Technology in Cancer Research & Treatment
Volume 21: 1-10

DOI: 10.1177/15330338221105718
journals.sagepub.com/home/tct
SAGE

Application of Controlled Hypotension During Surgery for Spinal Metastasis

Rong-xing Ma, MD[1,2], Rui-qi Qiao, MD[1,2,*], Ming-you Xu, MD[1,2], Rui-feng Li, MD[1,2], and Yong-cheng Hu, MD, PhD[1]

Abstract

With advances in tumor treatment, metastasis to bone is increasing, and surgery has become the only choice for most terminal patients. However, spinal surgery has a high risk and is prone to heavy bleeding. Controlled hypotension during surgery has outstanding advantages in reducing intraoperative bleeding and ensuring a clear field of vision, thus avoiding damage to important nerves and vessels. Antihypertensive drugs should be carefully selected after considering the patient's age, different diseases, etc, and a single or combined regimen can be used. Hypotension also inevitably leads to a decrease in perfusion of important organs, so the threshold of hypotension and the maintenance time of hypotension should be strictly limited, and the monitoring of important organs during the operation is particularly important. Information such as blood perfusion, blood oxygen saturation, cardiac output, and neurophysiological conduction potential changes should be obtained in a timely fashion, which will help to reduce the risk of hypotension. In short, when applying controlled hypotension, it is necessary to choose an appropriate threshold and duration, and appropriate monitoring should be conducted during the operation to ensure the safety of the patient.

Keywords

controlled hypotension, spinal metastasis, intraoperative hemostasis, complication, intraoperative monitoring

Introduction

The incidence of cancer is increasing year by year. In 2020, the number of diagnosed cancer patients reached 19.3 million, and 10 million died of cancer. In the next 20 years, there will be 30 million new cases and 16 million cancer deaths. Bone is the third most common site of metastatic tumors after the lung and liver. The primary tumors most prone to bone metastasis are breast cancer, prostate cancer, lung cancer, and so on. These tumors not only have an obvious tendency for bone metastasis, but they also have a high incidence. The spine is the most common site of bone metastasis, and with the continuous development of treatment and the prolonged survival time of cancer patients, the incidence of spinal metastases is increasing.[1,2]

Currently, the main method for treating spinal tumors is surgery, which is often applied when the estimated survival time of the patient is greater than 6 months, and in these patients, the malignant metastatic lesions should be removed as completely as possible. Surgical treatment can improve the quality of life of the patients by relieving the corresponding symptoms of spinal cord compression, increase their spinal stability, and prolong their survival time.[3]

However, orthopedic surgery usually involves cutting into the bone marrow, muscle tissue, and venous plexus. Because of the complex structure of the blood vessels, bleeding during orthopedic surgery is relatively heavy and is usually characterized by diffuse bleeding, which is difficult to control with traditional surgical techniques, especially when the operation involves intraosseous capillaries. A meta-analysis by Chen *et al* included 760 patients with spinal tumors and spinal metastases. The total perioperative blood loss was 2180 ml (95% CI, 1805-2554 ml).[4]

Therefore, blood transfusion is a common practice during orthopedic surgery. However, allogeneic blood transfusion has risks such as immunosuppression and disease transmission, and some patients may have transfusion-related reactions such as transfusion-related lung injury, renal failure, myocardial infarction, and even life-threatening reactions.[5] Other methods

[1] Tianjin Hospital, Tianjin, China
[2] Graduate School, Tianjin Medical University, Tianjin, China

*The first two authors contributed equally to this manuscript.

Corresponding Author:
Yong-cheng Hu, Department of Bone and Soft Tissue Oncology, Tianjin Hospital, 406 Jiefang Southern Road, Tianjin, China.
Email: huycdoctor@163.com

to reduce bleeding during spinal surgery include aseptic gauze packing and compression, acute hypervolemic or isovolumic hemodilution, perioperative blood recovery, antifibrinolytic drugs, and controlled hypotension. Although acute hypervolemic hemodilution and acute normovolemic hemodilution play an important role in blood protection, hemodilution may affect the blood coagulation function of the body.[6,7] Autologous blood recovery technology can minimize the need for allogeneic blood transfusion, but spinal surgery is traumatic and has a large amount of bleeding, so allogeneic blood transfusion cannot be avoided completely.[8] Antifibrinolytic drugs can reduce perioperative blood loss and the need for blood transfusion during spinal surgery, but it is controversial since it can increase the risk of venous thromboembolism.[9] Therefore, the application of controlled hypotension has fewer clinical challenges.

Controlled hypotension (CH) refers to the use of drugs and/or anesthetic techniques to reduce the mean arterial blood pressure (MAP) to 55~65 mm Hg, the systolic blood pressure to 80~90 mm Hg or to reduce MAP by 30% of the baseline value.[10] Controlled hypotension can reduce intraoperative bleeding and ensure a clear field of vision, avoiding damage to important nerves and vessels and shortening the operation time, and reducing the need for blood transfusion, ligation and cauterization of tissue, and the degree of edema, along with accelerating wound healing. It is an important method to reduce intraoperative bleeding during spinal surgery.[11] However, controlled hypotension also introduces risks of low perfusion injury to various organs, including the spinal cord, thrombosis, persistent hypotension, cardiac arrest, and so on, and it can be difficult to prevent these complications. Intraoperative monitoring of important organs is undoubtedly an effective means to solve this problem. Emerging technologies, such as intraoperative transcranial Doppler (TCD) monitoring of cerebral blood flow, somatosensory evoked potential (SSEP) monitoring of the spinal tract, transesophageal echocardiography (TEE) monitoring of cardiac function, and near-infrared spectroscopy (NIRS) monitoring of renal perfusion, can help clinicians determine the best strategy to reduce the risk of perioperative complications and monitor cerebral perfusion during the induction and maintenance of general anesthesia. They can help reduce the occurrence of perioperative ischemic complications.[12–14] These techniques make controlled hypotension safer, and thus it can be used more widely in the clinic.

Physiology of Hemorrhage During Spinal Surgery

Intraoperative blood loss is a common problem, and the definition of massive blood loss is usually considered to be 1 stroke 2 (adult 60 mL/kg) of the patient's total blood loss within 24 h, which constitutes severe blood loss.[15] Most spinal surgery studies have reported surgical blood loss requiring blood transfusions, which range from 650 ml to 2839 ml per case. Chen *et al* showed that among 760 patients undergoing spinal surgery, the mean estimated perioperative blood loss was 2180 ml (95% Cl 1805-2554), which is rather shocking.[4] Blood loss during spinal surgery for metastatic diseases may come from large numbers of tumor blood vessels and dilated epidural veins, as well as from soft tissue, paraspinal vessels, etc[16] The following discusses the physiology behind the ease of hemorrhage during spinal surgery from three aspects.

