6 Perioperative Anesthetic Management and Preoperative Precautions for Retroperitoneal Tumors

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1 Anesthetic Risk Assessment and Preparation for Retroperitoneal Tumor Surgery

Retroperitoneal tumors (RPTs) refer to neoplasms that occur in the retroperitoneal space, mainly arising from fat, loose connective tissue, muscle, fascia, blood vessels, nerves, and lymph tissue, within the retroperitoneum, but excluding the origin from retroperitoneal organs (such as the kidney, pancreas, suprarenal gland, and ureter). They are a relatively rare entity of tumor and mostly malignant (accounting for about 70% of total cases). Common benign RPTs include teratoma, nerve sheath tumor, and fibroma. Malignant RPTs include liposarcoma, fibrosarcoma, leiomyosarcoma, embryonal carcinoma, neurofibrosarcoma, and malignant lymphoma. These tumors are located deeply inside the abdominal cavity with a certain space for expansion. It is tough to diagnose these tumors at the early stage due to lack of typical signs or symptoms. As they grow larger, tumors may compress or invade the surrounding organs and tissues, resulting in subsequent presentations in patients. All of these factors contribute to a challenge for surgeons to radically remove RPTs. The key points in the assessments of anesthetic risk for patients include clinical presentations at baseline, concomitant diseases, current treatment, and organ system function. The preexisting disease of patients must be well controlled in order to create optimal conditions for surgery.

1.1 Patient Assessment

To ensure safe and smooth implementation of anesthesia procedure, each patient should receive a detailed assessment before anesthesia in clinics.

1.1.1 Medical Records Review

To make a comprehensive assessment requires full understanding of the patient's surgery and anesthesia-related conditions:

1. General condition: age, gender, development, nutrition, mental state, spine and extremities, activity, blood pressure, heart rate, respiration, body temperature, and so on.
2. History of the present illness, past medical history, past history of anesthesia, family history of tumor, histories of drug allergy, cigarette smoking and alcohol consumption,

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C.-H. Luo (ed.), *Retroperitoneal Tumors*, https://doi.org/10.1007/978-94-024-1167-6_6

as well as presence, severity, and pathologic effects of concomitant diseases such as neurological, respiratory, cardiovascular, endocrine, and other systemic disorders.
3. Routine blood, urine, and stool tests, blood biochemistry, water and electrolyte acid-base status, X-ray, ECG, liver and kidney function, as well as other special examinations.
4. Understand the administration of special anesthesia-related drugs and preoperative preparations.

1.1.2 Physical Examination

1. Give priority to reexamination of the nervous, circulatory, and respiratory systems.
2. Perform special tests depending on the specific type of anesthesia, e.g., patients who receive intrathecal block should be examined by X-ray, for the spine and skin of the chest and back; those who receive general anesthesia should be examined for dentures, dental caries and loose teeth, the extent of mouth opening, the activity of the head and neck, the height of the throat, and feasibility for tracheal intubation.
3. Understand the patients' mental state and anesthesia requirements.
4. Carefully explain to patients in order to eliminate their concerns and to enhance their confidence in the anesthetic procedure and their trust in anesthesiologists.
5. Determine the type and premedication of anesthesia according to physical condition and surgical requirements of the patients.
6. If any examination is not performed as scheduled or needs to be repeated or if the patient's physical condition does not allow undergoing anesthesia, anesthesiologists should directly notify the physician to seek for a resolution through consultation and report to the senior physician in the department.
7. Anesthesiologists must ask for advice from surgeons about the surgical site, requirements, options, and time length of duration, potential intraoperative risks, and anesthetic requirements.
8. Explain the choices of anesthesia, potential anesthesia complications, adverse effects of anesthetics, anesthesia accidents, as well as self-supporting drugs and supplies to the patients' relatives before anesthesia, in order to obtain their consent before asking them to sign the anesthesia consent form.

1.2 Preanesthetic Preparation for Patients with Common Concomitant Diseases

Anesthesia risk in hypertensive patients depends on the presence of secondary damages to vital organs and the extent of the damage, including the changes in the brain, heart, coronary blood supply, and renal function. Patients should be treated with antihypertensive drugs to keep their blood pressure below 160/90 mmHg, as well as with preoperative medication to improve the functions of vital organs and to maintain water and electrolyte balance before anesthesia.

Anesthesia is generally well tolerated in NYHA Class I and Class II patients whereas poorly tolerated in NYHA Class III and Class IV patients. It is necessary to improve the preoperative cardiac function and to control chronic heart failure for NYHA Class III and Class IV patients. The heart rate in atrial fibrillation should be controlled, with the ventricular rate of <100 bpm. Premature ventricular contractions (PVCs) should be less than 5 beats/min. Drugs that can effectively control PVCs should be administered appropriately except for multifocal PVCs or R on T. Patients with obvious ECG abnormalities should undergo consultation with cardiologists. For patients with ischemic heart disease, clinicians must clarify the patient's present history of angina and previous history of myocardial infarction, as well as the current status of cardiac decompensation. Patients should not undergo elective surgery anesthesia if they have experienced myocardial infarction within 6 months.

Respiratory diseases: As patients with acute respiratory infections are prone to developing atelectasis and pneumonia postoperatively, elective surgery should be scheduled 1–2 weeks after patients have shown complete response. Patients are asked to quit smoking 1–2 weeks before operation. Patients with pulmonary heart disease (cor pulmonale) should be treated with drugs to maintain an

optimal cardiac function. Prophylactic antibiotics may be administered 3–5 days before surgery.

For patients with diabetes, urine glucose should be basically controlled to be negatively or weakly positive, urine ketone bodies must be negative, and fasting blood glucose must be less than 8.0 mmol/L before operation. During the operation, these patients should be monitored for blood glucose and treated with insulin when appropriate, and attention should be paid to the maintenance of normal serum potassium. Before emergency surgery, blood glucose, serum potassium, sodium, chlorine, pH, urine glucose, and urine ketone bodies should be examined. Insulin should be administered accordingly. Anesthesia and surgery should not be considered until urine ketone bodies have been converted to negative and electrolyte levels have recovered to normal.

1.3 Physical Status Classification Before Anesthesia

Refer to physical status (PS) classification system of American Society of Anesthesiologists (ASA) (Table 6.1).

Table 6.1 ASA physical status (PS) classification system

Classification	Definition
I	Normal healthy
II	Mild systemic disease
III	Severe systemic disease that limits the daily activities but does not cause loss of working ability
IV	Severe systemic disease that causes loss of working ability and poses a threat to life
V	A moribund person who is not expected to survive for 24 h without or with the operation

Note: The addition of "E" denotes each class of emergency surgery. For Class I and Class II patients, anesthesia is generally well tolerated, while anesthesia poses a certain risk to Class III patients for whom clinicians should make appropriate preanesthesia preparation for the prevention and treatment of complications; anesthesia poses great risk to Class IV patients for whom active rescue should be given; simultaneously, the surgeons and the patients' families must be clearly informed of accidents that may occur during perianesthesia period before surgery.

1.4 Preparation of Anesthetic Instruments and Devices

Anesthesia devices are used to implement general anesthesia, supply oxygen, as well as assist in or control ventilation. Additionally, modern anesthesia devices are equipped with electronics and computer control and monitoring system, thus requiring better operative and management skills. Devices must be thoroughly examined before use in order to minimize accidents caused by mechanical failure.

1.4.1 Air Source

Oxygen, nitrous oxide, or compressed air has a distinctive mark. Gas source output pipeline should be connected to the corresponding gas source input joint of anesthesia machine, which cannot be mistakenly connected.

