An audit of red cell and blood product use after the institution of thromboelastometry in a cardiac intensive care unit

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SUMMARY. Cardiac surgery is estimated to use 20% of the UK blood supply. However, there has been much interest recently in decreasing red cell and blood product use not only to ease strain on blood stocks or avoid potential transmission of infection but also to decrease post-operative transfusion-related complications. Coagulopathies are not uncommon in cardiac surgical patients, but the time lapse for reporting conventional laboratory results has been highlighted as an obstacle to the appropriate use of blood products. Accordingly, much interest has arisen in rapid near-patient testing of coagulation and, in January 2002, a thromboelastometer (ROTEM®, Pentapharm, Germany) was purchased for our unit.

This audit sought to assess its impact by retrospective analysis of 990 sequential patients' demographic data and transfusion details covering 6 months prior to its introduction and 6 months after.

In the 6 months prior to its introduction, red cells were used in 60% of patients and fresh frozen plasma (FFP) and platelets used in 17 and 16% of patients, respectively. In the following 6 months, red cell use had fallen to 53% and FFP and platelets to 12 and 11%, respectively ($P < 0.05$).

Introduction of thromboelastometry has significantly decreased our use of red cells and blood products.

Key words: cardiac surgery, coagulopathy, post-operative haemorrhage, thromboelastometry.
cerebrovascular accident and post-operative infection (Spiess, 2001; Spiess et al., 2004). There are also anecdotal concerns over the effect of platelet transfusion on graft patency.

Worldwide, the largest avoidable risk to patients from transfusion is probably due to the administration of fresh frozen plasma (FFP) for inappropriate or unproven clinical indications (McClelland, 2001). Moreover, the administration of a standard dose of FFP in order to resolve factor deficiencies in critically ill patients is questioned (Casbard et al., 2004). Accordingly, many cardiac units have sought to decrease their red cell, FFP and platelet use and base their transfusion management on the actual requirements as diagnosed by specific coagulation tests. However, traditional tests of coagulation after bypass [prothrombin time, partial thromboplastin time (PTT), international normalized ratio (INR) and platelet count (PC)] have several problems, notably their inability to test platelet function and also the delay in receiving results from the laboratory. This has led to empirical rather than evidence-based use of blood products in the past. Thromboelastometry is a rapid near-patient method of analysing whole blood coagulation which assesses the interaction of platelets and the plasma coagulation system and their ability to form a functional clot from the formation of the first fibrin fibres and activated platelets to the formation of a three-dimensional whole blood clot until the eventual dissolution of the clot. This interaction, the process of clot polymerization and fibrinolysis are not assessed using standard laboratory tests. The principle was demonstrated by Hartert (1948) but has more recently been updated (Calatzis et al., 1996). By combining different activators and inhibitors, the localization of haemostatic disorders is possible within a short time. The aim of our audit was to assess whether the introduction of thromboelastometry to our unit decreased red cell, FFP and platelet use.

MATERIALS AND METHODS

A retrospective analysis of data from 990 patients was performed which covered a period 6 months prior to the introduction of ROTEM® thromboelastometry (Pentapharm, Germany) and 6 months after its introduction. During this study period, only trained anaesthetic personnel performed the ROTEM® test(s) providing a daytime service for theatre and intensive care patients.

The ROTEM® thromboelastometry analyser provides four independent measurement channels, each providing a Thromboelastometry (TEM) trace – a typical TEM trace is shown in Fig. 1. Its function has been described in detail elsewhere (Innerhofer et al., 2004; Luddington, 2005). In short, the original thromboelastographic procedure has been modified by allowing a computerized analysis of the trace and by adding different coagulation-inducing agents and/or platelet-inhibiting agents to allow the detection of specific coagulation defects such as hypofibrinogenaemia, factor deficiency, thrombocytopenia, the presence of heparin and hyperfibrinolysis. INTEM is a baseline test using an ellagic acid contact activator for analysing the general coagulatory status of the patient. The cloting time (CT) and clot formation time (CFT) give information about the activation
and dynamics of clot formation, allowing for the analysis of factor deficiencies or detection of the presence of anticoagulants. With a simultaneously performed HEPTEM test which adds heparinase, a heparin or residual heparin effect can be demonstrated when compared with the INTEM test, and the coagulation can be evaluated without the heparin effect (if it is present in the patient sample). The maximum clot firmness (MCF) gives information about clot strength and stability which is largely dependent on fibrinogen (FG) and platelets. In the FIBTEM test, cytochalasin D is used as a platelet inhibitor allowing the analysis of FG concentration and function in clot polymerization alone. In Fig. 2, two typical sets of traces from a patient with normal haemostasis and a patient with deficient haemostasis are shown.