Complexity of the Spinal Vessels

Extramedullary artery: there are three longitudinal arteries along the spinal cord, providing transverse branches to the white matter and gray matter. These arteries supply a network of circular arteries located on the surface of the spinal cord, called the "dural plexus." The first longitudinal artery is the anterior spinal artery (ASA). The other two longitudinal arteries are the paired posterior spinal arteries (PSA). The ASA provides blood flow to the first 2/3 of the spinal cord, while the PSA provides blood to the back 1/3 of the spinal cord. The branches of these arteries that reach the spinal cord are called radiculomedullary arteries. The largest one is the "great anterior radiculomedullary artery". This artery is particularly important because it anastomoses with the ASA and supplies the major part of the arterial flow to the lumbar enlargement.[17,18]

Arterial anastomotic systems: When considering the spinal cord in the axial plane, four anastomotic circles have been described: intramedullar, intradural, extradural, and extravertebral. They each bear the confluence and shunt of blood. The ASA and the PSA reach the conus medullaris, where they anastomose through the anastomotic loop of the conus medullaris. It represents the largest anastomotic system between the ASA and PSA. Many of the most invasive resections of spinal tumors endanger the extramedullary artery and intradural anastomotic network.[19]

Tumor Neovascularization

Tumor angiogenesis refers to new blood vessels formed by the existing vascular system in response to the tumor. To maintain growth beyond more than a few millimeters in diameter, all malignant tumors need to induce the growth of new blood vessels, which play a key role in the occurrence, invasion, and metastasis of solid tumors. Angiogenesis is considered a sign of tumor progression because the rich vascular network can provide sufficient oxygen and nutrition for tumor cells and contribute to tumor metastasis.[20]

Abnormalities of Tumor Angiogenesis

Tumor angiogenesis produces abnormal blood vessels, and they are more fragile than normal blood vessels: (a) due to an incomplete endothelium, lack of coverage of smooth muscle cells and surrounding tissue, the vessels are sparse, fragile, deformed and have high permeability; (b) the tumor interstitial pressure and blood volume are increased due to arteriovenous shunts and even acute vascular rupture.[21,22]

Effect of Controlled Hypotension

The main purpose of controlled hypotension is to reduce the intravascular tension, reduce bleeding and blood transfusions, clear the surgical field and improve the accuracy of the operation, thus reducing accidental injury to nerves and vessels, shortening the operation time, reducing preload and afterload and improving myocardial work, reducing ligation of cauterized tissue, reducing the degree of edema, and accelerating wound healing. To improve the safety of the perioperative patients, hypotension is suitable for spinal surgery and other operations with an expected large amount of blood loss and a high risk.[23–25]

Among the many advantages of controlled hypotension, the most important advantage is that it can effectively reduce the amount of intraoperative blood loss. Freeman *et al* studied 102 patients who underwent sacral tumor resection (59% of the total). The patients in the experimental group received hypotensive epidural anesthesia, and the control group received standard anesthesia care. The results showed that hypotensive anesthesia could reduce blood loss and blood transfusions.[26] Huh *et al* used milrinone to reduce intraoperative blood pressure and adjusted the infusion dose to reduce the systolic blood pressure or the average blood pressure to 60–65 mm Hg. Milrinone-controlled hypotension can reduce intraoperative blood loss and increase the urine volume compared with sodium nitroprusside or nitroglycerin in elderly patients undergoing spinal surgery.[27] Consistently, Hwang *et al* found that controlled hypotension can significantly reduce intraoperative blood loss and blood transfusion, improve the surgical field, and improve perfusion.[28] In addition, the use of controlled hypotension during spinal surgery can protect renal function and reduce the degree of renal damage. Park *et al* measured serum creatinine clearance, serum cystatin C, urine volume, and sodium excretion fraction in patients undergoing interpyramidal fusion before the operation, after the operation and on the first day after the operation. The results showed that renal function was preserved in patients undergoing spinal surgery under controlled hypotension[29] (Table 1).

Commonly Used Drugs for Controlled Hypotension and Pain Management in the Clinic

Vasodilators

Sodium nitroprusside is probably the most popular drug; it produces NO by metabolism in vascular smooth muscle and relaxes it. Sodium nitroprusside is a powerful vasodilator. Because the afterload is reduced, the myocardial oxygen consumption is reduced, so the cardiac output does not decrease, the effect is fast, the action time is short, and the blood pressure is easy to control; it has long been the first choice as an antihypertensive drug during surgery. However, its inhibition of platelets has a potential risk of increasing blood loss, and its other potential side effects include tachycardia, hypoxia of liver and skeletal muscle, and intrapulmonary shunt.[30,31]

Nitroglycerin mainly relaxes vascular smooth muscle, dilates the venous system, reduces peripheral circulation resistance and dilates volumetric blood vessels. In the clinic, nitroglycerin is recommended to be used in combination with esmolol to reduce the heart rate. Compared with sodium nitroprusside, nitroglycerin acts more slowly but does not cause myocardial ischemia, rebound hypertension, or toxic metabolites.[32]

β1 Adrenergic Receptor Blockers

Esmolol, as a highly selective β1 adrenergic receptor blocker, acts quickly and for a short time and can significantly reduce the heart rate, cardiac output, and blood pressure. Studies have shown that esmolol can reduce spinal cord ischemia–reperfusion injury in nerve injury model rats. In theory, the infusion of esmolol and nitroglycerin is more beneficial for the smooth implementation of controlled hypotension.

α2-adrenergic receptor agonists.

Dexmedetomidine, as a highly selective α2-adrenergic receptor agonist, has analgesic and sedative effects and reduces sympathetic nerve activity. It is used for controlled hypotension mainly by inhibiting sympathetic nerve activity, thus slowing down the heart rate and reducing blood pressure. At the same time, it can also reduce the rate of cerebral oxygen uptake, reduce the incidence of postoperative cognitive dysfunction, and have a neuroprotective effect.

