

Anesthetic management in untreated Bland-White-Garland syndrome: a case report and literature review

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Abstract: Bland-White-Garland syndrome (BWGS) is a rare congenital coronary artery malformation. In adult patients with BWGS, left coronary artery is supplied by collateral vessels from dilated right coronary artery. When high-pressure coronary flow drains into the low-pressure pulmonary artery with little ventricle perfusion, it causes a “coronary steal”. In this study, a 53-year-old man with untreated BWGS receiving choledochotomy under general anesthesia was presented. The patient suffered from chronic biliary calculi, atrial fibrillation, complete left bundle branch block, and chronic heart failure. The anesthetic management for choledochotomy in this patient presented a special challenge. Moreover, relevant literature search was performed for all the case reports of BWGS published in PubMed and MEDLINE from 1990 to 2018. In addition, a summary of underlying pathophysiology and anesthetic implications of patients with BWGS was provided.

Keywords: anesthesia, Bland-White-Garland syndrome, left main coronary artery, right coronary artery, pulmonary artery, coronary steal

Background

Bland-White-Garland syndrome (BWGS), also known as anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA), is a rare congenital malformation affecting 1 in every 300,000 live births and represents 0.24–0.46% of all congenital cardiac diseases. It is characterized by high mortality due to chronic myocardial ischemia, heart failure, ventricular arrhythmias, and sudden death. If the adequate collateral circulation between right and left coronary artery exists, only about 10–15% of the patients survive to adulthood.^{1,2} However, in 80–90% of the BWGS cases, sudden cardiac death occurs within the first year of life. The survival depends greatly on an adequate collateral circulation between the left and right coronary arteries. Moreover, identification of dilated collaterals is often the first indication of pathology. Survival to adulthood is unusual, and patients over the age of 50 are rare.

Here, a rare case of a patient with BWGS will be presented, who also suffered from chronic biliary calculi. Although his cardiac function was in poor status and the risk of anesthesia was extremely high, choledocholithiasis was the only chance for him to survive. This case is rare because it describes the anesthetic management of a patient with BWGS, and as far as the author knows there are very few studies that focus on the anesthetic management of patients with BWGS, especially ones undergoing noncardiac surgery.

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Case presentation

A 53-year-old man, diagnosed with choledocholithiasis, was scheduled for a choledochotomy under general anesthesia in our hospital. Written informed consent has been obtained by the patient and case details and accompanying images are allowed to be published by the patient and our hospital.

The patient presented with a 10-month history of whole body yellowing and severe abdominal pain and survived a cardiac arrest 1 year ago. His medication included furosemide, spironolactone, and perindopril. The blood pressure was 110/65 mmHg, heart rate 72 beats/min, oxygen saturation 99%. Blood tests showed hemoglobin: 99 g/L, albumin: 35.7 g/L, APTT: 45.9 s, TT: 14.9 s, total bilirubin: 55.3 $\mu\text{mol/L}$, gamma-glutamyltransferase: 554 u/L, PRO-BNP: 3262 pg/mL. The electrocardiogram showed fibrillation with a ventricular rate of 96 beats per minute (Figure 1), complete left bundle branch block, occasional premature ventricular beats. Transthoracic echocardiography (TTE) showed left main coronary artery (LMCA) originating from the pulmonary artery (PA), systolic and diastolic blood flow signals at the origin of LMCA, slightly decreased left ventricular function (ejection fraction 52%), enlargement of the ventricle and atrium, moderate pulmonary hypertension with pulmonary artery pressure of 56 mmHg, expansion of the right coronary artery (RCA), and severe mitral and tricuspid regurgitation (Figure 2). Then, PA computed tomography angiography (CTA) and double source CT coronary angiography revealed



Figure 1 Electrocardiogram showed fibrillation, complete left bundle branch block, and occasional premature ventricular beats.

a congenital anomalous LMCA originating from the PA with no identified connection to the aortic root and a severely dilated RCA originating from the normal sinus of Valsalva along with abundant intercoronary collaterals circulation (Figure 3). The diagnosis of BWGS was confirmed. Due to the poor hepatic function, he could not wait for cardiac surgery. Furthermore, he refused to undergo cardiac surgery because of its high risk.

