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Original Research Paper

Cardiology

TO STUDY RETROGRADE AUTOLOGUS PRIMING (RAP) AS AN IMPORTANT BLOOD CONSERVATION MODALITY AND ITS ROLE IN POST OPERATIVE OUTCOME - A STUDY OF 200 CASES IN MADRAS MEDICAL COLLEGE, CHENNAI.

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ABSTRACT

AIMS AND OBJECTIVES : To study the effect of retrograde autologous priming techniques on transfusion requirements and outcome in CABG patients.

1. The effect on peri-operative transfusion requirements.
2. The effect on post-operative morbidity.
3. The effect on duration of post operative stay.

MATERIALS AND METHODS :

We analysed the patient details retrospectively using the charts as well as our clinical clinical workstation. Categorical data were expressed as frequency and percentage. Categorical data were expressed as frequency and percentage. Continuous variable expressed as mean ± standard deviation. Significant differences between proportions determined by Chi-squared analysis or Fischer's exact test. All analysis were carried out using Statistical Package for Social Service version 16(SPSS Inc.,Chicago, IL, USA). Probablity values $p<0.05$ were considered significant.

RESULTS: We had a total of 200 patients in our series from 2014-15. Coronary artery disease is more common in males 83% of our study group. Commonly seen in Diabetics(60%), hypertensives(62%) and smokers(30%), their respective percentages in the study population. Analysing Retrograde autologus priming as a blood conservation modality we were able to derive at a reduction in hemodilution, transfusion rates, creatnine and lactate levels, period of stay but were not able to exhibit statistical significance. The factors like intra operative hemodilution($p=0.039$) and transfusion($p=0.050$). Post operative creatnine levels($p=0.026$) and Stay in the ICU($p=0.014$) were significant.

CONCLUSION:

We were able to establish Retrograde Autologus Priming as one of the blood conservation modalities. As in other literature, our study also suggests that Retrograde Autologus Priming of cardiopulmonary bypass circuit as an effective blood conservation modality. There is a significant reduction in the total transfusion rates of patients in the Retrograde Autologus Priming group in the overall study. Though only the intra op transfusion rates and post operative critical care stay were deemed statistically significant, in this retrograde study, It is promising to note and could get more gratifying results if there could be a prospective study with strict transfusion triggers.

KEYWORDS : Retrograde Autologus Priming, Hemodilution, Blood Transfusion, Cardiopulmonary Bypass.

PATIENTS AND METHODS

SETTING:

This retrospective study was performed at Madras Medical College, Chennai,

COHART:

A retrospective study, comparing the effect of retrograde autologous priming to standard priming techniques on perioperative transfusion requirements and morbidity, in patients undergoing elective primary coronary artery bypass grafting.

STUDY PROFILE & PORTFOLIO:

Inclusion Criteria

1: Patients aged between 20 and 70 years.
2: Patients presenting for elective primary coronary artery bypass grafting.

Exclusion Criteria

1: Patients aged <20 or >70 years.
2: Patients with left ventricular ejection fraction <40%.
3: Pre-operative Hemoglobin <10gm%.
4: Weight less than 45 kg.
5: Pre-existing renal impairment i.e. serum creatinine >1.4mg/dl.
6: Patients presenting for emergency surgery.
7: Re-do coronary artery bypass grafting.

The study included patients who satisfied the study's induction criteria from April 2014 to March 2015.

As it is a retrospective study there was no randomization followed the study was divided into 2 separate groups of patients who had undergone retrograde autologous priming(Group A) and the other who had undergone standard priming(GroupB) consisting of 100 subjects in each arm.

PRIMARY OUTCOME.

Reduction in transfusion requirements peri-operatively.

SECONDARY OUTCOME/S:

1. Reduction in post-operative morbidity.
2. Incidence of renal failure and stroke.
3. ICU stay and Hospital Stay.

TRANSFUSION TRIGGERS:

There was no set transfusion protocol. The institution criteria which was followed during the tenure of study is explained. Packed red cells was be transfused if hemoglobin was < 6.0gm% on cardio-pulmonary bypass and if hemoglobin was < 8.0gm% at any time after termination of cardio-pulmonary bypass. Packed red cells were transfused even at higher hemoglobin values if clinically symptomatic anemia, evidence of end organan failure and low cardiac output develops. Transfusion of packed red cells were carried out only after documenting the hemoglobin value. Use of blood products like platelets and plasma were performed on clinical evidence of bleeding.

STATISTICAL METHODS:

Statistical methods used for primary outcome analysis included description of methods to estimate the strength of the effect (Odds ratios). After checking for normality, appropriate parametric tests like 2 independent sample t test were used to assess the mean difference between participants of the retrograde autologous priming and standard priming groups for continuous variables like hemoglobin, lactate, creatinine. For categorical variables, like sex, pre-operative diagnosis, comorbidities, Chi square/ Fisher's exact was used. The p-value was computed using 2 proportion Z test for non-continuous variables like number of patients transfused with packed red cells. Multivariate analysis was done based on the variables which were significant at Bivariate level. P-value less than 0.05 taken as significant level. All the analysis were performed using

SPSS-16. A total of 200 patient charts were analysed and documented, out of which 100 were charts of patients in whom retrograde autologus priming of the cardiopulmonary bypass circuit was performed and the other 100 charts were of patients in whom standard priming was followed.

Sample size:
The pre op haemoglobin was taken as predictor. From the pilot study the effect size for the difference in haemoglobin among operated was calculated. Based on the information using following formula the sample size was calculated.

Proportion in group I0.26
Proportion in group II0.1
Estimated risk difference0.16
Power (1-beta) %80
Alpha error (%)5
1 or 2 sided2
Required sample size for each arm89
Considering that there is a dropout rate of about 10%, it can be approximately An adequate sample size of 100 is needed to detect a 40 % event rate with 0.64 effect size with pre haemoglobin as predictor of outcome(ablation / modified), with 80% power and 5% error.

ANAESTHETIC MANAGEMENT
Standard anesthetic techniques for induction, maintenance and inotrope management were followed in all patients. The surgical and perfusion teams were observed to be the same for patients in both groups. All patients in this study received only less than 250ml crystalloid infusion prior to initiation of cardiopulmonary bypass from the anesthesia team. Prior to initiation of cardio pulmonary bypass, all patients received Injection Porcine Heparin (>400U/kg) to obtain an activated clotting time of >450sec. On termination of cardio-pulmonary bypass, all patients received Injection Protamine (Img/l00U of heparin) for reversal of Heparin anti-coagulant effects. Hemodynamic goals included maintenance of mean arterial pressure >65mm of Hg prior to initiation of cardiopulmonary bypass & >50mm of Hg on cardio-pulmonary bypass using vasoactive agents like Injection Phenylephrine in bolus doses or Nor-adrenaline infusion.

