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Introducing retrograde autologous priming for bloodless open-heart surgery in a new cardiac centre: Initial outcomes

Murat Tavlasoglu[a,*], Ibrahim Samurcu[a], Munacettin Ceviz[a]

[a]*Private Buhara Hospital, Department of Cardiovascular Surgery, Erzurum, Türkiye*

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Abstract

Aim: The use of priming fluid in the cardiopulmonary bypass causes hemodilution and increases the need for blood transfusions. Retrograde autologous priming is known to be beneficial in reducing blood transfusion and hemodilution. In this article, 38 cases were retrospectively reviewed to demonstrate the feasibility of routine retrograde autologous priming in a newly established cardiac surgery center.

Materials and Methods: A total of 38 patients underwent open-heart surgery between January 2024 and July 2024. All patients were operated using a cardiopulmonary bypass machine primed with retrograde autologous blood. Perfusion and anesthesia techniques were the same for all patients. Hematocrit levels in the preoperative period, during weaning, on the first postoperative day, third day, discharge day, and 10th postoperative day were retrospectively analyzed. Postoperative hemodynamic parameters, pressor requirements, and fluid requirements were recorded. Length of stay in the hospital and intensive care unit, as well as blood requirements, were retrospectively analyzed.

Results: No major bleeding and mortality was observed. Hematocrit levels during cardiopulmonary bypass ranged from 28% to 31%. The transfusion rate for per patient was 0.13 units.

Conclusion: It was proven that the routine use of retrograde autologous priming, even in a newly established heart surgery institution, is safe, repeatable, and effective in decreasing hemodilution and red cell transfusion rates in cardiac operations.

Introduction

Cardiac surgical procedures can necessitate blood use in many cases. Red cell transfusions occur in approximately 40%–60% of patients during their hospitalization [1]. A blood transfusion is a kind of tissue transplantation, so efforts have been made for optimal blood conservation techniques in cardiac surgical procedures. Many approaches have been described to date to decrease blood transfusion rates, such as preoperative anemia management, smaller cardiopulmonary bypass (CPB) circuits, cell salvage, use of antifibrinolytics, reduction of transfusion triggers, and topical hemostatic agents [1,2].

One of the blood conservation approaches used in cardiac surgery is retrograde autologous priming (RAP). It was first described in 1960 by Panico and Neptune [3]. In this approach, the main principle for achieving blood conservation is draining the patient's blood into the CPB circuit and targeting high hematocrit levels, thus avoiding hemodilution from crystalloid-based prime solutions. This defined method for decreasing the need for transfusion was first tested by Rosengart et al. in a small randomized controlled trial (RCT) in 1998 [4]. Over the past 7 decades, there have been a number of small RCTs and studies to prove the beneficial effects of RAP on diminishing red blood cell transfusion rates. Although joint consensus has been recommending the use of RAP, previous grading has not been consistent, and the level of evidence has not included additional trials performed in the era [1,2,4]. However, it has been proven in recent studies that RAP is effective in decreasing transfusion rates [2,5].

This study seeks to evaluate the viability, cost-efficiency, and consistency of utilizing RAP in CPB circuits for open-heart surgery, even in a new cardiac surgery center, as a reliable method for optimizing blood conservation strategies.

Materials and Methods

Patient characteristics

This study was conducted at a newly established Cardiovascular Surgery Department in Private Buhara Hospital in Erzurum between January 2024 and July 2024. The

*Corresponding author:
Email address: mrttvls@gmail.com (Murat Tavlasoglu)

sample size determined by time period in which all patients underwent open heart surgery, except off-pump and minimally invasive procedures between 1st January 2024 and 31st July 2024. A total of 38 patients (34 males, 4 females; mean age: 57.29±10.8 years; range 34 to 74 years) were included in the study. Although all patients were included for the study except off-pump surgeries, the sample size was not large enough. This can be explained by utilizing RAP in a new heart center. due to a new center. The Hospital Ethics Committee approved the study based on retrospective data collection. This study complies with the Declaration of Helsinki.