Although a test is relatively cheap to run (approximately £4 per test) and cheaper to perform than a routine coagulation test, it was decided that it would be too costly to perform on every patient, and a decision was made to test only those patients who were bleeding excessively post-operatively.

Excess bleeding is difficult to define, and there are many nomograms in use throughout the UK. In our unit, excess bleeding is defined as more than 300 mL in the first post-operative hour, more than 250 mL in the second hour and more than 150 mL in any subsequent hour, as studies have shown that, in the absence of a coagulopathy, bleeding at these levels is surgical in origin (Michelson et al., 1980). In addition, a test was performed if specifically requested by the operating surgeon or anaesthetist if it was felt that the patient was bleeding diffusely.

Institution of thromboelastometry

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after protamine administration in the operating room.

There is a transfusion protocol (first introduced in our unit in 1998 and based on surgical consensus using the evidence available at that time) covering the first 24 h post-operatively; however, ultimately, the transfusion strategy is specific to each individual patient and is dictated by their clinical condition.

Few patients require transfusion of red cells preoperatively. In theatre, blood samples are taken pre- and post-cardiopulmonary bypass to measure arterial blood gases, biochemistry and haematocrits, and haematocrit levels are measured continuously during bypass. The minimum acceptable haematocrit on bypass is deemed to be 16%; all patients will be transfused if their haematocrit drops below this although some patients may be transfused red cells where the haematocrit is between 16 and 18% depending on that patient’s volume status. Immediately post-operatively, the patient is relatively haemodiluted from the pump prime given in theatre, so the haematocrit is ignored for the first 2 h assuming cardiovascular stability if it is greater than 18%. This should allow the patient’s own diuresis to haemoconcentrate the patient to a more satisfactory haematocrit. If the haematocrit is lower than 18% in this early post-operative phase, red cells will be transfused. Thereafter, patients are transfused with red cells when the haematocrit is less than 21%. Occasionally, red cells are transfused despite a haematocrit level of greater than 21% where the patient’s clinical condition dictates or as per surgeons’ instructions. After the first 24-h post-surgery Hb levels are checked daily. It is our aim that patients are discharged from hospital with Hb of not less than 12 g dL\(^{-1}\).

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Prior to the introduction of ROTEM\(^\text{®}\), FFP and platelets were transfused according to the results of laboratory coagulation screens performed post-operatively or by surgical request and only if the patient was bleeding excessively. Where the INR were measured at greater than 1.5, four units of FFP was given. Where PCs were less than 100 or less than one half of the pre-operative value, a unit of pooled platelets was administered. Occasionally, where surgery had been technically difficult, FFP and platelets were transfused in preference to re-exploration if bleeding was felt to be excessive but was not causing significant cardiovascular instability. After the introduction of ROTEM\(^\text{®}\), it was our aim that patients were managed based on the results of the ROTEM\(^\text{®}\). The INTEM test was performed as a basic test for the evaluation of coagulation. Where heparin excess was demonstrated (by a normalized CT value in the HEPTEM compared with a prolonged CT in the INTEM test), a further 50 mg protamine was administered; where factor deficiency or hypofibrinogenemia was demonstrated by prolonged CT values (in both INTEM and HEPTEM) or reduced clot firmness in the FIBTEM test, respectively, four units of FFP were administered; where platelet abnormality was suggested (reduced clot firmness in INTEM/HEPTEM with a normal clot firmness in FIBTEM), a unit of pooled platelets was administered. No platelet augmenting therapies such as desmopressin acetate (DDAVP) are used in our unit. Figure 3 is a flow chart of test use and their interpretation.

