Antegrade rapid prime displacement in elective coronary artery surgery is associated with lower perioperative blood transfusions and a shorter hospital stay

Priyadharshanan Ariyaratnam^{a,*}, Robert T. Bennett^b, Lindsay A. McLean^b, Kishore K. Jagannadham^b, Edward Turner^b, Steven Griffin^a, Mubarak A. Chaudhry^a and Mahmoud Loubani^a

^a Department of Cardiothoracic Surgery, Castle Hill Hospital, Cottingham, UK

^b Department of Cardiac Perfusion, Castle Hill Hospital, Cottingham, UK

* Corresponding author. Department of Cardiothoracic Surgery, Castle Hill Hospital, Cottingham HU16 5JQ, UK. Tel: +44-781-4118367; e-mail: priyadariyaratnam@yahoo.co.uk (P. Ariyaratnam).

Received 12 February 2013; received in revised form 10 April 2013; accepted 18 April 2013

Abstract

OBJECTIVES: Haemodilution during cardiopulmonary bypass is associated with increased perioperative blood transfusions and is thought to reduce intraoperative oxygen delivery to the brain. We sought to evaluate our method of rapid antegrade prime displacement in the context of the perioperative blood transfusion rate, intraoperative cerebral saturations and postoperative hospital stay.

METHODS: Retrospective analysis of 160 propensity-matched patients undergoing elective coronary artery bypass grafting was performed comparing different perfusion strategies on perioperative blood transfusion and length of postoperative stay. Eighty patients who had rapid antegrade prime displacement and vacuum-assisted venous drainage (RAD-VAD) were compared with 80 patients who had conventional cardiopulmonary bypass with gravity drainage (CB). RAD-VAD involved displacing all or most of the prime in the circuit with the patient's own blood prior to the initiation of cardiopulmonary bypass within a 15–20 s window. Within each group, 10 patients had intraoperative cerebral saturation measurements.

RESULTS: There were no differences in the baseline characteristics between the groups. Both groups had a significant fall ($P < 0.05$) in haematocrit during cardiopulmonary bypass from preoperative values, however, the fall in haematocrit was significantly less in the RAD-VAD group ($P < 0.05$). There was significantly ($P < 0.05$) less intraoperative and postoperative homologous blood transfusions in the RAD-VAD group ($47.892 \text{ ml} \pm 8.14$ and $76.58 \text{ ml} \pm 21.58$) compared with the CB group ($229.06 \text{ ml} \pm 105.03$ and $199.91 \text{ ml} \pm 47.13$). There was a significant fall in cerebral saturations within both groups ($P < 0.05$) but it was not significant between the groups. The postoperative stay was significantly ($P < 0.05$) shorter in the RAD-VAD group compared with the conventional group ($7.74 \text{ days} \pm 0.51$ vs $10.13 \text{ days} \pm 0.95$).

CONCLUSIONS: RAD-VAD is associated with a significantly lower blood transfusion rate perioperatively and shorter hospital stays compared with CB.

Keywords: Cardiopulmonary bypass • Blood transfusion

INTRODUCTION

Although the cardiopulmonary bypass (CPB) circuit has been dramatically refined since its conception by Gibbon, it still carries many imperfections [1, 2]. One such shortcoming is haemodilution during CPB, a significant determinant of postoperative blood transfusion. Both are significant risk factors for morbidity following cardiac surgery [3, 4].

Prime displacement during CPB is used to reduce the prime volume delivered to the patient, thus reducing haemodilution and preserving the haematocrit during bypass [5]. Various methods have been trialled, including retrograde autologous priming. However, the effectiveness and safety of *antegrade* approaches have yet to be fully discerned.

In this study, we compared our technique of rapid antegrade prime displacement using vacuum-assisted venous drainage (RAD-VAD) against conventional bypass using gravity drainage (CB). We explored the impact of these methods on haematocrit, cerebral saturations during CPB and postoperative outcomes.

METHODS

Study design

This study was approved by our institution's Audit Review Board. Retrospective analysis of data registered prospectively on to our database (Patient Analysis Tracking System) for patients

undergoing only elective coronary artery bypass surgery (CABG) between January 2009 and January 2010 was undertaken. Patients were excluded from the analysis if they were in renal failure or had an intra-aortic balloon pump inserted preoperatively.