VASOPRESSORS USED
1. Phenylephrine:
- Synthetic Noncatecholamine
- Selective l adrenergic agonist with minimal adrenergic effect.
- Causes vasoconstriction primarily in arterioles.

Advantages: Direct agonist with short duration of action(< 5min) Increases coronary perfusion pressure Myocardial oxygen consumption is not increased substantially

Disadvantages: May increase pulmonary vascular resistance Reflex bradycardia

Indication: Hypotension, SVT, Cyanotic spells.

Dose: Bolus: l-10mcg/kg
Infussion: 0.5-10mcg/kg/min

2. Ephedrine:
- Plant derieved alkaloid with sympathomimetic effects.
- Mild , i, 2 adrenergic agonist.
- Indirect NE release from neurons.

Advantages:
Short Duration(3-10 mins)
Safe in pregnancy
Good agent to correct sympathectomy induced relative hypovolemia and decreased Systemic Vascular Resistance(SVR) after spinal or epidural anaesthesia.

Disadvantages:
Efficacy is reduced when NE stores are depleted.
Risk of malignant hypertension with MAO inhibitor or cocaine
Tachyphylaxis with repeated doses.

Indication: Hypotension due to low SVR or low CO and HR is low, particularly spinal/ epidural anaesthesia. Temporary therapy to hypovolemia.

Dose: Bolus:5-10mg iv, 25-50mg im

3. Norepinephrine:
- Primary physiologic postganglionic sympathetic neurotransmitter.
- Direct l, 2, adrenergic agonist action.

Advantage:
Equivalent to Epinephrine at 1 agonist
Redistributes blood flow to brain and heart.
Elicits intense al and a2 agonist, effective vasoconstrictor.

Disadvantage:
Reduced Oxygen perfusion
Myocardial ischaemia possible
Pulmonary vasoconstriction
Arrythmia
Risk of Skin necrosis on extravasation.

Indication:
To increase systemic vascular resistance, esp. septic shock.

Vasoplegia - Post Cardiopulmonary Bypass.
Dose: 0.03-0.3 mcg/kg/min

CARDIO-PULMONARY BYPASS
Standardized cardio-pulmonary bypass equipment and technique for retrograde autologous priming was used for all patients who participated in this study. Terumo Systems cardio-pulmonary bypass machine and Affinity(Medtronic) oxygenator were used for patients in both groups. Extracorporeal circuit:

Arterial line: length - 270cms, diameter - 3/8"
Venous line: length - 270cms, diameter - 1/2"
Cardioplegia line: length - 500cms, diameter -1/4"
Vent line: length - 500cms, diameter -1/4"
Cardiotomy suction line(2nos): length - 500cms, diameter -1/4"
Recirculation line - 500cms, diameter -1/4"

Ringer lactate was the priming solution used for all patients, with 1200ml as standard volume in the standard prime group. Modified St. Thomas cardioplegia(1:4 blood cardioplegia) was used to arrest the heart in diastole in all patients. In the retrograde autologous priming group the volume of crystalloid prime displaced from the extracorporeal circuit was based on the clinical discretion of the surgeon and anesthetist. There was no major correlation between the BSA of the patient and prime displaced from the extracorporeal circuit. It was dependant on the surgeons intra-op assessment in conjunction with the anaesthetist. As low as 200ml of prime was displaced for patient with a BSA of 1.85m2 and as high as 500ml of prime was displaced for patient with a BSA of 1.44m2. Extracorporeal circuit volume was documented for all patients.

RETROGRADE A UTOLOGOUS PRIMING TECHNIQUE
For patients pertaining to the retrograde autologous priming group, after aortic and venous cannulation, mean arterial blood pressure was hiked up to approximately 70mm of Hg using 50-100gm bolus doses of phenylephrine and a mild head-low position. Retrograde autologous priming was performed on the arterial line initially, arterial line was undamped and crystalloid solution in the arterial line was gradually displaced back into the reservoir using the patients' blood. Just prior to the patients' blood entering the

reservoir, the arterial line was clamped. Once this is done, the main cardio-pulmonary bypass pump was switched on and the cardioplegia line was undamped to push the displaced crystalloid into the collecting bag, connected to the cardioplegia line. The crystalloid solution in the venous line was also displaced in a similar manner after completion of the procedure on the arterial line. Approximately 2-4 minutes were required for institution of retrograde autologous priming on both arterial and venous lines. All through this time, the cardiotomy suction is turned off to avoid mixing of the blood with the crystalloid solution in the reservoir.

A GEM Premier 3000 blood gas analyzer was used for measurement of hemoglobin and lactate levels for all patients.

Intra-op and post-op data from the perfusion data sheet and the ICU charts respectively of the 200 patients, 100 in each group who fulfilled the inclusion criteria, were collected by the primary investigator. Clinicians had followed the routine transfusion protocols, followed as departmental policy, in the ICU.

RESULTS

DEMOGRAPHIC VARIABLES

Two hundred patients (166 males and 34 females) who underwent elective primary coronary artery bypass grafting were analysed in the study 100 patients each were analysed underwent retrograde autologous priming group (RAP) and standard priming group (No RAP). Of the 200 participants 166(83%) were male and only 34(17%) were female.

Group A i.e. retrograde autologous priming group (RAP) had 81(81%) male and 19(19%) female patients while group B i.e. standard priming group (no RAP) had 85(85%) male and 15(15%) female patients. There are 73(36.5%) patients in the retrograde autologous priming group had triple vessel disease and 27(13.5%) had double vessel disease, whereas 81(40.5%) and 19(9.5%) patients had triple vessel disease and double vessel disease in the standard priming group respectively

Depicts the male to female distribution in both the retrograde autologus priming and the standard priming group in which the X axis is formed by the no of patients and Y axis representing the type of priming.

CATEGORICAL VARIABLES

Table 1 : There is no statistically significant difference in demographic variables (age, weight and body surface area) between the two groups .

