Autologous Platelet-Rich Plasma Reduces Transfusions During Ascending Aortic Arch Repair: A Prospective, Randomized, Controlled Trial

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Background. **Blood conservation using autologous platelet-rich plasma (aPRP), a technique of whole blood harvest that separates red blood cells from plasma and platelets before cardiopulmonary bypass with retransfusion of the preserved platelets after completion of cardiopulmonary bypass, has not been studied extensively. We sought to prospectively determine whether aPRP reduces blood transfusions during ascending and transverse aortic arch repair.**

Methods. **We randomly assigned 80 patients undergoing elective ascending and transverse aortic arch repair using deep hypothermic circulatory arrest to receive either aPRP (n = 38) or no aPRP (n = 42). Volume of aPRP retransfused was 726 ± 124 mL. The primary end point was transfusion amount. Secondary end points were death, stroke, renal failure, pulmonary failure, and transfusion costs. Perioperative transfusion rate was defined as blood transfusions given during surgery and up to 72 hours afterward. The surgeon and intensivist were blinded to the treatment arm. Because an anesthesiologist initiated the protocol, the surgeon was not aware of aPRP collection, as this occurred only after the sterile drape was in place. In addition, because cell salvage was performed on all cases, differentiation in perfusionist activities (during spinning of aPRP) was not evident. Platelet, fresh frozen plasma, and cryoprecipitate intraoperative transfusions were performed only after heparin was reversed and the patient was judged as coagulopathic on the basis of associated criteria: cryoprecipitate transfusion for fibrinogen level less than 150 μg/dL, platelet transfusion for platelet count less than 80,000, and fresh frozen plasma when thromboelastogram test was suggestive or a partial thromboplastin time was greater than 55 seconds, and prothrombin time was greater than 1.6 seconds.**

Results. **Early mortality, stroke, and respiratory complications were similar between groups. Only acute renal failure was reduced in the aPRP group, 7% versus 0% ($p < 0.014$). Mean transfusion rate of packed red blood cells was reduced by 34%, fresh frozen plasma by 52.8%, cryoprecipitate by 70%, and platelets by 56.7% in the aPRP group ($p < 0.02$). Hospital length of stay (9.4 ± 5.3 days versus 12.7 ± 6.3 days; $p < 0.014$) and transfusion costs ($1,396 ± $1,755 versus $2,762 ± $2,267; $p < 0.004$) were reduced in the aPRP group.**

Conclusions. **The use of aPRP reduced allogeneic transfusions during ascending and transverse aortic arch repair with deep hypothermic circulatory arrest. This translated to less acute renal failure, decreased length of stay, and lower transfusion costs. Further studies examining the coagulation factors of aPRP are required.**

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Bleeding requiring massive blood transfusions to correct coagulopathy may complicate the repair of thoracic aortic aneurysms and dissections. Thrombocytopathy, coagulation factor deficiencies, and deep hypothermia associated with thermal deregulation of the coagulation system during cardiopulmonary bypass (CPB) are contributing factors. Traditional therapy to correct bleeding depends on allogeneic blood and blood product transfusions (ie, red blood cells [RBCs], fresh frozen plasma [FFP], platelets, and cryoprecipitate). Unfortunately, blood transfusion therapy is often associated with adverse effects, which parallel blood product usage [1]. Moreover, blood transfusions have increased despite limited blood resources and rising health care costs [2]. Importantly, it is estimated that shortages of blood supply in the United States will worsen [3]. It is therefore important to adopt effective, safe, and economical blood conservation processes to better use our blood product resources and decrease morbidity and mortality associated with blood transfusions. Some blood conservation techniques include autologous predonation of blood products, blood salvaging systems, cell salvage techniques, minimized pump prime, and pharmacologic agents [4, 5]. The use of autologous platelet-rich plasma

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(aPRP) has been reported previously as a blood conservation approach but has been met with equivocal results [5–10].

Previously, our institution adopted the use of aPRP as an intraoperative blood conservation approach in aortic surgery [11]. It is a technique of whole blood harvest that separates RBCs from plasma and platelets before CPB with retransfusion of the "preserved" platelets after discontinuation of CPB. In a retrospective study, we demonstrated that intraoperative aPRP transfusion significantly reduced intraoperative and postoperative blood transfusion and decreased postoperative coagulopathy, acute renal failure, and pulmonary complications [11]. Although encouraging, this study was limited by its retrospective design and inherent biases. Therefore, the purpose of this prospective, randomized, controlled trial was to determine whether aPRP reduced blood transfusions during elective ascending and transverse aortic arch repair.

