Protocol guided bleeding management improves cardiac surgery patient outcomes

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Background and Objectives Excessive bleeding is a risk associated with cardiac surgery. Treatment invariably requires transfusion of blood products; however, the transfusion itself may contribute to postoperative sequelae. Our objective was to analyse a quality initiative designed to provide an evidenced-based approach to bleeding management.

Materials and Methods A retrospective analysis compared blood product transfusion and patient outcomes 15 months before and after implementation of a bleeding management protocol. The protocol incorporated point-of-care coagulation testing (POCCT) with ROTEM and Multiplate to diagnose the cause of bleeding and monitor treatment.

Results Use of the protocol led to decreases in the incidence of transfusion of PRBCs (47.3% vs. 32.4%; P < 0.0001), FFP (26.9% vs. 7.3%; P < 0.0001) and platelets (36.1% vs. 13.5%; P < 0.0001). During the intra-operative period, the percentage of patients receiving cryoprecipitate increased (2.7% vs. 5.1%; P = 0.002), as did the number of units transfused (248 vs. 692; P < 0.0001). The proportion of patients who received tranexamic acid increased (13.7% to 68.2%; P < 0.0001). There were reductions in re-exploration for bleeding (5.6% vs. 3.4%; P = 0.01), superficial chest wound (3.3% vs. 1.4%; P = 0.002), leg wound infection (4.6% vs. 2.0%; P < 0.0001) and a 12% reduction in mean length of stay from operation to discharge (95%: 9–16%, P < 0.0001). Acquisition cost of blood products decreased by $1 029 118 in the 15-month period with the protocol.

Conclusions The implementation of a bleeding management protocol supported by POCCT in a cardiac surgery programme was associated with significant reductions in the transfusion of allogeneic blood products, improved outcomes and reduced cost.

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Key words: bleeding management protocol, haemostasis, patient blood management, transfusion – surgery.

Introduction

Some bleeding is an inevitable consequence of cardiac surgery; however, up to 10% of patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) experience excessive bleeding which can negatively impact their outcome [1–3]. Treatment of such bleeding invariably necessitates the transfusion of blood products. However, there are accumulating data indicating these transfusions may independently contribute to postoperative sequelae and increased mortality [4–8]. Improving outcomes for these patients is therefore dependent on clinicians recognizing patients who have a high risk of bleeding, implementing a plan to reduce the likelihood of a bleeding event and the ability to promptly diagnose the aetiology of bleeding to guide appropriate management. The cause of excessive bleeding is frequently multifactorial, and a complex balance of treatment is often required to re-establish and maintain haemostasis. Effective bleeding management must focus on the real rather than an assumed cause of bleeding, with targeted haemostatic therapy administered with minimal delay.

Concerns surrounding the potential for transfusion-associated adverse events and increasing cost were drivers to establish an evidenced-based approach to bleeding management. This study compares blood product use, patient outcomes and cost before and after implementation of this patient blood management (PBM) strategy.

Materials and methods

This quality initiative was approved by the institutional ethics committee (HREC/13/QPCH/341). A retrospective cohort analysis was performed on patients who underwent cardiac surgery with CPB during 15 months before (1/04/2011–30/06/2012) and after (1/07/2012–30/09/2013) implementation of a bleeding management protocol. Patients undergoing heart and/or lung transplantation, or surgery with mechanical circulatory support were excluded from this analysis. The practice change involved the anaesthetic, cardiac and critical care departments, at The Prince Charles Hospital, a tertiary referral centre in Queensland, Australia. Cardiac surgery was performed by eight cardiac surgeons supported by 12 cardiac anaesthetists. A clinical nurse consultant developed, co-ordinated, implemented and evaluated the provision of the bleeding management protocol.

