

## DOES AUTO TRANSFUSION OF UNPROCESSED RESIDUAL BLOOD IN THE CARDIOPULMONARY BYPASS CIRCUIT LEAD TO UNFAVORABLE OUTCOMES?

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### ABSTRACT

**Objective:** Transfusion of residual blood left in the cardiopulmonary bypass circuit is recommended. Whether this blood should be processed or not before transfusion is not known.

**Study Design:** A prospective non-randomized case control study.

**Place and Duration of Study:** A tertiary care heart center, from Jan 2016 to Dec 2018.

**Methodology:** A prospective non-randomized case control study was designed. Consecutive patients operated at a tertiary care hospital were included in the study who underwent different open-heart procedures on cardiopulmonary bypass. Patients were divided into two groups. Those who received the unprocessed residual blood transfusion, residual volume retransfused at the end of cardiopulmonary bypass and those who did not, residual volume not retransfused (RVNR). Important perioperative data was collected from the hospital database and analyzed using IBM SPSS-statistics 23.0 (IBM, SPSS Inc., Chicago, IL).

**Results:** Of the 120 patients, 56 patients were included in the RVR group and 64 in the RVNR group. Mean age in the RVR group was  $49.41 \pm 14.38$  years and in the RVNR group  $49.27 \pm 16.36$  years ( $p=0.96$ ). Female patients were 9 (16.07%) in the RVR group and 20 (31.25%) in the RVNR group. Residual blood left in the circuit was  $271.43 \pm 52$  ml in the RVR group and  $264.06 \pm 54.5$  ml in the RVNR group ( $p=0.45$ ). Hemoglobin measured in ICU was  $10.5 \pm 1.12$  gm/dl in the RVR group and  $9.97 \pm 1.25$  gm/dl in the RVNR group (0.02). Blood products were needed in 27 patients in RVR group and 21 patients in RVNR group ( $p=0.57$ ). There was no significant difference between the two groups with respect to total drainage in the first 24 hours ( $p=0.89$ ). Similarly, the re-exploration rates were not different between the two groups ( $p=0.50$ ).

**Conclusion:** Re-transfusion of residual blood left in the CPB circuit is a safe practiced. If this blood is transfused in an unprocessed form, it does not lead to adverse outcomes.

**Keywords:** Cardiopulmonary bypass, Residual blood re-transfusion.

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### INTRODUCTION

Cardiopulmonary bypass (CPB) is used for a myriad of open-heart procedures. The safety and efficacy of CPB is well established and various modifications over the years have led to safer CPB practices and better patient outcomes. These modifications include and not limited to mini CPB circuits, heparin and phosphorylcholine coated circuits, centrifugal pumps and the use of cell savers to name a few<sup>1</sup>. But coagulopathy, increased use of blood products and various complications associated with blood transfusions are also known adverse effects of CPB<sup>2</sup>. Various blood conservation methods have been used to

mitigate these effects. Transfusion of the blood left in the CPB circuit after the patient is off bypass is practiced in almost all types of open-heart procedures performed on cardiopulmonary bypass. This residual blood can be transfused mainly in two ways; direct transfusion without processing and processing the blood in various ways before transfusion. Direct transfusion can be accomplished either by chasing it through the CPB circuit with a crystalloid solution through the arterial cannula or collecting it in a sterile infusion bag system and re-transfusing it. Various methods of processing are centrifugation, ultrafiltration and cell savers<sup>3</sup>.

Transfusion of residual blood in the CPB circuit is recommended in the European Association of Cardiothoracic Surgery guidelines as

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part of a blood management strategy<sup>4</sup>. Although this is a class I recommendation, the level of evidence is still C. There is a need for large scale randomized studies to demonstrate the safety and efficacy of this practice. Secondly, the re-transfusion of unprocessed blood may increase inflammatory markers in the circulation and cause bleeding postoperatively<sup>5,6</sup>. Data regarding its safety is sparse. We conducted this single centre study to show the safety of this technique in a sizeable cohort of patients.

## METHODOLOGY

A prospective comparative study was designed including all the consecutive patients undergoing open heart surgery at a tertiary care heart center from January 2016 to December 2018. Patients using coumarin derivatives or non-steroidal anti-inflammatory drugs in the immediate preoperative period were not included in the study. Patients with cardiogenic shock, use of intra-aortic balloon pump and unplanned intraoperative procedures were also excluded. Similarly, patients undergoing any type of emergency procedure, redo procedure, those with preoperative liver or kidney function derangement and any type of bleeding disorder were not included in the study. All the patients were operated using cardiopulmonary bypass. No patient received anti-fibrinolytic agent in the perioperative period. Patients were divided into two groups based upon the use of residual pump blood. Perioperative variables of interest were recorded in both the groups.

