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Commentary: Everyone is winging it, some just do it more confidently

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In the current issue of the *Journal*, Mavroudis and colleagues¹ from Philadelphia present an elegant study in which they try to determine the effect of various perfusion strategies on cerebral blood flow, oxygenation, mitochondrial function, and cellular injury. For that purpose, they assign 41 piglets to 5 different groups who underwent sham operation (n = 3), cardiopulmonary bypass (CPB) with normothermia (n = 8) or with hypothermia to 18°C (n = 10), deep hypothermic circulatory arrest (DHCA) at 18°C for 40 minutes (n = 10), and with selective antegrade cerebral perfusion (SACP) at 10 cc/kg/min for 40 minutes (n = 10). Novel noninvasive spectroscopy was used to assess cerebral blood flow and oxyhemoglobin saturation (supply) and oxygen extraction fraction (demand). Developing metabolic byproducts were analyzed with cerebral microdialysis from samples that were collected at specific intervals from the left frontal cortex. Laser Doppler also provided invasive cerebral blood flow measurement. Mitochondrial respiration and reactive oxygen species generation were assessed following animal sacrifice. The results are interesting and are well discussed in the aforementioned article and nicely summarized in the accompanying graphical abstract. In summary, compared with sham operation, normothermic CPB wasn't associated with major disturbances in cerebral perfusion and supply/demand ratio, DHCA was associated with decreased supply/demand ratio and with mitochondrial dysfunction and cellular injury, SACP stabilized the increased demand with better supply/demand ratio compared with DHCA and less mitochondrial

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CENTRAL MESSAGE

Much work is still needed to identify the optimal perfusion strategy for brain protection given the great practice variations, multitude of involved factors, and various mechanisms of cellular injury.

dysfunction and cellular injury, and finally hypothermic CPB was associated with increased supply/demand ratio and evidence of mitochondrial injury, likely from oversupply.

Aortic arch surgery represents an important share of congenital cardiac surgery, and brain protection during these procedures continues to be a subject of great interest to surgeons and researchers.^{2,3} There is a great deal of practice variation among surgeons and institutions, much of which seems to be based on preference, without clear evidence to support one strategy over another.²⁻⁵ First, there are variations in the perfusion techniques used during cooling, including flow rate, acid-base management strategy, speed and degree of cooling, hematocrit level, use of vasodilators, use of surface cooling or systemic medications, and others. In addition, there are variations in brain perfusion strategies during arch surgery, including DHCA alone, SACP, SACP and descending aortic perfusion (using various techniques), and even SACP with heart and descending aortic perfusion. Although SACP is the most commonly used strategy, there are great variations among surgeons in terms of systemic cooling (varying between 18°C and normothermia), cannulation strategy (graft vs direct, innominate artery alone vs with the left common carotid) and most importantly flow rate (10-80 cc/kg/min, with some advocating normal perfusion when descending aortic perfusion is applied as well). The adaptation of body

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organs to perfusion flow and pressure is not well understood, and the assumption that organs would autoregulate the flow when multiple cannulas are inserted to perfuse the brain, heart, and distal body is not well founded. In addition, there are variations in the modes of neuromonitoring and whether that should include spectroscopy of both hemispheres (given the incompleteness of the circle of Willis in many patients), or also should include somatic spectroscopy, electroencephalogram, cranial Doppler, etc.⁶ For sure, there are also variations in anesthesia management and differences in the tactics and vigilance to alter perfusion strategies in response to abnormalities in brain monitoring during arch surgery. The foregoing, in addition to abundant perioperative factors that could affect cerebral blood flow, show why illustrating advantages of one strategy over another is so complicated.⁷⁻⁹

This lack of consensus and persistent knowledge gaps with regard to brain protection and optimization of cerebral perfusion and metabolism during aortic arch surgery make it seem like we are forever “winging it.” However, this is not new to science and medicine; we constantly find ourselves in unfamiliar situations and are forced to adapt to these situations by making new decisions based on the information available at that time. This adaptive approach balanced with existing expertise is the basis of innovation and creation of new knowledge. This excellent work by Mavroudis and colleagues serves to raise more questions than to provide answers that bridge our knowledge gap in that topic. Nonetheless, several important messages can be derived from this work.

