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The Effect of Standardizing Autologous Prime Techniques in Patients Undergoing Cardiac Surgery with Cardiopulmonary Bypass

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Abstract: Autologous priming (AP) of the extracorporeal circuit has been used as a technique to reduce iatrogenic anemia in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB). The purpose of this study was to review the results of standardizing AP techniques to reduce variation among clinicians and its effect on clinical outcomes. Standardized goal-directed protocols for AP were established by the cardiac team and applied to all adult cardiac surgical patients where CPB was used. Following Institutional Review Board approval, data were analyzed for two sequential groups of patients: Non-standardized AP (NST-AP) and standardized AP (ST-AP). Exclusion criteria included pre-CPB hemodynamic instability and preoperative hematocrit (Hct) values less than 30%. The primary end point was the transfusion of red blood cells (RBCs), whereas secondary end points included Hct change and other perioperative allogeneic blood product transfusions. Data are presented as mean and SD. Of the 192 patients evaluated, 82 were in the NST-AP group and 110 in the ST-AP group. There were no preoperative demographic differences across groups. Total AP volume was lower in the NST-AP group than in the ST-AP patients (486.8 ± 259.6 mL vs. 1,048.2 ± 218.7 mL, $p < .001$). Whereas pre-CPB Hct values were identical between the groups, the first on-CPB (25.7% ± 4.5% vs. 27.9% ± 4.2%, $p < .001$), high CPB (27.7% ± 3.5% vs. 29.1% ± 3.6%, $p < .008$), and first postoperative (32.5% ± 4.0% vs. 34.3% ± 3.9%, $p < .003$) were all significantly higher in ST-AP patients. Perioperative transfusion rate was higher in NST-AP patients (63.6%) vs. ST-AP (44.6%), $p < .01$. There was no difference in intraoperative RBC transfusion, but postoperatively, more patients in the NST-AP group received RBCs than those in the ST-AP group (51.2% vs. 28.2%, $p < .01$). The application of an ST-AP protocol was effective in reducing hemodilution, which was associated within higher Hcts and lower postoperative transfusion rates. **Keywords:** cardiac surgery, autologous prime, blood management, cardiopulmonary bypass, allogenic blood transfusion. *J Extra Corpor Technol. 2019;51:227–37*

Managing cardiac patients is complicated by numerous factors, including the patient preoperative condition, severity of the cardiovascular lesions(s), and the type of operation to be performed. The utilization of the heart–lung machine to conduct cardiopulmonary bypass (CPB) results in a multitude of physiological alterations related to the extracorporealization of blood. All patients experience some degree of hemodilution as a result of both anesthetic and perfusion management where asanguineous solutions are administered for a number of reasons that include maintaining hemodynamic stability, priming of the CPB circuit, and for myocardial protection. Several modalities are used for the volumetric maintenance of these patients, all of which are components of comprehensive blood management programs used at most hospitals. These strategies include acute normovolemic hemodilution, hypotensive anesthesia, miniaturized low-prime circuitry, ultrafiltration (UF), and autologous priming (AP) of the CPB circuit (1–3).

AP of the extracorporeal circuit is achieved by using the patient's own blood to displace the asanguineous prime solution, which has been discussed since the advent of CPB, but did not gain popularity until the late 1990s (4–6). The benefits of this technique have included reduced transfusion rates (7–10), better maintenance of colloid osmotic pressure and reduced extravascular lung water accumulation (9,11),

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improved regional cerebral oxygenation (12), and shortened overall length of stay (7). In addition, this technique has also been cited as a recommendation by a perfusion professional society.[1] However, there have been a number of reports that have stated only meager or limited benefit in regards to transfusion rates or other outcomes (11,13–16). Because such controversy exists, the overall recommendations for its incorporation into standard clinical practice have not been shown to be conclusive (Class IIb) (17). There are many reasons that the use of AP remains equivocal. These include patient-related factors that include questionable benefits when preoperative anemia is seen and operative issues such as the potential for a period of hemodynamic instability when performed, and reduced circulating blood volumes during CPB. Furthermore, this is one technique that requires strict team attention to patient management during AP and standardization of protocol to minimize interclinician variability. The absence of either may be a primary determinant in affecting how successful the process will be in achieving desired goals of patient care. Therefore, the goal of this research was to evaluate the clinical results of standardizing how AP is applied in the clinical setting.

MATERIALS AND METHODS

Patient Population

All patients undergoing cardiac surgery with CPB operated on at a single center[2] over a 24-month period were considered for the study. Inclusion criteria included patients who were older than 19 years and underwent repair for acquired heart disease such as surgical coronary revascularization, valve repair or replacement, combined procedures, and non-emergent repair of aortic disease. Patients were excluded from the study if they underwent emergent cardiac surgery, had congenital heart disease, had preoperative anemia as determined by either a preoperative hematocrit (Hct) of 30% or less, an intraoperative post-heparinization Hct change of less than 26%, or required priming of the CPB circuit with allogeneic packed red blood cells (RBCs).

