The Student Section

Hypothermic Cerebral Perfusion: A Battlefield Against Neurologic Injuries In Patients On Cardiopulmonary Bypass

Weibin Liu

Cardiovascular Science Master Program,

Class of 2018

Midwestern University

Glendale, Arizona

Cardiac surgery, along with the development of cardiopulmonary bypass (CPB), significantly improve the capability of restoring patients' cardiac function and quality of life. Nevertheless, neurologic complications have been a source of concern since the inception of cardiac surgeries.[1] The incidence of major neurologic morbidity related to cardiac surgery falls between 1% and 6%, and up to 9% of selected patient populations may have shown clinical evidence of stroke.[1] In this student viewpoint essay, I will present a brief review of cerebral perfusion (CP) and perioperative risk factors, and various CP techniques. At the end, new paradigms of CP and hypothermia management are discussed.

Under resting physiologic conditions, 14% to 20 % of the cardiac output perfuses the brain tissue. Regulation of cerebral oxygen delivery (CDO_2) or cerebral blood flow is coupled with the cerebral metabolic rate of oxygen consumption ($CMRO_2$).[1, 2] In terms of perfusion pressure, the brain is a distinct organ. For most organ systems, perfusion pressure depends on the mean arterial pressure (MAP) versus central venous pressure gradient. In contrast, CP is dependent on the pressure gradient between MAP and intracranial pressure.[3]

With improved perioperative management and post-operative outcomes, the proportion of geriatric patients undergoing cardiac surgeries continues to grow.[4] Beyond the risk and physiologic stress factors on bypass, age-related pathophysiologic changes can exaggerate the incidence of neurologic complications post cardiac surgery and CPB procedures. Metabolic syndromes, including hypertension, hyperlipidemia, obesity, diabetes mellitus, and impaired glucose tolerance, are contributing factors for the development of cardiac surgical diseases and perioperative complications including neurologic injuries.[5] Previous stroke and abnormal serum albumin are identified as independent variables associated with delirium after cardiac surgery in elderly (≥ 60 years of age).[4]

With the goal to ensure adequate intraoperative systemic perfusion, CPB procedures impose non-physiologic stress to the whole body and bear risks to compromise CP. After initiation of CPB, acute hypothermia and rapid hemodilution potently disturb cerebral metabolism and oxygen delivery.[1] New balances between $CMRO_2$ and CDO_2 change dynamically on bypass. $CMRO_2$ is majorly determined by the tissue temperature in the brain, while CDO_2 is affected by hemoglobin concentration, pump flow and MAP.[1] Moreover, embolization, systemic inflammatory response, cerebral hyperthermia during the rewarming stage and extended ischemic time can contribute to neurologic damages. Furthermore, postoperative patient care, namely management of coagulopathy, control of hyperthermia, need for extracorporeal membrane oxygenation (ECMO) or assist device support, duration of hospital stay, etc., can have profound impact on neurologic outcomes.[1] Refinement in perioperative care, anesthetic management and surgical techniques over the past few decades have largely contributed to improved patient neurologic outcomes.[1]

Given the physiologic stress of cardiac surgery, CPB and incidence of

Continued from Page 5

neurologic injury, assessment of adequacy of CDO_2 remains a persistent point of care during CPB. Some currently-used techniques include near-infrared optical spectroscopy (NIRS), measurement of venous oxyhemoglobin saturation at the jugular bulb, transcranial Doppler and bispectral EEG analysis (BIS).[1]

During complex adult cardiac surgeries usually involving aortic arch, different techniques have been employed for optimal CP. Such techniques include deep hypothermic circulatory arrest (DHCA), antegrade CP (ACP) and retrograde CP (RCP). Hypothermia is the principal neuroprotectant for straight DHCA. Intermittent CP, selective ACP and RCP are used to reduce the chances or degrees of neurological injury. ACP is achieved by direct cannulation in the innominate, carotid or axillary arteries. ACP is usually conducted with a flow rate range at 10-20 ml/kg/min to maintain a perfusion pressure at 50-70 mmHg at the right radial artery.[2] During DHCA, RCP delivers oxygenated blood into the snared superior vena cava (SVC) at a flow rate of 150 to 700 ml/min. The mean RCP pressure of 25 mmHg, up to 40 mmHg, has been shown to be safe.[2]

There is still no consensus on the optimal CP methods despite multiple studies with varied degrees of clinical efficacy.[6] The retrospective findings of these studies, plus a patient population with greater surgical risk factors and preoperative neurologic morbidity rates, further complicates the comparison.[6] DHCA, with patient core temperature below 20°C, is a globally accepted technique with CPB for adult aortic arch repair. DHCA is generally recognized as safe for short procedures. Increased stroke and death rate has been associated with duration of DHCA greater than 45 minutes and 65 minutes respectively.[11]

In contrast to straight DHCA, both ACP and RCP allow continuous cerebral cooling, supply of oxygenated blood and washout of metabolites.[2] ACP allows independent control of blood temperature to the cerebral and systemic circulation with potential risk for embolization and extra cannula. The RCP approach is capable of flushing potential air emboli from cerebral circulation. RCP avoids additional manipulation of the arch vessels, therefore reducing procedure time and potential risk of dislodging atherosclerotic emboli. However, the retrograde cerebral perfusion flow limit remains unclear, complicated by significant extra-cranial collateral flows.