Patients were divided into two groups: those undergoing conventional gravity drainage CB and those undergoing RAD-VAD. Propensity scores were assigned to each preoperative patient characteristic and matched 1:1 between the two groups of patients. The propensity score represented the probability of a patient being assigned to the case group given the covariables of that patient. It was calculated for each patient using a logistic regression model from the following variables: age, body mass index, logistic EuroSCORE, left ventricular ejection fraction, New York Heart Association (NYHA) functional class, chronic obstructive pulmonary disease (use of bronchodilators or steroids due to lung disease), previous myocardial infarction, diabetes, smoking, previous cardiac surgery, peripheral vascular disease and previous stroke/transitory ischaemic attack. Patients were randomly selected from the RAD-VAD group and matched with for a partner in the CB who had the nearest logit-transformed propensity score. Balance of matching variables was assessed by formal statistical comparison (Kolmogorov-Smirnov test for continuous variables and Fisher's exact test for categorical variables). A *P*-values of >0.05 were considered as evidence for balance of the quantity.

After propensity matching, we identified a final cohort of 140 patients: those using CB ($n = 70$) or RAD-VAD ($n = 70$).

Ten further matched patients in each group had intraoperative cerebral saturation measurements.

Perfusion systems and common strategies

Three oxygenators were used; Admiral (Eurosets, Italia), D903 (Sorin Biomedica) and EOS (Sorin Biomedica), which were integral oxygenator/cardiotomy systems with the facility to separate the cardiotomy blood from the venous blood and were designed to allow vacuum-assisted venous drainage (VAVD). The size of the oxygenator was determined by the ideal mid flow value based on the patient's body surface area. The D903 has a prime volume of 250 ml, the Admiral has 190 ml and the EOS has 160 ml prime volume.

All tubing and oxygenators were phosphorylcholine (PC) coated. The cardiotomy reservoir was connected to a cell saver (Medtronic Autolog or Sorin Electa) to allow the removal of excess prime and cardiotomy suction blood.

Bypass circuits were flushed with carbon dioxide before priming with ~ 1250 – 1500 ml of Hartmann's solution in the CB group and 1000 ml of prime in the RAD-VAD group. Both groups had circuits primed with 5000 IU heparin.

Perfusion strategies

Conventional bypass with gravity drainage. The conventional circuit consisted of an integral oxygenator/cardiotomy system, a $\frac{1}{2}$ ' venous line and a $\frac{3}{8}$ ' arterial line incorporating an arterial filter (Sorin D734 or Eurosets Sherlock). CPB was established using gravity venous drainage and maintained as described above. The arterial line filters had the same pore size.

RAD-VAD method. The circuit used for our Cottingham RAD-VAD technique (Fig. 1) was the same as for CB with the following modifications:

- (i) A regulated vacuum was applied to the venous reservoir (max -100 mmHg, Amvex Corporation) to augment the venous return. The negative pressure in the venous reservoir was measured and maintained at more than -40 mmHg.
- (ii) A $\frac{1}{4}$ ' 'prime displacement line' was inserted into the arterial line, distal to the arterial line filter and connected to the cardiotomy reservoir.

VAVD facilitated a reduction in prime volume by; allowing the oxygenator to be placed closer to the operating field at the level of the patient, which reduced the length of the arterial and venous lines by 40%, and enabling the $\frac{1}{2}$ ' venous line to be replaced with a $\frac{3}{8}$ ' venous line.

The venous reservoir (under vacuum) was emptied and cleared of prime before opening the venous line.

When the surgeon had cannulated and attached the arterial and venous lines to the patient and when both the perfusionist and anaesthetist were satisfied that the patient was ready for CPB, the order for commencement of CPB was given. Immediately following this order, antegrade prime displacement was performed in a rapid manner before the initiation of full bypass: the arterial line was clamped distal to the prime displacement line. The venous line clamp was then removed. The prime displacement line was opened and prime pumped into the cardiotomy reservoir. When the patient's blood had displaced the clear prime, the prime displacement line was clamped and the arterial line opened to establish full CPB. This whole process from the verbal order for CPB to the rapid antegrade prime displacement to the initiation of full CPB takes under 15 s. The displaced prime in the cardiotomy was transferred to the cell saver.

