Head forward inclination, significantly flexed extremities.
IV. Accompanying movements of upper extremities
1: Decreased movement on one side;
2: One arm fails to swing;
3: Both arms fail to swing.
V. Gait
0: Good;
1: Slightly reduced step distance, but no difficulty in turning;
2: Small step distance and laborious turning;
3: Minimal step, slow turn.
VI. Tremor
1: Mild tremor was observed in extremities and head at rest or during walking;
2: Severe but non-sustained tremor of the hands, head or other extremities;
3: There is severe and constant tremor and is unable to write and eat independently.
VII. Seating disorder
1: Mild difficulty;
2: Moderate difficulty, but no need for help;
3: Need help.
VIII. Speech
0: Clear;
1: Mild hoarseness;
2: Moderate hoarseness with stuttering;
3: Very hoarse and weak.
IX. Face expression
1: Mildly stiff;
2: Moderately stiff with salivation;
3: Mask face.
X. Self-care ability
0: Completely self-care;
1: General things can be handled, can adhere to work;
2: Slowed movement, some activities need care;
3: Basic loss of self-care ability, need to be taken care of.

Note: The scores of the above 10 items are added up. The total score of 1 ~ 10 is mild, 11 ~ 20 is moderate, and 21 ~ 30 is severe

Rotigotine is a novel long-acting dopamine agonist whose transdermal patch can maintain a stable plasma concentration for more than 24 hours and is relatively safe and effective. The specific dosage should be given by a neurologist according to the patient's usual dosage, duration of Parkinson's disease, and the surgery [97, 99].

[Recommendation] Regional anesthesia is preferred for patients with Parkinson's disease. In those with severe motor deficits, general anesthesia and endotracheal intubation should be considered. Patients with worsened parkinsonian symptoms during surgery can be treated either by nasogastric feeding of drugs, or by replacement of usual dopaminergic agents with rotigotine transdermal patches. Halothane inhalation anesthesia should be avoided in patients taking levodopa.

Table 12 Perioperative Adjustment of Commonly Used Drugs in Patients with Parkinson's Disease

Drug	Preoperative	Intraoperative	Postoperative
Parkinsonian drugs			
Levodopa	Maintained	Maintained	Maintained
Dopamine agonists	Maintained	Maintained	Maintained
Amantadine	Maintained	Maintained	Maintained
Monoamine oxidase B (MAO-B) inhibitor catechol-	Discontinued	Discontinued	Discontinued
o-methyltransferase (COMT) inhibitors	Maintained	Maintained	Maintained
Anticholinergic drug	Maintained	Maintained	Maintained
Psychiatric drugs			
Clozapine	Maintained	Maintained	Maintained

Quetiapine	Use with caution	Use with caution	Use with caution
Tricyclic antidepressants	Use with caution	Use with caution	Use with caution
Selective serotonin reuptake inhibitors antidepressants	Use with caution	Use with caution	Use with caution

(III) Postoperative Medication and Management

1. Postoperative analgesia: Peripheral nerve block is a safe and effective method for postoperative analgesia. Opioids are commonly used for postoperative analgesia. However, fentanyl has been reported to result in severe bradykinesia, which cannot be improved by anti-parkinsonian therapy. This may be related to the alteration of dopamine receptor expression by opioid in the basal ganglia [100]. Morphine may increase or decrease levodopa-induced dyskinesia [101]. In the present, non-steroidal anti-inflammatory drugs (NSAIDs) are considered relatively safe for patients with Parkinson's disease. Although NSAIDs are associated with increased risk of bleeding, renal impairment and cardiovascular adverse events, inflammatory reactions may also be a possible pathophysiological mechanism for Parkinson's disease. Moreover, there are evidences supporting that NSAIDs may have neuroprotective effects. Non-steroidal anti-inflammatory drugs are recommended as an alternative to opioids for postoperative analgesia in patients with Parkinson's disease as long as the adverse effects are tolerated.

2. Prevention and treatment of postoperative complications: (1) Aspiration pneumonia: Patients with Parkinson's disease are prone to postoperative aspiration pneumonia due to dysphagia. Treatment with anti-parkinsonian drugs (other than monoamine oxidase B inhibitors) should be resumed as soon as possible, and the individual schedule should be adhered to, and the patient's habits should not be adjusted at will. (2) Urinary retention, urinary tract infection: Early completion of routine urinalysis to examine the existence of urinary retention. Urethral catheter should be removed whenever possible. Anti-infective therapy should be initiated as soon as possible if urinary tract infection is highly suspected.

(3) Blood pressure fluctuation and postural hypotension: It is recommended to increase water intake appropriately, pay attention to blood pressure monitoring, and stop monoamine oxidase B inhibitors 1 to 2 weeks before surgery. (4) Deep venous thrombosis of the lower extremities: Patients with Parkinson's disease require early initiation of prophylaxis and monitoring of deep venous thrombosis of the lower extremities due to long-term reduced activity due to dyskinesia and bed rest after surgery. (5) Postoperative nausea and vomiting: Dopamine antagonists (e.g., haloperidol, metoclopramide) exacerbate Parkinson's symptoms, whereas domperidone is associated with severe cardiovascular adverse effects and risk of sudden cardiac death. Serotonin receptor antagonists (e.g., ondansetron) are recommended to control vomiting in Parkinson's patients [95, 102].

[Recommendation] Nerve block analgesia is preferred after surgery. If tolerated, non-steroidal anti-inflammatory drugs are recommended as an alternative to opioids for postoperative analgesia in patients with Parkinson's disease. Antiparkinsonian medications other than monoamine oxidase B inhibitors should be resumed as soon as possible after surgery. It is recommended that a serotonin receptor antagonist (e.g., ondansetron) be used instead of a dopamine antagonist (e.g., haloperidol, metoclopramide) to control postoperative nausea and vomiting.

IV. Management of Psychiatric Symptoms in Patients with Parkinson's Disease

Psychiatric symptoms are seen in patients with advanced Parkinson's disease and other Parkinson's syndrome (e.g., Parkinson's dementia and diffuse Lewy body dementia), with clinical manifestations of anxiety, hallucinations, paranoia, delusions, and delirium. The most common causes of acute deterioration of Parkinson's disease symptoms and mental changes are toxins and metabolic abnormalities. Infection and metabolic disturbances should be investigated first when acute psychiatric disorders occur. If an underlying cause is identified, the aetiology should be managed before any adjustment of the antiparkinsonian medication is made.

Most antipsychotics (e.g., haloperidol, risperidone, olanzapine, aripiprazole, ziprasidone, etc.) should be avoided in patients with hallucinations and delusions, as they exacerbate parkinsonian symptoms. Only clozapine, and possibly quetiapine, does not worsen Parkinson's disease symptoms, and is the preferred antipsychotic for these patients. Benzodiazepines have some roles in alleviating psychiatric symptoms in patients with Parkinson's disease, but low doses are recommended for patients with advanced Parkinson's disease, since they increase the occurrence of psychobehavioral symptoms such as confusion or agitation due to the increased sensitivity to benzodiazepines [95, 103].

Depression is the most common non-motor symptom of Parkinson's disease, which usually precedes the onset of motor symptoms and impairs patients' quality of life. Selective serotonin reuptake inhibitors may be given for the treatment of depression and/or anxiety. Alternatively, dopamine agonists, especially pramipexole, can be used to improve both motor and depressive symptoms [104].

[Recommendation] Clozapine or quetiapine can be used for treating postoperative psychiatric symptoms such as hallucinations, delusions in patients with Parkinson's disease. Selective serotonin reuptake inhibitors or dopamine agonists (pramipexole) can be administered to those with depression or anxiety.

Alzheimer's Disease

I. Incidence of Alzheimer's Disease

Alzheimer's disease (AD) is the leading cause of dementia. According to the China Cognition and Aging Study (COAST study), there are 9.2 million patients with dementia diagnosed in China by 2009, 62.5% of which were caused by AD [105].

II. Basic Symptoms and Treatment of Alzheimer's Disease

Dementia is defined as a state of impaired cognitive function (memory, executive, verbal, or visual spatial impairment) or abnormal mental behavior developed after a normal intelligence that affects work or daily life and cannot be explained by delirium or other psychiatric disorders. Cognitive or psychosocial impairment can be objectively confirmed by medical history review or neuropsychological assessment, which displays impairments in at least two of the following fields: (1) memory and learning; (2) executive function including reasoning, judgment, and complex task handling; (3) visual-spatial ability; (4) language capability; (5) personality or behavior [106].

The diagnosis of AD consists of 3 aspects: (1) meeting the criteria for dementia; (2) the occurrence and development of dementia accord with the characteristics of AD: insidious onset and slowly progressive deterioration; (3) dementia due to other causes is excluded. As the primary cause of dementia, AD begins 15 to 20 years before the onset of symptoms, and can be divided into three sequential stages: preclinical, mild cognitive impairment (MCI) and dementia [107-109]. Biomarkers of AD include diagnostic and progression markers. CSF tau protein and beta-amyloid (Aβ), amyloid positron emission tomography (PET), and AD pathogenic gene are diagnostic markers. Brain structure magnetic resonance imaging (MRI) and 2-fluoro-2-deoxy-D-glucose (18F-FDG) PET are markers of progression. Mutations include those in genes encoding amyloid precursor protein (APP), presenilin 1 (PS1), and presenilin 2 (PS2), which are causative for early-onset autosomal dominant AD.

The treatments of AD include: (1) cholinesterase inhibitors (ChEIs): ChEIs increase the acetylcholine concentration in the synaptic cleft and are the first-line treatment for mild to moderate AD. These include donepezil, gabardine, galantamine and huperzine A; (2) excitatory amino acid receptor antagonists: mainly memantine hydrochloride, which is the first drug used for moderate to severe dementia. It improves cognitive function, daily living and psycho-behavioral symptoms.

III. Perioperative Management of Alzheimer's Disease

(I) Association between Surgery and Alzheimer's Disease

Anesthesia and surgery can lead to delirium and cognitive dysfunction, especially in older patients [110-111]. In clinical studies, patients with AD were at higher risk of delirium during hospitalization, while patients with preclinical AD were more likely to experience cognitive decline postoperatively [112-113].

So far, the relationship of postoperative delirium and cognitive dysfunction with risk factors and pathogenesis of AD is unclear, but may be partially overlapped [114-115]. Postoperative delirium and cognitive dysfunction were not significantly associated with structural imaging findings of neurodegenerative lesions, but were associated with the angiographic changes [116]; PET imaging follow-up studies revealed no significant correlation between Aβ deposition and cognitive dysfunction within 1 year after surgery [117]. By contrast, the inflammatory responses during the anesthetic and surgical process may initiate or worsen cognitive decline in the elderly [118]. In conclusion, more studies are needed to elucidate the relationship between perioperative delirium, cognitive dysfunction and AD, as well as the underlying mechanisms.

(II) Preoperative Evaluation of Patients with Alzheimer's Disease

Since 30%-50% of AD patients have depressive symptoms, and dementia and depression usually share some symptoms, patients with AD need to be simultaneously assessed for cognitive function and depressive status before surgery [119].

1. Depression status assessment (see Anxiety and Depression section): The degree of depressive, guilty

sense and other symptoms were assessed using the Hamilton Depression Scale (HAMD). The total score < 8 is normal. 8-20 may be depressed; Score 20 to 35: Affirmative depression; > 35 is classified as major depression (Table 13).

2. Cognitive function assessment (refer to the Cognitive Dysfunction section): Mini-Mental State Examination (MMSE) is used, including time-orientation, location-orientation, immediate memory, attention and calculation, short-term memory, language and visual-spatial structure. Language tests include naming, retelling, listening comprehension (level 3 instruction), reading comprehension and writing. With a total score of 30, the test scores are closely related to the level of culture. The normal cut-off scores are as follows: illiteracy > 17, primary school > 20, and junior middle school or above > 24 (Table 14).

[Recommendation] Preoperative assessment of cognitive function and depression is recommended in patients with AD.

(III) Intraoperative Management of Alzheimer's Disease (see Cognitive Dysfunction section)

Sensitivity to narcotic drugs is increased in patients with AD [120]. Regional anesthesia is recommended as a priority in patients with AD. If general anesthesia is necessary, it is recommended to maintain appropriate anesthesia depth (e.g., BIS40-60) under EEG anesthesia monitoring [121-123] and to choose propofol total intravenous anesthesia [124-125] to reduce postoperative delirium and cognitive dysfunction in patients with AD. For patients with known MCI or AD, total intravenous propofol anesthesia or local anesthesia is better than general anesthesia with inhalation anesthetics, such as sevoflurane [126]. Opioid analgesics have increased efficacy and decreased clearance in the elderly. Therefore, the initial dose chosen can be comparable to that for younger patients, but subsequent doses should be reduced and the intervals between repeated doses should be extended. Among opioids, remifentanil has the advantages of rapid acting and clearance, and definite analgesic effect. Although remifentanil does not prevent POCD compared with other fentanyl classes, postoperative cognitive recovery is more rapid in patients maintained with remifentanil. Elderly patients require a reduction in infusion rate when remifentanil is administered. In patients older than 60-70 years, it is recommended that infusion rates do not exceed 30% to 40% of that administered to younger patients [127].

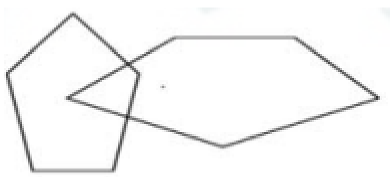
Anticholinergic agents (e.g., atropine, scopolamine, etc.) should be avoided in patients with AD and MCI who are sensitive to anticholinergics. Succinylcholine should be avoided if the patient is taking an acetylcholinesterase inhibitor (e.g., donepezil, rivastigmine, etc.).

Table 13 Hamilton Depression Rating Scale (HAMD)

Serial number	Content	0 = None	1 = Mild	2 = Moderate	3 = Severe	4 = Extremely severe	Score
1	Depressed mood	None	Say when asked	Spontaneous expression of depression	Display in expression tone	Excellent words and deeds	
2	Feelings of guilt	None	Blame oneself	Rumination over past errors	Delusion of sin	Threat hallucination	
3	Suicide	None	Feeling like life is meaningless	Thoughts about death	Ideas of suicide	Have severe suicidal behavior	
4	Difficulty in falling asleep	None	Sometimes	Nightly	-	-	
5	Sleep not deep	None	Mild	Severe	-	-	
6	Early awakening	None	Can sleeping after waking up	Can't sleep after waking up	-	-	
7	Work and interest	None	Say when asked	Decreased spontaneous expression of interest	Less activity, reduced efficiency	Stop working	
8	Retardation (slowness)	None	Slight slow	Marked slowness	Difficulty in talking	Stupor	
9	Agitation	None	A little restless	Marked restlessness	Unable to sit still	More small movements	
10	Psychic anxiety	None	Say when asked	Spontaneous expression	Display in expression tone	Marked panic	
11	Somatic anxiety	None	Slight	Moderate	Severe	affect life	
12	Gastrointestinal symptom	None	Loss of appetite	Require digestive drugs	-	-	
13	General symptoms	None	Pain or tiredness	Symptoms	-	-	
14	Genital symptoms	None	Hyposexuality	Symptoms	-	-	
15	Hypochondriasis	None	Too much attention to the body	Repeated consideration of health issues	Paranoid delusion	Concomitant hallucinations	
16	Loss of weight	None	Probable	Definite	-	-	
17	Insight	None	Acknowledging illness	Denial of illness	-	-	
Total score							

Table 14 Mini-Mental State Examination (MMSE)

Item	Question contents	Correct	Wrong
1 (5 points)	(1) What is the year?	0	1
	(2) What is the season?	0	1
	(3) What is the day?	0	1
	(4) What month is it now?	0	1
	(5) What day is it?	0	1
2 (5 points)	(1) Which province (city) are you in now?	0	1
	(2) Which county (district) are you in now?	0	1
	(3) Which township (town, street) are you in now?	0	1
	(4) What floor are you on now?	0	1
	(5) Where is this?	0	1
3 (3 points)	Say 3 article names (1 s means 1 name, 1 point is counted per mistake, and it is not repeated, and the maximum number of statements is 6)	0	1
	A. Rubber ball	0	1
	B. National flag	0	1
	C. Trees		
4 (5 points)	Count backward from 100 by sevens. (repeat 5 times)	0	1
	93	0	1
	86	0	1
	79	0	1
	72	0	1
	65		
5 (3 points)	Repeat the item name in question 3 one more time	0	1
	A. Rubber ball	0	1
	B. National flag	0	1
	C. Trees		
6 (2 points)	(1) What is this? (Show the watch to the subject)	0	1
	(2) What is this (show the pen to the subject)	0	1
7 (1 point)	Repeat this sentence: "Forty-four stone lions."	0	1
8 (3 points)	"Please keep the paper in your right hand."	0	1
	"Then fold the paper in half."	0	1
	"Please hand me the paper."	0	1
	(Order in 3 phases)		
9 (1 point)	Read the following sentence and follow its instructions: "Please raise your right hand."	0	1
10 (1 point)	Please say one full sentence (as long as possible)	0	1
11 (1 point)	Please draw the following figure:	0	1



Note: The full score of this scale is 30 points, and 1 point is obtained for each question answered correctly. Illiteracy ≤ 17 points, ≤ 20 points for those with primary school education, ≤ 24 points for those with secondary school education or above

If muscle relaxants are necessary, a higher than normal dose of non-depolarised muscle relaxant is required, but the antagonist will fail at this time [128].

[Recommendation] Regional anesthesia is preferred. Those who mandatorily need general anesthesia should maintain proper anesthesia depth under the monitoring of anesthesia depth and choose propofol for total intravenous anesthesia. Short-acting opioids (e.g., remifentanil) are recommended and anticholinergics are avoided.

(IV) Postoperative Management of Alzheimer's Disease (see Cognitive Dysfunction).

Regional block analgesia is preferred. Since medications, electrolyte disturbances, and anxiety can cause delirium aggravate cognitive impairment, medications influencing cognitive function should be avoided. Meanwhile, electrolyte disturbances should be promptly corrected and anxiety and other adverse emotions should be improved.

Postoperative sleep disturbances can also worsen cognitive impairment in patients with AD and may induce delirium. Thus, non-pharmacological measures should be taken to improve sleep status. In addition, elderly patients with AD are prone to postoperative complications such as pneumonia and urinary tract infection, which require active prevention, early recognition and intervention.
[Recommendation] Regional blockade of analgesia is preferred. Medications worsening cognitive impairment should be avoided. Care should be taken to prevent complications such as delirium.

Anxiety and Depression

I. Overview
Anxiety and depression are the most common perioperative mood disorders.
The core symptoms of anxiety are excessive worry, expressed as fear of a dangerous or unfortunate event that may occur in the future and is unpredictable. Individuals will have anxious reaction under stress condition. Moderate anxiety is helpful to mobilize the subjective initiative, but pathological anxiety is often accompanied by significant autonomic dysfunction and motor restlessness, as well as subjective pain and social function impairment. The occurrence of preoperative anxiety is related to surgical stress, which can be manifested as an acute episode or generalized anxiety disorder (GAD). A cross-sectional survey showed that the incidence of preoperative anxiety was as high as 92.6%, of which patients with anxiety more severe than moderate accounted for about 40.5% [129]. Preoperative anxiety is accompanied by increased postoperative pain, cognitive impairment, complications, and mortality, and is associated with decreased long-term postoperative quality of life and reduced survival rate [130-133].
The core symptoms of depression is depressed mood, which is characterized by unhappiness, loss of interest, feeling pessimistic, and even self-injurious or suicidal thoughts or behaviors; often accompanied by symptoms such as slower reaction, memory decline, easy fatigue, loss of appetite, and insomnia. The incidence of preoperative depression is approximately 9% to 15% in cardiac surgery patients and 21% to 31% in orthopedic surgery patients [134-137].
The incidence of depression is even up to 56% in patients with comorbid chronic disease [138].
Preoperative depression is accompanied by deterioration in patient outcomes, including increased postoperative complications and mortality, prolonged postoperative in-hospitalization, and reduced long-term postoperative quality of life and survival rate [137, 139–143].
Anxiety and depression often coexist, and the pathogenesis are diverse. Pain, lack of access to adequate medical information, impaired physical function, comorbid mental illness, and work and financial stress are the most common and major risk factors; other risk factors include low education level and loss of hope for the future [144–145].
[Recommendation] Perioperative anxiety and depression are common and will cause adverse effects on brain health and prognosis, so adequate attention is required.

II. Diagnosis and Assessment of Anxiety and Depression
(I) Diagnosis and Assessment of Anxiety
The diagnosis of anxiety requires a combination of medical history, clinical presentation, and associated ancillary tests. According to the ICD-10 diagnostic criteria, the basic feature of GAD is generalized and persistent anxiety. Patients usually have the following symptoms: (1) panic; (2) motor tension; (3) vegetative nerve hyperactivity. The basic features of panic disorder are recurrent, unpredictable, episodic anxious fear, panic attacks more than three times in a month, occurring in defined situations without objective dangerous environment; other types of anxiety disorders may refer to the corresponding diagnostic criteria. Non-psychiatrists could assess symptoms by the Anxiety Assessment Scale (Table 15).
(II) Diagnosis and Assessment of Depression
The diagnostic criteria for depressive disorders in the ICD-10 include three core symptoms: (1) depressed mood; (2) loss of interest and pleasure; (3) reduced energy leading to increased feelings of exertion and reduced activity; and seven additional symptoms: (1) reduced attention; (2) low self-esteem and self-confidence; (3) self-incrimination and a sense of worthlessness; (4) thinking of the future as bleak and pessimistic;

Table 15 Commonly Used Anxiety Screening Scale

Scale	Characteristic
Hamilton Anxiety Rating Scale (HAMA) [146]	Observer-rating scale, taking 15 to 20 minutes; the most commonly used scale, can be used to assess the severity of anxiety; the total score is 56, while more than 14 is anxiety, and more than 29 is severe anxiety; it needs to be performed by trained professionals
Generalized Anxiety Disorder 7-item Scale (GAD-7) [147]	Self-rating scale, taking 5 minutes; mainly used for generalized anxiety screening; the total score is 21, with 0 ~ 4 being normal, 5 ~ 9 being mild anxiety, 10 ~ 14 being moderate anxiety, and 15 and above being severe anxiety
Hospital Anxiety and Depression Scale (HADS) [148-149]	Self-rating scale, taking 5 minutes; including two sub-scales of anxiety and depression, having 7 questions for anxiety and depression respectively; 0 ~ 7 points belong to asymptomatic; 8 ~ 10 points belong to may exist; 11 ~ 21 points belong to definitely exist; at the time of scoring, 8 points are taken as the starting point, i.e., both suspicious and symptomatic persons are positive; more often used for anxiety and depression screening in general hospitals
State-Trait Anxiety Inventory (STAI) [150]	Include the state anxiety subscale (S-AI) and the trait anxiety subscale (T-AI), with 20 items each; the self-rating scale, taking 10 ~ 20 min; the total score of each subscale is 20 ~ 80 points, with high scores reflecting severe anxiety symptoms; and the total score exceeding the 95th percentile value is abnormal.
Self-Rating Anxiety Scale (SAS) [151-152]	Self-rating scale, taking 5 ~ 10 min; can provide the reference cut-off value of anxiety severity; 20 items, with a total score of 20 ~ 80 points, 44 points or less as normal, 45 ~ 59 as mild to moderate anxiety, 60 ~ 74 as severe anxiety, and more than 75 as very severe anxiety.

(5) self-injurious or suicidal idea or behavior; (6) sleep disorder; (7) loss of appetite. Mild depression has at least two core symptoms and at least two additional symptoms, and the patient should experience some difficulties in daily work and social activities, which means a mild impact on the patient's social function. Moderate depression has at least two core symptoms and at least three (preferably four) additional symptoms and the patient has considerable difficulty in work, social, and household activities. Severe depression has all three core symptoms and at least four additional symptoms, and the patient's social, work, and life functions are all severely impaired. Non-psychiatrists can assess symptoms by using the Depression Assessment Scale (Table 16).
[Recommendation] Perioperative assessment of anxiety and depression in elderly patients is recommended.

III. Perioperative Management of Patients with Depression and Anxiety
(I) Non-pharmacological Intervention
Active psychological intervention can effectively alleviate preoperative anxiety and depression and reduce the incidence of postoperative complications [137, 159–160]. Commonly used psychological intervention including preoperative visits by anesthesiologists and preoperative written/oral/video education by professionals can significantly reduce the incidence of anxiety and depression; the core content of psychological intervention is establishing a trusting relationship with the patient and reducing anxiety and depression in patients by providing detailed medical information [161-163].
[Recommendation] Non-pharmacological interventions based on psychological behavioral therapy are recommended for patients with preoperative anxiety and depression.
(II) Pharmacological Intervention
1. Treatment of perioperative transient anxiety: Studies have shown that low-dose anxiolytics (e.g., midazolam 0.02 to 0.04 mg/kg), passion fruit flavone (500 mg), gabapentin (1200 mg) orally, or dexmedetomidine (0.5 to 1.0 μg/kg) intravenous infusion can effectively relieve preoperative anxiety in patients [164-168]. However, a meta-analysis showed that preoperative application of anxiolytics had no significant effect on clinical outcomes such as length of hospital stay [169].
[Recommendation] Routine use of anxiolytics is not recommended for patients with mild anxiety. However, for patients with moderate or severe anxiety or symptoms affecting perioperative safety, pharmaceutical therapy should be considered.

2. Perioperative medication management in patients with chronic anxiety disorders: Systemic treatment with anxiolytics, antidepressants, and psychotherapy is recommended for patients with chronic anxiety disorders. Perioperative use of benzodiazepines increases the risk of complications such as delayed emergence and postoperative delirium, while withdrawal may lead to acute withdrawal symptoms [170-171]. Antidepressants such as paroxetine, venlafaxine, sertraline, and escitalopram are also effective in relieving anxiety symptoms [170]. For perioperative management, please refer to the section on perioperative management of patients with chronic depression.
[Recommendation] Attention should be paid to the potential risks of benzodiazepines, and it is recommended that psychiatrists should be consulted for perioperative medication suggestion.
3. Treatment of perioperative transient depression: about 80% to 90% of patients with preoperative depression can return to non-depressive state after surgery, and drug intervention for preoperative depression does not change the prognosis significantly [172]. Pharmacological intervention on preoperative transient depression is not supported by sufficient evidence.
[Recommendation] Routine use of antidepressants is not recommended for perioperative transient depression. Consultation with a psychiatrist is recommended if the patient has moderate to severe depression or if their symptoms affect prognosis and treatment.
4. Perioperative management of patients with chronic depression: Patients with chronic depression often require continuous pharmaceutical therapy, and the major antidepressants used are monoamine oxidase inhibitors, serotonin reuptake inhibitors, and tricyclic and tetracyclic antidepressants (Table 17). Long-term antidepressant application was associated with a 1.33-fold increased risk of death and a 1.14-fold increased risk of new cardiovascular events; in subgroup analyses, there is no significant difference in the effect on mortality between serotonin reuptake inhibitors and tricyclic antidepressants, but other antidepressants are associated with an increased risk of death compared with tricyclic antidepressants [173].

Table 16 Commonly Used Depression Assessment Scale

Scale	Characteristic
Hamilton Depression Rating Scale (HAMD) [153]	The observer-rating scale, used for depression severity assessment, takes 15 min; the gold standard of the depression assessment scale, rating should be performed by trained professionals; the scale has 17, 21, and 24 items in three versions; when using the 17-item form, the maximum score is 56, with 0 to 7 being normal, 8 to 14 being mild depression, 15 to 23 being moderate depression, and 24 and above being severe depression.
Geriatric Depression Scale (GDS) [154]	The self-rating scale, used for depression screening, takes 5 ~ 15 min; there are 30, 15, 10, and 6-item versions; the maximum score of the 30-item question scale is 30, with 0 ~ 10 being normal, 11 ~ 20 being mild depression, and 21 ~ 30 being moderate to severe depression; it is applicable to the elderly population.
Hospital Anxiety and Depression Scale (HADS) [155-156]	Including 2 sub-scales: anxiety and depression, having 7 questions for anxiety and depression respectively; the self-rating scale, used for depression screening, takes 5 min; 0 ~ 7 points belong to asymptomatic; 8 ~ 10 points belong to suspicious existence; 11 ~ 21 points belong to definite existence; applicable to general hospitals.
Patient Health Questionnaire (PHQ) [157]	Self-rating scale, taking 5 ~ 10 min; depression screening questionnaire recommended by WHO; 9-item or 2-item version; 9-item version with a total score of 0 ~ 27 points, the higher the scores are, the more severe the depressive symptoms are; very simple, with high reliability and validity.
Self-Rating Depression Scale (SDS) [158]	The self-rating scale, used to assess the severity of depression, takes 5 to 10 minutes and contains 20 items that are rated on a four-point scale. The standard cut-off value of the Chinese norm is 53 points, of which 53 ~ 62 points are mild depression, 63 ~ 72 points are moderate depression, and more than 73 points are severe depression; it can be used in the elderly population.

Table 17 Commonly Used Antidepressant Drugs

Category	Representative drug
Reversible monoamine oxidase inhibitor	Moclobemide
Tricyclic antidepressants	Amitriptyline, clomipramine, imipramine
Selective serotonin reuptake inhibitors	Citalopram, fluoxetine, sertraline
Selective norepinephrine reuptake Inhibitors	Reboxetine
Norepinephrine and dopamine reuptake Inhibitors	Bupropion
Serotonin and norepinephrine reuptake Inhibitors	Venlafaxine, duloxetine
Serotonin antagonism/serotonin reuptake inhibitors	Mirtazapine

A meta-analysis showed that small doses of ketamine can effectively reduce depression in patients, and the effect lasts for 2 to 3 days [174]. In patients undergoing radical mastectomy, perioperative continuous administration of low-dose ketamine (0.5 mg/kg for 7 days) can effectively reduce hospital anxiety and depression scale scores [175].

[Recommendation] The dosage of antidepressants varies widely among individuals, and drug arrest may lead to withdrawal reactions. Sudden perioperative discontinuation of antidepressants is not recommended for patients using high dose of antidepressants. Small doses of ketamine may be effective for perioperative depression. Psychiatric consultation is recommended for severely depressed patients.

(III) Interactions between Antidepressants and General Anesthetics

Monoamine oxidase inhibitors are the first used antidepressants and are rarely used in clinical practice now. Commonly used medications in this category include phenelzine, toloxatone, phencypromine, and selegiline. When used in combination with opioids (mainly piperidine, tramadol, dextromethadone, etc.), monoamine oxidase inhibitors can prevent their metabolic inactivation by inhibiting the hepatic drug-enzyme system, causing severe nervous system dysfunction, respiratory and circulatory dysfunction, or even death [176-177].

Opioids (especially meperidine), etomidate may cause symptoms of acute serotonin intoxication when used in combination with antidepressants such as monoamine oxidase inhibitors and serotonin reuptake inhibitors in a dose-dependent pattern [178-179]. Serotonin toxicity is a series of toxic reactions caused by the accumulation of serotonin in the body. Common symptoms include neuromuscular hyperresponsiveness (tremor, spasm, positive tendon reflex and extrapyramidal muscle rigidity, etc.), autonomic hyperactivity (diaphoresis, fever, tachycardia and rapid breathing) and mental disorders (agitation, excitement and coma) [178]. Treatment options include the administration of serotonin antagonists or serotonin receptor blockers, such as chlorpromazine, cyproheptadine, and risperidone; while haloperidol is ineffective in the treatment of toxic reactions, bromocryptine may also aggravate toxic reactions [178].

[Recommendation] Be vigilant for the interactions and toxicity of antidepressants and general anesthetics.

(IV) Selection of Anesthetic Methods and Drugs

Isoflurane anesthesia (inhaling 4% isoflurane to achieve 80% suppression of brain waves, followed by maintaining twice the MAC value; lasting 40 to 45 minutes for each and for 3 weeks) has been shown to improve symptoms in patients with treatment-resistant depression compared with electroconvulsive therapy [178]. It suggests that isoflurane anesthesia may be beneficial to depressive patients. Patients who received electroconvulsive therapy under ketamine anesthesia have faster postoperative recovery and less cognitive impairment than those under thiopental anesthesia [179-181]. However, evidence in this area is very limited.

[Recommendation] There is insufficient evidence to clarify the effects of anesthesia on patients with anxiety and depression and which anesthetic is more reasonable.

IV. Postoperative Anxiety and Depression

The incidence of postoperative depression is about 20% to 30% [182]. The incidence of postoperative anxiety is about 9.4% to 13.3% [183]. Preoperative depression and functional impairment caused by surgery may be important factors contributing to postoperative depression [182-184]. Postoperative psychological intervention and functional rehabilitation may alleviate the severity of depression [182, 184]. Serotonin reuptake inhibitors have been shown in a systematic review to be beneficial in the treatment of perioperative depression, but with the caveat of an increased risk of bleeding and death [185]. Severely depressed patients should be managed by a psychiatrist.

[Recommendation] Pay attention to postoperative anxiety and depression, especially patients with severe illness who may be at risk for self-injury or suicide. Evidence on prevention and treatment is still limited, and consultation with a psychiatrist is recommended.

Conflict of interest All authors declare that there is no conflict of interest.

Reference

[1] Beard JR, Bloom DE. Towards a comprehensive public health response to population ageing[J]. Lancet, 2015, 385(9968): 658-661.DOI:10.1016/S0140-6736(14)61461-6.

[2] Manku K, Bacchetti P, Leung JM. Prognostic significance of postoperative in-hospital complications in elderly patients. I. Long-Term Survival[J]. Anesth Analg, 2003, 96(2): 583-589, tableofcontents.DOI:10.1213/00000539-200302000-00051.

[3] Oresanya LB, Lyons WL, Finlayson E. Preoperative assessment of the older patient: an arrative review[J]. JAMA,2014,311(20): 2110-2120.DOI:10.1001/jama.2014.4573.

[4] Badenes R, Gruenbaum SE, Bilotta F. Cerebral protection during neurosurgery and cerebral apoplexy[J]. Curr Opin Anaesthesiol, 2015,28(5):532-536.DOI:10.1097/ACO.0000000000000232.