The primary end-points were as follows: the incidence of patients receiving transfusion of allogeneic packed red blood cells (PRBCs), fresh frozen plasma (FFP), platelets or cryoprecipitate. Secondary end-points included the total number of units transfused (intra-operative and postoperative), unplanned surgical re-exploration for bleeding, length of stay (LOS) from surgery to discharge, the incidence of infectious and embolic complications, new renal replacement therapy and in-hospital mortality. The incidence of tranexamic acid (TXA; Cyklokapron, Pfizer, Pty Ltd, Perth, Australia), prothrombin complex concentrate (PCC; Prothrombinex VF, CSL Behring, Melbourne, Victoria Australia) and recombinant factor VIIa use (rFVIIa; NovoSeven: Novo Nordisk, Bagsvaerd, Gladsaxe Denmark), as well as blood product acquisition costs, was analysed.

Clinical management prior to the introduction of the bleeding management protocol

Anaesthesia utilized a balanced approach aimed at fast-track extubation where possible. This included intravenous midazolam, fentanyl and titrated propofol for anaesthetic induction, with rocuronium or pancuronium administered for endotracheal intubation. TXA was used based on surgical or anaesthetic preference. If significant blood loss was anticipated, cell salvage was utilized from commencement of procedure, or postheparin reversal in the event of excessive bleeding. Systemic heparinization was administered for aortic cannulation to achieve a target activated clotting time (ACT, Hemochron Junior) of >400 seconds before commencing CPB. The circuit was primed with Plasmalyte-148 (Baxter Healthcare Pty Ltd, Toongabbie, NSW, Australia) and 10 000 IU heparin (Pfizer, Pty Ltd) and buffered with sodium bicarbonate (Pfizer, Pty Ltd). Anaesthesia was maintained with an intravenous propofol infusion and intermittent dosing of fentanyl. Haemoglobin concentration was maintained above 7 g/dl but was dependent on physiological circumstances specific to the individual patient. Pacing and inotropic support were utilized as required. After separation from CPB, heparin was reversed with a dose of protamine that accounted for total heparin dose including CPB prime and expected heparin elimination. A propofol infusion was continued for transfer of the intubated/ventilated patient to the cardiac intensive care unit (ICU). Sedation was ceased to allow extubation when the patient was haemodynamically stable and normothermic with minimal blood loss.

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In the presence of clinically significant bleeding, FFP was commonly the first line of treatment, with additional platelet transfusion for a history of antiplatelet therapy. Cryoprecipitate was given for sustained bleeding. PCC and rFVIIa were used as last line procoagulant treatment. Optimization of haemostatic conditions involved ensuring calcium levels were above 1 mmol, nasopharyngeal temperature was above 36°C, and pH was above 7.3. The previously described clinical management remained unchanged during the postprotocol period unless specified below.

Clinical management with the bleeding management protocol

A bleeding management protocol was developed to formalize and standardize practice (Fig. 1) [9]. Decisions regarding bleeding risk, diagnostic testing and treatment options were made by the anaesthetist, surgeon and/or intensive care consultant. TXA was optional for patients identified at high risk of bleeding, and the dose was commonly a 15-mg/kg bolus with an infusion of up to 5 mg/kg/h. The protocol supported preoperative impedance platelet aggregometry (Multiplate®; Roche Diagnostics, Rotkreuz, Zug Switzerland) for patients taking antiplatelet medication during the week prior to surgery. If platelet function indicated high risk of bleeding (ADP < 30 AUC; APSI < 30 AUC; TRAP < 50 AUC), blood banks were notified to ensure appropriately matched platelets were on site. Rotational thromboelastometry assay (ROTEM; Tem International GmbH, Munich, Germany) was recommended for high-risk patients when the patient reached 36°C coming off pump. Post protamine, diagnostic POCCTs were performed for clinically significant bleeding. Assessment of bleeding risk and treatment options were based on clinical judgment in conjunction with the protocol.

To support the use of the protocol, a range of educational tools, materials and multiple instruction sessions were conducted. Anaesthetic technicians and a core group of ICU clinical nurses were trained as operators of both POCCT instruments.