Preoperative and intraoperative practices and preferences

Two patients who underwent off-pump coronary bypass surgery were excluded from the study. After obtaining approval from the hospital ethics committee, the retrospective study was initiated. All antiplatelet drugs were discontinued before each surgery. Clopidogrel was stopped 4 days before surgery, acetylsalicylic acid 1 day before surgery, and anticoagulant drugs 3 days before the day of surgery. Patients were administered Enoxaparin Sodium (100 IU/day) twice daily during the preoperative period. Patients were given 10 mg of oral diazepam the night before surgery. Anesthesia induction was performed with 2 mg/kg etomidate, 1 µg/kg fentanyl, and 1 mg/kg vecuronium, and maintenance anesthesia was performed with 1 MAC isoflurane.

Autologous blood was collected from all patients with a hematocrit value of 40% or greater during anesthesia induction. RAP was the routine approach for all patients undergoing open heart surgery, and RAP volumes maintained between 900-400cc (mean: 711.8±107.44, max 900cc, min 400cc). In each cardiopulmonary bypass procedure, the priming solution volumes were maintained between 1400-1000cc (mean: 1201.315±129.701, max 1400cc, min 1,000 cc) using the balanced electrolyte solution Isolyte-S® (Eczacıbaşı-Baxter, Istanbul). Additionally, 5000 units of heparin were added to each priming solution. The CPB circuit was kept as short as possible in all cases to reduce the amount of priming solution. After achieving anticoagulation with 300 IU/kg heparin, the activated clotting time (ACT) value was maintained above 400 seconds. A roller pump and membrane oxygenators (Eurosets Kompass A.L One, Eurosets Horizon AF Plus, Eurosets Skipper AF Plus, Medolla, ITALY) (Paragon Adult Midi Integrated Oxygenator, Nottinghamshire, UK) (Capiox FX15 and FX25 Oxygenator, Terumo Global, Europe) were used for cardiopulmonary bypass. After aortic clamping, 1,000 cc of Modified Del Nido cold (4-8°C) blood cardioplegia (40 cc 7.5% potassium, 16.3 cc 8.4% $NaHCO_3$, 16.3 cc 15% $MgSO_4$, 6.5 cc 2% Lidocaine Hydrochloride, 20 cc 20% Mannitol) was administered at a 4:1 ratio (800 cc blood and 200 cc Modified Del Nido solution), with an additional 500 cc dose administered every 35-40 minutes (antegrade from the aortic root and venous grafts). The average flow rate was set to 2.2 to 2.4 L/min/m^2. Operations were performed at moderate hypothermia (rectal temperature) of 32°C. The room temperature was maintained at 18-20°C. After reaching 35°C, cross clamp was removed, and heating continued until the rectal temperature reached 37°C before separation from cardiopulmonary bypass. Heparin was neutralized with protamine sulfate at a 1:1.3 ratio. Intravenous metoprolol and inotropic agents were used to control heart rate and arterial pressure, respectively. Tranexamic Acid was administered at a dose of 50 mg/kg after heparin neutralization with protamine. In the postoperative period, fluid replacement was adjusted to maintain central venous pressure at 8-12 mm Hg. Erythrocyte suspension was given when the hematocrit level fell below 22% and clinical symptoms associated with low hematocrit levels appeared. Fresh frozen plasma and platelet suspension were administered in cases of demonstrated bleeding disorder (international normalized ratio > 1.5, activated prothrombin time > 60 s, and platelet count $< 80{,}000/mm^3$) or suspected postoperative platelet and coagulation factor dysfunction. The decision for reoperation due to bleeding was made if the bleeding amount was 200 cc/hour or more, or if the bleeding amount was 300 cc/hour or more for the following two hours. ACT values were routinely measured in patients admitted to the intensive care unit, and additional protamine was administered if the entry value was exceeded. Parameters such as postoperative bleeding amount, chest tube removal time, intensive care unit stay duration, discharge time, revision rates, changes in renal function, and hematocrit levels (postoperative day 1, postoperative day 3, at discharge, and postoperative day 10) were investigated.