1.4.2 Anesthesia Machine

Anesthesia machine is the most important device in anesthesia. It has fast oxygen supply and assisted respiration and other special functions, which is an indispensable element of anesthetic procedure. Modern anesthesia machine must have the following functions:

1. Flowmeter: The scales should be accurate, the knob can be opened and closed freely, and the float can move up and down flexibly and shouldn't bounce when starting. Float should point to zero when the meter is turned off. Glass tube should be intact without steam, and the knob shouldn't be closed too tightly.
2. Evaporator: Inhaled anesthetics are placed into the corresponding evaporator after checking their names, and the volume should not exceed the "maximum" mark. Vaporizer's concentration dial should be rotating properly, and the dial can be closed by a "padlock." The accuracy of output concentration marker of the evaporator can be verified by anesthetic concentration monitor.
3. Loop system: Check the components for leaks before implementation of anesthesia. Inhalation and exhalation valves should be opened and closed flexibly, free from condensed water vapor or soda lime dust. Each

joint must be matched to each other. It should be noted that residual water in the loop during anesthesia should be removed timely if any; attention should be paid to the degree of discoloration or heating of soda lime; if any, soda lime should be timely replaced.
4. Attention should be paid to the activity of ventilator balloon. If any joggling or shaking occurs or the balloon does not empty completely, the fresh gas flow should be adjusted.
5. Once the respirator is disconnected from the connecting pipe of anesthesia machine and the nozzle is shut off with the palm, the pressure gauge rises immediately. When it is fully inflated, the balloon does not move up and down any longer, suggesting that it is intact without leakage.
6. Modern anesthesia machine is equipped with a variety of breathing patterns, adjustable respiratory parameters that can apply to both adults and children, perfect respiratory monitoring system (such as inhaled oxygen concentration, tidal volume, respiratory rate, respiratory ratio, peak airway pressure, and mean pressure), and even respiratory function monitoring feature.

1.4.3 Monitoring Equipment

Vital signs of patients should be monitored during surgery. Routine monitoring includes noninvasive blood pressure, ECG, and pulse wave oxygen saturation. Patients who undergo general anesthesia should also be monitored for end-tidal carbon dioxide and body temperature. Special operation may require special monitoring. Therefore, further requirements have been raised for monitors.

1. Invasive blood pressure monitoring: Monitors with blood pressure monitoring feature must be selected during major surgery, and those with multichannel invasive pressure monitoring features should be preferred as they can be used to monitor various pressures simultaneously, such as arterial pressure, central venous pressure, and pulmonary artery pressure.
2. Cardiac output monitoring: Cardiac output monitoring can be conducted as a part of the multifunctional monitor or by a separate monitor.
3. Neuromuscular monitoring: For patients with neuromuscular diseases or severe liver and kidney dysfunction, muscle relaxation monitoring is required during general anesthesia.
4. Monitoring depth of anesthesia: Adjust medication according to monitoring results.

1.4.4 Testing Device

As tests are often performed during anesthesia, including routine blood, biochemical, coagulation, and arterial blood gas (ABG) tests, appropriate devices should be equipped in the anesthesiology department.

1.4.5 Insulation Devices

Insulation devices include insulation mattress, hot air heater, and infusion warmer.

1.4.6 Infusion Set

Infusion set includes various infusion pumps, syringe pumps, target-controlled infusion pumps, and blood transfusion devices.

1.5 Preparation of Anesthetics

1.5.1 Preanesthetic Medication

1. Sedative hypnotics: such as phenobarbital sodium, diazepam, and midazolam.
2. Narcotic analgesics: such as meperidine and morphine.
3. Anticholinergics: such as atropine and scopolamine.
4. Antihistamines: hormones and gastric mucosal protective agents.

1.5.2 Local Anesthetics

1. Lipids: such as procaine, chloroprocaine, and tetracaine.
2. Amides: such as lidocaine, bupivacaine, and ropivacaine.

1.5.3 General Anesthetics

1. Intravenous anesthetics: such as propofol, ketamine, thiopental, midazolam, etomidate, and sodium oxybate (sodium γ-hydroxybutyrate).
2. Inhaled anesthetics: such as enflurane, isoflurane, sevoflurane, desflurane, halothane, and nitrous oxide.

3. Narcotic analgesics: such as morphine, pethidine, fentanyl, sufentanil, remifentanil, tramadol, and nonsteroidal anti-inflammatory drugs (NSAIDs).
4. Muscle relaxant: such as succinylcholine, mivacurium, vecuronium, pipecuronium bromide, atracurium, pancuronium, and rocuronium.

1.5.4 Autonomic Nervous System Drugs

1. Cholinergic drugs
   Atropine, scopolamine, anisodamine, neostigmine, and edrophonium chloride
2. Adrenergic drugs
   Norepinephrine, epinephrine, phenylephrine, dopamine, dobutamine, isoproterenol, ephedrine, metaraminol clonidine, phentolamine, urapidil, metoprolol, esmolol, and labetalol.

1.5.5 Vasoactive Drugs

1. Vasodilator

   Prazosin, urapidil, phentolamine, diazoxide, nitroprusside, nitroglycerin, hydralazine, and indapamide

2. Calcium channel blockers

   Nifedipine, nimodipine, nicardipine, felodipine, lacidipine, amlodipine, diltiazem, verapamil, and flunarizine

3. Antiarrhythmic drugs

   Quinidine, procainamide, lidocaine, phenytoin, mexiletine, propafenone, amiodarone, bretylium, and adenosine

1.5.6 Infusion

Infusion includes crystalloid solutions, colloidal solution, and electrolyte supplements, of which:

1. Crystalloid solution: such as normal saline, multiple electrolytes injection, balanced salt solution, and dextrose and sodium chloride injection.
2. Colloidal solution: such as hydroxyethyl starch (HEAS), all kinds of gelatin preparation, and dextran preparation.
3. Electrolyte supplements: such as sodium chloride, potassium chloride, calcium chloride, magnesium sulfate, and sodium bicarbonate at high concentration.
4. Dehydration diuretic drugs: such as furosemide and mannitol.

1.5.7 Drugs Acting on Coagulation System

Heparin such as unfractionated heparin and low molecular weight heparin; prothrombin complex; fibrinogen; V/VII factor preparation; and antifibrinolytic drugs, such as tranexamic acid injection, aminocaproic acid, and protamine.

In each operation requiring anesthesia, clinicians should fully assess patients' preoperative risks of anesthesia and surgery and thus prepare for appropriate medication according to perioperative accidents that may occur.

2 Selection of Anesthetic Method and Regulation of Intraoperatively Anesthetic Depth

2.1 Selection of Anesthetic Method

In general, the choice of anesthetic method for patients who undergo surgical procedures is determined by anesthesiologists based on the size of the surgery, the patient's physical condition, and their proficient in anesthesia.

In early stage, retroperitoneal tumors which are confined to relatively small areas with intact envelopes can be resected under epidural anesthesia. However, most of the tumors are located more deeply into the abdomen with greater space for expansion and generally asymptomatic in the early stage. When they grow larger and larger over time, tumors may fulfill the retroperitoneal space. Symptoms don't occur until the boundary between the tumor and intestine or blood vessels becomes ill-defined. At this point, general anesthesia is necessary because spinal anesthesia alone cannot meet the operative requirements. In addition, spinal anesthesia interferes with the compensatory mechanisms that are activated in

response to blood loss, as it can block the sympathetic ganglia, causing dilation of the blood vessels. Therefore, hypovolemic shock is a contraindication to spinal anesthesia. By contrast, general anesthesia not only alleviates the suffering of patients but also facilitates the maintenance of respiration and circulation as well as monitoring the changes in vital signs and hemodynamics. General anesthesia is a more popular choice for patients with retroperitoneal tumors who often experience loss of a large amount of blood intraoperatively. If necessary, general anesthesia may be combined with epidural anesthesia in order to reduce medication/dosage.

2.2 Regulation of Intraoperative Anesthetic Depth

Anesthesia is far more than maintaining hemodynamic stability and keeping patients in unconscious state. As postsurgical traumatic syndrome often occurs, forgetting and consciousness have become more and more important components in the field of anesthetic depth. A suitable anesthesia should at least meet two standards:

1. Loss of awareness and memory (implicit memory).
2. Blockage of noxious stimulation response (i.e., analgesia, muscle relaxation, loss of autonomic response) which has been shown to occur at a subcortical level and therefore may be unrelated to consciousness.

2.2.1 Anesthetic Depth and Noxious Stimulation Response

A variety of noxious stimulation responses during anesthesia may be acquired by somatic and autonomic responses of patients. Somatic responses can be reflected by pain and body movement, while autonomic responses can be reflected by sympathetic, parasympathetic, endocrine, and neural responses.

Clinical Presentations

With the wide use of muscle relaxants, the body movement and breathing types have lost their original indication. Clinically, the depth of anesthesia is estimated only based on the blood pressure, heart rate, and autonomic nervous reaction; however, such indicators vary greatly depending on individual differences, medication, diseases, and surgical procedures, thus causing certain difficulty in accurately determining the depth of anesthesia.