Point-of-care coagulation testing

Rotational thromboelastometry assay diagnostics utilize citrated whole blood with four independent measuring channels to allow a combination of appropriate assays [10–14]. The EXTEM assay detects deficiencies of vitamin K-dependent coagulation factors, fibrinogen, platelets and factor XIII. The FIBTEM assay supports the assessment of isolated fibrinogen contribution to clot quality, where any contribution of platelets to clot firmness is inhibited by cytochalasin D. The FIBTEM result, when evaluated against the EXTEM result, provides the ability to diagnose platelet or fibrinogen deficiency. The APTEM assay contains the antifibrinolytic drug aprotinin; comparison of APTEM results with EXTEM can confirm hyperfibrinolysis and the efficacy of antifibrinolytic treatment. The INTEM and HEPTEM assays are intrinsically activated by ellagic acid. As the HEPTEM assay contains heparinase, comparison with the INTEM will reveal the influence of heparin.

Results were available for interpretation within 15 min from the time of drawn sample and streamed live into the operating theatre (OT) or ICU. ROTEM results were interpreted using the amplitude at 10 min (A10) which have been shown to reliably predict maximum clot firmness (MCF) [15–17]. Platelet function was assessed on the Multiplate using hirudin anticoagulated whole blood. Assays included platelet stimulation by arachidonic acid (ASPItest), adenine diphosphate (ADPtest) and thrombin receptor activating peptide 6 (TRAPtest) [18–21]. The area under the curve (AUC) was expressed in arbitrary units/min. Results were available within 15 min.

Acquisition cost of allogeneic blood products

The cost of blood and blood products was based on the Australian National Blood Authority list price in 2012, with 1 unit PRBC, AUD 352; 1 unit FFP, AUD 287; 1 unit pooled platelets AUD 377; 1 unit cryoprecipitate AUD 38; 500 units PCC, AUD 265; and 1 mg rFVIIa, AUD 1197 [22].

Statistical analysis

Data are presented as means [±standard deviation (SD)], medians (25th, 75th percentile), numbers and percentages as appropriate. Statistical calculations were performed in R version 2.15.2 for Windows (R Development Core Team, 2008, Vienna, Austria). The Wilcoxon signed-rank test was used to test the difference in samples (before peri-operative bleeding management compared to after peri-operative bleeding management) for continuous variables. Fisher’s exact test was used to perform analysis of frequencies, and the binomial test was used to determine differences in proportions before peri-operative bleeding management compared to after peri-operative bleeding management. In all of the tests performed, a significance level of α = 0.05 was used. Relative risks (and 95% CI) were also calculated for the binary outcome variables. The relative risks indicates how much more likely (when the value is >1) or how much less likely (when the value is <1) an event is likely to occur in the cohort after the introduction of peri-operative bleeding management.
compared to cohort before the introduction peri-operative bleeding management. Regressions were also performed on the mean LOS in hospital (from operation to discharge) as well as the incidence of infection (deep sternal, superficial chest, and leg wound) to determine what factors affected these outcomes. A generalized linear model (GLM) with a gamma error distribution and log-link function was used to model the LOS in the hospital. Logistic regressions (logit link) were performed to model the incidence of infection.

Results

A total of 1295 patients underwent cardiac surgery during the 15 months before the introduction of the bleeding management protocol and 1265 patients during the 15-month period after. Patient demographics and surgical characteristics are summarized in Table 1.

Percentage patients receiving transfusion

Introduction of the protocol resulted in a significant reduction in three of the four primary end-points (Fig. 2). There were decreases in PRBC transfusion (47 vs. 32%; *P* < 0.0001), FFP (26 vs. 7%; *P* < 0.0001) and platelets (36 vs. 13%; *P* < 0.0001; Fig. 2). In contrast, the incidence of patients receiving cryoprecipitate was not statistically different (9 vs. 8%; *P* = 0.323; Fig. 2).