	RAP(n=100)	No RAP(n=100)	p Value
Age(years)	56.05±8.983	57.67±8.351	0.188
Weight(kg)	68.35±7.683	69.23±9.432	0.632
BSA(m2)	1.689±0.140	1.698+0.154	0.649

COMORBIDITIES

Table 2 : Represents frequency of co-morbid conditions among participants of study

	RAP(n=100)	No RAP(n=100)
Hypertension	73	51
Diabetes	62	58
COPD	28	31
Peripheral Vascular Disease	4	1

Table 3 : Frequency and distribution of Diabetes among both the group.

			Group		Total
DIABETES			RAP	NO RAP	
	Yes	Count	62	58	120
		% within DIABETES	51.7%	48.3%	100.0%
		% within Group	62.0%	58.0%	60.0%
	No	Count	38	42	80
		% within DIABETES	47.5%	52.5%	100.0%
		% within Group	38.0%	42.0%	40.0%
	Total	Count	100	100	200
		% within DIABETES	50.0%	50.0%	100.0%
		% within Group	100.0%	100.0%	100.0%

Table 4: Significance among the RAP & Non RAP group of diabetes by Chi-Square test

N=100	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (l-sided)
Pearson Chi-Square	.333a	1	.564	.665	.333
Continuity Correctionb	.188	1	.665		
Fisher's Exact Test Linear-by-Linear Association	.332	1	.565		

Table 5: Frequency and distribution of Hypertension among both the group.

			Group		Total
DIABETES			RAP	NO RAP	
	Yes	Count	73	51	124
		% within HTN	58.9%	41.1%	100.0%
		% within Group	73.0%	51.0%	62.0%
	No	Count	27	49	76
		% within HTN	35.5%	64.5%	100.0%
		% within Group	27.0%	49.0%	38.0%
	Total	Count	100	100	200
		% within HTN	50.0%	50.0%	100.0%
		% within Group	100.0%	100.0%	100.0%

Table 6: Significance among the RAP & Non RAP group of Hypertension by Chi-Square test.

N=100	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (l-sided)
Pearson Chi-Square	10,272*	1	.001	.002	.001
Continuity Correctionb	9.359	1	.002		
Fisher's Exact TestLinear-by-LinearAssociation	10.220	1	.001		
No. of Valid Cases	200				

Table 7: Frequency and distribution of Smoking among both the group.

			Group		Total
DIABETES			RAP	NO RAP	
	Yes	Count	28	31	59
		% within COPD_Smoker	47.5%	52.5%	100.0%
		% within Group	28.0%	31.0%	29.5%
	No	Count	72	69	141
		% within COPD_Smoker	51.1%	48.9%	100.0%
		% within Group	72.0%	69.0%	70.5%
	Tota l	Count	100	100	200
		% within COPD_Smoker	50.0%	50.0%	100.0%
		% within Group	100.0°/	100.0%	100.0%

Table 8: Significance among the RAP & Non RAP group of Smoker by Chi-Square test.

N=100	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (l-sided)
Pearson Chi-Square	.216[a]	1	.642	.002	.001

Continuity Correctionb	.096	1	.756		
Fisher's Exact TestLinear-by-LinearAssociation	.215	1	.643		

Table 9: Frequency and distribution of Peripheral vascular disease among both the group.

			Group		Total
DIABETES			RAP	NO RAP	
	Yes	Count	4	1	5
		% within PVD	80.0%	20.0%	100.0%
		% within Group	4.0%	1.0%	2.5%
	No	Count	96	99	195
		% within PVD	49.2%	50.8%	100.0%
		% within Group	96.0%	99.0%	97.5%
	Total	Count	100	100	200
		% within PVD	50.0%	50.0%	100.0%
		% within Group	100.0°/	100.0%	100.0%

Table 10: Significance among the RAP & Non RAP group of peripheral vascular disease by Chi-Square test.

N=100	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (l-sided)
Pearson Chi-Square	1.846	1	.174	.369	.184
Continuity Correction[b]	.821	1	.365		
Fisher's Exact TestLinear-by-LinearAssociation	1.837	1	.175		
No. of Valid Cases	200				

Table 11: Frequency and distribution of Cerebro vascular accidents among both the group.

			Group		Total
DIABETES			RAP	NO RAP	
	Yes	Count	0	3	3
		% within PVD	0.0%	100.0%	100.0%
		% within Group	0.0%	3.0%	1.5%
	No	Count	100	97	197
		% within PVD	50.8%	49.2%	100.0%
		% within Group	100.0%	97.0%	98.5%
	Total	Count	100	100	200
		% within PVD	50.0%	50.0%	100.0%
		% within Group	100.0°/	100.0%	100.0%

Table 12: Significance among the RAP & Non RAP group of CVA by Chi-Square test.

N=100	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (l-sided)
Pearson Chi-Square	3.046[3]	1	.081	.246	.123
Continuity Correction[b]	1.354	1	.245		
Fisher's Exact TestLinear-by-LinearAssociation	3.030	1	.082		
No. of Valid Cases	200				

PRE-OPERATIVE VARIABLES

Table 13 : Shows the comparison of the Pre operative variables, mean± SD and p value calculated by 2 proportion Z test.

	RAP(n=100)	NoRAP(n=100)	p Value
Hemoglobin (gm%)	13.350*1.567	13.008±1.473	0.114
Creatinine	0.933±0.2067	0.9638±0.2278	0.321
Ejection Fraction (%)	52.99±5.676	53.54±5.700	0.495

The mean hemoglobin in the study population has been 13-13.5 gm% , creatnine 0.93-0.96 mg% with ejection fraction of 53-53.5% with no evidence of statistical significance between two groups.

INTRA-OPERATIVE VARIABLES

Table 14 : Shows the comparison of the intra operative variables, mean± SD calculated by 2 independent sample t test and p value calculated by 2 proportion Z test.

	RAP(n=100)	No RAP(n=100)	p Value
CPB Volume(ml)	919.80±95.184	1313.00±48.783	0.000
Aortic Cross-Clamp Time (hrs.)	49.84±12.839	47,44±14.036	0.209
CPB Time (hrs.)	92.76±24.196	87.69±29.732	0.188

Mean cardio-pulmonary bypass volumes were 919.80±95.184ml in the retrograde autologous priming group and 1313.00±48.783ml in the standard priming group (Table: 18). The mean value of the prime displaced from the cardiopulmonary bypass circuit is 368±79.6203ml. The cardio-pulmonary bypass and the aortic cross clamp times were insignificant in the two groups.

