A structured blood conservation programme reduces transfusions and costs in cardiac surgery

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INTRODUCTION

Transfusions of blood products can be lifesaving, but they are also associated with well-recognized risks and adverse effects. There is a small but non-negligible risk of transmission of pathogens, and blood products can also result in immune response modulation, with an increased risk of infections and malignancies [1–3]. Recent data suggested that transfusion with blood products is an independent risk factor for both short- and long-term mortality after cardiac surgery [4–8]. Blood products are associated with high direct and indirect costs, and a shortage of blood products is a reality. Thus, there are many reasons for limiting the use of blood products to only necessary transfusions.

There is wide variation in the prevalence of perioperative transfusions in cardiac surgery [9–11]. The large differences between institutions cannot be explained just by differences in patient characteristics. Most likely, institutional and individual differences in transfusion practice, guidelines and attitudes influence the frequency and number of transfusions. The decision to transfuse is based on multiple patient factors and it is impossible to designate a single transfusion trigger. At our institution, 61% of patients who underwent cardiac surgery in 2009 were transfused perioperatively. At that time, there was no written transfusion policy at our institution. This high prevalence initiated a multifactorial blood conservation programme with the intention of reducing transfusions by 30% without compromising patient safety.

The aim of the present prospective study was to evaluate the effect of a blood conservation programme on transfusion prevalence, transfusion volumes and costs for blood products in acute and elective cardiac surgery. In addition, we investigated whether the programme was associated with any measurable effects on early complication rates. Finally, we studied the effects of the...
programme over a 24-month period after the project was completed.

**METHODS**

**Patients**

All adult patients \((n=2162, \text{mean age } 65 \pm 12\text{ years, } 75\% \text{ men})\) who underwent cardiac surgery at Sahlgrenska University Hospital during a 24-month period from February 2009 to January 2011 were included in the study. The patients were divided into two groups. The first group comprised all patients operated on during the previous 12 months before the start of the blood conservation programme, from 1 February 2009 to 31 January 2010 \((n=1128)\). The second group comprised all patients who were operated on after the start of the programme \((n=1034)\), from 1 February 2010 to 31 January 2011. The study was approved by the Regional Research Ethics Committee, which waived individual patient consent. Patient characteristics are given in **Table 1**.

**Study design**

The following preoperative variables were prospectively registered for all patients: age, gender, body mass index, additive EuroSCORE, antithrombin therapy, preoperative haemoglobin, activated partial thromboplastin time \((\text{aPTT})\), prothrombin time, platelet count, serum creatinine and plasma fibrinogen concentration. The following perioperative and postoperative variables were registered: surgical procedure, cardiopulmonary bypass \((\text{CPB})\) time and aortic clamp time, acuteness, number of red blood cells \((\text{RBCs})\), plasma- and platelet transfusions, reoperation for bleeding within 24 h postoperatively, chest drain loss during the first 12 postoperative hours, length of stay in the intensive care unit \((\text{ICU})\) and total length of hospital stay, ventilation time, mediastinitis, defined as infection involving deep tissues with either purulent drainage or microorganisms isolated from fluid or tissue, highest postoperative serum creatinine and haemoglobin levels on Day 4 after surgery. Acute surgery was defined as surgery commencing within 24 h of the decision to operate. The proportion of patients transfused with any blood was registered for 3 consecutive years after the programme was initiated.

Preoperative, perioperative and postoperative data were compared between the two groups and in subpopulations based on gender, age, surgical procedure and preoperative haemoglobin levels. The cost calculations were based on the institutional price list for blood products 2009 \((\text{RBC concentrate: } 102\text{ €/unit; plasma: } 35\text{ €/unit; and platelets: } 290\text{ €/unit})\). The same price list was used to calculate costs for the patients operated during 2010.

**Blood conservation programme**

The programme had three parts:

(i) **Education.** All the staff involved in the care of the patients, including surgeons, anaesthetists, residents, OR-, ICU- and ward nurses, nurse helpers, physiotherapists and perfusionists were educated about the risks and benefits of blood transfusions and the new transfusion guidelines in a 45-min lesson. The lesson was repeated for all new employees.

(ii) **Guidelines.** We revised our guidelines for transfusions based on the Society of Thoracic Surgeons and the Society of Cardiac Anaesthetists Guidelines (2007 edition) [12]. In the institutional guidelines, the decision to transfuse red cells perioperatively should be based on clinical judgement of the patient’s clinical and haemodynamic status, and/or signs of low oxygen delivery with mixed venous saturation below 55%, haemoglobin levels below 60 g/l were an absolute indication for RBC transfusion. In patients with ongoing significant bleeding, a haemoglobin level of 100 g/l was aimed for. Plasma was transfused in patients with ongoing significant bleeding (>200 ml/h) and prolonged coagulation time in the absence of a sustained heparin effect by thromboelastometry \((\text{TEM})\), indicating a coagulation factor deficiency. Platelets were transfused in patients with ongoing significant bleeding (>200 ml/h) and low platelet count (<100 \times 10^9/l) and/or suspected platelet dysfunction, e.g. treatment with platelet inhibitors. The final decision to transfuse or not was always at the discretion of the physician responsible.