Pupillary Light Reflex

Pupillary light reflex is commonly used to evaluate the effects of anesthetics and the function of brain stem during the surgery. It can be used to assess surgical stimulation; however, its clinical reliability is affected by opioids, advanced age, the disease itself, and other factors.

Lower Esophageal Contractility (LEC)

In human, the lower esophageal sphincter is composed of smooth muscle, and its spontaneous contraction is controlled by the vagus nerve center and reticular activating system (RAS) within the brain stem. Spontaneous contraction of esophagus only occurs in patients who are awake and sober. Under anesthesia, the spontaneous contraction disappears, resulting in a decrease in waveform amplitude even with stimulation, which can be used to determine the depth of anesthesia.

Heart Rate Variability (HRV)

HRV refers to minor variation in the time interval between consecutive heartbeats. Under physiological conditions, HRV that originates from the self-regulatory activity of the sinoatrial node is regulated by advanced innervation of the brain as well as spontaneous rhythm and pressure chemoreceptor activities of central nervous system (CNS) via the sympathetic and vagal nerves. Heart rate variability may be used to assess quantitatively the tension and balance of cardiac sympathetic nerve and vagus nerve. When any harm or injury stimulates human body, the sympathetic system will be activated, thus increasing heart rate variability. Studies have indicated a correlation between the depth of anesthesia and the change in heart rate variability, which can serve as an index for objectively evaluating the depth of anesthesia.

2.2.2 Depth of Anesthetic and Level of Consciousness

How to prevent intraoperative awareness by reasonably regulating the depth of anesthesia has become a common concern in today's anesthesiology community. Indicators such as heart rate, blood pressure, respiration, eye symptoms, lacrimation, and sweating that were previously widely used in clinical judgment on the depth of anesthesia are independent of awareness, so the intraoperative awareness cannot be completely eliminated even if the depth of anesthesia is maintained stable during the surgery. The consciousness state under anesthesia can be divided by cognitive function into four stages as follows: (1) conscious awareness with explicit memory, (2) conscious awareness without explicit memory, (3) unconscious awareness with implicit memory but not explicit memory, and (4) no awareness. The elimination of implicit memory constitutes the sole basis for eliminating the underlying cause of awareness. Studies on electroneurophysiology (ENP) have proved that bispectral index (BIS), auditory evoked potential (AEP), auditory evoked potentials index (AEPI), and EEG-nonlinear are closely associated with alterations in consciousness during general anesthesia, thus providing supporting evidence for the objective monitoring of consciousness components under general anesthesia.

3 Intraoperative Monitoring of Patients with Retroperitoneal Tumors

During surgery, electrocardiogram (EKG), noninvasive blood pressure (NIBP), and noninvasive pulse oximetry (SpO_2) should be routinely monitored. For patients who undergo major surgery and are critically ill, invasive blood pressure (IBP), central venous pressure (CVP), pulmonary capillary wedge pressure, cardiac output, and even end-tidal carbon dioxide ($PETCO_2$) under general endotracheal anesthesia should be monitored. In the elderly, children, and patients who undergo major surgery, the body temperature should be monitored.

3.1 Monitoring of Respiratory Function

3.1.1 Tidal Volume (VT) and Minute Ventilation (VE)

These parameters are measured by the flowmeter of the anesthesia machine. Normal range in adults is as follows: VT: 350–500 mL and VE: 5000–8000 mL. During mechanical ventilation, the expiratory volume should be monitored.

3.1.2 Airway Pressure (Paw)

Airway pressure is related to tidal volume, inspiratory flow, airway resistance, and lung compliance. During mechanical ventilation, the peak inspiratory pressure is 12–15 cm H_2O in adults and 10–12 cm H_2O in children. The mean airway pressure may be raised by increasing tidal volume and inspiratory flow or using end-expiratory pressure (PEEP).

3.1.3 Noninvasive Pulse Oximetry (SPO_2)

The pulse oximeter probe is usually placed on a finger, and the light source is aligned with the fingernail; pediatric probe is placed around the fingers, toes, or dorsum of the hand and foot. SPO_2: normal range in inspiratory air is 96–97% in adults and 91–92% in newborns.

3.1.4 End-Tidal Carbon Dioxide Partial Pressure (PET CO_2)

The clinical significance of PET CO_2: Clinically, the monitoring of PET CO_2 is used in endotracheal intubation under general anesthesia, mechanical ventilation, critically ill patients, and cardiopulmonary resuscitation.

3.2 ECG Monitoring

During surgery requiring anesthesia, the purpose of routine ECG monitoring is to timely detect and prevent cardiac arrhythmias and cardiac arrest, to identify the presence of myocardial ischemia or electrolyte imbalance, as well as to evaluate pacemaker function. Common leads include chest lead V5 or modified lead CM5 which are

suitable for monitoring any changes in S-T segment and the presence of myocardial ischemia. Limb lead II showing clear P-wave is suitable for monitoring cardiac arrhythmias. Note: the instrument should have special anti-interference ability, the earth wire should be connected carefully, the integrity of the lead wire should be checked, and the electrode patch should be closely attached to the skin.

3.3 Blood Pressure Monitoring

Noninvasive blood pressure monitoring is suitable for all types of surgeries. Invasive blood pressure (IBP) monitoring can be used for cardiovascular and complex procedures, patients with shock and critical illness, hypothermia, and controlled hypotension (during hypotensive anesthesia).

3.3.1 Noninvasive Blood Pressure Monitoring (NIBP)

The ideal width of the cuff should be 40% of the limb circumference. The measured value is accurate when the cuff is deflated at a rate of 2–3 mmHg per second. If deflation is too rapid, the measured value may be underestimated.

3.3.2 Invasive Blood Pressure (IBP) Monitoring

Clinically, 22G and 20G catheters are usually inserted into the radial artery or dorsal pedal (dorsalis pedis) artery, or 18G catheter is inserted into the femoral artery for continuous measurement of arterial pressure. Normal blood pressure is 90–130/60–90 mmHg in adults and less than 140/90 mmHg in patients under 40 years without a history of hypertension; in patients over 40 years, systolic blood pressure (SBP) increases by 10 mmHg for each 10-year increment in age, whereas diastolic blood pressure (DBP) remains unchanged. In adults, the blood pressure of the lower limb is about 20–40 mmHg higher than that of the upper limb. The difference in blood pressure between the left and right limbs is about 10 mmHg. Normal SBP in children is calculated with the formula (mmHg) = age × 2 + 80, and DBP is calculated as 2/3 or 3/5 of SBP.

3.3.3 Central Venous Pressure (CVP)

The central veins most commonly used for catheter insertion are femoral vein, internal jugular vein, and subclavian vein. An accurate reading may be obtained when measuring CVP from the superior vena cava. Normal range of CVP is 6–12 cm H_2O.

CVP value of 0–5 cm H_2O indicates insufficient blood circulation. CVP > 15 cm H_2O suggests heart failure, cardiac tamponade, excessive infusion, or peripheral vascular contraction; clinicians should make the diagnosis combined with clinical symptoms and other hemodynamic monitoring indicators such as pulmonary capillary wedge pressure (PCWP).

3.4 Blood Gas Analysis

1. Acidity or alkalinity (pH value): The normal pH of arterial blood is between 7.35 and 7.45, while the venous blood pH is usually 0.05 units lower than the arterial. The pH below 6.8 or above 7.8 indicates severe acid-base imbalance, which can lead to severe, even life-threatening medical conditions.
2. Partial pressure of carbon dioxide (PCO_2) refers to the pressure exerted by the amount of CO_2 that is physically dissolved in the blood. It can reflect the acid-base status when breathing. The normal range for PCO_2 of arterial blood is 35–45 mmHg, and PCO_2 of the venous blood is 6–7 mmHg higher than that of arterial blood. The PCO2, along with the pH, can be used to distinguish among metabolic acidosis, metabolic alkalosis, respiratory acidosis, and respiratory alkalosis.
3. Buffer base (BB) refers to the sum of all the buffer bases in the whole blood. Normal range is 45–50 mmol/L. BB can reflect the body's buffering capacity in response to acid-base disorders.
4. Base excess (BE) refers to the amount of acid or base required to titrate whole blood at 37 degrees Celsius with $PaCO_2$ of 40 mmHg back to a standardized blood pH of 7.4. BE is an important indicator to reflect the metabolic acid-base status, with a normal range of +/− 3 mmol/L.