CARDIO-PULMONARY BYPASS PARAMETERS

Table 15 : Shows the comparison of the intra operative variables, mean± SD calculated by 2 independent sample t test and p value calculated by 2 proportion Z test.

	RAP(n=100)	No RAP(n=100)	p Value
Hemoglobin(gm%)	7.845±1.1141	7.502±1.2162	0.039
Lactate(mg/dl)	2.893±0.8328	3.128±1.1009	0.268
Patients transfused PRBCs	3	11	0.050

Mean hemoglobin levels during cardio-pulmonary bypass were significantly lower in the standard priming group as depicted in Table: 15. Mean lactate levels were not statistical significance. As depicted only 3 patients in the retrograde autologous priming group were transfused packed red cells as compared to 11 patients in the standard priming group, again a statistically significant difference. There was no intraoperative transfusion of any platelet concentrates or fresh frozen plasma during cardio-pulmonary bypass.

POST CARDIO-PULMONARY BYPASS PARAMETERS

Table 16 : Shows the comparison of the post operative variables, mean± SD calculated by 2 independent sample t test and p value calculated by 2 proportion Z test.

	RAP(n=100)	No RAP(n=100)	p Value
Hemoglobin (gm%)	9.856± 1.336	9.796±0.9615	0.687
Lactate(mg/dl)	3.529± 1.9047	3.422± 1.5034	0.660

In the post-cardio-pulmonary bypass period, i.e. in the critical care unit, mean hemoglobin levels and lactates were not statistically different between the two groups.

POST-OPERATIVE DAY 1 PARAMETERS

The mean hemoglobin levels on the first post operative day, i.e. from the time of receiving the patient in the intensive care unit till midnight of the same day was 10.419± 1.264 in the retrograde autologus priming group exhibiting no much statistical significance from its control group. There was no statistically significant difference between the two groups with regard to lactate and mean volumes of first 24 hour drain output for study participants.

Table 17 : Shows the comparison of the post operative variables, and Table 8 post operative blood transfusion, meant SD calculated by 2 independent sample t test and p value calculated by 2 proportion Z test.

	RAP(n=100)	No RAP(n=100)	p Value
Hemoglobin (gm %)	10.419± 1.264	10.202±1.0912	0.195
Lactate(mg/dl)	1.986±0.854	1.881±0.6012	0.312
Intercoastal Drains	438.30±164.64	464.80±139.642	0.221

Table 18 : Blood and Blood products transfused on POD1

Patients Transfused	RAP(n=100)	No RAP(n=100)	p Value
PRBCs	22	33	0.11
FFP	7	8	
Platelet Concentrate	13	15	0.83

During the post cardio-pulmonary bypass period, 22 patients in the retrograde autologous priming group were transfused packed red cells against 33 in the standard priming group.

With regard to fresh frozen plasma, only 7 participants in the retrograde autologous priming group were transfused and 571.428±293.463 ml was the mean volume transfused. In the standard priming group, only one patient was transfused with 750ml. 13 patient received 150ml of platelet rich concentrate in the retrograde autologous priming group vs. 15 patients with a mean volume of 112.50+53.033 ml in the standard priming group, again of no statistical significance.

POST-OPERATIVE DAY 2 PARAMETERS

Table 19 : Shows the comparison of the post-operative day2 variables and transfusion rate, mean± SD calculated by 2 independent sample t test and p value calculated by 2 proportion Z test.

	RAP(n=100)	No RAP(n=100)	p Value
Hemoglobin (gm%)	9.995±0.9199	9.774±0.9550	0.278
Creatininc(mg/dl)	1.2602±0.15938	1.2521 ±0.25549	0.860
Lactate(mg/dl)	3.830+1.7612	3.979±1.9553	0.712
Patients Transfused	9	9	1

There was no statistically significant difference in the hemoglobin, creatinine and lactate values between the retrograde autologous priming group and standard priming group on the second post-operative day. There was no difference in the transfusion rates among the retrograde autologous priming group and the standard priming group, (p value: 1)

POST-OPERATIVE DAY 3 PARAMETERS

Table 20 : Shows the comparison of the post-operative day 3 variables, mean± SD calculated by 2 independent sample t test and p value calculated by 2 proportion Z test.

	RAP(n=100)	No RAP(n=100)	p Value
Hemoglobin (gm%)	9.906±1.2256	9.66±0.3024	0.139
Creatinine(mg/dl)	0.9211 ±0.30245	1.0293±0.37597	0.026
Patients Transfused PRBCs	12	9	0.64

On the third post-operative day, there was no clinically significant difference in the hemoglobin between the retrograde autologous priming group and the standard priming group. There was statistically significant difference in the creatinine on the third post operative day. On the third post-operative day, twelve patients in the retrograde autologous priming group were transfused packed red blood cells while only nine patients in the standard priming group were transfused.

TIME AT ICU AND DISCHARGE

Table 21 : Shows the comparison of the post operative stay in ICU and ward, mcan± SD calculated by 2 independent sample t test and p value calculated by 2 proportion Z test

	RAP(n=100)	NoRAP(n=100)	p Value
Discharge from ICU (days)	3.28±0.6371	3.53±0.7843	0.014
Discharge from hospital (days)	7.95+2.6681	8.69±3.4692	0.092

MULTI VARIATE ANALYSIS

Table 22: With the sample size of 200, it was amenable to include 10 variables in the analysis, in which Odds Ratio is calculated describing the chances of occurance following which p value with 95% confidence interval is suggested.

Risk Variable	**OR**	**95% CI**	**P value**
Blood Post OP		0.63-2.42	0.54
Yes	1.00		
No	1.23		
Lactate Post OP	1.05	0.89-1.25	0.55
HB Post OP	0.82	0.59-1.13	0.23
HB Intra OP	1.40	1.04-1.88	0.03
Drain post OP	0.99	0.99-1.00	0.35
Creatnine POD3	0.54	0.20-1.42	0.54
ICU Stay	0.44	0.20-0.96	0.04
Total Stay	1.11	0.93-1.33	0.25

Multivariate analysis of the components of the study was studied on, after suitable correction, in order to derive the clinical significance of parameters due to interdependence. Considering that some of the parameters were statistically significant individually their significance between the retrograde autologus priming group and the standard priming group were confirmed in correlation to each other. Hence it was noted that Intra operative haemoglobin and Post op ICU stay were clinically as well as statistically significant.