(iii) **Transfusion log.** A specific transfusion log was added to the patient records. In this log, all transfusion episodes were registered together with time of transfusion, indication for transfusion, type of blood product, amount \((\text{units})\), patient status including blood pressure, pulse, mixed venous oxygenation, haemoglobin levels and the prescribing physician (Fig. 1).

All patient and transfusion data were collected from patient records and local data registries into a database by a designated research nurse.
Clinical management

In all patients, anaesthesia was induced with 200–300 μg fentanyl and thiopentone (3–5 mg/kg body weight), followed by pancuronium (0.1 mg/kg) and maintained with sevoflurane. During CPB, anaesthesia was maintained with propofol. The patients received heparin (350 units/kg body weight) to maintain an activated clotting time of more than 480 s. After CPB, the heparin was reversed by the administration of protamine sulphate (1 mg protamine/100 units of heparin). The CPB circuit included a membrane oxygenator and roller pumps. The standard non-pulsatile CPB technique with normothermia and haemodilution was used in most cases. The CPB circuit was primed with 1400 ml Ringer acetate (Fresenius Kabi AB, Uppsala, Sweden) and 200 ml mannitol (150 mg/ml) (Fresenius Kabi AB). Cardioprotection was achieved with antegrade cold blood cardioplegia. Weaning off CPB was performed after rewarming to a bladder temperature of 36°C. Aspirin was not discontinued before surgery. If possible, clopidogrel was discontinued 5 days before surgery. All patients received 2 g tranexamic acid intravenously at anaesthesia induction and at the end of surgery. Aprotinin was not used in any of the study patients. Thromboelastography (TEG) or TEM was used to monitor haemostasis in patients with ongoing bleeding in the operating theatre and in the ICU [13].

Statistics

Results are expressed as mean and standard deviation (SD) and/or median and 25th and 75th percentiles, or as a number and percentage. Statistical significance was defined as a P-value <0.05. The independent sample t-test was used to compare normally
distributed continuous variables, the Mann–Whitney U-test was used to compare non-normally distributed continuous variables and categorical variables were compared with a χ² test. Normal distribution of data was tested with the Kolmogorov–Smirnov test. All descriptive and statistical analyses were performed in Statistica 12 (StatSoft, OK, USA).

RESULTS

General

Preoperative fibrinogen levels were significantly lower and aPTT was somewhat longer in the patients who were included after the start of the programme (Table 1). The mean preoperative haemoglobin concentration tended to be lower, and the proportion of patients undergoing acute surgery tended to be larger after the start of the programme (P = 0.07 both). Other factors before and after the programme started are given in Table 1.

Transfusions

Red blood cells. There was a significant decrease in RBC transfusions when the programme was started (Fig. 2). The proportion of patients transfused with RBCs was reduced by 21.8% (from 58.2 to 45.5%, P < 0.001). The mean number of RBC transfusions was 3.6 ± 7.5 units per patient before and 2.8 ± 6.6 units per patient after the start (P = 0.010). The median number of transfusions was 2 (25th and 75th percentiles 0–4) before and 0 (0–3) after the start (P < 0.001). Before the programme, 37.3% of the transfused patients were transfused with 1–2 RBC units, 36.9% with 3–6 units and 25.8% with ≥6 units when compared with 40.6, 32.1 and 27.2%, respectively, after the programme was started (P = 0.25).

Plasma. There was a significant decrease in plasma transfusions after the programme was launched (Fig. 2). The proportion of patients transfused with plasma was reduced by 37.4% (from 30.8 to 19.3%, P < 0.001). The mean number of plasma transfusions was 2.4 ± 7.9 units per patient before and 1.9 ± 7.3 units per patient after the start (P = 0.10). The median number was 0 (0–2) before and 0 (0–0) after the start (P < 0.001). The reduction in plasma transfusion prevalence was consistent in all subgroups of patients.

Platelets. There was a significant decrease in platelet transfusions after the programme was started (Fig. 2). The proportion of patients transfused with platelets was reduced by 21.0% (from 20.5 to 16.2%, P = 0.010). The mean number of platelet transfusions was 0.77 ± 2.3 units per patient before and 0.57 ± 1.7 units per patient after the start (P = 0.019). The median number was 0 (0–0) before and 0 (0–0) after the start (P = 0.09). The reduction in platelet transfusion prevalence was consistent in all subgroups of patients.