Calcium Channel Blockers

Nicardipine is a calcium channel antagonist injected intravenously that can moderately and quickly control blood pressure, relax vascular smooth muscle, and reduce systemic vascular resistance.[33,34] By comparing nicardipine with sodium nitroprusside, Lustik *et al* found that nicardipine caused a lower rate of severe hypotension than sodium nitroprusside, although both drugs were acceptable options for achieving the goal of controlled hypotension.[35]

Phosphodiesterase Type III Inhibitor

Milrinone is a selective phosphodiesterase type III inhibitor used in patients with congestive heart failure or during cardiac surgery. Phosphodiesterase inhibitors can increase cyclic adenosine monophosphate and promote the influx of calcium into cardiomyocytes and vascular smooth muscle. Vascular dilatation occurs in both arterial and venous smooth muscle, which reduces systemic blood pressure.[36] Milrinone-controlled hypotension reduced the intraoperative blood loss and increased the urine volume compared with sodium nitroprusside or nitroglycerin.[37]

Narcotic Drugs

Propofol, as a general intravenous anesthetic, inhibits myocardial contractility and the circulatory baroreceptor response to hypotension by directly reducing the peripheral vascular resistance and inhibiting endoplasmic reticulum calcium release.

Table 1. Clinical outcomes of controlled hypotension reported in different studies.

Study	Drugs	Blood pressure range（mm Hg）	Measuring index (experimental group vs control group)		Conclusions
Freeman *et al*[26]	Propofol plus either remifentanil or ketamine	MAP 53mm Hg	Intraoperative blood loss: 1457mL vs 2421mL	Red cells transfused: 2.7units vs 3.9units	Hypotensive anesthesia resulted in less blood loss and fewer blood units transfused
Huh *et al*[27]	Milrinone, sodium nitroprusside, nitroglycerine	A fall of 30% in systolic blood pressure	Intraoperative blood loss: 288.5mL vs 399.8mL and 367.0mL	Hourly urine output: 1.4mL vs 0.7mL and 0.9mL	Milrinone for induced hypotension led to less intraoperative blood loss and higher urine output
Hwang *et al*[28]	Milrinone	MAP was not less than 60 mm Hg	Intraoperative blood loss: 445.0mL vs 765.0mL	Hourly urine output: 1.4mL vs 0.8mL	Reduced intraoperative blood loss and while urine output increased
Park *et al*[29]	Nicardipine	Mean arterial pressure at 50–65 mm Hg	Creatinine clearance: 200mL/min/1.73m^3 vs 150mL/min/1.73m^3	Serum cystatin C: 0.58mg/L vs 0.63mg/L	Nicardipine increased creatinine clearance and renal function was preserved

Abbreviation: MAP, mean arterial pressure.

Its inhibition of circulation is weak, so it is often used in combination with a variety of drugs to achieve antihypertensive effects. Sevoflurane has been shown to reduce systemic vascular resistance in a variety of ways. Albertin *et al* found that patients treated with propofol had more local blood flow than those in the sevoflurane group but had less intraoperative bleeding.[25]

Anesthetic management during spinal surgery is often faced with the challenges of massive blood loss, difficult pain control, a long operation time, and posture-related complications. In the systematic review by Alboog *et al*, three main factors were considered most important during anesthesia for complex spinal surgery in adults: blood loss, pain management, and posture-related complications. Prophylaxis of tranexamic acid and an optimal prone position have been shown to be effective blood protection strategies with the least risk to patients, while a combination of gabapentin, ketamine, and opioids can achieve the best analgesic effect.[37] In addition, Waelken *et al* pointed out that for surgical analgesia, different operative time periods should be treated differently. Paracetamol and nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 specific inhibitors should be used before or during the operation, ketamine can also be injected intravenously, and epidural anesthesia should be used alone or in combination with opioids.[38] Therefore, it can be seen that the single or combined use of different drugs, and how to choose and match them, is still the core issue of clinical concern and should be fully evaluated before surgery, according to the patient's specific operation and the postoperative goals. At the same time, new drug discoveries also provide more room for controlled hypotension and pain management (Table 2).

Table 2. Overall recommendations for peri-operative pain management in patients undergoing complex spine surgery.

Pre-operative and intra-operative recommendations
Oral or i.v. paracetamol (Grade D)
Oral or i.v. NSAIDs / COX-2 specific inhibitors (Grade A)
i.v. Ketamine infusion (Grade A)
Postoperative recommendations
Epidural analgesia with local anaesthetics and with or without opioids (Grade B)
Oral or i.v. paracetamol (Grade D)
Oral or i.v. NSAIDs/COX-2 specific inhibitors (Grade A)
Opioids as rescue medication (Grade D)

Abbreviations: COX, cyclooxygenase; i.v., intravenous.

Effects of Controlled Hypotension on Vital Organs (Heart, Brain, Kidney, Vision)

Controlled hypotension is mostly safe, but this does not mean that there are no complications. Most of the complications or deaths are closely related to the selection of the antihypertensive indications, the mastery of the antihypertensive techniques and management, excessive hypotension, excessive drug dosage and insufficient blood volume, and the lack of understanding of potential risk factors before the operation. Therefore, before applying controlled hypotension, we must fully consider the advantages and disadvantages before choosing to use it.

Effects of Controlled Hypotension on the Brain

Due to its characteristics of a high metabolic rate, high oxygen consumption and sensitivity to hypoxia, the greatest concern of controlled hypotension is cerebral ischemia and hypoxia caused by insufficient cerebral blood flow. Therefore, ensuring the blood perfusion of the brain tissue and the balance of oxygen supply and demand is a basic safety requirement of controlled hypotension. When the arterial blood pressure changes, intracranial arterioles can maintain a relatively stable cerebral blood volume through contraction or relaxation to maintain normal physiological function, which is called automatic regulation of cerebral blood flow. When the blood pressure is lower than the lower limit of the ability of cerebral blood flow regulation, with a continuous decrease in blood pressure, the cerebral blood flow will continue to decrease, and finally, there will be irreversible brain damage.[39] These injuries include central nervous system injury, increased local tissue pressure, hypertension, and a decrease in lateral limb circulation and they can significantly affect the functional activity of hippocampal CAl neurons in the brain.[40]