Mean units per patient

Post implementation of the protocol, there were significant decreases in mean units per patients for PRBCs, ASPI (2.2 vs. 1.34; *P* < 0.0001), FFP (1.27 vs. 0.29; *P* < 0.0001) and platelets (0.76 vs. 0.26; *P* < 0.0001; Fig. 3). There was an increase in the mean units per patient of cryoprecipitate.
Table 1 Demographics of patient cohorts

<table>
<thead>
<tr>
<th></th>
<th>Before bleeding management (n = 1295)</th>
<th>After bleeding management (n = 1265)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>63.1 ± 15.2</td>
<td>63.9 ± 14.2</td>
<td>0.301</td>
</tr>
<tr>
<td>BMI</td>
<td>28.5 ± 5.6</td>
<td>28.5 ± 5.6</td>
<td>0.916</td>
</tr>
<tr>
<td>Male/female [n (%)]</td>
<td>940/355 (72.6/27.4)</td>
<td>906/359 (71.6/28.4)</td>
<td>0.597</td>
</tr>
<tr>
<td>Anaemic/not anaemic [n (%)]</td>
<td>388/907 (30.0/70.0)</td>
<td>352/913 (27.8/72.2)</td>
<td>0.239</td>
</tr>
<tr>
<td>Cardiac reoperation/no cardiac reoperation [n (%)]</td>
<td>157/1138 (12.1/87.9)</td>
<td>127/1134 (10.9/89.0)</td>
<td>0.102</td>
</tr>
<tr>
<td>Elective/emergency surgery [n (%)]</td>
<td>709/586 (54.7/45.3)</td>
<td>689/576 (54.5/45.5)</td>
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<tr>
<td>Operation [n (%)]</td>
<td></td>
<td></td>
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<tr>
<td>CABG</td>
<td>572 (44.2)</td>
<td>567 (44.8)</td>
<td>0.093</td>
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<tr>
<td>Valve(s)</td>
<td>356 (27.5)</td>
<td>344 (27.2)</td>
<td></td>
</tr>
<tr>
<td>CABG + Valve(s)</td>
<td>175 (13.5)</td>
<td>136 (10.8)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>192 (14.8)</td>
<td>218 (17.2)</td>
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<td>Ceased Aspirin [n (%)]</td>
<td>510 (39.4)</td>
<td>522 (41.3)</td>
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<td>&lt;24 h</td>
<td>201 (15.5)</td>
<td>196 (15.5)</td>
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<td>24-48 h</td>
<td>220 (17.0)</td>
<td>201 (15.9)</td>
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<td>48-168 h</td>
<td>175 (13.5)</td>
<td>159 (12.6)</td>
<td></td>
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<tr>
<td>&gt;7 days</td>
<td>189 (14.6)</td>
<td>187 (14.8)</td>
<td></td>
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<tr>
<td>Ceased Clopidogrel [n (%)]</td>
<td>940 (72.6)</td>
<td>924 (73.0)</td>
<td>0.830</td>
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<tr>
<td>&lt;24 h</td>
<td>34 (2.6)</td>
<td>13 (1.0)</td>
<td></td>
</tr>
<tr>
<td>24-48 h</td>
<td>46 (3.6)</td>
<td>35 (2.8)</td>
<td></td>
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<tr>
<td>48-168 h</td>
<td>128 (9.9)</td>
<td>143 (11.3)</td>
<td></td>
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<tr>
<td>&gt;7 days</td>
<td>144 (11.1)</td>
<td>150 (11.9)</td>
<td></td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>90.0 (66.5, 121.5)</td>
<td>84.0 (62.1, 121)</td>
<td>0.006</td>
</tr>
<tr>
<td>Cross-clamp time (min)</td>
<td>64.0 (43.0, 87.5)</td>
<td>60.0 (42.0, 86.0)</td>
<td>0.111</td>
</tr>
<tr>
<td>EF (%)</td>
<td>60.0 (50.0, 64.0)</td>
<td>60.0 (50.0, 65.0)</td>
<td>0.522</td>
</tr>
<tr>
<td>EuroSCORE</td>
<td>5.11 (2.37, 9.78)</td>
<td>4.93 (2.35, 10.38)</td>
<td>0.888</td>
</tr>
<tr>
<td>Pre Op HB</td>
<td>135.0 (123, 147)</td>
<td>136.0 (124, 147)</td>
<td>0.213</td>
</tr>
<tr>
<td>Diabetes/no diabetes [n (%)]</td>
<td>324/971 (25.0/75.0)</td>
<td>297/968 (23.5/76.5)</td>
<td>0.363</td>
</tr>
<tr>
<td>Circulatory arrest/No circulatory arrest [n (%)]</td>
<td>32/1263 (2.5/97.5)</td>
<td>44/1221 (3.5/96.5)</td>
<td>0.134</td>
</tr>
</tbody>
</table>