A temporary pacemaker was implanted prior to the induction of anesthesia. The arterial blood gas analysis was normal ($\text{pH}=7.39$, $\text{PaCO}_2=35$ mmHg, $\text{PaO}_2=88$ mmHg, $\text{HCO}_3=22.4$ mmol/L, $\text{HCT}=33\%$, $\text{K}=3.4$ mmol/L). The patient was put under general endotracheal anesthesia with steady intravenous induction. Fentanyl 8 $\mu\text{g/kg}$, atracurium 0.2 mg/kg, propofol 1.5 mg/kg, and midazolam 0.05 mg/kg were administered with syringe pumps separately, and the duration of intravenous administration was more than 10 mins. The infusion rate was slightly adjusted according to the BIS value, so that the bispectral index (BIS) value was slowly descended from 100 to 60, and then the patient was intubated. Ultrasound-guided transversus abdominis plane block and rectus sheath block were performed to reduce the pain stress response with 0.5% ropivacaine (0.5 mL/kg). Intraoperative transesophageal echocardiography (TEE) showed severely dilated RCA and the LMCA originating from PA, 16 mm distal to the pulmonic valve, with the retrograde flow draining from dilated LMCA into the PA, causing coronary “steal phenomenon” (Figure 4).

The anesthesia was maintained by sevoflurane supplied at 1 minimum alveolar concentration, and continuous infusion of 1% propofol with infusion rate around 15–20 mL/hr. Anesthetic depth was accurately monitored by BIS (50–60). Oxygen was given by pressure-controlled mechanical ventilation (airway pressure 13 cm H_2O , oxygen/air ratio 1:1, end-tidal CO_2 35–38 mmHg). The mean arterial pressure was maintained above 80 mmHg and the heart rate between 70 and 90/min, with cardiac function monitored by TEE. Norepinephrine 0.03–0.08 $\mu\text{g/kg/min}$ and dopamine 3–6 $\mu\text{g/kg/min}$ were required during the surgery.

The laparotomy lasted 2 hrs. The patient was extubated shortly after surgery and was transported to intensive care unit. His cardiac function remained stable and he was transferred to the general ward on postoperative day 1. He was subsequently discharged 7 days after surgery. A 6-month follow up showed the patient was convalescing smoothly.

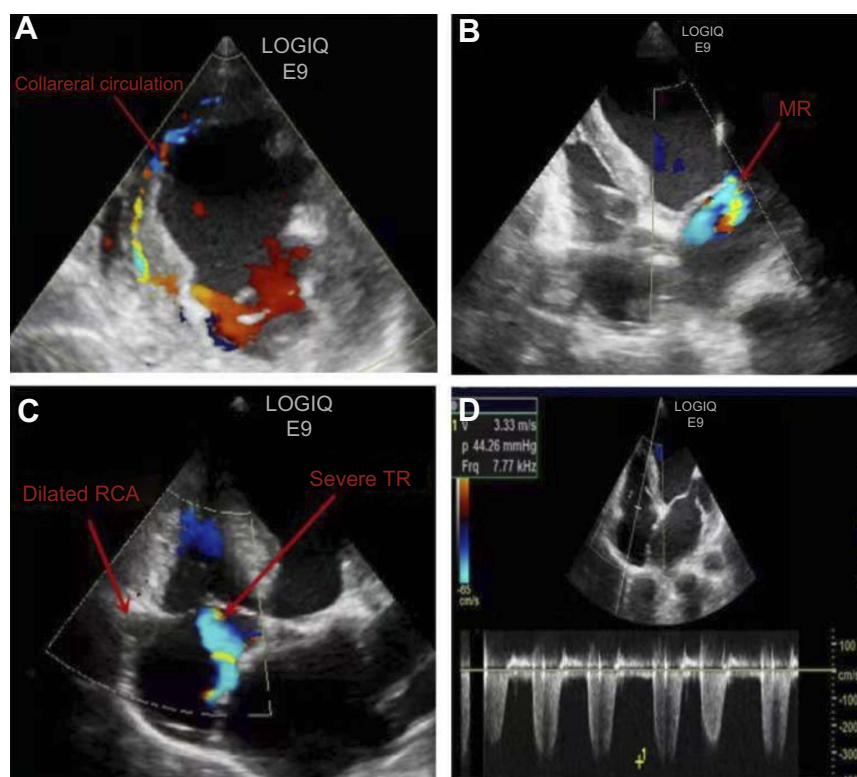


Figure 2 Transthoracic echocardiography. (A) Abundant collateral circulation. (B) Severe mitral regurgitation. (C) Dilated right coronary artery and severe tricuspid regurgitation. (D) Moderate pulmonary hypertension with pulmonary artery pressure of 56 mmHg.