All data were collected prospectively and loaded into a perfusion quality improvement database as a normal process of caring for patients undergoing cardiac surgery.[3] A power analysis was performed using a statistical software package.[4] The variable used was first Hct on CPB historical controls (25%) with an expected change in the Hct with successful AP of an increase of 2%. The power of the test was set at .80 and the SD of 6%. The calculated sample size using these conditions was found to be 71. The local Research Ethics Committee approved the research and determined that informed consent was not necessary for the study.[5]

Before the start of this study, AP was practiced at our center but was not standardized according to patient-specific criteria, and a target AP volume to be displaced was not defined. The attending perfusionist attempted AP, but the technique could be terminated, or partially completed, as a result of clinician prerogative when either hemodynamic instability was encountered or if there was intolerance to the time necessary to complete AP. An initial analysis of the perfusionist AP performance was completed as the preliminary evaluation to identify the extent of interclinician variability. During this time, there were three perfusionists performing CPB each with their own AP technique, which resulted in varying prime volumes and volumes of AP displaced. This degree of variation seen was deemed unacceptable and a process for standardizing how AP was being performed begun. A literature review of the current literature and best practices was completed and reviewed by the cardiac surgeons, anesthesiologists, and perfusionists. The agreed-upon techniques were incorporated into a standard protocol, which all team members followed for non-emergent surgeries. These included retrograde displacement of the arterial line contents to the arterial outlet port of the oxygenator and displacement of the prime solution from the venous line into the venous reservoir with a volume sufficient to replace the remaining oxygenator, centrifugal pump, and tubing into the priming bags stopping approximately when red blood entered the bags. A concerted effort to standardize performance among the staff using the protocol outlined below was performed for all patients who met the inclusion criteria. During the study, the surgical team did not change and included two cardiac surgeons, three cardiovascular anesthesiologists, and two perfusionists. There was no change in clinical practice during the study period.

Surgical Technique

Surgery was performed through a median sternotomy except for minimally invasive procedures for aortic valve surgery where a hemi-sternotomy was used. For coronary artery bypass (CAB) graft surgery, a left internal thoracic artery was always used with greater saphenous vein harvesting performed endoscopically. Cannulation was achieved with a 24-Fr aortic cannula (EZF24TA®, Edwards Lifesciences, Irvine, CA), a 36/46 Fr triple-stage

[1]Amercian Society of Extracorporeal Technology, Standards and Guidelines for Perfusion Practice. http://www.amsect.org/p/cm/ld/fid=1617. Accessed August 6, 2019.
[2]Lehigh Valley Hospital - Pocono, East Stroudsburg, PA.
[3]The contents of the database are shown in the Addendum 1.
[4]http://www.statisticalsolutions.net/pss_calc.php.
[5]Wright Center for Graduate Medical Education, Institutional Review Board, Scranton, PA. Study # PMC061814AL.

venous cannula (TF364602A®, Edwards Lifesciences), and both antegrade (ARO14V®, Edwards Lifesciences) and retrograde (RCO14IT®, Edwards Lifesciences) cardioplegia cannulae. Venting of the heart was achieved through a 20-Fr catheter (12,112, DLP®, Medtronic, Minneapolis, MN) placed either into the right superior pulmonary vein and advanced into the left ventricle or placed in the pulmonary artery.

Anesthetic Technique

All patients were anesthetized with a balanced technique combining narcotics and inhalation gases. Indwelling catheters were placed for the measurement and continuous monitoring of arterial and pulmonary artery blood pressure (BP). Additional continuous monitoring included electrocardiogram, near infrared spectroscopy (NIRS) (INVOS™ 5100, Covidien Corporation, Mansfield, MA), and urine output. Premedication consisted of intravenous midazolam, and anesthesia was induced with either propofol or etomidate as a hypnotic, fentanyl as the narcotic, and rocuronium for muscle paralysis and maintained with the inhalational agent desflurane or sevoflurane. The anesthetic agents were titrated to effect during surgery based on vital signs (heart rate, BP) and bispectral (BIS) (Bispectral Index™, Covidien, Mansfield, MA) values, and muscle relaxant supplemented based on the train-of-four response. Certain patients who were anticipated to undergo rapid extubation also received a continuous infusion of dexmedetomidine dependent on the preoperative clinical assessment, which was initiated upon institution of CPB. Ventilation was achieved to normocapnia under volume control at a frequency of 10–12 breaths per minute, and a tidal volume of 8–10 mL kg^{-1} of ideal body weight and positive end-expiratory pressure of 5 cm H_2O were maintained. Glycemic control throughout the perioperative period was achieved by maintaining glucose levels at 120–150 mg dL^{-1} by the use of insulin infusion or bolus, as necessary. At the conclusion of the surgery, patients were transported to the cardiovascular intensive care unit (CVICU) with oxygen and monitoring of arterial BP, heart rate, and pulse oximetry. Patients were weaned from CPB as per standard protocols. NIRS and BIS analysis monitoring were routinely used with interventions for improving cerebral saturation instituted once the levels dropped below 25% of baseline (pre-anesthetic induction) levels or if saturation values were to decrease below 40%. These interventions included increasing cardiac output, increasing mean arterial pressure, increasing $PaCO_2$ levels, administering additional anesthetic agents, correcting hemodilution through urine output, or the administration of RBCs.