Comparison of cohorts from the 15 months, before (n = 1295) and after (n = 1265) implementation of peri-operative bleeding management. Data are presented as numbers (%), means ± SD or medians (25th/75th percentile). CPB, cardiopulmonary bypass.

0.68 vs. 0.90; P = 0.465, but this was not statistically significant (Fig. 3).

Intra and post operative transfusion of allogeneic blood products

Breakdown analysis of blood product use post protocol revealed a significant intra-operative decrease in the number of transfused units (PRBCs P < 0.0001, FFP P < 0.0001, platelets P < 0.0001; Fig. 4). The percentage of patients receiving transfusion of PRBCs, (P < 0.0001), FFP (P < 0.0001) and platelets (P < 0.0001) also decreased (Fig. 4). Conversely for cryoprecipitate, the number of units transfused intra-operatively increased (P < 0.0001), as did the percentage patients receiving cryoprecipitate (P = 0.002; Fig. 4 and Table 2). In the postoperative period, the percentage of patients transfused, as well as the total number of units transfused, decreased for all products following the introduction of the protocol (PRBCs; P < 0.0001, FFP; P < 0.0001, platelets; P < 0.0001, cryoprecipitate; P < 0.0001; Fig. 4 and Table 2).

Large volume and massive transfusion

The incidence of large volume transfusion (defined as ≥5 units of PRBCs) was 15.9%, and this decreased to 8.5% (P < 0.0001) post introduction of the bleeding management protocol. There was also a reduction in the incidence of massive transfusion (defined as ≥10 units of PRBCs) from 4.6% to 2.6% (P = 0.007). Intra-operatively, with the introduction of the bleeding management protocol, there was a statistically significant reduction in large volume transfusion (4.5% vs. 2.9%; P = 0.035), but

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reduction in massive transfusion (0.8% vs. 0.6%; $P = 0.647$) did not reach significance.

Chest tube drainage

Mean chest tube blood loss at 2, 4 and 12 hours was lower during protocol use by 41% (95%; 38–45%; $P < 0.001$), 35% (95%; 32–39%; $P < 0.001$) and 27% (95%; 23–32%; $P < 0.001$), respectively (Fig. 5).

Bleeding management outcomes excluding patients who received POCCT

Analyses were performed to determine the incidence of allogeneic and fractionated blood products in patients where neither ROTEM, nor Multiplate were used, before and after the implementation of the bleeding management protocol. All allogeneic blood product transfusion incidence was significantly reduced (PRBCs: 43.3% vs. 25%; $P < 0.0001$, FFP: 26.9% vs. 4.5%; $P < 0.0001$, platelets: 36% vs. 5.5%; $P < 0.0001$, cryoprecipitate: 9.1% vs. 3%; $P < 0.0001$, PCC: 4.3% vs. 1.8%; $P = 0.001$, rFVIIa: 1.9% vs. 0.5%; $P = 0.004$). There were also statistically significant decreases in the use of PCC (4.3 vs. 1.8; $P = 0.001$) and rFVIIa (1.9 vs. 0.5; $P = 0.004$).

Protocol interventions

Following the implementation of the protocol, 274 (21.7%) and 224 (17.7%) patients were assessed by ROTEM and Multiplate, respectively. The proportion of patients who received TXA increased (13.7% vs. 68.2%; $P < 0.0001$; Table 2). There were insignificant changes to the percentage of patients receiving rFVIIa (1.9% vs. 1.5%; $P = 0.540$) and PCC (4.3% vs. 4.5%; $P = 0.848$; Table 2).

