PBLD 7 – Rewarming the cardiac surgical patient:
What is the best management on cardiopulmonary bypass?

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Learning Objectives

1. To understand the relationship between rewarming rate and peak temperature on neurologic and other outcomes after cardiac surgery

2. To understand how to interpret the information provided by the various temperature monitoring sites to optimize cooling, rewarming, and prevent temperature afterdrop

3. To understand how to integrate the current recommendations for rewarming rates, temperature gradients and maximum temperature following cooling during cardiopulmonary bypass

Case #1:

A 72 year old male professor with a history of crescendo angina and a history of Type II diabetes, hypertension, hyperlipidemia, renal insufficiency and peripheral vascular disease is diagnosed with multi-vessel coronary artery disease. He had a left CEA two years ago for a critical left ICA occlusion found following a TIA. He is scheduled for on-pump 3-vessel CABG. A decision is made to cool on bypass to 33°C, but just prior to removal of the cross-clamp, the surgeon instructs the perfusionist to “crank up” the temperature to facilitate the rewarming process.

Questions:

1. What is the effect of bypass temperature on outcome (cerebral and other) after cardiac surgery?
2. In routine cases, is there a role for hypothermia during bypass?
3. Which site(s) should be chosen for temperature monitoring?
4. Is there an optimal rewarming strategy?
5. During rewarming, how do temperature measurements at standard monitoring sites deviate from cerebral temperature?
6. Is there value to monitoring the bypass circuit arterial inflow temperature while on CPB?
7. Is there a maximum temperature limit to which arterial blood should be warmed on CPB?
8. What is the association between perioperative hyperthermia and neuropsychological dysfunction?
9. What is the relationship of rewarming rate to neuropsychological dysfunction?

Case #2

A 66 year old woman presents with a 5.5 cm aneurysm of the ascending aorta and aortic arch. Due to the aneurysmal involvement of the proximal aortic arch, she will require operative repair utilizing deep hypothermic circulatory arrest (DHCA). Her medical history is otherwise significant for hypertension and hyperlipidemia.
Questions:

1. What should be the target temperature prior to initiating circulatory arrest?
2. What is the role for antegrade cerebral perfusion during DHCA?
3. Should you apply ice to the head?
4. Is there any pharmacology that you can use to protect the brain?
5. What are the considerations for rewarming from DHCA?
6. What is your target temperature (and desired monitoring site) to separate from CPB without having a hypothermic rebound?

Discussion

Although cardiac surgery allows for life-saving therapy, it also represents a unique injury paradigm resulting from derangements in numerous homeostatic pathways. Organ injury, most notably cerebral injury, may result as a consequence of these various perturbations in inflammatory, hemostatic and oxidative stress pathways, all of which have been implicated in the pathogenesis of end organ injury. Indeed, significant adverse cerebral outcomes can occur after major cardiovascular surgery. Despite advances in surgical, anesthetic, and neuroprotective strategies, the incidence of perioperative stroke after cardiac surgery remains at 2-5%, while other temporary neurological dysfunction (TND) and long-term cognitive decline both having a much higher rate. The incidence of adverse cerebral outcomes is particularly high in patients undergoing repair or replacement of the ascending aorta or aortic arch, particularly when deep hypothermic circulatory arrest (DHCA) is used. Preventing or treating perioperative cerebral injury remains difficult, partly because the underlying mechanisms associated with the ischemia-reperfusion injury introduced by CPB (and DHCA, if used) are incompletely understood. Temperature management strategies have been implicated as factors available to mitigate cerebral injury.

Fundamental in the consideration of hypothermia for CPB is its putative global organ protective effects. Hypothermia, while having a suppressing effect on cerebral metabolism (approx. 6-7% decline per °C), likely has other neuroprotective effects that are mediated by non-metabolic pathways. Moderate hypothermia has multimodal effects in the ischemic brain including blocking the release of glutamate, reducing calcium influx, hastening recovery of protein synthesis, diminishing membrane-bound protein kinase C activity, slowing of the time to onset of depolarization, reducing formation of reactive oxygen species, and suppressing nitric oxide synthase activity. It is likely that the additive effect of these mechanisms conveys neuroprotection from hypothermia. Although experimental demonstrations of the neuroprotective benefits of hypothermia are abundant, definitive clinical examples, until the recent demonstrations of its efficacy following cardiac arrest, have been few.

Without question, hypothermia has allowed for the conduct of lifesaving cardiovascular procedures on the heart and aorta that would otherwise not be possible. No more dramatic an example of this are procedures requiring DHCA. Completely arresting the circulation is critical for the conduct of a number of procedures, examples of which include surgery on the aortic arch and pulmonary embolectomy. Although the use of these low temperatures can clearly serve to preserve organ function (most notably the brain), the actual target temperature at arrest, as well
as the strategies used to obtain that temperature and rewarm from it, have undergone considerable revision in recent decades. Furthermore, modifications in the choice of cannulation sites and perfusion technique, (most notably, selective cerebral perfusion), has again allowed for the modification of these hypothermic strategies.