Extracorporeal Circuit

A standard modular heart–lung machine (Advanced Perfusion System 1, Terumo Cardiovascular, Ann Arbor, MI) with a central control monitor was used for all patients with the following safety devices in place: bubble and level detection systems, pressure monitoring for the arterial line, and vacuum-assisted venous drainage when performed, cardioplegia circuit, and both antegrade and retrograde cardioplegia administration. All safety devices had preprogrammed limits of operation that were not altered throughout the experimental time period. Vacuum-assisted venous drainage was used only for minimally invasive aortic valve procedures with negative pressure not exceeding negative 40 mmHg. The CPB circuit contained a membrane oxygenator[6] with an integrated arterial filter (Terumo FX15, Terumo Cardiovascular, or Inspire 6 or LivaNova, Mirandola, Italy), a centrifugal pump (Delphin®, Terumo Cardiovascular), a tip-to-tip coated tubing pack (XCoating®, Terumo Cardiovascular), a 4 to 1 blood to crystalloid cardioplegia circuit (Capiox CP50®, Terumo Cardiovascular), and an in-line arterial and venous blood gas monitor (CDI 500®, Terumo Cardiovascular). Intraoperative autotransfusion (IAT) was used in every case (CATS®, Terumo Cardiovascular) with autotransfusate reinfused through a 20-micron blood filter. The prime constituents included a balanced physiologic saline solution (PSS), 2,000 mL (Plasma-Lyte 148, Baxter Healthcare Corporation, Deerfield, IL); porcine heparin, 10 mL (1,000 IU mL^{-1}); 25% salt-poor albumin, 100 mL; 25% mannitol, 50 mL; and epsilon aminocaproic acid, 20 mL (10 g in 20 mL). Blood flow during CPB was maintained between 1.8 and 2.4 liters per minute (LPM) m^2 with a mean arterial BP between 50 and 80 mmHg. An alpha-stat acid–base regimen was maintained and mild hypothermia (32–35°C bladder temperature) used in all cases with rewarming to 36.5–37°C core temperature before separating from CPB. Arterial blood gas parameters were maintained as follows: pH 7, 30–7.45; PaO_2, 150–250 mmHg; $PaCO_2$, 35–55 mmHg; HCO_3, 23–27 mEq; base excess, 2 to 2; and mixed venous oxygen saturation (SvO_2) greater than 65%. Sevoflurane was administered to all patients during CPB and supplemented with fentanyl to achieve appropriate anesthesia as described previously. At the end of the case and after protamine had been administered, the residual CPB contents were transferred to the IAT machine and processed using the device quality mode. All autotransfusate was returned to the patient either in the operating room (OR) or while in the CVICU.

Transfusion Strategy

Patients were transfused with RBCs if their on-CPB Hct dropped below 24% with either a drop in SvO_2 below 65% and/or an NIRS decline of 25% below the baseline, or an absolute value under 40% unresponsive to increased CPB blood flow or increased depth of anesthesia. All

[6]Oxygenators were used in an alternating fashion without patient specific decisions for use.

intraoperative allogeneic RBC units were washed with an IAT machine (CATS®, Terumo Cardiovascular) before infusion. Transfusion of RBCs in the CVICU was achieved if the patient's Hct decreased below 24% and if there was a concurrent hypoxic indication unresponsive to changes in ventilator settings, such as a reduced SvO_2 or low cardiac index (less than 2 LPM m^{2-1}). Intraoperative transfusion of other blood products occurred when excessive bleeding was encountered, as assessed by the surgeon, and postoperatively when chest tube output exceeded 300 mL $hour^{-1}$ for two consecutive hours. Fresh frozen plasma (FFP) was given when international normalized ratio (INR) exceeded 1.5, with two FFP units administered before repeat INR assessment. The use of FFP during CPB was administered if the perfusionist felt the response to additional heparin to achieve an activated clotting time (ACT) of more than 400 seconds in three consecutive assessments could not be reached. Single-donor platelets (SDPs) were transfused for platelet counts lower than 100,000 uL^{-1} with active bleeding, with patients receiving one SDP before reassessment. Cryoprecipitate (CRYO) (CRYO, 10 pack units) was administered if fibrinogen levels were below 100 mg dL^{-1}. These criteria were the same for the entire hospital stay. Chest tube drainage was measured but was not reinfused in any patient.

AP Technique

All patients were evaluated for AP with those presenting with a pre-CPB Hct of 26% or below excluded because of a calculated post-dilutional CPB Hct of less than 23%. In all patients, the arterial cannula was inserted approximately 3–5 minutes after the administration of porcine heparin (400 IU per kg^{-1}) with a target ACT of greater than 500 seconds. A blood sample was drawn approximately 3 minutes post-heparinization for the measurement of an ACT and arterial blood gas, with the Hct from this sample serving as the Pre-CPB value. The venous and cardioplegia cannulae were inserted next. Once the ACT had reached 300 seconds, the AP procedure commenced.

Non-Standardized AP (NST-AP) Protocol

Before standardization, the perfusionist removed volume primarily from the arterial and venous lines and oxygenator without targeting a specific volume of crystalloid solution to be removed. The decision to use AP was made by the perfusionist and anesthesiologist based on the patients arterial BP post-heparinization and immediately before AP. If the patient's systolic BP pressure was 100 or less, the anesthesiologist administered a small dose of vasopressor (phenylephrine) and once the pressure increased, AP was started. If the arterial systolic BP did not increase, AP was not attempted. The patient's blood volume was drained by a syphon into the circuit and used to displace the asanguineous CPB solution into the two crystalloid 1,000-mL PSS bags used to prime the circuit. The bags were connected to the top of the venous reservoir using the prime port as shown in the manufacturer's instructions for use, with a recirculation line connected via two "wye" connectors: one just distal to the arterial port of the oxygenator and a second at the top of the venous reservoir proximal to the prime port. The order of volume displacement by the device was as follows: arterial line, oxygenator, venous line, venous reservoir, and recirculation line. Once the volume had been displaced, clamps were placed on both the arterial and venous lines and the centrifugal pump turned on to displace the volume into the 1,000-mL bags. As soon as the displaced volume was seen to transition from an asanguineous to a sanguineous solution, the recirculation line was clamped, and the cardiac team was alerted that CPB could commence concurrently with the ACT rising above 500 seconds. The entire AP process usually did not exceed 3 minutes. There was no target AP or end prime volume of the circuit. Patients undergoing this technique comprise the NST-AP group.