Material and Methods

Study Design

The University of Texas Medical School at Houston's Committee for the Protection of Human Subjects approved this study, with written consent obtained from all enrolled patients. By computer-generated randomization, we assigned 80 patients from May 2010 through February 2013 undergoing elective ascending and transverse aortic arch repair using deep hypothermic circulatory arrest (DHCA) to receive either aPRP or no aPRP. The patients included in the study arose from a total of 299 patients who underwent ascending and transverse aortic arch repair during the study period. Of the 299 patients, 96 were excluded because they underwent acute type A dissection repair, and 123 patients were excluded because of recent anticoagulants, preoperative renal failure requiring dialysis, and refusal to consent. Patients were divided into two groups. In the aPRP group, 38 patients (47.5%) received aPRP. This was compared with the non-aPRP control group of 42 patients (52.5%). The primary end point was total perioperative transfusions. Secondary end points were early mortality, stroke, renal failure, pulmonary failure, time to extubation, hospital length of stay (LOS), and transfusion costs.

Definitions

Early mortality was defined as all-cause in-hospital and 30-day mortality [12]. Intraoperative transfusion was defined as transfusions given during the procedure until the end of the operation. Perioperative transfusions were any transfusions given from the beginning of the operation to 72 hours after sternal closure, even if delayed closure was used. Stroke was defined as a prolonged (72 hours) or permanent neurologic deficit that was associated with abnormal results of magnetic resonance imaging or computed tomographic scans. Acute renal failure was defined as an increase of serum creatinine to greater than 2.0 mg/dL, or twice the most recent preoperative creatinine level, or a new requirement for dialysis postoperatively. Pulmonary insufficiency was defined as prolonged ventilator support greater than 24 hours, the development of acute respiratory distress syndrome, pulmonary edema, pneumonia, or reintubation. The transfusion direct cost was the dollar charge to the hospital by the blood banking service for only the blood product transfusions. This did not include the service costs related to administering the transfusions.

Study Population

Inclusion criteria were adults older than 18 years of age who were not pregnant and undergoing elective ascending aortic arch repair with DHCA. Exclusion criteria included patients with American Society of Anesthesia class V or E status, known coagulation disorder, anemia (hemoglobin < 11 mg/dL), intraaortic balloon pump or other ventricular assist devices, end-stage renal disease dependent on hemodialysis, recent anticoagulants (anti-glycoprotein IIb-IIIa agents) less than 5 days, and weight less than 50 kg. A standardized blood conservation protocol was applied to all patients per The Society of Thoracic Surgeons guidelines [1]. This included preoperative avoidance of anticoagulants and antiplatelet medication, intraoperative use of cell-salvage techniques, administration of antifibrinolytics, and standardized transfusion criteria.

Anesthetic Management

All patients were monitored according to the American Society of Anesthesia guidelines with a five-lead electrocardiograph. In addition, cerebral oximetry and both nasal and bladder temperatures were monitored, along with continuous blood pressure, central venous pressure, and pulmonary artery pressure and mixed venous oxygen saturation measured by arterial catheter, central venous catheter, and pulmonary catheter, respectively. Transesophageal echocardiography was used for all cases. Routine general anesthesia was a balanced technique using bolus administration of propofol (0.5 to 2 mg/kg), fentanyl (10 to 15 μg/kg), midazolam (0.05 to 0.1 mg/kg), and a paralytic agent. Anesthesia was maintained with an inhalational agent (isoflurane or sevoflurane) at 0.5 to 1 minimum alveolar concentration. The hemodynamic variables were monitored throughout the case and continued in the intensive care unit. All patients received tranexamic acid as a 0.5- to 1-g loading dose followed by an infusion of 0.5 to 1 g/h. The maximal dose of tranexamic acid was 6 g or 80 mg/kg per case. The dose was reduced 50% in patients with chronic kidney disease (glomerular filtration rate < 60 mL $\cdot$ min^{-1} $\cdot$ 1.73 m^{-2}). Glomerular filtration rate can be calculated by the following equation:

$$\text{GFR} = (140 - \text{age}) \times \text{wt (kg)} \times (0.85\ \text{woman}) / (72 \times \text{creatinine})$$

The thromboelastogram test assessed fibrinolytic activity on completion of the procedure.