Platelet—monocyte pro-coagulant interactions in on-pump coronary surgery

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Abstract

Objective: Platelets and monocytes possess haemostatic properties, but the clinical effect of platelet—monocyte interactions on haemostasis following coronary surgery is not known. The study characterises the platelet and monocyte responses in cardiac surgery and its impact on haemostasis.

Methods: In 1342 patients, changes in white blood cell counts (WBC), monocyte counts and platelet counts were measured. PMC formation was analysed by flow-cytometry using monoclonal antibodies against pan-leucocyte marker CD45, monocyte marker CD14 and platelet marker CD42. TF expression was determined using monoclonal antibodies against CD45, CD14 and human-TF. Continuous variables were expressed as mean ± SD. Changes in monocyte and platelet counts over time were considered as repeated measures data, and analysed using Generalised Estimating Equations (GEE). Multivariate regression analysis was used to evaluate the effect of several factors on blood loss.

Results: A monocytosis occurs with on-pump coronary surgery, but is less pronounced than with off-pump surgery. No difference was seen in patients having redo-surgery or more complex cardiac surgery. Factors associated with monocytosis on multivariate analysis were higher body mass index (p = 0.02), diabetes (p = 0.035) and smoking (p = 0.01). Older patients manifested a lower response (p < 0.001). Cross-clamp fibrillation was associated with a lower (p = 0.048) monocytic response than was cardioplegia. PMC formation dropped following administration of heparin, peaked at 5 min of CPB, and declined by 2 h of CPB (p = 0.04). A return towards preoperative levels was found during postoperative days 1—5. No significant change in monocyte TF expression occurred. The mean postoperative blood loss was 581.2 ± 292.8 ml, and inversely related to increasing preoperative platelet counts (p < 0.001), and to higher monocyte % counts (p = 0.012). Patients, who were female (p < 0.001), had higher body mass indices (p < 0.001), and higher core body temperatures during surgery (p = 0.013), as well as patients having perioperative aprotinin (p < 0.001) related to less blood loss.

Conclusions: A higher postoperative platelet count as well as monocyte% significantly and independently decreases postoperative blood loss following cardiac surgery.

Keywords: Platelets; Monocyte; Cardiopulmonary bypass; Coronary artery bypass surgery

1. Introduction

Circulating platelets and monocytes possess direct haemostatic properties that may become activated during coronary surgery. Studies suggest that platelet-derived tissue factor (TF), associated with platelet—monocyte conjugate (PMC) formation, or transcriptionally derived monocyte TF is responsible for potentiating coagulation [1,2].

Interestingly, only 10—20% of the total extractable tissue factor activity is expressed on the surface of intact monocytes. Thus, most TF is latent or encrypted in the cell membrane. Platelets, through platelet-derived microparticles are a source of tissue factor to circulating monocytes, resulting in rapid pro-coagulant responses. These involve the formation of thrombin via a TF/factor VII-dependent and factor XII-independent pathway [3].

In contrast, a delayed, transcriptionally mediated monocyte TF expression is thought to involve not only platelet interaction but also stimulation by circulating cytokines generated perioperatively. When co-incubated, leucocytes and platelets generate more TF activity than either cell type alone. Platelets play a pivotal role in decrypting TF activity of monocytes, generating a hybrid TF terrain, which both triggers and favours thrombogenesis [4].

Despite the awareness of these platelet—monocyte coagulant interactions, it is not known whether these monocyctic and platelet count changes are related to the complexity of procedure performed and the use of...
cardiopulmonary bypass, and also if they have a clinically significant impact on haemostasis following conventional on-pump coronary surgery. The specific objectives of this study were to

1. ascertain if the complexity of the procedure affected the monocyctic and platelet count changes?
2. ascertain if there was a difference between on- and off-pump coronary artery bypass grafting in terms of monocyctic and platelet count changes?
3. characterise elements of the monocyctic response elicited by cardiac surgery that potentially relate to haemostasis, and to determine whether preoperative and/or intraoperative factors influenced this response?
4. characterise the interaction between monocytes and platelets after conventional on-pump coronary surgery?
5. ascertain if there was a clinically discernable influence on haemostatic outcome after on-pump coronary surgery that confirmed the known potential haemostatic nature of these interactions between monocytes and platelets?