Standardized AP (ST-AP) Protocol

The ST-AP protocol was similar to that described previously with the following modification. The surgeon, anesthesiologist, and perfusionist communicated before starting AP. The surgeon allowed AP to proceed as part of the care management plan and did not intercede to stop AP unless hemodynamic instability could not be corrected with vasopressors. Similar to the NST-AP process, the anesthesiologist used phenylephrine to maintain systolic BP but was more cognizant of the ensuing process. The displaced volume was targeted to achieve a minimum of 1,000 mL and displaced this quantity regardless of the change from asanguineous to sanguineous seen entering the prime bags. Several prime constituents were not added to the prime until after the AP process. This included albumin, mannitol, and epsilon-aminocaproic acid which were added after the volume was displaced and immediately before initialing CPB. The targeted end prime volume of the circuit was between 800 and 900 mL. The total time for the ST-AP process did not exceed 120 seconds.

During the study, no attempt was made to displace volume from the cardioplegia circuit. Pump suckers and ancillary vents were not started till the arterial line and oxygenator volume had been displaced, and the ACT exceeded 400 seconds. Additional heparin was titrated throughout the CPB period to achieve a minimal ACT value of greater than 500 seconds. At the end of the surgery, heparin was reversed with protamine administered at a ratio of 100 mg of protamine to every 10,000 IU of total heparin.

Study Groups

The two study groups comprised the NST-AP and the ST-AP groups. Because this was a sequential study, neither group overlapped with the other in regard to patient enrollment. The primary end point was the transfusion of RBCs, whereas the secondary end points included Hct and other perioperative allogeneic blood product transfusions (FFP, SDP, and CRYO).

Statistical Analysis

Statistical analysis of the study data was limited to bivariate descriptive summaries and crude assessment of group difference (no simultaneous statistical adjustment for other known risk factors). Continuous variables were reported as mean with SD and group differences were assessed using Welch's ANOVA. Categorical variables were summarized using count and percent of within-group total, with group differences assessed using the chi-squared test. All statistical analyses were conducted using the R statistical computing environment (version 3.5.2) (18) together with "tableone" analysis package (19–21).

RESULTS

A total of 192 patients were enrolled with 82 in the NST-AP group and 110 in the ST-AP group. In all cases, the use of AP did not result in any adverse events associated with its application, and no one on the cardiac team expressed concerns about the safe conduct of the process. There were no perioperative deaths, defined as a failure to be discharged from the facility, in any patient involved in this study. There were no preoperative demographic differences across the groups (Table 1). There were no statistically significant differences in CPB times, cross clamp times, or types of procedures performed (Table 2). However, there was a slightly higher number of minimally invasive aortic valve replacements in the ST-AP group.

The results of the various volumes are shown in Figure 1 and Table 3. The net crystalloid prime volume in the NST-AP group was 433 mL higher than the ST-AP group, and the total displaced AP volume was 561 mL lower in the NST-AP group (486.8 ± 259.6 mL vs. 1,048 ± 218.7 mL, $p < .001$). The use of UF was highest in the NST-AP group (75.6% vs. 9.1%) and the total volume of the ultrafiltrate removed was three times higher in NST-AP patients. The total asanguineous volume added during CPB was 421 mL higher in the NST-AP group. Anesthesia asanguineous crystalloid volumes were highest in the ST-AP group averaging 379 mL higher than the NST-AP patients. Total urine output was higher in the ST-AP patients averaging over 150 mL more than that in the NST-AP group. There was a higher amount of IAT returned volume given in the NST-AP group vs. ST-AP.

Whereas intraoperative pre-CPB Hcts were identical between groups, all subsequent Hct levels were higher in the ST-AP group except for the last Hct in the OR which were similar (Table 4). Postoperatively, Hct levels were initially higher in the ST-AP patients, but by postoperative day 1, there were no differences between the groups. In those patients who did not receive a periopaertive RBC transfusion, there were no differences in Hct between groups. However, in patients who were transfused with one or more units of RBC, the ST-AP group had higher Hct levels at all time points once on CPB and through entry into the ICU (Figure 2).

There were no differences in intraoperative RBC transfusion, but postoperatively, more patients in the NST-AP group received RBCs than in the ST-AP group (51.2% vs. 28.2%, $p < .01$). The perioperative units of RBC transfusion are shown in Figure 3. The use of FFP during CPB was given in more patients in the NST-AP group. More patients in the ST-AP group received intraoperative SDP, but this trend reversed in the ICU. Although the perioperative transfusion rate of RBC was not different between groups, more patients in the NST-AP received a higher number of RBC units (Table 5).

DISCUSSION

The acceptance of AP as a blood management technique varies in clinical practice and ranges from 17.9% use worldwide (22) to more than 96% at hospitals performing cardiac surgery in America (2). The reasons for this disparity may be traced to the publication of clinical practice guidelines that identified AP as only a mid-level recommendation (17). This discrepancy may be related to several factors, including a paucity of well-constructed studies in the literature along with the heterogeneity in

Table 1. Demographic data for all patients.