Retrograde autologous priming (RAP)

In CPB circuits, we use a connection line that extends between output of arterial filter and the venous line. The connecting line is one of the easiest ways for deairing arterial line during the arterial cannulation process (Figure 1, black arrow). Micro air bubbles are evacuated from arterial line through to venous reservoir via connecting line, such deairing of CPB circuits is a very effortless approach. RAP procedure begins after completion of cannulation. The procedure consists of four steps. First one consists of draining priming solution from arterial line distal to

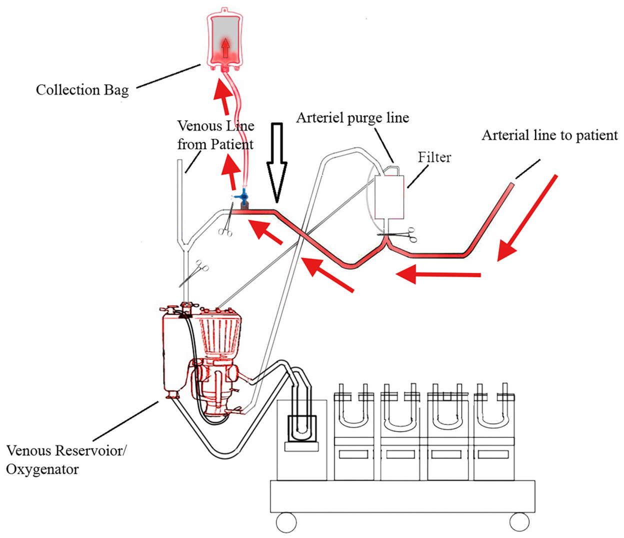

Figure 1. RAP procedure, step 1.

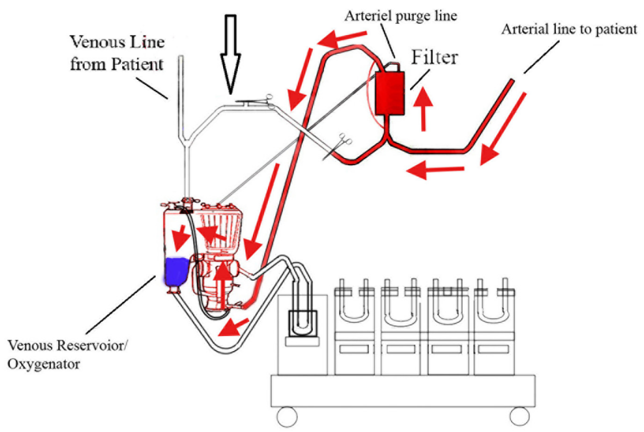

Figure 2. RAP procedure, step 2.

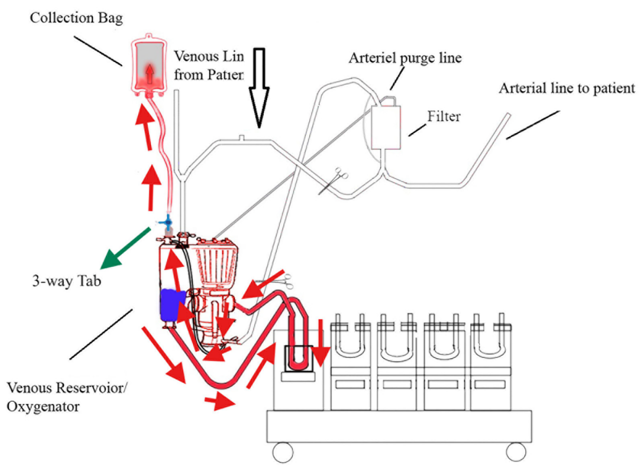

Figure 3. RAP procedure, step 3.