Common strategies. CPB was maintained with a cardiac index of 2.2 – 2.4 l/min/m², mean arterial pressure (MAP) of 60 – 70 mmHg, partial pressure of oxygen (PO₂) of 150 – 225 mmHg and partial pressure of carbon dioxide (PCO₂) of 36 – 39 mmHg.

Figure 1: Schematic for Cottingham rapid antegrade prime displacement and vacuum-assisted venous drainage technique.

Pressures were maintained by altering pump flow, administering intravascular volume administration when necessary (Hartmann's Crystalloid or Volplex Colloid solutions) or by the vasoconstrictor, metaraminol. We used an alpha-stat perfusion strategy with all our patients.

Patients were transfused with red cells if the haemoglobin on the arterial blood gas fell <6.5 g/dl.

All cardiotomy suction blood was separated from the venous return and washed with the cell saver before being returned to the patient.

At the end of all procedures the residual blood in the perfusion circuit was flushed to the cell saver and concentrated before being returned to the patient.

Following the administration of protamine and discontinuation of CPB, patients had a thromboelastogram test to determine if any clotting products were required.

In vivo optical spectroscopy technique. *In vivo* optical spectroscopy (INVOS) (Somanetics) allows for the measurement venous-weighted regional saturations of the brain using a disposable oximeter sticker placed on the skin of the patient's head. This is useful because although peripheral pulse oximetry or blood gases may indicate adequate oxygen saturations, regional inadequacies, particularly in the brain, may concurrently exist. INVOS, therefore, allows for regional brain oxygen saturation (rSO₂) to be measured so as to act rather like a real-time early warning system for cerebral under-perfusion.

If cerebral saturations fell 20% below the baseline, the following strategies were implemented to increase the rSO₂:

- (i) Increase the MAP during CPB to >50 mmHg.
- (ii) Increase the cardiac index to >2.5 l/m²/min.
- (iii) Increase FIO₂.
- (iv) Decrease cerebral O₂ demand by increasing anaesthesia.

Statistical analysis. Our primary endpoint was perioperative blood transfusion rates. Secondary endpoints were morbidity and

length of postoperative hospital stay. Morbidity was defined as: (a) cardiac (confirmed myocardial infarction or sustained reduction in ventricular function), (b) renal (confirmed reduction in glomerular filtration rate/new dialysis), (c) neurological (confirmed cerebrovascular accident or hypoxic brain injury) and (d) wound infection (confirmed graft site or sternal wound infection). Data were analysed using SPSS statistics 19. The continuous variables with a normal distribution were compared by means of the unpaired Student's *t*-test. Those without a normal distribution were compared by means of the Mann-Whitney *U*-test. Categorical variables were analysed using the χ^2 -test or Fisher's exact test when sample size or expected results were too small. For time trends analysis of haematocrit during CPB, three consecutive periods were considered (initiation of CPB, lowest mean values during CPB and termination of CPB), and repeated measurement analysis of variance was used to evaluate changes in haematocrit between groups. Multivariate regression analysis was used to assess the association of base-line variables with perioperative blood transfusion and postoperative stay. *P*-values ≤0.05 were considered statistically significant.

RESULTS

Baseline characteristics

The baseline demographic data for the prime displacement (PD) vs conventional CPB (CB) study is given in Table 1. As can be seen, the groups were closely matched. There was also no significant difference between the patients in the INVOS cohort.

Intraoperative characteristics

The mean cross-clamp time, cumulative bypass time and number of coronary anastomoses did not vary between the groups (Table 2).