	Non-Standardized	Standardized	*p*-Value
Number	82	110	
Age (years) (mean [SD])	65.3 (10.1)	66.8 (11.8)	.345
Gender (male) (count [%])	52 (63.4)	75 (68.2)	.592
Weight (kg) (mean [SD])	90.7 (22.4)	86.5 (20.1)	.176
Height (cm) (mean [SD])	170.4 (10.9)	170.5 (10.7)	.938
Body surface area (mean [SD])	2.02 (.28)	1.97 (.24)	.29

Table 2. Operative data for all patients.

	Non-Standardized	Standardized	*p*-Value
Number	82	110	
CPB time (min) (mean [SD])	102.7 (56.1)	114.2 (55.1)	.159
Cross clamp time (min) (mean [SD])	70.6 (41.0)	69.2 (44.0)	.818
Procedure type			
Aortic procedure (count [%])	1 (1.2)	3 (2.7)	–
AVR (count [%])	14 (17.1)	18 (16.4)	–
AVR combined (count [%])	11 (13.4)	15 (13.6)	–
Coronary artery bypass graft (count [%])	40 (48.8)	51 (46.4)	–
MVR (count [%])	7 (8.5)	10 (9.1)	–
MVR combined (count [%])	5 (6.1)	7 (6.4)	–
AVR/MVR (count [%])	4 (4.9)	6 (5.5)	–
Minimally invasive AVR which are part of the AVR group (count [%])	5 (6.1)	11 (10.0)	–

AVR, aortic valve replacement; MVR, mitral valve replacement or repair.

how techniques of AP are applied (11,13–16). Most articles do not report the frequency of which AP was attempted but prematurely stopped, nor do they state the reasons for such cessation. The reasons that AP has not gained universal acceptance may be related to a number of observations, including the degree of hemodynamic instability that occurs with fluid shifts immediately before CPB and intolerance by the attending perfusionist to conduct CPB with lower volumes in the extracorporeal circuit. Indeed, it is not inconceivable for the displaced volume to be added back to the patient soon after initiating CPB with AP because of a zero-balance effect of rehydration. One possible benefit of performing AP may be the maintenance of a more rheological equivalent solution coursing through the arterial circuit into the ascending aorta at the onset of CPB. The aortic arch and brachiocephalic vessels contain both aortic and carotid bodies which consist of several small clusters of chemoreceptors and baroreceptors made of highly vascularized glomus cells that release a variety of neurotransmitters affecting BP. With the onset of CPB, the clear solution that initially perfuses the aorta and carotid arteries may elicit a neuroendocrine response that stimulates these cells, which may not occur or results at a slower rate, when the blood solution from AP perfuses the ascending aorta. Nevertheless, AP is widely practiced, at least in North

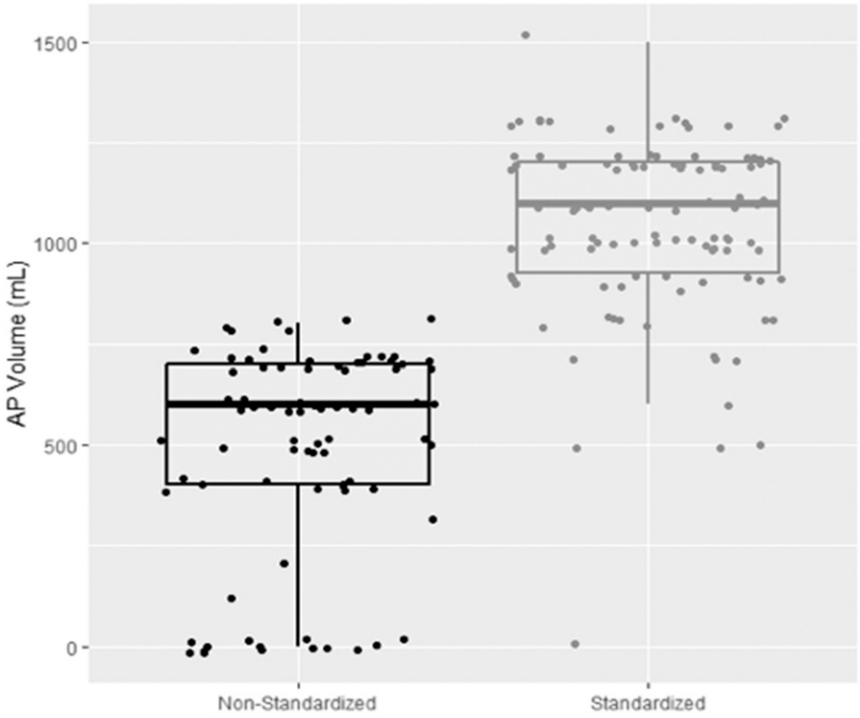

Figure 1. Autologous prime volume (APV) removed from study groups.

Table 3. Perioperative volume administration and removal.

	Non-Standardized	Standardized	*p* Test
Number	82	110	
Net crystalloid prime volume (mL) (mean [SD])	1,415.7 (295.4)	982.7 (282.8)	<.001
APV (mL) (mean [SD])	486.8 (259.6)	1,048.2 (218.7)	<.001
CPB Asang. (mL) (mean [SD])	1,198.4 (835.6)	776.8 (711.9)	<.001
CPB urine (mL) (mean [SD])	226.3 (168.8)	328.0 (207.6)	<.001
UF use (Yes) (count [%])	62 (75.6)	10 (9.1)	<.001
Ultrafiltration volume (mL) (mean [SD])	563.5 (408.9)	170.9 (614.7)	<.001
Anesthesia Asang. (mL) (mean [SD])	1,497.6 (703.5)	1,877.4 (696.6)	<.001
Total urine (mL) (mean [SD])	517.3 (274.3)	753.2 (369.7)	<.001
IAT returned (mL) (mean [SD])	1,204.7 (575.7)	803.3 (488.8)	<.001
ICU chest tube output (mL) (mean [SD])	1,301.0 (977.8)	1,447.1 (1,403.2)	.427

Asang., asanguineous.

