Clinical Review

Complications of Cardiopulmonary Bypass From an Anesthesia Perspective: A Clinical Review

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Abstract

Description

Cardiopulmonary bypass (CPB) is frequently used for open heart surgery and other procedures that utilize temporary substitution or support of heart and lung function. While it is widely accepted as the predominant method to carry out these procedures, it is not without possible complications. CPB can be seen as the ultimate "team sport" as it includes and is dependent on contributions from multiple professionals including anesthesiologists, cardiothoracic surgeons, and perfusion technicians. In this clinical review paper, we examine possible complications of CPB, primarily from the perspective of the anesthesiologist, and how to troubleshoot them if they arise, which often requires the involvement of other essential team members.

Keywords

cardiopulmonary bypass; extracorporeal circulation/adverse effects; intraoperative complications; anesthesia

Introduction

Cardiopulmonary bypass (CPB) is commonly used for open heart surgery and other procedures that require temporary substitution or support of heart and lung function. Most cardiac surgery is performed with some version of CPB, and the tremendous success of these operations reflects how safe and effective the modern perfusionist and "heart-lung machines" have become. During CPB, venous blood is drained from the patient via a venous or outflow cannula, usually into a reservoir, and then flows through a heat exchanger and filter to control the temperature of the blood and remove larger particles. Next, the blood flows through an oxygenator where gas exchange takes place, and then is returned to the patient through an arterial or inflow cannula.[1] Extracorporeal membrane oxygenation (ECMO) is similar, but intended for longer periods of time and uses appropriately modified equipment.[2] For many open heart operations, an aortic cross-clamp is applied, separating the heart from the systemic circulation, and a high-potassium solution called cardioplegia is infused via the aortic root or the coronary sinus to achieve diastolic arrest of the myocardium.

CPB is carried out by certified clinical perfusionists who work closely with cardiac surgeons and the cardiac anesthesia team during open heart surgery. Indeed, the interaction of the cardiac anesthesiologist, the cardiac surgeon, and the perfusionist is truly one of the great ballets in modern medicine. Although there are many safeguards in place, including pre-operative checklists that were developed long before the surgical "time-out" became fashionable[3], there may be complications of CPB that the anesthesia team should be aware of and prepared to help resolve quickly. It is important to recognize that the life of the patient is literally in the hands of the surgical team, and a well-coordinated response to unusual circum-

stances can make an important difference. The purpose of this paper is to enumerate complications that can and do happen in the cardiac operating room related to CPB, and briefly describe potential responses by the anesthesia team that may aid in the resolution of the problem, and improve both patient safety and teamwork.

It is worthwhile to note that the physiology of CPB is not exactly the same as human heart and lung function.[4] For example, most CPB is carried out with non-pulsatile arterial blood flow. Although the vascular physiologic impact of laminar flow has been discussed for years, there is no clear evidence that pulsatile flow is superior.[5] The difference between mean arterial pressure and central venous pressure during CPB reflects the perfusion pressure for all organs. Accurate and reliable measurement of these values is essential for the safe conduct of CPB. One should bear in mind, although overall perfusion pressure may be within an acceptable range (60-80 mmHg), the distribution to renal, visceral, brain, and musculoskeletal vascular beds remains somewhat unpredictable.[6] Typically, at a mean arterial pressure less than 65 mmHg, the central nervous system's auto-regulatory mechanisms have reduced effectiveness at recruiting additional parenchymal blood flow.[7-8] Moreover, the impact of hemodilution, cooling and rewarming, and anesthetic effects may contribute to relative ischemia[9], despite adequate overall delivery of oxygen (Global Oxygen Delivery [DO2], is the total amount of oxygen delivered to the tissues per minute irrespective of the distribution of blood flow; a parameter measured continuously by many perfusionists). Even a perfectly executed CPB "run" can result in hematologic, inflammatory, micro-embolic, and immunologic injuries that become manifest subsequently in the cardiovascular intensive care unit.[10] These injuries are dose-dependent, meaning that the duration of CPB is something that the anesthesiologist should be aware of as a potentially modifiable risk factor.[11]

