



## What's new with alpha-stat versus pH-stat?

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When hypothermic cardiopulmonary bypass (HCPB) or deep hypothermic circulatory arrest (DHCA) is used during cardiac surgery, anesthesiologists and perfusionists are faced with an important question: Should one temperature correct blood gasses to patient temperature (pH-stat) or not ( $\alpha$ -stat)? With pH-stat management, turning down CPB gas sweep rate or adding CO<sub>2</sub> to the oxygenator counteracts increased gas

solubility, lower PaCO<sub>2</sub>, and alkaline pH that would otherwise occur naturally with cooler temperatures.

Thus, pH-stat requires an increased total body CO<sub>2</sub> content to maintain neutrality at cooler temperatures.

pH-stat causes cerebral vasodilatation above metabolic demands (loss of autoregulation) and possibly faster, more homogenous cooling. Proponents argue that pH-stat also improves oxygen delivery by counteracting the pH- and hypothermia- associated leftward shift in the oxyhemoglobin dissociation curve.

$\alpha$ -stat (not temperature correcting) requires that neutrality is maintained only at 37°C, and permits the hypothermic alkaline drift. Thus, additional CO<sub>2</sub> is not needed and cerebral autoregulation is maintained.

Proponents of  $\alpha$ -stat cite that cellular transmembrane pH gradients, protein functioning, and enzyme activity are more normal when the pH is allowed to drift alkaline in parallel with the temperature dependent pKa's of proteins and the neutral pH of water. They also argue that a relatively alkaline pH is beneficial before the ischemic insult of circulatory arrest. Despite considerable laboratory and animal research into these mechanisms, substantial controversy remains over which strategy produces the best clinical outcomes. Recent animal, pediatric, and adult investigations, however, have advanced our understanding of the competing benefits of each technique.

Considerable recent animal data suggest pH-stat management confers cerebral protection during DHCA when compared with  $\alpha$ -stat.<sup>1-4</sup> For example, experiments involving a porcine DHCA model and intracranial monitoring of temperature, oxygen tension, and cerebral metabolites (via a microdialysis catheter), revealed pH-stat management was associated with fewer metabolic derangements and improved survival after 75 minutes of DHCA at 18°C, when compared with  $\alpha$ -stat.<sup>1</sup> In a study involving DHCA in piglets, improved cerebral oxygenation by near infrared spectroscopy, improved short term neurological performance, and improved brain histopathology was associated with pH-stat when compared with  $\alpha$ -stat.<sup>5</sup> Similarly, in a piglet



model involving DHCA and intravital microscopy through a cranial window, improved cerebral oxygenation at the end of cooling, and faster recovery of cerebral oxygenation upon rewarming, was associated with pH-stat when compared with  $\alpha$ -stat.<sup>4</sup> Other recent data have suggested that pH-stat antegrade cerebral perfusion improves cerebral oxygenation and reduces lactate formation in dogs with cerebral infarcts when compared to  $\alpha$ -stat.<sup>2</sup> Proposed mechanisms for the benefits of pH-stat include a relative rightward shift of the oxyhemoglobin dissociation curve aiding oxygen delivery, increased cerebral blood flow and volume providing a greater depot of oxygen stores during circulatory arrest, more complete cooling, and greater suppression of cerebral metabolic rate.

The pediatric literature also generally supports the use of pH-stat management during HCPB and DHCA for providing both cerebral and myocardial protection. Clinical studies suggest that pH-stat is particularly beneficial in cyanotic neonates and infants because it shifts more CPB flow away from the aortopulmonary collateral circulation and towards the cerebral circulation, both improving cerebral cooling and oxygen supply.<sup>6</sup> Recent studies have also revealed a decrease in peak postoperative troponin levels, reduced ventilator dependence, and reduced ICU stays with pH-stat versus  $\alpha$ -stat.<sup>7</sup> Despite such evidence, however, conflicting clinical outcome data persist. For example, a randomized controlled trial of over 100 neonates and infants revealed that neither strategy was consistently associated with improved neurodevelopmental outcome.<sup>8</sup>

The data are even less conclusive for adults, unfortunately. Recent studies favoring pH-stat revealed significantly fewer episodes of jugular venous desaturation upon rewarming and a reduction in cerebral arteriovenous glucose and oxygen gradients when compared with  $\alpha$ -stat.<sup>9-10</sup> Studies such as these supporting pH stat management without evaluating long term follow-up, however, hardly challenge the widely-cited evidence Murkin and colleagues presented in 1995 showing poorer neurological outcomes with pH-stat HCPB.<sup>11</sup> Many speculate that, in adults, any potential benefits of excessive cerebral blood flow during HCPB are outweighed by an increased cerebral embolic load (microemboli and macroemboli).<sup>12</sup> Interestingly, this putative mechanism has been recently challenged by a study involving a controlled microembolic load and DHCA in pigs that revealed that pH-stat was still associated with improved outcomes when compared with  $\alpha$ -stat.<sup>13</sup> Clinical applicability of these results are limited, however, and these results alone should not impact current clinical practice.

In summary, the debate over optimal blood gas management during HCBP and DHCA continues. Most clinicians believe pH-stat offers substantial protection in neonatal and infant cardiac surgery where aortopulmonary steal often exists and embolic risk is low (despite a lack of consistent outcome data). Conversely, most clinicians apply an  $\alpha$ -stat strategy for adults undergoing HCPB and/or DHCA, in order to maintain cerebral autoregulation and limit cerebral embolic load. With definitive outcome data lacking, further research is certainly warranted.

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