2. Materials and methods

2.1. Patient selection

The computerised prospective cardiac surgical database at the Hammersmith Hospital, London, maintains data on cardiac operations performed at the Hospital. One thousand and forty-two consecutive patients having isolated first time coronary artery bypass graft surgery were selected for inclusion into the main study group. We also selected a secondary study group including 300 of the most recent consecutive cardiac surgery patients having first time or redo surgery at St. Mary’s Hospital.

Preoperative and postoperative white blood cell counts, monocyte counts and platelet counts were measured on all patients as part of their automated full blood count. Monocyte counts were expressed as a percentage of the total white cell count to give the monocyte percentage, thus aiming to detect if a relative monocytosis occurred following surgery and to differentiate this from a rise reflecting an overall leucocytosis. The preoperative and intraoperative variables used for the multivariate models in the study are shown in Table 1 along with the distribution of patients within each variable.

2.2. Surgical techniques

2.2.1. On-pump technique, Hammersmith Hospital

Cardiopulmonary bypass was performed using aortic-caval cannulation, a Stockert roller pump (Stockert Instruments, Munich) and a Bard or Quadrox hollow fibre membrane oxygenator (Jostra Medizintechnik AG, Germany). The mean cardiopulmonary bypass time was 80.45 ± 27.45 min and the mean cross-clamp time was 42.75 ± 19.70 min. The method of myocardial protection was cardioplegia in 584 (56%) patients and cross-clamp fibrillation in the remaining 458 (44%). The mean blood pressure on cardiopulmonary bypass was maintained at 50–60 mmHg. The lowest core temperature whilst on cardiopulmonary bypass in degree Celsius was noted as the core temperature of the body during the operation.

2.2.2. On-pump technique, St. Mary’s Hospital

CPB was instituted with aorto-caval cannulation. Standard bypass management included membrane oxygenators, arterial line filters and, non-pulsatile flow of 2.4 l/min/m² with a mean arterial blood pressure 50–60 mmHg. Myocardial protection was achieved mainly by intermittent antegrade cold blood cardioplegia (4:1 blood to crystalloid ratio). Retrograde blood cardioplegia was used occasionally in addition, particularly if there was left main stem disease with tight right coronary artery stenosis, which might cause inadequate delivery of the cardioplegia to the targeted myocardium and consequently incomplete myocardial protection. Temperature management was again with moderate hypothermia.

2.2.3. Off-pump technique, St. Mary’s Hospital

Off pump surgery was performed with proximal occlusion of the target coronary vessel with a sildastic sling and the use of epicardial stabilising devices and apical suction devices [Octopus™ 3 or 4 (Medronic Inc., Minneapolis, USA), Starfish™ (Medronic Inc.) or the Guidant Vortex Vacuum Assist (Cupertino, USA)]. Intracoronary shunts were

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### Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>61.85 ± 9.4</td>
</tr>
<tr>
<td>BMI (mean ± SD)</td>
<td>26.42 ± 4.15</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>866 (83.11)</td>
</tr>
<tr>
<td>Female</td>
<td>176 (16.89)</td>
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<tr>
<td>Diabetes mellitus, n (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>241 (23.13)</td>
</tr>
<tr>
<td>No</td>
<td>801 (76.87)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>451 (43.28)</td>
</tr>
<tr>
<td>No</td>
<td>591 (56.72)</td>
</tr>
<tr>
<td>Hypercholesterolaemia, n (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>436 (41.84)</td>
</tr>
<tr>
<td>No</td>
<td>606 (58.16)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td></td>
</tr>
<tr>
<td>Ever</td>
<td>743 (71.30)</td>
</tr>
<tr>
<td>Never</td>
<td>299 (28.70)</td>
</tr>
<tr>
<td>Ejection fraction &lt; 30%, n (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>123 (11.80)</td>
</tr>
<tr>
<td>No</td>
<td>919 (88.20)</td>
</tr>
<tr>
<td>Aprotinin, n (%)</td>
<td></td>
</tr>
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<td>Yes</td>
<td>108 (10.37)</td>
</tr>
<tr>
<td>No</td>
<td>934 (89.63)</td>
</tr>
<tr>
<td>Myocardial protection, n (%)</td>
<td></td>
</tr>
<tr>
<td>Cardioplegia</td>
<td>584 (55.99)</td>
</tr>
<tr>
<td>Cross-clamp fibrillation</td>
<td>458 (43.95)</td>
</tr>
<tr>
<td>Preoperative monocyctic $(%)$</td>
<td>8.26 ± 2.20</td>
</tr>
<tr>
<td>Preoperative platelet count $(%)$</td>
<td>243.50 ± 66.22</td>
</tr>
<tr>
<td>Core temperature on bypass $(%)$</td>
<td>32.90 ± 2.60</td>
</tr>
<tr>
<td>CPB time $(%)$</td>
<td>80.45 ± 27.76</td>
</tr>
</tbody>
</table>
not used routinely during the distal anastomoses. Systolic arterial pressures were maintained at a minimum of 70 mmHg during distal anastomoses utilising venous volume regulation, rate control, inotropes or vasoconstrictors. Proximal anastomoses were performed with a side-biting aortic clamp, with systemic pressures that were dictated by individual surgeon preference. The target ACT during surgery was 300. Normothermia was maintained by using warm intravenous fluids, heating mattress and a humidified airway, in addition to maintaining a warm operating theatre. A standby perfusionist with primed bypass circuit was available for all OPCAB cases.