[5] Bilotta F, Guerra C, Rosa G. Update on anesthesia for craniotomy[J]. Curr Opin Anaesthesiol, 2013, 26(5): 517-522. DOI:10.1097/01.aco.0000432513.92822.c2.

[6] Riedel B, Browne K, Silbert B. Cerebral protection: inflammation, endothelial dysfunction, and postoperative cognitive dysfunction[J]. Curr Opin Anaesthesiol, 2014,27(1):89-97.DOI: 10.1097/ACO.0000000000000032.

[7] Mehdi Z, Birns J, Partridge J, et al. Perioperative management of adult patients with a history of cerebral apoplexy or transient ischaemic attack undergoing elective non-cardiac surgery[J]. Clin Med (Lond),2016,16(6):535-540.

[8] Chinese Society of Neurology, Group of Cerebral Vascular Disease, Chinese Classification of Cerebrovascular Diseases 2015 [J]. Chinese Journal of Neurology, 2017, 50 (3): 168-171. DOI:10.3760/cma.j.issn.1006-7876.2017.03.003.

[9] Liu Ming, Liu Junfeng, Wu Bo. Progress and interpretation of classification of cerebrovascular disease [J]. Chinese Journal of Neurology, 2017, 50 (3): 163-167. DOI: 10.3760/cma.j.issn.1006-7876.2017.03.002.

[10] Selim M. Perioperative cerebral apoplexy[J]. N Engl J Med,2007,356(7): 706-713.DOI:10.1056/NEJMra062668.

[11] Likosky DS, Caplan LR, Weintraub RM, et al. Intraoperative and postoperative variables associated with strokes following cardiac surgery[J]. Heart Surg Forum,2004,7(4):E271-276.DOI: 10.1532/HSF98.20041035.

[12] Mashour GA, Sharifpour M, Freundlich RE, et al. Perioperative metoprolol and risk of cerebral apoplexy after noncardiac surgery[J]. Anesthesiology, 2013, 119(6): 1340-1346. DOI: 10.1097 / ALN.0b013e318295a25f.

[13] Smilowitz NR, Gupta N, Ramakrishna H, et al. Perioperative major adverse cardiovascular and cerebrovascular events associated with noncardiac surgery[J]. JAMA Cardiol, 2017, 2(2):181-187.DOI:10.1001/jamacardio.2016.4792.

[14] European Stroke Organisation, Tendera M, Aboyans V, et al. ESC guidelines on the diagnosis and treatment of peripheral artery diseases: document covering at herosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries: the task force on the diagnosis and treatment of peripheral artery diseases of the European Society of Cardiology(ESC) [J]. Eur Heart J, 2011, 32(22): 2851-2906. DOI:10.1093/eurheartj/ehr211.

[15] Rothwell PM, Warlow CP. Timing of TIA spreceding stroke: time window for prevention is very short[J]. Neurology,2005,64 (5):817-820.DOI:10.1212/01.WNL.0000152985.32732.EE.

[16] Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC / ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the joint task force on non-cardiacsurgery: cardiovascular assessment and management of the European Society of Cardiology(ESC) and the European Society of Anaesthesiology(ESA) [J]. Eur J Anaesthesiol, 2014, 31(10): 517-573.DOI:10.1097/EJA.0000000000000150.

[17] Johnston DF, Sondekoppam RV. Continuous quadratus lumborum block analgesia fort otal hip arthroplasty revision[J]. J ClinAnesth, 2016, 35:235-237. DOI:10.1016/j.jclinane.2016. 08.002.

[18] Sacco RL, Adams R, Albers G, et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association / American Stroke Association Councilon Stroke: cosponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline[J]. Stroke,2006,37(2):577-617.DOI:10.1161/01.STR.0000199147. 30016.74.

[19] Engelhard K.Anaesthetic techniques to prevent perioperative cerebral apoplexy[J]. Curr Opin Anaesthesiol, 2013, 26(3): 368-374. DOI: 10.1097/ACO.0b013e3283608239.
[20] Ng JL, Chan MT, Gelb AW, et al. Perioperative cerebral apoplexy in noncardiac, nonneurosurgical surgery[J]. Anesthesiology,2011, 115(4):879-890.DOI:10.1097/ALN.0b013e31822e9499.
[21] O′Donnell MJ, Xavier D, Liu L, et al. Risk factors for ischaemic and intracerebral haemorrhagic cerebral apoplexy in 22 countries (the INTERCEREBRAL APOPLEXY study): a case-control study[J]. Lancet, 2010, 376(9735):112-123.DOI: 10.1016/S0140-6736(10)60834-3.
[22] Chinese Guidelines 2014 for Secondary Prevention of Ischemic Cerebral Apoplexy and Transient Ischemic Attack, Cerebrovascular Disease Group Ischemic Cerebral Apoplexy Secondary Prevention Guidelines Writing Group, Chinese Society of Neurology, [J] Chinese Journal of Neurology, 2015, 48 (4): 258-273.DOI:10.3760/cma.j.issn.1006-7876.2015.04.003.
[23] Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association [J].Stroke, 2014,45(7):2160-2236.DOI:10.1161/STR.00000000 00000024.
[24] James PA, Oparil S, Carter BL, et al. 2014 Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee(JNC8) [J]. JAMA, 2014, 311(5): 507-520. DOI:10.1001/jama.2013.284427.
[25] Pergola PE, White CL, Szychowski JM, et al. Achieved blood pressures in the secondary prevention of small subcortical cerebral apoplexys(SPS3) study: challenges and lessons learned[J]. Am J Hypertens,2014,27(8):1052-1060.DOI:10.1093/ajh/hpu027.
[26] Forster A, Szabo K, Hennerici MG. Pathophysiological concepts of cerebral apoplexy in hemodynamic risk zones—do hypoperfusion and embolism interact? [J]. Nat Clin Pract Neurol, 2008, 4(4): 216-225.DOI:10.1038/ncpneuro0752.
[27] Jia Q, Zhao X, Wang C, et al. Diabetes and poor outcomes within 6 months after acute ischemic stroke: the China National Stroke Registry[J]. Stroke, 2011, 42(10): 2758-2762. DOI: 10.1161/STROKEAHA.111.621649.
[28] Control Group, Turnbull FM, Abraira C, et al. Intensive glucose control and macrovascular outcomes in type2 diabetes[J]. Diabetologia, 2009, 52(11): 2288-2298. DOI: 10.1007 / s00125-009-1470-0.
[29] Fullerton B, Jeitler K, Seitz M, et al. Intensive glucose control versus conventional glucose control for type1 diabetes mellitus [J].Cochrane Database Syst Rev,2014,14(2):CD009122. DOI: 10.1002/14651858.CD009122.pub2.
[30] Gerstein NS, Schulman PM, Gerstein WH, et al. Should more patients continue aspirin therapy perioperatively?: clinical impact of aspirin withdrawal syndrome[J]. Ann Surg,2012,255 (5):811-819.DOI:10.1097/SLA.0b013e318250504e.
[31] Devereaux PJ, Mrkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery[J]. N Engl J Med,2014,370(16): 1494-1503.DOI:10.1056/NEJMoa1401105.
[32] Levine GN, Bates ER, Bittl JA, et al.2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines: an update of the 2011 ACCF/ AHA/SCAI guideline for percutaneous coronary intervention, 2011ACCF / AHA guideline for coronary artery bypass graft surgery, 2012ACC / AHA / ACP / AATS / PCNA / SCAI / STS guideline for the diagnosis and management of patients with stable ischemic heart disease,2013ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA / ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014ACC / AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery[J]. Circulation, 2016,134(10):e123-155.DOI:10.1161/CIR.000000 0000000404.
[33] Douketis JD, Spyropoulos AC, Spencer FA, et al. Perioperative management of antithrombotic therapy[J]. Chest, 2012, 141 (2 Suppl): e326S-e350S.DOI:10.1378/chest.11-2298.
[34] Pisters R, Lane DA, Nieuwlaat R, et al. A novel user-friendly score(HAS-BLED)to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey[J]. Chest,2010,138(5):1093-1100.DOI:10.1378/chest.10-0134.
[35] Epstein AE, Alexander JC, Gutterman DD, et al. American college of chest physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery[J]. Chest, 2005, 128(2 Suppl): 24S-27S. DOI: 10.1378 / chest.128.2_suppl.24s.
[36] Douketis JD, Berger PB, Dunn AS, et al. The perioperative management of antithrombotic therapy: American college of chest physicians evidence-based clinical practice guidelines (8th edition)

[J]. Chest, 2008, 133(6 Suppl): 299S-339S. DOI: 10.1378/chest.08-0675.
[37] Dunn AS, Turpie AG. Perioperative management of patients receiving oral anticoagulants a systematic review[J]. Arch Intern Med, 2003, 163(8):901-908.DOI:10.1001/archinte.163. 8.901.
[38] Group PEPPTC. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention(PEP) trial[J]. Lancet,2000,355(9212):1295-1302.
[39] McKenna R. Abnormal coagulation in the postoperative period contributing to excessive bleeding[J]. Med Clin North Am, 2001, 85(5):1277-1310.DOI:10.1016/S0025-7125(05)70378-3.
[40] Torn M, Rosendaal FR. Oral anticoagulation in surgical procedures: risks and recommendations[J]. Br J Haematol,2003, 123(4):676-682.DOI:10.1046/j.1365-2141.2003.04652.x.
[41] Siegal D, Yudin J, Kaatz S, et al. Periprocedural heparin bridging in patients receiving vitamin K antagonists: systematic review and meta-analysis of bleeding and thromboembolic rates[J]. Circulation,2012,126(13):1630-1639. DOI:10.1161/CIRCULATIONAHA.112.105221.
[42] Steinberg BA, Peterson ED, Kim S, et al. Use and outcomes associated with bridging during anticoagulation interruptions in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) [J]. Circulation, 2015, 131(5): 488-494. DOI: 10.1161/CIRCULATIONAHA.114.011777.
[43] Heidbuchel H, Verhamme P, Alings M, et al. EHRA practical guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation: executive summary[J]. Eur Heart J,2013,34(27):2094-2106.DOI:10.1093/eurheartj/eht134.
[44] Lai A, Davidson N, Galloway SW, et al. Perioperative management of patients on new oral anticoagulants[J]. Br J Surg,2014,101(7):742-749.DOI:10.1002/bjs.9485.
[45] POISE Study Group, Devereaux PJ, Yang H, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiacsurgery(POISEtrial): a randomised controlled trial [J]. Lancet, 2008, 371(9627): 1839-1847. DOI: 10.1016 / S0140-6736(08)60601-7.
[46] VanLier F, Schouten O, Hoeks SE, et al. Impact of prophylactic beta-blocker therapy to prevent cerebral apoplexy after noncardiac surgery [J]. Am J Cardiol, 2010, 105(1): 43-47. DOI: 10.1016 / j. amjcard.2009.08.646.
[47] Fleisher LA, Fleischmann KE, Auerbach AD, et al.2014 ACC/ AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology / American Heart Association Task Force on practice guidelines. Developed in collaboration with the American College of Surgeons, American Society of Anesthesiologists, American Society of Echo cardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Vascular Medicine Endorsed by the Society of Hospital Medicine[J]. J Nucl Cardiol,2015,22(1):162-215.DOI: 10.1007/s12350-014-0025-z.
[48] Powers WJ, Rabinstein AA, Ackerson T, et al.2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association[J]. Stroke, 2018, 49(3):e46-e110.DOI:10.1161/STR.0000000000 000158.
[49] Jorgensen ME, Torp-Pedersen C, Gislason GH, et al. Time elapsed after ischemic cerebral apoplexy and risk of adverse cardiovascular events and mortality following elective noncardiac surgery[J]. JAMA, 2014, 312(3): 269-277. DOI: 10.1001/jama.2014.8165.
[50] Blacker DJ, Flemming KD, Link MJ, et al. The preoperative cerebrovascular consultation: common cerebrovascular questions before general or cardiac surgery[J]. Mayo Clin Proc, 2004,79(2):223-229.DOI:10.4065/79.2.223.
[51] Feng S, Yang S, Xiao W, et al. Effects of perioperative goal-directed fluid therapy combined with the application of alpha-1adrenergic agonists on postoperative outcomes: a systematic review and meta-analysis[J]. BMC Anesthesiol,2018, 18(1):113.DOI:10.1186/s12871-018-0564-y.
[52] Geriatric Anesthesiology Group, Chinese Society of Anesthesiology. Guideline on Perioperative Anesthesia Management for Chinese Elderly Patients (Continued) [J]. International Journal of Anesthesiology and Resuscitation, 2014, 35(12):1057-1069. DOI:10.3760/cma.j.issn.1673-4378. 2014.12.001.
[53] Moritz S, Kasprzak P, Arlt M, et al. Accuracy of cerebral monitoring in detecting cerebral ischemia during carotidendarterectomy: a comparison of transcranial Doppler sonography, near-infrared spectroscopy, stump pressure, and somatosensory evoked potentials[J]. Anesthesiology,2007,107 (4):563-569.DOI:10.1097/01.anes.0000281894.69422.ff.
[54] Alexandrov AV, Sloan MA, Tegeler CH, et al. Practice standards for transcranial Doppler(TCD) ultrasound. Part II. Clinical indications and expected outcomes[J]. J Neuroimaging,2012,22 (3):215-224.DOI:10.1111/j.1552-6569.2010.00523.x.

[55] Fischer GW, Lin HM, Krol M, et al. Noninvasive cerebral oxygenation may predict outcome in patients undergoing aorticarchsurgery[J]. J Thorac Cardiovasc Surg, 2011, 141(3): 815-821.DOI:10.1016/j.jtcvs.2010.05.017.
[56] Heringlake M, Garbers C, Kabler JH, et al. Preoperative cerebral oxygen saturation and clinical outcomes in cardiac surgery[J]. Anesthesiology, 2011, 114(1): 58-69. DOI: 10.1097 / ALN.0b013e3181fef34e.
[57] Mashour GA, Sharifpour M, Freundlich RE, et al. Perioperative metoprolol and risk of cerebral apoplexy after noncardiac surgery [J]. Anesthesiology, 2013, 119(6): 1340-1346. DOI: 10.1097 / ALN.0b013e318295a25f.
[58] Mashour GA, Moore LE, Lele AV, et al. Perioperative care of patients at high risk for cerebral apoplexy during or after non-cardiac, non-neurologic surgery: consensus statement from the Society for Neuroscience in Anesthesiology and Critical Care[J]. J Neurosurg Anesthesiol, 2014, 26(4):273-285. DOI:10.1097/ ANA.0000000000000087.
[59] Mortazavi SM, Kakli H, Bican O, et al. Perioperative cerebral apoplexy after total joint arthroplasty: prevalence, predictors, and outcome[J]. J Bone Joint Surg Am,2010,92(11):2095-2101.DOI:10.2106/ JBJS.I.00940.
[60] Memtsoudis SG, Sun X, Chiu YL, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients[J].Anesthesiology,2013,118(5):1046-1058. DOI:10.1097/ALN.0b013e318286061d.
[61] Talke PO, Sharma D, Heyer EJ, et al. Society for neuroscience in anesthesiology and critical care expert consensus statement: anesthetic management of endovascular treatment for acute ischemic cerebral apoplexy: endorsed by the society of neuro interventional surgery and the neuro critical care society[J]. J Neurosurg Anesthesiol, 2014, 26(2): 95-108. DOI: 10.1097 / ANA.0000000000000042.
[62] Sessler DI, Sigl JC, Kelley SD, et al. Hospital stay and mortality are increased in patients having a “triple low” of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia[J]. Anesthesiology, 2012, 116(6):1195-1203.DOI:10.1097/ALN.0b013e31825683dc.
[63] Bijker JB, Persoon S, Peelen LM, et al. Intraoperative hypotension and perioperative ischemic cerebral apoplexy after general surgery: anested case-control study[J]. Anesthesiology, 2012, 116(3):658-664.DOI:10.1097/ALN.0b013e3182472320.
[64] Geriatric Anesthesiology Group, Chinese Society of Anesthesiology. Guideline on Perioperative Anesthesia Management for Chinese Elderly Patients [J]. International Journal of Anesthesiology and Resuscitation, 2014, 35 (10): 870-881, 901.DOI: 10.3760/cma.j.issn.1673-4378.2014.10.002.
[65] Laflam A, Joshi B, Brady K, et al. Shoulder surgery in the beach chair position is associated with diminished cerebral autoregulation but no differences in postoperative cognition or brain injury biomarker levels compared with supine positioning: the anesthesia patient safety foundation beach chair study[J]. Anesth Analg, 2015, 120(1): 176-185. DOI: 10.1213/ANE.0000000000000455.
[66] McCulloch TJ, Liyanagama K, Petchell J. Relative hypotension in the beach-chair position: effects on middle cerebral artery blood velocity[J]. Anaesth Intensive Care,2010,38(3):486-491. DOI:10.1177/0310057X1003800312.
[67] Bahrainwala ZS, Grega MA, Hogue CW, et al. Intraoperative hemoglobin levels and transfusion independently predict cerebral apoplexy after cardiac operations[J]. Ann Thorac Surg,2011,91(4): 1113-1118.DOI:10.1016/j.athoracsur.2010.12.049.
[68] Group PS, Devereaux PJ, Yang H, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery(POISE trial):a randomised controlled trial [J]. Lancet, 2008, 371(9627): 1839-1847. DOI: 10.1016 / S0140-6736(08)60601-7.
[69] Ashes C, Judelman S, Wijeysundera DN, et al. Selective beta1-antagonism with bisoprololis associated with fewer postoperative cerebral apoplexys than atenololor metoprolol: a single-center cohort study of 44,092 consecutive patients [J]. Anesthesiology, 2013, 119(4): 777-787. DOI: 10.1097 / ALN.0b013e3182a17f12.
[70] Carson JL, Terrin ML, Noveck H, et al. Liberalor restrictive transfusion in high-risk patients after hip surgery[J].N Engl J Med,2011,365(26):2453-2462.DOI:10.1056/NEJMoa1012452.
[71] Hare GM, Tsui AK, McLaren AT, et al. Anemia and cerebral outcomes: many questions, fewer answers[J].AnesthAnalg,2008, 107(4):1356-1370.DOI:10.1213/ane.0b013e318184cfe9.
[72] Stringer WA, Hasso AN, Thompson JR, et al. Hyperventilation-induced cerebral ischemia in patients with acute brain lesions: demonstration by xenon-enhanced CT[J]. AJNR Am J Neuroradiol,1993,14(2):475-484.
[73] Murkin JM. Pro: tight intraoperative glucose control improves outcome in cardiovascular surgery[J]. J Cardiothorac Vasc Anesth,2000,14(4):475-478.DOI:10.1053/jcan.2000.7967.

[74] McGirt MJ, Woodworth GF, Brooke BS, et al. Hyperglycemia independently increases the risk of perioperative cerebral apoplexy, myocardial infarction, and death after carotidendarterectomy[J]. Neurosurgery, 2006, 58(6): 1066-1073; discussion1066-1073. DOI:10.1227/01.NEU.0000215887.59922.36.
[75] Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial[J].Ann Intern Med, 2007, 146(4):233-243. DOI:10.7326/0003-4819-146-4-20070 2200-00002.
[76] January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology / American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society[J]. J Am Coll Cardiol, 2014,649(21):e1-76.DOI:10.1016/j.jacc.2014.03.022.
[77] Doherty JU, Gluckman TJ, Hucker WJ, et al. 2017ACC expert consensus decision pathway for periprocedural management of anticoagulation in patients with nonvalvular atrial fibrillation: a report of the American college of cardiology clinical expert consensus document task force[J].J Am Coll Cardiol,2017,69 (7):871-898.DOI:10.1016/j.jacc.2016.11.024.
[78] Cerebral Apoplexy Prevention Engineering Committee, National Health and Family Planning Commission. Consensus of Chinese experts on the perioperative application of antiplatelet drugs in patients with ischemic cerebral apoplexy 2016 [J]. National Medical Journal of China, 2016, 96 (43): 3443-3453.DOI: 10.3760/cma.j.issn.0376-2491.2016.43.002.
[79] Emergency Medicine Quality Control Center, National Health Commission. Expert consensus on emergency diagnosis and treatment of acute ischemic cerebral apoplexy in China [J]. Chinese Journal of Emergency Medicine, 2018, 38 (4): 281-287.DOI: 10.3969/jz.issn.1002-1949.2018.04.001.
[80] Stroke Unit Tria lists C. Organised in patient (stroke unit) care for stroke[J]. Cochrane Database Syst Rev, 2013, 11(9): CD000197.DOI:10.1002/14651858.CD000197.pub3.
[81] Nor AM, McAllister C, Louw SJ, et al. Agreement between ambulance paramedic-and physician-recorded neurological signs with Face Arm Speech Test(FAST)in acute stroke patients[J]. Stroke, 2004, 35(6): 1355-1359. DOI: 10.1161 / 01. STR.0000128529.63156.c5.
[82] Kidwell CS, Starkman S, Eckstein M, et al. Identifying stroke in the field. Prospective validation of the Los Angeles prehospital stroke screen(LAPSS) [J]. Stroke, 2000, 31(1): 71-76. DOI: 10.1161/01.STR.31.1.71.
[83] Bray JE, Martin J, Cooper G, et al. Paramedic identification of cerebral apoplexy: community validation of the melbourne ambulance cerebral apoplexy screen[J]. Cerebrovasc Dis, 2005, 20(1): 28-33. DOI: 10.1159/000086201.
[84] Nor AM, Davis J, Sen B, et al. The recognition of cerebral apoplexy in the emergency room(ROSIER) scale: development and validation of a cerebral apoplexy recognition instrument[J]. Lancet Neurol,2005,4(11): 727-734.DOI:10.1016/S1474-4422(05)70201-5.
[85] Ciccone A, Valvassori L, Nichelatti M, et al. Endovascular treatment for acute ischemic cerebral apoplexy[J]. N Engl J Med,2013,368 (10):904-913.DOI:10.1056/NEJMoa1213701.
[86] Chinese Diagnostic Criteria for Parkinson's Disease (2016 Edition), Parkinson's Disease and Movement Disorders Professional Committee, China Neurologist Association of Chinese Medical Doctor Association; Parkinson's Disease and Movement Disorders Group, Chinese Society of Neurology [J]. Chinese Journal of Neurology, 2016, 49 (4): 268-271.DOI: 10.3760/cma.j.issn.1006-7876.2016.04.002.
[87] Mueller MC, Jüptner U, Wuellner U, et al. Parkinson′s disease influences the perioperative risk profile in surgery[J]. Langenbecks Arch Surg,2009,394(3): 511-515.DOI:10.1007/ s00423-008-0404-5.
[88] Ebihara S, Saito H, Kanda A, et al. Impaired efficacy of cough in patients with Parkinson disease[J]. Chest, 2003, 124(3): 1009-1015.DOI:10.1378/chest.124.3.1009.
[89] Malek NM, Grosset KA, Stewart D, et al. Prescription of drugs with potential adverse effects on cardiac conduction in Parkinson′s disease[J]. Parkinsonism Relat Disord,2013,19(6): 586-589.DOI:10.1016/j.parkreldis.2013.02.004.
[90] Arora A, Fletcher P. Parkinsonism hyperpyrexia syndrome caused by abrupt withdrawal of ropini role[J]. Br J Hosp Med (Lond), 2013, 74(12):698-699. DOI:10.12968/hmed.2013.74. 12.698.
[91] Cheung YF, Hui CH, Chan JH. Parkinsonism-hyperpyrexia syndrome due to abrupt withdrawal of amantadine[J]. Hong Kong Med J,2011,17(2):167-168.
[92] Newman EJ, Grosset DG, Kennedy PG. The parkinsonism- hyperpyrexia syndrome[J]. Neurocrit Care,2009,10(1):136-140. DOI:10.1007/s12028-008-9125-4.Epub2008Aug20.
[93] Brennan KA, Genever RW. Managing Parkinson′s disease during surgery[J]. BMJ, 2010, 341: c5718. DOI: 10.1136 / bmj. c5718.
[94] Katus L, Shtilbans A. Perioperative management of patients with Parkinson′s disease[J]. Am J

Med,2014,127(4):275-280. DOI:10.1016/j.amjmed.2013.11.014.
[95] Burton DA, Nicholson G, Hall GM. Anaesthesia in elderly patients with neurodegenerative disorders: special considerations[J]. Drugs Aging, 2004, 21(4): 229-242. DOI: 10.2165/00002512-200421040-00002.
[96] Jamwal S, Kumar P. Insight into the emerging role of striatal neurotransmitters in the pathophysiology of Parkinson′s disease and Huntington′s disease: a review[J]. Curr Neuropharma Col, 2019, 17(2): 165-175. DOI: 10.2174 / 1570159X16666180302115032.
[97] Roberts DP, Lewis SJG. Considerations for general anaesthesia in Parkinson′s disease[J]. J Clin Neurosci,2018,48:34-41.DOI: 10.1016/j.jocn.2017.10.062.
[98] Stagg P, Grice T. Nasogastric medication for perioperative Parkinson′s rigidity during anaesthesia emergence[J]. Anaesth Intensive Care, 2011, 39(6): 1128-1130. DOI: 10.1177 / 0310057X1103900623.
[99] Wullner U, Kassubek J, Odin P, et al. Transdermal rotigotine for the perioperative management of Parkinson′s disease[J]. J Neural Transm(Vienna),2010,117(7):855-859.DOI:10.1007/s00702-010-0425-4.
[100] Zesiewicz TA, Hauser RA, Freeman A, et al. Fentanyl-induced bradykinesia and rigidity after deep brain stimulation in a patient with Parkinson disease[J]. Clin Neuropharmacol,2009, 32(1):48-50.DOI:10.1097/WNF.0b013e31817e23e3.
[101] Yan T, Rizak JD, Yang S, et al. Acute morphine treatments alleviate tremorin1-methyl-4-phenyl-1,2,3,6-tetrahydropyridi- netreated monkeys[J]. PLoS One, 2014, 9(2): e88404. DOI: 10.1371/journal.pone.0088404.eCollection2014.
[102] Zoldan J, Friedberg G, Livneh M, et al. Psychosis in advanced Parkinson′s disease: treatment with ondansetron, a 5-HT 3 receptor antagonist[J].Neurology,1995,45(7):1305-1308.DOI: 10.1212/WNL.45.7.1305.
[103] Horstink M, Tolosa E, Bonuccelli U, et al. Review of the therapeutic management of Parkinson′s disease. Report of a joint task force of the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society- European Section(MDS-ES). Part II: late (complicated) Parkinson′s disease[J]. Eur J Neurol,2006,13(11):1186-1202. DOI:10.1111/j.1468-1331.2006.01548.x.
[104] Seppi K, Weintraub D, Coelho M, et al. The movement disorder society evidence-based medicine review update: treatments for the non-motor symptoms of Parkinson′s disease[J]. Mov Disord, 2011, 26(Suppl 3):S42-80.DOI:10.1002/mds.23884.
[105] Jia J, Wang F, Wei C, et al. The prevalence of dementia in urban and rural areas of China[J]. Alzheimers Dement, 2014, 10(1):1-9. DOI: 10.1016/j.jalz.2013.01.012.
[106] 2018 Chinese Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Impairment (II): Guidelines for the Diagnosis and Treatment of Alzheimer's Disease, Chinese Writing Group of Dementia and Cognitive Disorders, Professional Committee of Cognitive Disorders, China Neurologist Association of Chinese Medical Doctor Association. [J]. National Medical Journal of China, 2018, 98(13):971-977. DOI: 10.3760/cma.j.issn.0376-2491. 2018.13.004.
[107] Sperling RA, Aisen PS, Beckett LA, et al. Toward defining the preclinical stages of Alzheimer′s disease: recommendations from the national institute on aging-Alzheimer′s association work groups on diagnostic guidelines for Alzheimer′s disease [J]. Alzheimers Dement, 2011,7(3):280-292. DOI: 10.1016/j. jalz.2011.03.003.
[108] Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer′s disease: recommendations from the national institute on aging-Alzheimer′s association work groups on diagnostic guidelines for Alzheimer′s disease[J]. Alzheimers Dement, 2011,7(3):270-279. DOI: 10.1016/j.jalz.2011.03.008.
[109] McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer′s disease: recommendations from the national institute on aging-Alzheimer′s association work groups on diagnostic guidelines for Alzheimer′s disease [J]. Alzheimers Dement, 2011,7(3):263-269. DOI: 10.1016/j. jalz.2011.03.005.
[110] Newman MF, Kirchner JL, Phillips-Bute B, et al. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery[J]. N Engl J Med,2001,344(24):395-402. DOI: 10.1056/NEJM200102083440601.
[111] Evered L, Scott DA, Silbert B, et al. Postoperative cognitive dysfunction is independent of type of surgery and anesthetic [J]. Anesth Analg, 2011, 112(5): 1179-1185. DOI: 10.1213 / ANE.0b013e318215217e.
[112] Arora SS, Gooch JL, Garcia PS. Postoperative cognitive dysfunction, Alzheimer′s disease, and anesthesia[J]. Int J Neurosci,2014,124(4):236-242. DOI: 10.3109/00207454.2013. 833919.
[113] Rolandi E, Cavedo E, Pievani M, et al. Association of postoperative delirium with markers of neurodegeneration and brain amyloidosis: a pilot study[J]. Neurobiol Aging, 2018,61: 93-101. DOI:

10.1016/j.neurobiolaging.2017.09.020.
[114] Bilotta F, Doronzio A, Stazi E, et al. Postoperative cognitive dysfunction: toward the Alzheimer's disease pathomechanism hypothesis[J]. J Alzheimers Dis,2010,22(Suppl 3):81-89. DOI: 10.3233/JAD-2010-100825.
[115] Cortese GP, Burger C. Neuroinflammatory challenges compromise neuronal function in the aging brain: Postoperative cognitive delirium and Alzheimer's disease[J]. Behav Brain Res, 2017,322(Pt B):269-279. DOI: 10.1016/j. bbr.2016.08.027.
[116] Kant I, de Bresser J, van Montfort S, et al. MRI markers of neurodegenerative and neurovascular changes in relation to postoperative delirium and postoperative cognitive decline[J]. Am J Geriatr Psychiatry, 2017, 25(10): 1048-1061. DOI: 10.1016/j.jagp.2017.06.016.
[117] Klinger RY, James OG, Borges-Neto S, et al. 18F-florbetapir positron emission tomography-determined cerebral beta-amyloid deposition and neurocognitive performance after cardiac surgery[J]. Anesthesiology,2018,128(4):728-744. DOI: 10.1097/ALN.0000000000002103.
[118] Evered L, Scott DA, Silbert B. Cognitive decline associated with anesthesia and surgery in the elderly: does this contribute to dementia prevalence?[J]. Curr Opin Psychiatry,2017,30(3): 220-226.
[119] Starkstein SE, Jorge R, Mizrahi R, et al. The construct of minor and major depression in Alzheimer's disease[J]. Am J Psychiatry,2005,162(11):2086-2093.DOI:10.1097/YCO.0000 000000000321.
[120] Moller JT, Cluitmans P, Rasmussen LS, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction[J]. Lancet, 1998, 351 (9106):857-861. DOI: 10.1016/s0140-6736(97)07382-0.
[121] Chan MT, Cheng BC, Lee TM, et al. BIS-guided anesthesia decreases postoperative delirium and cognitive decline[J]. J Neurosurg Anesthesiol, 2013, 25(1): 33-42. DOI: 10.1097 / ANA.0b013e3182712fba.
[122] Radtke FM, Franck M, Lendner J, et al. Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction[J]. Br J Anaesth, 2013, 110(Suppl 1): i98-i105. DOI: 10.1093/bja/aet055.
[123] Punjasawadwong Y, Chau-In W, Laopaiboon M, et al. Processed electroencephalogram and evoked potential techniques for amelioration of postoperative delirium and cognitive dysfunction following non-cardiac and non-neurosurgical procedures in adults[J]. Cochrane Database Syst Rev, 2018, 15(5): D11283. DOI: 10.1002 / 14651858. CD011283.pub2. [124] Miller D, Lewis SR, Pritchard MW, et al. Intravenous versus inhalational maintenance of anaesthesia for postoperative cognitive outcomes in elderly people undergoing non-cardiac surgery[J]. Cochrane Database Syst Rev, 2018,21(8):D12317. DOI: 10.1002/14651858.CD012317.pub2.
[125] Zhang Y, Shan GJ, Zhang YX, et al. Propofol compared with sevoflurane general anaesthesia is associated with decreased delayed neurocognitive recovery in older adults[J]. Br J Anaesth, 2018, 121(3):595-604. DOI: 10.1016/j.bja.2018.05. 059.
[126] Liu Y, Pan N, Ma Y, et al. Inhaled sevoflurane may promote progression of amnestic mild cognitive impairment: a prospective, randomized parallel-group study[J]. Am J Med Sci, 2013, 345(5):355-360. DOI: 10.1097/MAJ.0b013e31825a 674d.
[127] Funder KS, Steinmetz J, Rasmussen LS. Anaesthesia for the patient with dementia undergoing outpatient surgery[J]. Curr Opin Anaesthesiol, 2009, 22(6): 712-717. DOI: 10.1097 / ACO.0b013e328331a4eb.
[128] Berger M, Burke J, Eckenhoff R, et al. Alzheimer's disease, anesthesia, and surgery: a clinically focused review[J]. J Cardiothorac Vasc Anesth, 2014, 28(6): 1609-1623. DOI: 10.1053/j.jvca.2014.04.014.
[129] Aust H, Eberhart L, Sturm T, et al. A cross-sectional study on preoperative anxiety in adults[J]. J Psychosom Res,2018,111: 133-139. DOI: 10.1016/j.jpsychores.2018.05.012.
[130] Mimic A, Bantel C, Jovicic J, et al.Psychological factors as predictors of early postoperative pain after open nephrectomy [J]. J Pain Res, 2018,11:955-966. DOI: 10.2147/JPR.S152282.
[131] Su SH, Xu W, Hai J, et al. Cognitive function, depression, anxiety and quality of life in Chinese patients with untreated unruptured intracranial aneurysms[J]. J Clin Neurosci,2014,21 (10):1734-1739. DOI: 10.1016/j.jocn.2013.12.032.
[132] Cserep Z, Balog P, Szekely J, et al. Psychosocial factors and major adverse cardiac and cerebrovascular events after cardiac surgery[J]. Interact Cardiovasc Thorac Surg, 2010,11 (5):567-572. DOI: 10.1510/icvts.2010.244582.
[133] Cserep Z, Losoncz E, Balog P, et al. The impact of preoperative anxiety and education level on long-term mortality after cardiac surgery[J]. J Cardiothorac Surg, 2012,7: 86. DOI: 10.1186/1749-8090-7-86.
[134] Sowden G, Mastromauro CA, Januzzi JL, et al. Detection of depression in cardiac inpatients:

feasibility and results of systematic screening[J]. Am Heart J, 2010, 159(5): 780-787. DOI: 10.1016/j.ahj.2010.02.029.
[135] Stenman M, Sartipy U.Depression screening in cardiac surgery patients[J]. Heart Lung Circ, 2019, 28(6): 953-958. DOI: 10.1016/j.hlc.2018.04.298.
[136] Visser MA, Howard KJ, Ellis HB. The influence of major depressive disorder at both the preoperative and postoperative evaluations for total knee arthroplasty outcomes[J]. Pain Med, 2019,20(4):826-833. DOI: 10.1093/pm/pny107.
[137] MacDowall A, Skeppholm M, Lindhagen L, et al. Effects of preoperative mental distress versus surgical modality, arthroplasty, or fusion on long-term outcome in patients with cervical radiculopathy[J]. J Neurosurg Spine, 2018, 29(4): 371-379. DOI: 10.3171/2018.2.SPINE171378.
[138] Schonberger RB, Feinleib J, Holt N, et al. Preoperative depression symptom severity and its impact on adherence to preoperative beta-blocker therapy[J]. J Cardiothorac Vasc Anesth, 2014, 28(6):1467-1473. DOI: 10.1053/j.jvca.2014.05. 006.
[139] Ghoneim MM, O′Hara MW. Depression and postoperative complications: an overview[J]. BMC Surg, 2016, 16: 5. DOI: 10.1186/s12893-016-0120-y.
[140] Stenman M, Holzmann MJ, Sartipy U. Relation of major depression to survival after coronary artery bypass grafting[J]. Am J Cardiol, 2014, 114(5): 698-703. DOI: 10.1016 / j. amjcard.2014.05.058.
[141] Kerper LF, Spies CD, Buspavanich P, et al. Preoperative depression and hospital length of stay in surgical patients[J]. Minerva Anestesiol,2014,80(9):984-991.
[142] Miller JA, Derakhshan A, Lubelski D, et al. The impact of preoperative depression on quality of life outcomes after lumbar surgery[J]. Spine J, 2015,15(1):58-64. DOI: 10.1016/j. spinee.2014.06.020.
[143] Stenman M, Holzmann MJ, Sartipy U. Association between preoperative depression and long-term survival following coronary artery bypass surgery -a systematic review and meta-analysis[J]. Int J Cardiol, 2016, 222: 462-466. DOI: 10.1016/j.ijcard.2016.07.216.
[144] Caumo W, Schmidt AP, Schneider CN, et al. Risk factors for preoperative anxiety in adults[J]. Acta Anaesthesiol Scand, 2001, 45(3):298-307. DOI: 10.1034/j.1399-6576.2001.04500 3298.x.
[145] Strøm J, Bjerrum MB, Nielsen CV, et al. Anxiety and depression in spine surgery-a systematic integrative review[J]. Spine J, 2018, 18(7):1272-1285. DOI: 10.1016/j.spinee.2018. 03.017.
[146] Leung CM, Wing YK, Kwong PK, et al. Validation of the Chinese-Cantonese version of the hospital anxiety and depression scale and comparison with the Hamilton Rating Scale of Depression[J]. Acta Psychiatr Scand, 1999, 100(6): 456-461.DOI: 10.1111/j.1600-0447.1999.tb10897.x.
[147] Tong X, An D, McGonigal A, et al. Validation of the generalized anxiety disorder-7 (GAD-7) among Chinese people with epilepsy[J]. Epilepsy Res,2016,120:31-36. DOI: 10.1016/ j.eplepsyres.2015.11.019.
[148] Zigmond AS, Snaith RP. The hospital anxiety and depression scale[J]. Acta psychiatrica Scandinavica,1983, 67(6):361-370. DOI:10.1111/j.1600-0447.1983.tb09716.x.
[149] Zheng Leilei, Wang Yeling, Li Huichun. Application of Hospital Anxiety and Depression Scale in General Hospital [J]. Shanghai Psychiatric Medicine, 2003, 15 (5): 264-266.DOI: 10.3969/j.issn.1002-0829.2003.05.003.
[150] Zheng Xiaohua, Shu Liang, Zhang Ailin, et al. Test report for State-Trait anxiety problem in Changchun [J]. Chinese Mental Health Journal, 1993, 7 (2): 60-62.
[151] Zung WW. A rating instrument for anxiety disorders[J]. Psychosomatics, 1971, 12(6):371-379. DOI:10.1016/S0033- 3182(71)71479-0.
[152] Tao Ming, Gao Jingfang. Revision of reliability and validity of self-rating anxiety scale (SAS-CR) [J]. Chinese Journal of Nervous and Mental Diseases, 1994, 20 (5): 301-303.
[153] Ju HB, Kang EC, Jeon DW, et al. Associations among plasma stress markers and symptoms of anxiety and depression in patients with breast cancer following surgery[J]. Psychiatry Investig,2018,15(2):133-140. DOI: 10.30773/pi.2017.07.26.
[154] Niu L, Jia C, Ma Z, et al. Validating the geriatric depression scale with proxy-based data: a case-control psychological autopsy study in rural China[J]. J Affect Disord, 2018, 241: 533-538. DOI: 10.1016/j.jad.2018.08.066.
[155] Wu Y, Fu C, Zhang W, et al. The dermatology life quality in Chinese rosacea patients[J]. Psychol Health Med, 2018,23 (4):369-374. DOI: 10.1080/13548506.2017.1361540.
[156] Li Q, Lin Y, Hu C, et al. The Chinese version of hospital anxiety and depression scale: psychometric properties in Chinese cancer patients and their family caregivers[J]. Eur J Oncol Nurs,2016,25:16-23. DOI: 10.1016/j.ejon.2016.09.004.
[157] Sun XY, Li YX, Yu CQ, et al. Reliability and validity of depression scales of Chinese version: a systematic review [J]. Zhonghua Liu Xing Bing Xue Za Zhi, 2017, 38(1): 110-116. DOI: 10.3760/cma.j.issn.0254-6450.2017.01.021.

[158] Lee HC, Chiu HF, Wing YK, et al. The zung self-rating depression scale: screening for depression among the Hong Kong Chinese elderly[J]. J Geriatr Psychiatry Neurol,1994,7 (4):216-220. DOI:10.1177/089198879400700404.
[159] Renouf T, Leary A, Wiseman T. Do psychological interventions reduce preoperative anxiety?[J]. Br J Nurs,2014, 23(22):1208-1212. DOI: 10.12968/bjon.2014.23.22.1208.
[160] Tulgar S, Boga I, Piroglu MD, et al. Preoperative anxiety before spinal anesthesia: does internet-based visual information / multimedia research decrease anxiety and information desire? A prospective multicentered study[J]. Anesth Essays Res, 2017, 11(2): 390-396. DOI: 10.4103 / 0259-1162.206278.
[161] Nagrampa D, Bazargan-Hejazi S, Neelakanta G, et al. A survey of anesthesiologists′ role, trust in anesthesiologists, and knowledge and fears about anesthesia among predominantly hispanic patients from an inner-city county preoperative anesthesia clinic[J]. J Clin Anesth, 2015,27(2):97-104. DOI: 10.1016/j.jclinane.2014.05.012.
[162] McDonald S, Page MJ, Beringer K, et al. Preoperative education for hip or knee replacement[J]. Cochrane Database Syst Rev, 2014, 5: CD003526. DOI: 10.1002 / 14651858. CD003526.pub3.
[163] Klaiber U, Stephan-Paulsen LM, Bruckner T, et al. Impact of preoperative patient education on the prevention of postoperative complications after major visceral surgery: the cluster randomized controlled PEDUCAT trial[J]. Trials,2018, 19(1):288. DOI: 10.1186/s13063-018-2676-6.
[164] Senses E, Apan A, Kose EA, et al. The effects of midazolam and dexmedetomidine infusion on peri-operative anxiety in regional anesthesia[J]. Middle East J Anaesthesiol, 2013,22(1): 35-40.
[165] De Witte JL, Alegret C, Sessler DI, et al. Preoperative alprazolam reduces anxiety in ambulatory surgery patients: a comparison with oral midazolam[J]. Anesth Analg,2002,95(6): 1601-1606.
[166] Kim D, Lee S, Pyeon T,et al. Use of triazolam and alprazolam as premedication for general anesthesia[J]. Korean J Anesthesiol, 2015, 68(4):346-351. DOI: 10.4097/kjae.2015.68. 4.346.
[167] Movafegh A, Alizadeh R, Hajimohamadi F, et al. Preoperative oral passiflora incarnata reduces anxiety in ambulatory surgery patients: a double-blind, placebo-controlled study[J]. Anesth Analg, 2008, 106(6): 1728-1732. DOI: 10.1213 / ane.0b013e318172c3f9.
[168] Clarke H, Kirkham KR, Orser BA, er al. Gabapentin reduces preoperative anxiety and pain catastrophizing in highly anxious patients prior to major surgery: a blinded randomized placebo-controlled trial[J]. Can J Anaesth, 2013, 60(5): 432-443. DOI: 10.1007/s12630-013-9890-1.
[169] Walker KJ, Smith AF. Premedication for anxiety in adult day surgery[J]. Cochrane Database Syst Rev, 2009, 4: CD002192. DOI: 10.1002/14651858.CD002192.pub2.
[170] Swedish Council on Health Technology Assessment. Treatment of anxiety disorders: a systematic review [EB/OL]. Stockholm: Swedish Council on Health Technology Assessment (SBU),2005.
[171] Weinstein SM, Poultsides L, Baaklini LR, et al. Postoperative delirium in total knee and hip arthroplasty patients: a study of perioperative modifiable risk factors[J]. Br J Anaesth, 2018, 120(5):999-1008. DOI: 10.1016/j.bja.2017.12.046.
[172] Kohring JM, Erickson JA, Anderson MB, et al. Treated versus untreated depression in total joint arthroplasty impacts outcomes[J]. J Arthroplasty, 2018, 33(7S): S81-S85. DOI: 10.1016/j.arth.2018.01.065.
[173] Maslej MM, Bolker BM, Russell MJ, et al. The mortality and myocardial effects of antidepressants are moderated by preexisting cardiovascular disease: a meta-analysis[J]. Psychother Psychosom, 2017,86(5):268-282. DOI: 10.1159/ 000477940.
[174] Fond G, Loundou A, Rabu C, et al. Ketamine administration in depressive disorders: a systematic review and meta-analysis [J]. Psychopharmacology (Berl), 2014, 231(18): 3663-3676. DOI: 10.1007/s00213-014-3664-5.
[175] Lou QB, Nan K, Xiang FF, et al. Effect of perioperative multi-day low dose ketamine infusion on prevention of postmastectomy pain syndrome[J]. Zhonghua Yi Xue Za Zhi, 2017, 97(46):3636-3641. DOI: 10.3760/cma.j.issn.0376-2491. 2017.46.008.
[176] Hedrich WD, Hassan HE, Wang H. Insights into CYP2B6-mediated drug-drug interactions[J]. Acta Pharm Sin B,2016,6(5):413-425.DOI: 10.1016/j.apsb.2016.07.016.
[177] Stack CG, Rogers P, Linter SP. Monoamine oxidase inhibitors and anaesthesia. A review[J]. Br J Anaesth, 1988, 60(2): 222-227.DOI: 10.1093/bja/60.2.222.
[178] Baldo BA. Opioid analgesic drugs and serotonin toxicity (syndrome): mechanisms, animal models, and links to clinical effects[J]. Arch Toxicol, 2018,92(8):2457-2473. DOI: 10.1007/ s00204-018-2244-6.
[179] Kurhe Y, Mahesh R. Ondansetron attenuates co-morbid depression and anxiety associated

with obesity by inhibiting the biochemical alterations and improving serotonergic neurotransmission[J]. Pharmacol Biochem Behav, 2015, 136: 107-116. DOI: 10.1016/j.pbb.2015.07.004.
[180] Weeks HR 3rd, Tadler SC, Smith KW, et al. Antidepressant and neurocognitive effects of isoflurane anesthesia versus electroconvulsive therapy in refractory depression[J]. PLoS One, 2013,8(7):e69809. DOI: 10.1371/journal.pone.0069809.
[181] Yoosefi A, Sepehri AS, Kargar M, et al. Comparing effects of ketamine and thiopental administration during electroconvulsive therapy in patients with major depressive disorder: a randomized, double-blind study[J]. J ECT, 2014,30 (1):15-21. DOI: 10.1097/YCT.0b013e3182a4b4c6.
[182] Adachi Y, Kimura H, Sato N, et al. Preoperative level of depression is a predictor of postoperative levels of depression in patients with head and neck cancer[J]. Jpn J Clin Oncol, 2014,44(4):311-317. DOI: 10.1093/jjco/hyu002.
[183] Duivenvoorden T, Vissers MM, Verhaar JA, et al. Anxiety and depressive symptoms before and after total hip and knee arthroplasty: a prospective multicentre study[J]. Osteoarthritis Cartilage, 2013, 21(12):1834-1840. DOI: 10.1016/j.joca.2013. 08.022.
[184] Li Z, Geng W, Yin J, et al. Effect of one comprehensive education course to lower anxiety and depression among Chinese breast cancer patients during the postoperative radiotherapy period -one randomized clinical trial[J]. Radiat Oncol, 2018,13(1):111. DOI: 10.1186/s13014-018-1054-6.
[185] Sepehripour AH, Eckersley M, Jiskani A, et al. Selective serotonin reuptake inhibitor use and outcomes following cardiac surgery-a systematic review[J]. J Thorac Dis, 2018,10 (2):1112-1120. DOI: 10.21037/jtd.2018.01.69.

Chinese Multidisciplinary Expert Consensus of Perioperative Brain Health in Elderly Patients (II)

Perioperative Neurocognitive Disorders

I. Concepts
Perioperative neurocognitive disorders (PND) includes neurocognitive impairment that is already present preoperatively and newly developed postoperatively [e.g., postoperative cognitive disorder (POCD)] [1].
II. Preoperative Cognitive Impairment
As the population ages, the number of elderly patients requiring surgery increases year by year. Some studies have shown that cognitive impairment exists in 22% to 23% of elderly patients undergoing elective surgery [2]. Preoperative cognitive impairment is not only closely associated with postoperative complications, delirium, exacerbation of cognitive impairment, and increased mortality, but also accompanied by prolonged postoperative hospital stay and increased medical costs [3-6]. Therefore, assessing preoperative cognitive function is of great clinical importance (Table 1).
[Recommendation] For patients with poorly controlled diabetes, chronic obstructive pulmonary disease (COPD) with hypoxemia, history of cerebral apoplexy, history of Parkinson's disease, depression, and tumor radiotherapy/chemotherapy, be highly vigilant to whether there is preoperative cognitive impairment and it is recommended to assess their cognitive function
III. Assessment of Cognitive Function
Both the American College of Surgeons (ACS) and the American Geriatrics Society (AGS) recommend preoperative cognitive assessment in elderly patients by health care providers in their guidelines on Geriatric Preoperative Assessment as well as guidelines on Geriatric Postoperative Delirium [40]. Knowledge of the patient's cognitive status prior to surgery is crucial for risk assessment stratification and influences subsequent monitoring, and treatment.
1. Preoperative cognitive function assessment: The Mini-Mental State Examination (MMSE) is one of the most popular screening tools for cognitive impairment in the world.
The test covers time, place orientation, immediate memory, attention, numeracy, short-term memory, language and visuospatial ability. The total score of MMSE is 30 points, and < 27 points is considered as cognitive impairment. It takes 5 ~ 10 min to complete the entire test. The correlation between MMSE score and the verbal and performance test score of the Wechsler Adult Intelligence Scale (WAIS) are 0.78 and 0.66, respectively, indicating a good correlation with the WAIS [41]. However, the MMSE is currently under copyright and may require licensing agreement to use.
Preoperative screening of cognitive function can also be performed using the Mini-Cognitive Assessment Instrument (Mini-Cog) [40]. The Mini-Cog involves three words recall tests of memory and a clock drawing test as interference; it tests visuospatial presentation, recall, and executive function.

The Mini-Cog is scored on a 5-point scale, where 5 is full and 2 or less is possibly cognitive impaired [42]. The Montreal Cognitive Assessment (MoCA) covers a wider range of cognitive domains than the MMSE, including attention, executive function, memory, language, visuospatial skills, abstract thinking, numeracy, and orientation; It has a full score of 30 points, and the cut score for cognitive impairment shall be 25 or less. It is more sensitive than MMSE to detect mild cognitive impairment (MCI) (Table 2).

2. Further examination of preoperative cognitive impairment: For patients with mild cognitive impairment and dementia, the ability to perform daily activities in life (e.g., Barthel Index Scale, total score 0 to 100; the higher score suggesting more independence), the psycho-behavioral symptoms (e.g., anxiety, depression, etc.), and the cognitive function in specific domains should be further tested. Further biomarker tests (e.g., amyloid, etc.) and imaging (e.g., MRI and CT) may be performed as necessary [18, 38].

Neuropsychological tests currently used to diagnose cognitive impairment mainly involve four aspects including memory, language, psychomotor speed, and attention/concentration.

Table 1 Common Diseases Leading to Preoperative Cognitive Impairment and Their Incidence

Disease Type	Incidence
Endocrine, nutritional, metabolic disease	
Diabetic mellitus	In elderly population with type 2 diabetes, the incidence of cognitive impairment is 11.3% [7], the annual incidence of dementia is 1.64% ~ 5.31%, and the annual incidence of conversion from mild cognitive impairment (MCI) to dementia is 8.79% [8]. Severe recurrent hypoglycemia and poor initial cognitive function are associated with accelerated cognitive decline [9].
Obesity	Age influences the relationship between obesity (BMI > 30 kg/m^2) and dementia: at age < 65 years, the obesity is positively associated with dementia (*RR* = 1.41); while at age ≥ 65 years, the obesity is negatively associated with dementia (*RR* = 0.83) [10].
Undernutrition	Patients with dementia have significantly lower serum vitamin D concentrations than patients with mild cognitive impairment and cognitively normal individuals [11]. Folic acid, vitamin B6, and B12 supplementation can reduce the incidence of brain atrophy by 30% in patients with mild cognitive impairment, particularly in the hippocampus and medial temporal lobe regions [12]. Among people > 80 years of age, those who consume soy products daily have a 20% lower risk of dementia than those who never consume soy products [12].
Respiratory system disorder	
Chronic obstructive pulmonary disease (COPD)	In patients with COPD and hypoxemia, the incidence of cognitive impairment is 77% [13]; Low oxygen saturation is associated with an increased risk of cognitive impairment (when oxygen saturation ≤ 88%, *OR* = 5.45); frequent oxygen therapy reduces the risk of cognitive impairment in such patients (*OR* = 0.14) [14-15].
Disorder circulatory system	
Hypertension	The incidence of dementia in untreated hypertensive patients is 1.78% ~ 8.31%; the incidence of dementia in hypertensive patients receiving antihypertensive treatment is 0.89% ~ 7.47% [16].
Cardiovascular disease	Among patients undergoing elective coronary artery bypass graft surgery, 35% have preoperative cognitive impairment [17]. 68% of patients over the age of 60 undergoing vascular surgery have preoperative cognitive impairment or dementia and 88.3% are missed for diagnose [18].
Nervous system disease	
Cerebral apoplexy	10% patients have coexisting dementia before the first cerebral apoplexy, 10% patients develop new dementia shortly after the first cerebral apoplexy, and more than 1/3 patients develop dementia after recurrent cerebral apoplexy [19]; 3 months after cerebral apoplexy, the incidence of dementia is 15% ~ 30% [20]; The incidence of dementia ranges from 7% to 41% in the first year after cerebral apoplexy and increases at a rate of 1.7% to 3% per year [19].
Other associated dementia	In the elderly Chinese population > 60 years of age, the incidence of mild cognitive impairment is 15.3% ~ 42.0% [21-23]. The incidence of dementia ranges from 4.7% to 10.44% [24-26]. Among the causes of dementia, Alzheimer's disease (AD) is the most common; followed by vascular dementia (VaD), which accounts for approximately 15% of patients with dementia [20].
Parkinson's disease (PD)	The incidence of mild cognitive impairment in patients newly diagnosed with Parkinson's disease is twice that of healthy elderly; the incidence of mild cognitive impairment in patients

	diagnosed with Parkinson's disease within 3 to 5 years of diagnosis is 20% to 57% [27]. In Parkinson's disease patients with mild cognitive impairment, the incidence of dementia after 36 months is 8% [28]. The patients with Parkinson's disease are 3 to 5 times more likely to develop dementia than healthy individuals, and the incidence of dementia in patients of Parkinson's disease is estimated to be 2% to 3% [27].
Encephalitis	The mortality of encephalitis is usually 5% to 15%, and cognitive impairment is prevalent among survivors [29].
Sleep disorder	
Obstructive sleep apnea syndrome (OSA)	Dementia is more likely to occur in the first 2.5 years of OSA diagnosis; the hazard ratio for developing dementia is 1.7 for OSA patients overall and 2.38 for women; and the risk of developing dementia increased 5.08 times for 50-year-old male OSA patients, and 2.20 times for female OSA patients ≥ 70 years [30].
Other	Patients with insomnia and use of hypnotics have a higher risk of dementia (*HR* = 2.34) [31].
Mental and behavioral disorders	
Depression	30% to 40% of non-demented elderly patients with depression show executive disorder in cognitive examination [32-33].
Tumor	
Central	The incidence of disabling cognitive impairment is 50% to 90% in patients with brain tumors surviving more than 6 months after radiation therapy [34].
Non-central	The incidence of chemotherapy-related cognitive impairment ranges from 14% to 85% [35].
Digestive system	
Liver cirrhosis	Cirrhotic patients who have had episodes of hepatic encephalopathy show persistent cognitive impairment with loss of learning ability, and the severity of impairment increases with the number of episodes of hepatic encephalopathy [36-37].
Other	
Frailty syndrome	The definition of frailty syndrome: Satisfying more than 3 items of poor grip strength, slow gait speed, low physical activity, weight loss without cause, and exhaustion [38]. Frailty syndrome, a short-term predictor of dementia and vascular dementia, is significantly associated with an increased risk of dementia (adjusted hazard ratio, 1.85), particularly vascular dementia (adjusted hazard ratio, 2.68) [39].

Note: MCI: mild cognitive impairment; BMI: body mass index; *RR:* relative risk; COPD: chronic obstructive pulmonary disease; *OR*: odds ratio; VaD: vascular dementia; PD: Parkinson's disease; *HR*: hazard ratio; OSA: obstructive sleep apnea syndrome

Table 2 Common Cognitive Function Assessment Scale

Scale	Sensitivity [a] (%)	Specificity [a] (%)	Assessment time (min)
MMSE [38]	63.4	65.4	5 ~ 10
Mini-cog [39]	76 ~ 100	54 ~ 85	2 ~ 4
MoCA [38]	80 ~ 100	50 ~ 70	10 ~ 15

Note: MMSE: Mini-Mental State Examination; Mini-cog: Mini-Cognitive Assessment Instrument; MoCA: Montreal Cognitive Assessment; [a] Sensitivity and specificity in identifying mild cognitive impairment (MCI)

Most frequently used neuropsychological tests include the Addition (attention, concentration), Visual Reproduction (visual perception and visual memory), Associate Learning (verbal memory and verbal learning), and Digit Span – forward/backward (attention, concentration, and short-term memory) tests from the Wechsler Memory Scale and Digit Symbol Test (visual-motor coordination, motor and mental speed) from the Wechsler Adult Intelligence Scale (Revised). Higher scores on above test items represent better function; Trail Making Test (visual spatial scanning, attention, and motor sequencing skills) and Purdue Pegboard Test – preferred/non-preferred hand (manual dexterity) from the Wechsler Adult Intelligence Scale (Revised), with lower scores on these two tests representing better function [42-43].

3. Diagnosis of new-onset postoperative cognitive disorder (POCD): according to the traditional definition, POCD refers to new-onset impairment lasting for more than two weeks in two or more cognitive domains after surgery [44]. Based on this, the classical approach is to analyze the test results using the reliable change index rule (I-RCI rule) [45]. This method requires a control group of normal subjects who don't have surgery take neuropsychological tests at the same time intervals as the patients. First, the value after the same interval is subtracted from the baseline value of the control

group to obtain the qualified learning effect. The patients' postoperative test value is then subtracted from the preoperative baseline value and the mean learning effect. Result is divided by the standard deviation of the learning effect from control group to obtain the Z value for each test; the Z values of all tests of a single patient are summed and then divided by the standard deviation of the sum of the Z values of all tests in the control group to obtain the total Z value of that patient. Patients with more than two test items having Z value ≤ 1.96 or total Z values ≤ 1.96 are diagnosed as POCD. For consistency with the literatures, POCD is still used in this document.
According to the new nomenclature in 2018, traditional POCD is divided into three categories according to the time of occurrence: delayed neurocognitive recovery within 30 days after surgery, postoperative mild/major neurocognitive disorder from 30 days to one year after surgery, and mild/major neurocognitive disorder after 1 year [1]. Their diagnoses are all made following the DSM-V criteria for mild/major neurocognitive impairment. This criterion requires that within one or more cognitive domains (complex attention, executive function, learning and memory, language, perception, or social cognition), there is a mild/significant cognitive decline compared to the level of previous performance. Among them, mild NCD refers to a decrease of one ~ two standard deviations in cognitive function score compared with the baseline value or the control group, and the cognitive deficit does not interfere with the independence of daily activities; major NCD refers to a decrease of more than two standard deviations in cognitive function score compared with the baseline value or the control group, and the cognitive deficit interferes with the independence of daily activities [46].
[Recommendation] Routine screening for cognitive impairment in high-risk elderly patients is recommended prior to surgery. For patients with preoperative cognitive impairment and dementia, their ability of daily living and mental or behavioral symptoms should be further assessed, and neuropsychological tests, laboratory or imaging examinations should be performed when necessary. Repeated cognitive function screening or neuropsychological tests after surgery can help identify new-onset cognitive impairment.
IV. Preoperative Preparation and Intervention
1. Improvement of basal state and cognitive function: as mentioned above, lack of sleep, chronic stress, chronic alcohol consumption, disorders of perceptual functions (e.g., audiovisual sensations), metabolic and endocrine dyscrasia, diseases, etc., all have a negative impact on cognitive function. Frailty and malnutrition are also accompanied by an increased risk of cognitive impairment [43]. While preoperative cognitive impairment is an important risk factor for postoperative cognitive complications.
Correcting bad living habits, improving perception (correcting vision, wearing hearing aids), maintaining normal metabolic and endocrine functions, and actively treating coexisting diseases are the basis for improving the preoperative physical condition. In addition, targeted interventions can be implemented. Participation in physical exercise, developing social contacts and mindfulness training have been shown to improve patients' physical and mental health and cognitive performance [43]. For patients with mild cognitive impairment, meta-analysis has shown that multiple cognitive trainings may prompt recruitment of alternate neural processes as well as support primary networks, resulting in improved cognitive function in patients [45]. Preoperative improvement of nutritional status, physical exercise, behavioral intervention, and implementation of cognitive function training can effectively improve cognitive function and reduce the incidence of POCD [18, 40, 43].
The importance of teamwork in optimizing perioperative management of the elderly should be valued. Meta-analysis shows that preoperative geriatrics specialist consultation and intervention can reduce the occurrence of postoperative delirium in elderly patients with cognitive impairment [47]. If possible, drug abuse patients should be referred to a specialist for detoxification treatment.
[Recommendation] For patients with preoperative cognitive impairment, in addition to basic treatment, it is recommended to actively implement targeted interventions, including nutritional status improvement, physical exercise and cognitive function training.
2. Management of cognitive enhancing drugs: Currently there are a variety of drugs that can be used to improve cognitive function in patients with existing cognitive impairment, including vitamins, gamma-aminobutyric acids (such as piracetam, oxiracetam), ergot alkaloids (such as dihydroergotoxine), calcium antagonists (such as nimodipine), cholinesterase inhibitors (such as donepezil and rivastigmine), glutamate receptor antagonists (such as memantine), neurotrophic factors (such as nerve growth factor, ganglioside), etc. [17, 38]. However, the effect of these drugs on surgical patients remains to be demonstrated.
Attention should be paid to the interaction between these drugs and anesthetic drugs during perioperative period. For example, ergot alkaloids have a strong alpha-receptor blocking effect which can inhibit vasoconstriction, lower blood pressure, and may increase the risk of perioperative hypotension. Cholinesterase inhibitors inhibit acetylcholinesterase and increase the concentration of acetylcholine at the neuromuscular junction, prolonging the duration of succinylcholine to 50 min;

non-depolarizing muscle relaxants may be considered for patients using such drugs, but it should be noted that succinylcholine can't be reversed by anticholinergics [18, 40]. Other adverse effects of cholinesterase inhibitors are sinus bradycardia, increased smooth muscle tone, or convulsions [40]. Patients with cognitive impairment may be treated concomitantly with psychotropic drugs including antidepressants, so it is also necessary to pay attention to the interaction between psychotropic drugs and anesthetic drugs (see Anxiety and Depression sections).

[Recommendation] The patient's preoperative medication should be inquired in detail, and if necessary, neurologist or psychiatrist should be involved to guide the perioperative medication; adverse drug reactions and possible interactions with anesthetic drugs should be noted.

V. Anesthesia and Intraoperative Management

(I) Preoperative Medication

Anticholinergic drugs can interfere with information storage in the brain, resulting in decreased memory, learning ability, and attention. Anticholinergic drugs are contraindicated preoperatively in patients with cognitive impairment; if such drugs must be used, drugs that cross the blood-brain barrier as little as possible should be selected. Blood-brain barrier passage rates of commonly used anticholinergics: glycopyrrolate < atropine < scopolamine < penehyclidine.

Midazolam is used to eliminate patients' bad memories in anesthesia because of its anterograde amnesia effect, but large doses or repeated use can also produce retrograde amnesia and destabilize memory function. Repeated or high-dose use of benzodiazepines should be avoided in patients with preoperative cognitive impairment.

[Recommendation] Anticholinergics are contraindicated preoperatively and benzodiazepines should be used with caution.

(II) Selection of Anesthetics

1. Propofol: In the early postoperative period of propofol anesthesia, patients' spatial cognitive ability, memory and thinking ability are reduced to varying degrees, and will gradually recover after 24 h [48]. Intravenous anesthesia has less effect on cognitive function than inhalation anesthesia [49-51].

2. Etomidate: There are few reports of postoperative cognitive dysfunction in elderly patients with etomidate anesthesia, and some studies have shown that there is no significant difference between etomidate and propofol in the incidence of POCD in elderly patients after surgery [52]. However, in animal studies, even a single anesthetic dose of etomidate causes long-term (up to one week) impairment of memory function, and this effect is associated with its caused increase in α5 subunit-containing GABA receptors on the surface of hippocampal neurons [53]. However, reversing this effect can improve the memory function of animals [54-55]. Although etomidate has the advantage of small hemodynamic effects in elderly patients, it is not recommended for routine anesthesia in elderly patients, given its potential adverse effects on postoperative memory function and adrenocortical function.

3. Ketamine: The results of studies on the neuroprotective effects of ketamine on neurological function are controversial [56-60]. Although a meta-analysis in 2018 showed that intraoperative low-dose ketamine decreased the occurrence of POCD, the included studies were of small sample sizes and low quality [60]. According to a large sample size randomized controlled study, intraoperative low-dose ketamine did not reduce postoperative delirium in elderly patients, but instead increased psychiatric symptoms adverse events [60].

4. Inhaled anesthetic drugs: Inhaled anesthetic drugs (e.g., sevoflurane, desflurane, isoflurane) have been reported to be associated with neurological protection and injury, but it is not clear which drug has an advantage in reducing the occurrence of POCD [61-63].

5. Intravenous analgesic drugs: Opioids are commonly used as analgesic drugs in the perioperative period, but high doses of opioids increase the risk of postoperative delirium [64]. Among all opioids, meperidine has an effect that significantly increases delirium [64]. Delirium is associated with an increased risk of cognitive impairment. In addition, meperidine may cause symptoms of acute serotonin toxicity when combined with antidepressant drugs including monoamine oxidase inhibitors and serotonin reuptake inhibitors (see Anxiety and Depression section) [65]. Therefore, pethidine is contraindicated in elderly patients. The effect of other opioids on postoperative cognitive function needs further investigation [66-67]. On the other hand, nonsteroidal anti-inflammatory drugs (e.g., parecoxib sodium, flurbiprofen axetil) and acetaminophen have been demonstrated to reduce the occurrence of postoperative delirium and may help improve postoperative cognitive function [68-69].

6. Muscle relaxants: No effect on cognitive function has been found [70-71].

7. Local anesthesia drug: The effect of intravenous continuous infusion of lidocaine on POCD after surgery is still controversial, and large sample size randomized controlled studies have not found perioperative lidocaine to be brain protective in patients undergoing cardiac surgery [72–74].

8. Dexmedetomidine: Dexmedetomidine is highly selective α2 adrenergic agonists. Several meta-

analyses have shown that perioperative administration of dexmedetomidine reduces the occurrence of postoperative cognitive dysfunction [75-79]. A recent meta-analysis also showed that perioperative dexmedetomidine also reduced the occurrence of postoperative delirium [80-81]; Delirium is an important risk factor for cognitive impairment.

9. Ulinastatin: Ulinastatin is a broad-spectrum protease inhibitor used intraoperatively to reduce excessive inflammation induced by surgery. Several randomized controlled studies have shown that intraoperative administration of ulinastatin reduces the occurrence of early postoperative cognitive impairment [82-84].