America, and remains one component of a multifaceted blood conservation program, including the one at our center. What we did notice, however, was that the techniques being used by our perfusion team varied among clinicians despite the mantra that AP was being administered. The concern arose that the lack of an ST-AP protocol could affect outcomes and prompted the current investigation as an effort for continuous quality improvement for clinical practice.

The standardization of healthcare delivery techniques that are formulated on the best available evidence has been shown to improve outcomes and reduce costs (23). Clinical practice guidelines are useful tools in identifying techniques that possess high-level evidence either that they be incorporated or omitted from care plans. In cardiac surgery, the assessment of compliance with these guidelines is often missing or non-existent, making it difficult to determine the effect on outcomes. We have previously identified that efforts to improve quality are often taken at a macro level which requires complex methods for change and requires buy-in from multiple levels to avoid a top-down management approach (24). However, it is at the institutional level where performance is more readily modifiable, resulting in improvements for patient care with more rapidity.

One of the most important aspects of standardizing the AP process was the discussion that occurred among the cardiac team concerning the critical nature of the reducing variation. The team met formally on a monthly basis and more frequently in informal settings. All team members were involved, which included surgeons, anesthesiologists, perfusionists, physician assistants, and nurses (OR and ICU). Once the protocol had been devised and all agreed to its applicability, it was applied across all patients. Teman et al. have described a comparison of AP vs. non-AP techniques in a patient population where the study groups were established by the perfusionist preference to either use the technique or not (25). Although the authors did find a benefit to use AP, the lack of standardization within the clinical practice creates an element of inter-clinician bias and may influence the results. We chose to establish an agreed-upon protocol that the entire team would follow to reduce variation related to clinician preference.

Most research published on AP has compared patients who have either undergone AP or who have not, which expands the volumetric differences and may influence RBC transfusion rates (26,27). Our study was unique in so far as all patients had undergone the displacement of volume

Table 4. Hct and platelet values throughout hospital stay.

	Non-Standardized	Standardized	*p*-Value
Number	82	110	
HCT post-induction (%) (mean [SD])	36.2 (4.5)	36.4 (5.1)	.758
HCT pre-CPB (%) (mean [SD])	33.7 (4.8)	33.9 (4.9)	.727
HCT first CPB (%) (mean [SD])	25.7 (4.5)	27.9 (4.2)	<.001
HCT low CPB (%) (mean [SD])	24.1 (4.5)	25.7 (4.0)	.01
HCT high CPB (%) (mean [SD])	27.7 (3.5)	29.1 (3.6)	.008
HCT last in room (%) (mean [SD])	27.0 (4.1)	27.6 (3.5)	.279
HCT ICU entry (%) (mean [SD])	32.5 (4.0)	34.3 (4.0)	.003
HCT POD 1 (%) (mean [SD])	32.0 (3.8)	32.6 (3.7)	.279
PLT preoperative (uL^{-1}) (mean [SD])	214.3 (57.3)	213.2 (62.9)	.901
PLT ICU entry (uL^{-1}) (mean [SD])	132.6 (45.2)	137.6 (48.7)	.471
PLT POD 1 (uL^{-1}) (mean [SD])	135.8 (46.6)	135.9 (50.8)	.983

PLT, platelet count; POD, postoperative day.

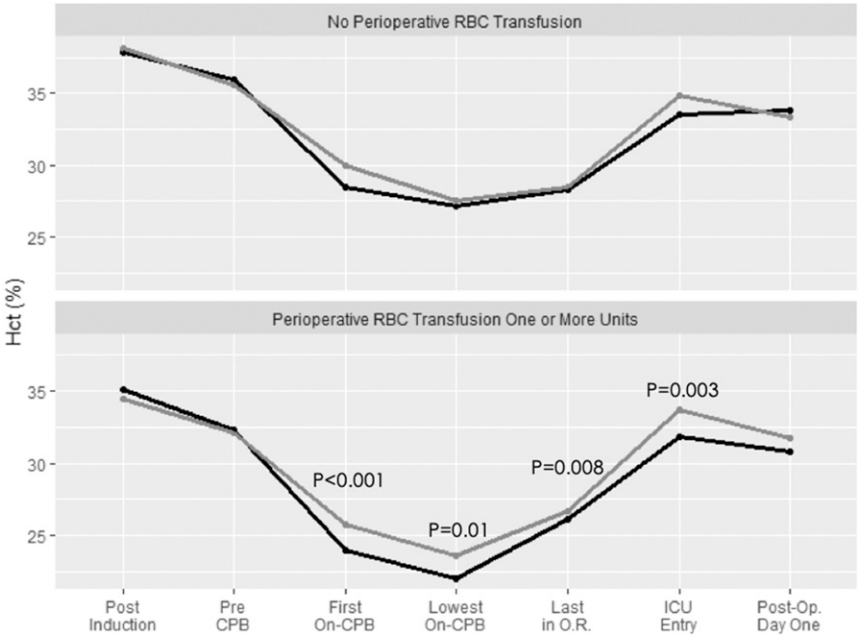

Figure 2. Intraoperative Hct values among study groups. CPB, cardiopulmonary bypass; ICU, intensive care unit; Post-Op, postoperative. The standardized autologous prime group is shown in gray.