DISCUSSION

Society of Cardio-thoracic Surgeons 2011 Guidelines recommend Retrograde autologous priming of the cardio-pulmonary bypass circuit as a strategy with level Hb evidence to reduce haemodilution and thereby transfusion requirements [1,7]. Retrograde autologous priming was first described by Panico and Neptune in 1960[18,20].

Our study analysed data of 200 patients undergoing elective coronary artery surgery retrospectively in a comparative study among the retrograde autologus priming group and standard priming group. Rosengart T K et al, who performed a prospective randomized control study, on primary coronary artery bypass grafting patients, modified the technique, to demonstrate the efficiency of retrograde autologous priming in reducing transfusion requirements[19]. The groups were comparable in terms of demographic data and comorbidities. Left ventricular dysfunction has been identified as a risk factor for transfusions during cardiac surgery[1,7]. On analysis of our data, 10 patients had an ejection fraction of less than 45%; 7 were recruited in the standard priming group and 3 were recruited in the retrograde autologous priming group. None of the patients received transfusion of packed red cells. The mean weight of patients recruited in our study was 68.35±8. 983 kg and 69.23±9.432kg in the retrograde autologous priming group and standard priming group respectively. All previous studies evaluating the efficacy of retrograde autologous priming had a minimum mean weight of 76 kg or higher [19,20,22,26].

The degree of intra operative haemoglobin and the resultant hemodilution documented in our study was comparable to Shapira et al's randomized control study in 1998, at Boston Medical Centre who concluded their success in reduction of homologous transfusion rates and costs by using a multimodality approach[29].

In the study conducted in Seoul(Asia), the mean weight was 45 kg and the mean hematocrit was 39%[23]. The mean preoperative haemoglobin in the audit done in AIIMS by S.M.Reddy et al in 2009 had a mean of 11.8±3.154gm%[25]. The mean hemoglobin level of patients recruited in our study was 13.35±1.567 gm% and 13.008±1.473 gm% in the retrograde autologous priming group and standard priming group respectively.

The two groups were similar with respect to operating teams and techniques. Both the groups were similar with respect to risk factors for hemorrhage and transfusions peri-operatively.

We were able to reduce prime volumes by approximately 31 % in the retrograde autologous priming group, with a mean prime volume of 919.80±95.184ml. The mean of reduction in prime in RAP patients is 368±79.6203ml. Vandewiele K et al identified optimal retrograde autologous priming volume as 475 ml in patients with BSA more than 1.7 m^2 and 375 ml in patients with BSA less than 1.7 m^2, for reducing transfusion requirements[27]. But our study couldn't establish a relationship between the BSA and the amount of prime displaced from the Cardiopulmonary bypass circuit, we had

displaced maximum of 500 ml of prime for a patient with BSA of 1.4 m^2 and as less as 200 ml of prime for a patient with BSA of 1.9 m^2

Cardio-pulmonary bypass durations were approximately 92.76±24.196mins and 87.69±29.732mins in the retrograde autologous priming and standard priming groups respectively. Aortic cross clamp times were 49.84±12.839mins and 47.44±14.036mins in the retrograde autologous priming and standard priming groups respectively. In our study the cohort comprised of patients operated by multiple surgeons unlike Murphy et al. Glenn S. Murphy et al, could not demonstrate a reduction in transfusion requirements with retrograde autologous priming, had an average aortic cross clamp time of 1.46 hrs and cardio-pulmonary bypass time of 1.91 hrs[22]. Prolonged cardio-pulmonary bypass and cross clamp durations have been identified as a risk factor for transfusions and this probably explains the failure of Glenn S. Murphy et al to obtain a positive result[18].

Retrograde autologous priming has been proven to be an effective method in reducing haemodilution and transfusion requirements during cardiopulmonary bypass[19,21,23,25-27]. The introduction of retrograde autologous priming resulted in significantly lower levels of intra-operative haemodilution; in our study only 3(1.5%) patients in the retrograde autologous priming group vs 11(5.5%) patients in the standard priming group were transfused packed red cells, during cardio-pulmonary. Haemoglobin levels during cardio-pulmonary bypass were 7.845±1.114 in the retrograde autologous priming group and 7.502±1.2162gm% in standard priming group (p value: 0.039). Hemoglobin levels were also significantly higher in the retrograde autologous priming group during cardiopulmonary bypass. These results were comparable to Rosengart et al, Balachandran et al, Hou et al, Saczkowski et al and Vandewiele et al[19,21,23,25,26]. As the standard prime group patients 11 members were transfused during CP Bypass the mean haemoglobin values were comparable between the groups. Hence, as discussed earlier the mean number of units transfused during cardio-pulmonary bypass was significantly higher in the standard priming group.As confirmed by the anaesthetist we administer patients with mean volumes of 750 ml intraoperatively. Fluid given to patients intraoperatively has notably caused significant hemodilution. The contributing factor to Murphy's negative results may be the the higher volumes of crystalloids administered during surgery (mean volumes of 3 litres) [22].

Our study is comparable to Nithin et al's prospective randomized control study conducted in Vellore in 2012. Both the studies have a comparable Body Surface Area in the study cohart and resultant reduction in hemodilution intraoperatively. The prior study was handicapped in doing the multivariate analysis due to the lower study population(n=86). But were able to establish better results due to strict adherence to protocol in view of its prospective nature.

The Society of Cardio-thoracic Surgeons 2011 Guidelines has identified major risk factor for receiving transfusion of packed red cells during cardiac surgery[1,7]. The risk factors identified were

- reduced red cell mass
- patients presenting for emergency surgeries or re-operations,
- advanced age,
- non-cardiac risk factors like renal failure and
- patients who were prescribed anti-platelet or anti-thrombotic drug pre-operatively[1,7].

Many Indian patients have reduced red cell mass due to either lower body mass or preoperative aneamia, or even both. Studies have identified Asians have a higher percentage body fat compared to Western population[28]. So even with comparable body weights and heamatocrits our population may have reduced RBC mass as compared to the other studies[19,20,22,26].

This trial was conducted exclusively on primary coronary artery bypass grafting patients, unlike other studies like Murphy's where authors recruited all cardiopulmonary bypass patients[22]. In coronary artery bypass grafting excessive hemodilution due to irrigation is limited when compared to other cardiac surgical procedures.