For this retrospective audit, data from our unit’s database was analysed. This database comprises information on patient demographics and characteristics including the European System for Cardiac Operative Evaluation (EuroSCORE) risk index, pre-operative coagulation laboratory results, admission Hb concentration, details of the surgery performed, time in the operating room including cross clamp and bypass times, CRCs, FFP and platelet administration, discharge Hb concentration and patient outcome data.

These data were analysed comparing the two time periods before (July 2001–December 2001) and after institution of thromboelastometry (February 2002–July 2002). The two 6-month periods were chosen in order to have matching sample sizes. Although there are comprehensive data for 18 months after its introduction, it was felt that this extended period could bias the results because of unequal sample size. There were no changes in senior- or middle-grade staff or to the transfusion protocol over the 12-month period. Although the most junior surgical staff change every 4 months, they have no influence on transfusion practice. This 4-month rotation continued throughout the 12-month study period, both before and after starting the ROTEM\(^\text{®}\) analyses.

Continuous data such as age and Hb concentration were analysed for the two time periods before and after institution of thromboelastometry by t-test (after viewing histograms for normal distribution and confirming homogeneity of variance by Levene Median test) or by Mann–Whitney U-test [EuroSCORE, length of stay in intensive care unit (ITU) or hospital, numbers of CRCs, FFP or platelets transfused] as appropriate. For the analysis of absolute frequencies (sex, surgery performed, re-explorations, numbers of patients transfused with red cells, FFP and platelets), the \(\chi^2\) test was performed. In all tests, a \(P\)-value of less than 0.05 was
considered statistically significant. The statistical calculations were performed with Statistica '99 Edition (Statsoft, Tulsa, OK, USA).

RESULTS
In the 12 months described in this audit, 488 patients were followed during the 6 months before the implementation of ROTEM® and 502 patients in the first 6 months thereafter. Patient characteristics, pre-operative laboratory results and surgical variables are summarized in Table 1. Demographics were similar before and after implementation of ROTEM® (341 males and 147 females before and 359 males and 142 females after ROTEM® was established; mean age 64.4 years before and after, ns). Also the mean pre-operative Hb value and the coagulation laboratory parameters (PC, FG and INR) did not

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differ between groups. The activated PTT was slightly shorter in the group before the introduction of ROTEM® (31 vs. 32 s, \(P = 0.014\)), slight differences were also seen in the EuroSCORE (medians 4 and 3 before and after the introduction of ROTEM®, \(P = 0.026\)). As a more relevant factor for post-operative bleeding, the frequencies of the types of procedures performed differed slightly, with more coronary artery bypass grafting (76 vs. 68%, \(P = 0.008\)) and less combined valve and bypass procedures (6 vs. 11%, \(P = 0.007\)) before the introduction of ROTEM®. Time in theatre also differed slightly between groups before and after ROTEM® (173.6 vs. 161.1 min, \(P < 0.001\)) as did bypass times (73.8 vs. 68.6 min, \(P = 0.015\)) and cross clamp times (45.9 vs. 45.9 min, ns).

Table 2. Transfusion requirements before and after the introduction of ROTEM®

<table>
<thead>
<tr>
<th></th>
<th>Before introduction of ROTEM®</th>
<th>After introduction of ROTEM®</th>
<th>(P)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients transfused with CRCs (n)</td>
<td>294/488 (60%)</td>
<td>270/502 (53%)</td>
<td>0.040</td>
</tr>
<tr>
<td>CRCs transfused (units)</td>
<td>1094, 2 (3)</td>
<td>931, 1 (2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Patients transfused with FFP (n)</td>
<td>81/488 (17%)</td>
<td>60/502 (12%)</td>
<td>0.037</td>
</tr>
<tr>
<td>FFP transfused (units)</td>
<td>343, 0 (0)</td>
<td>271, 0 (0)</td>
<td>0.036</td>
</tr>
<tr>
<td>Patients transfused with platelets (n)</td>
<td>77/488 (16%)</td>
<td>56/502 (11%)</td>
<td>0.033</td>
</tr>
<tr>
<td>Platelets transfused (units)</td>
<td>96, 0 (0)</td>
<td>75, 0 (0)</td>
<td>0.032</td>
</tr>
</tbody>
</table>

CRC, concentrated red cell; FFP, fresh frozen plasma.
Frequency data (patients transfused with CRCs, FFP and platelets) are presented as \(n\) (%); data which are continuous but not normally distributed (units of CRCs, FFP and platelets transfused) are presented as absolute number, median (interquartile range).