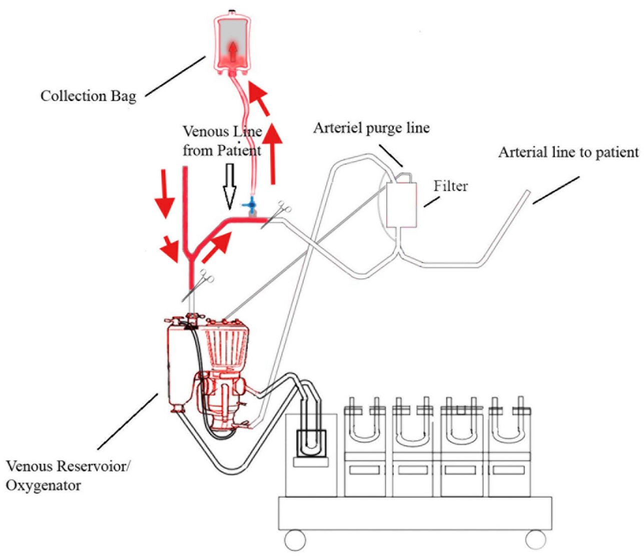

Figure 4. RAP procedure, step 4.

the filter through to the collecting bag via connecting line between distal end of arterial filter and venous line (Figure 1). In this step, line occluding clamp is applied arterial line just proksimal to the bifurcation level of arterial line at the output portion of filter, depicted in Figure1. Here collecting bag is placed at the middle portion of connecting line. I In the second step, retrogradely arterial filter drainage and then drainage of arterial line which is proximal to filter and finally priming solution of oxygenator are drained to the reservoir, thus drainage of filter, arterial line and oxygenator are completed (Figure 2). Here, clamp is applied to the connecting line side of bifurcation. Third step consists of draining priming solution from reservoir to the collecting bag placed on 3-way tap (Figure 3, dark green arrow) at the right upper part of reservoir via direct connection between arterial output of oxygenator and 3-way tap (Figure 3). Here, clamp is applied on arterial line after it leaves oxygenator. Finally, fourth step consists of draining priming solution from venous line through the collecting bag placed at the middle portion of connecting line and clamps are applied on connecting line after collecting bag and venous line before venous inflow of reservoir (Figure 4). Red arrows represent the direction of drainagein each step. Thus, prime solution previously used in order to evacuate air from CPB lines and parts such as filter, oxigenator and reservorior replaced with autologous blood which provides higher hematocrit levels, and decreased amount of prime solution. To decrease the risk of hemodynamic deterioration when implementing RAP procedure, CPB circuits were kept as short as possible. We strictly obey this rule in the institution. Strict monitorization is essential in RAP procedure.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The categorical data in this study were reported as percentages, reflecting the proportion of individuals within each category. The Shapiro-Wilk test was performed to assess the normality of each parameter. If a p-value greater than 0.05 suggests that the data is normally distributed, while a p-value less than 0.05 indicates deviation from normality. Arithmetic mean, standard deviation, and associated confidence interval presented for normally distributed variables and median, interquartile range, and associated confidence interval presented for the data which do not follow a normal distribution. Correlation analysis was performed to analyze the relationships between parameters. Regression analysis was performed for identifying and quantifying the relationship and modeling the relationship between a dependent variable and one or more independent variables.

Results

RAP diagram and the sequence of RAP preparation were depicted in Figure 1, 2, 3, 4, respectively. Preoperative demographic variables, patient characteristics and surgical data for 38 patients were demostrated in Table 1. All patients underwent cardiac surgical procedures using heart lung machine included in the study. Off – pump surgical procedures and minimally invasive procedures were also excluded. The Shapiro-Wilk test for determining normal distribution and descriptive statistics for parameters

Table 1. Preoperative demographic variables, patient characteristics and surgical data.