Table 1: Preoperative patient characteristics

	Conventional CPB	Prime displacement	<i>P</i> -value
Mean age in years (±SD)	67.64 (9.649)	65.01 (9.886)	0.114
Female (prop) (%)	20 (14/70)	14.3 (10/70)	0.373
CCS I (prop) (%)	11.4 (8/70)	8.6 (6/70)	0.631
CCS II (prop) (%)	50 (35/70)	54.3 (38/70)	
CCS III (prop) (%)	27.1 (19/70)	30 (21/70)	
CCS IV (prop) (%)	7.1 (5/70)	7.1 (5/70)	
NYHA I (prop) (%)	31.4 (22)	35.7 (25/70)	0.978
NYHA II (prop) (%)	57.1 (40/70)	50 (35/70)	
NYHA III (prop) (%)	10 (7/70)	14.3 (10/70)	
NYHA IV (prop) (%)	1.4 (1/70)	0	
With chronic obstructive pulmonary disease (prop) (%)	12.9 (9/70)	10 (7/70)	0.598
No previous myocardial infarctions (prop) (%)	40 (28/70)	37.1 (26/70)	0.731
Insulin dependent diabetes mellitus (prop) (%)	11.4 (8/70)	4.3 (3/70)	0.711
Chronic kidney disease (prop) (%)	0	0	0.854
Peripheral vascular disease (prop) (%)	11.4 (8/70)	11.4 (8/70)	N/A
Three-vessel disease (prop) (%)	81.4 (57/70)	80 (56/70)	0.832
Ejection fraction <30% (prop) (%)	10 (7/70)	5.7 (4/70)	0.863
Mean body mass index (±SD)	28.94 (4.66)	29 (4.44)	0.295
Mean body surface area (±SD)	1.97 (0.22)	2.02 (0.21)	0.120
Mean logistic EuroSCORE I	4.86 (8.22)	4.83 (4.83)	0.295

CCS: Canadian Cardiovascular Society scoring system; NYHA: New York Heart Association scoring system; prop: proportion out of 70.

Table 2: Operative characteristics

	Conventional CPB	Prime displacement	P-value
Patients using Avant oxygenator (%)	92.86 (65/70)	77.14 (54/70)	0.007
Mean CPB time (min) (SD)	88.20 (25.71)	81.16 (23.49)	0.093
Mean cross-clamp time (min) (SD)	52.01 (16.29)	49.94 (14.1)	0.302
Mean Pre-CPB HCT (SD)	37.03 (4.093)	39.41 (4.599)	0.078
Mean lowest CPB HCT (SD)	24.66 (3.540)	28.76 (4.325)	<0.001
Mean post-CPB HCT (SD)	28.259 (3.4997)	31.080 (5.1323)	<0.001
Mean volume of prime delivered (ml) (SD)	1429.29 (209.985)	363.57 (270.79)	<0.001
Mean intraoperative crystalloid delivered (ml) (SD)	386.43 (52.51)	372.06 (56.50)	0.861
Mean intraoperative colloid delivered (ml) (SD)	252.86 (35.58)	292.15 (38.83)	0.457
Mean intraoperative autologous blood transfusion (ml) (SD)	62.658 (10.09)	105.116 (33.49)	0.112
Mean intraoperative homologous blood transfusion (ml) (SD)	229.06 (105.03)	47.892 (8.14)	<0.001
Mean amount of blood retrieved from cell saver (ml) (SD)	268.50 (57.30)	271.111 (29.176)	0.855
Mean amount of metaraminol given during CPB (mg) (SD)	12.65 (7.12)	14.50 (7.80)	0.743
Mean cerebral saturation % (L and R) pre-CPB (%) (SD) <i>n</i> = 10	75.1(6.1)	69.2 (4.3)	0.841
Mean cerebral saturation % (L and R) during CPB (%) (SD) <i>n</i> = 10	66.11 (5.47)	62.58 (4.06)	0.08

The Admiral oxygenator was used significantly more in the CB group than the RAD-VAD ($P = 0.007$). However, this did not influence the blood transfusion rate or the postoperative stay.

The intraoperative (asanguineous) prime delivered was confirmed to be significantly more in the CB group compared with the RAD-VAD group (1429.29 ml $\pm$ 25.098 vs 363.57 ml $\pm$ 32.37, $P < 0.001$).

There was no significant difference ($P > 0.05$) observed between RAD-VAD and the CB in the total volume of crystalloid (372.06 ml $\pm$ 56.50 vs 386.43 ml $\pm$ 52.51) or colloid (252.86 ml $\pm$ 35.58 vs 292.15 ml $\pm$ 38.83) given during CPB.

There was a significant initial fall in haematocrit (%) from the initiation of CPB to the mean of the lowest [Hb] through CPB in both the CB (37.03 $\pm$ 4.093–24.66 $\pm$ 3.546) and the RAD-VAD group (39.91 $\pm$ 4.599–28.76 $\pm$ 4.325) ($P < 0.001$). This is followed by an increase at the end of CPB. This fall and rise was significantly less ($P < 0.001$) in the RAD-VAD group compared with the CB group (Fig. 2).