Abbreviations: MR, mitral regurgitation; TR, tricuspid regurgitation; RCA, right coronary artery.

Literature review

Recent literature on anesthetic management of patients with BWGS were reviewed by conducting a thorough search on PubMed and MEDLINE of all the case reports of Bland-White-Garland syndrome published from 1950 to 2018. The keywords used included “Bland-white-Garland Syndrome”, “ALCAPA”, “coronary anomaly”, “anaesthesia”, “anomalous origin of the left coronary artery from the pulmonary artery”. The references of the selected literature have also been included. In addition, cases without definitive diagnosis of BWGS, reports only about surgical procedures, ultrasound or radiologic diagnosis were excluded.

Our literature search showed a total of 6 cases related to anesthetic management between 1996 and 2008. The characteristics of the reported cases of BWGS patients undergoing general anesthesia are listed in Table 1, and the clinical course of anesthetic management in Table 2. These patients were between the ages of 7 weeks and 68 years. Cardiovascular surgery with CPB took place in 5 cases (5/6), and noncardiac surgery took place only in 1 case (1/6). Suspicion and diagnostic modalities of BWGS were completed before surgery (5/6), during or after the

surgery (1/6). Five cases had symptoms of myocardial ischemia (5/6).

Discussion

The hemodynamic changes of BWGS are based on the pressure imbalance. Although the abnormal connection between coronary artery and PA exists during the fetal period, since there is a pressure balance between pulmonary and systemic circulation, the direction of blood flow in the left coronary artery (LCA) is still antegrade. After birth, the pressure of pulmonary circulation decreases rapidly. This “pressure imbalance” between the systemic and pulmonary circulation leads to a significant decrease of the antegrade blood flow and oxygen concentration in the LCA, leading to myocardial ischemia. Infant-type BWGS causes death of infants. If the lateral branches between the left and right coronary arteries can form rapidly, the blood of the RCA enters the LCA through the collateral branches, and the perfusion of the left ventricle can be improved. The mechanism of the high-pressure coronary flow draining into the low-pressure PA with little ventricle perfusion is called the “coronary steal”.⁷ Moreover, the perfusion of the left ventricle caused by