2.3. Flow cytometry

2.3.1. Platelet—monocyte conjugate analysis

Blood was drawn preoperatively and at 2 h post-bypass and anti-coagulated with sodium citrate. Platelet—monocyte conjugate formation was analysed by tricolour flow cytometry using whole blood as described by us previously [5]. Briefly, whole blood was diluted (3:7) in a modified Tyrode’s buffer and 100 μl aliquots were fixed with 1% paraformaldehyde and stained with the following monoclonal antibodies: pan-leucocyte marker CD45-FITC, the monocyte marker CD14-ECD and the platelet marker CD42b-PE (Beckman Coulter). The monocyte population was identified using CD45-FITC and CD14-ECD fluorescence, and then CD42b-PE was used to calculate the percentage of platelets adherent to the monocyte sub-population.

TF expression was determined using whole blood prepared as described above and stained with the pan-leucocyte marker CD45-PE, the monocyte marker CD14-ECD and the anti-human TF-FITC (America Diagnostica, Stamford, CT, USA). The monocyte population was identified using CD45-FITC and CD14-ECD fluorescence, and then mean TF fluorescence on the monocyte population was used to calculate the mean relative fluorescent intensity (RFI) of staining, calculated by dividing the mean fluorescent staining intensity of the anti-TF antibody at any given time point by the staining intensity of a class-matched and fluorochrome matched control antibody.

2.4. Statistical analysis

Continuous variables were expressed as mean ± SD. p-values <0.05 were considered statistically significant. We evaluated the effect of several factors on blood loss by using stepwise multivariable regression analysis with both forward and backward variable selection. Changes in the monocyte and platelet counts over time were considered as repeated measures data and analysed by using Generalised Estimating Equations (GEE) [6,7]. Marginal models (unstructured correlation matrix) based on generalised estimation equations were used to perform regression analysis. Variables significant at the 5% level were retained in the final multivariable models. Analysis was conducted by using the statistical software SPSS version 12.0 for Windows (SPSS Inc., Chicago, IL, USA), and Intercooled Stata version 8.0 for Windows (Stata Corporation, USA).

3. Results

3.1. Monocyte response to cardiac surgery and factors affecting the response

3.1.1. In more complex cardiac surgery

More complex cardiac surgery was defined as either redo-operations or multiple procedures (at least two of coronary or valve or aortic surgery). We observed that patients having redo-operations did not mount a different monocytic response to those having first time surgery (beta coefficient = −0.003, p = 0.95 and 95% CI −0.14 to 0.13).

Patients having complex operations again did not show a difference in the monocytic response to surgery (beta coefficient = −0.02, p = 0.18 and 95% CI −0.06 to 0.12).

3.1.2. In off-pump coronary surgery

We next ascertained how the above findings compared to the response of these cells in off-pump coronary surgery. It was apparent that at every postoperative time point, monocyte counts were significantly higher in the off-pump group when compared with the on-pump group having coronary surgery (beta coefficient = −0.07, p = 0.03 and 95% CI −0.14 to −0.01) and significantly, higher platelet count at 2 h post-bypass.

Fig. 1. Changes in white cell, monocyte and platelet counts from preoperative levels to the end of the first postoperative week. PRE denotes preoperative and PO denotes postoperative with the numerical value being the postoperative day of the sample.
counts directly predicted a greater monocytic response (beta coefficient = 0.0004, p = 0.003, 95% CI 0.0004 to 0.0007).