Postoperative outcomes

There was no mortality in either group, nor were there any postoperative cardiac, renal, neurological or wound complications in either group. However, the postoperative stay was significantly less in the RAD-VAD group compared with the CB group (7.74 days $\pm$ 0.519 vs 10.13 days $\pm$ 0.959, $P = 0.030$) (Table 3). When evaluating whether intraoperative and postoperative blood transfusions were independent predictors of length of postoperative stay, only a higher postoperative transfusion amount of red cells was a significant ($P < 0.001$) predictor of a longer postoperative stay. Homologous ($P = 0.389$) and autologous ($P = 0.465$) were not predictors of hospital stay.

Haematological and transfusion characteristics of PD vs conventional CPB study

There was significantly ($P < 0.05$) less intraoperative and postoperative homologous blood transfusions in the RAD-VAD group (47.892 ml $\pm$ 8.14 and 76.58 ml $\pm$ 21.58) compared with the CB

Figure 2: Estimated marginal means of haematocrit.

group (229.06 ml $\pm$ 105.03 and 199.91 ml $\pm$ 47.13). Regarding actual numbers of patients receiving blood, 2/70 (2.86%) patients received red cells intraoperatively in RAD-VAD vs 14/70 (20%) in the CB group while 13/70 (18.6%) patients were given postoperative red cells in the RAD-VAD group vs 20/70 (28.6%) patients in the CB group.

There was no significant difference ($P > 0.05$) in the amount of clotting products given between the groups in the postoperative period.

INVOS data

Within the INVOS groups, there was a significant fall in the mean rSO_2 during CPB ($P < 0.05$) over time. Although not statistically significant, the percentage fall in mean rSO_2 from pre-bypass baseline was less in the prime displacement group than in the conventional bypass group (-6.7 ± 4.8 vs -9.0 ± 3.0 rSO_2

Table 3: Postoperative complications

	Conventional CPB	Prime displacement	P-value
Total blood loss	864.74 (616.23)	774.2 (443.29)	0.320
Postoperative blood transfusion (ml)	199.91 ± 47.137	76.58 ± 21.583	0.022
Total clotting factor replacement	341.274 (112.93)	229.872 (60.06)	0.284
Mortality (%)	0	0	N/A
Acute renal failure (%)	0	0	N/A
Deep sternal wound infection (%)	0	0	N/A
Reoperation (%)	0	0	N/A
Intra-aortic balloon pump (%)	0	0	N/A
Neurological complications (%)	0	0	N/A
Myocardial infarctions (%)	0	0	N/A
Mean postoperative hospital stay (days) (SD)	10.13 (8.025)	7.74 (4.349)	0.030

index units). Representative INVOS traces for the conventional bypass group and PD group and are shown in (Figs 3 and 4), respectively.

Cost analysis

There was no cost incurred in including the prime displacement line into the CB circuit to create the RAD-VAD circuit as this was covered in the manufacturer's costs.

The cost of intraoperative blood transfusion for the CB group was £64.76 (±16.88) per patient compared with £5.02 (±3.53) for the RAD-VAD group ($P < 0.001$).

The cost of postoperative blood transfusions for the CB group was £123.25 (±29.06) per patient compared with £47.22 (±13.31) for the RAD-VAD group ($P < 0.001$).

DISCUSSION

Uniqueness of our method

Prime displacement CPB has been practiced as an alternative method of perfusion for over a decade. The technique varies from centre to centre and is very much operator dependent [6, 7]. The advantages of our low cost RAD-VAD method over other techniques are 2-fold. First, we are able to prevent the haemodilution of the patient during CPB by displacing all/most of the prime with the patient's own blood prior to commencing CPB in a rapid fashion that takes under 15 s.

Secondly by having VAVD, we are able to raise the oxygenator to the level of the patient and thus shorten the table times compared with gravity drainage where the oxygenator is well below the patient, thereby reducing the exposure of the patients' blood to the foreign surfaces of the tubing, thus reducing any possible inflammatory response to this [8].