Preoperative demographic variables		
Variables	Number (n)	Percentage (%)
Smoking	34	89.47
Diabetes mellitus	28	73.68
Hypertension	24	63.15
Preoperative clopidogrel medication	12	31.57
Preoperative TIA history	3	7.89
Carotid artery disease	3	7.89
COPD	8	21
Cronic Renal insufficiency	1	2.6
Characteristics of patients and surgical data		
Characteristics of patients	Mean	SD
Age (year)	57.29	10.8
Weight	82.32	12.6
Preoperative hematocrit (%)	43.3	15.12
Ejection fraction (%)	42.3	5.7
Sex	Number (n)	Percentage (%)
Male	34	89.47
Female	4	10.52
Surgical procedures	Number (n)	Percentage (%)
CABG	28	73.6
CABG + Giantic Goitre	1	2.6
CABG + Ascending Aortic Replacement	1	2.6
AVR	1	2.6
MVR	1	2.6
AVR+MVR	3	7.9
BENTALL	3	7.9

TIA: Transient Ischemic Attack COPD: Chronic Obstructive Pulmonary Disease CABG: Coronary Artery Bypass Grafting. AVR: Aortic Valve Replacement. MVR: Mitral Valve Replacement.

following normal and abnormal distribution were summarized in Table 2.

In total, 38 patients underwent open-heart surgery, 4 of who were female. Performed surgical procedures were coronary artery bypass surgery (CABG) (28 patients, 73.6%), Bentall procedure (3 patients,7.9%), double valve replacement (3 patients, 7.9%), aortic valve replacement (1 patient, 2.6%), CABG + ascending aortic replacement (1 patient, 2.6%), mitral valve replacement (1 patient 2.6%), and CABG + gigantic goitre (1 patient 2.6%). Intraoperative x-clamp time and total perfusion time were 56.36 ± 22.43 and 84.21± 33.85, respectively. Correlation analysis showed strong positive correlations between parameters were shown in Table 3. However, RAP and Used package of Blood presented weak, but negative correlation (r = -0.15). Regression Analysis suggested correlation between RAP and other variables (Figure 5). Higher RAP values were associated with better short-term hematocrit levels (weaning, postoperative day 1, and day 3). The impacts of RAP on Hct values diminished by discharge and were not significant by postoperative day 10. Regression analysis demonstrated some key findings about Impact of RAP on Patient Recovery. They are as follows: 1- Higher RAP values significantly predicted higher weaning Hct values. Approximately 34% of the variability in weaning Hct value can be explained by RAP (Coefficient: 0.0186, $p<0.001$, R-squared: 0.338). 2- RAP was a significant predictor of Hct values on postoperative day 1, though the relationship was weaker compared to weaning Hct value (Coefficient: 0.0087, $p = 0.027$, R-squared: 0.130). 3- RAP significantly impacted Hct values on postoperative day 3, explaining about 40% of the variability (Coefficient: 0.0095, $p = 0.002$, R-squared: 0.401). 4- While there was a positive relationship, RAP was not a statistically significant predictor of discharge Hct value at the 0.05 level (Coefficient: 0.0065, $p = 0.103$, R-squared: 0.199). 5- RAP did not significantly predict Hct values on postoperative day 10, with very low explanatory power (Coefficient: 0.0084, $p = 0.296$, R-squared: 0.030). The relationship between RAP and postoperative Hct levels are showed a significant positive impact at time series analysis.

Postoperative drainage was ranged from 150cc to 550cc (mean: 351,32cc ±129,70cc). None of patients underwent revision for bleeding. All patients followed up in intensive care unit after surgery for 2 days even if they were hemodynamicly stable. Chest tubes were removed in postoperative third day. Hospital stays ranged between 4 days to 8 days (mean: 5.25 days ±1.11days). No hospital mortality was observed. Renal function tests were in normal range in all patients. In postoperative period patient volume replacement was 100 cc/hour.