Patient outcomes

After the introduction of the protocol, there was significant reductions in re-exploration for bleeding (5.6% vs. 3.4%; $P = 0.01$), incidence of superficial chest wound (3.3% vs. 1.4%; $P = 0.002$) and leg wound infection (4.6% vs. 2.0%; $P < 0.0001$; Table 2). There was no significant difference in the incidence of deep sternal wound infection, postoperative pneumonia, atrial fibrillation,
permanent or transient neurological complications, post-operative pulmonary embolus or new renal replacement therapy (Table 2). Mean LOS from operation to hospital discharge was 12% lower (95%; 9–16%; \( P < 0.0001 \)) after the introduction of protocol, but in-hospital mortality remained unchanged (2.1 vs. 1.7%; \( P = 0.566 \)).

**Discussion**

Introduction of a bleeding management protocol in our cardiac surgery unit has led to significant reductions in the incidence of patients receiving transfusions, as well as a substantial decrease in the total number of blood products transfused. It has also resulted in significant reductions in unplanned re-exploration surgery, superficial chest and leg wound infections and LOS from operation date to discharge.

The past decade has seen a move from ‘product centred transfusion practice’ to ‘PBM’[23–25]. This is a result of accumulating evidence that transfusion of allogeneic blood products is not risk free and has been reinforced by an increase in societal guidelines supporting more appropriate management of the patients’ own blood [26–29] (Fig. 1). The protocol is a sequential decision support algorithm intended to assist balancing competing risks when making treatment decisions at multiple time-points: (i) pre surgery, (ii) when 36°C was reached on pump, (iii) post reversal of heparin with protamine and (iv) in the event of ongoing or delayed bleeding.

The protocol includes the identification of the patient at high risk of bleeding for early intervention with TXA. As a result, TXA use increased significantly (13.9% vs. 68.8%; \( P < 0.0001 \)) (Table 2) and was associated with declines in postoperative chest tube blood loss at 2 h by 41% (95%; 38–45%), at 4 h by 35% (95%; 32–39%) and at 12 h by 27% (95%; 23–32%; Fig. 5). This is consistent with decreases in the volume of postoperative blood loss in cardiac surgery associated with TXA as reported by other observational studies and randomized controlled trials [32–34].

The protocol promoted scheduled POCCTs at multiple time-points to support early identification of haemostatic obstacles to implementing a change in practice, economic issues or a combination of these factors. In our centre, prior to the implementation of our bleeding management protocol, decisions regarding treatment of bleeding varied widely amongst clinicians.

To facilitate the move to a patient-centred approach, we introduced a bleeding management protocol incorporating point-of-care coagulation testing based on recommendations from multiple published guidelines [26–29] (Fig. 1). The protocol is a sequential decision support algorithm intended to assist balancing competing risks when making treatment decisions at multiple time-points: (i) pre surgery, (ii) when 36°C was reached on pump, (iii) post reversal of heparin with protamine and (iv) in the event of ongoing or delayed bleeding.

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The protocol promoted scheduled POCCTs at multiple time-points to support early identification of haemostatic
derangements. The short result turnaround time of POCCT was a major advantage allowing clinicians diagnose and treat bleeding promptly, and also track treatment response [12, 35, 36]. To facilitate this approach, the POCCT instruments were located in a laboratory adjacent to the OT and ICU. Hence, the rapid turnaround time was achieved by (i) not having to transport samples to the main laboratory, (ii) not centrifuging samples to separate...

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plasma for testing and (iii) live streaming of results into OT or ICU. Furthermore, live streaming of results into the appropriate OT enabled joint, timely diagnosis and management by the surgeons and anaesthetists.