Mechanical and Technical Problems

Tubing or connectors may kink, crack, disconnect, rupture, be stepped on, compressed, or obstructed with thrombus, creating a situation that may require swift repair. If the mechanical problem interferes with the venous return to the pump or arterial inflow to the patient, periods of low flow can occur. If these periods are not brief, then hypothermia, packing the head in ice, providing an anesthetic that inhibits excitatory neurotransmitters, and perhaps the administration of steroids should be considered.[12] If the mechanical or technical problems impact the cardioplegia delivery circuit, hopefully, this can be discovered and addressed before the aortic cross-clamp goes on. If it occurs once the heart is arrested, options include additional cooling of the patient and the heart, direct administration of potassium or esmolol via the coronary arteries or coronary sinus (potentially passing these drugs directly from the anesthesiologist to the surgical field, while the perfusionist is fixing the pump), or releasing the aortic cross-clamp if possible and allowing the heart to be re-perfused with blood.[13]

The venous reservoir, whether "open" or "closed" to the atmosphere, may be the first place that thrombus is noted. It is worthwhile to inspect this, especially at times when the activated clotting time (ACT) may be subtherapeutic or procoagulant agents such as plasma or platelets have been administered while CPB is taking place.[14] If vacuum-assisted venous drainage (with a closed circuit) is used, the venous system may become over-pressurized, creating too much negative pressure, leading to worse venous drainage, or an implosion of the venous reservoir.[15] The anesthesiologist may be able to observe, by direct inspection or with echocardiography, whether venous cannulae are appropriately placed and whether the heart is adequately drained. It could be helpful to remind the team that the repositioning of the venous cannula, additional venting of the heart, and less vacuum assistance may actually improve venous drainage.

The centrifugal head, which pumps the blood using centrifugal force, can crack, or its magnets can de-couple, leading to pump failure.[16] The oxygenator itself may fail during CPB (estimated to occur in about 1 in 4000 cases, due to structural damage or manufacturing defect). This can be noted initially as rising partial pressure of carbon dioxide, then falling partial pressure of oxygen in the blood.[17] A crack in the heat exchanger may lead to blood in the heat-

er-cooler (water lines), or unexpected rising levels in the venous reservoir.

The oxygenator can also be a place where the clot is noticed, particularly when there is inadequate anticoagulation, the patient has a hypercoagulable condition, or there is a particularly long CPB episode.[18] The patient with cold agglutinins presents a special problem, and sludging of blood in the oxygenator for those patients can be treated by assuring therapeutic anticoagulation and avoidance of temperatures below the patient's thermal amplitude, if known.[19] For example, tepid blood cardioplegia delivered more frequently is a good solution that does not require much alteration in usual techniques or protocols.

The anesthesia team should be prepared to support the patient and assist the perfusionist if an emergency replacement of the centrifugal pump, integrated oxygenator, or heat exchanger is required.[20] The perfusionist is also heavily dependent on anesthetic monitoring equipment during CPB, including properly functioning cerebral oximetry, an arterial line for blood pressure monitoring, BIS monitoring, and Foley catheter drainage.

Human error is among the most common causes of malfunction of the bypass circuit.[21] For example, oxygen and anesthesia gas lines may not be properly connected to the oxygenator. The attentive cardiac anesthesiologist might have some familiarity with how these gas lines are attached in their particular operating room. In another example, tubing may be connected to the circuit in a manner that allows it to kink, causing any number of issues. Bearing in mind that this circumstance might be extremely stressful to the perfusionist, the capable anesthesiologist can quietly inspect and "trouble-shoot" the circuit along with the perfusionist, to more quickly resolve the issue.

Cannulation and Potential Problems

Adequate outflow and inflow, from and to the patient, depends on well-placed cannulae and connections. An uncommon error is switching the arterial and venous lines from the pump, which should be noticed immediately, before significant arterial blood has drained back towards the pump.