For the relationship between intraoperative mild hypotension and stroke, Bijker *et al* found that the duration of a decrease in mean arterial pressure from the baseline value of more than 30% was significantly correlated with postoperative stroke and that postoperative hypotension may be associated with perioperative stroke.[41] However, Hsieh *et al* found no correlation between stroke and intraoperative hypotension. The risk of hypotension among stroke patients was not higher than that in the normal control group.[42] Bijker *et al* explained that there is a statistically significant correlation between a decrease of more than 30% of MAP from the base value and the occurrence of postoperative stroke, and the definition of "baseline" is different, depending on the baseline used, which may affect the correlation between the degree of intraoperative hypotension and the risk of postoperative ischemic stroke. In addition, stroke risk is also associated with the duration of intraoperative hypotension. When the duration is extended by one minute, the risk of stroke increases by 1.013 times.[41]

Effect of Controlled Hypotension on the Myocardium

The overall incidence of myocardial injury during noncardiac surgery is 3.1%. There is no fixed definition of perioperative myocardial injury, generally defined as occurring within 7 days after the operation, reflected by the peak value of fourth-generation troponin exceeding 0.03~0.04 ng/ml once, and the peak value of CK-MB exceeding 8.8 ng/ml once.[43] Walsh *et al* evaluated the relationship between intraoperative hypotension (MAP < 55-75 mm Hg) and postoperative acute renal injury (AKI) and myocardial injury in 33330 patients to determine the MAP threshold of increased risk of damage. The incidences of AKI and myocardial injury were 2478 (7.4%) and 770 (2.3%), respectively. The increased risk of both MAP thresholds was lower than that of 55 mm Hg, and it is worth noting that there does not seem to be any safe duration when MAP is lower than 55 mm Hg.[44]

Salmasi *et al* evaluated whether the relationship between intraoperative hypotension and myocardial injury depended on the baseline MAP. The results showed that an absolute threshold of MAP lower than 65 mm Hg was progressively related to myocardial damage. The lower the absolute threshold is, the longer the duration of hypotension and the more common the injury. When MAP is 50 mm Hg, only 1 min can significantly increase the risk of myocardial and kidney damage. When MAP is lower than 65 mm Hg, a duration longer than 13 min is significantly related to an increased risk of myocardial and renal injury. When MAP is lower than 50% before surgery, 5 min significantly increased the risk of myocardial and kidney injury.[45] From the same point of view, Waes *et al* showed that a relative MAP less than 40% of the preoperative blood pressure for more than 30 min was associated with an increased incidence of myocardial injury, and even a short period of hypotension below 40% of preoperative MAP was associated with kidney and myocardial injury. Therefore, the classic recommendation that intraoperative blood pressure should be maintained within 20% of preoperative blood pressure seems reasonable.[46]

Effect of Controlled Hypotension on the Kidney

The effect of controlled hypotension on the kidney is mainly reflected by AKI. AKI is defined as a relative 50% increase in creatinine or an absolute increase of 0.3 mg/dl in the first two days after the operation.[47] In adults, the renal blood flow remains constant between MAP 75 and 170 mm Hg, but beyond this range, it becomes dependent on blood pressure. MAP of 50 to 60 mm Hg is the lower limit of renal blood flow autoregulation.[48] Rhee *et al* recently measured the reactivity of renal vessels using near-infrared spectroscopy. When MAP decreased to 60, 45, and 40 mm Hg, renal blood flow decreased to 75%, 50%, and 25% of the baseline, respectively.[49] To study the relationship between intraoperative hypotension and acute renal injury, Sun *et al* conducted a retrospective cohort study of 5127 patients undergoing noncardiac surgery, and the results showed that when the MAP was lower than 60 mm Hg, the incidence of AKI was 1.84%. However, when the MAP was lower than 55 mm Hg, the incidence of AKI was 2.34%, and when the time was extended for more than 20 min, the incidence of AKI was 3.53%.[50] The degree of reduction of the MAP level is very important; therefore, the appropriate baseline level and duration of hypotension should be selected according to the age and renal function level before the operation; it should not be less than 55 mm Hg; and the duration should not generally exceed 20 min.

Effect of Controlled Hypotension on Vision

Vision loss is a complication encountered in 0.2% of spinal surgeries. Bilateral optic nerve involvement is common in patients with perioperative posterior ischemic optic neuropathy, and bilateral optic nerve involvement occurs in approximately half of patients and 70% of patients after lumbar surgery.[51] Intraoperative anemia and controlled maintenance hypotension are the main risk factors for vision loss in patients with ischemic optic neuropathy after lumbar surgery,[52] which may increase the central venous pressure and decrease the intraocular perfusion pressure.[53,54]

Mione *et al* studied bilateral occipital watershed ischemic stroke caused by hypotension during spinal surgery. They reported a patient with vision loss due to bilateral symmetrical occipital infarction caused by intraoperative hypotension after lumbar laminectomy. The patient was 55 years old, without any underlying disease. The preoperative blood pressure was 176/114 mm Hg. To prevent bleeding, the systolic blood pressure was controlled below 80 mm Hg for 75 min. He did not receive a blood transfusion during the operation. When he woke up, he complained of complete blindness. Two years later, he still had serious visual impairment and spatial neglect. Patients undergoing spinal surgery are particularly prone to intraoperative hypotension, and there is a risk of vision loss due to eye infarction and cortical infarction, especially due to the presence of variations in the cerebral arterial ring[55] (Table 3).

New Progress in the Prevention of Complications

Intraoperative Monitoring of Cerebral Blood Flow by Transcranial Doppler

TCD analysis of pulsatile cerebral blood flow velocity waveforms of intracranial arteries can provide information on various cerebrovascular changes.[56] The latest TCD includes the use of spectral and color Doppler as well as grayscale tissue imaging, allowing direct display of major intracranial arteries and the identification of arteries and their hemodynamics.[57] Cerebral blood flow resistance can be measured by the Pulsatility Index (PI).[58] The results of Abdelhaleem *et al* show that there is a significant difference between PI and the mean blood flow velocity of the middle cerebral artery before and after the operation, so TCD measurement of PI can be regarded as a more effective monitoring method.[59] Chaix *et al* used TCD to monitor the blood flow velocity of the middle cerebral artery (Vm) and recorded the systolic velocity (Vs.), diastolic velocity (Vd), and pulsatile index ([Vs.−Vd]/Vm) to evaluate cerebral perfusion during the induction and maintenance of general anesthesia. It was found that the decrease in cerebral perfusion measured by Vm was related to the decrease in MAP in high-risk patients.[12] Similarly, Larsen *et al* reported that a decrease in MAP was positively correlated with Vm, although changes in MAP within the range of brain autoregulation should not affect cerebral blood flow.[60]