5. Partial pressure of oxygen (PO_2) refers to the pressure exerted by the amount of oxygen molecules that are physically dissolved in plasma. Normal range of PaO_2 is 80–110 mmHg; and normal mixed venous oxygen tension (PvO_2) value is 40 mmHg. It is a critical indicator in the diagnosis of hypoxia.
6. Arterial oxygen saturation (SaO_2) refers to the extent of oxygen binding to hemoglobin. Normal range of SaO_2 is greater than 95%, whereas 64 to 88% for venous blood.

3.5 Monitoring of Cardiac Output (CO) and Stroke Volume (SV)

Cardiac output (CO) is able to reflect the cardiac ejection function. The abnormality in cardiac output is related to insufficient preload as well as cardiac systolic and diastolic dysfunction. Monitoring of capacity indicators is helpful to rule out causal factors for inadequate capacity, analyze the etiology and pathophysiology of cardiac systolic and diastolic dysfunction, and thus implement individualized treatment during surgery. Both minimally invasive and noninvasive cardiac function monitoring devices can be used for monitoring CO and stroke volume (SV). Swan-Ganz catheter may be considered for critically ill patients who should be monitored for mixed venous oxygen saturation, pulmonary artery pressure, pulmonary vascular resistance, and pulmonary artery wedge pressure (PAWP), because of its high specificity in evaluating the abovementioned indicators. Pulse index continuous cardiac output (PiCCO) can be used to obtain pulse contour cardiac output (PCCO) and to calculate intrathoracic blood volume (ITBV) and extravascular lung water (EVLW), which is helpful to evaluate hemodynamic changes and distribution capacity of patients during surgery.

3.6 Urine Volume

Urine volume not only reliably reflects renal blood perfusion but also indirectly reflects the systemic circulation. The method for monitoring urine volume is simple. During surgery, the nature and total volume of urine are determined. The amount of creatinine, protein, and other chemicals released into the urine during this period is often tested.

3.7 Monitoring of Body Temperature

If the patient's body temperature rises during anesthesia, firstly, several factors should be ruled out, such as ambient over-temperature, malignant hyperthermia, carbon dioxide accumulation, transfusion reaction, septic shock or sepsis, and thyroid crisis. If hypothermia occurs during anesthesia, first of all, the following factors should be ruled out: uncontrollable rewarming after hypothermic anesthesia, liver dysfunction after liver transplantation, disease progression, long-term exposure of body chamber to low-temperature environment, and a large amount of blood transfusion.

3.8 Monitoring of Effects of Muscle Relaxants

The commonly used patterns of electrical nerve stimulation are single twitch, train of four (TOF), tetanic, post-tetanic count (PTC), and double-burst stimulus (DBS). Monitoring of muscle relaxants is helpful to identify the cause for postoperative respiratory depression and to provide guidance for the administration of antagonists. The respiratory depression induced by residual muscle relaxants should be prevented.

3.9 Monitoring of Concentration of General Anesthetics

The concentration of volatile anesthetics (such as enflurane, isoflurane, sevoflurane, desflurane, and nitrous oxide) in breathing air is usually determined by an infrared analyzer. Clinically, the monitoring of inspired and expired concentration of anesthetics is helpful to evaluate the

uptake and distribution of anesthetics, depth of anesthesia, as well as tolerance and response of patients to the specific concentration of anesthetics.

4 Anesthesia for Patients with Retroperitoneal Tumors with Endocrine Function

Retroperitoneal tumors (RPTs) can be divided into benign and malignant categories, of which malignant RPT accounts for about 60–80% (~80% reported in international literatures vs. 56% reported in Chinese literatures). Common malignant RPTs include liposarcoma, fibrosarcoma, nerve fiber sarcoma, and malignant lymphoma, whereas benign RPTs include fibroma and teratoma. Generally, cystic RPTs are benign, whereas solid RPTs are malignant. Retroperitoneal space is a huge compartment of the extraperitoneal space located in the posterior abdomen, which extends from the diaphragm superiorly to the pelvis inferiorly. RPTs may be derived from fat, connective tissue, fascia, muscles, blood vessels, nerves, and lymphatic tissue or residual embryonic tissues in the retroperitoneal space, of which two-thirds are malignant in nature. Therefore, there are a variety pathological subtypes of RPTs. Several RPTs derived from chromaffin tissue with endocrine function can secrete norepinephrine and epinephrine, also known as pheochromocytoma.

4.1 Clinical Characteristics of Pheochromocytoma

1. Hypertension: Hypertension is the most important clinical symptom of pheochromocytoma and mostly paroxysmal. At the time of onset, SBP may rise up to 300 mmHg and DBP up to 180 mmHg, accompanied by headache, palpitations, nausea, vomiting, sweating, paleness, anxiety, panic attacks, blurred vision, tachycardia, arrhythmia, and precordial distress (sense of urgency). In severe cases, hypertension can induce left ventricular failure and cerebral stroke.
2. Arrhythmia: Symptoms of arrhythmia include tachycardia and atrial fibrillation.
3. Metabolic disorder syndrome: Patients may experience increased basal metabolic rate (BMR), low-grade fever, sweating, elevated blood glucose (hyperglycemia) and impaired glucose tolerance (IGT), glycosuria, limb weakness, weight loss, and skinny (for those with history of chronic disease).

4.2 Preoperative Preparation

1. Preoperative depressurization, volume expansion, and correction of arrhythmia: Pheochromocytoma not only secretes large amounts of catecholamines but also results in changes in renin-angiotensin-aldosterone system, thus maintaining contraction of peripheral vascular vessels. Although pheochromocytoma presents with increased blood pressure, patient's blood volume can be decreased by ~30% as compared to the normal physiological state. Two weeks before surgery, selective α1-blockers are used to decrease the blood pressure by gradually dilating the peripheral vascular beds in contracted state. If a desired effect is not achieved by α1-blocker monotherapy, the concomitant administration of Ca^{2+} channel blockers such as nifedipine may be used to block the source of intracellular Ca^{2+}, thus achieving a satisfactory effect. An ideal preoperative blood pressure is within or close to normal range, at which the patients do not experience obvious discomfort such as dizziness and palpitations after minor activities. Long-acting α-blocker should be discontinued 1 day before surgery in order to prevent the occurrence of sustained hypotension after adrenalectomy.
2. When part of the interstitial fluid moves into the blood vessels due to the decline in blood pressure, the intravascular blood volume is partially complementary but remains in an insufficient state. Therefore, a certain amount of liquids such as colloidal solutions and plasma is required for volume expansion,

which should be performed at least 3 days before surgery, with daily volume of no less than 1500 mL and maintaining hematocrit level below 45%. However, attention should be paid to the blood pressure during the preoperative volume expansion; otherwise patients are susceptible to suffer from increased cardiac loading and subsequently induced heart failure.

3. Tachycardia (>100 beats per min) is the most common type of arrhythmia observed in pheochromocytoma. Concomitant administration of propranolol can reduce the patient's heart rate. However, the addition of β-blockers cannot be given less than 1 week after the administration of α-blockers. Domestic scholars believe that the heart rate should be controlled at less than 90 beats/min during preoperative preparation.
4. Preoperative medication: Atropine is not recommended because it inhibits the vagus nerve, thus causing an increase in heart rate and arrhythmia. Scopolamine is commonly used before operation.
5. Anesthesia method

An ideal anesthetic method is expected to properly suppress or relieve stress response caused by surgical trauma.

a. Epidural anesthesia has been gradually abandoned due to its obvious disadvantages, such as induction of anxiety, fear and other psychological stress response in patients during the operation, incomplete block, traction reaction, and high incidence of hypotension after tumor resection.
b. General anesthesia can make up for deficiencies of epidural anesthesia but has its limitations in inhibition of the perioperative traumatic stress. Now, it is commonly used in surgery.
c. The combination of general anesthesia and epidural anesthesia is worth advocating because it can draw upon each other's strengths while removing their respective shortcomings. Epidural puncture is firstly conducted. Until a plateau is reached, the induction of general anesthesia won't be performed. The stable induction and smooth catheterization should be guaranteed during general anesthesia. Succinylcholine is not recommended as it can cause muscle tremors, easily leading to an increase in the secretion of catecholamine or potassium. Fentanyl is an ideal drug due to its role in slowing heart rate.