The Society of Cardio-thoracic Surgeons advocates the use of tranexamic acid as class 1(A) recommendation, however its safety profile during coronary artery bypass grafting surgery is still being investigated[1,7]. As a routine protocol tranexamix acid was administered to patients of this study, contrary to most previous trials. The administration of tranexamic acid postoperatively in the ICU's too, helped in reducing mediastinal bleeding, hence further reduction of haemorrhage and transfusion requirements in both groups.

Although hemoglobin levels were not statistically different in the immediate postoperative period and during the first post-operative day. Hemoglobin levels were higher in the retrograde autologous priming group. Mean haemogloin values were 9.906±1.2256 and 9.66±0.3024gm% in the retrograde autologous priming and standard priming groups respectively (p value:0.139).

Reported transfusion rates for cardiac surgical patients (30%) are comparable with transfusion rates in our standard priming group (40%) group. Whereas use of a single intervention (retrograde autologous priming) resulted in reduction of transfusion requirements by more than 10% (30% in the retrograde autologous priming group)[1,7].

The transfusion trigger of <8.0gm% for the post-cardio-pulmonary bypass period adopted in our study as institutional policy, were not strictly adhered to accounted for comparatively liberal transfusion protocol, when compared to previous studies. If we had adopted a more strict protocols transfusion for the post-cardio-pulmonary bypass period, like previous authors, our transfusion rates would have been much lesser. 23 out of 55 patients who received transfusions in the post-cardio-pulmonary bypass period had haemoglobin concentrations between 8 and 8.5gm%.

There was no statistically significant difference in the volume of fresh frozen plasma or platelet rich concentrate transfused or the number of patients receiving these blood products at any point of time during the hospital stay between the two groups.

On analysis of lactate levels at different intervals, we could not demonstrate any significant advantage of retrograde autologous priming over standard priming techniques. We could demonstrate statistically significant difference between the retrograde autologous priming group and the standard priming group with regard to trends of creatinine levels. Both low hematocrits and transfusion of packed red cells are associated with renal dysfunction in cardiac surgical patients[12]. The has been documented worsening of renal function as a result of transfusion and there has end organ damage as a result of low hematocrit values, which has been documented as transfusion protocol by STS 2011 guidelines.

There was a significance in the post operative day 3 creatnine levels(p=0.026>, wherein the levels were significantly lower in the retrograde autologus priming group compared to that of standard priming. Exclusion of patients with preoperative renal dysfunction and low ejection fractions has eluded the presence of post-operative renal dysfunction requiring dialysis.

However our study did not demonstrate any statistically significant difference between the two groups with regard to renal failure requiring hemodailysis and stroke. Intra-operative transfusion of packed red cells can result in increased risk of adverse effects like sternal wound infection, renal and pulmonary dysfunction, prolonged length of stay in the intensive care unit and hospital[11]. There was also no statistically significant difference between times of discharge from hospital between patients of both the groups. The study has demonstrated significant reduction in the number of days of stay in the intensive care unit between these two subset of population.

Investigators have compared either direct infusion vs centrifugation and or ultrafiltration (Salvage of pump blood - level Hb) of pump blood for reinfusion, and found centrifugation to be most reasonable[(I)]. All the other blood conservation modalities are documented to incur additional expenses. Retrograde autologus priming of the cardiopulmonary bypass circuit reduces the incidence of intraoperative transfusion rates without incurring any additional cost neither on the patient nor the institution .

Among the various intra-operative strategies available to reduce transfusion requirements, retrograde autologous priming and minimalized cardio-pulmonary bypass circuit were based on the principle of reducing haemodiltion. The use of a haemo-concentrator will not attenuate the initial drop in haemoglobin concentrations and the correction of haemodilution is slow. Haemo-concentrators require increased pump flows to facilitate filtration and are again expensive.

Retrograde autologous priming is a safe and inexpensive technique of reduction of transfusion requirements intra-operatively. We shall recommend Retrograde autologus priming as one of the blood conservation modalities to be carried out in the institutions carrying out Cardiac surgeries.

LIMITATIONS

The study had patients who were managed under different circumstances without a preset protocol for the study, we were successful in displacing higher prime volume in patients with low BSA and vice versa.

The study excluded all patients with high risk factors for transfusion of packed red cells. Hence was handicapped in establishing the benefits of having lower levels of haemodilution therby avoiding transfusion of packed red cells.

As the study is a retrospective analysis we were unable to strictly adhere to transfusion triggers and accept the carried out measures. There were instances of transfusion inspite of hemoglobin levels documented more than 8gm%, which was on the sole discreation of the clinician with his clinical acumen, this might have resulted in higher transfusion rates. A Strict protocol on transfusion policy with a post-cardio-pulmonary bypass transfusion trigger of 8gm% would have been more appropriate.

The cohort consisted of patient population operated and managed by multiple teams unlike Glenn S M et al's single surgeon cohart.

As the study is a retrospective an analysis we could not ascertain colloid osmotic pressure and extra vascular lung volume.

CONCLUSION

Retrograde autologous priming has proved to effectively reduce hemodilution on cardiopulmonary bypass whereby maintaining better hematocrit levels as noted (p=0.039) .

Retrograde autologous priming has been found to have significantly low creatinine in the post operative period(p=0.026), though there was elevated creatinine values, they could be managed conservatively and there was no requirement for hemodialysis.

Retrograde autologous priming has not shown any significance in the transfusion requirements though we were able to establish reduced hemodilution. There was no reduction in the transfusion requirements during the entire length of hospital stay either. Retrograde autologous priming has no effect on morbidity with respect to stroke.

With respect to hospital stay Retrograde autologous priming has no effect on duration. But there has been statistically significant difference in the intensive care stay(p=0.014).

Our inferences were based on the bivariate analysis of the data collected, these were subjected to multivariate analysis and found to have a significant difference.

Retrograde autologous priming group edging over the standard priming group in reducing intra operative hemodilution (p=0.04) and the stay in critical care(0.03). Retrograde autologous priming has not incurred any extra expenditure in the patient care nor has incurred any additional expenses to the institution per se. We would suggest that it should be part of the blood conservation strategy for reduction of allogeneic transfusions. With strict adherence to transfusion triggers we would be able to establish further reduction in the rate of transfusion and thereby would also reduce the related complications, extending safer post operative care.