[Recommendation] Propofol based intravenous anesthesia is preferred in elderly surgical patients and can be combined with dexmedetomidine during perioperative period, NSAIDs or acetaminophen can be given in patients without contraindications, and ulinastatin can be given prophylactically in high-risk patients.

(III) Selection of Anesthesia Methods

1. Total intravenous anesthesia versus inhalation anesthesia: A meta-analysis in 2018 included 28 randomized controlled studies involving 4507 elderly patients undergoing various procedures, including cardiovascular surgery. The results showed that the use of propofol based maintenance of total intravenous anesthesia reduced the occurrence of early postoperative cognitive dysfunction compared with the maintenance of inhaled anesthesia (low quality evidence) [85]. A subsequent randomized controlled study also demonstrated that propofol intravenous anesthesia reduced the occurrence of early postoperative cognitive dysfunction in elderly patients undergoing tumor surgery compared with sevoflurane inhalation anesthesia [86].

2. General anesthesia versus regional block anesthesia: A 2014 systematic review showed that regional block anesthesia reduced the occurrence of early (within one week) postoperative cognitive impairment compared with general anesthesia, but there was no difference in cognitive recovery after one week [87].

Several randomized controlled studies later also reported similar results that regional block improved early postoperative cognitive recovery, but there was no significant difference between the two groups in cognitive outcome after one week [88-91].

3. Regional anesthesia combined with sedation: There are studies comparing the effects of different depths of propofol sedation during spinal anesthesia and found that, compared with patients with deep sedation, patients with shallow sedation had better postoperative cognitive recovery, especially for patients with comorbidities [92-93]. In critically ill patients with comorbid conditions, long-term survival was also improved in the shallow sedation group compared with the deep sedation group [94]. Another retrospective cohort study looked at elderly patients undergoing orthopedic surgery under regional block anesthesia and found that sedation with dexmedetomidine was able to reduce the occurrence of postoperative agitation compared with propofol sedation [95].

[Recommendation] For elderly surgical patients, regional block anesthesia is recommended as the first choice. Propofol based intravenous anesthesia is recommended for patients requiring general anesthesia. Shallow sedation with dexmedetomidine is recommended for regional block anesthesia patients requiring sedation.

(IV) Intraoperative Monitoring and Management

1. Monitoring of depth of anesthesia: Bispectral index (BIS) is the most widely used means of monitoring depth of anesthesia in clinical practice. Patients with preoperative cognitive impairment are more likely to have low BIS during anesthesia [96]. In several clinical studies, the use of intraoperative anesthesia depth monitoring (BIS) to avoid excessive anesthesia can reduce the incidence of postoperative delirium and/or POCD [97-103], although there are different results [104]. A meta-analysis found that intraoperative anesthesia depth monitoring could reduce POCD occurrence [105].

[Recommendation] Anesthesia depth monitoring is recommended during general anesthesia to avoid excessive anesthesia.

2. Non-invasive cerebral oxygen saturation monitoring: Non-invasive cerebral oxygen saturation monitoring can reflect changes in cerebral perfusion and guide the management of cerebral oxygen supply and demand balance. Noninvasive cerebral oxygen saturation monitoring in adults has a high degree of variability, approximately (71±6) %. Intraoperative low cerebral oxygen saturation values (e.g., less than 50%) are associated with an increased risk of new-onset postoperative brain injury and cognitive decline, and the duration of the decline is associated with the degree of postoperative cognitive impairment; whereas, circulatory management based on noninvasive cerebral oxygen saturation monitoring may improve postoperative cognitive recovery [106-108], even though the study results are not completely consistent [109]. Meta-analyses have shown that circulatory management under intraoperative cerebral oxygen saturation monitoring may reduce early postoperative cognitive impairment [110].

[Recommendation] It is recommended to maintain the balance of cerebral oxygen supply and demand under the monitoring of cerebral oxygen protection for high-risk patients.

3. Intraoperative circulatory management: Elderly patients with preoperative cognitive impairment tend to have varying degrees of impaired cerebrovascular self-regulation [111]. In previous studies, intraoperative hypotension was accompanied by an increased occurrence of cerebral apoplexy [112-113] and postoperative delirium [114-115]. However, a recent randomized controlled study failed to find that intraoperative goal-directed blood pressure management reduced cognitive impairment occurrence 3 months after surgery [116]. Nevertheless, for surgical patients with preoperative cognitive impairment, care should be taken to maintain stable blood pressure during surgery, and blood pressure fluctuations should not exceed 20% of the preoperative baseline blood pressure. It has been shown that anemia accompanies an increased risk of cognitive impairment in critically ill patients [117-118]. Perioperative hemoglobin levels in elderly patients should be maintained above 100 g/L as far as possible.

[Recommendation] The perioperative blood pressure of elderly patients should be maintained stable, and the fluctuation range should not exceed 20% of preoperative baseline blood pressure; the hemoglobin level of critically ill patients should be maintained above 100 g/L as far as possible.

4. Intraoperative respiratory management: Some studies have found that the use of a lung-protective ventilation mode (adjusting tidal volume frequency according to the patient's condition) during surgery can reduce postoperative delirium and cognitive impairment, which is possibly related to the reduction of systemic inflammatory response [119]. In elderly patients with cognitive impairment, maintaining the inspired oxygen concentration between 30% and 40% during maintenance of anesthesia helps to reduce the incidence of postoperative cognitive impairment and neurodegenerative diseases [120]. However, hypoxemia, which can also lead to decreased neurotransmitter release and cognitive impairment, should be avoided. Intraoperative hyperventilation ($PaCO_2$) can decrease cerebral blood flow and oxygen supply [121], which are particularly unfavorable for patients with preexisting cognitive impairment; therefore, excessive ventilation should be avoided and $PaCO_2$ should be maintained at a normal level (35 ~ 45 mmHg, 1 mmHg = 0.133 kPa).

[Recommendation] Lung protective ventilation strategy (small tidal volume, PEEP and lung recruitment strategy, etc.) is recommended; avoid excessive ventilation and maintain $PaCO_2$ at 35 ~ 45 mmHg; hypoxemia should be avoided and SpO_2 be maintained not less than 90% in perioperative period.

5. Body temperature management: Intraoperative hypothermia can lead to increased incidence of postoperative wound infection, delayed wound healing, significantly increased perioperative bleeding, and increased cardiovascular events in patients, which increase the risk of postoperative cognitive impairment in elderly patients with fragile brain function. In the elderly, hypothermia is very likely to occur during surgery due to body thermoregulation decline.

The body temperature during surgery of elderly patients should be routinely monitored and maintained no less than 36℃ by warming equipment [122].

[Recommendation] Routine monitoring of body temperature should be performed during the surgery to actively keep warm and maintain an intraoperative body temperature of no less than 36℃.

VI. Postoperative Management

Preoperative and intraoperative issues requiring preventive management are equally applicable after surgery. In the postoperative management of patients with cognitive impairment, a patient-centered medical care model should be established to allow patients' family members or people familiar with the patient to participate in medical care and improve patient outcomes.

(I) General Treatment

The patients continue to be monitored as necessary, and in addition to basic vital signs, blood glucose, electrolytes, invasive arterial blood pressure, fluid intake and output, and organ function indicators will be monitored when necessary.

Pay attention to timely correct acid-base and electrolyte disturbances, maintain stable blood glucose levels and homeostasis, and continue to treat primary diseases leading to cognitive impairment. Actively provide nutritional support; be alert to the risk of aspiration and asphyxia in patients with dysphagia and nasogastric feeding [123]. According to the patient's individual condition, perform passive or active activities at an early stage; however, the principle of individualization should be emphasized, and attention should be paid to the prevention of bed falls and tumbles. Perform cognitive function assessment and individualized cognitive function training, including memory training, orientation training, language communication ability training, visuospatial and executive ability training, and calculation ability training [123–124].

(II) Postoperative Pain Management

Inadequate postoperative analgesia can affect sleep, induce delirium and postoperative cognitive dysfunction and other adverse consequences, and prolong hospital stay and increase economic burden. Adequate postoperative analgesia is particularly important for patients with preexisting cognitive impairment.

1. Pain assessment: For patients with cognitive impairment, pain assessment may be more difficult due to concomitant memory, cognitive, expressive, communication impairments [125]. Patients with mild to moderate cognitive impairment can choose visual analogue scale (VAS), numeric rating scale (NRS) or verbal rating scale (VRS); patients who cannot express (e.g., endotracheal intubation) can use Wong-Baker facial expression scale [126]. For patients with severe cognitive impairment, the Chinese Version of Pain Assessment Scale for Advanced Dementia (C-PAINAD) can be selected [127–128], with total score of 0 to 10 and higher scores indicating severer pain (Table 3). It should be noted that pain assessment should be repeated after surgery, and pay attention to the patient's pain assessment during activities; tolerance of cough or general activities can be considered enough analgesia for the patients [127].

2. Analgesic management: For elderly patients, especially those with cognitive impairment, more precise individualized analgesic regimens and closer monitoring must be used to minimize adverse reactions while achieving the desired analgesic effect. Multimodal analgesia is recommended, i.e., an analgesic approach combined with peripheral (e.g., intraspinal block, peripheral nerve block, or local infiltration) and systemic analgesia, and analgesic drugs combined with opioids, tramadol, acetaminophen, nonsteroidal anti-inflammatory drugs, local anesthetics, and/or dexmedetomidine [126].

It should be noted that a systematic review of the use of opioids for postoperative pain management showed that meperidine was the only opioid that was positively associated with the development of delirium (see Anesthetic Drug Selection section); therefore pethidine analgesia should be avoided in elderly patients, especially those with preoperative cognitive impairment.

(III) Prevention of Postoperative Complications

Most elderly patients often have a combination of diseases and are more likely to have postoperative complications, require longer hospital stay, and have higher perioperative mortality [6, 18, 129–135]. Compared with patients without cognitive impairment before surgery, patients with cognitive impairment are more likely to develop delirium [6, 130–131, 133–135], pulmonary infection [6, 129, 132], urinary tract infection [129 – 130, 132, 134] and other complications after surgery, which can further aggravate cognitive impairment and worsen patient outcomes. So, it is essential to prevent the occurrence of postoperative complications. In elderly patients, the complication symptoms are not obvious or typical and thus difficult to be detected in the early stage of the disease, especially in patients with perception and communication difficulties due to cognitive impairment, so early identification and active intervention become more necessary to improve the prognosis of patients.

1. Delirium (see Delirium section): Preoperative cognitive impairment [131, 134–135] and dementia [6, 130–131, 133] are considered independent risk factors for the development of delirium, which occurs in more than two-thirds of patients with dementia. For the prevention, diagnosis and treatment of postoperative delirium in elderly patients, please refer to the delirium section of this Expert Consensus [136-138].

2. Pulmonary infections: Postoperative pulmonary infections occur 2 to 3 times more frequently in patients with dementia than in those without dementia. In order to reduce the occurrence of pulmonary infections, it is recommended to provide education and training for relevant personnel and implement the following measures in daily clinical practice: Raise the head of the bed 30° ~ 45° when there are no contraindications; adequate postoperative analgesia; active prevention of thrombosis; give priority to enteral nutrition; early pulmonary rehabilitation, such as breathing exercises, patting back for sputum aspiration; attention should be paid to avoid aspiration by mistake in patients with dysphagia; get out of bed as soon as possible [139].

3. Other complications: (1) Prevention of urinary tract infections: regular cleaning of the urethra, perineum, bladder irrigation if necessary [123] (2) Prevention of pressure ulcers: regularly turn over, assist the patient to perform slight activities on the bed, timely change clothes, keep the skin dry and clean, and conditionally apply the air cushion bed [125].

Table 3 Chinese Version of Pain Assessment Scale for Advanced Dementia (C-PAINAD)

Item	0 point	1 point	2 points	Score
Respiration	Normal	Occasional labored breathing/short period of hyperventilation	Dyspnea with noise/Long period of hyperventilation/tidal breathing [a]	
Negative vocalization	None	Occasional groan/low voice with negative tone	Repetitive yelling/Loud moaning or groaning / crying	

Facial expression	Smiling or inexpressive	Sad/frightened/frown	Facial grimacing
Body language	Relaxed	Tense/Distressed pacing/Fidgeting	Rigid /Fists clenched /Knees pulled up /Pulling or pushing away /Stiff/clenched fist/knee lift/pull or push/jostling
Consolability	No need to console	Solace the patient by distraction or touch, comfort	Cannot solace the patient by distraction or touch

Note: The observation time is about 5 min, and the total score is 10 points; [a] Also known as Cheyne-Strokes respiration, it is a kind of respiration that gradually changes from shallow slow to deep fast, then from deep fast to shallow slow, and then after a period of apnea, it begins to repeat the above periodic changes, and its shape is like tidal fluctuations.

[Recommendation] (1) elderly patients still need close monitoring after surgery, and in addition to the original treatment, supportive treatment should also be actively provided, including nutritional support, early mobilization and cognitive function training; (2) carefully assess the pain, give multimodal analgesia according to the principle of individualization, so as to achieve the ideal analgesic effect while minimizing adverse reactions; (3) early identification and active prevention of postoperative complications, especially delirium, lung infection and urinary tract infection, to improve patient prognosis.

Delirium

I. Overview
Delirium is an acute temporary abnormality of brain function that often occurs within hours to days and is characterized by inattention, altered level of consciousness, and cognitive impairment, and the condition tends to fluctuate over a short period of time [140]. The development of delirium is associated with worsened prognosis, including increased recent postoperative complications, prolonged in-hospital stay, increased medical costs, increased mortality [141-143], decreased long-term cognitive ability and quality of life and shortened survival time after surgery [143-145].
The incidence of delirium in elderly hospitalized patients ranges from 7% to 35%; in elderly patients requiring surgery for emergency and traumatic fractures and the like, the incidence of preoperative delirium can be as high as 60% [146-147]. The incidence of postoperative delirium is correlated with the severity of trauma of the surgery. Studies have shown a delirium incidence of 4% after cataract surgery and 10% to 30% after major non-cardiac surgery, while the incidence of delirium after cardiac surgery can be as high as 50% [148-151].
II Risk Factors for Delirium
The development of delirium is often the result of the interaction of predisposing and precipitating factors (Table 4). Susceptibility factors are closely related to the patient's underlying condition, among which brain aging, frailty, and dementia are important susceptibility factors for the development of delirium. For postoperative patients, perioperative stress, anesthetic/analgesic drugs, pain, and electrolyte disturbances are important precipitating factors of delirium.
III. Diagnosis of Delirium
1. The "gold standard" diagnosis of delirium: The definition of delirium in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) and the International Classification of Diseases-10 (ICD-10) are the "gold standards" used to diagnose delirium (Table 5). However, these standards lack structured test methods and standardized operating procedures, and each assessment takes about 30 min, which is mainly applicable to psychiatrists [152-153].
2. Quantitative diagnostic assessment tool for delirium: When untrained non-psychiatric medical staff (e.g., nurses, etc.) perform delirium assessment, the rate of underdiagnosis and misdiagnosis of delirium can be as high as 70% [154].

Table 4 Predisposing and Precipitating Factors for Postoperative Delirium [152-174]

Predisposing factor	Precipitating factor
Advanced age (≥ 65 years)	Drug
Reduced cognitive reserve	Sedative hypnotic
Dementia	Anticholinergic
Cognitive impairment	Polypharmacy
Depression	Alcohol or drug withdrawal
Brain atrophy	Surgery

Reduced physiological functional reserve	Cardiovascular surgery
Hyposthenia	Orthopedic procedures
Restriction of spontaneous movement	Prolonged extracorporeal circulation
Decreased exercise tolerance	Non-cardiac surgery
Visual or hearing impairment	Various diagnostic procedures
Decreased oral intake	Intraoperative hypotension
Dehydration	Intraoperative low cerebral oxygen saturation
Electrolyte disorder	Admission to ICU
Undernutrition	Environmental change
Co-existing disease	Physical restraint
Serious illness	Urethral catheter and various drainage tubes
Multiple coexisting conditions	Pain stimulation
Psychiatric disorder	Mental tension
Cerebral apoplexy history	Intercurrent illness
Metabolic disturbances	Infection
Trauma or fracture	Iatrogenic complications
Terminal illness	Severe acute illness
Co-infection with HIV	Metabolic disturbances
Sleep disordered breathing/insomnia	Fever or hypothermia
Drug use	Shock
Psychoactive drugs	Hypoxemia
Application of multiple drugs	Anemia
Drug dependence	Dehydration
Alcoholism	Hypoproteinemia
ApoE4 genotype	Malnutrition
-	Pain
-	Sleep disorder
-	Cerebral apoplexy

Note: "-" indicates that this item has no content.

To facilitate non-psychiatric physicians to administer rapid and accurate delirium assessments, investigators developed a variety of structured scales (Table 6). Among them, the Confusion Assessment Method (CAM) is currently one of the most widely used scales [155]. It makes a diagnosis based on nine common features of delirium, including acute onset, inattention, disorganized thinking, altered level of consciousness, disorientation, memory impairment, decreased comprehension, neurogenic agitation, and altered sleep-wake cycle. The sensitivity and specificity of this scale in the Chinese population are 76% and 100%, respectively [156]. The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) is designed for mechanically ventilated patients and is also of great value for the diagnosis of certain special subgroups of patients, such as patients at age of >65 years, with suspected dementia and Acute Physiology and Chronic Health Evaluation II (APCHHE II) of ≥ 23 points [157].

Table 5 Definition of Delirium in DSM-5 and ICD-10

Gold standard	Definition of delirium
DSM-5	1. Disturbances in attention (e.g., disturbance of attention directing, concentration, retention, and shifting) and consciousness (e.g., impairment of orientation to the environment) 2. It occurs over a short period of time (usually hours to days) and is characterized by acute changes in attention and cognitive function from baseline state, and the severity fluctuates within one day 3. It may be accompanied by impairment of cognitive function (e.g., impairment of memory, orientation, language, vision, spatial perception, and comprehension) 4. The occurrence of symptoms A and C cannot be explained by preexisting, established, progressive neuropsychiatric disorders; and does not occur in patients with severely impaired levels of consciousness (e.g., coma) 5. Causative factors such as drug intoxication/withdrawal, exposure to toxic substances, or multifactorial pathogenesis can be identified based on history, physical examination, and laboratory tests
ICD-10	1. Consciousness disturbances (from consciousness obscurity to coma) and impaired attention (reduced ability to concentrate, maintain, and shift)

2. Global deterioration of cognitive function (perceptual distortion, illusions and hallucinations, impairment of abstract thinking and comprehension, impairment of immediate and recent memory with relatively intact long-term memory, disorientation to time, place, person)
3. Psychomotor disturbances (hypoactive or hyperactive and non-premonitory interconversion, prolonged reaction time, increased or decreased speech rate, increased startle response)
4. Disturbance of the sleep-wake cycle (insomnia or total sleeplessness or inversion of the sleep-wake cycle, daytime sleepiness, worsening of nocturnal symptoms, dreaminess or nightmares, hallucinations upon awakening)
5. Affective disorders (e.g., depression, anxiety or fear, irritability, euphoria, apathy, confusion)
6. Symptoms often sudden occur, fluctuate within one day, with a total duration of less than six months

Its sensitivity and specificity in the Chinese population ranged from 81.8% to 93.4% and 87.7% to 90.8%, respectively [158].
[Recommendation] Assessment of delirium in perioperative elderly patients is recommended.

IV. Perioperative Management
1. Preoperative Assessment and Preparation: A detailed preoperative assessment of the patient's medical history and examinations can help identify high-risk patients and risk factors to take targeted preventive measures [163]. Preoperative assessment includes patient's medical history, comorbidities, mental status, activity status, nutritional status, drug treatment and other conditions, and checking whether the patient has abnormal examination results such as electrolyte imbalance. Preoperative depression and anxiety are important risk factors of delirium, and interventions including preoperative education can effectively alleviate depression and anxiety, thereby reducing the incidence of delirium [164-165]. Preoperative cognitive training, improvement of nutritional status, correction of electrolyte imbalance, and improvement of sleep have all been demonstrated to reduce the incidence of delirium [166-168].
A meta-analysis showed that preoperative avoidance of benzodiazepines and anticholinergics reduced the incidence of postoperative delirium [169]. However, in patients who have been taking benzodiazepines for a long time, stopping the drug before surgery may induce withdrawal symptoms. It is recommended that psychiatrists be invited to guide the perioperative medication management of such patients (see Anxiety and Depression section).

Table 6 Common Delirium Assessment Scale

Scale	Sensitivity (%)	Specificity (%)	Characteristics and applicable population
CAM	76.0	100	Developed based on DSM-3R; has been validated in Chinese population; applicable to hospitalized elderly patients [156]
CAM-ICU	81.8 ~ 93.4	87.7 ~ 90.8	Developed based on DSM-IV; has been validated in Chinese population; applicable to tracheal intubation, intensive care unit and emergency patients [158]
3D-CAM	95.0	94.0	Designed based on CAM and provides a standardized assessment method; has not yet been validated in Chinese population; applicable to elderly and patients with comorbid dementia [159]
DRS-98	-	-	Designed based on DSM-III R; has not been validated in Chinese population; contains 10 diagnostic criteria with scores of 0 – 4, respectively, with higher scores representing more severer symptoms; can be used to grade the severity of delirium [160]
Nu-DESC	80.0	92.0	Diagnostic cut-off of 3 points; has been validated in Chinese population; suitable for delirium screening [161]
MDAS	91.8	99.0	Diagnostic cut-off of 7.5 points; has been validated in Chinese population; suitable for delirium screening [162]

Note: CAM: Confusion Assessment Method; CAM-ICU: Confusion Assessment Method – ICU; 3D-CAM: 3D-Confusion Assessment Method; DRS-98: Delirium Rating Scale – 98; Nu-DESC: Nursing

Delirium Screening Scale; MDAS: Memorial Delirium Assessment Scale; DSM: Diagnostic and Statistical Manual of Mental Disorders

[Recommendation] For high-risk patients, non-pharmacological preventive measures, such as cognitive function training, psychological intervention, improvement of basal status, and sleep, are recommended before surgery; avoid preoperative use of drugs that increase the risk of delirium.
2. Anesthesia type: In patients undergoing prosthetic joint replacement surgery, it has been shown that spinal anesthesia and nerve block reduce the incidence of postoperative delirium [170–172]. However, a meta-analysis that included 15 observational studies of patients with hip fractures showed there was no statistically significant difference in the effect of general anesthesia versus regional block anesthesia on the incidence of delirium [173]. Another meta-analysis included 104 studies (including randomized controlled studies) on hip fracture patients also found no statistical difference between local and general anesthesia on the incidence of postoperative delirium [174].
[Recommendation] Available evidence did not find a difference in the effect of anesthesia type (general anesthesia or regional block anesthesia) on the incidence of postoperative delirium.
3. Anesthetics: A meta-analysis included 28 randomized controlled studies involving 4507 elderly patients undergoing various procedures, including cardiovascular surgery.
The results showed that compared with inhalation anesthesia, total intravenous anesthesia based on propofol reduced the incidence of early postoperative cognitive dysfunction (low-quality evidence), but there was no significant difference in the effect on postoperative delirium, mortality and hospital stay [85]. A subsequent randomized controlled study also demonstrated that, compared with sevoflurane anesthesia, propofol anesthesia reduced the occurrence of early postoperative cognitive dysfunction in elderly patients undergoing tumor surgery [86].
[Recommendation] Propofol total intravenous anesthesia may be more useful than inhalational anesthesia for improving early postoperative cognitive recovery in elderly patients undergoing major surgery.
4. Intraoperative anesthesia depth monitoring: There are three prospective randomized controlled studies showing that the use of anesthesia depth monitoring during general anesthesia to avoid deep anesthesia can reduce the risk of postoperative delirium in elderly patients [97, 175–176]. A meta-analysis also showed that in non-cardiac, non-neurosurgical elderly patients, the use of processed electroencephalography (EEG) and evoked potential monitoring to optimize anesthesia depth could reduce the occurrence of postoperative delirium; there was no significant effect on postoperative hospital stay and mortality [177]. However, a recent randomized controlled study showed that depth of anesthesia based on EEG monitoring failed to reduce early postoperative delirium [178].
[Recommendation] It is recommended to maintain an appropriate depth of anesthesia under EEG monitoring during surgery to avoid deep anesthesia.
5. Depth of intraoperative sedation: A randomized controlled study comparing the effects of two propofol sedation depths, BIS 50 and 80, on the incidence of postoperative delirium in elderly patients undergoing spinal anesthesia showed that patients in the lighter sedation (BIS 80) group had an approximately 50% lower risk of delirium development than those in the deep sedation (BIS 50) group [92]. Another randomized controlled study comparing the effect of different depth of propofol sedation (OASS sedation score 0 ~ 2 versus 3 ~ 5) on the incidence of postoperative delirium in elderly patients undergoing hip fracture surgery under spinal anesthesia showed no statistically significant difference in the incidence of delirium between the two groups; however, in patients without preoperative comorbidity, the incidence of postoperative delirium was lower in patients with light sedation [93].
[Recommendation] For elderly patients undergoing regional block anesthesia, it is recommended that deep sedation should be avoided during surgery.
6. Cerebral oxygen saturation monitoring: Cerebral oxygen saturation can be continuously monitored and reflected in real time using noninvasive techniques (e.g., near-infrared spectroscopy) [179]. A prospective cohort study observing the relationship between cerebral oxygen saturation and delirium in 20 elderly patients undergoing abdominal surgery showed that preoperative cerebral oxygen saturation was lower in patients with delirium than in those without delirium, but there was no significant difference in changes of cerebral oxygen saturation during surgery between the two groups [180]. Circulatory management based on cerebral oxygen saturation monitoring has been shown to reduce delirium rates in cardiac surgery and intensive care unit patients in several cohort studies [181-183]. A meta-analysis of 15 randomized controlled studies showed that intraoperative management of circulation under cerebral oxygen saturation

monitoring reduced postoperative cognitive impairment and shortened ICU stay, but did not reduce postoperative delirium occurrence [184].

[Recommendation] For patients at high risk of cerebral ischemia, management of circulation under cerebral oxygen saturation monitoring may help improve postoperative cognitive recovery.

7. Intraoperative blood pressure management: Intraoperative hypotension was accompanied by an increased risk of postoperative cerebral stroke in the POISE study and a nested case-control study [185–186]. In a cohort study of cardiac surgery patients and a systematic review of gastrointestinal surgery patients, intraoperative hypotension was accompanied by an increased risk of postoperative delirium [114-115]. However, a recent randomized controlled study failed to find that intraoperative goal-directed blood pressure management reduced cognitive impairment occurrence 3 months after surgery [116]. In a cohort study of patients undergoing cardiac surgery under cardiopulmonary bypass, excessive blood pressure during cardiopulmonary bypass (beyond the range of cerebrovascular autoregulation) was also accompanied by increased postoperative delirium [187].

[Recommendation] Goal-directed blood pressure management is recommended during surgery to avoid hypotension or excessive blood pressure.

8. Postoperative analgesia: Opioids are currently commonly used as analgesic drugs, but high doses of opioids increase the risk of postoperative delirium [64]. Several randomized controlled studies have shown that multimodal analgesia can improve analgesia, reduce opioid consumption, and reduce the incidence of postoperative delirium. Multimodal analgesic modalities include combined use of acetaminophen or nonsteroidal anti-inflammatory drugs, or combined regional blocks (peripheral nerve blocks and epidural blocks), among others [68–69, 177, 188–189].

[Recommendation] Multimodal analgesia is recommended to improve the analgesic effect and reduce the dose of opioids.

9. Depth of sedation in mechanically ventilated patients: For mechanically ventilated patients in the care unit, the use of shallow sedation may reduce the occurrence of delirium; the use of daily sedation interruptions or goal-directed sedation strategies may help to avoid excessive sedation [190]. A meta-analysis comparing the use of BIS monitoring with sedation scales to assess the depth of sedation in relation to patient outcome in the intensive care unit showed that BIS does not have advantage in deep sedation monitoring in the ICU [191].

[Recommendation] For mechanically ventilated patients in the intensive care unit, avoiding excessive sedation can reduce the incidence of delirium.

10. Selection of sedation drugs for mechanically ventilated patients: Meta-analysis shows that sedation with benzodiazepines is associated with a 2.59-fold increased risk of delirium and increased length of stay in the care unit and mechanical ventilation; non-benzodiazepines (dexmedetomidine, propofol) have a significant advantage in ICU patient sedation [192-194].

[Recommendation] Sedation with benzodiazepines should be avoided in mechanically ventilated patients in the care unit, and a preference for non-benzodiazepines (propofol and dexmedetomidine) is recommended.

V. Prevention of Delirium

1. Non-pharmacological prophylaxis: Non-pharmacological measures are the first choice to prevent delirium. Non-pharmacological interventions are mainly targeted at modifiable risk factors, such as cognitive impairment, sleep deprivation, immobilization, visual impairment, auditory impairment, and dehydration for delirium, and measures taken usually include maintaining orientation, improving cognitive function, early mobilization, improving sleep, active communication, wearing glasses and hearing aids, and preventing dehydration (Table 7). Multiple meta-analyses have shown that non-pharmacological interventions can reduce the risk of delirium by about 53% [195–196].

Table 7 Non-pharmacological Prophylaxis for Delirium

Risk factor	Intervention measures
Cognitive impairment	Improve cognitive function; improve orientation; avoid medications that affect cognitive function
Limited mobility	Early mobilization; daily physiotherapy or rehabilitation
Water electrolyte imbalance	Maintain normal serum sodium and potassium; control blood glucose; timely detect and handle dehydration or fluid overload

High risk drugs	Dose reduction or discontinuation of benzodiazepines, anticholinergics, antihistamines, and meperidine; dose reduction or discontinuation of other drugs to reduce drug interactions and adverse reactions
Pain	Use of paracetamol or non-steroidal anti-inflammatory drugs; use of nerve block; effective control of postoperative pain; avoidance of pethidine
Visual and hearing impairment	Wear glasses or use magnifying glasses to improve vision; wear hearing aids to improve hearing
Undernutrition	Proper use of dentures; nutritional support
Iatrogenic complications	Remove the urinary catheter as soon as possible after surgery to avoid urine retention or urinary incontinence; strengthen skin care to prevent pressure sores; promote the recovery of gastrointestinal function; if necessary, use drugs to promote gastrointestinal peristalsis; if necessary, perform chest physiotherapy or oxygen inhalation; appropriate anticoagulant therapy; prevent urinary tract infection
Sleep deprivation	Reducing environmental disturbances including sound and lighting; non-pharmacological measures to improve sleep

[Recommendation] Non-pharmacological measures should be taken for all elderly patients to prevent delirium.

2. Pharmacological prevention: Several meta-analyses have shown that perioperative use of dexmedetomidine can reduce the incidence of postoperative delirium [81, 197]; although there are also different opinions in this regard [198-199]. A 3-year follow-up study showed that low-dose dexmedetomidine after surgery may improve long-term outcomes while reducing the occurrence of postoperative delirium in elderly patients [200].

A meta-analysis showed that the effect of prophylactic administration of haloperidol on the incidence of postoperative delirium is not clear [201]. A large sample size randomized controlled study showed that prophylactic administration of ketamine did not reduce the incidence of postoperative delirium [59]. In addition, the use of haloperidol, ketamine, etc., in ICU patients was not found to improve other clinical outcomes [190].

[Recommendation] Perioperative administration of dexmedetomidine reduces postoperative delirium. Its impact on long-term outcome requires further investigation.

VI. Treatment of delirium

(I) Non-drug therapy

Non-pharmacological interventions may reduce the risk of delirium [195-196]. These measures are equally applicable to the treatment of delirium patients (Table 7) [155, 202-207]. Non-pharmacological measures are the first choice for the treatment of delirium [208].

[Recommendation] Non-pharmacological measures are preferred for the treatment of delirium patients.

(II) Drug therapy

1. Psychiatric drugs: Haloperidol and non-classical psychotropic drugs including quetiapine and olanzapine are used on average to treat agitated delirium [209-212]. However, it is necessary to be alert to the side effect of such drugs, such as extrapyramidal reactions and QT interval prolongation.

[Recommendation] Postoperative agitated delirium can be treated with haloperidol or atypical antipsychotics.

2. Dexmedetomidine: A meta-analysis showed that use of dexmedetomidine for the treatment of patients with agitated delirium reduced the duration of delirium [213].

[Recommendation] Dexmedetomidine is recommended for the treatment of postoperative agitated delirium.

Conflict of interest All authors declare that there is no conflict of interest.

Reference

[1] Evered L, Silbert B, Knopman DS, et al. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery-2018[J]. Br J Anaesth,2018,121(5): 1005-1012. DOI: 10.1016/j.bja.2017.11.087.

[2] Culley DJ, Flaherty D, Reddy S, et al. Preoperative cognitive stratification of older elective surgical patients: across-sectional study[J]. Anesth Analg,2016,123(1):186-192. DOI:10.1213/ANE.0000000000001277.

