Hemodilution and Hematocrit on Cardiopulmonary Bypass: How Low Can We Go?

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Background

Since 1953 when Dr. John Gibbons, Jr. and colleagues first successfully used cardiopulmonary bypass to perform an open mitral comissurotomy, the technology of the cardiopulmonary bypass (CPB) circuit and the physiologic management of patients during extracorporeal circulatory support have undergone a tremendous evolution. Despite major technologic advances and half a century of experience with cardiopulmonary bypass, the pathophysiologic consequences of CPB remain significant. Efforts to study and identify factors that contribute to poor outcomes in patients undergoing CPB have yielded important information, but nevertheless definitive answers and consensus on optimal practices have been difficult to realize. In 2009, Murphy et al reviewed the existing evidence for management of physiologic variables including hematocrit during cardiopulmonary bypass. He concluded that a paucity of data prevents strong recommendations and that randomized clinical trials are critically needed.

Physiology and Outcomes of Cardiopulmonary Bypass Anemia

The transition away from “blood prime” to the use crystalloid prime solution in an effort to avoid the risks of homologous blood exposure introduced significant degrees of hemodilution and anemia during CPB. Physiologic studies of anemia in animal models supported this practice. Hemodilution is associated with decreased viscosity and decrease systemic vascular resistance and promotes microvascular blood flow. Although oxygen carrying capacity is decreased, several studies indicate that cerebral blood flow increases in response to anemia are sufficient to maintain adequate oxygen delivery. Cook et al studied healthy dogs during normothermic cardiopulmonary bypass and found that cerebral blood flow (CBF) increases 43% for a 30% decrease in hematocrit (HCT). These increases in CBF were noted to be blunted in the setting of hypothermia. Studies by Cook suggested that the coupling of CBF and CMRO2 was lost with hypothermia. A study in dogs with a HCT 10% demonstrated that CBF increased above baseline to a greater extent at 38°C than 28°C and the least at 18°C. Duebener in piglets studies showed that a HCT 10% during DHCA (Temp 15°C) was associated with worsened cerebral tissue oxygenation and endothelial activation markers than HCT 20% or 30%. Other work suggested that increased CBF may have some negative consequences, namely increasing the embolic load to the cerebral vasculature. Nevertheless extreme hemodilution does not appear to precipitate ischemic injury and a wide plateau for relationship between HCT and cerebral oxygen balance is observed. Cook et al. showed CMRO2 remains stable at HCT 14% (for 38°C), 11% (for 28°C), 10% (18°C). Mathru et al. reported results 8 anesthetized patients who were exposed to an HCT of 15% after elective CABG surgery and a body temperature of 37°C, which led to a significant, but not ‘critical’, reduction in DO2. Other research by Mathru in awake humans demonstrated that oxygen consumption remained stable to HCT 15%.

Morbidity Outcomes

In the last decade, retrospective studies have raised concerns about the widespread use of extreme hemodilution on bypass. Fang and colleagues performed a retrospective review of 2738 patients...
undergoing CABG on CPB. They reported a doubling (2.7-fold) of mortality risk demonstrated when the lowest nadir HCT reached <14% during CPB. For high risk patients, 2.2 times probability of mortality when nadir HCT ≤17% during CPB. Similar findings were reported by Defoe and colleagues in a prospective observational study of 6980 consecutive patients undergoing CPB for CABG. DeFoe found that a HCT <19% during CPB was associated with >2x risk mortality and a trend toward increased death was observed for a HCT <23%. Habib et al in another large retrospective study of 5000 consecutive patients for cardiac surgery with CPB demonstrated that a nadir HCT <22% was associated with statistically significant increases in risk of stroke, MI, low CO, cardiac arrest, renal failure, prolonged ventilation, reoperation for bleeding, sepsis, multi-organ failure, prolong ICU stay. Lowest HCT CPB was also associated with reduced survival at 6 yrs. In this study, the rate of transfusion was significantly higher patients with HCT <22%, raising questions about the role transfusion played in the observation of increased morbidity in the setting of hemodilution.