4.3 Intraoperative Anesthetic Management

Once entering the operation room, patients will undergo opening of venous access route. Patients with mental stress or sympathetic hyperactivity can be given a small dose of midazolam and intravenous pump infusion of sodium nitroprusside (1–5 μg kg^{-1} min^{-1}) or nitroglycerin (5–20 μg • kg^{-1} • min^{-1}) in order to control the rapid rise in blood pressure and maintain it within the normal range before surgery. Simultaneously, phentolamine, metoprolol, esmolol, cedilanid, dopamine, norepinephrine, and other first-line drugs are diluted and labeled until use. Invasive monitoring of mean arterial pressure (MAP) and CVP, as well as noninvasive monitoring of heart rate, ECG, SpO_2, $PETCO_2$, minimum alveolar concentration (MAC), and urine volume should be initiated.

Patients with pheochromocytoma may encounter risks during surgery, such as arrhythmia and severe fluctuations in blood pressure, which frequently occur in the catheterization under induction of anesthesia, especially during surgical resection and vascular ligation of tumor. Therefore, the maintenance of stable hemodynamics during these periods is pivotal to guarantee the surgical safety.

1. Treatment of hypertensive crisis: Once hypertensive crisis occurs, monitor the patient's heart rate, MAP, CVP, and ECG; maintain the original controlled hypotension medicine such as nitroglycerin or sodium nitroglycerine, while immediately administering 0.5–3 mg of phentolamine via intravenous bolus; and expand the blood volume slowly.

The above intervention is able to prevent a sudden drop in the blood pressure as well as a sharp rise in compensatory heart rate resulting from the dilating effect of phentolamine. When the blood volume of patients is slowly expanded with crystalloid solution and crystalloid solution during controlled hypotension, the incidence of hypotension and shock after tumor excision may be effectively reduced. Usually, the blood pressure and heart rate would be gradually declined following the abovementioned treatment. If the ventricular rate remains fast (greater than 140 beats/min), slow speed and low-dose administration of propranolol, metoprolol, or esmolol may be given under ECG monitoring. Notably β-blockers are not recommended for controlling heart rate of patients with hypertension accompanied by tachycardia due to its risk of inducing heart failure. Thus, α-blockers such as phentolamine are preferred as the first treatment option when hypertension and tachycardia occur simultaneously. Phentolamine should be intravenously administered, while gradual expansion is conducted. If necessary, β-blockers may be employed to control heart rate.

2. Prevention and treatment of hypotension after tumor resection: Slow expansion is performed before tumor resection, while the blocking test is conducted to observe the changes in blood pressure, and the expansion volume is adjusted accordingly. After removal of the tumor, the endogenous catecholamine levels are expected to drop suddenly; therefore, norepinephrine (dopamine or dobutamine) should be supplemented. The administration dose should be adjusted according to blood pressure. The volume is timely expanded by rapid infusion of blood and liquid according to CVP and urine volume to maintain systolic blood pressure above 100 mmHg. Patients with preexisting heart failure may be given cedilanid and a small dose of dopamine or dobutamine (2–10 μg kg^{-1} min^{-1}) after tumor resection to maintain stable hemodynamics.
3. Blood transfusion and liquid infusion during surgery: While monitoring the CVP and urine volume, an appropriate volume of blood or liquid may be transfused or infused. During the infusion, the filling extent of external jugular vein should be carefully monitored. The breath sounds at the base of lung should be auscultated. In addition, attention should be paid to maintain cardiac function.
4. Monitoring of blood glucose is conducted intraoperatively. Hypoglycemia induced by tumor resection should be prevented. Metabolic homeostasis of blood glucose and carbohydrate should be maintained.

4.4 Postoperative Management and Analgesia

Heart failure and hypotension are common postoperative risks. Since malignant hypertension caused by pheochromocytoma results in cardiovascular damage, patients are susceptible to die because of poor compensatory capability in response to excessive cardiac load and hypovolemia. Clinicians should pay attention to this serious problem. Close monitoring and careful adjustment are guaranteed. Effective postoperative pain management not only alleviates the stress response but also blocks the cardiac sympathetic nerve and improves the balance between supply and demand of myocardial oxygen, thus providing better conditions for recovery of patients.

5 Bloodless Medicine and Surgery for Retroperitoneal Tumor

In recent years, the shortage in blood supply is becoming more and more severe with a sharp increase in blood consumption. With in-depth exploration of blood transfusion, clinical studies have shown that blood transfusion may arouse more serious problems in cancer patients, such as tumor recurrence and metastasis, poor quality of life, and reduced survival time. To alleviate the shortage in blood supply, reduce the occurrence of transfusion-related complications and improve long-term prognosis of patients with tumors; a concept of bloodless medicine has been proposed

by scholars worldwide. The bloodless medicine refers to a variety of techniques that allow a patient to be treated without blood transfusions through optimal blood manipulation. The purpose of bloodless medicine is to reduce blood transfusion-related complications and prolong survival of patients by minimizing or avoiding allogeneic blood transfusion. Common approaches applied in bloodless medicine include correction of anemia before surgery, autologous blood reservation, control of perioperative bleeding, blood recovery and hemodilution by surgeons, strengthening of blood conservation for patients at high risk of bleeding, multidisciplinary collaboration, as well as sustained and effective continuing education. For patients with retroperitoneal tumors (RPTs), surgery remains the only effective therapeutic approach. Due to its special nature, RPT does not cause symptoms until it develops to an advanced stage. As it invades the large blood vessels and adjacent organs, advanced disease will bring extreme difficulty achieving a complete surgical resection, leading to a large amount of bleeding. Therefore, the bloodless medicine plays a pivotal role in reducing allogeneic blood transfusion and providing long-term prognosis in patients with RPTs.

5.1 Implementation of Bloodless Medicine

5.1.1 Implementation of Preoperative Autologous Blood Donation and Reservation

A certain amount of autologous blood can be collected from patients within the preoperative period (2–4 weeks) to prepare for blood transfusion during surgical procedures.

Case Selection

Generally, patients with Hb > 110 g/L and Hct > 33% are eligible to donate blood, without limitation on age. For a patient with body weight ≥50 kg, the volume of blood collection is about 450 mL each time, which may be appropriately reduced for a patient with body weight <50 kg. The volume of blood collection is usually controlled at 10–15% of circulating blood volume each time. Contraindications include combined congestive heart failure, unstable angina, severe coronary artery stenosis or myocardial infarction within 3 months, and severe aortic valve stenosis.

Detailed Implementation

Simple method is similar to ordinary blood donation; however, it is difficult to meet the requirement of retroperitoneal tumor surgery due to very limited volume of blood collection.

Switchback method can obtain sufficient autologous blood to meet the requirements of surgery within a certain period. The process is as follows: the first unit is collected for reservation at 4 weeks before operation; the second and third units are collected for reservation at 3 weeks before operation while the first unit is transfused back into the body; and the fourth, fifth, and sixth units are collected for reservation at 2 weeks before operation while the second and third units are transfused back into the body; finally, the seventh, eighth, ninth, and tenth units are collected for reservation at 1 week before operation while the fourth and fifth units are transfused back into the body. In such way, approximately 5 units of autologous blood can be obtained (about 1000–1500 mL), thus substantially meeting the surgical requirements.

Erythropoietin (EPO) as an enhancer for blood reservation: Clinical studies have shown that only one-thirds of red blood cells (RBCs) is compensated within 4 weeks when a moderate blood loss lasts for a short period (10 days). By contrast, the proliferative response of RBCs in bone marrow with the aid of EPO can be enhanced by 3–4 times, thus producing adequate amounts of RBCs that can meet the reservation requirements on autologous blood donation.