In addition to DHCA, promising results using ACP with "moderate" hypothermia (25°-28°C) have been reported.[7, 8, 13] Preventza O, et al. reported that aortic arch surgery patients of moderate hypothermia with ACP for >30 min had significantly improved long-term survival rate compared with the deep hyperthermia group.[13] Avoidance of deep hypothermia, prolonged perfusion time for warming and cooling is one of the major advantages of this strategy. Hypothermic circulatory arrest (HCA)/RCP and ACP provide comparable clinical outcomes with regard to mortality and stroke rates, but HCA with RCP resulted in a higher incidence of prolonged intensive care unit stay.[9] ACP might be preferred as the brain protection method for complicated aortic arch procedures.[10]

In a small scale survey published in 2010 of aortic arch surgeons at several academic medical centers in the United States (n=16), 50% stated they prefer selective ACP and 38% used some combination of ACP and RCP.[11] The international aortic arch surgery study group proposed new paradigms for adult aortic arch repair as "mild hypothermia without circulatory arrest," further extending the gradual return to normal physiology in the conduct of aortic arch repairs.[12] Considering the nature of HCA and the diversity of clinical cases, algorithm-based individualized care plan of cerebral perfusion and circulatory arrest should be developed. Furthermore, improved understanding of CP under hypothermic conditions is required to embrace the practice of goal-directed perfusion targeting neurologic complications.

References

1. Gravlee GP, Davis RF, Hammon J, Kussman B. Cardiopulmonary Bypass and Mechanical Support: Principles and Practice. Fourth Edition. Wolters Kluwer. 2016. Ch. 15: 385-417.
2. Ghosh S, Falter F, Perrino AC. Cardiopulmonary Bypass. Second Edition. Cambridge Medicine. 2015. Ch. 12: 186-202.
3. Hill L, Gwinnutt C. Cerebral Blood Flow and Intracranial Pressure. http://www.frca.co.uk/Documents/170907%20Cerebral%20physiology%20I.pdf Retrieved on April 5th, 2017.
4. Castillo JG, Silvay G, Chikwe J. Cardiac anesthesia and surgery in geriatric patients: epidemiology, current surgical outcomes, and future directions. *HSR Proc Intensive Care Cardiovasc Anesth.* 2009;1(2):6-19.
5. Malik S, Wong ND, Franklin SS, et al. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in

Continued on Page 10

Continued from Page 9

United States adults. *Circulation.* 2004;110:1245-1250.
6. Stoicea N, Bergese SD, Joseph N, et al. Pro: Antegrade/Retrograde Cerebral Perfusion Should Be Used During Major Aortic Surgery With Deep Hypothermic Circulatory Arrest. *J Cardiothorac Vasc Anesth*. 2016; 70(16):30418-30419.
7. Salazar J, Coleman R, Griffith S, et al. Brain preservation with selective cerebral perfusion for operations requiring circulatory arrest: protection at 25 degrees C is similar to 18 degrees C with shorter operating times. *Eur J Cardiothorac Surg*. 2009;36(3):524-531.
8. Algarni KD, Yanagawa B, Rao V, et al. Profound hypothermia compared with moderate hypothermia in repair of acute type A aortic dissection. *J Thorac Cardiovasc Surg.* 2014;148:2888-2894.
9. Okita Y, Miyata H, Motomura N, et al. A study of brain protection during total arch replacement comparing antegrade cerebral perfusion versus hypothermic circulatory arrest, with or without retrograde cerebral perfusion: analysis based on the Japan Adult Cardiovascular Surgery Database. *J Thorac Cardiovasc Surg*. 2015;149(2):S65-S73.
10. Poon SS, Estrera A, Oo A, et al. Is moderate hypothermic circulatory arrest with selective antegrade cerebral perfusion superior to deep hypothermic circulatory arrest in elective aortic arch surgery? *Interact CardioVasc Thorac Surg*. 2016; 23(3): 462-468.
11. Stein LH, Elefteriades JA. Protecting the brain during aortic surgery: an enduring debate with unanswered questions. *J Cardiothoracic Vascular Anesthesia*. 2010; 24(2): 316-321.
12. Gutsche JT, Ghadimi K, Patel PA, et al. New frontiers in aortic therapy: focus on deep hypothermic circulatory arrest. *J Cardiothorac Vasc Anesth*. 2014; 28 (4):1159-1163.
13. Preventza O, Coselli JS, Akvan S, et al. The impact of temperature in aortic arch surgery patients receiving antegrade cerebral perfusion for>30 minutes: How relevant is it really? *J Thorac Cardiovasc Surg*. 2016 (16):31684-31691.