First, ongoing metabolic requirement during DHCA results in significant mismatch between cerebral blood flow (lacking in DHCA) and demand, with subsequent significant disruption to cerebral hemodynamics, cellular injury, and mitochondrial function. Irrespective of the lack of demonstrable neurodevelopmental advantage, I, along with many others, have experienced a significant decrease in operative mortality with the use of SACP during arch reconstruction and Norwood operations. This, in addition to the data presented by Mavroudis and colleagues, makes the argument for using DHCA alone during arch surgery very weak.

Second, although SACP seems to improve the mismatch between supply and demand, with consequent reduced cellular injury and improved mitochondrial function, there

is evidence that excessive supply also can result in mitochondrial dysfunction and cellular injury that does not seem to be ischemia-related. Therefore, an impulsive and automatic increase in SACP rate is unlikely to completely solve the problem and might be harmful, and it seems to me that more research and better intraoperative monitoring are needed to bridge the knowledge gap and maybe provide a customized perfusion approach, given that a blanket strategy that fits all seems improbable.

Finally, this study raises the question of what end points should we be looking at when examining diverse cerebral perfusion strategies? Neurodevelopmental markers that have been used traditionally might reflect a cumulative effect of all influential factors and thus are nonspecific and likely underpowered to detect a difference. On the other hand, collection of metabolites representing cellular injury and mitochondrial dysfunction might not be clinically realistic. Research to develop practical noninvasive optimal monitoring strategies that correlate with these markers might be a necessary adjunct to the perioperative care of these patients.

References

1. Mavroudis CD, Ko T, Volk LE, Smood B, Morgan RW, Lynch JM, et al. Does supply meet demand? A comparison of perfusion strategies on cerebral metabolism in a neonatal swine model. *J Thorac Cardiovasc Surg.* 2022;163:e47-58.
2. Amir G, Ramamoorthy C, Riemer RK, Reddy VM, Hanley FL. Neonatal brain protection and deep hypothermic circulatory arrest: pathophysiology of ischemic neuronal injury and protective strategies. *Ann Thorac Surg.* 2005;80:1955-64.
3. McKenzie ED, Andropoulos DB, DiBardino D, Fraser CD Jr. Congenital heart surgery 2005. The brain: it's the heart of the matter. *Am J Surg.* 2005;190:289-94.
4. De Paulis R, Czerny M, Weltert L, Bavaria J, Borger MA, Carrel TP, et al. Current trends in cannulation and neuroprotection during surgery of the aortic arch in Europe. *Eur J Cardiothorac Surg.* 2015;47:917-23.
5. Hammel JM. Supplemental perfusion techniques for aortic arch reconstruction, with emphasis on direct cannulation of the descending aorta. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann.* 2019;22:14-20.
6. Edmonds HL Jr, Ganzel BL, Austin EH III. Cerebral oximetry for cardiac and vascular surgery. *Semin Cardiothorac Vasc Anesth.* 2004;8:147-66.
7. Fuller S, Rajagopalan R, Jarvik GP, Gerdes M, Bernbaum J, Wernovsky G, et al. Maxwell Chamberlain Memorial Paper for congenital heart surgery. Deep hypothermic circulatory arrest does not impair neurodevelopmental outcome in school-age children after infant cardiac surgery. *Ann Thorac Surg.* 2010;90:1985-94.
8. Goldberg CS, Bove EL, Devaney EJ, Mollen E, Schwartz E, Tindall S, et al. A randomized clinical trial of regional cerebral perfusion versus deep hypothermic circulatory arrest: outcomes for infants with functional single ventricle. *J Thorac Cardiovasc Surg.* 2007;133:880-7.
9. Visconti KJ, Rimmer D, Gauvreau K, del Nido P, Mayer JE Jr, Hagino I, et al. Regional low-flow perfusion versus circulatory arrest in neonates: one-year neurodevelopmental outcome. *Ann Thorac Surg.* 2006;82:2207-11.