during the study. Therefore, our results may not have been as dramatic as if we had compared two groups based on undergoing AP or not. Furthermore, although we standardized the AP technique through adherence to a protocol, we did not achieve our target of 1,000 mL of displaced volume on all patients. In fact, 28 of the 110 patients (25.4%) in the ST-AP group did not meet our target. The decision to keep these patients in the analysis was made because the standardized protocol was followed and the final outcomes were not realized until the data were analyzed. To remove these observations may have biased the results and were not identified in the initial exclusion criteria and may have

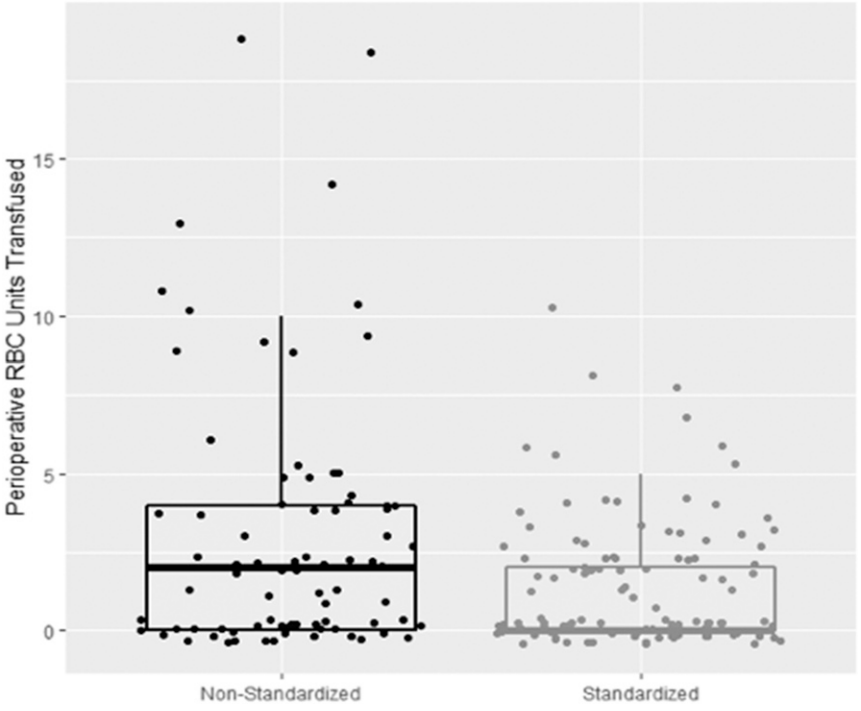

Figure 3. Perioperative allogeneic units of RBC transfusion in study groups.

Table 5. Perioperative transfusion data.

	Non-Standardized	Standardized	*p*-Value
Number	82	110	
CPB RBC (U) (mean [SD])	.9 (1.7)	.7 (1.2)	.463
CPB RBC (mL) (mean [SD])	259.8 (511.6)	213.2 (364.0)	.463
CPB FFP (U) (mean [SD])	.32 (1.08)	.04 (.23)	.009
CPB FFP (mL) (mean [SD])	88.8 (301.2)	10.9 (69.5)	.009
Anesthesia RBC (U) (mean [SD])	.12 (.46)	.15 (.52)	.745
Anesthesia RBC (mL) (mean [SD])	36.6 (136.6)	44.0 (157.1)	.734
Anesthesia FFP (U) (mean [SD])	.18 (.65)	.15 (.6)	.763
Anesthesia PLT (U) (mean [SD])	.24 (.69)	.30 (1.2)	.516
Anesthesia PLT (mL) (mean [SD])	24.4 (69.5)	30.0 (112.8)	.691
Anesthesia CRYO - U (mean [SD])	.00 (.00)	.05 (.31)	.192
Anesthesia CRYO - mL (mean [SD])	.00 (.00)	4.55 (31.44)	.192
ICU RBC (U) (mean [SD])	2.0 (3.2)	.6 (1.1)	<.001
ICU RBC (mL) (mean [SD])	607.1 (941.0)	191.8 (354.2)	<.001
ICU RBC transfusion (yes) (%)	42 (51.2)	31 (28.2)	.002
ICU FFP (U) (mean [SD])	.82 (1.89)	.23 (.68)	.003
ICU FFP (mL) (mean [SD])	238.7 (549.0)	68.1 (200.5)	.003
ICU PLT (U) (mean [SD])	.72 (2.34)	.04 (.27)	.003
ICU PLTS (mL) (mean [SD])	71.3 (232.4)	3.69 (27.10)	.003
ICU CRYO (U) (mean [SD])	.01 (.11)	.04 (.23)	.384
ICU CRYO (mL) (mean [SD])	1.52 (13.80)	4.60 (28.26)	.366
Perioperative RBCs transfusion (Yes) (%)	49 (59.8)	52 (47.3)	.117
Perioperative RBCs (U) (mean [SD])	3.0 (4.1)	1.5 (2.1)	.001
Perioperative RBCs (U) When Txd. (mean [SD])	5.0 (4.3)	3.1 (2.0)	.007

PLT, platelets; Txd., transfused; When Txd., grouping patients as to whether they have received a RBC transfusion or not.

resulted in a smaller intergroup difference in both primary and secondary end points. However, this reflects the normal clinical variation that is seen in fluid environments that occur in cardiac surgery and better reflect the diverse operative conditions by which these treatments are applied.

