



## Nadir hematocrits lower than 21% on cardiopulmonary bypass are associated with greater cerebrovascular and renal complication rates and should trigger transfusion.

### PRO:

The management of nadir hematocrits during cardiopulmonary bypass (CPB) has changed dramatically over the years. Initially, all CPB circuits were primed with whole blood, reducing the level of hemodilution and limiting how low the patient's hematocrit would drop.<sup>1</sup> Concerns arose over exposing patients to blood transfusions from numerous donors (triggering antibodies, increasing risks of transfusion related reactions, and infection) and depleting the relative scarce commodity of available blood.

Currently, while variable, most CPB prime is composed of crystalloid and colloid solutions that can lead to marked levels of hemodilution. There are advantages of hemodilution: a reduction in the viscosity of blood allows for maintenance of blood flow without elevated arterial pressures (which can lead to dissection). Hypothermia also aids in reducing oxygen requirements of vital organs during CPB, allowing for the lower hematocrit, but the question remains: to what nadir hematocrit should we hemodilute?<sup>2,3</sup>

Several recent studies have found that the severity of hemodilution during CPB correlates strongly with increased perioperative morbidity and/or mortality.<sup>3,4,5,6</sup> These clinical studies have built upon the animal models in the literature that suggested severe hemodilution could lead to increased end-organ damage and touted potential benefits of maintaining higher hematocrits.<sup>7,8</sup> Additionally, the definition of "severe" hemodilution in these studies varies. Increased complications are seen with nadir hematocrits anywhere in the range of 17-23.<sup>2,3,4,5,6</sup> For the purposes of this discussion, I will consider nadir hematocrits less than 21 severe, and highlight the evidence in the literature that exists for maintaining patients at or above this number.

In 1997, Fang et al. found that so-called "high-risk" patients (defined as those who had one or more of 8 significant independent predictors of mortality including: previous open heart surgery, renal failure, congestive heart failure, etc) had increased mortality with nadir hematocrits less than 17, while "low-risk" patients had increased mortality at < 14. This was one of the first studies in a human population that actually identified a number where morbidity/mortality was increased at a certain nadir hematocrit. Previous work had all shown either no benefit or safety at hematocrits even as low as 13.<sup>4</sup> It should be noted, however, that these studies, including even Fang's work, were done in a surgical population that is very different than the one we deal with today- almost all of our patients would fall into the "high-risk" category.

Additionally, subsequent, more recent work in larger groups of patients has demonstrated that increased complications occur well



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above the first nadir established by Fang. DeFoe et al. reported a trend towards increasing risk of death at all hematocrits < 23 in a much larger group of patients. The mortality at a nadir hematocrit of < 19 was double that of when the nadir hematocrit was 25 or above. Additionally, patients with low hematocrits had an increased risk of intra- or post-operative placement of intra-aortic balloon pumps and return to CPB after initial separation.<sup>2</sup> Smaller patients had increased risk and inherently this makes sense as their hemodilution would presumably be more severe if identical CPB circuits were employed regardless of weight.

Habib et al. found that at nadir hematocrits lower than 22, patients had significantly increased risk for myocardial infarction, renal failure, prolonged ventilation, sepsis and longer intensive care unit (ICU)/hospital stays. Long term survival also was improved systematically with increasing nadir hematocrits. Both early and late mortality figures were worse for patients with nadir hematocrits < 20, and worsened significantly the lower the hematocrit fell versus patients with hematocrits in the high 20's.<sup>6</sup>

In addition to mortality outcomes, evidence for significant morbidity associated with hematocrits lower than 21 is prevalent throughout the literature and the pathways for such injury better delineated. Of note, the renal and neurological organ systems seem particularly susceptible to injury after excessive hemodilution.

The effect of hemodilution on brain function is thought to be related to the increase in the embolic load to the brain.<sup>9</sup> Additionally, while oxygen delivery to the brain is maintained during hemodilution in normal brain cells, ischemic cells may lack the compensatory measures needed for survival and extraction of oxygen decreases with decreased hematocrit.<sup>3</sup>

Karkouti et al examined almost 11,000 patients prospectively undergoing cardiac surgery with CPB. For every percent decrease in nadir hematocrits during CPB, patients had a 10% increase in the odds of suffering a perioperative stroke. If patients had a nadir hematocrit < 18, their risk of stroke was 3x that of patients who had nadir hematocrits 21-23.<sup>3</sup> In another retrospective review of 5000 consecutive patients, Habib et al. found a significantly increased risk of stroke with nadir hematocrits of less than 22.<sup>5</sup>

Some authors maintain that hematocrits should actually be maintained much higher than 21, even as high as 30 for preservation of neurological function.<sup>10</sup> Jonas et al., found that in a pediatric population, patients with hematocrits higher than 27 had significantly better motor skills at one year than their counterparts who had nadir hematocrits of 21.<sup>5,11</sup> Noting that the adult brain may be even more sensitive to hypoxic brain injury than the neonatal brain, he advocates hematocrits of at least 25.<sup>10</sup>

Like neurological injury, renal failure as sequelae of cardiac surgery is a dreaded complication. It can occur in 1-5% of patients undergoing cardiac surgery and has been identified as an independent risk for increased mortality.<sup>12,13</sup> With respect to renal function, even slight reductions in renal oxygen delivery (as a result of hemodilution) can cause ischemic damage. This may actually be

exacerbated by increased renal blood flow, as this increases renal energy requirements which cannot be met in the face of diminishing oxygen delivery.<sup>13</sup> Additionally, much like in the brain, increased embolic load is also thought to contribute to renal dysfunction perioperatively.

Recent studies have confirmed the deleterious effects of low nadir hematocrits on renal function. Karkouti et al. studied over 9000 patients prospectively and found an independent relationship between nadir hematocrit on CPB and acute renal failure requiring dialysis. Hematocrits lower than 21 had the highest risk; interestingly, hematocrits above 25 also had greater risk compared to those between 21-25.<sup>13</sup> Habib et al, found that patients with CPB hemodilution to hematocrits < 24 had an increased likelihood of renal injury and worse operative outcomes.<sup>5</sup> In another study, the same authors found that as nadir hematocrits on CPB decreased lower than 22, the risk of postoperative renal dysfunction increased.<sup>6</sup>

It is clear from these studies that the current practice of hemodilution, while with some benefits, carries inherent risks of increased morbidity and mortality. While most of these studies have been observational or retrospective in their design, their results are consistent. There exists a need for randomized, controlled trials that may better elucidate how low we should allow hematocrits to fall during CPB (as has been called for by many of these authors). Certainly there are concerns with transfusions, but there exist possible alternatives where excessive hemodilution as well as transfusion can be minimized. These include the practice of retrograde, autologous priming of the CPB circuit or the use of smaller circuits, especially in smaller patients. When these measures cannot be undertaken, hematocrits below 21 should spur transfusions as the neurological/renal morbidity and overall increases in mortality outweigh the benefits of hemodilution.

(Endnotes)

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