3.1.3. In first time on-pump coronary surgery

Changes in total white blood cell (WBC), monocyte and platelet counts are shown in Fig. 1. The WBC significantly increased following surgery (p < 0.001). A rapid peak by the second postoperative day was followed by a moderate drop on the third, fourth and fifth day. This was followed by a second rise by the sixth and seventh postoperative days. The monocyte count was seen to similarly increase on the first two postoperative days, but then in contrast to the WBC continued to rise steadily until the fifth postoperative day. Using the monocyte%, it was apparent that the initial rise in the monocyte count was a reflection of the rise in the total WBC. In contrast, over subsequent days an absolute monocytosis was seen, independent of total WBC. In comparison, the platelet count mirrored the WBC initially and showed a trough by the second postoperative day. This was followed by a subsequent rise that was significantly above the preoperative levels after the sixth postoperative day.

Factors associated with relative monocytosis after on-pump coronary surgery were studied using multivariable regression analysis. Variables analysed are shown in Table 1. Patients with a higher body mass index (BMI) had a greater increase in M% (p = 0.02), as did diabetic patients (p = 0.035) and patients who smoked (p = 0.01). In contrast, older patients manifested a lower monocytic response to cardiac surgery (p < 0.001). Interestingly, myocardial protection using cross-clamp fibrillation as opposed to cardioplegia was associated with a significantly lower monocytic response postoperatively (p = 0.048). These results are shown in Table 2.

The regression equation is as follows:

$$\Delta M_o = 3.58 - 0.05(A) + 0.03(BMI) + 0.31(DM) + 0.39(S) - 1.4(MP)$$

where $\Delta M_o$: the change in monocyte fraction, A: age in years, BMI: body mass index, DM: diabetic status (non-diabetic = 0, diabetic = 1), S: smoking status (non-smoker = 0, smoker = 1) and MP: the type of myocardial protection used (cross-clamp fibrillation = 0, cardioplegia = 1).

3.2. Platelet—monocyte conjugate formation and role of TF

Since monocytes exert some of their potential haemostatic effects in association with the formation of PMCs, we characterised actual PMC formation in association with on-pump coronary surgery. PMC formation (Fig. 2) did not initially demonstrate a significant change although a slight downward trend following administration of heparin, followed by a subsequent peak at 5 min following the onset of CPB was seen. In contrast, 2 h after the onset of CPB, a significant decline in circulating PMCs was observed (p = 0.04). A rise and return towards preoperative levels was then found between 24 h and 5 days postoperatively.

Since circulating monocyte TF expression may itself exert haemostatic effects and influence PMC formation, we used flow cytometric analysis to characterise this parameter.

Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>p-value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.05</td>
<td>&lt;0.001</td>
<td>-0.006 to -0.034</td>
</tr>
<tr>
<td>BMI</td>
<td>0.03</td>
<td>0.02</td>
<td>0.005 to 0.063</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.31</td>
<td>0.035</td>
<td>0.022 to 0.595</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.39</td>
<td>0.01</td>
<td>0.094 to 0.688</td>
</tr>
<tr>
<td>Cross-clamp fibrillation</td>
<td>-1.40</td>
<td>0.048</td>
<td>-2.779 to -0.011</td>
</tr>
</tbody>
</table>

Fig. 2. Formation of platelet—monocyte conjugates. The percentage of monocytes forming conjugates with platelets is indicated by the day of the sample. PRE denotes preoperative and subsequent samples are immediately after the administration of heparin, after 5 min of bypass, at the end of bypass, at 2 h and at 24 h after bypass and on postoperative day 5.

Fig. 3. (A) Colour densitometry plot showing leucocyte populations defined using pan-leucocyte marker (CD-45-PE) on the x-axis and monocyte marker (CD14-ECD) on the y-axis. (B) A histogram plot showing (on the y-axis) fluorescence of monocyte bound tissue factor (Tissue Factor-PE).
Use of aprotinin

Platelet count if <160 × 10^9 l⁻¹ was inversely related to postoperative bleeding as we observed that both circulating platelet and monocyte counts were inversely related to postoperative blood loss following on-pump coronary surgery. The impact of cardiopulmonary bypass on platelet function and post-operative haemostasis is well known and has previously been reviewed by our group [9]. In contrast, a potential haemostatic role for circulating monocytes has only been suggested from basic science studies and has never previously been investigated in the clinical setting of cardiac surgery. Our data using multivariable analysis suggest for the first time that a higher postoperative monocyte% significantly and independently decreases postoperative blood loss. Haemostatic mechanisms involved may include monocyte TF interactions with clotting factor VII and platelets as previously described [10—12] and also elaborated in Section 1. Activated platelets are known to adhere to blood monocytes, and this adhesion is mainly mediated by the surface exposure of the platelet granule protein CD62P (P-selectin). Platelets as well as platelet-derived microvesicles contain and transfer TF (the most important initiator of intravascular thrombin and fibrin formation), to monocytes in addition to decrypting monocyte TF. This potentially helps plug surgically transacted vasculature by activating the clotting cascade around platelet—monocyte conjugates.