The inclusion of POCCTs in the protocol provided an objective, evidenced-based approach to bleeding management. Despite decreases in the number of units and percentage of patients transfused, analysis demonstrated an increase in the percentage of patients receiving cryoprecipitate intra-operatively (2.7% vs. 5.1%; \( P = 0.002 \)), as well as the number of units transfused (\( P < 0.0001 \)). In this study, cryoprecipitate was used to supplement fibrinogen levels, as fibrinogen concentrate was not available in Australia for acquired hypofibrinogenemia. During major surgical blood loss, fibrinogen is the first coagulation factor to reduce to a critical level [37]. In addition, the plasma concentration of fibrinogen is decreased immediately after CPB [38, 39]. Literature refers to the critical role of fibrinogen in clot development and the importance of fibrinogen supplementation in situations with excessive or protracted bleeding [40–43]. We also noted a decrease in the percentage of patients and number of units of cryoprecipitate transfused postoperatively. We propose that this reflects the achievement of effective haemostasis intra-operatively using POCCT results to provide prompt, targeted treatment. This is supported by the decrease in the return to OT for investigation of excessive bleeding (5.6% vs. 3.4%; \( P = 0.01 \)) which aligns with studies published by Gorlinger et al. and Weber et al.[12, 35]. In addition, we noted significant reductions in the incidence of large volume transfusion (15.9% to 8.5%; \( P < 0.0001 \)), as well as massive transfusion (4.6% to 2.6%; \( P = 0.007 \)). These reductions may be important as Karkouti et al. and Ranucci et al. reported large volume transfusion as an independent risk factor for morbidity and mortality in cardiac surgery [2, 8]. Following the implementation of the protocol, the relative risk of mortality was 0.81. The absence of any significant reduction in the mortality rate can be expected because of the low baseline mortality rate of 2.1% and the cohort size.

The development of infection in cardiac surgery patients has been associated with smoking, transfusion of PRBCs, CPB duration, increased BMI and diabetes mellitus [4, 7, 44]. Both cohorts in this study had comparable BMI and diabetes mellitus (Table 1). Postbleeding management reductions were seen in CPB time (90 min vs. 84 min; \( P < 0.006 \)), as well the incidence of PRBCs (47.3% to 32.4%; \( P < 0.0001 \)). We observed a drop in the percentage of patients developing deep sternal wound infection, but this was not statistically significant (0.6% vs. 0.3%; \( P = 0.387 \)). However, significant reductions were observed with superficial chest wound infections (3.3% vs. 1.4%; \( P = 0.002 \)), as well as leg wound infections (4.6% vs. 2.0%; \( P < 0.0001 \)). Our analysis revealed that for every 1 unit increase in the total number of units of PRBCs transfused per patient, the calculated odds of having a superficial chest wound increased by 7% (95%;1–14%), and the odds of having a leg wound infection by increased by 6% (95%;2–11%). Since both a reduction in CPB time and the mean units of PRBCs transfused per patient were observed after the treatment algorithm was implemented, and as both are associated with infection, it is unclear as

![Fig. 5 Box plot of chest tube blood loss at (a) 2 h, (b) 4 h and (c) 12 h of surgery, before (n = 1295) and after (n = 1265) implementation of a bleeding management protocol.](image-url)
to whether one or a combination of these factors had an impact on the decreased incidence of superficial chest and leg wound infection. We demonstrated significant decreases in FFP (26-9% vs. 7.3%; \( P < 0.0001 \)) and platelet (36-1% vs. 13.5%; \( P < 0.0001 \)) transfusion. This may also be important as there is accumulating evidence indicating inappropriate plasma and platelet transfusion may have a negative impact on patient outcomes including infection [45–50].

In 2011 in the State of Queensland, 37% of the cost of blood products was devolved to local hospitals, and although this was not the only driver for the development of the bleeding management protocol, the resulting economic benefits have been significant. Despite a POCCT consumable cost of $44,411, the use of this new protocol has resulted in a $1,029,118 decrease in the acquisition cost of blood products. This is in line with other studies using similar bleeding management protocols that incorporate POCCT as well as a recently published Health Technology Assessment [12, 35, 36, 51]. In addition, there were indirect cost savings associated with the reduction in re-exploration for bleeding (Table 2) and a reduction in LOS from operation to hospital discharge that was 12% lower (95%; 9–16%; \( P < 0.0001 \)). This is consistent with other studies demonstrating an association between a reduction in LOS and reduced blood product transfusion and postoperative bleeding [52, 53].