[3] Robinson TN, Wu DS, Pointer LF, et al. Preoperative cognitive dysfunction is related to adverse postoperative

outcomes in the elderly[J]. J Am Coll Surg,2012,215(1):12-18. DOI: 10.1016/j.jamcollsurg.2012.02.007.
[4] Chiu HC, Chen CM, Su TY, et al. Dementia predicted one-year mortality for patients with first hip fracture: a population-based study[J]. Bone Joint J, 2018, 100-B(9): 1220-1226. DOI: 10.1302 / 0301-620X. 100B9. BJJ-2017-1342.R1.
[5] Harrington MB, Kraft M, Grande LJ, et al. Independent association between preoperative cognitive status and discharge location after cardiac surgery[J]. Am J Crit Care, 2011,20(2):129-137. DOI: 10.4037/ajcc2011275.
[6] Kassahun WT. The effects of pre-existing dementia on surgical outcomes in emergent and nonemergent general surgical procedures: assessing differences in surgical risk with dementia[J]. BMC Geriatr, 2018, 18(1): 153. DOI: 10.1186 / s12877-018-0844-x.
[7] Kodl CT, Seaquist ER. Cognitive dysfunction and diabetes mellitus[J]. Endocr Rev,2008,29(4):494-511. DOI: 10.1210/ er.2007-0034.
[8] Ma F, Wu T, Miao R, et al. Conversion of mild cognitive impairment to dementia among subjects with diabetes: a population-based study of incidence and risk factors with five years of follow-up[J]. J Alzheimers Dis,2015,43(4):1441-1449. DOI: 10.3233/JAD-141566.
[9] Feinkohl I, Aung PP, Keller M, et al. Severe hypoglycemia and cognitive decline in older people with type 2 diabetes: the Edinburgh type 2 diabetes study[J]. Diabetes Care,2014,37(2): 507-515. DOI: 10.2337/dc13-1384.
[10] Pedditzi E, Peters R, Beckett N. The risk of overweight/obesity in mid-life and late life for the development of dementia: a systematic review and meta-analysis of longitudinal studies[J]. Age Ageing,2016,45(1):14-21. DOI: 10.1093/ageing/afv151.
[11] Wise J. Low vitamin D is linked to faster cognitive decline in older adults[J]. BMJ, 2015, 351: h4916. DOI: 10.1136/bmj. h4916.
[12] Hogervorst E, Kassam S, Kridawati A, et al. Nutrition research in cognitive impairment/dementia, with a focus on soya and folate[J]. Proc Nutr Soc,2017,76(4):437-442. DOI: 10.1017/ S0029665117000404.
[13] Grant I, Heaton RK, McSweeny AJ, et al. Neuropsychologic findings in hypoxemic chronic obstructive pulmonary disease [J]. Arch Intern Med,1982,142(8):1470-1476. DOI: 10.1001/ archinte.1982.00340210062015.
[14] Fried TR, Vaz FC, Rabow MW. Caring for the older person with chronic obstructive pulmonary disease[J]. JAMA, 2012, 308(12):1254-1263. DOI: 10.1001/jama.2012.12422.
[15] Thakur N, Blanc PD, Julian LJ, et al. COPD and cognitive impairment: the role of hypoxemia and oxygen therapy[J]. Int J Chron Obstruct Pulmon Dis,2010,5:263-269. DOI: 10.2147/ COPD.S10684.
[16] McGuinness B, Todd S, Passmore P, et al. Blood pressure lowering in patients without prior cerebrovascular disease for prevention of cognitive impairment and dementia[J]. Cochrane Database Syst Rev, 2009, 4: CD004034. DOI: 10.1002 / 14651858.CD004034.pub3.
[17] Silbert BS, Scott DA, Evered LA, et al. Preexisting cognitive impairment in patients scheduled for elective coronary artery bypass graft surgery[J]. Anesth Analg,2007,104(5):1023-1028. DOI: 10.1213/01.ane.0000263285.03361.3a.
[18] Partridge JS, Dhesi JK, Cross JD, et al. The prevalence and impact of undiagnosed cognitive impairment in older vascular surgical patients[J]. J Vasc Surg,2014,60(4):1002-1011. DOI: 10.1016/j.jvs.2014.04.041.
[19] Pendlebury ST, Rothwell PM. Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis[J]. Lancet Neurol,2009,8 (11):1006-1018. DOI:10.1016/S1474-4422(09)70236-4.
[20] O′Brien JT, Thomas A. Vascular dementia[J]. Lancet,2015,386 (10004):1698-1706. DOI: 10.1016/S0140-6736(15)00463-8.
[21] Vancampfort D, Stubbs B, Lara E, et al. Mild cognitive impairment and physical activity in the general population: Findings from six low-and middle-income countries[J]. Exp Gerontol, 2017, 100: 100-105. DOI: 10.1016 / j. exger.2017.10.028.
[22] Hao L, Wang X, Zhang L, et al. Prevalence, risk factors, and complaints screening tool exploration of subjective cognitive decline in a large cohort of the Chinese population[J]. J Alzheimers Dis, 2017, 60(2): 371-388. DOI: 10.3233 / JAD-170347.
[23] Liu W, Wu Y, Bai L, et al. Sex differences in the prevalence of and risk factors for nonvascular cognitive function in rural, low-income elderly in Tianjin, China[J]. Neuroepidemiology, 2018,51(3-4):138-148. DOI: 10.1159/000490496.
[24] Bakre AT, Chen R, Khutan R, et al. Association between fish consumption and risk of dementia: a new study from China and a systematic literature review and meta-analysis[J]. Public Health Nutr, 2018, 21(10): 1921-1932. DOI: 10.1017 / S136898001800037X.
[25] Deng J, Cao C, Jiang Y, et al. Prevalence and effect factors of dementia among the community elderly in Chongqing, China [J]. Psychogeriatrics, 2018, 18(5): 412-420. DOI: 10.1111 / psyg.12343.
[26 Jia J, Wang F, Wei C, et al. The prevalence of dementia in urban and rural areas of China[J]. Alzheimers Dement,2014,10 (1):1-9. DOI: 10.1016/j.jalz.2013.01.012.
[27] Kehagia AA, Barker RA, Robbins TW. Neuropsychological and clinical heterogeneity of cognitive impairment and dementia in patients with Parkinson′s disease[J]. Lancet Neurol,2010,9(12):1200-1213. DOI: 10.1016/S1474-4422(10) 70212-X.
[28] Lawson RA, Yarnall AJ, Duncan GW, et al. Stability of mild cognitive impairment in newly diagnosed Parkinson′s disease [J]. J Neurol Neurosurg Psychiatry,2017,88(8):648-652. DOI: 10.1136/jnnp-2016-315099.
[29] Venkatesan A. Epidemiology and outcomes of acute encephalitis[J]. Curr Opin Neurol,2015,28(3):277-282. DOI: 10.1097/WCO.0000000000000199.
[30] Pan W, Kastin AJ. Can sleep apnea cause Alzheimer's disease? [J]. Neurosci Biobehav Rev,2014,47:656-669. DOI: 10.1016/j.neubiorev.2014.10.019.
[31] Yaffe K, Falvey CM, Hoang T. Connections between sleep and cognition in older adults[J]. Lancet Neurol, 2014, 13(10): 1017-1028. DOI: 10.1016/S1474-4422(14)70172-3.
[32] Morimoto SS, Kanellopoulos D, Manning KJ, et al. Diagnosis and treatment of depression and cognitive impairment in late life[J]. Ann N Y Acad Sci,2015,1345:36-46. DOI: 10.1111/ nyas.12669.
[33] Alexopoulos GS, Kiosses DN, Heo M, et al. Executive dysfunction and the course of geriatric depression[J]. Biol

Psychiatry, 2005, 58(3): 204-210. DOI: 10.1016 / j. biopsych. 2005. 04.024.
[34] Makale MT, McDonald CR, Hattangadi-Gluth JA, et al. Mechanisms of radiotherapy-associated cognitive disability in patients with brain tumours[J]. Nat Rev Neurol, 2017, 13(1): 52-64. DOI: 10.1038/nrneurol.2016.185.
[35] Hodgson KD, Hutchinson AD, Wilson CJ, et al. A meta-analysis of the effects of chemotherapy on cognition in patients with cancer[J]. Cancer Treat Rev,2013,39(3):297-304. DOI: 10.1016/j.ctrv.2012.11.001.
[36] Umapathy S, Dhiman RK, Grover S, et al. Persistence of cognitive impairment after resolution of overt hepatic encephalopathy[J]. Am J Gastroenterol, 2014, 109(7): 1011-1019. DOI: 10.1038/ajg.2014.107.
[37] Bajaj JS, Schubert CM, Heuman DM, et al. Persistence of cognitive impairment after resolution of overt hepatic encephalopathy[J]. Gastroenterology,2010,138(7):2332-2340. DOI: 10.1053/j.gastro.2010.02.015.
[38] Robertson DA, Savva GM, Coen RF, et al. Cognitive function in the prefrailty and frailty syndrome[J]. J Am Geriatr Soc, 2014,62(11):2118-2124. DOI: 10.1111/jgs.13111.
[39] Solfrizzi V, Scafato E, Frisardi V, et al. Frailty syndrome and the risk of vascular dementia: the Italian Longitudinal Study on Aging[J]. Alzheimers Dement, 2013, 9(2): 113-122. DOI: 10.1016/j.jalz.2011.09.223.
[40] Chow WB, Rosenthal RA, Merkow RP, et al. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society[J]. J Am Coll Surg,2012,215 (4):453-466. DOI: 10.1016/j.jamcollsurg.2012.06.017.
[41] Zhou Xiaoxuan, Xie Min, Tao Jing, et al. Study and application of mini-mental state examination scale [J]. Chinese Journal of Rehabilitation Medicine, 2016, 31 (6): 694-696, 706. DOI: 10.3969/j.issn.1001-1242.2016.06.019.
[42] Borson S, Scanlan JM, Chen P, et al. The Mini-Cog as a screen for dementia: validation in a population-based sample[J]. J Am Geriatr Soc, 2003, 51(10): 1451-1454. DOI: 10.1046 / j.1532-5415.2003.51465.x.
[43] Bruhl AB, Sahakian BJ. Drugs, games, and devices for enhancing cognition: implications for work and society[J]. Ann N Y Acad Sci, 2016, 1369(1): 195-217. DOI: 10.1111 / nyas.13040.
[44] Association AP. Diagnostic and statistical manual of mental disorder[M]. 4th ed. Washington DC: American Psychiatirc Association,1994:143-146.
[45] Sherman DS, Mauser J, Nuno M, et al. The efficacy of cognitive intervention in mild cognitive impairment (MCI): a meta-analysis of outcomes on neuropsychological measures[J]. Neuropsychol Rev, 2017, 27(4): 440-484. DOI: 10.1007 / s11065-017-9363-3.
[46] Association AP. Diagnostic and statistical manual of mental disorders(DSM-5®)[M]. Washington DC:American Psychiatric Pub,2013.
[47] Moyce Z, Rodseth RN, Biccard BM. The efficacy of peri-operative interventions to decrease postoperative delirium in non-cardiac surgery: a systematic review and meta-analysis [J]. Anaesthesia, 2014, 69(3): 259-269. DOI: 10.1111 / anae. 12539.
[48] Padmanabhan U, Leslie K, Eer AS, et al. Early cognitive impairment after sedation for colonoscopy: the effect of adding midazolam and/or fentanyl to propofol[J]. Anesth Analg,2009, 109(5):1448-1455. DOI: 10.1213/ane.0b013e3181a6ad31.
[49] Yang Qilin. Comparison of the effect of intravenous anesthesia and inhalation anesthesia on postoperative cognitive function in elderly patients [J]. China Modern Medicine, 2017(5):112-114, 127.DOI: 10.3969/j.issn.1674-4721.2017.05.036.
[50] Xu D, Yang W, Zhao G. Effect of propofol and inhalation anesthesia on postoperative cognitive dysfunction in the elderly: a meta-analysis[J]. Nan Fang Yi Ke Da Xue Xue Bao, 2012, 32(11): 1623-1627. DOI: 10.3969 / j. issn. 1673-4254. 2012.11.022.
[51] Tang N, Ou C, Liu Y, et al. Effect of inhalational anaesthetic on postoperative cognitive dysfunction following radical rectal resection in elderly patients with mild cognitive impairment[J]. J Int Med Res, 2014, 42(6): 1252-1261. DOI: 10.1177 / 0300060514549781.
[52] Li Lin, Han Jicheng, Lu Xiangyu. Research progress and related prevention of postoperative cognitive dysfunction in elderly patients after general anesthesia [J/CD]. Chinese Journal of Clinicians (Electronic Edition), 2016(11): 305-306.
[53] Zurek AA, Yu J, Wang DS, et al. Sustained increase in alpha5 GABAA receptor function impairs memory after anesthesia[J]. J Clin Invest, 2014, 124(12): 5437-5441. DOI: 10.1172 / JCI76669.
[54] Martin LJ, Oh GH, Orser BA. Etomidate targets alpha5 gamma-aminobutyric acid subtype A receptors to regulate synaptic plasticity and memory blockade[J]. Anesthesiology, 2009, 111(5): 1025-1035. DOI: 10.1097 / ALN. 0b013e3181bbc961.
[55] Wang DS, Kaneshwaran K, Lei G, et al. Dexmedetomidine prevents excessive gamma-aminobutyric acid type A receptor function after anesthesia[J]. Anesthesiology, 2018, 129(3): 477-489. DOI: 10.1097/ALN.0000000000002311.
[56] Lee KH, Kim JY, Kim JW, et al. Influence of ketamine on early postoperative cognitive function after orthopedic surgery in elderly patients[J]. Anesth Pain Med, 2015, 5(5): e28844. DOI: 10.5812/aapm.28844.
[57] Hudetz JA, Iqbal Z, Gandhi SD, et al. Ketamine attenuates post-operative cognitive dysfunction after cardiac surgery[J]. Acta Anaesthesiol Scand,2009,53(7):864-872. DOI: 10.1111/ j.1399-6576.2009.01978.x.
[58] Rascon-Martinez DM, Fresan-Orellana A, Ocharan-Hernandez ME, et al. The effects of ketamine on cognitive function in elderly patients undergoing ophthalmic surgery: a pilot study [J]. Anesth Analg, 2016, 122(4): 969-975. DOI: 10.1213 / ANE.0000000000001153.
[59] Avidan MS, Maybrier HR, Abdallah AB, et al. Intraoperative ketamine for prevention of postoperative delirium or pain after major surgery in older adults: an international, multicentre, double-blind, randomised clinical trial[J]. Lancet, 2017, 390 (10091):267-275. DOI: 10.1016/S0140-6736(17)31467-8.
[60] Hovaguimian F, Tschopp C, Beck-Schimmer B, et al. Intraoperative ketamine administration to prevent delirium or postoperative cognitive dysfunction: A systematic review and meta-analysis[J]. Acta Anaesthesiol Scand, 2018, 62(9): 1182-1193. DOI: 10.1111/aas.13168.
[61] Cascella M, Bimonte S. The role of general anesthetics and the mechanisms of hippocampal and extra-hippocampal dysfunctions in the genesis of postoperative cognitive dysfunction[J]. Neural Regen Res, 2017, 12(11): 1780-1785.

DOI: 10.4103/1673-5374.219032.
[62] Manatpon P, Kofke WA. Toxicity of inhaled agents after prolonged administration[J]. J Clin Monit Comput,2018,32(4): 651-666. DOI: 10.1007/s10877-017-0077-0.
[63] Alalawi R, Yasmeen N. Postoperative cognitive dysfunction in the elderly: a review comparing the effects of desflurane and sevflurane[J]. J Perianesth Nurs, 2018, 33(5): 732-740. DOI: 10.1016/j.jopan.2017.04.009.
[64] Swart LM, van der Zanden V, Spies PE, et al. The comparative risk of delirium with different opioids: a systematic review[J].·Drugs Aging,2017,34(6):437-443. DOI: 10.1007/s40266-017-0455-9.
[65] Baldo BA. Opioid analgesic drugs and serotonin toxicity (syndrome): mechanisms, animal models, and links to clinical effects[J]. Arch Toxicol,2018,92(8):2457-2473. DOI: 10.1007/ s00204-018-2244-6.
[66] Khodayari-Rostamabad A, Olesen SS, Graversen C, et al. Disruption of cortical connectivity during remifentanil administration is associated with cognitive impairment but not with analgesia[J]. Anesthesiology,2015,122(1):140-149. DOI: 10.1097/ALN.0000000000000510.
[67] Silbert BS, Scott DA, Evered LA, et al. A comparison of the effect of high-and low-dose fentanyl on the incidence of postoperative cognitive dysfunction after coronary artery bypass surgery in the elderly[J]. Anesthesiology,2006,104(6): 1137-1145. DOI: 10.1097/00000542-200606000-00007.
[68] Mu DL, Zhang DZ, Wang DX, et al. Parecoxib supplementation to morphine analgesia decreases incidence of delirium in elderly patients after hip or knee replacement surgery: a randomized controlled trial[J]. Anesth Analg,2017, 124(6):1992-2000. DOI: 10.1213/ANE.0000000000002095.
[69] Subramaniam B, Shankar P, Shaefi S, et al. Effect of intravenous acetaminophen vs placebo combined with propofol or dexmedetomidine on postoperative delirium among older patients following cardiac surgery: the DEXACET randomized clinical trial[J]. JAMA,2019,321(7):686-696. DOI: 10.1001/ jama.2019.0234.
[70] Berger M, Burke J, Eckenhoff R, et al. Alzheimer′s disease, anesthesia, and surgery: a clinically focused review[J]. J Cardiothorac Vasc Anesth, 2014, 28(6): 1609-1623. DOI: 10.1053/j.jvca.2014.04.014.
[71] Di Nino G, Adversi M, Samolsky DB, et al. Peri-operative risk management in patients with Alzheimer′s disease[J]. J Alzheimers Dis, 2010, 22(Suppl 3): 121-127. DOI: 10.3233 / JAD-2010-101299.
[72] Mathew JP, Mackensen GB, Phillips-Bute B, et al. Randomized, double-blinded, placebo controlled study of neuroprotection with lidocaine in cardiac surgery[J]. Stroke, 2009, 40(3): 880-887. DOI: 10.1161 / STROKEAHA. 108. 531236.
[73] Mitchell SJ, Merry AF. Lignocaine: neuro-protective or wishful thinking? [J]. J Extra Corpor Technol,2009,41(1):P37-P42.
[74] Habibi MR, Habibi V, Habibi A, et al. Lidocaine dose-response effect on postoperative cognitive deficit: meta-analysis and meta-regression[J]. Expert Rev Clin Pharmacol, 2018, 11(4): 361-371. DOI: 10.1080 / 17512433. 2018. 1425614.
[75] Valentin LS, Pereira VF, Pietrobon RS, et al. Effects of single low dose of dexamethasone before noncardiac and nonneurologic surgery and general anesthesia on postoperative cognitive dysfunction-a phase III double blind, randomized clinical trial[J]. PLoS One, 2016, 11(5): e0152308. DOI: 10.1371/journal.pone.0152308.
[76] Hirsch J, Vacas S, Terrando N, et al. Perioperative cerebrospinal fluid and plasma inflammatory markers after orthopedic surgery[J]. J Neuroinflammation, 2016, 13(1): 211. DOI: 10.1186/s12974-016-0681-9.
[77] Zhou C, Zhu Y, Liu Z, et al. Effect of dexmedetomidine on postoperative cognitive dysfunction in elderly patients after general anaesthesia: a meta-analysis[J]. J Int Med Res,2016,44 (6):1182-1190. DOI: 10.1177/0300060516671623.
[78] Man Y, Guo Z, Cao J, et al. Efficacy of perioperative dexmedetomidine in postoperative neurocognitive function: a meta-analysis[J]. Clin Exp Pharmacol Physiol, 2015, 42(8): 837-842. DOI: 10.1111/1440-1681.12432.
[79] Li B, Wang H, Wu H, et al. Neurocognitive dysfunction risk alleviation with the use of dexmedetomidine in perioperative conditions or as ICU sedation: a meta-analysis[J]. Medicine (Baltimore), 2015, 94(14): e597. DOI: 10.1097 / MD. 0000000000000597.
[80] Duan X, Coburn M, Rossaint R, et al. Efficacy of perioperative dexmedetomidine on postoperative delirium: systematic review and meta-analysis with trial sequential analysis of randomised controlled trials[J]. Br J Anaesth,2018,121(2):384-397. DOI: 10.1016/j.bja.2018.04.046.
[81] Wu M, Liang Y, Dai Z, et al. Perioperative dexmedetomidine reduces delirium after cardiac surgery: A meta-analysis of randomized controlled trials[J]. J Clin Anesth,2018,50:33-42. DOI: 10.1016/j.jclinane.2018.06.045.
[82] Lv ZT, Huang JM, Zhang JM, et al. Effect of ulinastatin in the treatment of postperative cognitive dysfunction: review of current literature[J]. Biomed Res Int, 2016, 2016: 2571080. DOI: 10.1155/2016/2571080.
[83] Wang KY, Yang QY, Tang P, et al. Effects of ulinastatin on early postoperative cognitive function after one-lung ventilation surgery in elderly patients receiving neoadjuvant chemotherapy[J]. Metab Brain Dis,2017,32(2):427-435. DOI: 10.1007/s11011-016-9926-7.
[84] Zhang M, Zhang YH, Fu HQ, et al. Ulinastatin may significantly improve postoperative cognitive function of elderly patients undergoing spinal surgery by reducing the translocation of lipopolysaccharide and systemic inflammation [J]. Front Pharmacol, 2018, 9: 1007. DOI: 10.3389 / fphar.2018.01007.
[85] Miller D, Lewis SR, Pritchard MW, et al. Intravenous versus inhalational maintenance of anaesthesia for postoperative cognitive outcomes in elderly people undergoing non-cardiac surgery[J]. Cochrane Database Syst Rev, 2018, 8: CD012317. DOI: 10.1002/14651858.CD012317.pub2.
[86] Zhang Y, Shan GJ, Zhang YX, et al. Propofol compared with sevoflurane general anaesthesia is associated with decreased delayed neurocognitive recovery in older adults[J]. Br J Anaesth, 2018, 121(3): 595-604. DOI: 10.1016 / j. bja. 2018. 05. 059.
[87] Zywiel MG, Prabhu A, Perruccio AV, et al. The influence of anesthesia and pain management on cognitive dysfunction after joint arthroplasty: a systematic review[J]. Clin Orthop Relat Res, 2014, 472(5): 1453-1466. DOI: 10.1007 / s11999-013-3363-2.
[88] Liu J, Yuan W, Wang X, et al. Peripheral nerve blocks versus general anesthesia for total knee replacement in elderly patients on the postoperative quality of recovery[J]. Clin Interv Aging,2014,9:341-350. DOI: 10.2147/CIA.S56116.
[89] Mei B, Zha H, Lu X, et al. Peripheral nerve block as a supplement to light or deep general anesthesia in elderly

patients receiving total hip arthroplasty: a prospective randomized study[J]. Clin J Pain, 2017, 33(12): 1053-1059. DOI: 10.1097/AJP.0000000000000502.
[90] Tzimas P, Samara E, Petrou A, et al. The influence of anesthetic techniques on postoperative cognitive function in elderly patients undergoing hip fracture surgery: General vs spinal anesthesia[J]. Injury, 2018, 49(12): 2221-2226. DOI: 10.1016/j.injury.2018.09.023.
[91] Wang Y, Cheng J, Yang L, et al. Ropivacaine for intercostal nerve block improves early postoperative cognitive dysfunction in patients following thoracotomy for esophageal cancer[J]. Med Sci Monit,2019,25:460-465. DOI: 10.12659/ MSM.912328.
[92] Sieber FE, Zakriya KJ, Gottschalk A, et al. Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair[J]. Mayo Clin Proc, 2010, 85(1): 18-26. DOI: 10.4065 / mcp.2009.0469.
[93] Sieber FE, Neufeld KJ, Gottschalk A, et al. Effect of depth of sedation in older patients undergoing hip fracture repair on postoperative delirium: the STRIDE randomized clinical trial [J]. Jama Surg, 2018, 153(11): 987-995. DOI: 10.1001 / jamasurg.2018.2602.
[94] Brown CT, Azman AS, Gottschalk A, et al. Sedation depth during spinal anesthesia and survival in elderly patients undergoing hip fracture repair[J]. Anesth Analg,2014,118(5): 977-980. DOI: 10.1213/ANE.0000000000000157.
[95] Shin HJ, Koo BW, Bang SU, et al. Intraoperative dexmedetomidine sedation reduces the postoperative agitated behavior in elderly patients undergoing orthopedic surgery compared to the propofol sedation[J]. Minerva Anestesiol,2017, 83(10):1042-1050. DOI: 10.23736/S0375-9393.17.11794-3.
[96] Drummond JC. Depth of anesthesia causality dilemmas: the next generation[J]. Can J Anaesth,2016,63(2):142-147. DOI: 10.1007/s12630-015-0489-6.
[97] Chan MT, Cheng BC, Lee TM, et al. BIS-guided anesthesia decreases postoperative delirium and cognitive decline[J]. J Neurosurg Anesthesiol, 2013, 25(1): 33-42. DOI: 10.1097 / ANA.0b013e3182712fba.
[98] Radtke FM, Franck M, Lendner J, et al. Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction[J]. Br J Anaesth,2013,110 Suppl 1:i98-i105. DOI: 10.1093/bja/aet055.
[99] Willingham MD, Avidan MS. Triple low, double low: it′s time to deal achilles heel a single deadly blow[J]. Br J Anaesth, 2017,119(1):1-4. DOI: 10.1093/bja/aex132.
[100] Moller PA, Kamenik M. Bispectral index-guided induction of general anaesthesia in patients undergoing major abdominal surgery using propofol or etomidate: a double-blind, randomized, clinical trial[J]. Br J Anaesth, 2013, 110(3): 388-396. DOI: 10.1093/bja/aes416.
[101] Sessler DI, Sigl JC, Kelley SD, et al. Hospital stay and mortality are increased in patients having a “triple low” of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia[J]. Anesthesiology, 2012, 116(6): 1195-1203. DOI: 10.1097 / ALN. 0b013e31825683dc.
[102] Shu AH, Wang Q, Chen XB. Effect of different depths of anesthesia on postoperative cognitive function in laparoscopic patients: a randomized clinical trial[J]. Curr Med Res Opin, 2015, 31(10): 1883-1887. DOI: 10.1185 / 03007995. 2015. 1075968.
[103] Hou R, Wang H, Chen L, et al. POCD in patients receiving total knee replacement under deep vs light anesthesia: A randomized controlled trial[J]. Brain Behav, 2018, 8(2): e910. DOI: 10.1002/brb3.910.
[104] Steinmetz J, Funder KS, Dahl BT, et al. Depth of anaesthesia and post-operative cognitive dysfunction[J]. Acta Anaesthesiol Scand, 2010, 54(2): 162-168. DOI: 10.1111 / j. 1399-6576. 2009.02098.x.
[105] Lu X, Jin X, Yang S, et al. The correlation of the depth of anesthesia and postoperative cognitive impairment: A meta-analysis based on randomized controlled trials[J]. J Clin Anesth,2018,45:55-59. DOI: 10.1016/j.jclinane.2017.12.002.
[106] Cho H, Nemoto EM, Yonas H, et al. Cerebral monitoring by means of oximetry and somatosensory evoked potentials during carotid endarterectomy[J]. J Neurosurg, 1998, 89(4): 533-538. DOI: 10.3171/jns.1998.89.4.0533.
[107] Yao FS, Tseng CC, Ho CY, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery[J]. J Cardiothorac Vasc Anesth,2004,18(5):552-558. DOI: 0.1053/j. jvca.2004.07.007.
[108] Trafidlo T, Gaszynski T, Gaszynski W, et al. Intraoperative monitoring of cerebral NIRS oximetry leads to better postoperative cognitive performance: a pilot study[J]. Int J Surg,2015,16(Pt A):23-30. DOI: 10.1016/j.ijsu.2015.02.009.
[109] Goettel N, Burkhart CS, Rossi A, et al. Associations between impaired cerebral blood flow autoregulation, cerebral oxygenation, and biomarkers of brain injury and postoperative cognitive dysfunction in elderly patients after major noncardiac surgery[J]. Anesth Analg, 2017, 124(3): 934-942. DOI: 10.1213/ANE.0000000000001803.
[110] Yu Y, Zhang K, Zhang L, et al. Cerebral near-infrared spectroscopy (NIRS) for perioperative monitoring of brain oxygenation in children and adults[J]. Cochrane Database Syst Rev, 2018, 1: D10947. DOI: 10.1002 / 14651858. CD010947. pub2.
[111] Burkhart CS, Rossi A, Dell-Kuster S, et al. Effect of age on intraoperative cerebrovascular autoregulation and near-infrared spectroscopy-derived cerebral oxygenation[J]. Br J Anaesth,2011,107(5):742-748. DOI: 10.1093/bja/aer252.
[112] Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial[J]. Lancet, 2008, 371(9627): 1839-1847. DOI: 10.1016 / S0140-6736(08)60601-7.
[113] Bijker JB, Persoon S, Peelen LM, et al. Intraoperative hypotension and perioperative ischemic stroke after general surgery: a nested case-control study[J]. Anesthesiology,2012, 116(3):658-664. DOI: 10.1097/ALN.0b013e3182472320.
[114] Wesselink EM, Kappen TH, van Klei WA, et al. Intraoperative hypotension and delirium after on-pump cardiac surgery[J]. Br J Anaesth,2015,115(3):427-433. DOI: 10.1093/bja/aev256.
[115] Scholz AF, Oldroyd C, McCarthy K, et al. Systematic review and meta-analysis of risk factors for postoperative delirium among older patients undergoing gastrointestinal surgery[J]. Br J Surg,2016,103(2):e21-e28. DOI: 10.1002/bjs.10062.

[116] Langer T, Santini A, Zadek F, et al. Intraoperative hypotension is not associated with postoperative cognitive dysfunction in elderly patients undergoing general anesthesia for surgery: results of a randomized controlled pilot trial[J]. J Clin Anesth, 2019, 52: 111-118. DOI: 10.1016 / j. jclinane. 2018.09.021.
[117] Ge Y, Ma Z, Shi H, et al. Incidence and risk factors of postoperative cognitive dysfunction in patients underwent coronary artery bypass grafting surgery[J]. Zhong Nan Da Xue Xue Bao Yi Xue Ban,2014,39(10):1049-1055. DOI: 10.11817/ j.issn.1672-7347.2014.10.011.
[118] Schneider AL, Jonassaint C, Sharrett AR, et al. Hemoglobin, anemia, and cognitive function: the atherosclerosis risk in communities study[J]. J Gerontol A Biol Sci Med Sci,2016,71 (6):772-779. DOI: 10.1093/gerona/glv158.
[119] Wang R, Chen J, Wu G. Variable lung protective mechanical ventilation decreases incidence of postoperative delirium and cognitive dysfunction during open abdominal surgery[J]. Int J Clin Exp Med,2015,8(11):21208-21214.
[120] Habre W, Petak F. Perioperative use of oxygen: variabilities across age[J]. Br J Anaesth,2014,113 (Suppl 2):i26-i36. DOI: 10.1093/bja/aeu380.
[121] Grune F, Kazmaier S, Sonntag H, et al. Moderate hyperventilation during intravenous anesthesia increases net cerebral lactate efflux[J]. Anesthesiology, 2014, 120(2): 335-342. DOI: 10.1097/ALN.0b013e3182a8eb09.
[122] Madrid E, Urrutia G, Roque IFM, et al. Active body surface warming systems for preventing complications caused by inadvertent perioperative hypothermia in adults[J]. Cochrane Database Syst Rev,2016,4:D9016. DOI: 10.1002/14651858. CD009016.pub2.
[123] Expert Consensus Writing Group on the Care and Management of Patients with Cognitive Disorders, Cognitive Disorders Branch, Chinese Geriatrics Medicine Society. Expert consensus on the care management of patients with cognitive impairment in China [J]. Chinese Journal of Geriatrics, 2016, 35 (10): 1051-1060. DOI: 10.3760/cma.j.issn.0254-9026.2016.10.007.
[124] Shaji KS, Sivakumar PT, Rao GP, et al. Clinical practice guidelines for management of dementia[J]. Indian J Psychiatry, 2018, 60(Suppl 3): S312-S328. DOI: 10.4103 / 0019-5545. 224472.
[125] Andrade DC, Faria JW, Caramelli P, et al. The assessment and management of pain in the demented and non-demented elderly patient[J]. Arq Neuropsiquiatr,2011,69(2B):387-394. DOI: 10.1590/S0004-282X2011000300023.
[126] Xu Jianguo. Expert consensus on postoperative pain management in adults [J]. Clinical Anesthesiology Journal, 2017, 33 (9): 911-917.
[127] Falzone E, Hoffmann C, Keita H. Postoperative analgesia in elderly patients[J]. Drugs Aging, 2013, 30(2): 81-90. DOI: 10.1007/s40266-012-0047-7.
[128] Peng Meici, Zhong Peiwen, Liang Yingqin, et al. Chinese version of preliminary evaluation of the pain assessment scale for advanced dementia [J]. Chinese Journal of Nursing, 2007, 42 (8): 677-680.
[129] Hu CJ, Liao CC, Chang CC, et al. Postoperative adverse outcomes in surgical patients with dementia: a retrospective cohort study[J]. World J Surg, 2012, 36(9): 2051-2058. DOI: 10.1007/s00268-012-1609-x.
[130] Bail K, Berry H, Grealish L, et al. Potentially preventable complications of urinary tract infections, pressure areas, pneumonia, and delirium in hospitalised dementia patients: retrospective cohort study[J]. BMJ Open,2013, 3(6):e002770. DOI: 10.1136/bmjopen-2013-002770.
[131] Racine AM, Fong TG, Gou Y, et al. Clinical outcomes in older surgical patients with mild cognitive impairment[J]. Alzheimers Dement, 2018, 14(5): 590-600. DOI: 10.1016 / j. jalz.2017.10.010.
[132] Gajdos C, Kile D, Hawn MT, et al. The significance of preoperative impaired sensorium on surgical outcomes in nonemergent general surgical operations[J]. JAMA Surg,2015, 150(1):30-36. DOI: 10.1001/jamasurg.2014.863.
[133] Culley DJ, Flaherty D, Fahey MC, et al. Poor performance on a preoperative cognitive screening test predicts postoperative complications in older orthopedic surgical patients[J]. Anesthesiology, 2017, 127(5): 765-774. DOI: 10.1097 / ALN 0000000000001859.
[134] Trubnikova OA, Mamontova AS, Syrova ID, et al. Does preoperative mild cognitive impairment predict postoperative cognitive dysfunction after on-pump coronary bypass surgery? [J]. J Alzheimers Dis,2014,42 Suppl 3:S45-S51. DOI: 10.3233/ JAD-132540.
[135] Kazmierski J, Banys A, Latek J, et al. Mild cognitive impairment with associated inflammatory and cortisol alterations as independent risk factor for postoperative delirium[J]. Dement Geriatr Cogn Disord,2014,38(1-2):65-78. DOI: 10.1159/000357454.
[136] Wan Xiaojian, Wang Dongxin, Fang Xiangming, et al. Expert consensus on the prevention and treatment of postoperative delirium in adults [EB/OL]. (2014-07-15) [2018-12-08]. http://www.csahq.cn/guide/detail_214.html.
[137] Aldecoa C, Bettelli G, Bilotta F, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium[J]. Eur J Anaesthesiol, 2017,34(4):192-214. DOI: 10.1097/EJA.0000000000000594.
[138] Alcorn S, Foo I. Perioperative management of patients with dementia[J]. BJA Education,2016,17(3):94-98. DOI: 10.1093/ bjaed/mkw038.
[139] Key Infection Prevention and Control Group of the Fourth Committee of Hospital Infection Control Branch of Chinese Preventive Medicine Association. Expert consensus on prevention and control of postoperative pneumonia [J]. Chinese Journal of Clinical Infectious Diseases, 2018, 11 (1): 11-19.DOI: 10.3760/cma.j.issn.1674-2397.2018.01.003.
[140] Guenther U, Radtke FM. Delirium in the postanaesthesia period[J]. Curr Opin Anaesthesiol,2011, 24(6):670-675. DOI: 10.1097/ACO.0b013e32834c7b44.
[141] Ouimet S, Kavanagh BP, Gottfried SB, et al. Incidence, risk factors and consequences of ICU delirium[J]. Intensive Care Med,2007, 33(1):66-73.DOI: 10.1007/s00134-006-0399-8.
[142] Thomason JW, Shintani A, Peterson JF, et al. Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients[J]. Crit Care,2005, 9(4):R375-381.DOI: 10.1186/cc3729.
[143] Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients[J]. Crit Care Med, 2004, 32(4): 955-962. DOI: 10.1097 / 01. CCM.0000119429.16055.92.
[144] Hopkins RO, Jackson JC. Short-and long-term cognitive outcomes in intensive care unit survivors[J]. Clin Chest Med, 2009, 30(1):143-153, ix. DOI: 10.1016/j.ccm.2008.11.001.