The results of changes in Hct in this study agree with what others have found. Severdija et al. have shown that when AP is applied when the nadir intraoperative Hct was similar to that of the current study (26). However, the ICU entry Hct was only 28%, which was 6% lower than that of our AP patients. This may reflect the use of IAT which the authors only stated was used to process pericardial shed blood. In our institution, IAT is used throughout the entire case, including the processing of residual pump contents. Most autotransfusate was collected post-protamine administration, and this volume was reinfused both intraoperatively and in the ICU. The NST-AP group had significantly higher autotransfusate, which was more than 400 mL higher than the ST-AP patients, which may explain the higher ICU entry Hct in that group. Trapp and colleagues also have shown that AP is beneficial in reducing allogenic RBC transfusion but were unable to demonstrate that it resulted in reduced levels of biological markers of injury or postoperative outcomes (1). This effect was also shown in another study (13), which failed to show patient benefit beyond maintaining higher intraoperative Hct levels. However, all these studies did identify that AP can be achieved safely without increased risk or negative outcomes. Although the reasons for this are unknown, it may be related to the absolute level of hemodilution related to the volume of asanguineous solution displaced. The removal of 300 mL of clear volume did not have an effect on lowering RBC transfusion rates (16), which may reflect hesitation on the perfusionist, and cardiac team, to remove higher volumes. The AP volumes displaced ranged from just under 500 mL in the non-standardized group to just more than 1,000 mL once standardized. This difference did result in higher sustained Hct levels which were approximately 2% higher, but the overall effect on RBC transfusion was not seen intraoperatively, whereas in the ICU, more patients were transfused with higher RBC volumes. The reason for this disparity may reflect that even removal of 500 mL of AP volume may be beneficial and that extending beyond that confers reduced hemodilution but does not affect RBC transfusion. It is unknown why the ST-AP group had more crystalloid volume given by the anesthesiologist. Because we only measured the total volumes given and not the pre-CPB or post-CPB time periods, we cannot determine if the additional volume was given after CPB and is related to lower prime volumes.

The decision to use UF during CPB was made by the attending perfusionist and was not standardized in the AP protocol. Before standardizing AP, the perfusion team used UF significantly more than in the post standardization period, falling from 75.6 to 9.1%. Similarly, the total volume of ultrafiltrate declined several fold. It is more than likely that the use of UF would have declined even further, but there were more minimally invasive aortic valve

procedures performed in the ST-AP group where the myocardial protection technique used a pure crystalloid solution,[7] which proactively resulted in the need for UF. The large reduction in the use of UF resulted in better management of resources and an inherent cost-savings to the hospital. We had previously shown that the use of UF may negatively impact urine output (28). The negative impact of UF on kidney function may be exacerbated when patients present with preoperative renal impairment and that increasing the volume of UF may further increase the risk of acute kidney injury (29). Although the mechanism of this reaction, if found to be true, is elusive, it may be related to the volume shift and resultant renal perfusion. Although we did not measure renal function during this study, the lower urine output seen in the NST-AP group is the reason to examine this effect in further prospective research.

The protocol for either AP technique did not include displacing the volume from the cardioplegia circuit, which has been described by others (30). This may have had an additional positive effect on the first, and ensuing, Hcts during CPB. However, the total prime volume of the cardioplegia heat exchanger (52 mL) and tubing (60 mL) represented approximately 10% of our net prime volume. Whether this would have influenced our results is questionable but undoubtedly may have had a summative benefit.

Another difference in our study as compared with others was the decision to include all procedure types in the population. Many studies limit the patient population to CAB and/or valve operations (3,7,8). We decided to evaluate the effect in adults undergoing cardiac surgery for diverse procedures, excluding emergencies and patients presenting with a preoperative anemia. Such a diverse patient population may have influenced outcomes because cardiac valvular surgeries and resternotomy procedures are known to result in an increased risk for transfusion (31).

Limitations

The present study has several imitations. First, it is a retrospective single-center study without randomization that used prospectively obtained quality improvement data to populate a database. Therefore, we cannot state the cause and effect and concede that the lack of randomization may have influenced results. The study was performed sequentially, so differences that occur in one time period cannot be discounted in having an effect on outcomes. However, the entire cardiac team, less one perfusionist who was involved only in the first few months of the study, was the same. There was no control group of patients who did not undergo AP. Such a cohort would not have been possible because the practice of AP is well engrained in the culture of the cardiac team, and the omission of this would not have been ethically achievable. And finally, although we tried to establish specific criteria for the administration of blood products, we cannot rule out the fact that patients may have been transfused outside of the guidelines established.

[7]Custodiol HTK Solution, Essential Pharmaceuticals LLC, Durham, NC.

CONCLUSIONS

The use of AP of the heart–lung machine during cardiac surgery with CPB resulted in a reduction in hemodilution as evidenced intraoperative by Hcts that averaged above 24%. The standardization of AP techniques further limited hemodilution resulting in Hct values that were sustained at over 2% higher than patients with non-standardized techniques. The application of an ST-AP protocol was safely applied in a clinical setting demonstrating the benefit of communication among the cardiac team members to establish an evidence-based process to optimize patient benefit.

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