Any blood product. There was a significant decrease in transfusions of any blood product after the start of the programme (Fig. 2). The proportion of patients transfused with any blood product was reduced by 20.7% (from 60.9 to 48.3%, P < 0.001). The mean number of transfusions was 6.8 ± 17 units per patient before and 5.3 ± 15 units per patient after the start of the programme (P = 0.028). The median number was 2 (0–6) before and 0 (0–4) after the start (P < 0.001). The reductions in subgroups of patients are shown in Fig. 3. The association between risk score (EuroSCORE) and transfusion is illustrated in Fig. 4. The proportions of patients transfused with any blood product during Year 2 and Year 3 after the start were 54.0 and 50.7%, respectively.

Patient outcome. There was no significant difference in the incidence of reoperation for bleeding, length of stay at ICU, overall incidence of mediastinitis, incidence of new dialysis or 30-day mortality before and after the start of the programme. Ventilation time and hospital stay were statistically longer, haemoglobin levels 4 days after operation were higher and chest drain loss during the first 12 postoperative hours, but the absolute differences were minimal (Table 2).

Costs. The total cost of blood products before the start was 1 301 261 € per year. During the 12-month period after the start, the programme reduced the total amount of transfused RBCs by 806 units, plasma by 558 units and platelets by 207 units compared with the period before the start. This corresponds to savings of 161 623 € or 12.4% of the total cost of blood products over a 12-month period at our institution (Table 3).

DISCUSSION

The results of the present study demonstrate that a structured blood conservation programme reduces transfusion prevalence and costs for blood products. This can be achieved without compromising patient safety. The reduction in transfusion prevalence was maintained for at least 3 years.

Patients undergoing cardiac surgery remain at high risk of the need for transfusion of blood products. The optimal level of transfusion is unknown. Direct risks associated with transfusion include immune modulation and transmission of pathogens [1–3]. Several recent studies have also indicated that transfusion of RBCs increases both early and late mortality in cardiac surgery patients [4–8]. However, contradictory reports also exist [14]. Although it is difficult to isolate the effect of blood transfusion from other known or unknown risk factors, the studies indicate that patients should only be transfused when it is considered necessary. Furthermore, recent studies in large patient materials have shown that the introduction of different blood conservation programmes reduces morbidity and mortality in cardiac surgery patients [15–19].

In the present study, we investigated the effects of a structured inexpensive blood conservation programme on transfusion prevalence and costs. A more restrictive approach to transfusion than
the historical one was advocated, where more liberal use of blood products was considered the best form of patient care. The results show that the programme reduced the prevalence rate of any transfusion by 22% despite the fact that changes in patient mix between the two periods indicate that there would be an increased need for transfusions. Mean fibrinogen levels were lower and there was a strong tendency towards more acute patients and a reduced proportion of CABG's after the start of the programme. These factors have previously been shown to increase bleeding and transfusions after cardiac surgery [1, 10, 20]. The median additive EuroSCORE did not differ significantly between the two periods. There is a close association between preoperative risk and transfusion prevalence, as shown in Fig. 4. This might have implications for transfusion prevalence if older patients and patients with more comorbidities are accepted for cardiac surgery. Our results demonstrate further that the effects of the programme were maintained at an acceptable level over at least a 3-year period despite the programme initially being envisaged as a 1-year project.

![Figure 3](image_url) Percentage of patients in different subgroups who were transfused with any blood product before (white bars) and after (black bars) the blood conservation programme was started. ***P < 0.001. CABG: coronary artery bypass grafting.

![Figure 4](image_url) Percentage of patients with a different additive EuroSCORE who were transfused with any blood product before (white bars) and after (black bars) the blood conservation programme was started. *P < 0.05, **P < 0.01, ***P < 0.001