All the patients were operated using cardiopulmonary bypass using standardized techniques for preoperative preparation, anesthesia and surgery. Before commencement of cardiopulmonary bypass (CPB), full dose heparin was given according to the weight of the patient i.e. 300-400 U/Kg. The target activated coagulation time (ACT) for establishing CPB was at least 480 seconds. Additional doses of heparin were given as required to keep the ACT above 480 seconds. At the end of the procedure, the residual blood was collected in a bag and transfused slowly.

Continuous variables were tested for normality with Shapiro-Wilk test and reported as mean and standard deviations. Depending upon normality, continuous variables were compared with Student t-test when continuous and Chi square test when categorical or Wilcoxon-Mann-Whitney U test. Categorical variables are reported as percentages and compared with chi square test. A *p*-value less than 0.05 (two tailed) was considered as significant. Statistical analysis was performed using IBM SPSS-statistics 23.0 (IBM, SPSS Inc., Chicago, IL).

## RESULTS

The total number of patients included in the study was 120. The residual pump volume was returned (RVR) in 56 patients while in 64 patients, the volume was not returned (RVNR). Mean age in the RVR group was  $49.41 \pm 14.38$  years and in the RVNR group  $49.27 \pm 16.36$  years ( $p=0.96$ ). Female patients were 9 (16.07%) in the RVR group and 20 (31.25%) in the RVNR group. Other baseline characteristics of the two groups are shown in table-I.

The mean cross clamp time and bypass times was not significantly different in the two groups ( $p=0.12$  and  $p=0.06$ ). Total protamine given in RVR group was  $208.64 \pm 41.3$  and in the RVNR group it was  $207.67 \pm 45.5$  ( $p=0.90$ ). Activated coagulation time measured in seconds after the procedure in ICU was  $132.2 \pm 23.25$  seconds in the RVR group and  $132.3 \pm 34.45$  seconds in the RVNR group ( $p=0.98$ ). Residual blood left in the circuit was  $271.43 \pm 52$  ml in the RVR group and  $264.06 \pm 54.5$  ml in the RVNR group ( $p=0.45$ ). Different procedures performed in the two groups are given in table-II. The postoperative outcome variables of interest are compared in table-III. Haemoglobin measured in ICU was  $10.5 \pm 1.12$  gm/dl in the RVR group and  $9.97 \pm 1.25$  gm/dl in the RVNR group ( $p=0.02$ ). Blood products were needed in 27 patients in RVR group and 21 patients in RVNR group ( $p=0.57$ ). There was no significant difference between the two groups with respect to total drainage in the first 24 hours ( $p=0.89$ ). Similarly, the re-

exploration rates were not different between the two groups ( $p=0.50$ ). Added protamine was given after arrival in the ICU was significantly high in the RVR group. A mild to moderate correlation

**Table-I: Baseline characteristics of the groups (n=120).**

		Residual volume returned (n=56)	Residual volume not returned (n=64)	p-value
Age (years)		49.41 ± 14.38	49.27 ± 16.36	0.96
Gender	Male	47 (83.9%)	44 (68.7%)	0.05
	Female	9 (16.07%)	20 (31.25%)	
Body surface area (Kg/m <sup>2</sup> )		1.75 ± 0.17	1.74 ± 0.18	0.84
Preoperative haemoglobin (g/dl)		14.97 ± 1.3	12.69 ± 1.7	0.18
Preoperative platelet count (×10 <sup>9</sup> )		239 ± 62	236 ± 96	0.82
Preoperative INR		1.03 ± 0.32	0.99 ± 0.21	0.44
Preoperative creatinine (mg/dl)		1.05 ± 0.25	0.92 ± 0.30	0.02
ACT before the procedure		137.11 ± 24.8	138.9 ± 29.37	0.72

**Table-II: Intraoperative variables (n=120).**

		Transfusion	No transfusion	p-value
Cross clamp time (minutes)		59.00 ± 32.12	47.2 ± 20.81	0.12
CPB time		89.80 ± 43.1	77.27 ± 28.9	0.06
Total protamine given at the end of CPB		208.64 ± 41.3	207.67 ± 45.5	0.90
ACT after the procedure		132.2 ± 23.25	132.3 ± 34.45	0.98
Residual blood in the circuit		271.43 ± 52	264.06 ± 54.5	0.45
Added protamine used (mg)	0	51	60	0.76
	25	2	1	
	50	3	3	
Procedure Done	CABG	34	44	NS
	MVR	15	11	
	AVR	2	2	
	CABG+MVR	1	1	
	LA Myxoma	1	1	
	Bentall	1	1	
	VSR	1	3	
	RSOV	0	1	
LV tumour	1	0		