[145] Pisani MA, Kong SY, Kasl SV, et al. Days of delirium are associated with 1-year mortality in an older intensive care unit population[J]. Am J Respir Crit Care Med, 2009, 180(11): 1092-1097. DOI: 10.1164/rccm.200904-0537oc.
[146] Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people[J]. Lancet,2014, 383(9920):911-922.
[147] Vasilevskis EE, Han JH, Hughes CG, et al. Epidemiology and risk factors for delirium across hospital settings[J]. Best Pract Res Clin Anaesthesiol,2012, 26(3):277-287. DOI: 10.1016/j. bpa.2012.07.003.
[148] Milstein A, Pollack A, Kleinman G, et al. Confusion/delirium following cataract surgery: an incidence study of 1-year duration[J]. Int Psychogeriatr, 2002, 14(3): 301-306. DOI: 10.1017/S1041610202008499.
[149] Su X, Meng ZT, Wu XH, et al. Dexmedetomidine for prevention of delirium in elderly patients after non-cardiac surgery: a randomised, double-blind, placebo-controlled trial [J]. Lancet, 2016, 388(10054): 1893-1902. DOI: 10.1016 / S0140-6736(16)30580-3.
[150] Pioli G, Bendini C, Giusti A, et al. Surgical delay is a risk factor of delirium in hip fracture patients with mild-moderate cognitive impairment[J]. Aging Clin Exp Res, 2019, 31(1): 41-47.DOI: 10.1007/s40520-018-0985-y.
[151] Gosselt AN, Slooter AJ, Boere PR, et al. Risk factors for delirium after on-pump cardiac surgery: a systematic review [J]. Crit Care,2015,19:346. DOI: 10.1186/s13054-015-1060-0.
[152] Association AP. Diagnostic and statistical manual of mental disorders (Dsm-51) [M]. 5th ed. Amer Psychiatric Pub Inc, 2013.
[153] Sepulveda E, Franco JG, Trzepacz PT, et al. Delirium diagnosis defined by cluster analysis of symptoms versus diagnosis by DSM and ICD criteria: diagnostic accuracy study [J]. BMC Psychiatry, 2016, 16: 167. DOI: 10.1186 / s12888-016-0878-6.
[154] Ritter SRF, Cardoso AF, Lins MMP, et al. Underdiagnosis of delirium in the elderly in acute care hospital settings: lessons not learned[J]. Psychogeriatrics, 2018, 18(4): 268-275. DOI: 10.1111/psyg.12324.
[155] Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: the confusion assessment method. A new method for detection of delirium[J]. Ann Intern Med, 1990, 113(12): 941-948. DOI: 10.7326/0003-4819-113-12-941.
[156] Leung J, Leung V, Leung CM, et al. Clinical utility and validation of two instruments (the Confusion Assessment Method Algorithm and the Chinese version of Nursing Delirium Screening Scale) to detect delirium in geriatric inpatients[J]. Gen Hosp Psychiatry,2008, 30(2):171-176. DOI: 10.1016/j.genhosppsych.2007.12.007.
[157] Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) [J]. Crit Care Med, 2001, 29(7): 1370-1379. DOI: 10.1097 / 00003246- 200107000-00012.
[158] Wang C, Wu Y, Yue P, et al. Delirium assessment using confusion assessment method for the intensive care unit in Chinese critically ill patients[J]. J Crit Care, 2013, 28(3): 223-229. DOI: 10.1016/j.jcrc.2012.10.004.
[159] Marcantonio ER, Ngo LH, O′Connor M, et al. 3D-CAM: derivation and validation of a 3-minute diagnostic interview for CAM-defined delirium: a cross-sectional diagnostic test study[J]. Ann Intern Med, 2014, 161(8): 554-561. DOI: 10.7326/L14-5026-2.
[160] Rosen J, Sweet RA, Mulsant BH, et al. The delirium rating scale in a psychogeriatric inpatient setting[J]. J Neuropsychiatry Clin Neurosci, 1994, 6(1): 30-35. DOI: 10.1176/jnp.6.1.30.
[161] Mei Wei, Liu Shangkun, Zhang Zhiguo, et al. Reliability and validity study of Chinese version of Nursing Delirium Screening Scale [J]. Chinese Journal of Nursing, 2010, 45 (2):4. DOI: 10.3761/j.issn.0254-1769.2010.02.001.
[162] Shi Z, Wu Y, Li C, et al. Using the Chinese version of Memorial Delirium Assessment Scale to describe postoperative delirium after hip surgery[J]. Front Aging Neurosci,2014,6:297. DOI: 10.3389/fnagi.2014.00297.
[163] Aldecoa C, Bettelli G, Bilotta F, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium[J]. Eur J Anaesthesiol, 2017, 34(4):192-214. DOI: 10.1097/EJA.0000000000000594.
[164] Downing LJ, Caprio TV, Lyness JM. Geriatric psychiatry review: differential diagnosis and treatment of the 3 D′s-delirium, dementia, and depression[J]. Curr Psychiatry Rep,2013, 15(6):365. DOI: 10.1007/s11920-013-0365-4.
[165] Chevillon C, Hellyar M, Madani C, et al. Preoperative education on postoperative delirium, anxiety, and knowledge in pulmonary thromboendarterectomy patients[J]. Am J Crit Care,2015, 24(2):164-171. DOI: 10.4037/ajcc2015658.
[166] Eijlers R, Legerstee JS, Dierckx B, et al. Development of a virtual reality exposure tool as psychological preparation for elective pediatric day care surgery: methodological approach for a randomized controlled trial[J]. JMIR Res Protoc,2017, 6 (9):e174. DOI: 10.2196/resprot.7617.
[167] Mazzola P, Ward L, Zazzetta S, et al. Association between preoperative malnutrition and postoperative delirium after hip fracture surgery in older adults[J]. J Am Geriatr Soc,2017, 65 (6):1222-1228. DOI: 10.1111/jgs.14764.
[168] Kratz T, Heinrich M, Schlauss E, et al. Preventing postoperative delirium[J]. Dtsch Arztebl Int, 2015, 112(17): 289-296. DOI: 10.3238/arztebl.2015.0289.
[169] Kassie GM, Nguyen TA, Kalisch Ellett LM, et al. Preoperative medication use and postoperative delirium: a systematic review [J]. BMC Geriatr, 2017, 17(1): 298. DOI: 10.1186 / s12877-017-0695-x.
[170] Papaioannou A, Fraidakis O, Michaloudis D, et al. The impact of the type of anaesthesia on cognitive status and delirium during the first postoperative days in elderly patients[J]. Eur J Anaesthesiol, 2005, 22(7): 492-499. DOI: 10.1017 / s0265021505000840.
[171] Steenberg J, Moller AM. Systematic review of the effects of fascia iliaca compartment block on hip fracture patients before operation[J]. Br J Anaesth, 2018, 120(6): 1368-1380. DOI: 10.1016/j.bja.2017.12.042.
[172] Weinstein SM, Poultsides L, Baaklini LR, et al. Postoperative delirium in total knee and hip arthroplasty patients: a study of perioperative modifiable risk factors[J]. Br J Anaesth, 2018, 120(5):999-1008. DOI: 10.1016/j.bja.2017.12.046.
[173] O′Donnell CM, McLoughlin L, Patterson CC, et al. Perioperative outcomes in the context of mode of anaesthesia for patients undergoing hip fracture surgery: systematic review and meta-analysis[J]. Br J Anaesth,2018, 120(1):37-50. DOI: 10.1016/j.bja.2017.09.002.
[174] Mason SE, Noel-Storr A, Ritchie CW. The impact of general and regional anesthesia on the incidence of post-operative cognitive dysfunction and post-operative delirium: a systematic review with meta-analysis[J]. J Alzheimers Dis, 2010, 22 Suppl 3:67-79. DOI: 10.3233/JAD-2010-101086.
[175] Radtke FM, Franck M, Lendner J, et al. Monitoring depth of anaesthesia in a randomized trial decreases the rate of

postoperative delirium but not postoperative cognitive dysfunction[J]. Br J Anaesth,2013, 110 Suppl 1:i98-105. DOI: 10.1093/bja/aet055.
[176] Sahni N, Anand LK, Gombar K, et al. Effect of intraoperative depth of anesthesia on postoperative pain and analgesic requirement: A randomized prospective observer blinded study [J]. J Anaesthesiol Clin Pharmacol,2011, 27(4):500-505. DOI: 10.4103/0970-9185.86595.
[177] Punjasawadwong Y, Chau-In W, Laopaiboon M, et al. Processed electroencephalogram and evoked potential techniques for amelioration of postoperative delirium and cognitive dysfunction following non-cardiac and non-neurosurgical procedures in adults[J]. Cochrane Database Syst Rev, 2018, 5: Cd011283. DOI: 10.1002 / 14651858. CD011283.pub2.
[178] Wildes TS, Mickle AM, Ben Abdallah A, et al. Effect of electroencephalography-guided anesthetic administration on postoperative delirium among older adults undergoing major surgery: the ENGAGES randomized clinical trial[J]. JAMA, 2019, 321(5):473-483. DOI: 10.1001/jama.2018.22005.
[179] Calderon-Arnulphi M, Alaraj A, Slavin KV. Near infrared technology in neuroscience: past, present and future[J]. Neurol Res,2009, 31(6):605-614.DOI: 10.1179/174313209X383286.
[180] Morimoto Y, Yoshimura M, Utada K, et al. Prediction of postoperative delirium after abdominal surgery in the elderly [J]. J Anesth,2009, 23(1):51-56. DOI: 10.1034/j.1399-0012. 2000.0140s3037.x.
[181] Palmbergen WA, van Sonderen A, Keyhan-Falsafi AM, et al. Improved perioperative neurological monitoring of coronary artery bypass graft patients reduces the incidence of postoperative delirium: the Haga Brain Care Strategy[J]. Interact Cardiovasc Thorac Surg,2012, 15(4):671-677. DOI: 10.1093/icvts/ivs317.
[182] Lopez MG, Pandharipande P, Morse J, et al. Intraoperative cerebral oxygenation, oxidative injury, and delirium following cardiac surgery[J]. Free Radic Biol Med,2017,103:192-198. DOI: 10.1016/j.freeradbiomed.2016.12.039.
[183] Wood MD, Maslove DM, Muscedere JG, et al. Low brain tissue oxygenation contributes to the development of delirium in critically ill patients: A prospective observational study[J]. J Crit Care,2017,41:289-295. DOI: 10.1016/j.jcrc.2017.06.009.
[184] Zorrilla-Vaca A, Healy R, Grant MC, et al. Intraoperative cerebral oximetry-based management for optimizing perioperative outcomes: a meta-analysis of randomized controlled trials[J]. Can J Anaesth,2018, 65(5):529-542. DOI: 10.1007/s12630-018-1065-7.
[185] Group PS, Devereaux PJ, Yang H, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial[J]. Lancet, 2008, 371(9627): 1839-1847. DOI: 10.1016 / S0140-6736(08)60601-7.
[186] Bijker JB, Persoon S, Peelen LM, et al. Intraoperative hypotension and perioperative ischemic stroke after general surgery: a nested case-control study[J]. Anesthesiology,2012, 116(3):658-664. DOI: 10.1097/ALN.0b013e3182472320.
[187] Hori D, Brown C, Ono M, et al. Arterial pressure above the upper cerebral autoregulation limit during cardiopulmonary bypass is associated with postoperative delirium[J]. Br J Anaesth,2014, 113(6):1009-1017. DOI: 10.1093/bja/aeu319.
[188] Bjorkelund KB, Hommel A, Thorngren KG, et al. Reducing delirium in elderly patients with hip fracture: a multi-factorial intervention study[J]. Acta Anaesthesiol Scand, 2010, 54(6): 678-688. DOI: 10.1111/j.1399-6576.2010.02232.x.
[189] Tokita K, Tanaka H, Kawamoto M, et al. Patient-controlled epidural analgesia with bupivacaine and fentanyl suppresses postoperative delirium following hepatectomy[J]. Masui,2001, 50(7):742-746.
[190] Devlin JW, Skrobik Y, Gelinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU[J]. Crit Care Med, 2018, 46(9): e825-e873. DOI: 10.1097/CCM.0000000000003299.
[191] Shetty RM, Bellini A, Wijayatilake DS, et al. BIS monitoring versus clinical assessment for sedation in mechanically ventilated adults in the intensive care unit and its impact on clinical outcomes and resource utilization[J]. Cochrane Database Syst Rev, 2018, 2: Cd011240. DOI: 10.1002 / 14651858.CD011240.
[192] Wang H, Wang C, Wang Y, et al. Sedative drugs used for mechanically ventilated patients in Intensive Care Units: a systematic review and network meta-analysis[J]. Curr Med Res Opin, 2019, 35(3): 435-446. DOI: 10.1080 / 03007995.2018.1509573.
[193] Fraser GL, Devlin JW, Worby CP, et al. Benzodiazepine versus nonbenzodiazepine-based sedation for mechanically ventilated, critically ill adults: a systematic review and meta-analysis of randomized trials[J]. Crit Care Med,2013, 41 (9 Suppl 1):S30-38. DOI: 10.1097/ccm.0b013e3182a16898.
[194] Burry L, Rose L, McCullagh IJ, et al. Daily sedation interruption versus no daily sedation interruption for critically ill adult patients requiring invasive mechanical ventilation[J]. Cochrane Database Syst Rev, 2014, 7: CD009176. DOI: 10.1002/14651858.CD009176.
[195] Hu RF, Jiang XY, Chen J, et al. Non-pharmacological interventions for sleep promotion in the intensive care unit[J]. Cochrane Database Syst Rev, 2015, 10: CD008808. DOI: 10. 1002/14651858.CD008808.pub2.
[196] Hshieh TT, Yue J, Oh E, et al. Effectiveness of multicomponent nonpharmacological delirium interventions: a meta-analysis[J]. JAMA Intern Med, 2015, 175(4): 512-520. DOI: 10.1001/jamainternmed.2014.7779.
[197] Duan X, Coburn M, Rossaint R, et al.Efficacy of perioperative dexmedetomidine on postoperative delirium: systematic review and meta-analysis with trial sequential analysis of randomised controlled trials[J]. Br J Anaesth,2018, 121(2):384-397. DOI: 10.1016/j.bja.2018.04.046.
[198] Li X, Yang J, Nie XL, et al. Impact of dexmedetomidine on the incidence of delirium in elderly patients after cardiac surgery: A randomized controlled trial[J]. PLoS One, 2017, 12(2): e0170757. DOI: 10.1371/journal.pone.0170757.
[199] Deiner S, Luo X, Lin HM, et al. Intraoperative infusion of dexmedetomidine for prevention of postoperative delirium and cognitive dysfunction in elderly patients undergoing major elective noncardiac surgery: a randomized clinical trial[J]. JAMA Surg,2017, 152(8):e171505. DOI: 10.1001/jamasurg. 2017.1505.
[200] Zhang DF, Su X, Meng ZT, et al. Impact of dexmedetomidine on long-term outcomes after noncardiac surgery in elderly: 3-year follow-up of a randomized controlled trial[J]. Ann Surg, 2018. DOI: 10.1097/SLA.0000000000002801.

[201] Santos E, Cardoso D, Neves H, et al. Effectiveness of haloperidol prophylaxis in critically ill patients with a high risk of delirium: a systematic review[J]. JBI Database System Rev Implement Rep,2017, 15(5):1440-1472. DOI: 10.11124/ JBISRIR-2017-003391.
[202] Mehta S, Cook D, Devlin JW, et al. Prevalence, risk factors, and outcomes of delirium in mechanically ventilated adults[J]. Crit Care Med, 2015, 43(3): 557-566. DOI: 10.1097 / CCM.0000000000000727.
[203] Pan Y, Jiang Z, Yuan C, et al. Influence of physical restraint on delirium of adult patients in ICU: A nested case-control study[J]. J Clin Nurs, 2018, 27(9-10): 1950-1957. DOI: 10.1111/jocn.14334.
[204] Martinez F, Donoso AM, Marquez C, et al. Implementing a multicomponent intervention to prevent delirium among critically ill patients[J]. Crit Care Nurse, 2017, 37(6): 36-46. DOI: 10.4037/ccn2017531.
[205] Litton E, Carnegie V, Elliott R, et al. The efficacy of earplugs as a sleep hygiene strategy for reducing delirium in the ICU: a systematic review and meta-analysis[J]. Crit Care Med,2016, 44(5):992-999. DOI: 10.1097/CCM.0000000000001557.
[206] Cheong CY, Tan JA, Foong YL, et al. Creative music therapy in an acute care setting for older patients with delirium and dementia[J]. Dement Geriatr Cogn Dis Extra, 2016, 6(2): 268-275. DOI: 10.1159/000445883.
[207] Johnson K, Fleury J, McClain D. Music intervention to prevent delirium among older patients admitted to a trauma intensive care unit and a trauma orthopaedic unit[J]. Intensive Crit Care Nurs, 2018, 47:7-14. DOI: 10.1016/j.iccn.2018.03.007.
[208] Barnes-Daly MA, Phillips G, Ely EW. Improving hospital survival and reducing brain dysfunction at seven california community hospitals: implementing PAD guidelines via the ABCDEF bundle in 6,064 Patients[J]. Crit Care Med,2017,45 (2):171-178. DOI: 10.1097/CCM.0000000000002149.
[209] Girard TD, Pandharipande PP, Carson SS, et al. Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial[J]. Crit Care Med, 2010, 38(2): 428-437. DOI: 10.1097 / ccm. 0b013e3181c58715.
[210] Devlin JW, Roberts RJ, Fong JJ, et al. Efficacy and safety of quetiapine in critically ill patients with delirium: a prospective, multicenter, randomized, double-blind, placebo-controlled pilot study[J]. Crit Care Med,2010, 38(2): 419-427. DOI: 10.1097/ccm.0b013e3181b9e302.
[211] Skrobik YK, Bergeron N, Dumont M, et al. Olanzapine vs haloperidol: treating delirium in a critical care setting[J]. Intensive Care Med, 2004, 30(3): 444-449. DOI: 10.1007 / s00134-003-2117-0.
[212] Wang EH, Mabasa VH, Loh GW, et al. Haloperidol dosing strategies in the treatment of delirium in the critically ill[J]. Neurocritical Care, 2012, 16(1): 170-183. DOI: 10.1007 / s12028-011-9643-3.
[213] Flukiger J, Hollinger A, Speich B, et al. Dexmedetomidine in prevention and treatment of postoperative and intensive care unit delirium: a systematic review and meta-analysis[J]. Ann Intensive Care, 2018, 8(1): 92. DOI: 10.1186 / s13613-018-0437-z.

Chinese Multidisciplinary Expert Consensus of Perioperative Brain Health in Elderly Patients (III)

Perioperative Sleep

I. Normal Sleep Physiology

Normal adults sleep about 7 to 8 hours a day. Sleep monitoring techniques, based on electroencephalography (EEG), electrooculography (EOG), and submental electromyography (EMG) during sleep, revealed cyclical changes in sleep, and each cycle consists of non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. Sleep normally begins with NREM sleep, with four to five NREM/REM sleep cycles per night, usually 90 ~ 120 min per cycle.

Eye movements are slow or completely absent during NREM sleep, and EMG activity is lower than in the awake state and may also reach a night-long minimum state. NREM sleep is divided into three stages according to EEG characteristics: Stage 1 (N1 stage): it is a transition stage between waking and other sleep stages, and the EEG frequency is characterized by low-amplitude mixed-frequency waves of 4.0~7.0 Hz. During this sleep stage, the perception of sleep is quite different, and about half of the people do not think they are sleeping after being awakened during this period; Stage 2 (N2 stage): the EEG can be characterized by biphasic K-complexes of >0.5s duration and sleep spindles of 11.0~16.0 Hz; Stage 3 (N3 stage): the EEG frequency is 0.5~2.0 Hz, the amplitude is >75μV, and the duration of slow-wave EEG activity accounts for 20% or more of an epoch. This stage of sleep is also called deep sleep, sometimes called slow-wave sleep or synchronized sleep, and most of the N3 stage appears in the first half of the night.

REM sleep (R-stage) is characterized by periodic bursts of rapid eye movements. EEG shows low amplitude mixed frequencies and sawtooth EEG waves of 2~6 Hz are also observed, but there are no K complex/sleep spindle waves. Skeletal muscle EMG activity levels are the lowest, and transient EMG activity is observed with large fluctuations in respiratory rate, heart rhythm variability, and vascular tone.

REM sleep predominates in the latter part of the night. The time from sleep onset to the appearance of the first segment of REM sleep is called REM latency, and REM sleep deprivation or discontinuation of REM inhibitors can lead to a decrease in REM latency. Sleep onset REM (SOREM) is defined when REM latency is 0~15 min, which is one of the objective indicators for the diagnosis of narcolepsy. Tricyclic antidepressants, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and lithium may prolong REM latency.

The ratio of the time of each sleep stage to the total sleep time in the whole night sleep of healthy adults is 2%~5% in N1 stage, 45%~55% in N2 stage, 10%~20% in N3 stage; 75%~80% in NREM sleep, 20%~25% in REM sleep. Human sleep architecture also changes with age. In men, the N3 stage decreases and the N1 stage increases with age. In women, stage N3 sleep changes little with age. Body temperature decreases gradually during sleep, and core body temperature is lowest 2 h before waking up. Core body temperature and dim light melatonin release onset time are objective indicators to assess sleep-awake circadian rhythms [1].

Sleep quality needs to be assessed in terms of ability to fall asleep, ability to maintain sleep, presence or absence of early awakening, total sleep time, sleep efficiency, sleep architecture, and wake state. Sleep latency is usually used as an objective evaluation index of ability to fall asleep. Sleep latency is defined as the time from lights off to the appearance of the first epoch of sleep (stage N1, N2, N3, or R). Normal adults generally need about 20 minutes from awake to falling asleep, and sleep latency more than 30 min indicates difficulty in falling asleep. Sleep latency can be shortened or prolonged by behavioral factors, sleep and its related diseases, or drug factors. Sleep maintenance refers to the continuity of sleep, usually sleep throughout the night will also have fragments of awake, but after awakening it is easy to fall asleep.

Having more than two awakenings per night and/or difficulty falling asleep after awaking indicate poor sleep continuity. Early awakening is defined as more than 30 min earlier than habitual awakening. Total sleep time (TST) is the sum of the time spent in each sleep stage during the overnight sleep period. Sleep efficiency is the percentage of total sleep time to total in bed time (the period of time from lying in bed with lights off until light on), which should be ≥ 85% in normal. Good sleep is defined as normal total sleep time during the main sleep period. Sleep architecture is consistent with age changes, with refreshing minds upon awakening, loss or significant alleviation of fatigue before bedtime, energetic daytime, and cognitive function and work ability unaffected [2].

In addition to the diaphragm, the tension of the pharyngeal opening muscles, genioglossus, intercostal muscles and abdominal muscles is reduced during the transition from wakefulness to sleep, and is significantly associated with the sleep stage (awake > NREM sleep > REM sleep), and voluntary respiratory regulation is basically disappeared, and the hypercapnic ventilatory response (HCVR) and hypoxic ventilatory response (HVR) of the respiratory center are reduced compared with those in wakefulness, especially in the REM sleep [3]. These changes can lead to a decrease in minute ventilation, with an increase in PaCO2 of 4 to 8 mmHg (1 mmHg = 0.133 kPa) and a decrease in PaO2 of 3 to 10 mmHg compared with the awake period [4]. In elderly patients with chronic respiratory insufficiency or pulmonary vascular disease, particularly during recovery from general anesthesia or surgical procedures affecting ventilation, sleep-related hypoventilation/hypoxemia may be caused, inducing or aggravating respiratory failure.

Studies have confirmed that general anesthesia, perioperative psychological and physiological stress, and the use of certain drugs can cause changes in sleep-wake circadian rhythms and decrease sleep quality. Epidemiological studies have found that acute or chronic sleep deprivation (especially deep sleep deprivation) can significantly affect the health of the body, leading to daytime drowsiness, fatigue, memory loss, reduced alertness, inattention and operational errors, irritability, etc.; decreased coordination of action and increased risk of falls in the elderly; decreased humoral or cellular immunity and increased chances of infection; decreased leptin secretion and abnormal fat metabolism causing obesity; impaired islet function and reduced insulin receptor sensitivity leading to abnormal glucose metabolism or aggravating diabetes; increased sympathetic activity, impaired vascular endothelial function, inducing or aggravating hypertension, or leading to an increased risk of arrhythmia and sudden death [5–8].

II. Preoperative Sleep Disorders

According to the International Classification of Sleep Disorders, Third Edition (ICSD-3), there are currently more than 90 known sleep disorders, which are distributed at all ages. Common sleep disorders are insomnia disorders (referred to as insomnia), sleep-related breathing disorders, sleep-related movement disorders, among which insomnia is the most common. The sleep disorders in this expert consensus focus on insomnia. According to the course of the disease and other specific conditions, insomnia can be divided into chronic insomnia, short-term insomnia and other insomnia. The risk of insomnia in the elderly population is significantly higher than that in other age groups, which may cause adverse effects on their cardiovascular system, endocrine system, immune system, and nervous system. Therefore, it is important to pay attention to the diagnosis and treatment of insomnia in the elderly population, especially in the perioperative elderly population.

(I) Occurrence and Harm of Insomnia

Epidemiological surveys in 2006 found that the prevalence of insomnia among adults in mainland China was as high as 57%, which is much higher than in developed countries such as Europe and the United States [9-10]. The prevalence of insomnia in the elderly population was significantly higher than that in other age groups. Chronic insomnia has been reported in 40% to 70% of the elderly. The prevalence of insomnia is further increased in elderly patients with various mental and physical disorders; moreover, the prevalence of insomnia is higher with more types of comorbid disorders [11-12]. For preoperative patients, sleep disturbances are more likely to occur in the presence of a combination of disease, psychological, and environmental factors. Small sample size surveys have shown that the prevalence of insomnia within 1 month before surgery is 60% ~ 80% in different surgical patients [13-15]. Insomnia has adverse effects on the mental, physical and social functions of patients, which can lead to emotional disorder and mental weakness, and even psychological disorders and suicide in severe cases; it can also lead to immune dysfunction, inducing or aggravating heart disease, hypertension, diabetes, etc. [16-19]. Patients with preoperative insomnia are more likely to experience anxiety, which can affect their hemodynamic stability, lead to increased blood pressure and cardiovascular events, increase the sensitivity of patients to pain, affect the dosage and effect of anesthetic drugs, and also lead to an increased risk of postoperative delirium and cognitive impairment; these will have a negative impact on early postoperative recovery and increase medical and nursing costs [17-20]. Therefore, preoperative insomnia should be highly valued by surgeons and anesthesiologists.

(II) Risk Factors for Preoperative Insomnia

The risk factors of preoperative insomnia are divided into physiological factors, pathological factors and environmental factors. Physiological factors include age, gender, genetics, personality characteristics, etc.; age is an important risk factor for insomnia, and the higher the age, the greater the risk of insomnia (the prevalence of chronic insomnia increases from 4% in children and 9.3% in young adults to 38.2% in the elderly); pathological factors mainly refer to previous history of insomnia, various mental disorders and physical diseases, and the use of drugs that may affect sleep; environmental factors include negative life events, environmental changes, and the negative impact of the surrounding population on patients [9].

(III) Assessment of Preoperative Insomnia

Clinical assessment of sleep conditions should include clinical comprehensive assessment, subjective assessment and objective assessment. Clinical comprehensive assessment is the basis and main method of insomnia diagnosis, when necessary, subjective or objective assessment can be carried out to more accurately evaluate the characteristics and influencing factors of insomnia.

1. Clinical comprehensive assessment: Clinical comprehensive assessment should obtain the patient's

sleep characteristics, daytime activity and function, comorbid conditions, basic physical examination, and family history of sleep or psychiatric disorders. Among them, sleep characteristics include the background, performance, evolution process, whether accompanied by daytime symptoms and its basic performance, duration and so on.
(1) Context of occurrence: Assess behavior and mental activity from late afternoon until bedtime. Bedtime status assessment is the main way to understand the cognitive and behavioral characteristics of patients with insomnia, and is also the basis for the development of psychological treatment program. Understand the patient's sleep environment, including bedroom temperature, humidity, light (natural light and lighting) conditions, bed area, hardness, and outside environment of bedroom, especially noise, bright light and air pollution. 2) Sleep-wake circadian rhythm: Understand the daily routines of patients, preliminarily assess the sleep-wake circadian rhythm, and eliminate various circadian rhythm sleep-wake disorders. Among them, sleep-wake phase disorder is more common in elderly patients. For those who complain of difficulty in falling asleep at night, and early waking up and difficulty in falling asleep again, special attention should be paid to further assess their sleep-wake circadian rhythm (the patient often has slept for a while on the sofa after dinner). 3) Nocturnal symptoms: sleep-related symptoms that may occur during sleep from nighttime to early morning awakening, which are clues to the diagnosis of insomnia disorder and other sleep-related diseases. 4) Daytime activity and function: The influence of insomnia on work and daily life, including the state of wakefulness or alertness, emotional state, degree of mental distress, cognitive function such as attention and memory, and changes in the working state of daily life after the occurrence of insomnia. (5) Other medical history: including physical diseases, mental disorders, other sleep disorders, stress factors, pregnancy, menstrual period and perimenopause.
2. Subjective assessment: Subjective assessment methods include self-assessment (e.g., sleep diary, self-rating scale, etc.) and observer-assessment. (1) Sleep diary: An "objective" assessment of subjective sleep perception. Usually, patients are asked to complete a sleep diary lasting for 2 weeks, which includes recording the daily time of going to bed and getting up, estimating sleep latency, recording the number of nocturnal awakenings and total time in bed, estimating the actual sleep time, and calculating the sleep efficiency of patients. This method is simple, easy and widely used in clinical practice. 2) Scale or questionnaire assessment: It is a method for "objectively" assessing subjective experience. It is divided into self-rating scale and observer-rating scale according to different subjects who fill in the items of the scale. The self-rating scale refers to the scale in which the item is scored by the tested object itself; the observer-rating scale is a scale in which the professional personnel specially trained in the use of specific scale make a comprehensive score based on the information obtained from the inquiry and professional observation of the tested object. The selection of scale shall be made according to the assessment purpose and the reliability and validity of the scale itself. For the preoperative patient, select scale according to demand (Table 1).
3. Objective assessment: Objective assessment is not a routine test for the diagnosis of insomnia disorder and is recommended for the suspected combination of other sleep disorders, undiagnosed, persistent and intractable insomnia disorder, violent behavior during sleep, and the presence of comorbid and interacting physical disorders with insomnia disorder. (1) Physical examination: Some common physical diseases such as hypertension, hyperthyroidism or hypothyroidism, cerebrovascular disease, organic brain disease, cardiovascular disease, severe liver and kidney function damage, etc., may be the predisposing factors of insomnia, and may also be comorbid with insomnia disorder for a long time and have mutual influence, so corresponding examination shall be performed when necessary. 2) Polysomnography (PSG): It is a basic technique for conducting sleep medicine research and sleep disease diagnosis, a standard method for evaluating sleep-related pathophysiology and sleep architecture, and an objective examination for scoring wakefulness or sleep. PSG is not recommended as a routine examination for patients with insomnia because insomnia can be diagnosed by medical history, clinical presentation, and questionnaires; PSG is only used in patients in which the presence of other sleep disorders, sleep cognitive abnormalities, or intractable insomnia is suspected. (3) Actigraphy: It is an effective method for assessing sleep-wake circadian rhythm and determining sleep pattern. The actigraphy can, in the form of value or chart, reflect the waking and sleeping pattern, and estimate the sleep latency, total sleep time, awake times, sleep efficiency, etc. It is recommended for people with insomnia and suspected to be accompanied by abnormal sleep rhythm, as well as the evaluation of sleep quality before and after treatment [21]. (4) Multiple sleep latency test (MSLT): Objective determination of propensity to fall asleep and the possibility of sleep onset REM. It is recommended for the definitive diagnosis of suspected narcolepsy and differential diagnosis of suspected idiopathic hypersomnia, and is not recommended for those with a definite diagnosis of simple short-term insomnia or chronic insomnia.
[Recommendation] Because insomnia has adverse effects on the intraoperative risks and postoperative

recovery of mental, physical and social functions of elderly perioperative patients, it is recommended to perform a comprehensive clinical assessment and subjective assessment of the patient's sleep status before surgery, and when necessary, perform corresponding objective assessment.