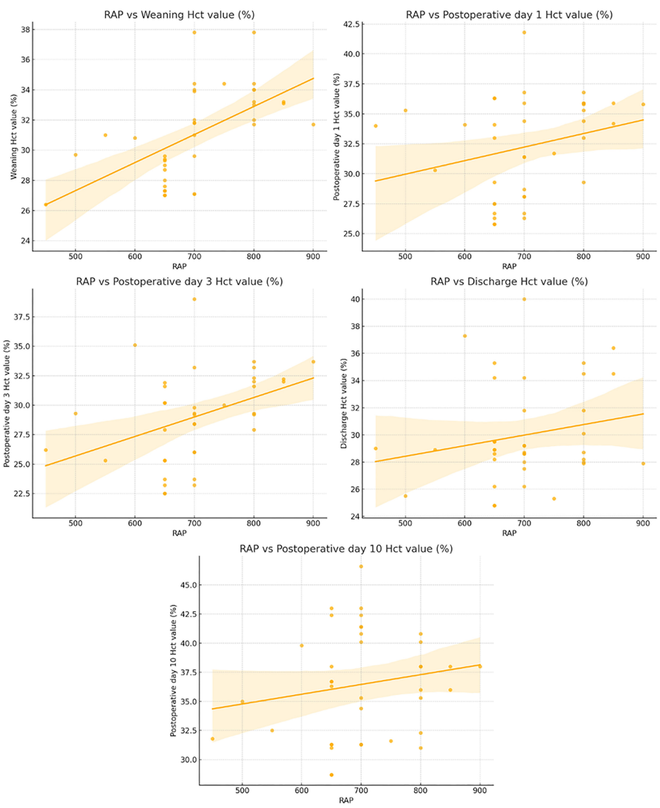

Figure 5. Regression analysis shows the impact of RAP on Hct value changes in weaning from CPB, postoperative day 1, 3, discharge and postoperative day 10.

Table 2. The Shapiro-Wilk test results for determining normal distribution and descriptive statistics of variables in preoperative and postoperative periods.

	W-statistic	p-value	Distribution
Preoperative Hct value (%)	0.96	0.288	Normally distributed (p>0.05)
Priming solution (cc)	0.76	0.000001	Abnormal distribution (p<0.05)
RAP	0.91	0.005	Abnormal distribution (p<0.05)
Authologus Blood (cc)	0.81	0.000052	Abnormal distribution (p<0.05)
CPB urine output (cc)	0.96	0.20	Normally distributed (p>0.05)
Weaning Hct value (%)	0.93	0.03	Abnormal distribution (p<0.05)
BALANCE in CPB (cc)	0.94	0.058	Normally distributed (p>0.05)
Postoperative day 1 Hct value (%)	0.92	0.01	Abnormal distribution (p<0.05)
Postoperative day 3 Hct value (%)	0.96	0.32	Normally distributed (p>0.05)
Discharge Hct value (%)	0.89	0.002	Abnormal distribution (p<0.05)
Postoperative day 10 Hct value (%)	0.96	0.195	Normally distributed (p>0.05)
Used package of Blood (Unit)	0.40	0.0000027	Abnormal distribution (p<0.05)

The Shapiro-Wilk test. A p-value greater than 0.05 suggests that the data is normally distributed, while a p-value less than 0.05 indicates deviation from normality.

Descriptive statistics

Descriptive statistics for normally distributed variables				
	Mean	Standard Deviation	95% CI Lower	95% CI Upper
Preoperative Hct value (%)	43.71	4.07	42.36	45.05
CPB urine output (cc)	689.47	262.82	603.08	775.86
BALANCE in CPB (cc)	139.47	253.39	56.18	222.76
Postoperative day 3 Hct value (%)	29.03	3.89	27.76	30.31
Postoperative day 10 Hct value (%)	36.48	4.56	34.98	37.98

Descriptive statistics for variables not following normally distribution				
	Median	IQR	95% CI Lower	95% CI Upper
Priming solution (cc)	1300.0	200.0	1100.0	1300.0
Authologus Blood (cc)	400.0	100.0	400.0	400.0
Weaning Hct value (%)	30.9	3.475	29.3	31.65
Postoperative day 1 Hct value (%)	33.5	7.549	29.8	34.4
Discharge Hct value (%)	28.9	3.800	28.4	29.5
Used package of Blood (Unit)	0.0	0.0	0.0	0.0

Used package of Blood (Unit) in 38 patients were only 5 unit in total ranged from 0 to 1(mean: 0.13 ±0.34).