5.1.2 Implementation of Intraoperative Autologous Blood Donation and Blood Dilution

a. Preoperative management: Patients with deep vein thrombosis combined with chronic venous diseases should be excluded before operation. Tumor embolization should be

conducted for patients with large tumors preoperatively to reduce 50–90% of the blood supply to tumors. Drugs that can promote proliferation of RBCs should be given to patients with preoperative hemoglobin (Hb) <12 g/L until it recovers to normal. The erythropoietin (EPO) 300 U/kg plus iron sucrose 500 mg should be administered on days 1, 7, 14, and 21.

b. Management of intraoperative anesthesia: Catheterization via radial artery (the gauge on artery catheter needle must be >20G) and central vein is performed under local anesthesia. Patients' indicators such as blood pressure, heart rate, oxygen saturation, and end-tidal carbon dioxide should be monitored.
c. Blood donation: After patients are placed in a Trendelenburg (15°) position, radial artery blood is drawn for 15–30 min. Blood volume (mL) = body weight (kg) × 1000 × 7% × 2 × (actual Hct − target Hct)/(actual Hct + target Hct). Hct is hematocrit. The blood is stored in a collection bag containing ACD (antibiotic coagulate drug).
d. Fluid replacement: When 6% hydroxyethyl starch (Voluven at a dose of 15 mL/kg) and compound sodium lactate (at a dose of 10 mL/kg) are intravenously infused at a rate of 50 mL/min after blood donation, patient's Hct may decrease to 28.8%; however, the actual increase in volume is only 10–15% of circulation volume, thus exerting less effect on the load capacity of circulation.
e. Intraoperatively controlled hypotension: The combination of nitroglycerin at a dose of 1–6 μg/kg/min and esmolol may be used depending on patient's heart rate. MAP should be controlled at no less than 50–55 mmHg.
f. Blood transfusion: Blood gas, routine blood, and five indicators of blood coagulation should be reexamined intraoperatively. The target range of Hb or Hct is 6–7 g/L or 24–26%, respectively. When Hb is <6 g/dL or Hct is <24%, the autologous blood should be reinfused. If a large amount of bleeding (>3000 mL) occurs, the allogeneic blood should be transfused. The Hb should be controlled to be equal to or less than 7 g/L intraoperatively. Excessive blood transfusion should be avoided before tumor resection in order to prevent blood loss in the tumor. Artificial colloids (hydroxyethyl starch or gelatin) and vasoactive drugs (such as phenylephrine) may be used to maintain systemic blood pressure.
g. Postoperative management—modified iron shock therapy: Iron is a vital component in the production of erythropoiesis. Iron deficiency affects not only the hematopoiesis of bone marrow but also the synthesis of various key enzymes and coenzyme involved in cell metabolism. Clinically, patients are given intravenous infusion of iron sucrose 500 mg/500 mL or low molecular weight iron dextran 1 g/500 mL.

5.2 Key Technologies of Bloodless Medicine

5.2.1 Correction of Anemia

Patients with retroperitoneal tumors may experience weight loss, fatigue, sodium reduction, fever, ascites, jaundice, and even cachexia and severe anemia due to long duration, high consumption, as well as compression and displacement of adjacent organs caused by the increased tumor volume. Common medications include anti-anemia drug (iron, folic acid, and vitamin B12), erythropoietin (EPO), and traditional Chinese medicine (such as Siwu decoction, *Angelica sinensis* blood- supplementing decoction, and all nourishing decoction).

1. Iron supplements: As an essential component of hemoglobin, myoglobin, and cytochrome system, iron is the main raw material for hematopoiesis. Iron deficiency affects not only the hematopoiesis of bone marrow but also the synthesis of a variety of important enzymes and coenzyme involved in cell metabolism, causing microcytic hypochromic anemia (John et al. 2009). Iron is indicated for different types of iron deficiency anemia, while attention should be also paid to elimi-

nate the cause of anemia. Commonly used drugs include ferrous sulfate, iron dextran, and ammonium ferric citrate syrup. Folic acid and vitamin B12 are major therapies for megaloblastic anemia and malignant anemia.

2. Erythropoietin (EPO): EPO is an endocrine hormone that acts on the bone marrow hematopoietic cells to promote proliferation, differentiation, and ultimate nature of erythroid progenitor cells. It plays an important role in oxygen supply to the body. In the early embryo development, EPO is generated by the liver, and then the production site of EPO gradually shifts to the kidney after birth. In practice, EPO has been widely used in the treatment of various anemias. It is mostly effective in treating anemia caused by renal failure and uremia. EPO also shows efficacy in cancer-related anemia, anemia of prematurity, and maternal anemia, as well as reduction in perioperative allogeneic blood transfusion. In previous studies on cancer-related anemia, a single dose of EPO was 100–150 U/kg, which cannot meet the surgical requirements due to long-treatment duration and low efficacy. For this reason, an alternative regimen was implemented, namely, single dose of erythropoietin (EPO) of 300 U/kg plus iron sucrose of 500 mg on days 1, 7, 14, and 21, respectively. As its role in enhancing the production of RBCs may cause long-term tumor recurrence, EPO is only indicated for patients with Hb of less than 12 g/L. In order to avoid the adverse effect of EPO postoperatively, we apply pulse therapy with low molecular weight iron dextran at a dose of 1 g/500 mL and periodically reexamine the serum iron concentration afterward.
3. Traditional Chinese medicine: In Chinese medicine theory, blood is generated by transforming the vital energy from water and food. Its generation is closely associated with the functions of the heart, spleen, stomach, and kidney. The generated blood is dominated by and stored in the heart, spleen, and liver, respectively, i.e., the blood is generated by the heart, stored in the liver, and governed by the spleen. Vital energy that is closely related to blood plays a key role in promoting its generation and circulation. Therefore, deficiency of vital energy often leads to blood deficiency and vice versa. Promoting vital energy and replenishing blood are mutually beneficial. Commonly used blood-replenishing recipes include Siwu decoction, *Angelica sinensis* blood-supplementing decoction, and all nourishing decoction. Commonly used blood-replenishing traditional medicine includes blood-supplementing *Angelica sinensis* extract, mulberry-honey extract, blood-supplementing donkey-hide gelatin extract, blood-nourishing granule, promising longevity extract, blood-nourishing and hair growth capsule, Angelicae sinensis, and herbaceous peony and rehmannia pill.

5.2.2 Autologous Blood Transfusion

Preoperative Autologous Blood Donation

It is applicable to patients with good performance status, weight of 45 kg (maternal weight of 55 kg) and above; blood pressure of 90–140/60–90 mmHg, pulse difference of >30 mmHg; normal function of the heart, lung, liver, and kidney; Hb > 110 g/L or Hct > 33%; and platelet count > 100×10^9/L. For patients with low platelet count for a long term, without bleeding tendency, platelet restriction may be relaxed to >80×10^9/L, with normal platelet function and normal blood coagulation.

Specific procedures: Doctors should estimate the possible blood loss during surgery and accordingly make decision on the amount, method, and timing of blood collection. Each blood collection volume should be controlled at about 8 mL/kg. Simple blood collection is suitable for patients with a small amount of expected blood loss and blood donation. If 400 mL of blood is required, the collection should be conducted 3–5 days before surgery; if 800–1200 mL of blood is required, the collection should be conducted 14–21 days before surgery. Leapfrog blood collection is suitable for patients with a large amount of expected blood loss and blood donation. Conversion/switchback blood collection: Firstly, 400 mL of blood is collected 30 days

before surgery. Secondly, 800 mL of blood is collected 7 days later, while the previously collected blood is transfused back into the body. Thirdly, 1200 mL of blood is collected thereafter, while the whole blood volume collected in the second time is transfused back into the body and so forth. Before and after blood collection, patients may be given iron, vitamin B12, folic acid, and recombinant human erythropoietin. Relevant examinations should be conducted before blood collection, and patients are asked to sign the consent form for autologous blood donation and fill in the application form by themselves (Sanders et al. 2004).

Previous studies have reported leapfrog blood collection, namely, the conversion of the preoperative blood collection within the wards. Autologous blood is collected before surgery, with the volume not exceeding 12% of the total generally. The amount of collected blood accounting for 10% of the total is equivalent to the amount of blood collected from donors with the same blood group in blood bank. For patients who are not dehydrated, liquid supplementation is not necessary; if a single blood volume collected reaches 12%, supplementation of appropriate crystalloid solution is recommended. Collected blood can be stored in blood bank generally for not more than 10 days. If the plasma is removed, the remaining packed RBCs may be stored in the −80 °C freezer for several months to years. During the blood collection, oral administration of ferrous sulfate at a dose of 200–300 mg 3 times a day is effective for regenerating RBCs and preventing anemia. After 4 weeks of treatment, 1000 mL blood can be reserved (Arthur and Bracey 2008). However, this method also has disadvantages, i.e., the cycle is long, and the patients remain in a state of iatrogenic anemia.