In addition to the use of profound hypothermia for aortic surgery, selective antegrade or retrograde brain perfusion techniques are an essential part of the neuroprotective strategy in patients undergoing DHCA. Institutional experiences appear to be an important factor in selecting the specific technique. [22-28] Cooling for DHCA is routinely performed using the heart-lung machine and target temperatures range anywhere from 14 to 22°C. Selective cerebral perfusion, by either direct cannulation of the brachiocephalic vasculature or a graft anastomosis to the axillary artery (or of a portion of a newly implanted graft) allows the delivery of low-flow (5-25 ml/kg) antegrade cerebral perfusion with an arterial blood pressure target of 50-65 mm Hg (measured via the right radial arterial catheter). Procedural aspects of antegrade cerebral perfusion vary in regard to the cannulation site and strategy, the target flows and target mean arterial pressure, the pressure monitoring site, as well as the target temperature of selective perfusion. Selective antegrade perfusion combined with either DHCA for less profound hypothermia (in the 25-28° range) seems to be associated with reasonable cerebral outcomes. [29]

Outside the DHCA setting, the optimal temperature strategy for cardiac surgery has been debated for decades. Some of the most illustrative data outlining the pros and cons of various temperature strategies during CPB have come within the past 15-20 years. In the late 1980’s and early 1990’s, warm CPB (along with continuous warm cardioplegia) was revisited because of its potential myocardial salvaging effects.[30-33] Possible cerebral effects of this warmer CPB were investigated as there was a concern that cerebral outcome could be compromised. Several large studies have been undertaken examining the effects of temperature management on cerebral outcome after cardiac surgery. The Warm Heart Investigators group, performed a trial at Emory University,[34] and a later trial at Duke University,[35] although demonstrating important methodological differences, had very similar neurocognitive outcome results,[36,37] but remarkably different results pertaining to stroke.[30] None of the studies demonstrated any neuroprotective benefit from hypothermia on neurocognitive outcome. A more recent trial by Nathan et al also failed to show any neurocognitive benefit to hypothermia.[38] The Warm Heart Investigators trial and the Duke trial similarly showed no difference with respect to stroke. This was in contrast to the Emory trial that demonstrated an apparent injurious effect (higher stroke incidence) of what was most likely mild degrees of hyperthermia during CPB. These divergent results could partly be explained by differences in how temperature was monitored (i.e., nasopharyngeal vs. bladder), what the peak and nadir temperatures were, and how normothermia was maintained (actively warmed vs. allowing the patient’s temperature to passively drift). Most relevant to the issue of stroke was that in the Emory trial, patients were actively warmed, which in itself is not injurious if it is precisely carried out. Furthermore, they did not measure nasopharyngeal temperature, making it highly likely that they exposed the brain to hyperthermic temperatures. These data suggest that active warming to maintain temperatures at (or greater) than 37°C may pose an unnecessary risk of stroke.

Critically important to the issue of temperature management is how to accurately measure temperature in situations where the brain is at risk. Whereas measuring temperature within the
brain itself cannot practically be done, when this is not directly possible, a surrogate of brain temperature should be chosen. These include nasopharyngeal temperature as well as tympanic membrane temperature. More invasive brain temperature surrogates have also been used including the measurement of jugular bulb temperature with a thermistor placed retrogradely from the internal jugular vein. It is clear from these different temperature sites that significant temperature gradients exist across the body and across the brain during bypass. It is likely that during periods of rapid flux (such as during rewarming[40]), that these temperature gradients are maximal making a non-cerebral brain temperature site particularly prone to misrepresenting brain temperature.

Related to the issue of temperature and organ injury is the counter current argument related to *hyperthermia*. Compared to hypothermia, *hyperthermia*, in an opposite and disproportionate fashion, has injurious effects.[11] Although the normothermic vs. hypothermic CPB studies referred to previously [30,34,35] demonstrated no neuroprotective effects, a potential explanation for this lack of effect may be related to the obligate rewarming that occurs at the end of bypass. Indeed, Grigore et al.[41] studied the effect of different rewarming rates on neurocognitive outcome after CABG. These investigators compared conventional “fast” rewarming to slower rewarming and found a lower incidence of neurocognitive dysfunction six weeks after cardiac surgery. These slower rewarming rates were accompanied by lower peak cerebral temperatures during rewarming, consistent with past observations that rapid rewarming can lead to an overshoot in cerebral temperature resulting with the occurrence of inadvertent cerebral hyperthermia.[42] By reducing this rewarming rate, one limits and ideally prevents, the overshoot in temperature and thereby avoids the negative effects of cerebral hyperthermia. Supporting the concept that limiting rewarming may be neuroprotective was a study by Nathan et al.[43] that demonstrated a neurocognitive benefit for patients who had limited rewarming and were maintained between 34 and 36º for a prolonged (12 hours) period post-operatively. Indeed, the beneficial effect may actually have been mediated by the avoidance of cerebral hyperthermia during rewarming rather than the prolonged hypothermia.[43] These rewarming studies, when coupled with the post-operative temperature data suggesting that early postoperative fever is associated with worse neurocognitive decline,[44] suggests that avoiding hyperthermia may be beneficial in this population.

The post-operative period may be equally important with respect to temperature management and cerebral injury in cardiac surgery patients. Grocott et al demonstrated a direct relationship between postoperative hyperthermia and cognitive loss at six weeks after surgery.[44] It is unclear, however, whether this hyperthermia is directly responsible for the cognitive decline, or the hypothermia is secondary to the cerebral injury itself, such as injury to hypothalamic thermoregulatory areas. Taken together, the postoperative period represents a potentially important time period in which to intervene with a strategy of preventing hyperthermia and associated cognitive impairment. Thus, we have no convincing evidence from clinical trials that mild hypothermia during non-DHCA CPB is neuroprotective. A possible explanation for this is that any degree of neuroprotection afforded by hypothermia is negated by the obligatory rewarming period that ensues.[41]
References & Suggested Reading