Problems with aortic cannulation include a cannula that is not in the true lumen of the aorta. This can lead to dissection, which can be noted by a transesophageal echocardiogram.[22] To prevent this, the perfusionist checks for pulsatile blood pressure in the arterial line and correlates it with the arterial catheter before a test infusion is given. The aortic cannulation site should be inspected for calcification, not just by palpation by the surgeon, but also with the transesophageal echocardiogram (TEE), or better still, epicardial ultrasound imaging. Aortic cannulation is less likely to be malpositioned given its intraluminal part is designed to be very short. When peripheral cannulations from femoral, axillary, or subclavian sites are required, the positioning of the guidewire should be confirmed to be in the true lumen with TEE. Echo guidance should be provided to advance the cannulae to the correct position in the ascending aorta. The aortic arterial cannula can also be misdirected. If, for example, the tip of the cannula is oriented into the innominate artery, there may be hyperperfusion in that vascular bed (high pressure in a right radial artery catheter; eventually engorgement of the right side of the head) with hypoperfusion of the remainder of the body (low pressure in left-sided and femoral arterial catheters; unequal cerebral oximetry). Similarly, direct axillary artery cannulation can miss the true lumen, again resulting in dissection and inadequate flow to the body. A kink in the artery, or in a graft connected to it, can also result in high resistance to arterial in-flow. If an axillary artery cannula is placed too deeply, it may become obstructed upon clamping of the innominate artery during periods of circulatory arrest. Similarly, femoral artery cannulation can result in dissection of the vessel, with inadequate flow to the body.[23] "Through and through" injury of that vessel may lead to retroperitoneal bleeding, which will manifest as falling blood volume and hematocrit.[24] If the femoral artery is used for initial cannulation to treat aortic dissection, the chances of persistent dissection in the non-replaced aorta are increased if CPB is resumed through that cannula after a period of circulatory arrest.[25]

Venous cannulation is usually achieved with a dual or triple-stage cannula via the right atrium. If a cannula is placed too deeply, it can be wedged in the inferior vena cava, resulting in

poor venous drainage. In addition, inferior vena cava venous cannulae can further be misplaced in the hepatic vein, compounding diminishing venous return. If the cannula is not deep enough, exposing drainage holes to the atmosphere, air will be directed towards the pump and can result in “air lock”, a complete cessation of venous drainage. A venous cannula that is too big can cause collapse of the inferior vena cava and right atrium around the cannula and manifest as "chatter" in the venous line with poor venous drainage and congestion of the lower part of the body. This venous hypertension can lead to a decrease in perfusion pressure and subsequent renal and visceral ischemic injury.[26] A similar problem can occur with bicaval cannulation; the inferior vena cava cannula should not be too large or too deep. The TEE is not very helpful for the placement of these venous cannulae. However, TEE guidance is extremely important when femoral venous cannulation is carried out.[27] In order to be properly placed, this long cannula, with multiple side holes, must end in the superior vena cava. If the guiding wire, and therefore the tip of the cannula, is not engaged in the superior vena cava (SVC), perforation of the heart or very poor venous drainage becomes possible.

Cardioplegia cannulae are usually placed in the aortic root or in the coronary sinus. Misplacement of the aortic root cannula can cause aortic dissection, again notable on TEE. Echocardiography can also be used to confirm or guide the placement of the coronary sinus catheter. Problems with that cannula include perforation or rupture of the coronary sinus, or inadequate depth of cannulation leading to inadequate cardioplegia delivery. In open aortic cases, coronary ostial perfusion catheters may be used, and these can cause dissection of the coronary arteries themselves. This may not be manifest until attempts to wean from CPB reveal ischemic myocardial dysfunction and electrocardiographic (EKG) changes.[28]

Embolization

Air in the circuit can be a problem during CPB.[29] This can range from small bubbles visualized by careful inspection of the venous lines to a massive air embolus into the patient. Air entering the venous return side of the circuit usually occurs due to the misplacement of cannulae, surgical injury of the atrium or veins, excessive negative pressure in the circuit, or an inadvertent opening such as uncapped central venous catheters. As previously mentioned, a large amount of venous air can result in “air-lock” and impeded venous return. While filters in the circuit are effective in removing most bubbles, a large amount of venous air can result in air in the arterial line. Obviously, this can have disastrous effects on the brain and other organs, resulting in seizure and other ischemic neurological injuries. The appropriate response to a large amount of venous air is to place the patient in Trendelenburg position, transiently reduce arterial inflow while maintaining some blood in the venous reservoir, and quickly identify the source of the air. If air has been observed to enter the arterial system, the anesthesia team should be prepared to place the patient in Trendelenburg position, inspect with TEE, and assist with de-airing maneuvers.[30] Adequacy of de-airing should always be confirmed by TEE before weaning the patient off CPB, especially in procedures where the surgeon opened the cardiac cavities, as required in valve replacements. It is not unusual to have a transient ischemia post-pump, especially in the right coronary artery (RCA) distribution, since the RCA ostium is superior in a supine patient, where the air rises. One may have to re-initiate CPB if raising the pressure with pressors does not remove the air.

Small particulate matter may also embolize during CPB, perhaps entering the coronary circulation. This may not manifest until weaning from CPB, when ischemic electrocardiogram (EKG) changes and myocardial dysfunction may appear. The anesthesia team can aid with TEE examination (ie, reporting specific wall motion abnormalities), administration of nitroglycerin while on CPB, and support with inotropes as needed.