REFERENCES

1. Victor A. Ferraris, Jeremiah R. et al. Update to The Society of Thoracic Surgeonsand the Society of Cardiovascular Anesthesiologists Blood Conservation Clinical Practice Guidelines. Ann Thorac Surg 2011 ;91:944-82.
2. Severdija EE, Heijmans JH, Theunissen M . Retrograde autologous priming reduces transfusion requirements in coronary artery bypass surgery. Perfusion. 2011 Jul;26(4):315-21.
3. Teman N, Delavari N, Romano M. Effects of autologous priming on blood conservation after cardiac surgery Perfusion July 1, 2014 29: 333-339
4. Lahanas A, Argerakis PW et al. A retrospective comparison of blood transfusion requirements during cardiopulmonary bypass with two different small adult oxygenators Perfusion November 1,2013 28: 541-545
5. Nanjappa A, Gill J, Sadat U, Colah S. The effect of retrograde autologous priming on intraoperative blood product transfusion in coronary artery bypass grafting Perfusion November 1,2013 28: 530-535
6. Severdija EE al. Extracorporeal circuity prime reduces blood transfusion requirements in coronary artery surgery. NeSECC editie 2007 ur2: 9-16
7. Ferraris VA, Ferraris SP et al. Perioperative blood transfusion and blood conservation in cardiac surgery: The Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists clinical practice guideline. Ann Thorac Surg 2007;83(Suppl):27- 86.
8. Romaine-Davis A. John Gibbon and His Heart-Lung Machine. Philadelphia, Pa: University of Pennsylvania Press; 1991.
9. Ascione R, Williams S et al. Reduced postoperative blood loss and transfusion requirement after beating heart coronary operations: a prospective randomized study. J Thorac Cardiovasc Surg 2001; 121:689 -96.
10. Engoren MC, Habib RH et al. Effect of blood transfusion on long-term survival after cardiac operation.Ann Thorac Surg 2002;74:1180-6.
11. Reges RV, Vicente WV, Rodrigues AJ et al. Retrograde autologous priming in cardiopulmonary bypass in adult patients: effects on blood transfusion and hemodilution. Rev Bras Cir Cardiovasc. 2011 Oct-Dec;26(4):609-16.
12. Senay S, Torman F et al;The impact of allogenic red cell transfusion and coated bypass circuit on the inflammatory response during cardiopulmonary bypass: a randomized study. Int Cardiovascular and Thoracic Surg 2009;8:93-99.
13. Kearsey C, Thekkudan J et al. Assessing the effectiveness of retrograde autologus priming of the cardiopulmonary bypass machine in isolated coronary artery bypass grafts. Ann R Coll Surg Engl 2013;95:207 -210.
14. Mangu H R et al. Blood transfusion practices in cardiac anaesthesia. Indian J. of Anaesthesia 2014: 58(5):616-621.
15. Spiess BD et al. Transfusion of blood products affects outcome in cardiac surgery. Semin Cardiothorac Vase Anesth 2004;8:267-81.
16. Trapp C, Schiller W, Mellert F, Halbe M. Retrograde Autologous Priming as a Safe and Easy Method to Reduce Hemodilution and Transfusion Requirements during Cardiac Surgery. Thorac Cardiovasc Surg. 2015 Oct;63(7):628-34.
17. Rosengart TK, DeBois W, O'Hara M. Retrograde autologous priming for cardiopulmonary bypass: a safe and effective means of decreasing hemodilution and transfusion requirements. J Thorac Cardiovasc Surg. 1998 Feb;l 15(2):426-38; discussion 438-9.
18. Helm RE, Rosengart TK et al. Comprehensive multimodality blood conservation: 100 consecutive CABG operations without transfusion. Ann Thorac Surg. 1998 Jan; 65(l) : 125-36.
19. Shapira et al. Role of allogenic Transfusions after open heart surgeries by lowering cardiopulmonary bypass prime volume.Ann thorac Surg. 1998:65(3):724-30.
20. Balachandran S, Cross M H. Retrograde Autologous Priming of the Cardiopulmonary Bypass Circuit Reduces BloodTransfusion After Coronary Artery Surgery. Ann Thorac Surg 1913, 2002;73:1912-8.
21. Gregory P. Eising, Martin Pfauder, Markus Niemeyer. Retrograde autologous priming: is it useful in elective on-pump coronary artery bypass surgery. Lange Ann Thorac Surg 2003;75:23-27.
22. Murphy GS, Szokol JW et al. Retrograde autologous priming of the cardiopulmonary bypass circuit: safety and impact on postoperative outcomes. J Cardiothorac Vase Anesth. 2006 Apr;20(2): 156-61. Epub 2006 Jan 6. pp 156-161.
23. Saczkowski R, Bernier PL, Tchervenkov CI. Retrograde autologous priming and allogeneic blood transfusions: a meta-analysis. Interact Cardiovasc Thorac Surg. 2009 Mar;8(3):373-6.
24. Xiaotong H; Yang Feng; Ruifang Liu. Retrograde autologous priming of the cardiopulmonary bypass circuit reduces blood transfusion in small adults: a prospective, randomized trial. European Journal of Anesthesiology: December 2009 - Volume 26 - Issue 12 - p 1061-1066
25. Srikrishna Modugula Reddy, Sachin Talwar et al. Multi-modality blood conservation strategy in open-heart surgery: an audit. Interact Cardiovasc Thorac Surg. 2009 Sep;9(3):480-2.
26. Sun P, Ji B, Sun Y, Zhu X, Liu J, Long C. Effects of retrograde autologous priming on blood transfusion and clinical outcomes in adults: a meta-analysis. Perfusion. 2013 May;28(3):238-43.