Acute Hemodilution Technique

It mainly consists of three types: a) acute normovolemic hemodilution (ANH), b) acute non-normovolemic hemodilution (ANNH), and c) hypervolemic hemodilution (HVH). ANH is the most commonly used method in anesthesiology department. The principle of ANH is as follows: while removing a portion of RBCs, plasma, or blood, substitute will be transfused into the patients' body to maintain their intravascular volume and oxygen-carrying capacity. Specific procedures are as follows: blood is collected from arteries or deep veins, and the collection volume is calculated based on the initial and target Hct in combination with the patient's height, weight, and gender. Meanwhile, equivalent volume of crystalline or colloidal solution is rapidly infused via the unobstructed venous access. In general, crystalloids are replaced in a ratio of 3:1 (crystalloid/blood, v/v) whereas colloids in a ratio of 1:1 (colloids/blood, v/v). Dilution can be achieved by mixing crystalloid solution and colloidal solution.

Acute hypervolemic hemodilution (AHH): When a certain amount of mixture of crystalloid and colloidal solution (usually 20–30% of blood volume) is rapidly infused using reserved elasticity of blood vessels after anesthesia, the intravascular volume may increase above the baseline level, thereby achieving the purpose of hemodilution. Thanks to its easy accessibility, this method has been widely used in the early management of cerebral infarction.

Theoretically, any degree of hemodilution may be achieved by normovolemic hemodilution. However, with the higher degree of hemodilution, blood volume and fluid volume will be dramatically raised, thus increasing the difficulty for the operation. The extent of AHH depends on the ability of dilation of capacity vessels in patients. Fluid dynamics have indicated that the expansion efficiency of hypervolemic hemodilution can be improved only when the blood vessels are effectively dilated under general anesthesia or epidural block; otherwise a considerable amount of the expansion liquid may affect the efficiency of expansion and cause interstitial edema after entering the blood vessels according to Starling's laws.

In view of the abovementioned facts, the concept of non-normovolemic hemodilution has been proposed, i.e., the blood donation is performed before fluid expansion on the day of surgery, and the volume of blood collection is 10–15% of the patient's total circulating blood volume, and then the liquid equal to 2–2.5 times the volume of blood donation is administered for

rapid expansion during induction of general anesthesia. Since a portion of intravascular volume has been reduced prior to hemodilution, the actual preload increment of the system is only one-half of the expansion volume, thus improving the safety of hemodilution. As blood donation performed prior to hemodilution removes a portion of RBCs, a greater degree of hemodilution can be achieved more easily with non-normovolemic hemodilution as compared to AHH when supplementing the same volume of expansion liquid. Compared with ANH, the volume of blood donation required for non-normovolemic hemodilution is reduced by one-half when the same degree of blood dilution is achieved, which simplifies the procedures of the hemodilution. In addition, the blood volume of patients who receive acute non-normovolemic hemodilution is higher than the baseline level, while to the same extent of dilution, the blood volume of patients who receive ANH is essentially equal to the baseline level. Thus, acute non-normovolemic hemodilution may improve the tolerance of patients to bleeding.

Non-normovolemic hemodilution process: After induction of anesthesia, the volume of whole blood (mL) = body weight (kg) × 1000 × 7% × 2 × (actual Hct –target Hct)/(actual Hct + target Hct) is collected via arteries or veins before surgery. Following blood donation, 6% hydroxyethyl starch Voluven at a dose of 15 mL/kg and compound sodium lactate at a dose of 10 mL/kg are intravenously infused at a rate of 50 mL/min. On one hand, this method only exerts a minor effect on the circulating load capacity. As a portion of RBCs is removed prior to dilution, the patients' Hct may drop to 0.28 ± 0.09. In this sense, non-normovolemic hemodilution is superior to acute normovolemic hemodilution (ANH). On the other hand, this method has little effect on the hydrostatic pressure of the system, thus maintaining intravascular retention of expansion liquid at a higher level as compared with acute hypervolemic hemodilution (AHH). For example, the blood volume of an adult with body weight of 70 kg is 70 mL/kg, and the volume of blood collection is about 800–1200 mL; the changes in the patient's circulating blood volume is [(15 + 10/3) − 800/70]/70 × 100%, so the actual increase in capacity is only 10–15% of total circulating volume. As this method only exerts minor effect on the circulating volume, its indications for hemodilution may be widened. This method can obtain high-quality blood which is helpful for postoperative recovery of the blood coagulation function.

Controlled Hypotension

In order to reduce blood loss in surgical field, create favorable conditions for surgical procedures, and decrease the amount of blood transfusion, controlled hypotension is intentionally performed using various drugs and methods during surgery. However, the blood perfusion to vital tissues and organs must be guaranteed in the implementation process to meet the minimum needs of the body metabolism and to prevent hypoxic-ischemic damage (Spahn et al. 2008). Quick-acting vasoactive drugs with shorter half-life (e.g., nitroglycerin) in combination with β-blockers (e.g., esmolol) can be applied intraoperatively to reduce blood pressure as much as possible for the purpose of reducing blood loss as long as the mean arterial pressure (MAP) of the radial artery is not less than 50–55 mmHg. Controlled hypotension should be discontinued when substantial blood loss causes a sudden drop in blood pressure. Before tumor resection, blood transfusion should be minimized to prevent a large amount of blood loss in the surgery. Once heavy blood loss is encountered perioperatively, artificial colloids and vasopressors may be applied to maintain stable circulation. As for vasopressor, a combination of a small dose of norepinephrine and dobutamine is recommended for those patients.

Intraoperative Blood Doping Technology

Indications for autologous blood doping: a) Operative bleeding is estimated to be more than 600 mL, such as cardiovascular surgery, total hip replacement, spine surgery, and intracranial aneurysm clamping operation, b) liver and spleen rupture and rupture of the femoral artery with subsequent massive hemorrhage, and c) massive hemorrhage caused by ruptured ectopic pregnancy. Contraindications: a) sepsis, b) serious

bacterial contaminations in blood, and c) malignant cell contaminations in blood.

Nowadays, safety in blood transfusion during tumor surgery remains controversial. In the review of literatures involving intraoperative blood recycle in patients with tumors between 1968 and 2000, Elias pointed out via meta-analysis that tumor cells were present in all recycled blood and tumor spread was independent of collected blood. Leukocyte filter is expected to reduce the number of circulating tumor cells; however, in vitro experiments demonstrate that only 75% of liver tumor cells can be removed by leukocyte filter. X-ray irradiation can only inhibit tumor cell proliferation without killing them. Therefore, intraoperative blood in patients with malignant tumors may not be recycled in order to avoid the spread of cancer, but further investigation is guaranteed.

5.3 Treatment of Refractory Hypotension in Retroperitoneal Tumor Surgery

It is very difficult to completely resect retroperitoneal tumors due to its special location. Especially, malignant tumors do not cause symptoms until they are in the advanced stage. At the time of diagnosis, large blood vessels and adjacent organs have been invaded by tumors, resulting in a larger amount of blood loss during surgery. Therefore, intraoperative and postoperative refractory hypotension frequently occurs.

5.3.1 Definition of Refractory Hypotension

Refractory hypotension is a shock-like state. When experiencing hypotension during surgery, patients whose arterial pressure is less than 12/8 kpa (90/60 mmHg) or declined by more than 40 mmHg from baseline, with a low perfusion state (lactic acidosis, oliguria, or acute confusion) or organ dysfunction, can be diagnosed as refractory hypotension, if their blood pressure remains low after receiving blood transfusion, fluid replacement, vasopressors, and other anti-shock therapy. Refractory shock means decompensated shock lasting more than 1 h. Chinese scholars define refractory shock as decompensated shock lasting for more than 12 h or recurrent hypotension despite adequate treatment. Its occurrence is related to the decline in the reactivity of small arterial smooth muscle cells (ASMCs) to endogenous or exogenous vasoconstrictor.

Refractory hypotension that results in hypoperfusion of the brain, heart, and other vital organs is one of the critical causes of severe shock-related death. However, the mechanism has not yet been elucidated. According to literatures, severe shock may be possibly related to free radicals that lead to inactivation of endogenous catecholamines, desensitization of adrenergic receptor, metabolite accumulation, energy depletion, and action of cytokines (NO and ET).