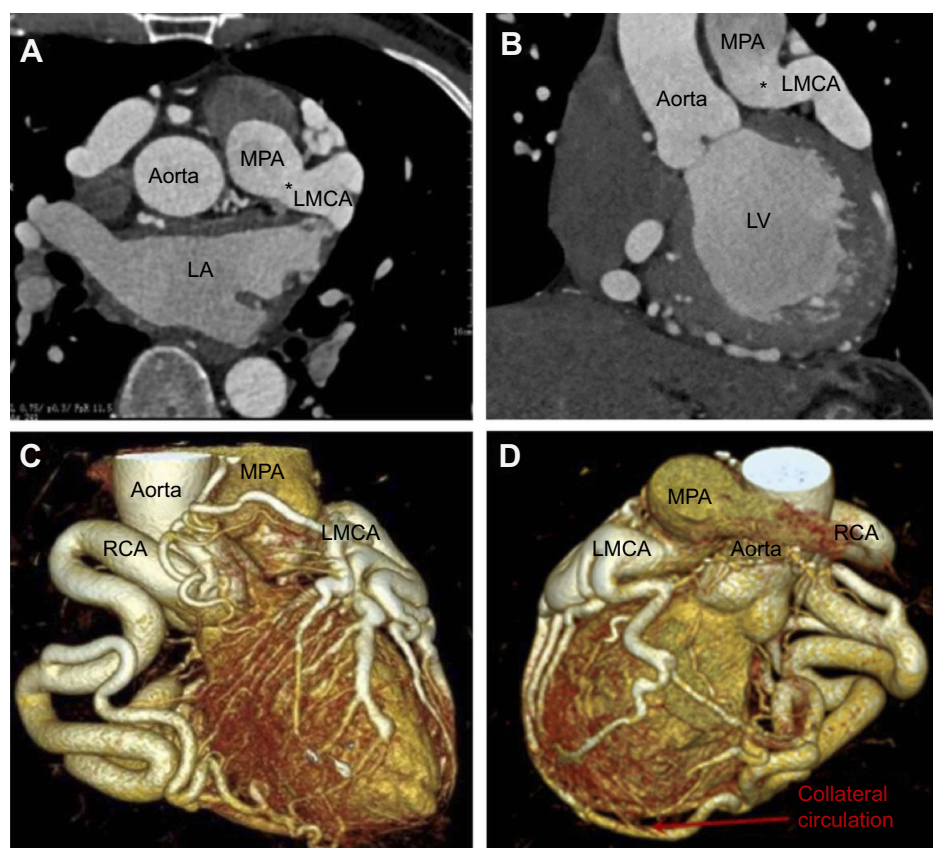


Figure 3 Coronary computed tomography angiography (CTA) clearly identifies the anomalous origin of the left main coronary artery (LMCA) from pulmonary artery (PA) (asterisks, **A** and **B**). The construction image of the double source coronary CTA shows the LMCA originating from the PA with no identified connection to the aortic root, a severely dilated right coronary artery (RCA), and the abundant intercoronary collaterals.

(**C**) Anterior position; (**D**) posterior position.

Abbreviations: LA, left atrium; RA, right atrium; RCA, right coronary artery.

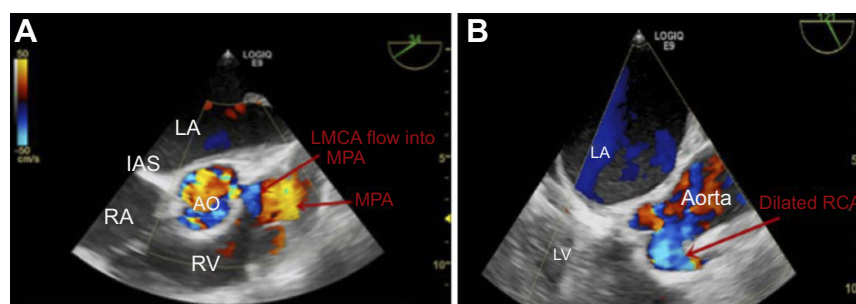


Figure 4 Intraoperative TEE. (**A**) Modified mid-esophageal aortic valve short view, color flow Doppler examination showed that the left main coronary artery (LMCA) origin was showed arising from pulmonary artery (PA), with the retrograde flow draining from dilated LMCA into the PA. (**B**) Modified mid-esophageal aortic valve long view showed severely dilated right coronary artery (RCA).

Abbreviations: RV, right ventricle; IAS, interatrial septum; LA, left atrium; RA, right atrium; TEE, transesophageal echocardiography.

this retrograde blood flow is still inadequate. Therefore, patients are at high risk of myocardial infarction, left ventricular dysfunction, mitral regurgitation, recurring ventricular arrhythmia, and even sudden death. Our patient had no obvious physiological abnormalities after birth and did not present with clinical symptoms throughout his

childhood. He has a right dominant coronary artery, which is an important factor for the survival of BWGS patients into adulthood, since this may be related to the increased blood oxygen supply from the right dominant coronary artery through the collateral vessels to the left coronary artery.

Table 1 Characteristic of reported cases of BWGS undergoing general anesthesia

Study	Age	Symptoms	Diagnostic methods	Surgery	Monitor
Stefan Kleinschmidt 1996 ³	5 months	Dyspnea, perspiration, tachycardia	TTE (EF16%), left heart catheterization, coronary angiography	LCA reimplantion, CPB	A; V
S. Michael Roberts 2016 ⁴	68 years	1 year progressively increasing dyspnea on exertion	TTE, left heart catheterization, CTA	LMCA reimplantion, CPB	PA catheter TEE
Cormac J Fahy 2011 ⁵	4 months	Resting tachypnea and diaphoresis	TTE (retrograde flow, EF<15%) no cardiac catheterization	LCA reimplantion, CPB	TEE no arterial catheter
Cormac J Fahy 2011 ⁵	7 weeks	Irritability, tachypnea	TTE	VSD repair CPB	A; V
Madan Mohan Maddali 2011 ²	18 years	Angina	TTE, CTA	LAD revascularized; OPCAB; no CPB	TEE
Anudeep Jafra 2017 ⁶	54 years	Unstable angina	TTE (EF40%), coronary angiogram	Mastectomy	TTE

Abbreviations: CPB, cardiopulmonary bypass; OPCAB, off-pump coronary artery bypass; A, arterial pressure monitoring; V, venous pressure monitoring; CTA, computed tomography angiography; LMCA, left main coronary artery; PA, pulmonary artery; TTE, transthoracic echocardiography; EF, ejection fraction; LCA, left coronary artery; LAD, left ascending artery; VSD, ventricular septal defect.