27. Vandewielea K, Boveb T, Filip M.J.J. The effect of retrograde autologous priming volume on haemodilution and transfusion requirements during cardiac surgery. Interactive Cardiovascular and Thoracic Surgery 16 (2013) 778-784.
28. Nithin et al. A randomized control study comparing bthe effect of retrograde autologus priming to standard priming technique on perioperative transfusion requirements and morbidity in patients undergoing elective coronary artery bypass grafting. CMC Audit Apr 2014.
29. Scott BH, Seifert FC, Glass PS. Blood use in patients undergoing coronary artery bypass surgery: impact of cardiopulmonary bypass pump, hematocrit, gender, age, and body weight. Anesth Analg. 2003 Oct;97(4):958-63.
30. Deurenberg-Yap M, Schmidt G, van Staveren WA, Deurenberg P. The paradox of low body mass index and high body fat percentage among Chinese, Malays and Indians in Singapore. Int J Obes Relat Metab Disord. 2000;24:1011-7.
31. Wen CP, David Cheng TY, Tsai SP, et al. Are Asians at greater mortality risks for being overweight than Caucasians? Redefining obesity for Asians. Public Health Nutr. 2009;12:497-506.
32. Zelinka ES, Ryan P, McDonald J .Retrograde autologous prime with shortened bypass circuits decreases blood transfusion in high-risk coronary artery surgery patients. J Extra Corpor Technol. 2004 Dec; 36(4):343-7.
33. Menkis AH, Martin J, Spiess B, et al. Drug, devices, technologies, and techniques for blood management in minimally invasive and conventional cardiothoracic surgery: Innovations (Phila). 2012 Jul-Aug; 7(4):229-41.
34. Hwang J, Huh J, Kim J, Park S.The effect of retrograde autologous priming of the cardiopulmonary bypass circuit on cerebral oxygenation. J Cardiothorac Vase Anesth. 2011 Dec;25(6):995-9.
35. Trapp C, Schiller W, Mellert F, Halbe M. Retrograde Autologous Priming as a Safe and Easy Method to Reduce Hemodilution and Transfusion Requirements during Cardiac Surgery. Thorac Cardiovasc Surg. 2015 Oct;63(7):628-34.
36. Habib RH, Zacharias A, Schwann TA. Role of hemodilutional anemia and transfusion during cardiopulmonary bypass in renal injury after coronary revascularization: implications on operative outcome. Crit Care Med. 2005 Aug;33(8): 1749-56.
37. Cormack JE, Forest RJ, Groom RC. Size makes a difference: use of a low-prime cardiopulmonary bypass circuit and autologous priming in small adults. Perfusion. 2000 Mar;15(2):129-35.
38. Perry AF, Jost J, Sievers H. Reduction of homologous blood requirements by blood-pooling at the onset of cardiopulmonary bypass.J Thorac Cardiovasc Surg. 1994 May;107(5):1210-4.
39. Pappalardo F, Corno C, Franco A, Giardina G. Reduction of hemodilution in small adults undergoing open heart surgery: a prospective, randomized trial.Perfusion. 2007 Sep;22(5):317-22.
40. Ranucci M, Pistuddi V, Carboni G. Effects of priming volume reduction on allogeneic red blood cell transfusions and renal outcome after heart surgery. Perfusion. 2015 Mar;30(2): 120-6.
41. Analysis of cardiopulmonary bypass diluted autologous blood transfusion: a report of 5000 cases.Li J, Huang MJ. Zhonghua Yi Xue Za Zhi. 2013 May 7;93(17): 1324-6. Chinese.
42. Loubser PG, Morell RI, Loubser I A. Impact of extracorporeal circuit prime volume reduction on whole blood sequestration during acute normovolemic hemodilution for adult cardiac surgery patients. J Extra Corpor Technol. 2004 Dec;36(4):329-35.
43. Campbell JA, Holt DW, Shostrom VK, Durham SJ. Influence of intraoperative fluid volume on cardiopulmonary bypass hematocrit and blood transfusions in coronary artery bypass surgery. J Extra Corpor Technol. 2008 Jun;40(2):99-108.
44. Wiefferink A, Weerwind PW, van Heerde W. Autotransfusion management during and after cardiopulmonary bypass alters fibrin degradation and transfusion requirements.J Extra Corpor Technol. 2007 Jun;39(2):66-70.
45. Cromer MJ, Wolk DR. A minimal priming technique that allows for a higher circulating hemoglobin on cardiopulmonary bypass.Perfusion. 1998 Sep;13(5) :311-3.
46. Sobieski MA, Slaughter MS, Hart DE. Prospective study on cardiopulmonary bypass prime reduction and its effect on intraoperative blood product and hemoconcentrator use.Perfusion. 2005 Jan;20(l):31-7.
47. Saxena P, Saxena N, Jain A, Sharma VK. Intraoperative autologous blood donation and retrograde autologous priming for cardiopulmonary bypass: a safe and effective technique for blood conservation.Ann Card Anaesth. 2003 Jan;6(l):47-51.
48. Kahraman S, Altunkaya H, Celebioglu B. The effect of acute normovolemic hemodilution on homologous blood requirements and total estimated red blood cell volume lost.Acta Anaesthesiol Scand. 1997 May;41(5):614-7.
49. Kearsey C, Thekkudan J, Robbins S. Assessing the effectiveness of retrograde autologous priming of the cardiopulmonary bypass machine in isolated coronary artery bypass grafts.Ann R Coll Surg Engl. 2013 Apr;95(3):207-10.
50. Abdel Aal M, ElNahal N, Bakir BM. Mini-cardiopulmonary bypass impact on blood conservation strategy in coronary artery bypass grafting. Interact Cardiovasc Thorac Surg. 2011 Apr;12(4):600-4.
51. Myers GJ, Legare JF, Sullivan JA. Use of autologous blood as part of the perfusate for cardiopulmonary bypass: a priming technique. Perfusion. 2002 May; 17(3) :211-6.
52. Virmani S, Tempe DK, Pandey BC, Cheema AS. Acute normovolemic hemodilution is not beneficial in patients undergoing primary elective valve surgery.Ann Card Anaesth. 2010 Jan-Apr;13(l):34-8.
53. Kamiya R, Hirose Y, Gamo M. Hemoglobin levels and weight gain after coronary bypass grafting by use of intraoperative hemodilution and autologous blood transfusion. Masui. 2002 Feb;51(2): 150-3. Japanese.
54. Rousou JA, Engelman RM, Flack JE. The 'primeless pump1: a novel technique for intraoperative blood conservation. Cardiovasc Surg. 1999 Mar;7(2):228-35.
55. Giinday M, Bingol H. Is crystalloid cardioplegia a strong predictor of intra¬operative hemodilution? J Cardiothorac Surg. 2014 Jan 27;9:23.
56. Ariyaratnam P, Bennett RT, McLean LA. Antegrade rapid prime displacement in elective coronary artery surgery is associated with lower perioperative blood transfusions and a shorter hospital stay.Interact Cardiovasc Thorac Surg. 2013 Sep;17(3):485-91.
57. Avgerinos DV, DeBois W, Salemi A.Blood conservation strategies in cardiac surgery: more is better.Eur J Cardiothorac Surg. 2014 Nov;46(5):865-70
58. Kiessling AH, Wedde S, Keller H Pre-filling of the extracorporeal circuit with autologous blood is safe, but not effective in optimizing biocompatibility in high-risk patients. Perfusion. 2012 Sep;27(5):371