Table 1 Common Self-Rating Scales for Insomnia

Scale	Characteristic	Meaning
Pittsburgh sleep quality index (PSQI)	Self-rating scale for sleep quality, widely used, the validity and reliability of Chinese version of scale is better; mainly assessing sleep quality over a 1-month time interval	The total score ranges from 0 to 21, with higher scores representing more severe sleep disturbances and a score of > 5 points is considered to indicate the presence of disturbed sleep
Epworth sleepiness scale (ESS)	Used to assess daytime distress, sleepiness	The total score is 0-24 points, and the higher the score is, the more severe the degree of sleepiness is; the normal score is ≤ 10 points, and ≥ 16 points is severe sleepiness; when necessary, further examination can be performed to exclude narcolepsy, sleep-disordered breathing and other diseases
Dysfunctional beliefs and attitudes about sleep (DBAS)	Used to assess the degree to which insomnia patients have misconceptions or behaviors about sleep and the consequences of insomnia	Those with high scores, suggesting the presence of corresponding false beliefs or behaviors, have a higher risk of insomnia chronicity and are more in need of psychological treatment such as cognitive behavior
Beck depression inventory (BDI-I, BDI-II)	Self-rating scale for evaluating depressive manifestations	BDI-I < 10 is considered as no depression or minimal; BDI-II < 14 is considered as no depression or minimal

(IV) Preoperative Diagnosis of Insomnia

1. Diagnostic criteria: ICSD-3 diagnostic criteria for insomnia are recommended (Table 2).
2. Diagnostic process: The diagnosis of insomnia is based primarily on subjective symptoms. Objective tests, including biochemistry, polysomnography, multiple sleep latency test, and actigraphy, may be performed when detailed knowledge of sleep architecture and analysis of the etiology of insomnia or identification of other sleep-related disorders is required. However, objective examination is not a routine examination for insomnia (Figure 1).

[Recommendation] The diagnosis of insomnia is mainly based on subjective symptoms, and objective examinations can be performed when necessary.

(V) Preoperative Management of Insomnia

Preoperative sleep status is affected by many aspects such as physiological characteristics, types of diseases, types of surgeries, psychological status, economic status, preoperative preparation operations, and behaviors of medical staff. Therefore, a combination of non-pharmacological and pharmacological treatments is recommended to improve insomnia in patients prior to surgery.

1. Non-pharmacological treatment: It is the basis for treating insomnia, including improving the sleep environment, implementing sleep cognitive behavioral therapy, psychotherapy, and physical therapy.
2. Pharmacotherapy: It includes medication adjustments made to improve sleep directly by applying hypnotic drugs and by treating various diseases that affect sleep and correcting the adverse effects of non-hypnotic drugs on sleep. At present, the commonly used hypnotic drugs mainly include benzodiazepine receptor agonists (BzRAs), melatonin receptor agonists, sedative antidepressants, and orexin receptor antagonists etc..

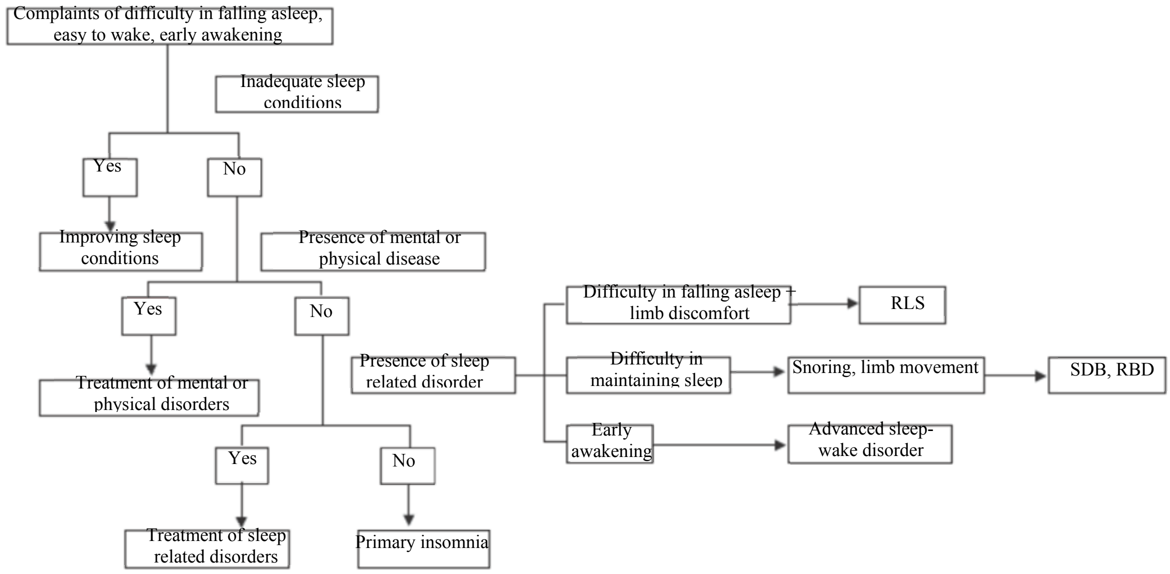
Among them, benzodiazepine receptor agonists include benzodiazepines (BZDs) and non-benzodiazepines (NBZDs). The specific drugs and characteristics are shown in Table 3.

3. Preoperative management of patients with acute insomnia: In elderly patients with preoperative acute insomnia, non-benzodiazepines among benzodiazepine receptor agonists (e.g., zaleplon, zolpidem, zopiclone, etc.) and some antidepressant drugs (e.g., mirtazapine, trazodone hydrochloride, etc.) may be selected on the basis of non-pharmacological treatment. Preoperative correction of insomnia is beneficial to reduce the dosage of anesthetic drugs and reduce the risk of anesthesia.

However, because sedative-hypnotic drugs have central sedative effects, combined use with general anesthetic drugs will produce synergistic effects and aggravate the degree of central depression. Therefore, for patients who use sedative hypnotics for acute insomnia before surgery, it is necessary to closely monitor vital signs and adjust the dosage of anesthetic drugs in time during surgery.
4. Preoperative management of patients with chronic insomnia: Whether chronic insomnia patients are chronically treated with hypnotic drugs is debated. Some studies suggest that long-term users gradually reduce the response to drugs; some studies suggest that the drug effect is stable after long-term use, the latter mainly refers to estazolam, zopiclone, zolpidem, melatonin receptor agonists, orexin receptor inhibitors [10]. Meta-studies showed [22] insomnia patients can get 60% hypnotic effect with placebo, in which the majority of the hypnotic drugs are benzodiazepine receptor agonists and melatonin receptors agonists and antidepressants;

Table 2 International Classification of Sleep Disorders, Third Edition (ICSD-3) Diagnostic Criteria for Insomnia

Criteria A ~ F must be met
A. The patient reports or the patient's parent or caregivers observes, one or more of the following: (1) Difficulty initiating sleep (2) Difficulty maintaining sleep (3) Waking up earlier than desired (4) Resistance to going to bed on appropriate schedule (5) Difficulty sleeping without parent or caregiver intervention B. The patient reports or the patient's parent or caregiver observes, one or more of the following related to the nighttime sleep difficulty: (1) Fatigue/malaise (2) Attention, concentration, or memory impairment (3) Impaired social, family, occupational, or academic performance (4) Mood disturbance/irritability (5) Daytime sleepiness (6) Behavior problems (e.g., hyperactivity, impulsivity, or aggression) (7) Reduced motivation/energy/initiative (8) Proneness for errors/accidents (9) Concerns about or dissatisfaction with sleep C. The reported sleep/wake complaints cannot be explained purely by inadequate opportunity (i.e., enough time is allotted for sleep) or inadequate circumstances (i.e., the environment is safe, dark, quiet, and comfortable) D. The sleep disturbance and associated daytime symptoms occur at least three times per week E. The sleep disturbance and associated daytime symptoms have been present for at least three months F. The sleep/wake difficulty is not better explained by another sleep disorder
The diagnostic criteria for short-term insomnia disorder are similar to those for chronic insomnia disorder, but the disease duration is less than 3 months and there is no frequency requirement



Note: RLS: Restless legs syndrome; SDB: Sleep disordered breathing; RBD: Rapid eye movement sleep behavior disorder

Figure 1 Diagnostic Procedures for Insomnia

Table 3 Mechanism of Action and Pharmacokinetic Characteristics of Common Hypnotics

Name	Site of Action	Indication	Time to peak (h)	Half-life (h)	Metabolic pattern
Benzodiazepine					
Alprazolam	$GABA_A$ receptor	Anxiety	1.0 ~ 3. 0	12.0 ~ 14.0	CYP3A4/5, CYP2C19
Estazolam	$GABA_A$ receptor	Early awakening and easy awakening at night	2. 0	15.0 (10.0 ~ 24.0)	CYP3A 4
Triazolam	$GABA_A$ receptor	Difficulty in falling asleep	1.0 ~ 3.0	1.5 ~ 5.5	CYP3A4
Diazepam	$GABA_A$ receptor	Anxiety	1.0 ~ 2.0	20.0 ~ 80.0	CYP3A4, CYP2C19, CYP2B
Lorazepam	$GABA_A$ receptor	Anxiety	1.0 ~ 3.0	10.0 ~ 20.0	Glucuronic acid
Non-benzodiazepine					
Zaleplon	Selective activation of w1, w2 sites on $GABA_A$ receptor complex	Difficulty in falling asleep	1.1	0.9 ~ 1.1	Aldehyde Oxidase, CYP3A4
Zolpidem	BZ_1 receptor site on $GABA_A$ receptor complex	Difficulty in falling asleep, difficulty in maintaining sleep	1.7 ~ 2.5	2.0 ~ 5.5	CYP3A4, CYP1A2, CYP2C9

Zopiclone	GABA receptor complex	Difficulty in falling asleep, difficulty in maintaining sleep	3.5 ~ 6.5	5.0 ~ 6.0	P450
Eszopiclone	GABA receptor complex	Difficulty in falling asleep, difficulty in maintaining sleep	1.3 ~ 1.6	6.0 ~ 7.0	CYP3A1, CYP2E1
Sedative antidepressants					
Amitriptyline	H_1, adrenergic α1, mAch	Depressive disorder	2.0 ~ 5.0	30.0(10.0 ~ 100.0)	CYP3A4, CYP2C19, CYP2D6, CYP2C9
Trazodone	5-HT_2, Adrenergic-alpha1	Depressive disorder	1.0 ~ 2.0	7.0 ~ 15.0	CYP3A4, CYP2D6, CYP1A2
Mirtazapine	H_1, 5-HT_2	Depressive disorder	0.3 ~ 2.0	20.0 ~ 40.0	CYP2D6, CYP1A2, CYP3A4
Melatonin receptor agonists					
Ramelteon	Melatonin type 1 receptor and type 2 receptor	Difficulty in falling asleep	0.7 ~ 1.0	0.8 ~ 2.0	CYP1A2, CYP2C, CYP3A4
Orexin receptor inhibitor					
Suvoreson	Orexin receptor	Difficulty in falling asleep, difficulty in maintaining sleep	9.0 ~ 13.0	-	-

Note: "-" indicates that this item has no content.

long-term use of benzodiazepines is associated with an increased risk of dementia [23]. Based on the above findings, long-term use of sedative-hypnotic drugs is not recommended. Patients with chronic insomnia preferred cognitive behavioral therapy, if necessary, oral hypnotic drugs can be added, but the course of medication should be controlled within 4 weeks as far as possible.

For patients with long-term use of sedative-hypnotic drugs due to chronic insomnia, it is recommended that: (1) those who use benzodiazepines may continue to use, change to short-acting benzodiazepines (such as triazolam) or change to non-benzodiazepines; (2) for those who use non-benzodiazepines, it is recommended to continue to use the original drugs; (3) for those who use antidepressant for sleep aids, continue to use the original drugs. It is also necessary to be alert to the severe central depressant effects of these drugs in combination with anesthetic drugs.

[Recommendation] Preoperative insomnia patients preferred non-pharmacological treatment, if necessary, medication can be added to improve sleep; however, benzodiazepines, especially long-acting benzodiazepines, were avoided as much as possible.

(VI) Anesthesia and Perioperative Management of Insomnia Patients

1. Choice of anesthesia method: Regional block anesthesia is helpful in reducing postoperative sleep disturbances compared with general anesthesia in patients undergoing the same procedure [24-25]. One of the possible reasons is that regional block anesthesia reduces opioid consumption [24] that may cause sleep disturbances [26]. Regional block anesthesia should therefore be performed whenever possible. For patients in whom general anesthesia is necessary, regional blocks or peripheral nerve blocks should be combined as much as possible to reduce opioid consumption.

For patients taking sedative-hypnotic drugs before surgery, attention should be paid to the following aspects during anesthesia: (1) Closely monitor vital signs and anesthetic effect, and judge the depth of

anesthesia by EEG monitoring as far as possible [27] to timely adjust the dosage of anesthetic drugs; (2) Fully consider the effect of preoperative hypnotic drugs on GABA system and the synergistic effect with general anesthetic drugs to adjust the type or dosage of anesthetic drugs; (3) Dexmedetomidine can be used as a compound drug for that it does not function through GABA system and can reduce the dosage of general anesthetic drugs. However, evidence for its effect on postoperative sleep is lacking.
2. Selection of surgical methods: The degree of postoperative sleep disturbance is significantly aggravated after major surgery [25]. For example, after open cholecystectomy, patients have significant sleep disturbances, as indicated by increased N2 sleep, and reduced or absent N3 and REM sleep [26]. However, the degree of postoperative sleep disturbance was reduced in patients who underwent laparoscopic cholecystectomy under general anesthesia, as shown by decreased N3 sleep, but preserved REM sleep [28]. The extent of surgical trauma was therefore minimized whenever possible.
3. Postoperative analgesia: Pain is the most important cause of postoperative sleep disturbance [29-30]. It should be noted that opioids worsen postoperative sleep disturbances, including reduced REM sleep [25-26]. Therefore, non-opioid measures for analgesia are recommended, including regional or peripheral nerve blocks, non-steroidal anti-inflammatory drugs, and acetaminophen.
[Recommendation] Regional block anesthesia should be used whenever possible; for patients who have to receive general anesthesia, regional block or peripheral nerve block are combined as much as possible to reduce opioid use.
For patients taking sedative-hypnotic drugs before surgery, attention should be paid to their synergistic effect with general anesthetic drugs, and the dosage of anesthetic drugs should be adjusted under close monitoring of depth of anesthesia. Non-opioid drugs should be used for postoperative analgesia as far as possible, and the analgesic effect should be guaranteed.
(VII) Measures to Improve Postoperative Sleep
1. Non-pharmacological measures: Minimize the factors interfering with sleep in the environment, including the control of lights and noise at night, appropriately reduce the interference of nursing activities, remove the endotracheal tube, nasogastric tube, urinary catheter and drainage tube as early as possible, and use earplugs, eye masks, etc., which can effectively improve the postoperative sleep of patients [29, 31–33].
2. Pharmacological measures: There is insufficient evidence to show that the drug improves sleep quality in patients [34]. However, the following medications are currently used to improve sleep quality in postoperative patients. (1) Non-benzodiazepine GABA receptor agonists: e.g., zaleplon, zolpidem, zopiclone, etc., are short-acting non-benzodiazepine GABA receptor agonists. Zolpidem has been shown to improve subjective sleep quality and reduce fatigue but not sleep architecture when taken the evening before surgery or the night of surgery [35]. (2) Melatonin and melatonin receptor agonists: such as melatonin, ramelteon, etc. A meta-analysis showed that preoperative administration of melatonin reduced the degree of anxiety in patients [36]. In some randomized controlled studies with small sample sizes, perioperative administration of melatonin improved subjective sleep quality and improved analgesia without significantly increasing the incidence of adverse events [37-40]. (3) Orexin receptor inhibitors: e.g., suvorexant, newly approved for insomnia quality [39, 41]. Some studies have reported that it has an effect of improving sleep in postoperative patients [39]. However, it still needs further observation. (4) Dexmedetomidine: Selective α2 receptor agonists, which can exert sedative effects through endogenous sleep-stimulating pathways [42]. Study shows [43] for postoperative patients without mechanical ventilation, low-dose dexmedetomidine infusion in the evening has the effect of improving sleep quality, including increasing N2 sleep (reducing N1 sleep), prolonging sleep duration, and improving subjective sleep quality.
[Recommendation] Non-pharmacological measures (i.e., by reducing interfering factors in the environment, including the use of earplugs and eye masks) are preferred to improve postoperative sleep. In patients with unsatisfactory results of non-pharmacological measures, oral administration of non-benzodiazepine GABA receptor agonists, melatonin and melatonin receptor agonists or orexin-receptor inhibitors, or intravenous infusion of low-dose dexmedetomidine may be considered.

III. Preoperative Sleep-related Breathing Disorders
(I) Concept of Obstructive Sleep Apnea
Sleep-related breathing disorders are a class of disorders characterized by the presence of respiratory abnormalities during sleep, including obstructive sleep apnea disorders, central sleep apnea syndromes, sleep-related hypoventilation disorders, and sleep-related hypoxemia disorder.
Obstructive sleep apnea (OSA) is the most common in clinical practice, so sleep-related breathing disorders in this expert consensus are mainly aimed at OSA. OSA is characterized by repeated collapse of the upper airway during sleep, obstruction causing hypopnea or apnea, which subsequently leads to frequent hypoxemia, hypercapnia, significant fluctuations in intrathoracic pressure, disturbed sleep

architecture, and increased sympathetic tone, which can lead to impaired function of multiple organ systems in the long term. Clinically, patients usually complain of snoring and gasping or choking during sleep, which may be accompanied by daytime sleepiness, difficulty in concentration, memory loss, mood disorder and other symptoms, and an increased risk of hypertension, ischemic heart disease, stroke, and type 2 diabetes.

(II) Perioperative Significance of OSA Evaluation

With the improvement of living standards as well as population aging, the prevalence of OSA has increased year by year. Epidemiological investigations abroad found [44-45] in the population aged 30~70 years that, the prevalence of moderate to major OSA (sleep apnea-hypopnea index ≥ 15) increased from 8.8% (1988–1994) to 13.0% (2007–2010) in men; and from 3.9% (1988–1994) to 5.6% (2007–2010) in women. There is still a lack of nationwide epidemiological survey data on the prevalence of OAS in China, but the survey results in some regions also showed a significant increase in its prevalence [46-50]. Study found [51-54] that the proportion of OSA patients with difficult insertion/extubation during surgery, the incidence of postoperative respiratory and cardiovascular and cerebrovascular complications, and the postoperative ICU entry rate were significantly higher than those of non-OSA patients. Accurate preoperative assessment and intervention of OSA patients can help predict surgical risk and select anesthesia, thereby reducing postoperative cardio-cerebral and pulmonary complications and shortening postoperative hospital stay. However, the preoperative diagnosis of OSA is currently missed at a high rate [55]. Therefore, anesthesiologists and surgeons should be more aware of the importance of OSA and improve the ability to screen for the disease.

(III) Impact of OSA on Perioperative Patients

OSA patients have abnormal upper airway anatomy, decreased muscle tone, and recurrent upper airway narrowing or collapse during sleep, which are related to sleep stage, body position, location and degree of upper airway narrowing/obstruction, muscle tone, and respiratory drive. There are many factors that may aggravate the degree of upper airway obstruction in patients with OSA during perioperative period. For example, sedation and anesthesia increase the critical closing pressure of upper airway, further increasing the risk of passive collapse of upper airway; hypnotics may reduce muscle tension and aggravate upper airway collapse during recovery period of general anesthesia; the inhibitory effect of sedative and analgesic drugs on the central nervous system may reduce the body's ability to regulate the respiratory response to hypoxia; the effect of surgical trauma on sleep architecture and posture may make patients more likely to have upper airway collapse or even occlusion. With the combined effect of the above factors, patients with OSA have an increased risk of upper airway obstruction and respiratory center depression during perioperative period (especially during induction of anesthesia and postoperative period), leading to increased apnea and hypoxemia, hypercapnia, cardiovascular and cerebrovascular complications, respiratory failure and even death due to asphyxia.

[Recommendation] Anesthesiologists and surgeons should pay attention to the preoperative screening and diagnosis and management of OSA, which helps to reduce the anesthetic risk and postoperative cardio cerebral and pulmonary complications in such patients.

(IV) Risk Factors for OSA

OSA occurs as a result of the interaction between genetic polymorphisms and the environment. There are many predisposing factors for OSA, and most of them have interactions; there are also individual differences in the main risk factors of patients. It is for these reasons that the treatment of patients with OSA should also follow the principles of individualization. Common risk factors include the following:

1. Genetic factors: The risk of OSA in first-degree relatives is 2.9 to 4.0 times higher than in the general population; and the greater the number of affected relatives, the higher the risk. Studies have shown that genetic factors have an impact on obesity, fat distribution characteristics, regulation of upper airway dilator muscle activity, ventilation-driven chemoreceptor sensitivity, anatomical characteristics of the upper respiratory tract, secondary pathophysiological responses to OSA, and symptom presentation.

2. Anatomical factors: Anatomical abnormalities of the upper respiratory tract are one of the most important risk factors for the development of OSA. The pharyngeal cavity and supraglottic region are the most common sites of obstruction in OSA. Among them, the common anatomical risk factors for pharyngeal collapse include: (1) diseases that lead to increased nasal resistance; (2) pharyngeal soft tissue hypertrophy, such as soft palate hypertrophy or drooping, palatal sagging and thickening or lengthening, tonsil or adenoid hypertrophy, and tongue hypertrophy; (3) excessive mucosal folds in the aryepiglottic folds; and (4) maxillary and mandibular dysplasia, such as micrognathia.

3. Obesity: Obesity is an important risk factor for OSA. The prevalence of OSA in overweight and obese people is 31%, and each 10% increase in body mass index increases the risk approximately fourfold. This is associated with the fact that obesity can lead to fat accumulation in the pharyngeal wall, increased collapsibility of the pharyngeal space, reduced lung volume, and impaired regulation of

airway dilator muscle tone.
4. Age and gender: The risk of OSA increases gradually with increasing age, which may be related to the decrease in upper airway muscle tone and decreased central or peripheral neuromuscular reactivity that occurs with increasing age. The prevalence of OSA is significantly higher in men than in women, and the prevalence of OSA increases in women after menopause, which may be related to the following factors: (1) obesity tends to be centrally distributed in male patients and tends to affect lung volume; (2) estrogen and progesterone have a protective effect on the incidence of OSA in women; (3) the airways may be longer and therefore more unstable in men than in women; and (4) the symptoms of snoring are not significant in female patients, which easily leads to missed diagnosis.
5. Body position: Body position affects airway obstruction or collapse by affecting the upper airway structure and/or the direction of gravity effect on upper airway structure. For example, supine position is more likely to have airway obstruction than lateral and prone positions, and head tilting can significantly reduce the collapse of upper airway.
6. Alcohol and smoking: Alcohol inhibits the sensitivity of the respiratory center to hypoxia and hypercapnia, and subsequently causes or worsens upper airway obstruction. The mechanism by which cigarette smoking causes OSA may be related to increased levels of upper airway inflammation, impaired airway receptors, and elevated arousal thresholds.
7. Effects of drugs: Certain drugs may increase the potential for airway collapse by decreasing the responsiveness of airway dilators, such as muscle relaxants, phenobarbital, and benzodiazepine sedative-hypnotics; others may increase the occurrence of apnea through central depressant effects, such as morphine and other opioid analgesic drugs.
(V) Assessment of OSA patients
Polysomnography is the "gold standard" for the diagnostic of OSA. However, due to the higher requirements for environment, equipment, operation and analysis capacity of this examination, it is difficult to meet the clinical needs. In recent years, with the increasing understanding of OSA and the improvement of sleep monitoring technology, the accuracy of portable sleep respiratory monitoring technology for the diagnosis of OSA has been recognized. The current process is to clinically screen the high-risk groups of OSA such as snoring and daytime sleepiness with questionnaires, and select objective sleep monitoring methods to confirm the diagnosis based on the screening results.
1. Screening of OSA patients: Commonly used screening questionnaires are the Berlin Questionnaire, STOP-Bang Score, Epworth Sleepiness Scale (ESS), etc., and there are differences in the sensitivity and specificity of different questionnaires for OSA screening. Among them, there are more studies on the STOP-Bang score in surgical patients, which has higher sensitivity and specificity for OSA, especially moderate to severe OSA, and has a good predictive effect on the occurrence of postoperative complications.
The STOP-Bang consists of eight items (Table 4), each of which receives a positive answer score of 1 out of 8. STOP-Bang is recommended for two-step screening: a score of < 3 indicates low risk of OSA, exclude moderate to severe OSA; score ≥ 5 is classified as high risk of OSA, which requires sufficient preoperative preparation, postoperative monitoring and non-invasive ventilation, and preoperative sleep study is feasible when conditions permit so as to accurately understand the patient's OSA; scores of 3~4 are classified as suspected high risk group. Preoperative sleep study is recommended to accurately evaluate the presence and severity of OSA (Figure 2) [56-60]. In addition, the STOP-Bang score predicts the risk of postoperative complications, score of ≥ 3 is associated with a significantly higher risk of postoperative cardiopulmonary complications (arrhythmia, myocardial infarction, laryngeal or bronchospasm, acute pulmonary edema, congestive heart failure), reintubation after extubation, prolonged mechanical ventilation, ICU admission, and longer postoperative hospital stay [60–61].
It should be noted that: (1) due to racial and regional differences, some scholars suggested that neck circumference and body mass index (BMI) in Asian population should be 36 cm and 25 kg/m2, respectively, which need to be confirmed by further studies; (2) the score has better sensitivity but lower specificity for predicting OSA in patients with atrial fibrillation, which may be due to the overlap of gender, age, hypertension in the score with the risk factors of atrial fibrillation. Class II sleep equipment is recommended for patients with atrial fibrillation for OSA diagnosis, without considering the results of STOP score; (3) for obese patients (i.e. BMI $\geq$ 30 kg/m2), STOP-Bang $\geq$ 4 is a cut-off point with good sensitivity and specificity for the evaluation of moderate-to-severe OSA [62].

Table 4 STOP-Bang Scoring Content

Serial number	Item	Content
1	Snoring	Do you snore loudly (louder than talking, or loud enough to be heard through closed doors)?

2	Tiredness	Do you feel tired, fatigued or sleepy during daytime?
3	Observation	Has anyone observed an apneic episode during your sleep?
4	Blood pressure	Have you ever or currently been a hypertensive patient?
5	BMI	BMI more than 35 kg/m^2?
6	Age	Age over 50 years old?
7	Neck circumference	Neck circumference > 40 cm?
8	Gender	Male

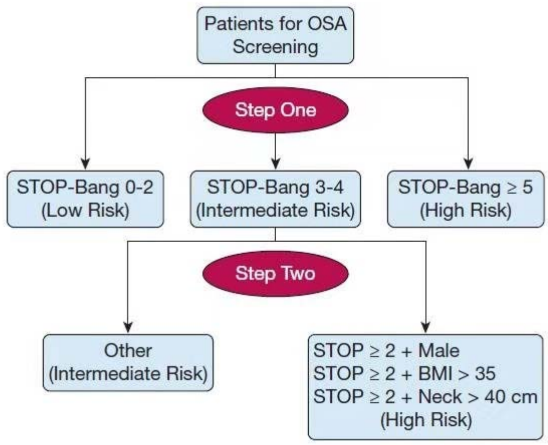


Figure 2 – *STOP-Bang algorithm with a two-step scoring strategy. See Figure 1 legend for expansion of abbreviation.*

2. Sleep study and report interpretation: Sleep study is an objective method of evaluating OSA and is divided into polysomnography (PSG) and portable monitoring (PM) based on the condition of the monitoring channels. Because portable monitoring does not record EEG, the sleep apnea-hypopnea index (AHI) provided by portable monitoring is based on total monitoring time rather than total sleep time, and thus will be less than the AHI value obtained by polysomnography, resulting in false negative results. In addition, polysomnography may be performed in people with mild OSA who do not have significant symptoms, who have severe cardiopulmonary disease, who are suspected of having other sleep disorders (e.g., severe insomnia), and who have a negative results of PM test but still have a suspicion of OSA [63].

For sleep study results, the following should be focused: (1) AHI: refers to the number of apneas and hypopneas that occur per hour of sleep and is a primary indicator for the diagnosis and evaluation of the severity of OSA. Greater AHI values are associated with greater OSA severity as AHI ≥ 5 is mild, AHI ≥ 15 is moderate, and AHI ≥ 30 is severe (2) REM sleep apnea-hypopnea index:

In patients under general anesthesia, the degree of upper airway collapse is correlated with the apnea index before anesthesia, especially AHI in REM sleep [64]. (3) AHI in supine sleep: The risk of upper airway obstruction is increased in the supine position, which is the most commonly used position for perioperative patients. Therefore, attention to the degree of apnea-hypopnea in the preoperative supine position helps to make a more accurate assessment of the risk of airway obstruction during and after surgery. 4) Degree of decrease of pulse oxygen saturation: The degree of decrease of pulse oxygen saturation is related to the degree of secondary organ dysfunction. The more pulse oxygen desaturation, the more severe the secondary organ dysfunction. Preoperative sleep pulse oxygen saturation decreased further during and after surgery due to anesthesia, trauma, body position and other factors. Therefore, attention should be paid to the degree of preoperative pulse oxygen desaturation.

[Recommendation] Screening for preoperative OSA is recommended for patients undergoing elective surgery. The STOP-Bang score is recommended for OSA screening. For patients in the high-risk group, adequate preoperative preparation is recommended, and sleep study can be recommended when necessary to further clarify the degree and characteristics of OSA; for patients in the intermediate-risk group, the necessity of objective examination should be determined by the surgeon and anesthesiologist in combination with the patient's surgical needs and underlying comorbidities.

3. Further assessment and management of OSA patients: For patients screened as high risk of OSA by

two-step method or with a definite diagnosis of OSA, not only the characteristics and severity of OSA should be assessed, but also their risk factors (such as obesity, upper airway structure, maxillofacial structure, etc.) and comorbidities (such as hypertension, cardiovascular and cerebrovascular diseases, obesity hypoventilation syndrome, etc.) should be further assessed. Patients, their families, and surgeons should be clearly informed of the increased risk of perioperative complications in such patients [65-70]. For patients undergoing non-emergency surgery, the need to postpone surgery for sleep study and necessary pre-operative treatment should be decided jointly by the anesthesiologist, the operating surgeon, and the patient [71].

(1) Difficult airway assessment: Up to 60% of moderate to severe OSA is due to obesity and may be associated with anatomical abnormalities of the upper airway, making it difficult to intubate the trachea. Induction of general anesthesia and administration of muscle relaxants can decrease muscle tone and collapse the upper airway, resulting in difficulty in glottic exposure and further increasing the difficulty of airway management. Therefore, for patients with high-risk or confirmed OSA, a detailed and comprehensive airway assessment should be performed before surgery. The anesthesiologist should know whether there is a difficult airway; whether there is facial deformity, such as micrognathia, mandibular retrusion, hyoid position, etc.; whether there is anatomical abnormality of upper respiratory tract, such as narrow oropharyngeal cavity, hypertrophy of tonsils or adenoids, tongue hypertrophy, etc.; and make a comprehensive judgment in combination with the results of Mallampati's classification, direct or indirect laryngoscopy, and imaging examination [65, 69, 72–73]. Strictly speaking, all OSA patients should be considered as difficult airway patients. For patients scheduled for general anesthesia with endotracheal intubation, the patency of the bilateral nasal cavities should be understood and the airway management protocol should be carefully designed.

It is necessary to prepare the corresponding airway management tools (nasal atypical tracheal catheter, video laryngoscope, fiber laryngoscope, laryngeal mask, special tracheal intubation equipment and emergency tracheotomy device, etc.); In addition, it is necessary to prepare the anesthesia machine, the monitor with the functions of end-tidal carbon dioxide partial pressure, pulse oxygen saturation, blood pressure and ECG monitoring, as well as the blood gas analyzer, transfer ventilator and necessary hemodynamic monitor. During the preoperative consultation, fully explain to the patients so that they can understand and cooperate the endotracheal intubation to be completed under conscious sedation.

[Recommendation] In patients with high risk or confirmed OSA, preoperative upper airway assessment and preparation as that for difficult airway should be performed; their risk factors and comorbid conditions should also be further assessed. Postpone surgery if necessary, perform sleep monitoring and give necessary preoperative therapeutic interventions.

(2) Assessment of vital organ function: The more severe the OSA, the greater the possibility and severity of involvement of heart, brain, kidney and other important organs, and the greater the potential risk during perioperative period. Therefore, attention should be paid to assess the involvement degree of organ systems such as cardiovascular and cerebrovascular system (such as hypertension, arrhythmia, coronary heart disease and cerebrovascular disease, etc.), respiratory system (such as decreased respiratory reserve, right ventricular hypertrophy, pulmonary hypertension, etc.) and kidney, and corresponding treatment should be given to achieve a better functional status of the damaged organs [65-66].

[Recommendation] OSA patients should pay attention to the assessment of vital organ function and the treatment of related diseases.

(3) Preoperative treatment of OSA: For patients with moderate to severe OSA or combining severe hypoxemia, whether preoperative continuous positive airway pressure therapy can improve outcomes is controversial. However, most studies support noninvasive positive pressure ventilation therapy before surgery to correct hypoxia, improve patient tolerance to surgery, and reduce the risk of anesthesia and surgical complications [74-75]. When conditions permit, weight loss treatment is feasible, and the therapeutic effect of OSA is assessed.

[Recommendation] For patients with preoperative assessed OSA or diagnosed with moderate to severe OSA, preoperative noninvasive ventilation treatment may be given, or continue previously effective treatment modalities (e.g., oral appliances).

(4) Preoperative medication: OSA patients are sensitive to various central depressants, and there are risks of apnea, upper airway obstruction, and excessive sedation after the use of sedative or narcotic analgesics, so such drugs should be used with caution before surgery. For OSA patients who experience insomnia preoperatively, non-benzodiazepine hypnotics may be selected when necessary, but oxygenation and ventilation status should be closely monitored and ventilation therapy should be prepared.