Table 2 Clinic course of anesthetic management

Study	Induction	Difficulties	Drug used to treat	Reasons	Follow up
Stefan Kleinschmidt 1996 ³	Fentanyl, 12 µg/kg etomidate, 0.2 mg/kg	Heart failure weaning from the CPB	Dopamine, 7 µg/kg/min Adrenaline, 2 µg/kg/min + noradrenaline 4 µg/kg/min dopamine 5 µg/kg/min	stimulation of a-R	Discharge:4th week Improved:7th month
S.Michael Roberts 2016 ⁴	stable	Unknown	Epinephrine 2 µg/min	Unknown	Discharge:7th day
Cormac J Fahy 2011 ⁵	sevoflurane gas induction, Pancuronium 0.1 mg/kg, fentanyl 2 µg/kg	15 min, HR decreased, cardiac arrest	CPR, defibrillation shock.	Inhalation induction; Etomidate not use	Discharge:4th day Improved:3 month
Cormac J Fahy 2011 ⁵	fentanyl 5 µg/kg, ketamine 2 mg/kg, pancuronium 0.1 mg/kg	On 3 rd day, developed tachypnea	An emergency cardiac catheterization; Emergency surgery	VSD repayment, PA flow decreased;	Discharge:5th day
Madan Mohan Maddali 2011 ²	Stable	Myocardial protection	Milirone; noradrenaline	Unknown	Discharge:6th day Improved:2nd week
Anudeep Jafra 2017 ⁶	Propofol, gas vecuronium 0.1 mg/kg	Unknown	100 mL fluid and 50 µg Phenylephrine was evaluated via TTE	Ventricular preload, function	Discharge:3rd day

Abbreviations: CPB, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; PA, pulmonary artery; TTE, transthoracic echocardiography; VSD, ventricular septal defect.

Coronary steal can be diagnosed by clinical symptoms, ECG, cardiac ultrasound, and angiography.^{8,9} Coronary steal causes complications as the result of decreasing myocardial perfusion, especially when there is an increased myocardial oxygen demand combined with reduced coronary perfusion, as well as a sudden drop in the pulmonary vascular resistance. This is why careful management is required during mechanical ventilation to prevent a sudden drop in pulmonary vascular resistance, which can be done by maintaining a reasonable arterial saturation without causing hyperoxia or hypocapnia.^{5,6} Subsequently, unintentional excessive ventilation should be avoided during mechanical ventilation to prevent the coronary steal. Diastolic blood pressure and diastolic duration are the two most important factors to determine the coronary blood flow. It is important to increase diastolic pressure and decrease heart rate in order to maintain coronary perfusion. A sharp increase of systemic vascular resistance should be prevented, as it would influence the forward output of the left ventricle, increasing mitral regurgitation.

This is a rare case about description of the anesthetic management of a patient with BWGS, especially ones undergoing noncardiac surgery. The difference or originality of this case compared to other case reports regarding anesthetic management for patients with BWGS syndrome is the concern about myocardial blood supply and coronary steal phenomenon throughout the whole anesthetic process. Anesthetic management was done to ensure adequate coronary perfusion and prevent coronary steal.

We searched both successful and unsuccessful cases that were relevant and organized our understanding of the underlying pathophysiologies and anesthetic implications with BWGS (summarized in Table 3). BWGS can be diagnosed by cardiac ultrasound, CTA, left heart catheterization, cardiac magnetic resonance imaging, and angiography, which were significant for anomalous LMCA originating from the PA and an enlarged right coronary artery.^{10–13} Genomics correlates of this rare disease are particularly missing, four mutations in three candidate genes potentially related to the ALCAPA phenotype, reporting the existence of mutations in CFTR, MEN1, and PKP2.¹⁴ The anesthetic technique influences myocardial ischemia with BWGS. Fentanyl, has vagotonic effects that sometimes result in severe bradycardia, combined with propofol the result is particularly hypotensive.¹⁵ Bolus injection for anesthesia induction was not adopted, because blood concentration would rise sharply, and then