Somatosensory Evoked Potential Monitoring of the Spinal Tract

SSEP is performed by applying an electrical stimulation to a specific mixed nerve or dermatome to generate a sensory stimulus and then recording the responses along the ascending neural pathway and the sensory cortex. The purpose of SSEP and other forms of intraoperative neuromonitoring is to detect reversible electrical changes as early as possible to prevent irreversible ischemic damage.[61] In view of this relationship, a decrease in SSEP amplitude can be used to indicate an increased risk of perioperative ischemic complications, such as stroke and optic nerve injury.[13] Thirumala *et al* also showed that intraoperative SSEP is highly specific for iatrogenic injury, dural traction, and a decrease in systemic blood pressure. A decrease in MAP leads to a significant reversible change in the potential amplitude of monitoring SSEP.[62] However, Abdelkader *et al* showed that the sensitivity of SSEP alone in monitoring selective corticospinal tract injury was low.[63] Kelleher *et al* suggested that the low sensitivity may be due to nerve root and corticospinal tract injury. EMG and motor evoked potentials (MEPs) are more sensitive methods to monitor these injuries.[64] A combination of MEP and SSEP has been shown to increase the sensitivity of SSEP from 59% to 92%.[65] Therefore, a combination of MEP and SSEP for multimode monitoring of the spinal tract is a more effective and reasonable method.

Monitoring of Cardiac Function by Transesophageal Echocardiography

Recently, the use of ultrasound has been shown to have an important impact on improving the monitoring and correction of hypovolemia and left ventricular dysfunction, with a trend toward a shorter operation time and reduced mortality.[66] Echocardiography can be divided into transthoracic echocardiography (TTE) and TEE. TEE provides a reliable acoustic window through the esophagus, reducing the variability of image generation and usually ensuring high-resolution images,[67] and TEE has been proven to outperform TTE in terms of the high clinical risk in critically ill patients.[68] From the point of view of hemodynamic monitoring, the evaluation of fluid response by TEE is mainly based on the changes of the aortic velocity time index, left ventricular systolic function, dynamic changes of the cardiac output to passive leg raising, and measurement of the inferior vena cava diameter. At the same time, TEE has very good specificity and moderate sensitivity in measuring the diameter of the superior vena cava during respiration.[69,70] Therefore, preoperative and intraoperative echocardiography may help clinicians determine the best strategies to reduce the risk of perioperative complications, including enhanced monitoring or a higher level of postoperative care.[14]

Monitoring Renal Perfusion Blood Flow by Near Infrared Spectroscopy

Different biomarkers (such as cystatin C and NGAL) are often used in the early detection of kidney injury. Nonetheless, renal oxygen saturation has been shown to be a better marker of acute renal hypoperfusion than serum creatinine, EGFR, and urinary NGAL.[71] NIRS is a noninvasive optical technique that continuously measures the difference between oxygenated and deoxyhemoglobin in the local tissue region, thus reflecting the local oxygen saturation.[72] A decrease in renal venous oxygen saturation (SrvO2) has been proven to be related to postoperative renal damage, so a decrease in renal oxygen saturation can predict acute renal injury intraoperatively and postoperatively.[73] Tholen *et al* compared the local tissue renal oxygen saturation (rSO2) obtained from skin sensors placed above the kidney with the invasive SrvO2 using NIRS. They found good agreement between rSO2 and SrvO2.[74] Malakasioti *et al* showed that a decrease in renal blood oxygen saturation

Table 3. The relationship between controlled hypotension and vital organs.

Study	Treatment	Thresholds of intraoperative MAP	Complication	Incidence	Conclusions
Bijker *et al*[41]	Cardiac or neurosurgical procedures were excluded	MAP was decreased more than 30% from baseline	Ischemic stroke	0.1-3%	Significantly associated with a postoperative stroke
Hsieh *et al*[42]	Nonneurological, noncardiac, and noncarotid surgery	Under a MAP of 70mm Hg	Ischemic stroke	0.1-3%	Not find an association between hypotension and postoperative stroke
Walsh *et al*[44]	Noncardiac surgery	Less than 55 mm Hg	Myocardial damage	2.3%	There does not any safe duration of a MAP less than 55mm Hg
Salmasi *et al*[45]	Noncardiac surgery	MAP below absolute thresholds of 65 mm Hg or relative thresholds of 20%	Myocardial damage	3.1%	Prolonged exposure was associated with increased odds
Sun *et al*[50]	Noncardiac surgery	Less than 55mm Hg	Acute kidney injury	2.34% or 3.53% (MAP<55mm Hg); 1.84% (MAP<60 mm Hg)	AKI is associated with sustained intraoperative periods
Murphy *et al*[51]	Lumbar spine fusion surgery	Systolic blood pressure ranging from 85 to 95 mm Hg and diastolic pressure between 40 and 60 mm Hg	Ischemic optic neuropathy	A case	Bilateral ischemic optic neuropathy was confirmed 2 months postoperatively

Abbreviation: MAP, mean arterial pressure.

Table 4. New progress in intraoperative monitoring.

Parameter	Method	Advantages	Limitation
Vessel blood flow	Transcranial Doppler sonography	Non-invasive Continuous Dynamic changes of vessels	Results dependent on probe position and user experience
Regional vascular oxygen saturation	Near-infrared spectroscopy	Non-invasive Continuous Applicable to all ages	High costs Possibility of extracranial contamination
Potential change	Somatosensory evoked potential	Offers real-time resolution of cerebral ischemia Sensitivity Surgical manipulations and to different types of injury Continuous	Ischemic insults to motor areas can only be detected Spatial resolution is limited
Hemodynamic monitoring	Trans-esophageal echocardiography	Offers a reliable acoustic window Assuring high-resolution images Less invasive	More time consuming Contraindication added

during the perioperative period or during shock reflects a decrease in blood transfer to vital organs and impairs renal perfusion.[75] Therefore, NIRS is a good noninvasive method for monitoring renal blood flow.

To a large extent, monitoring allows clinicians access to important information, such as the perfusion volume, blood oxygen saturation, cardiac output, and neurophysiological conduction potential changes in important organs under conditions of hypotension, which greatly reduces the occurrence of intraoperative complications. It should be pointed out that these new techniques are not only used to monitor specific organs, such as NIRS, which can also be used to monitor cerebral perfusion blood flow. TEE measurement of cardiac output can also indirectly predict changes in cerebral blood flow. TEE should be used singly or in combination according to the patient's condition (Table 4).