[Recommendation] For patients with OSA, sedative and analgesic drugs should be used with caution before surgery.

(VI) Intraoperative Anesthesia Management
Sedative hypnotics, narcotic analgesics, and muscle relaxants can all aggravate upper airway obstruction and even cause apnea.
In addition, these drugs not only inhibit the ventilatory response evoked by hypoxia and hypercapnia, but also inhibit the ability of patients with OSA to awaken from asphyxia and potentially be life-threatening [66, 68].
1. Intraoperative monitoring: Oxygen therapy will mask the decrease in blood oxygen caused by airway obstruction and may prolong the time of airway obstruction; however, end-tidal carbon dioxide monitoring can more accurately reflect the ventilation and effectively compensate for the deficiency of oxygen monitoring. Pulse oxygen saturation and end-tidal carbon dioxide levels should therefore be continuously monitored during induction of anesthesia, during surgery, before and after extubation after surgery, and in the early postoperative period.
During the perioperative period, continuous monitoring of ECG, timely detection and treatment of myocardial ischemia, and routine monitoring of non-invasive blood pressure should be conducted. Invasive arterial and central venous pressure monitoring should be performed during more complex surgery under general anesthesia. Special hemodynamic monitoring, such as stroke volume variation (SVV), may be considered when necessary. Anesthesia depth monitoring (such as BIS) is recommended in patients under general anesthesia or regional block combined sedation. Excessive anesthesia/sedation should be avoided during the surgery, and the patient should be fully awake at the end of the surgery. Other parameters are routinely monitored according to clinical presentation.
[Recommendation] Continuous monitoring of pulse oxygen saturation and end-tidal carbon dioxide levels is recommended. Perioperative monitoring should be strengthened.
2. Anesthesia method: The choice of anesthesia method depends on the anesthesia requirements for surgery and the patient's tolerance to anesthesia. Compared with general anesthesia, the use of regional block anesthesia (including local infiltration, peripheral nerve block or spinal block) can avoid or reduce the systemic use of sedative and analgesic drugs, which is beneficial to maintain the airway patency and increase the safety of patients. If it can meet the needs of surgery, it shall be listed as the first choice. If compound sedative or analgesic drugs are required during the use of regional block, the patient's ventilation and oxygenation status should be closely monitored. It should be noted that regional block combined with deep sedation poses a much higher risk to OSA patients than general anesthesia with endotracheal intubation. General anesthesia with endotracheal intubation should still be selected for procedures with large surgical trauma, complex procedures, excessive bleeding, and associated fluid loss/transfer, as well as for procedures that have a large impact on the patient's respiratory and circulatory functions (e.g., cardiac, thoracic, and neurosurgical procedures) [76-77].
[Recommendation] Regional block anesthesia is preferred in patients with OSA. If compound sedative and analgesic drugs are required during regional block anesthesia, the patient's ventilatory function and oxygenation status should be closely monitored. Attention must be paid to airway protection in patients undergoing general anesthesia.
3. Tracheal intubation technique: Difficult airway should be considered in all patients with OSA. Refer to "expert opinion on difficult airway management" [72, 76]. (1) Nasal intubation with conscious sedation: Conscious nasotracheal intubation has advantages in terms of safety and also facilitates exposure of the surgical field during oropharyngeal surgery. Perfect topical anesthesia (nasal, oropharyngeal, and endotracheal surface anesthesia) is the key to successful nasotracheal intubation. The nasal cavity of one side with better ventilation should be selected. If both sides have the same nasal ventilation, the left side is preferred. Nasal tracheal catheter with thin diameter and soft texture should be selected.
Fiberoptic bronchoscope-guided intubation is recommended. In order to reduce the patient's nervousness and discomfort, they are often supplemented with appropriate sedative and analgesic drugs; however, such patients are sensitive to drug effects and require titration under close monitoring. Intravenous infusion of short-acting drugs (e.g., propofol, remifentanil) or dexmedetomidine is recommended. (2) Rapid induction of oral intubation: Rapid induction of orotracheal intubation is feasible in patients with OSA without difficulty in ventilation and intubation. (3) Rapid induction of nasal intubation: In a qualified and skilled unit, rapid induction of nasal endotracheal intubation under fiberoptic bronchoscopic guidance is possible in patients with OSA who do not have difficult ventilation.
[Recommendation] The presence of a difficult airway should be considered in all patients with OSA and managed accordingly.
4. Intraoperative anesthetic management: (1) Anesthetic drugs: Drugs with rapid onset and short duration of action should be used, such as inhalation anesthetics (sevoflurane, desflurane), propofol and remifentanil for patients with general anesthesia, and short-acting or intermediate-acting non-

depolarizing muscle relaxants for muscle relaxation maintenance; propofol, remifentanil or dexmedetomidine for patients with compound sedation during surgery. Excessive anesthesia/sedation should be avoided during the surgery. At the end of the surgery, ensure that the patient is fully awake and that reflexes return to normal. 2) Respiratory management: Airway patency and satisfactory tidal volume shall be ensured for sedate patients. It should be noted that the depth of sedation in OSA patients correlates with the degree of airway collapse: Airway collapse is most severe in deep sedation, while snoring is most pronounced in shallow sedation. Therefore, the degree of airway patency cannot be judged based on snoring under sedation. The patient's ventilatory status can be monitored by end-tidal carbon dioxide and pulse oxygen saturation level to detect airway obstruction in time. Patients undergoing OSA corrective surgery under general anesthesia may choose to have the endotracheal tube reinforced with a steel wire, but it should still be noted that the mouth gag may squeeze the endotracheal tube, head displacement may cause distortion and displacement of the endotracheal tube, and the endotracheal tube is prone to bend obstruction at the nostril. So during the surgery, it is necessary to make close observation, timely communicate with the operator and adjust the position of catheter. End-tidal carbon dioxide level should be monitored continuously during surgery. Airway obstruction is more likely to occur after extubation due to the residual effects of anesthetics, oral secretions, and wound exudation, bleeding and edema after corrective surgery of OSA, especially in patients who are locally wrapped after nasal surgery. 3) Circulation management: pharyngolaryngeal operation and surgery have great stimulation to sympathetic nerve, which is easy to cause the increase of blood pressure, heart rate and arrhythmia, especially for the patients who have hypertension before surgery. Therefore, adequate depth of anesthesia must be ensured during endotracheal intubation and pharyngolaryngeal surgery, and vasodilators and/or esmolol may be given to control blood pressure and heart rate if necessary. In patients receiving remifentanil during surgery, effective analgesia should be given before discontinuation to avoid agitation, increased blood pressure, and increased heart rate due to hyperalgesia after discontinuation.

[Recommendation] Anesthetic drugs with rapid onset and short duration of action should be selected during general anesthesia. At the end of surgery, ensure that the patient is fully awake and that the reflexes return to normal.

(VII) Postoperative Management of OSA Patients

The postoperative condition of OSA patients is more complicated than that before surgery, and the reasons include: (1) residual sedative and analgesic drugs lead to central depression and aggravate upper airway collapse; (2) postoperative sleep disturbance is easy to occur, which is characterized by early postoperative sleep deprivation and increased rapid eye movement sleep rebound around 1 week after surgery, which may lead to the instability of sleep apnea time; (3) postoperative delirium is more likely to occur; (4) patients undergoing pharyngeal surgery are prone to upper airway edema [26, 78–83]. Therefore, OSA patients are more likely to have airway obstruction and fatal apnea after surgery, and postoperative management should be intensified until they return to the preoperative safe level.

1. Management of patients with retained endotracheal tubes after surgery: (1) Sedation and analgesia: In postoperative patients with retained endotracheal tubes, adequate analgesia should be given first. Non-opioid measures of analgesia are preferred, including regional or peripheral nerve blocks, non-steroidal anti-inflammatory drugs, acetaminophen, etc. Small doses of opioids may be combined if necessary. Patients who remain agitated after adequate analgesia may be given moderate sedation, preferably propofol and/or dexmedetomidine intravenously, but excessive sedation should be avoided [84]. (2) Principles and management of extubation: Patients with OSA are at high risk of developing airway obstruction after extubation. The timing of extubation should be determined by the patient's severity of OSA, body mass index, ease of mask ventilation and endotracheal intubation during induction of anesthesia, duration and type of surgery, and recovery of patient consciousness. Prepare post-extubation monitoring and subsequent support before extubation to reduce the risk of reintubation after extubation. Specific recommendations are as follows [65, 69, 76–77]: ① Severe OSA patients, or mild to moderate OSA patients with obvious difficult airway performance, should be considered to be extubated after the patient is fully awake; ② Sedative drugs should be discontinued before extubation to make the patient fully conscious, and the dose of analgesic drugs should also be reduced to the lowest effective dose of postoperative analgesia; ③ Patients should have complete recovery of orientation, cough and swallowing reflex, and complete recovery of neuromuscular transmission function [T4/T1 > 0.9, head-up test > 5 s, tidal volume > 8 ml/kg, maximum peak inspiratory pressure < -25 cmH_2O (1 cmH_2O = 0.098 kPa) and end-tidal carbon dioxide partial pressure < 45 mmHg]; ④ Patients undergoing pharyngeal and palatal plastic surgery or combined orthognathic surgery and patients with a difficult procedure of surgery should be considered for extubation after possible postoperative bleeding or airway obstruction is excluded; ⑤ Other risks of airway obstruction should be excluded, such as a large number of secretions and upper airway edema; ⑥Meet other indicators of

extubation; ⑦ Extubation in lateral, semi-recumbent or other non-supine position: if possible, the semi-upright position should be maintained after extubation; ⑧ Appropriate oropharyngeal or nasopharyngeal airway should be prepared before extubation, and prepare for mask ventilation. If you are uncertain whether a patient can be well ventilated after extubation and are not sure about reintubation, an endotracheal tube guide wire should be placed in advance before extubation so that the airway can be controlled in time if necessary. In case of poor spontaneous breathing in the early stage of extubation, continuous positive airway pressure (CPAP) ventilation or nasal high-flow oxygen therapy may be considered to ensure the upper airway opening and gradually reduce the inspired oxygen concentration until the transition to inhaled air maintenance; ⑨Routine preparation for re-intubation; ⑩ OSA patients should stay in the anesthesia recovery room for more than 3h after extubation, and most severe complications occurred within 2h after surgery. If respiratory obstruction or hypoxemia occurs after extubation, continuous monitoring should be performed in the anesthesia recovery room for at least 7 hours after the last adverse event; or transfer the patient to the intensive care unit.
[Recommendation] Patients with OSA should be extubated after full wakefulness from general anesthesia and complete recovery of autonomic reflexes. Mask ventilation and reintubation should be prepared before extubation.

2. Management of patients with endotracheal tube removal after surgery: (1) Monitoring: Patients with OSA should be monitored more closely after endotracheal tube removal. The following criteria should be assessed and met before the patient is transferred to a general ward: ①full recovery of consciousness and return to preoperative levels of arousal in response to abnormal ventilation; ②no need to use opioid analgesics or other sedatives to avoid aggravating respiratory events by inhibiting arousal; ③ ability to spontaneously apply CPAP to ensure a patent upper airway during sleep. Patients should still be routinely monitored for 24 h after returning to the ward, including electrocardiography, pulse oximetry, and noninvasive blood pressure monitoring, until the pulse oxygen saturation level remains above 90% while breathing air during sleep. (2) Postoperative analgesia: Patients with OSA are at great risk of developing upper airway obstruction and respiratory depression with opioids, and the combined use of sedative drugs with opioids further increases the risk of respiratory depression and airway obstruction. Therefore, it is recommended that non-opioid measures for analgesia be preferred, including regional or peripheral nerve blocks, non-steroidal anti-inflammatory drugs, acetaminophen, etc. Small doses of opioids may be combined if necessary. When patient-controlled intravenous analgesia or patient-controlled epidural analgesia is used, continuous infusion of background volume should be given with great caution or not given at all. All OSA patients receiving postoperative patient-controlled analgesia require close monitoring of snoring, sedation level, respiratory rate, and pulse oximetry [85]. (3) Respiratory management: It is recommended to apply non-invasive ventilation therapy after surgery for OSA patients. The parameters of non-invasive ventilation therapy [(CPAP or Bi-level Positive Airway Pressure (BiPAP), Adaptive Servo Ventilation (ASV), etc.)] are adjusted according to the monitoring results of respiration and blood oxygen, and oxygen therapy is provided at the same time, so as to maintain satisfactory pulse oxygen saturation level in the state of breathing air during sleep. (4) Body position: After returning to the ward, the patient should be in lateral or semi-recumbent position, avoiding supine position as much as possible, so as to improve the tidal volume of the patient and reduce the degree of tongue drop after extubation.
[Recommendation] Patients with OSA should continue to be closely monitored after extubation and should not return to the general ward until fully awake; monitoring should continue for 24 hours after they return to the ward. Nerve block, nonsteroidal anti-inflammatory drugs, and acetaminophen are preferred for analgesia in patients with OSA, and a small amount of opioid analgesic is given in combination if necessary. Postoperative noninvasive ventilation is recommended for patients with OSA. And the supine position should be avoided after surgery.

Conflict of interest All authors declare that there is no conflict of interest.

Reference

[1] Duffy JF, Dijk DJ, Klerman EB, et al. Later endogenous circadian temperature nadir relative to an earlier wake time in older people[J]. Am J Physiol,1998,275(5 Pt 2):R1478-R1487.
[2] Kryer MH, Roth T, Dement WC. Principles and practice of sleep medicine[M]. Sixth ed. Philadelphia, PA: ELSEVIER, 2017:15-24.
[3] Douglas NJ, White DP, Weil JV, et al. Hypercapnic ventilatory response in sleeping adults[J]. Am Rev Respir Dis, 1982,126(5):758-762. DOI: 10.1164/arrd.1982.126.5.758.

[4] Mohsenin V. Sleep in chronic obstructive pulmonary disease [J]. Semin Respir Crit Care Med,2005,26(1):109-116. DOI: 10.1055/s-2005-864204.
[5] Banks S, Dinges DF. Behavioral and physiological consequences of sleep restriction[J]. J Clin Sleep Med,2007,3 (5):519-528.
[6] Banks S, Van Dongen HP, Mai slin G, et al. Neurobehavioral dynamics following chronic sleep restriction: dose-response effects of one night for recovery[J]. Sleep, 2010, 33(8): 1013-1026. DOI: 10.1093/sleep/33.8.1013.
[7] Belenky G, Wesensten NJ, Thorne DR, et al. Patterns of performance degradation and restoration during sleep restriction an subsequent recovery: a sleep dose-response study[J]. J Sleep Res, 2003, 12(1): 1-12. DOI: 10.1046 / j.1365-2869.2003.00337.x.
[8] Cappuccio FP, D′Elia L, Strazzullo P, et al. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies[J]. Sleep, 2010, 33(5): 585-592. DOI: 10.1093/sleep/33.5.585.
[9] Chinese guidelines for the diagnosis and treatment of insomnia, China Sleep Research Society. [J]. National Medical Journal of China, 2017, 97 (24): 1844-1856. DOI: 10.3760 / cma.j.issn.0376-2491.2017.24.002.
[10] Riemann D, Baglioni C, Bassetti C, et al. European guideline for the diagnosis and treatment of insomnia[J]. J Sleep Res, 2017,26(6):675-700. DOI: 10.1111/jsr.12594.

[11] Foley D, Ancoli-Israel S, Britz P, et al. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey [J]. J Psychosom Res, 2004, 56(5):497-502. DOI: 10.1016/j.jpsychores.2004. 02.010.
[12] Bloom HG, Ahmed I, Alessi CA, et al. Evidence-based recommendations for the assessment and management of sleep disorders in older persons [J]. J Am Geriatr Soc, 2009, 57(5): 761-789.
[13] Xie Yuzhen. Investigation and analysis of preoperative sleep quality in patients with liver cancer [J]. China Practical Medicine, 2015, 10(28): 273-274, 275 DOI: 10.14163/j.cnki.11–5547/r.2015.28.200.
[14] Yang Lei, Wang Xuanjiu, Liu Wei, et al. Study on preoperative sleep status of patients with renal carcinoma [J]. World Journal of Sleep Medicine, 2018, 5(4): 16-19.
[15] Liu Yu, Bai Jiuxu, Liu Tao, et al. Investigation of preoperative sleep quality and analysis of influencing factors in patients with coronary heart disease [J]. Progress in Modern Biomedicine, 2016, 16(18): 3496-3499, 3568. DOI: 10.13241/j.cnki.pmb.2016.18.024.
[16] Vgontzas AN, Liao D, Bixler EO, et al. Insomnia with objective short sleep duration is associated with a high risk for hypertension[J]. Sleep, 2009, 32(4): 491-497. DOI: 10.1093 / sleep/32.4.491.
[17] Laugsand LE, Vatten LJ, Platou C, et al. Insomnia and the risk of acute myocardial infarction: a population study[J]. Circulation, 2011, 124(19): 2073-2081. DOI: 10.1161 / CIRCULATIONAHA.111.025858.
[18] Hayes D Jr, Anstead MI, Ho J, et al. Insomnia and chronic heart failure[J]. Heart Fail Rev, 2009, 14(3): 171-182. DOI: 10.1007/s10741-008-9102-1.
[19] Vgontzas AN, Liao D, Pejovic S, et al. Insomnia with objective short sleep duration is associated with type 2 diabetes: a population-based study[J]. Diabetes Care, 2009, 32(11): 1980-1985. DOI: 10.2337/dc09-0284.
[20] Li Li'e, Zhu Dandan, Lu Yueping. Preoperative sleep status of surgical inpatients and its influencing factors [J]. Modern Clinical Nursing, 2013,12(9):1-3, 4. DOI: 10.3969/ j.issn.1671-8283.2013.09.001.
[21] Smith MT, McCrae CS, Cheung J, et al. Use of actigraphy for the evaluation of sleep disorders and circadian rhythm sleep-wake disorders: an American academy of sleep medicine clinical practice guideline[J]. J Clin Sleep Med, 2018, 14(7): 1231-1237. DOI: 10.5664/jcsm.7230.
[22] Winkler A, Rief W. Effect of placebo conditions on polysomnographic parameters in primary insomnia: a meta-analysis[J]. Sleep, 2015, 38(6): 925-931. DOI: 10.5665 / sleep.4742.
[23] Islam MM, Iqbal U, Walther B, et al. Benzodiazepine use and risk of dementia in the elderly population: a systematic review and meta-analysis[J]. Neuroepidemiology, 2016, 47(3-4): 181-191. DOI: 10.1159/000454881.
[24] Kjolhede P, Langstrom P, Nilsson P, et al. The impact of quality of sleep on recovery from fast-track abdominal hysterectomy[J]. J Clin Sleep Med,2012,8(4):395-402. DOI: 10.5664/jcsm.2032.
[25] Chung F, Liao P, Elsaid H, et al. Factors associated with postoperative exacerbation of sleep-disordered breathing[J]. Anesthesiology, 2014, 120(2): 299-311. DOI: 10.1097 / ALN.0000000000000041.

[26] Knill RL, Moote CA, Skinner MI, et al. Anesthesia with abdominal surgery leads to intense REM sleep during the first postoperative week[J]. Anesthesiology,1990,73(1):52-61.
[27] Fahy BG, Chau DF. The technology of processed electroencephalogram monitoring devices for assessment of depth of anesthesia[J]. Anesth Analg, 2018, 126(1): 111-117. DOI: 10.1213/ANE.0000000000002331.
[28] Rosenberg-Adamsen S, Skarbye M, Wildschiodtz G, et al. Sleep after laparoscopic cholecystectomy[J]. Br J Anaesth, 1996,77(5):572-575. DOI: 10.1093/bja/77.5.572.
[29] Dolan R, Huh J, Tiwari N, et al. A prospective analysis of sleep deprivation and disturbance in surgical patients[J]. Ann Med Surg (Lond), 2016, 6:1-5. DOI: 10.1016/j.amsu.2015. 12.046.
[30] Celik S, Oztekin D, Akyolcu N, et al. Sleep disturbance: the patient care activities applied at the night shift in the intensive care unit[J]. J Clin Nurs,2005,14(1):102-106. DOI: 10.1111/ j.1365-2702.2004.01010.x.
[31] Fontana CJ, Pittiglio LI. Sleep deprivation among critical care patients[J]. Crit Care Nurs Q,2010,33(1):75-81. DOI: 10.1097/ CNQ.0b013e3181c8e030.
[32] Li SY, Wang TJ, Vivienne WS, et al. Efficacy of controlling night-time noise and activities to improve patients′ sleep quality in a surgical intensive care unit[J]. J Clin Nurs,2011,20 (3-4):396-407. DOI: 10.1111/j.1365-2702.2010.03507.x.
[33] Hu RF, Jiang XY, Chen J, et al. Non-pharmacological interventions for sleep promotion in the intensive care unit[J]. Cochrane Database Syst Rev, 2015, 10: CD008808. DOI: 10.1002/14651858.CD008808.pub2.
[34] Kanji S, Mera A, Hutton B, et al. Pharmacological interventions to improve sleep in hospitalised adults: a systematic review[J]. Bmj Open, 2016, 6(7): e12108. DOI: 10.1136/bmjopen-2016-012108.
[35] Krenk L, Jennum P, Kehlet H. Postoperative sleep disturbances after zolpidem treatment in fast-track hip and knee replacement[J]. J Clin Sleep Med,2014,10(3):321-326. DOI: 10.5664/jcsm.3540.
[36] Hansen MV, Halladin NL, Rosenberg J, et al. Melatonin for pre-and postoperative anxiety in adults[J]. Cochrane Database Syst Rev, 2015, 4: CD009861. DOI: 10.1002 / 14651858. CD009861.pub2.
[37] Borazan H, Tuncer S, Yalcin N, et al. Effects of preoperative oral melatonin medication on postoperative analgesia, sleep quality, and sedation in patients undergoing elective prostatectomy: a randomized clinical trial[J]. J Anesth,2010,24 (2):155-160. DOI: 10.1007/s00540-010-0891-8.
[38] Khare A, Thada B, Jain N, et al. Comparison of effects of oral melatonin with oral alprazolam used as a premedicant in adult patients undergoing various surgical procedures under general anesthesia: a prospective randomized placebo-controlled study [J]. Anesth Essays Res,2018,12(3):657-662. DOI: 10.4103/aer. AER_90_18.
[39] Kawada K, Ohta T, Tanaka K, et al. Addition of suvorexant to ramelteon therapy for improved sleep quality with reduced delirium risk in acute stroke patients[J]. J Stroke Cerebrovasc Dis, 2019, 28(1):142-148. DOI: 10.1016/j.jstrokecerebrovasdis. 2018.09.024.
[40] Madsen MT, Hansen MV, Andersen LT, et al. Effect of melatonin on sleep in the perioperative period after breast cancer surgery: a randomized, double-blind, placebo-controlled trial[J]. J Clin Sleep Med,2016,12(2):225-233. DOI: 10.5664/ jcsm.5490.
[41] Kishi T, Matsunaga S, Iwata N. Suvorexant for primary insomnia: a systematic review and meta-analysis of randomized placebo-controlled trials[J]. PLoS One,2015,10(8): e136910. DOI: 10.1371/journal.pone.0136910.
[42] Reardon DP, Anger KE, Adams CD, et al. Role of dexmedetomidine in adults in the intensive care unit: an update[J]. Am J Health Syst Pharm,2013,70(9):767-777. DOI: 10.2146/ajhp120211.
[43] Wu XH, Cui F, Zhang C, et al. Low-dose dexmedetomidine improves sleep quality pattern in elderly patients after noncardiac surgery in the intensive care unit: a pilot randomized controlled trial[J]. Anesthesiology, 2016, 125(5): 979-991. DOI: 10.1097/ALN.0000000000001325.
[44] Peppard PE, Young T, Barnet JH, et al. Increased prevalence of sleep-disordered breathing in adults[J]. Am J Epidemiol, 2013,177(9):1006-1014. DOI: 10.1093/aje/kws342.
[45] Tan A, Cheung YY, Yin J, et al. Prevalence of sleep-disordered breathing in a multiethnic Asian population in Singapore: a community-based study[J]. Respirology,2016, 21(5):943-950. DOI: 10.1111/resp.12747.
[46] Epidemiological survey of obstructive sleep apnea-hypopnea syndrome among people over 30 years old in Nantong, Zhang Ting. [J]. Collection of papers of 2017 International Orthodontic Conference & The 16th National Academic Conference on Orthodontic, Shanghai, 2017.
[47] Ma Hengjie, Wu Jingbo, Zhang Jing, et al. Study on epidemiological investigation of sleep apnea syndrome in Penglai population [J]. China Health Industry, 2017, 14 (21):1-2, 5. DOI:

10.16659/j.cnki.1672-5654.2017.21.001.
[48] Hu Qinglei, Yang Yang, Zhou Huan, et al. Epidemiological survey of obstructive sleep apnea hypopnea syndrome in children aged 4-7 years in Putuo District, Shanghai [J]. Chinese Journal of Ophthalmology and Otolaryngology, 2014, 14 (5): 316-319.
[49] Hu Qinglei, Du Cuiping, Yang Yang, et al. Epidemiological survey of obstructive sleep apnea hypopnea syndrome in people over 20 years old in Putuo District, Shanghai [J]. Chinese Journal of Ophthalmology and Otolaryngology, 2017,17(1):49-54. DOI: 10.14166/j.issn.1671- 2420.2017.01.015.
[50] Ma Yanning, Wang Xiaoqin, Bao Pingping. Epidemiological study on sleep apnea syndrome in Taiyuan area [J]. Guide of China Medicine, 2011,9(30):108-110. DOI: 10.3969/j.issn.1671-8194.2011.30.081.
[51] Hai F, Porhomayon J, Vermont L, et al. Postoperative complications in patients with obstructive sleep apnea: a meta-analysis[J]. J Clin Anesth, 2014, 26(8): 591-600. DOI: 10.1016/j.jclinane.2014.05.010.
[52] Mokhlesi B, Hovda MD, Vekhter B, et al. Sleep-disordered breathing and postoperative outcomes after elective surgery: analysis of the nationwide inpatient sample[J]. Chest,2013,144 (3):903-914. DOI: 10.1378/chest.12-2905.
[53] Gaddam S, Gunukula SK, Mador MJ. Post-operative outcomes in adult obstructive sleep apnea patients undergoing non-upper airway surgery: a systematic review and meta-analysis[J]. Sleep Breath, 2014, 18(3): 615-633. DOI: 10.1007/s11325-013-0925-1.
[54] Kaw R, Chung F, Pasupuleti V, et al. Meta-analysis of the association between obstructive sleep apnoea and postoperative outcome[J]. Br J Anaesth,2012,109(6):897-906. DOI: 10.1093/bja/aes308.
[55] Wang CL, Li XZ, Cai XL, et al. Anesthesiologist′s knowledge and attitudes about obstructive sleep apnea: a survey study[J]. Sleep Breath, 2012, 16(1):41-46. DOI: 10.1007/s11325-011- 0482-4.
[56] Singh M, Liao P, Kobah S, et al. Proportion of surgical patients with undiagnosed obstructive sleep apnoea[J]. Br J Anaesth, 2013,110(4):629-636. DOI: 10.1093/bja/aes465.
[57] Christensson E, Franklin KA, Sahlin C, et al. Can STOP-Bang and Pulse Oximetry Detect and Exclude Obstructive Sleep Apnea[J]. Anesth Analg,2018,127(3):736-743. DOI: 10.1213/ ANE.0000000000003607.
[58] Rebelo-Marques A, Vicente C, Valentim B, et al. STOP-Bang questionnaire: the validation of a portuguese version as a screening tool for obstructive sleep apnea (OSA) in primary care[J]. Sleep Breath, 2018, 22(3): 757-765. DOI: 10.1007 / s11325-017-1608-0.
[59] Mou J, Pflugeisen BM, Crick BA, et al. The discriminative power of STOP-Bang as a screening tool for suspected obstructive sleep apnea in clinically referred patients: considering gender differences[J]. Sleep Breath, 2019, 23(1): 65-75. DOI: 10.1007/s11325-018-1658-y.
[60] Chung F, Abdullah HR, Liao P. STOP-Bang questionnaire: a practical approach to screen for obstructive sleep apnea[J]. Chest,2016,149(3):631-638. DOI: 10.1378/chest.15-0903.
[61] Chung F, Chau E, Yang Y, et al. Serum bicarbonate level improves specificity of STOP-Bang screening for obstructive sleep apnea[J]. Chest,2013,143(5):1284-1293. DOI: 10.1378/ chest.12-1132.
[62] Nagappa M, Patra J, Wong J, et al. Association of STOP-Bang questionnaire as a screening tool for sleep apnea and postoperative complications: a systematic review and bayesian meta-analysis of prospective and retrospective cohort studies [J]. Anesth Analg, 2017, 125(4): 1301-1308. DOI: 10.1213 / ANE.0000000000002344.
[63] Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American academy of sleep medicine clinical practice guideline[J]. J Clin Sleep Med,2017,13(3):479-504. DOI: 10.5664/jcsm.6506.
[64] Karimi N, Kelava M, Kothari P, et al. Patients at high risk for obstructive sleep apnea are at increased risk for atrial fibrillation after cardiac surgery: a cohort analysis[J]. Anesth Analg, 2018, 126(6):2025-2031. DOI: 10.1213/ANE.0000000000002852.
[65] American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on perioperative management of patients with obstructive sleep apnea[J]. Anesthesiology,2014,120(2):268-286. DOI: 10.1097/ ALN.0000000000000053.
[66] Gross JB, Bachenberg KL, Benumof JL, et al. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists Task Force on perioperative management of patients with obstructive sleep apnea[J]. Anesthesiology,2006, 104(5):1081-1093, quiz1117-1118.
[67] Adesanya AO, Lee W, Greilich NB, et al. Perioperative management of obstructive sleep apnea[J]. Chest,2010,138(6): 1489-1498. DOI: 10.1378/chest.10-1108.

[68] Turner K, VanDenkerkhof E, Lam M, et al. Perioperative care of patients with obstructive sleep apnea -a survey of Canadian anesthesiologists[J]. Can J Anaesth,2006,53(3):299-304. DOI: 10.1007/BF03022219.
[69] Mickelson SA. Preoperative and postoperative management of obstructive sleep apnea patients[J]. Otolaryngol Clin North Am,2007,40(4):877-889. DOI: 10.1016/j.otc.2007.04.007.
[70] den Herder C, Schmeck J, Appelboom DJ, et al. Risks of general anaesthesia in people with obstructive sleep apnoea[J]. BMJ, 2004, 329(7472):955-959. DOI: 10.1136/bmj.329.7472. 955.
[71] Joshi GP, Ankichetty SP, Gan TJ, et al. Society for ambulatory anesthesia consensus statement on preoperative selection of adult patients with obstructive sleep apnea scheduled for ambulatory surgery[J]. Anesth Analg, 2012, 115(5):1060-1068. DOI:10.1213/ANE.0b013e318269cfd7.

[72] Benumof JL. Obstructive sleep apnea in the adult obese patient: implications for airway management[J]. J Clin Anesth, 2001,13(2):144-156. DOI: 10.1016/S0952-8180(01)00232-X.
[73] Meoli AL, Rosen CL, Kristo D, et al. Upper airway management of the adult patient with obstructive sleep apnea in the perioperative period--avoiding complications[J]. Sleep, 2003,26(8):1060-1065. DOI: 10.1093/sleep/26.8.1060.
[74] Chung F, Nagappa M, Singh M, et al. CPAP in the perioperative setting: evidence of support[J]. Chest,2016,149 (2):586-597. DOI: 10.1378/chest.15-1777.
[75] Singh PM, Borle A, Shah D, et al. Optimizing prophylactic CPAP in patients without obstructive sleep apnoea for high-risk abdominal surgeries: a meta-regression analysis[J]. Lung, 2016, 194(2):201-217. DOI: 10.1007/s00408-016- 9855-6.
[76] Chinese Anesthesiology Guidelines and Expert Consensus, Chinese Society of Anesthesiology. [M]. Beijing: People's Medical Publishing House, 2014:142-149.
[77] Kryer MH, Roth T, Dement WC. Principles and practice of sleep medicine[M]. 6th ed. Philadelphia,PA:ELSEVIER,2017: 1458-1462.
[78] Hillman DR, Platt PR, Eastwood PR. The upper airway during anaesthesia[J]. Br J Anaesth,2003,91(1):31-39. DOI: 10.1093/ bja/aeg126.
[79] Kellner P, Herzog B, Plossl S, et al. Depth-dependent changes of obstruction patterns under increasing sedation during drug-induced sedation endoscopy: results of a German monocentric clinical trial[J]. Sleep Breath, 2016, 20(3): 1035-1043. DOI: 10.1007/s11325-016-1348-6.
[80] Hiremath AS, Hillman DR, James AL, et al. Relationship between difficult tracheal intubation and obstructive sleep apnoea[J]. Br J Anaesth,1998,80(5):606-611. DOI: 10.1093/ bja/80.5.606.
[81] Siyam MA, Benhamou D. Difficult endotracheal intubation in patients with sleep apnea syndrome[J]. Anesth Analg,2002,95 (4):1098-1102. DOI: 10.1213/00000539-200210000-00058.
[82] Isono S, Tanaka A, Ishikawa T, et al. Sniffing position improves pharyngeal airway patency in anesthetized patients with obstructive sleep apnea[J]. Anesthesiology,2005,103(3): 489-494. DOI: 10.1097/00000542-200509000-00010.
[83] Aurell J, Elmqvist D. Sleep in the surgical intensive care unit: continuous polygraphic recording of sleep in nine patients receiving postoperative care[J]. Br Med J (Clin Res Ed),1985, 290(6474):1029-1032. DOI: 10.1136/bmj.290.6474.1029.
[84] Devlin JW, Skrobik Y, Gelinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU[J]. Crit Care Med, 2018, 46(9): e825-e873. DOI: 10.1097/CCM.0000000000003299.
[85] Cullen DJ. Obstructive sleep apnea and postoperative analgesia--a potentially dangerous combination[J]. J Clin Anesth, 2001, 13(2): 83-85. DOI: 10.1016 / S0952-8180(01) 00261-6.