the side effects of all the drugs are superimposed, leading to unwanted tachycardia and hypotension.^{16–19} Volatile agent for maintaining anesthesia is believed to have pleiotropic effects on protecting against myocardial ischemia, as well as maybe reduce the incidence of intraoperative awareness.^{6,20,21} The possible problems about the co-administration of inhalation and intravenous anesthetics for this patient are the decreases in systemic vascular resistance, which would decrease diastolic blood pressure and drop in left coronary artery blood flow from intercoronary collaterals.^{5,22} Less inhalation sevoflurane might have led to greater hemodynamic stability, so only 1% sevoflurane was used in this patient. Inotropes such as dopamine, dobutamine, and epinephrine should be used with extreme caution as they might result in tachycardia.²¹ Adequate dose of noradrenaline can increase coronary perfusion pressure by stimulation of alpha-adrenoreceptors.

In addition to routine monitoring, other equipment needs should be considered. Anudeep Jafra⁶ suggested the routine use of TTE in managing perioperative care when the underlying cardiac disease is rare, but the evidence base is insufficient. Anesthesiologists with a cardiac and echocardiography background can successfully perform TTE or TEE, which provides valuable new diagnostic information guiding changes in perioperative management.²³ In our case, echocardiography was performed to assess the preload and ventricular function.

For surgical procedures that may promote bradycardia, and particularly in patients with pre-existing severe cardiovascular disease (ie, NYHA C and D), cardiac pacing is indicated.²⁴ Since sudden death may occur in adult type BWGS, especially in patients with preexisting bundle branch block, the usage of temporary transvenous or transcutaneous pacing as a routine prophylactic measure is suggested, though it is an invasive procedure. In our patient, bradycardia did occur during the laparotomy, which may have been the result of anesthetics' vagal reflex, and when the heartbeat became slower than 70 per/min, the pacemaker was turned on.

Conclusion

Chronic ischemia in adult type BWGS leads to impaired myocardial function, which has potential for devastating outcomes. A successful management of anesthesia in an adult with diagnosed, but untreated BWGS was described in this study. Anesthetic management was done to ensure

Table 3 Anesthetic consideration and management of patients with BWGS

Preoperative evaluation	<p>Comprehensive preoperative evaluation can reduce complications</p> <ul style="list-style-type: none"> • Patient history History of angina, syncope, sudden cardiac arrest • Cardiac testing TTE, left heart catheterization, CTA, MRA
Pathophysiologic mechanism	<p>Understanding of pathophysiologic mechanism which runs through the whole anesthetic process</p> <ul style="list-style-type: none"> • Pressure imbalance between systemic and pulmonary circulation • Coronary steal and influence factors • Increase diastolic pressure to maintain coronary perfusion • Avoid tachycardia
Induction	<p>Goals: Ensure adequate coronary perfusion, use of a vasopressor, prevent coronary steal</p> <ul style="list-style-type: none"> • Fentanyl (has vagotonic effects that sometimes result in severe bradycardia) • Propofol (decrease SVR may reduce blood pressure and coronary perfusion) • Etomidate (provides a hemodynamically stable intravenous induction) • Midazolam • Succinylcholine (stimulates the emergence of different types of cardiac arrhythmias) • Volatile agent (with extreme caution)
Maintenance	<p>Goals: ensuring adequate anesthetic depth, adequate analgesia</p> <ul style="list-style-type: none"> • Intravenous • Volatile agent (with extreme caution)
Drugs	<p>Consideration of the agent's effect and side effect</p> <ul style="list-style-type: none"> • Inotropic support (increase myocardial oxygen consumption, should be used cautiously) Dopamine; dobutamine; Adrenaline • Vasoconstrictor Noradrenaline; Phenylephrine; Metaxalone • Esmolol (used primarily for tachycardia) • Antiarrhythmic drugs (Adenosine, Amiodarone)
Monitoring/equipment	<ul style="list-style-type: none"> • Temporary pacemaker; Defibrillator • Cardiac output monitoring • TTE/TEE (maybe considered to detect the status of preload or ventricular function) • Anesthesia depth • Temperature

Abbreviation: SVR, systemic vascular resistance; CTA, computed tomography angiography; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; MRA, magnetic resonance angiography.

adequate coronary perfusion, use a vasopressor, and prevent coronary steal. Comprehensive monitoring is suggested in perioperative management, as well as the routine use of pacemaker during surgery in managing this type of patients to prevent bradycardia and sudden cardiac arrest.

Disclosure

The authors report no conflicts of interest in this work.

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