Discussion

The main principles in heart surgery in recent years are to minimize all interventions, including surgical approaches and materials used, to reduce unnecessary patient interaction. There are many new researches trying to minimize heart lung machine lines or efforts to succeed bloodless operations by using patients own bloods. It is possible to mention such efforts advocating minimally invasive approaches are better for any surgical interventions [6]. Although all patients were included for the study except off-pump surgeries, the sample size was not large enough. This can be explained by utilizing RAP in a new heart center. In addition, this situation can be interpreted as a deficiency of the study, it is inevitable that the first results have a low sample size.

RAP and Used package of Blood presented weak, but negative correlation (r = -0.15) means as the volume of RAP increases, used package of Blood tends to decrease slightly. Higher RAP values were associated with better short-term hematocrit levels. This suggested that RAP played a significant role in early postoperative recovery, potentially through improved blood conservation and fluid management. Insignificant impact of RAP on Hct values in discharge and in postoperative day 10th can be explained by other factors which may influence long-term recovery more strongly.

We observed that RAP significantly decreased the actual priming volume, preserved the hematocrit level during CPB to a certain degree. Beneficial results of RAP were mentioned in various articles [3-10]. Also increased hematocrit levels during CPB can decrease lactate accumulation in CPB period [8]. Similarly, our results showed that RAP lowered the volume of transfusion. Moreover, in early postoperative period, RAP approach resulted in high a Hematocrit level which means improved tissue perfusion. Hofmann et al. and Severdija et al. reported intraoperative blood transfusion rates were significantly reduced in patients who underwent open heart surgery accompanied with RAP approach [9-10], in our retrospective study blood transfusion were not required for any patients in CPB procedure. Zelinka et al. reported not only per-

Table 3. Correlations analysis revealed strong relationship between parameters, r is greater than 0,7 and moderate relationship between parameters r is equal or greater than 0,3 or smaller than 0,7 (0,3 ≤ r < 0,7).

Strong and Moderate Correlations		
Strong Correlations (|correlation| ≥ 0.7)		
Variable 1	Variable 2	Correlation (r)
Preoperative Hct value (%)	Autologous blood	0.862
Preoperative Hct value (%)	Postoperative day 1 Hct value (%)	0.790
Autologous blood	Priming solution (cc)	0.709
Priming solution (cc)	RAP (%)	0.718
RAP (%)	Weaning Hct value (%)	0.863
Autologous blood (cc)	Postoperative day 1 Hct value (%)	0.87
Moderate Correlations (0.3 ≤ |correlation| < 0.7)		
Variable 1	Variable 2	Correlation (r)
Preoperative Hct value (%)	Postoperative day 3 Hct value (%)	0.540
Preoperative Hct value (%)	Postoperative day 10 Hct value (%)	0.620
Preoperative Hct value (%)	Discharge Hct value (%)	0.359
Autologous blood	Postoperative day 10 Hct value (%)	0.643
Priming solution (cc)	Postoperative day 10 Hct value (%)	0.504
Weaning Hct value (%)	Postoperative day 3 Hct value (%)	0.318
Postoperative day 1 Hct value (%)	Postoperative day 10 Hct value (%)	0.328
Postoperative day 3 Hct value (%)	Discharge Hct value (%)	0.415
Postoperative day 10 Hct value (%)	Discharge Hct value (%)	0.416