**Table 2**: Outcome variables before and after the start of the blood conservation programme

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Before start (n = 1128)</th>
<th>After start (n = 1034)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative drain loss (ml/12 h)</td>
<td>587 ± 416</td>
<td>553 ± 350</td>
<td>0.04</td>
</tr>
<tr>
<td>Reoperation for bleeding</td>
<td>65 (5.8%)</td>
<td>52 (5.0%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Postoperative serum creatinine</td>
<td>107 ± 67</td>
<td>108 ± 72</td>
<td>0.55</td>
</tr>
<tr>
<td>Postoperative dialysis</td>
<td>31 (2.7%)</td>
<td>29 (2.8%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Stroke</td>
<td>12 (1.1%)</td>
<td>18 (1.7%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Mediastinitis</td>
<td>17 (1.5%)</td>
<td>15 (1.5%)</td>
<td>0.91</td>
</tr>
<tr>
<td>Ventilation time (h)</td>
<td>3 (2–5)</td>
<td>3 (2–6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>2 (2–2)</td>
<td>2 (2–2)</td>
<td>0.07</td>
</tr>
<tr>
<td>Hb at Day 4 (g/l)</td>
<td>100 ± 11</td>
<td>98 ± 12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>7 (6–9)</td>
<td>7 (6–8)</td>
<td>0.013</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>28 (2.5%)</td>
<td>27 (2.6%)</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Mean ± SD, median and 25th and 75th percentiles, or number (%). Hb: haemoglobin; ICU: intensive care unit; SD: standard deviation.
Ventilation time and hospital stay were somewhat longer after the start but the absolute difference was marginal, and no difference in postoperative complications as mediastinitis, stroke, new dialysis or 30-day mortality was noted. Despite the reduction in blood product utilization, we were not able to demonstrate any clinical benefit after the programme started, which is in contrast to some previous publications [15–20]. This may be due to the limited study population. Most studies that have shown improved clinical outcome with a blood conservation programme [15–20] have included markedly larger study populations than in our study. Alternatively, the reduction in blood use in our study may not be large enough to imply any clinical benefit.

Interestingly, after the start, there was only a minimal difference in mean haemoglobin levels 4 days after surgery (2 g/l), despite the reduction in prevalence and in the mean number of RBC transfusions. This indicates that the effect of RBC transfusion on haemoglobin levels is short-lived and that a restrictive transfusion strategy would be expected to result in an increased number of transfusions later during the hospital stay.

Before the programme, 37% of our transfused patients had received 1–2 units and it was anticipated that this group would be markedly reduced after the programme started. However, the proportion of patients who received 1–2 units was not reduced despite the overall reduction in the prevalence of RBC transfusion. This indicates that there is still large room for improvement, since transfusion of only 1–2 units of RBCs may be redundant. This is supported by recent data that suggest that transfusion of as little as 1–2 units of RBCs influences survival after cardiac surgery [4,5].

The intention before the programme was started was to reduce transfusions by 30% without compromising medical safety. This objective was not reached since both the prevalence of transfused patients and the mean number of RBCs transfused were not reduced [5]. It is possible that our goal was too high. Alternatively, one may speculate that the adherence to our transfusion guidelines was too low. Nevertheless, we could not observe that the reduction in transfusions endangered medical safety.

The reduction in plasma transfusion after the start of the programme was considerably more pronounced than the reduction in RBC transfusion and plasma transfusion. This might be at least partly explained by the use of TEM in patients with ongoing bleeding. TEM can distinguish between impaired haemostasis caused by reduced clot initiation (i.e. coagulation factor deficiency or heparin effect) and impaired clot strength caused by low fibrinogen levels and/or low platelet count or dysfunction [13]. In our experience, very few patients have impaired clot initiation in the absence of sustained heparin effect, so plasma transfusion is rarely indicated, as also shown recently by our group in paediatric cardiac surgery [21].

We observed a large reduction in costs for blood products when the programme was started (Table 3), which is logical and in accordance with previous studies [15]. More importantly, there is often a shortage of blood products, and the reduction in blood used released almost 1400 units for other purposes during a 12-month period. The net reduction in total costs calculated was somewhat lower in reality since the reduced use of plasma resulted in an increase in the use of albumin and other plasma expanders. By contrast, our calculations were based on our blood bank’s prices for blood products, which may have led to underestimation of the total costs. There have been studies showing that the costs to society of blood products are markedly higher than institutional prices [22,23].

The present study has important limitations. Other factors not related to the transfusion policy may have changed during the studied periods. Non-adherence to transfusion guidelines may influence the results but were not covered in the present study. Furthermore, while the data for the period before the start of the project were retrieved from prospective registries, the data for the period after the start were collected prospectively. This may introduce bias with higher data quality from the second period. However, if the project had started with a collection period before the changes were introduced, all staff would have been aware of the upcoming changes, which may have influenced decision-making before the new transfusion policy was actually implemented. In addition, given the relative large study population, there were differences in some variables that become statistically significant between the study periods (e.g. aPTT, haemoglobin), which most likely are clinically irrelevant. Limitations in cost calculation and evaluation of clinically relevant endpoints are covered above.

In conclusion, the introduction of a blood conservation programme in cardiac surgery reduced blood product utilization and costs. Today, there is high awareness that blood transfusions are associated with well-recognized risks, and so a more restrictive approach to transfusions is necessary.

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### Conflict of interest

None declared.

### REFERENCES