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platelet use was reduced (96 units/488 patients vs. 75 units/502 patients, \( P = 0.032 \)).

In both groups, the outcome data were similar with no significant differences in discharge Hb, length of stay in ITU or hospital or in re-exploration rates (Table 3).

### DISCUSSION

This audit confirms the clinical impression that the percentage of patients receiving red cells, FFP and platelets fell significantly in our unit after the introduction of ROTEM\(^\circ\): subsequent analyses have demonstrated that this decrease has been maintained since. It is important to note that ROTEM\(^\circ\) analysis was only performed post-operatively in almost all patients and thus did not influence intra-operative management. Therefore, the changes observed seem solely due to changes in post-operative transfusion requirements. It is also important to note that admission and discharge Hb were not significantly different in the two time periods, because one possible explanation of the decreased use of red cells would be an acceptance of a lower discharge Hb; this is clearly not the case. Discharge Hb values are no different before and after the introduction of ROTEM\(^\circ\). It is our belief that ROTEM\(^\circ\) allows a more rapid diagnosis of the haemostatic defect. Indeed, results are often available from the ROTEM\(^\circ\) before the hospital porter has uplifted the coagulation sample destined for the laboratory. Earlier, more appropriate intervention is thus possible, minimizing post-operative blood loss and subsequent red cell transfusion. This would also explain the drop in the percentage of patients receiving FFP and platelets – a response to a more accurate diagnosis of the coagulation defect and a marked decrease in their speculative use. It has already been noted in a previous audit that, prior to the introduction of the ROTEM\(^\circ\), only 30% of patients receiving FFP or platelets had a confirmed coagulatory defect demonstrated by laboratory results (Anderson et al., 2003). If no haemostatic defect is identified, earlier surgical re-exploration is possible and blood loss may, again, be minimized.

When the ROTEM\(^\circ\) was introduced in our unit, it was initially a daytime, weekday service. However, accepting this limitation in its use may make the results even more impressive had they been extrapolated to our entire surgical population.

There are, of course, limitations in any retrospective audit of this type. Unfortunately, data on pre-operative medication are incomplete prior to the introduction of the ROTEM\(^\circ\) and could not be analysed. However, with the general trend towards the increased use of antiplatelet medication pre-operatively, it seems likely that the trend with regard to post-operative bleeding should, if anything, have increased blood loss post-operatively and therefore potentially increased our use of red cell and blood products. This has not been the case in our audit; red cell and product use fell. There was also a significant difference noted in the EuroSCORE risk indices for surgery. The EuroSCORE is a cumulative score which allocates points associated with certain risk factors such as complicated surgery, poor ventricular function and concurrent disease. The higher the score, the higher the predicted risk of mortality. There was a slightly higher risk score in patients in the 6-month period after the introduction of ROTEM\(^\circ\). However, both scores (median 3 before and 4 after introduction) are rated as medium surgical risk, and perhaps the statistics demonstrate a clinically (if not statistically) insignificant difference. Given that a higher EuroSCORE may reflect more complicated surgery or surgery on more systemically ill patients, the likely result with regard to blood loss would be an increase; this was not the case. The types of surgery performed during the two time periods analysed also demonstrated a small difference; there was less bypass grafting performed in the 6 months after the introduction of thromboelastometry and an increase in combined valve and graft surgery. With a trend towards higher risk surgery in the second

### Table 3. Outcome data

<table>
<thead>
<tr>
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<th>Before introduction of ROTEM(^\circ)</th>
<th>After introduction of ROTEM(^\circ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge Hb (g dL(^{-1}))</td>
<td>10 (1.2)</td>
<td>9.9 (1.2)</td>
</tr>
<tr>
<td>Length of stay in ITU (h)</td>
<td>23 (4)</td>
<td>24 (5)</td>
</tr>
<tr>
<td>Length of stay in hospital (days)</td>
<td>7 (2)</td>
<td>7 (3)</td>
</tr>
<tr>
<td>Re-exploration n (%)</td>
<td>19 (4%)</td>
<td>16 (3%)</td>
</tr>
</tbody>
</table>

Hb, haemoglobin; ITU, intensive care unit.