**Table-III: Important outcome variables.**

		Transfusion	No Transfusion	p-value
Haemoglobin in the ICU		10.5 ± 1.12	9.97 ± 1.25	0.02
Platelet count in ICU (×10 <sup>9</sup> )		210.5 ± 65.97	185.5 ± 78.87	0.06
INR in ICU		1.11 ± 0.18	1.06 ± 0.20	0.14
Packed Red cell transfusion (units)	0 units	37	35	0.57
	1 unit	20	16	
	2units	5	5	
	3 units	2	0	
		64	56	
Total drain output in the first 24 hours		531.6 ± 341.92	523.13 ± 373.01	0.89
Re-exploration for bleeding	No	54	60	0.50
	Yes	2	4	

in 5 patients in the RVR group and 4 patients in RVNR group ( $p=0.76$ ). Haemoglobin measured (Eta value 0.21) was observed for patients who

had transfusion of the residual blood and haemoglobin measured after arrival in the ICU.

## DISCUSSION

This study demonstrates the safety of re-transfusion of residual unprocessed CPB circuit blood. Although non-randomized, a good number of patients were included in the study with controls that proved that residual blood, if transfused in unprocessed form, does not lead to adverse outcomes with respect to postoperative blood loss and transfusion requirements.

An important finding in our study is the avoidance of added protamine in patients with transfusion of residual blood. Daane and colleagues used added dose of protamine to offset the effects of the heparin present in the re-transfused blood<sup>7</sup>. Our study showed that added protamine was required in a small quantity in both the groups and it did not differ between the groups. We used the Kaolin based activated coagulation time to decide about the additional protamine dose<sup>8</sup>. Although heparinase thromboelastography (TEG) has been used for this purpose, Levin and colleagues showed in a randomized controlled trial that the use of TEG compared to ACT did not show any difference in protamine dosing<sup>9</sup>.

Unprocessed blood contains inflammatory mediators and can cause activation of complement system<sup>10</sup>. Many of the untoward side effects of using cardiopulmonary bypass are due to the complement release subsequent to the inflammatory reaction initiated<sup>11</sup>. But as shown in our study, transfusion of residual blood did not lead to any adverse complication. Svenmarker and colleagues conducted a randomized study to investigate the cellular and inflammatory response that can be attributed to the suction blood processed with cell saver or the conventional cardiotomy suction<sup>12</sup>. They concluded that cardiotomy suction blood is a cause of hemolysis and increased plasma free hemoglobin but contributes insignificantly to inflammatory response. But this should be taken with caution in our results because the mean residual blood volume was much smaller in our study compared to some of the

previous studies<sup>7</sup>. This might be the reason of reduced inflammatory mediator load and hence comparatively better outcome.

A significant increase in the hemoglobin level was observed in those who received the residual blood from the circuit in our study. This effect was also demonstrated by Iyer and colleagues in their cohort of 40 patients where the transfusion of unprocessed blood lead to significantly increased hemoglobin post-operatively<sup>13</sup>. This improvement in hemoglobin has been attributed to the presence of a high volume of red cells in the residual pump blood. The same effect was shown by Srivanska and colleagues in their study<sup>14</sup>.

Various factors can lead to coagulopathy in the immediate postoperative period. Factors like residual heparin i.e. heparin rebound, thrombolysis and platelet dysfunction etc. are all associated with coagulopathy postoperatively<sup>15</sup>. Auto transfusion of the residual blood is expected to worsen the coagulation profile but this effect was not observed in our study. We demonstrated no change in the activated coagulation time done immediately after transfer to the ICU, and no change in the platelet count compared to the pre-operative values. Similarly, there was a non-significant change in the values of international normalized ratio. This effect has been described previously with the use of TEG measurements by Iyer and colleagues where they demonstrated no TEG evidence of fibrinolysis or platelet dysfunction<sup>8</sup>. In fact, the addition of protamine may lead to increased ACT<sup>16,17,18</sup>. The resulting effect was no increase in the total drainage in the first 24 hours and the rate of re-explorations in both the groups and also no increase in blood products.

## LIMITATION OF STUDY

Our study has some important limitations. We did not include patients at highest risk of bleeding so our results cannot be extrapolated to these patients. The study is not randomized, although includes a sizeable number of patients. This is a single center experience and the results cannot be generalized to other centers with different perioperative protocols especially related to

the heparin and protamine dosing. Also, our study had a heterogeneity of cardiac surgical procedures which may have different pathologies which was not accounted for in our study.

## CONCLUSION

Re-transfusion of residual blood in the CPB circuit does not lead to adverse outcomes. It can improve the hemoglobin as measured postoperatively at the cost of no increase in postoperative drainage in the first 24 hours or derangement in coagulation profile.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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