forming retrograde autologous priming but also shortening CPB circuits diminished use of blood during routine coronary artery bypass surgery [11]. In our institution CPB circuits are as short as possible and routine RAP approach is the preferred technique for minimizing blood requirement. In total, 5 packages (units) of red blood cell were used in 38 cases. 0.13 unit of red blood cell was used for per patient. Nanjappa et al. advocated that 300 cc RAP did not necessarily reduce red blood cell package requirements during CABG [12]. We think that RAP approach can be combined with other methods to further minimize transfusion rates including, 1. Shortening CPB circuits, 2. Obtaining autologous blood, 3. Decreasing reference hematocrit level for blood replacement, 4. taking into consideration of patients‘s homeland altitude where they live. This approach is not only beneficial in CPB, but also important for early recovery. Our newly settled cardiac centre is located in a high-altitude city that is why nearly all of the the patients had high hematocrit levels in preoperative period and were collected autologous blood during induction of anesthesia. This is our generally preferred approach.

Avoiding homologous blood transfusions may cause respiratory complications, and increase the risk of bacterial infections, and allergic transfusion reactions, as well as high costs. For this reason, blood transfusion should be avoided as much as possible and should be applied only in cases where the benefits outweigh the potential harm. The analysis of RAP reveals its significant role in improving early postoperative outcomes, particularly regarding hematocrit values. The findings indicate that higher RAP values are positively correlated with better weaning Hct values, postoperative day 1 Hct values, and postoperative day 3 Hct values. This correlation suggests that effective RAP can enhance blood conservation and fluid management during and immediately after surgery, leading to better initial recovery indicators. In literature there has been defined many beneficial effects of RAP applications including avoiding hemodilution, decreasing homologous blood infusion rates, decreasing volume of priming solutions [8-11]. RAP is a valuable technique in cardiac surgery, offering significant benefits in terms of blood conservation, hemodynamic stability, and postoperative outcomes [5,7].

Optimizing RAP during surgery could improve immediate postoperative outcomes, but continuous monitoring and additional interventions may be necessary to sustain these benefits throughout the recovery period. Although challenges remain, the continued refinement of RAP and its integration with other blood management strategies hold promise for improving patient care in cardiac surgery. The evidence supports RAP as an effective method to reduce the reliance on allogeneic blood transfusions, enhance patient outcomes, and potentially reduce healthcare costs [5-15]. Same beneficial effects of RAP applications were observed in aortic surgery reported by Williams et al. [1]. They reported RAP is a safe and easy method to reduce RBC transfusion in Thoracic aortic aneurysm surgery without any adverse effects on the clinical outcome [14]. Our results are parallels with the literature reveals evidence that rutin use of RAP even in newly settled cardiac surgery centre is promising, and effectively and easily applicable. Similar results were reported by Moscardelli et al. for minimally invasive mitral valve surgery [16]. Moreover, Hagedorn et al reported that RAP utilisations in combination with other techniques such as mini circuits, modified ultrafiltration, and use of a cell saver are methods adopted by pediatric heart programs to limit transfusions [17].

Although we have demonstrated beneficial effects of RAP as in literature [1-15], Prospective randomized controlled multicenter trials would provide a more useful contributions to the literature in order to obtain results beyond any doubt [18].

Conclusion

The strong correlation between RAP and early postoperative Hct values indicates that optimizing RAP could lead to better immediate postoperative outcomes. Ensuring high RAP values could help in minimizing blood loss and maintaining sufficient hematocrit levels, which are critical for patient stability and recovery. Combining other techniques with RAP such as shortened CPB circuits, and autologous blood collection reveales beter clinical results. Living in a high-altitude city seems to be an advantage for patients undergoing heart surgery procedures since collecting autologous blood is easier in such patients due to high hematocrit levels. This study suggested that performing RAP approach with combination of other techniques serves better result even in newly established cardiac surgery centre. However, to ensure sustained recovery, a comprehensive approach that includes RAP optimization and ongoing postoperative care is crucial.

Conflict of interest

None to declare

Ethical approval

Ethical approval was obtained for this study from the Private Buhara Hospital Non-Interventional Research Ethics Committee (Date: 12.07.2024, No: 1/KDC).

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