Neurologic Injury

The central nervous system may be injured during CPB due to inadequate delivery of oxygen, hypotension, periods of circulatory arrest (especially without cerebral perfusion), or embolization as described above.[8,31] Arterial emboli may be thromboemboli, atheroemboli, or air emboli. Major neurologic complications include stroke, neuropsychiatric abnormali-

ties such as cognitive dysfunction, spinal cord injury, and sometimes peripheral neuropathy.[32] The risk increases with patient age and underlying cerebrovascular disease.[33] An important monitoring tool is near-infrared spectroscopy (NIRS), which monitors cerebral oxygen saturation and provides early warning about the adequacy of oxygen delivery to the brain. The possible therapies and preventive measures for neurologic complications after CPB include the maintenance of adequate mean arterial blood pressure and the avoidance of intraoperative cerebral hypoperfusion. The anesthesiologist can also aid with careful pre-cannulation echocardiographic assessment, forewarning the team about heavy atherosclerotic burden.[34]

Anticoagulation, Thrombosis, and Hematologic Injury

In order for blood to pass safely through the CPB circuit without excess activation of coagulation or inflammatory systems, therapeutic anticoagulation, usually with heparin, must be achieved.[35] Different institutions have different tests and thresholds for measuring anticoagulation, but the most common is ACT, with point-of-care testing in the operating room. The anesthesia team must be familiar with the protocol used in their operating room and be prepared to treat subtherapeutic anticoagulation. A complete discussion of heparin resistance and the appropriate responses is beyond the scope of this paper, but as we have already mentioned, a high level of monitoring and inspection is required whenever anticoagulation is not within the therapeutic range.[36]

CPB also induces significant hemostatic changes.[37] Contact of blood with non-endothelial surfaces of the CPB circuit induces an intense pro-coagulant and inflammatory response, which results in coagulopathy due to platelet activation and dysfunction, initiation of the coagulation cascade, and decreased levels of circulating clotting factors. Thrombin generation and the activation of fibrinolytic pathways result in further consumption of platelets.[38] Both pro- and anti-coagulant proteins, especially fibrinogen and antithrombin, are generated during CPB.[39]

In addition, the priming solution of the CPB circuit results in hemodilution that exacerbates anemia and may worsen coagulopathy and bleeding. Due to these derangements in hemostasis, perioperative blood management strategies are required to successfully reduce transfusions during and after cardiac surgery with CPB.[40] It is important that the anesthesiologist be invested in blood management. Blood product administration should be guided by point-of-care hemoglobin and hematocrit testing, hemodynamic monitoring including EKG, and communication with operating room colleagues. Viscoelastic testing may be of benefit, and can also be the point of care in the cardiac operating room. Reversal of the anticoagulant should be communicated clearly and administered at an agreed-upon time. Hypothermia and metabolic abnormalities should be corrected prior to separation from CPB to prevent coagulopathy and hemodynamic instability.

Acute Kidney Injury

Acute kidney injury (AKI) may arise from a variety of causes, including intraoperative hypotension, postoperative cardiac complications that impair renal perfusion, hemolysis, atheroemboli, poor glucose control, or exposure to contrast media.[41] Reduced renal function due to transient hypoperfusion usually resolves within a few days, but some patients develop more severe and persistent kidney injury with a requirement for dialysis. In addition to baseline kidney dysfunction, preoperative risk factors for AKI include New York Heart Association functional class IV, valve surgery, peripheral arterial disease, emergency surgery, obesity, diabetes, and the need for a preoperative intra-aortic balloon pump. Perioperative factors such as anemia, red blood cell transfusions, hyperglycemia, and prolonged CPB are also associated with the development of AKI.[42]

Identifying that a patient is at risk is the first step in preventing AKI. Optimizing volume status with intravenous (IV) fluids, optimizing cardiac output, and ultimately renal blood flow and avoiding nephrotoxins are important contributions of the anesthesiologist, in conjunction with the surgical team, in mitigating AKI. Discontinuation of angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), discontinuation of SGLT2 inhibitors, avoidance of hyperglycemia,

and careful monitoring of urine output are additional measures the team can make to avoid AKI.[43] Pharmacologic agents such as diuretics, dopamine, or fenoldopam offer conflicting results in the prevention of CPB-associated AKI.[44]