This quality initiative was department wide and included significant education regarding bleeding management and PBM strategies from relevant societal guidelines [26–29]. The effect of learning and motivation to achieve practice improvement is a known confounder when making an analysis that involves human contribution; consequently, the ‘Hawthorne’ effect cannot be excluded [54]. To determine the effect of learning/motivation to embrace bleeding management and achieve practice improvement without the direct influence of POCCT, we investigated patients in whom neither ROTEM, nor Multiplate was used before and after the implementation of the bleeding management protocol. Independent of POCCT, post introduction of bleeding management, there were statistically significant reductions in transfusion of all allogeneic and fractionated blood products (Table 3). This implies large reductions in incidence of these interventions may have been achieved due to a learning effect. A formalized and ongoing education programme surrounding bleeding management, easy access to PBM support, more readily identifying patients at high risk of bleeding, including those who would benefit from TXA, may, at least in part, be responsible for fewer transfusions. It is also proposed that availability of rapid results from POCCT may have provided a level of reassurance, allowing clinicians to wait to treat patients ‘when’ they bleed not ‘in case they do’, and therefore a shift away from prophylactic to therapeutic transfusion.

This study has limitations associated with a retrospective review including factors that were not collected or analysed during the study period. Data on cell salvage were not collected. We excluded patients undergoing heart and/or lung transplantation, or surgery with mechanical circulatory support due to their non routine nature. This initiative was aimed at improving the overall

<table>
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<th>Table 3 Binary end-points of patient cohorts before and after bleeding management excluding POCCT</th>
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<tr>
<td>Before bleeding management (n = 1295)</td>
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<td>-----------------------------------------------</td>
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<tr>
<td>Incidence PRBC transfusion [n (%)]</td>
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<tr>
<td>Incidence of FFP transfusion [n (%)]</td>
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<td>Incidence of platelet transfusion [n (%)]</td>
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<td>Incidence of cryoprecipitate transfusion [n (%)]</td>
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<td>TXA [n (%)]</td>
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<td>PCC [n (%)]</td>
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<td>rFVIIa [n (%)]</td>
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Binary end-points comparing before (n = 1295) and after (n = 973) the introduction of bleeding management excluding patients receiving POCCT. Data are presented as relative risks (and 95% CI) indicating how much more likely (when the value is >1) or how much less likely (when the value is <1) an event is likely to occur in the cohort after the introduction of peri-operative bleeding management (excluding patients received POCCT) compared to cohort before the introduction peri-operative bleeding management.

FFP, fresh frozen plasma; PCC, prothrombin complex concentrate; POCCT, protocol incorporated point-of-care coagulation testing; PRBCs, packed red blood cells; TXA, tranexamic acid.
management of bleeding events and was not designed to establish causation for specific interventions and outcomes. Many possible interacting risks can contribute to the development of bleeding events, and equally management may require many treatment alternatives [55].

Conclusion

This tailored bleeding management protocol guided by POCCT facilitated early identification of patients at high risk of bleeding and rapid identification of the cause of bleeding to support appropriate treatment. The observed improvements in patient outcomes, decreases in blood product use and cost, indicate improved haemostasis management. This initiative has also led to a department wide change from a culture of ‘transfusion practice’ to one of ‘PBM’. As a result of effectiveness of this protocol in the cardiac surgery unit, efforts are now in progress to develop tailored bleeding management protocols for other surgical departments and general ICU.

Acknowledgements

We wish to acknowledgement and thank the surgeons, the anaesthetists, anaesthetic technicians, ICU specialists, ICU nurses, blood bank scientists and the TPCH Patient Blood Management Steering Committee for their support to implement the quality initiative described in this manuscript. A competitive grant was received though the Queensland Government ‘Queensland Health Innovation Funding’ for one annual salary for the project manager to develop, co-ordinate, implement and evaluate the bleeding management protocol described in this manuscript. The Prince Charles Hospital (TPCH) and Queensland Government Health Department ‘Clinical Access and Redesign Unit’ supported funding for POCCT consumables.

References


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