In conclusion, surgery is a common treatment method for patients with spinal tumors. Because of the special anatomical structure of the spine and the easy bleeding of tumor vessels, heavy intraoperative blood loss during spine surgery is common. The controlled hypotension technique can effectively reduce intraoperative blood loss and improve the clarity of the surgical field. Doctors must skillfully master and use the controlled hypotension technique to reduce blood pressure appropriately at critical moments. The decrease in blood pressure should be limited to maintain full perfusion of the heart, brain, kidney, and other important organs and keeping the blood pressure level as high as possible while meeting the surgical requirements. At the same time, the physiological functions of important organs must be strictly monitored to avoid complications and ensure the safety of the patients.

Acknowledgements

We thank Xiong-gang Yang MD and Hao-ran Zhang MD, for their encouragement and support during our study.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Yong-cheng Hu https://orcid.org/0000-0002-9846-6735

References

1. Salapura V, Jeromel M. Minimally invasive (percutaneous) treatment of metastatic spinal and extraspinal disease--a review. *Acta Clin Croat*. 2014;53(1):44-54. doi:10.1186/1471-2296-15-40
2. Harel R, Zach L. Spine radiosurgery for spinal metastases: indications, technique and outcome. *Neurol Res*. 2014;36(6):550-556. doi:10.1179/1743132814Y.0000000364
3. Luzzati AD, Shah S, Gagliano F, et al. Multilevel en bloc spondylectomy for tumors of the thoracic and lumbar spine is challenging but rewarding. *Clin Orthop Relat Res*. 2015;473(3):858-867. doi:10.1007/s11999-014-3578-x
4. Chen Y, Tai BC, Nayak D, et al. Blood loss in spinal tumour surgery and surgery for metastatic spinal disease: a meta-analysis. *Bone Joint J*. 2013;95–b(5):683-688. doi:10.1302/0301-620X.95B5.31270
5. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP. Transfusion medicine. First of two parts--blood transfusion. *N Engl J Med*. 1999;340(6):438-447. doi:10.1056/NEJM199902113400606
6. Saricaoglu F, Akinci SB, Celiker V, Aypar U. The effect of acute normovolemic hemodilution and acute hypervolemic hemodilution on coagulation and allogeneic transfusion. *Saudi Med J*. 2005;26(5):792-798. doi:10.1016/j.revmed.2005.02.001
7. Singbartl K, Innerhofer P, Radvan J, et al. Hemostasis and hemodilution: a quantitative mathematical guide for clinical practice. *Anesth Analg*. 2003;96(4):929-935. doi:10.1213/01.ANE.0000052711.68903.5D
8. Zhou LW, Li MQ, Wang XS, et al. Application of controlled hypotension combined with autotransfusion in spinal orthomorphia. *Anesth Essays Res*. 2014;8(2):145-149. doi:10.4103/0259-1162.134482
9. Yao AL, Zhu WM. Advances in intraoperative hemostatic techniques. *Chin J Pract Surg*. 2010;30(2):145-148.
10. Eckenhoff JE, Rich JC. Clinical experiences with deliberate hypotension. *Anesth Analg*. 1966;45(1):21-28. doi:10.1213/00000539-196601000-00006
11. Amr YM, Amin SM. Effects of preoperative β-blocker on blood loss and blood transfusion during spinal surgeries with sodium nitroprusside-controlled hypotension. *Saudi J Anaesth*. 2012;6(3):263-267. doi:10.4103/1658-354X.101219
12. Chaix I, Manquat E, Liu N, et al. Impact of hypotension on cerebral perfusion during general anesthesia induction: a prospective observational study in adults. *Acta Anaesthesiol Scand*. 2020;64(5):592-601. doi:10.1111/aas.13537
13. Nwachuku EL, Balzer JR, Yabes JG, et al. Diagnostic value of somatosensory evoked potential changes during carotid endarterectomy: a systematic review and meta-analysis. *JAMA Neurol*. 2015;72(1):73-80. doi:10.1001/jamaneurol.2014.3071
14. Vieillard-Baron A, Millington SJ, Sanfilippo F, et al. A decade of progress in critical care echocardiography: a narrative review. *Intensive Care Med*. 2019;45(6):770-788. doi:10.1007/s00134-019-05604-2
15. Elgafy H, Bransford RJ, McGuire RA, Dettori JR, Fischer D. Blood loss in major spine surgery: are there effective measures to decrease massive hemorrhage in major spine fusion surgery? *Spine (Phila Pa 1976)*. 2010;35(9 Suppl):S47-S56. doi:10.1097/BRS.0b013e3181d833f6
16. Bilsky MH, Fraser JF. Complication avoidance in vertebral column spine tumors. *Neurosurg Clin N Am*. 2006;17(3):317-329. doi:10.1016/j.nec.2006.04.007
17. Soubeyrand M, Court C, Fadel E, et al. Preoperative imaging study of the spinal cord vascularization: interest and limits in spine resection for primary tumors. *Eur J Radiol*. 2011;77(1):26-33. doi:10.1016/j.ejrad.2010.06.054
18. Biglioli P, Roberto M, Cannata A, et al. Upper and lower spinal cord blood supply: the continuity of the anterior spinal artery and the relevance of the lumbar arteries. *J Thorac Cardiovasc Surg*. 2004;127(4):1188-1192. doi:10.1016/j.jtcvs.2003.11.038
19. Lazorthes G, Gouaze A. [Supply routes of arterial vascularization of the spinal cord. Applications to the study of vascular myelopathies]. *Bull Acad Natl Med*. 1970;154(1):34-41.
20. Fukumura D, Jain RK. Imaging angiogenesis and the microenvironment. *Apmis*. 2008;116(7-8):695-715. doi:10.1111/j.1600-0463.2008.01148.x
21. Shi X, Zhou X, Wu S, Jin J, Zhou Z. Application of CT perfusion imaging in detection of tumor angiogenesis in osteosarcoma. *Chin-Ger J Clin Oncol*. 2011;10(3):174-177. doi:10.1007/s10330-011-0749-z
22. Goh V, Padhani AR, Rasheed S. Functional imaging of colorectal cancer angiogenesis. *Lancet Oncol*. 2007;8(3):245-255. doi:10.1016/S1470-2045(07)70075-X
23. Szpalski M, Gunzburg R, Sztern B. An overview of blood-sparing techniques used in spine surgery during the perioperative period. *Eur Spine J*. 2004;13 Suppl 1(Suppl 1):S18-S27. doi:10.1007/s00586-004-0752-y