Renal injury has also reported to be associated with extreme hemodilution. Swaminathan et al demonstrated an increase in renal dysfunction, measured by post-operative increase in serum Cr, in a retrospective study of 1404 patients undergoing CABG who experienced low HCT on CPB. Interestingly, in additional analyses, the authors noted that transfusion in response to low HCT actually worsened the degree of renal failure observed. Habib and colleagues concluded that a HCT <24% on CPB appeared to be a “critical threshold” triggering significantly worsened renal outcomes. They also observed a strong association between early transfusion on CPB in response to severe anemia and renal injury. Karkouti and colleagues retrospectively reviewed over 9000 patients undergoing CPB and reported that a nadir HCT <21% was associated with 2.34 times odds of post-op ARF. They noted a bimodal distribution of adverse outcomes with moderate hemodilution (HCT 21-25%) being associated with the best renal outcomes.

Neurologic morbidity has also been linked to extreme hemodilution on CPB. Animal studies illustrated larger cerebral infarct sizes after ischemic injury in the setting of extreme hemodilution. Karkouti et al reviewed over 10,000 patients and found that every 1% decrease in HCT was associated with a 10% increase the odds of developing a perioperative stroke. Mathew et al observed increased cognitive decline in elderly patients managed on CPB with HCT 15-18% compared to HCT>27%. Decreases in HCT by >12% from baseline was also associated with worsened cognitive outcome.

Although extreme hemodilution has been associated with poor outcome, low hematocrit during cardiac surgery is a significant risk factor for and closely associated with transfusion with red blood cells. An extensive body of literature now links transfusion to increased perioperative morbidity and mortality. Transfusion has never been demonstrated to improve tissue oxygenation, and, given changes that occur in stored red blood cells, transfused blood appears to have a significantly limited capacity to acutely deliver oxygen to tissues. Older stored blood appears to have a significantly worse profile, and several studies have suggested that transfusion of older units of RBC is associated with significantly increased outcome. Proinflammatory effects of transfusion with red blood cells or other blood components, namely platelets, may be more dramatic than the inflammatory effects observed with CPB. Transfusion has been associated with increased rates of pneumonia after CPB, increased incidence of low cardiac output heart failure, decreased long-term survival after CPB.

Several studies have attempted to tease out the relationship between extreme hemodilution, transfusion, and adverse outcome after CPB. Sophisticated analytical methodology has attempted to account for the influence of transfusion on the effects of low hematocrit. Similar to Swaminathan and Habib who found that transfusion in response to low hemocrit worsened renal outcomes, Surgenor et al found that risk of low cardiac output heart failure in patients with low nadir hematocrits was higher if patient received RBC transfusion. Ranucci and colleagues analyzed 3003 consecutive CABG patients who did not get transfused. Pre-operative HCT and lowest HCT on CPB were independent risk factors...
for major morbidity. Pre-operative HCT<40% is not a risk factor for major morbidity if nadir HCT on CPB is >28%.28

In analyses of cohorts of Jehovah Witness patients undergoing cardiac surgery demonstrates that blood transfusion can be avoided without significant adverse outcome. An analysis by Viele and colleagues of 61 reports of a total of 4722 Jehovah Witness patients undergoing cardiac surgery suggests that hemodilution to a Hbg 5.0g/dL can be tolerated with minimal morbidity.29 Other groups have described successful cardiac surgery in patients refusing blood transfusion by maximizing blood conservation techniques.30 Techniques for blood conservation such as pre-operative erythropoietin therapy, minimization of bypass circuit prime volume, use of retrograde autologous priming, heparin – coated bypass circuits, retransfusion of shed mediastinal and pleural blood post-operatively have all been described.31

Summary

Nevertheless, the optimal degree of hemodilution on CPB is still undefined. Given the risks inherent in transfusion with red blood cells and component therapies, efforts to avoid excess blood loss are paramount. More sophisticated measures of adequate tissue oxygenation may be needed to guide decision-making around transfusion and allow for the safe use more permissive degree of hemodilution.

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References


(29) Viele MK, Weiskopf RB. What can we learn about the need for transfusion from patients who refuse blood? The experience with Jehovah’s Witnesses. Transfusion 1994;34:396–401.