Safety concerns of our protocol

The period of haemodynamic instability during the time of prime displacement may present itself as a theoretical risk. However, the rapid displacement time of <20 s does not demonstrate any negative sequelae in our patients.

Further to this, during this rapid prime displacement period, there is a risk of reducing perfusion to the brain, which is demonstrated by our INVOS tracing. However, also from our INVOS tracing, it can be seen that this drop in cerebral sats is rapidly corrected within 5–10 s, again with no neurological sequelae.

Finally, the clamping and unclamping of the arterial line prior to prime displacement may cause the cardiectomy reservoir to become pressurized as it is a sealed chamber in a closed circuit. All our reservoirs are fitted with an over and under safety pressure release valve to prevent this from happening.

Effectiveness in lowering the requirement of red cell transfusion

Our method demonstrates a clear reduction in blood transfusion rate during CPB. This is likely due to the *haemodilution* effects of normal CB as there is no significant difference in the *blood loss* of our patients between the groups. A haemorrhagic explanation for the anaemia is further negated by the lack of any difference in the requirement of clotting products (Fresh Frozen Plasma, Platelets or Cryoprecipitate) after the operation.

Blood transfusion in itself is an expensive commodity associated with adverse postoperative outcomes. Our study shows a clear saving in blood transfusion costs in using PD over CB.

Our study did not demonstrate any clear differences in postoperative complications, including neurological disturbances, following cardiac surgery between the groups. We did not compare biochemical markers associated with morbidity such as inflammatory markers. Despite this, the PD group spent significantly fewer days postoperatively in our hospital. It is difficult to explain this prolonged hospital stay in the absence of any clear identifiable morbidity but studies have shown that blood transfusion is an independent predictor of hospital costs and morbidity [9]. Further to this, the lowest haematocrit on bypass was significantly more pronounced in the CB group compared with the RAD-VAD group and this is also an important determinant of outcome [10].

INVOS monitoring allows for implementing measures that have been shown to restrict the damage of persistently cerebral low saturations during CPB [11]. Our INVOS data show an interesting pattern over time of how well the brain is oxygenated during CPB. Both groups demonstrated a significant fall in cerebral saturations during CPB ($P < 0.05$), indicating that on-pump

Figure 3: Sample INVOS trace for conventional CPB.

Figure 4: Sample INVOS trace for rapid antegrade prime displacement and vacuum-assisted venous drainage.

CABG surgery may be associated with a reduction in cerebral saturations.

Although there was no difference between the groups, there is a trend ($P = 0.08$) towards improved saturations in the RAD-VAD group. Perhaps with a greater number of patients, this trend may have transpired into significant differences.

Limitations

This study suffers from the weakness inherent in any retrospective study, including potential inconsistency of the data acquired over time. Although we used a propensity-matched method it does not fully control or exclude confounding factors.

Secondly, we are comparing a hybrid procedure (VAVD and prime displacement) with conventional gravity-assisted CPB. Hence, one could argue that the effects seen could be either due to VAVD or prime displacement or both. Hence, a prospective study comparing VAVD with and without prime displacement may be useful.

Further to this, although we used the D903 oxygenator for the vast majority of our cases in both the PD and CB groups, we used it significantly more in the conventional bypass group. However, this did not significantly affect outcomes.

Finally, our patient cohort was a select group with a relatively low mean Logistic EuroSCORE, encompassing routine elective CABG operations. Hence, we cannot extrapolate the results for valve and complex non-CABG surgeries. Further studies would need to be done to evaluate the role of RAD-VAD in those patients.

Variations in techniques and results, between centres and studies, as well as the reliance on retrospective data precipitates a need for multicentre randomized control trials to compare different methods of prime displacement with each other as well as with conventional bypass.

CONCLUSION

Rapid antegrade prime displacement with VAVD is not associated with an increased perioperative risk to the patient undergoing elective CABG only. It is, however, associated with a significantly lower blood transfusion rate perioperatively and shorter hospital stays.

ACKNOWLEDGEMENTS

We thank other members of our perfusion team not attributed to in the author list: Wendy J Medlam, Rachel V Bennett, Jill Bell, Virginia Francis and Andrew Wallhead. We also thank Victoria Allgar from York University for helping with the statistical analysis.

Conflict of interest: none declared.

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