24. Dutton RP. Controlled hypotension for spinal surgery. *Eur Spine J*. 2004;13 Suppl 1(Suppl 1):S66-S71. doi:10.1007/s00586-004-0756-7
25. Albertin A, La Colla L, Gandolfi A, et al. Greater peripheral blood flow but less bleeding with propofol versus sevoflurane during spine surgery: a possible physiologic model? *Spine (Phila Pa 1976)*. 2008;33(18):2017-2022. doi:10.1002/stem.161
26. Freeman AK, Thorne CJ, Gaston CL, et al. Hypotensive epidural anesthesia reduces blood loss in pelvic and sacral bone tumor resections. *Clin Orthop Relat Res*. 2017;475(3):634-640. doi:10.1007/s11999-016-4858-4
27. Huh J, Chung H, Hwang W. Comparison of the effects of milrinone, sodium nitroprusside, and nitroglycerine for induced hypotension in elderly patients undergoing spine surgery: a randomized controlled trial. *Clin Spine Surg*. 2019;32(8):E366-e371. doi:10.1097/BSD.0000000000000884
28. Hwang W, Kim E. The effect of milrinone on induced hypotension in elderly patients during spinal surgery: a randomized controlled trial. *Spine J*. 2014;14(8):1532-1537. doi:10.1016/j.spinee.2013.09.028
29. Park C, Kim JY, Kim C, Chang CH. Nicardipine effects on renal function during spine surgery. *Clin Spine Surg*. 2017;30(7):E954-e958. doi:10.1097/BSD.0000000000000394
30. Bernard JM, Pinaud M, François T, et al. Deliberate hypotension with nicardipine or nitroprusside during total hip arthroplasty. *Anesth Analg*. 1991;73(3):341-345. doi:10.1213/00000539-199109000-00020
31. Testa LD, Tobias JD. Pharmacologic drugs for controlled hypotension. *J Clin Anesth*. 1995;7(4):326-337. doi:10.1016/0952-8180(95)00010-f
32. Degoute CS. Controlled hypotension: a guide to drug choice. *Drugs*. 2007;67(7):1053-1076. doi:10.2165/00003495-200767070-00007
33. IV Nicardipine Study Group. Efficacy and safety of intravenous nicardipine in the control of postoperative hypertension. *Chest*. 1991;99(2):393-398. doi:10.1378/chest.99.2.393
34. Halpern NA, Goldberg M, Neely C, et al. Postoperative hypertension: a multicenter, prospective, randomized comparison between intravenous nicardipine and sodium nitroprusside. *Crit Care Med*. 1992;20(12):1637-1643. doi:10.1097/00132586-199308000-00044
35. Lustik SJ, Papadakos PJ, Jackman KV, et al. Nicardipine versus nitroprusside for deliberate hypotension during idiopathic scoliosis repair. *J Clin Anesth*. 2004;16(1):25-33. doi:10.1016/j.jclinane.2003.05.002
36. Levy JH, Bailey JM, Deeb GM. Intravenous milrinone in cardiac surgery. *Ann Thorac Surg*. 2002;73(1):325-330. doi:10.1016/S0003-4975(01)02719-9
37. Alboog A, Bae S, Chui J. Anesthetic management of complex spine surgery in adult patients: a review based on outcome evidence. *Curr Opin Anaesthesiol*. 2019;32(5):600-608. doi:10.1097/ACO.0000000000000765
38. Waelkens P, Alsabbagh E, Sauter A, Joshi GP, Beloeil H. Pain management after complex spine surgery: a systematic review and procedure-specific postoperative pain management recommendations. *Eur J Anaesthesiol*. 2021;38(9):985-994. doi:10.1097/EJA.0000000000001448
39. Panerai RB. Cerebral autoregulation: from models to clinical applications. *Cardiovasc Eng*. 2008;8(1):42-59. doi:10.1007/s10558-007-9044-6
40. Drummond JC. Blood pressure and the brain: how low can you go? *Anesth Analg*. 2019;128(4):759-771. doi:10.1213/ANE.0000000000004034
41. Bijker JB, Persoon S, Peelen LM, et al. Intraoperative hypotension and perioperative ischemic stroke after general surgery: a nested case-control study. *Anesthesiology*. 2012;116(3):658-664. doi:10.1097/ALN.0b013e3182472320
42. Hsieh JK, Dalton JE, Yang D, et al. The association between mild intraoperative hypotension and stroke in general surgery patients. *Anesth Analg*. 2016;123(4):933-939. doi:10.1213/ANE.0000000000001526
43. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *Eur Heart J*. 2012;33(20):2551-2567. doi:10.1093/eurheartj/ehs184
44. Walsh M, Devereaux PJ, Garg AX, et al. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. *Anesthesiology*. 2013;119(3):507-515. doi:10.1097/ALN.0b013e3182a10e26
45. Salmasi V, Maheshwari K, Yang D, et al. Relationship between intraoperative hypotension, defined by either reduction from baseline or absolute thresholds, and acute kidney and myocardial injury after noncardiac surgery: a retrospective cohort analysis. *Anesthesiology*. 2017;126(1):47-65. doi:10.1097/ALN.0000000000001432
46. van Waes JA, van Klei WA, Wijeysundera DN, et al. Association between intraoperative hypotension and myocardial injury after vascular surgery. *Anesthesiology*. 2016;124(1):35-44. doi:10.1097/ALN.0000000000000922
47. Mehta RL, Kellum JA, Shah SV, et al. Acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11(2):R31. doi:10.1186/cc5713
48. Dolman J. Clinical anesthesia—6th edition. *Anesthesiology*. 2009;56(12):996. doi:10.1007/s12630-009-9173-z
49. Rhee CJ, Kibler KK, Easley RB, et al. Renovascular reactivity measured by near-infrared spectroscopy. *J Appl Physiol (1985)*. 2012;113(2):307-314. doi:10.1152/japplphysiol.00024.2012
50. Sun LY, Wijeysundera DN, Tait GA, Beattie WS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. *Anesthesiology*. 2015;123(3):515-523. doi:10.1097/ALN.0000000000000765
51. Murphy MA. Bilateral posterior ischemic optic neuropathy after lumbar spine surgery. *Ophthalmology*. 2003;110(7):1454-1457. doi:10.1016/S0161-6420(03)00480-9
52. Lee AG. Ischemic optic neuropathy following lumbar spine surgery. Case report. *J Neurosurg*. 1995;83(2):348-349. doi:10.3171/jns.1995.83.2.0348
53. Dilger JA, Tetzlaff JE, Bell GR, et al. Ischaemic optic neuropathy after spinal fusion. *Can J Anaesth*. 1998;45(1):63-66. doi:10.1007/BF03011996
54. Roth S, Nunez R, Schreider BD. Unexplained visual loss after lumbar spinal fusion. *J Neurosurg Anesthesiol*. 1997;9(4):346-348. doi:10.1097/00008506-199710000-00010
55. Mione G, Pische G, Wolff V, et al. Perioperative bioccipital watershed Strokes in bilateral fetal posterior cerebral arteries during spinal surgery. *World Neurosurg*. 2016;85:367.e317-321. doi:10.1016/j.wneu.2015.09.098