Continuous and normally distributed data (discharge Hb) are presented as mean (SD); data which are continuous but not normally distributed (length of stay in ITU and length of stay in hospital) are presented as median (interquartile range). Frequency data (re-exploration) are presented as n (%). \( P \)-values > 0.05 are not shown.
6-month period, blood loss and use of red cells and products should, if anything, have been greater. This did not occur. On the other hand, a slightly longer time in theatre (173.6 vs. 161.1 min, \(P < 0.001\)) with slightly longer cross clamp and bypass times was observed in the group of patients before the introduction of ROTEM®; that could account for a trend towards increased bleeding and transfusion requirements in this group. Nevertheless, with mean bypass times of just over 1 h in both groups, we would anticipate no clinically significant difference in bleeding between the two groups. Prolonged bypass times are associated with the development of coagulopathy and platelet dysfunction but, in particular, bypass times over 2 h (Spiess & Chang, 1993). Our bypass times rarely reached 2 h in either group (mean 73 vs. 68 min).

It is also true that there has been a concerted drive to decrease red cell and blood product use in recent years. It could be possible that our audit period merely reflected this trend. However, a previous audit performed over a 3-month period 1 year prior to the start of this audit demonstrated red cell use to be 60% and FFP and platelet use 15% which is almost identical to the pre-ROTEM® figures. This indicates that the decrease we observed in red cell and FFP/platelet use was not solely due to an interest in avoiding the use of blood or a reflection of an ongoing downward trend. Continuing audit in our unit suggests that there has been a steady state attained after the introduction of the ROTEM®, and there has been no continued downward trend. Extended data analysis of 1944 patients after the introduction of ROTEM® demonstrates red cell use in 49% of our patients and FFP and platelet use in 9.1 and 8.5% of our patient population, respectively.

In summary, there were a few variables which could have biased our analysis, but these factors tended to favour the group prior to the introduction of the ROTEM®. We felt that a multivariate analysis would not have overcome the limitations of a retrospective audit. However, a prospective trial is planned.

Other cardiac units have demonstrated improved red cell and/or blood product use after the institution of transfusion protocols or algorithms incorporating TEG alone, or a combination of various Point of Care coagulation tests (Shore-Lesserson et al., 1999; Nuttall et al., 2001; Royston & von Kier, 2001; Avidan et al., 2004). There is no doubt that this improved practice. However, we should emphasize that, in our study, there were no changes in protocols or personnel during the study period. The transfusion protocol we use has been in use in our unit since 1998, and there were no changes during this study period. Where red cells have been administered, the patient’s results are observed to ensure that appropriate transfusion triggers were used as per unit protocol. This ‘quality control’ is conducted several times per week, and there was no additional training or emphasis regarding the protocol in either of the two study periods. The only difference was the introduction of the ROTEM® analyser.

An important aspect of the audit is the cost implication of introducing a new test. An INTEM test costs £4. This is less expensive than routine laboratory tests of coagulation in our hospital and gives additional information on specific coagulatory defects and offers more specific management options. However, financial costs should not outweigh the cost of inappropriate transfusion to the recipient with regard to the risk of transfusion. These include well-known acute complications; however, in a situation where the majority of patients are expected to survive 10 years or longer as in cardiac surgery, this exposes patients to the risks of long-term complications. In the UK, vCJD is a particular concern in this regard, and it should be noted that transfusion-associated vCJD has been documented and vCJD has now been detected out with the UK. With changes to the donor pool, potential blood shortages and the increasing cost of blood products, it is increasingly important to optimize blood use. It is also not impossible that a test may be developed for vCJD and this would further pressure existing supplies. Any improvement in transfusion practice is to be welcomed. We have demonstrated that ROTEM® use has the potential to reduce overall blood product use in cardiac surgery patients.

ACKNOWLEDGMENTS

Many thanks are due to the Scottish National Blood Transfusion Service for funding the purchase of the ROTEM®.

REFERENCES


European System for Cardiac Operative Risk Evaluation (EuroSCORE) risk index. [Available at http://www.euroscore.org].