5.3.2 Treatment of Refractory Hypotension

1. Vascular reactivity recovery agent: Refractory hypotension during the surgery is mainly caused by declined reactivity of arterial smooth muscle cells (ASMCs) to endogenous or exogenous vasoconstrictor. Hyperpolarization of ASMCs is a major factor responsible for decrease in vascular reactivity. Hyperpolarization inhibits the voltage-dependent calcium channels (potential-operated channels [POC]), so that the intracellular calcium level cannot rise appropriately (only 50% of normal) when stimulated by norepinephrine (NE), resulting in a decrease in contractile response. The potassium efflux via activated potassium channels (ATP-sensitive potassium channels KATP, large conductance calcium-activated potassium channels BKCa) results in cellular hyperpolarization. In patients with shock, KATP is activated due to lack of ATP, increase in H^+, and formation of peroxynitrite ($ONOO^-$) anion induced by excessive NO in ASMCs; meanwhile the release of Ca^{2+} sparks from sarcoplasmic reticulum (RyR), enhanced coupling with BKCa, and the action of $ONOO^-$ jointly mediate activation of BKCa and increase in

spontaneous transient outward current (STOC), thereby leading to hyperpolarization of cell membrane. Based on this mechanism, vascular reactivity may be restored with drugs (called vascular reactivity recovery agent restituting vasoreactivity agent, RVA). For example, glyburide can be used to antagonize the activation of potassium channels in order to recover vascular reactivity.

2. Vasoactive drugs: High-dose dopamine results in vascular spasm and internal organ ischemia and hypoxia by activating dopamine receptors in blood vessels. That is why dopamine can worsen hypoperfusion of internal organs instead of significantly boosting blood pressure in the treatment of patients with shock accompanied by refractory hypotension. Ideal vasoactive drugs should be able to a) quickly raise blood pressure and improve heart and brain perfusion and b) improve or increase blood flow and perfusion of kidneys, intestine, and other organs, as well as correct tissue hypoxia to prevent multiple organ dysfunction syndrome (MODS). As a strong α receptor agonist, norepinephrine is effective in increasing blood pressure. It can rapidly improve hemodynamic status in patients with septic shock. However, Meier Hellmann et al. pointed out that monotherapy with norepinephrine can reduce visceral perfusion in septic shock due to its strong vasoconstrictor effect. A reduction in organ perfusion is the main pathophysiological feature of shock. Hypoxia of internal organs remains in patients with shock even after their blood pressure has been corrected, thus leading to MODS. Therefore, reversion of tissue ischemia by improving organ and tissue perfusion, particularly visceral organ perfusion, is the key for shock recovery and administration of vasoactive drugs. When evaluating shock resuscitation and efficacy of vasoactive drugs, special emphasis should be laid on improving organ perfusion rather than simply increasing blood pressure. Hemodynamic support must be strengthened to normalize cellular metabolism by restoring tissue perfusion. Dobutamine is the preferred choice, started at the initial dose of 10 μg/kg/min, titrated by 5 μg/kg/min very 10 min to a maximum of 20 μg/kg/min within 30 min. If it is still difficult to maintain blood pressure, norepinephrine may be used concomitantly at an initial dose of 0.1 μg/kg/min and titrated upward until MAP is maintained between 65 and 70 mmHg.
3. Vasopressin: The purpose of vasoactive drugs is to boost the blood pressure without inducing excessive contraction of blood vessels whereas ensuring visceral perfusion in patients with hypotension. Vasopressin (AVP), also known as antidiuretic hormone, is a peptide synthesized in hypothalamic nucleus and paraventricular nucleus of hypothalamus. AVP acts as agonists for V1, V2, and oxytocin receptors (OTRs). Its effect on V1 receptor is even stronger than angiotensin II and norepinephrine. The excitation of V2 receptors that are distributed in renal collecting tubules may promote reabsorption of water to help maintain a constant osmotic pressure and fluid volume. The excitation of vasopressin OTRs that are mainly located in the umbilical vein, aorta, and pulmonary artery may dilate blood vessels. A low-plasma concentration of AVP was found in patients with severe shock, thus laying a theoretical basis for its treatment of refractory hypotension. AVP may elevate the blood pressure in severe shock via two mechanisms: a) direct effect, namely, inducing contraction of vascular smooth muscle by directly activating V1 receptors, and b) indirect effect, namely, enhancing vasoconstriction of catecholamines. Short-term use of vasopressin can reduce the need for norepinephrine while increasing urine volume and creatinine clearance in patients with severe shock. AVP is especially suitable for children who need large doses of vasoactive drugs to maintain blood pressure, as it can reduce the dose of catecholamines and selectively affect systemic vascular vessels. Animal models have shown that AVP reduces blood flow to skeletal muscle and skin while relaxing the brain, coronary, and pulmonary blood vessels. AVP is superior to catecholamines for increasing the vital organ blood flow. Low dose of 0.0003–

0.001 U/kg is recommended since higher doses may cause splanchnic vascular, coronary ischemia and consequent decrease in cardiac output. In the treatment of severe shock, low dose of AVP exhibits diuretic effect possibly due to the following facts: (a) The elevation in mean arterial pressure caused by AVP increases the renal perfusion pressure and subsequently enhances urine output; (b) AVP increases glomerular filtration pressure by relaxing the afferent arterioles and contracting efferent arterioles; and (c) AVP increases urine output by regulating the secretion of atrial natriuretic hormone, renin, angiotensin, aldosterone, and other mediators.

4. Endorphin receptor antagonist: Inflammatory mediators involved in severe shock include tumor necrosis factor (TNF) α, interleukins (ILs), platelet-activating factor, leukotrienes, thromboxane A2, adhesion molecules, bradykinin, thrombin, myocardial inhibitory substance, β-endorphin, and heat shock protein. Among them, β-endorphin receptors are universally present in the central nervous system, heart, liver, kidney, and small intestine. The inhibitory role for β-endorphin in the cardiovascular effects of prostaglandins and catecholamines constitutes a key pathophysiological component of shock, thus providing a theoretical basis for the clinical use of naloxone in anti-shock therapy. Naloxone can reverse endotoxin shock by improving hemodynamics due to its antagonistic effect on endorphins. It was reported that naloxone was only effective for some septic shock and possibly associated with onset of pulmonary edema and seizures; therefore, it is still controversial on the efficacy and safety of naloxone in the treatment of severe shock. High dose of naloxone is suitable for vasoactive drug-dependent severe shock, which can effectively correct shock without vasopressors. The plasma half-life of naloxone is 90 min, and duration of action is 45–90 min. Therefore, naloxone should be continuously infused within 24 h to maintain an effective blood concentration. In case of emergency, the initial dose of 2 mg can be rapidly administered via intravenous route followed by a continuous maintenance infusion.
5. Fluid resuscitation: The supplementation of large volume of liquid may cause hypervolemia and hyperviscosity in patient with shock, thereby leading to adverse effects. Hypervolemia refers to hemoglobin concentration <70 gPL or hematocrit <0.20 as a result of transfusion. As shear stress is the product of shear rate times blood viscosity, a decrease in blood viscosity may reduce blood viscosity, shear stress, and the release of NO from endothelial cells. The reduction in NO that causes constriction of microarteries may result in reduction in perfusion pressure and capillaries collapse, thus affecting the cure rate of shock. When a large volume of dextran and artificial blood is transfused in the treatment of hemorrhagic shock, animals who received 100% of lost blood volume or 1.5 times the lost blood volume showed significantly lower survival rate than those who only received 50% of the lost blood volume. This may be explained by different degrees of reduction in blood viscosity. Particularly, a large volume of transfusion is not recommended for the treatment of uncontrolled hemorrhagic shock, and blood pressure should be firstly raised up to about 70 mmHg, rather than rapidly increased to a normal level. That is because a large volume of transfusion may worsen the hemorrhage by increasing blood pressure if the bleeding is uncontrolled; the transfusion may reduce the survival rate in hemorrhagic state. Furthermore, scholars have put forward new concepts such as “controlled resuscitation for uncontrolled hemorrhagic shock” and “permissive hypotensive resuscitation techniques.”

References

Arthur W, Bracey MD. Blood transfusion in cardiac surgery: a highly varied practice. Transfusion. 2008;48: 1271–3.

John AG, Veena C, Donghan L, et al. Initiation of epoetin-α therapy at a starting dose of 120,000 units

once every 3 weeks in patients with cancer receiving chemotherapy. Cancer. 2009;115:1121–31.

Sanders G, Mellor N, Richards K, et al. Prospective randomized controlled trial of acute normovolemic hemodilution in major gastrointestinal surgery. Br J Anaesth. 2004;93(6):775–81.

Spahn DR, Moch H, Hofmann A, Isbister JP. Patient blood management: the pragmatic solution for the problems with blood transfusions. Anesthesiology. 2008;109:951–3.