Perhaps the best data regarding the reduction of postoperative AKI point towards perioperative hemodynamic optimization.[45] This optimization can be initiated preoperatively, as well as intraoperatively and postoperatively, suggesting that ischemic injury can be prevented or effectively treated with prompt reperfusion. The preferred choice of IV fluids for volume expansion, such as crystalloid, bicarbonate solution, or colloid, is unclear.[46]

Pulsatile perfusion, with or without the use of an intra-aortic balloon pump, has not been proven to reduce the incidence of perioperative AKI.[47] Furosemide-induced diuresis and preservation of intravascular volume through an automated matched hydration system has been tested in randomized, controlled trials with mixed results in the prevention of radiocontrast-induced nephropathy and CPB-associated AKI.[48] More adequately powered studies are needed to better understand the role of furosemide-induced diuresis in this setting.

Lung Injury

Airway obstruction, bronchospasm, and pulmonary edema are relatively rare but potentially devastating pulmonary problems encountered in the patient undergoing CPB.[49] The anesthesiologist should be aware of any difficulties in ventilating the lungs before attempting to wean from CPB. The surgeon can help confirm that both lungs are expanded with positive pressure ventilation, and appropriate lung inflation should be confirmed. The differential diagnosis of poor lung inflation and/or deflation includes airway obstruction due to a kinked endotracheal tube, tracheal or bronchial obstruction (eg, mucus plug), airway compression by the TEE probe, right mainstem intubation, or pulmonary aspiration.[50] Blood in the airway is uncommon but may occur due to pulmonary parenchymal injury, pulmonary artery rupture caused by a pulmonary artery catheter, or injury during pulmonary thromboendarterectomy.[51] An initial step for the evaluation of airway obstruction is to pass a flexible suction catheter into the endotracheal tube. If the obstruction does not resolve after aspiration of secretions, bronchospasm is likely and should be treated.[52] In some cases, flexible bronchoscopy may be necessary.

Bronchospasm during weaning from CPB may be due to an allergic drug reaction (eg, protamine) or transfusion reaction (eg, blood products, plasma expanders), inadequate anesthesia, or pre-existing asthma or chronic obstructive pulmonary disease. Bronchospasm is largely managed by administering broncho-dilating pharmacologic agents.[53] The depth of anesthesia is also evaluated because bronchospasm may result from inadequate anesthesia. First-line therapies are inhaled beta-2 agonists such as albuterol or low doses of IV epinephrine. Also, H1 and H2 antihistamines are administered to reverse the effects of inflammatory mediator release.[54] In severe cases, a steroid such as methylprednisolone or hydrocortisone is administered to decrease airway swelling and reduce the likelihood of recurrence.[55]

Cardiogenic pulmonary edema may be due to pre-existing or new onset heart failure, exacerbated by additional fluid administration and decreased serum oncotic pressure during CPB.[56] Hemoconcentration during and after CPB and diuresis minimize the likelihood of this complication. Noncardiogenic pulmonary edema may be caused by protamine reaction, transfusion-related acute lung injury, or prolonged CPB duration.[57] Under these circumstances, noncardiogenic pulmonary edema is due to the sequestration of neutrophils in the pulmonary capillaries, elevation of lysosomal enzyme activity, localized inflammatory response, and ultimately increased capillary permeability.[58] Treatment involves the administration of a diuretic such as furosemide.[59] In patients with severely elevated pulmonary artery pressure, continuous inhalation of nitric oxide or epoprostenol is reasonable.[60] In rare cases of severe pulmonary edema, ECMO is necessary to temporarily replace lung function.[61]

Mesenteric Injury

Many of the above-mentioned complications can injure the abdominal viscera, including the intestines.[62] These injuries may not be manifest until sometime after the initial operation.[63] The

role of the anesthesiologist in identifying and treating this problem is therefore limited. Attention to perfusion pressure, DO2, lower body venous drainage and congestion, and kidney function are all important in mitigating mesenteric injury.

Conclusions

CPB is an important technique that allows safe and effective open-heart surgery. It comes with some potential costs, however, and complications must be anticipated, minimized, and responded to adroitly to optimize outcomes. While many of the complications of CPB are beyond the anesthesiologist's direct control, a well-informed and prepared anesthesia team can be extremely helpful in resolving these complications. Open communication and careful coordination with the perfusionist and cardiovascular surgeon are paramount in this ultimate "team sport".

Conflicts of Interest

The authors declare they have no conflicts of interest.

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