56. Thorpe SG, Thibeault CM, Canac N, et al. Toward automated classification of pathological transcranial Doppler waveform morphology via spectral clustering. *PloS one*. 2020;15(2):e0228642. doi:10.1371/journal.pone.0228642
57. Upadhyay S, Mallick P, Elmatite W. Transcranial Doppler (TCD) ultrasonography and its clinical application- A review and update. *Int J Vasc Med*. 2018;1(2):1-10.
58. Caldiera V, Caputi L, Ciceri E. Doppler Imaging: basic principles and clinical application. In: Prada F, Solbiati L, Martegani A, DiMeco F, eds. *Intraoperative Ultrasound (IOUS) in Neurosurgery*. Springer, Cham. 2016:101-120. doi:10.1007/978-3-319-25268-1_9
59. Abdelhaleem NF A. Verification of sphenopalatine ganglion block success using transcranial Doppler in management of patients with postdural. *Pain Physician*. 2021;24(5):E661-e668.
60. Larsen FS, Olsen KS, Hansen BA, Paulson OB, Knudsen GM. Transcranial Doppler is valid for determination of the lower limit of cerebral blood flow autoregulation. *Stroke*. 1994;25(10):1985-1988. doi:10.1161/01.str.25.10.1985
61. Kashkoush AI, Nguyen C, Balzer J, et al. Diagnostic accuracy of somatosensory evoked potentials during intracranial aneurysm clipping for perioperative stroke. *J Clin Monit Compu*. 2020;34(4):811-819. doi:10.1007/s10877-019-00369-x
62. Thirumala PD, Bodily L, Tint D, et al. Somatosensory-evoked potential monitoring during instrumented scoliosis corrective procedures: validity revisited. *Spine J*. 2014;14(8):1572-1580. doi:10.1016/j.spinee.2013.09.035
63. Kelleher MO, Tan G, Sarjeant R, Fehlings MG. Predictive value of intraoperative neurophysiological monitoring during cervical spine surgery: a prospective analysis of 1055 consecutive patients. *J Neurosurg Spine*. 2008;8(3):215-221. doi:10.3171/SPI/2008/8/3/215
64. Abdelkader AA, Zohdi A, El Gohary AM, El-Hadidy RA, AlMahdy RA. Somatosensory evoked potentials as a standalone tool during spine surgery: an Egyptian preliminary report. *J Clin Neurophysiol*. 2019;36(2):161-165. doi:10.1097/WNP.0000000000000562
65. Zhu F, Chui J, Herrick I, Martin J. Intraoperative evoked potential monitoring for detecting cerebral injury during adult aneurysm clipping surgery: a systematic review and meta-analysis of diagnostic test accuracy. *BMJ open*. 2019;9(2):e022810. doi:10.1136/bmjopen-2018-022810
66. Ferrada P, Evans D, Wolfe L, et al. Findings of a randomized controlled trial using limited transthoracic echocardiogram (LTTE) as a hemodynamic monitoring tool in the trauma bay. *J Trauma Acute Care Surg*. 2014;76(1):31-38. doi:10.1097/TA.0b013e3182a74ad9
67. Arntfield R, Pace J, Hewak M, Thompson D. Focused transesophageal echocardiography by emergency physicians is feasible and clinically influential: observational results from a novel ultrasound program. *J Emerg Med*. 2016;50(2):286-294. doi:10.1016/j.jemermed.2015.09.018
68. Arntfield RT, Millington SJ, Wu E. An elderly woman that presents with absent vital signs. *Chest*. 2014;146(5):e156-e159. doi:10.1378/chest.13-3029
69. Vieillard-Baron A, Evrard B, Repessé X, et al. Limited value of end-expiratory inferior vena cava diameter to predict fluid responsiveness impact of intra-abdominal pressure. *Intensive Care Med*. 2018;44(2):197-203. doi:10.1007/s00134-018-5067-2
70. Vignon P, Repessé X, Bégot E, et al. Comparison of echocardiographic indices used to predict fluid responsiveness in ventilated patients. *Am J Respir Crit Care Med*. 2017;195(8):1022-1032. doi:10.1164/rccm.201604-0844OC
71. Gist KM, Kaufman J, da Cruz EM, et al. A decline in intraoperative renal near-infrared spectroscopy is associated with adverse outcomes in children following cardiac surgery. *Pediatr Crit Care Med*. 2016;17(4):342-349. doi:10.1097/PCC.0000000000000674
72. Murkin JM, Arango M. Near-infrared spectroscopy as an index of brain and tissue oxygenation. *Br J Anaesth*. 2009;103(Suppl 1):i3-13. doi:10.1093/bja/aep299
73. Ortega-Loubon C, Fernández-Molina M, Fierro I, et al. Postoperative kidney oxygen saturation as a novel marker for acute kidney injury after adult cardiac surgery. *J Thorac Cardiovasc Surg*. 2019;157(6):2340-2351.e2343. doi:10.1016/j.jtcvs.2018.09.115
74. Tholén M, Ricksten SE, Lannemyr L. Renal near-infrared spectroscopy for assessment of renal oxygenation in adults undergoing cardiac surgery: a method validation study. *J Cardiothorac Vasc Anesth*. 2020;34(12):3300-3305. doi:10.1053/j.jvca.2020.04.044
75. Malakasioti G, Marks SD, Watson T, et al. Continuous monitoring of kidney transplant perfusion with near-infrared spectroscopy. *Nephrol Dial Transplant*. 2018;33(10):1863-1869. doi:10.1093/ndt/gfy116