A further observation was that patients with higher core body temperatures during coronary artery bypass grafting (relatively normothermic patients) were less likely to bleed in the postoperative period. Lower body temperatures may impair enzyme activity involved in the coagulation cascade. This is supported by in vitro studies, which have demonstrated that the clotting time of normal human plasma as measured by the activated partial thromboplastin times (APTT), pro-thrombin times (PT) and thrombin times (TT) is significantly prolonged by lower temperatures in an exponential manner [13]. Furthermore, it is also known that a lower body temperature during cardiopulmonary bypass causes increased platelet activation [14] and these pre-activated platelets are dysfunctional in the postoperative period. However, hypothermia may also affect monocyte function. This possibility is supported by in-vitro human monocyte studies in which the temperature dependence of their active uptake of colloidal gold particles has been demonstrated by electron microscopy [15].

The late increase in PMCs detected in peripheral blood may be related to the observed increase in absolute numbers of available monocytes and platelets or due to their increased affinity as a result of cellular activation. In keeping with this, work by Wahba and Videm [16] has shown that platelets increase both in number and in state of activation towards the end of the first week after cardiac surgery. Although monocyte up-regulation of surface TF would theoretically further contribute to PMC formation through platelet—P-selectin interaction, we did not, in this study, detect any significant change in expression perioperatively. Therefore, the late rise in circulating PMCs following cardiac surgery is likely to be related to the observed monocytosis and thrombocytosis that occurs at the end of the first postoperative week and/or maybe mediated through TF-independent interactions. This increased number of circulating PMCs if reflective of an increased adhesive state, may potentially mediate thrombo-embolic phenomena that contribute to early graft occlusion as well as to neurological

Table 3
Multivariate analysis of factors affecting postoperative blood loss after coronary artery bypass grafting

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>p-value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>132.50</td>
<td>&lt;0.001</td>
<td>−178.82 to −86.18</td>
</tr>
<tr>
<td>BMI</td>
<td>12.74</td>
<td>&lt;0.001</td>
<td>16.96 to −8.52</td>
</tr>
<tr>
<td>Platelet count if &gt;160 × 10^9 l⁻¹</td>
<td>−0.933</td>
<td>&lt;0.001</td>
<td>1.31 to 0.55</td>
</tr>
<tr>
<td>Monocyte% count</td>
<td>−7.90</td>
<td>0.012</td>
<td>14.08 to −1.72</td>
</tr>
<tr>
<td>Core temperature</td>
<td>−8.26</td>
<td>0.013</td>
<td>−14.78 to −1.73</td>
</tr>
<tr>
<td>Use of aprotinin</td>
<td>−117.49</td>
<td>&lt;0.001</td>
<td>−158.83 to −76.16</td>
</tr>
</tbody>
</table>

perioperatively (Fig. 3). We were unable to detect any significant change in monocyte TF expression in association with on-pump coronary surgery.

3.2.1. Contribution of monocytes to early postoperative blood loss

Having characterised potential monocyte haemostatic responses and levels of PMC formation perioperatively, we next studied the effects of absolute numbers of circulating platelets and monocytes on postoperative blood loss (Table 3). The chest drain output in the first 12 postoperative hours was used as a measure of postoperative blood loss. The mean postoperative blood loss in millilitres was 581.2 ± 292.8. Blood loss was found to be inversely related to increasing preoperative platelet count, in an exponential rather than linear manner. On this basis, platelet counts were categorised into three groups based on tertiles (platelet count <123 × 10^9 l⁻¹, platelet count (123—160) × 10^9 l⁻¹, and platelet count >160 × 10^9 l⁻¹). Our analysis demonstrated that postoperative blood loss was decreased significantly by preoperative platelet counts >160 × 10^9 l⁻¹ (p < 0.001), and also by higher preoperative monocyte counts (p = 0.012). Furthermore, female patients (p < 0.001), patients with higher body mass indices (p < 0.001), higher core body temperatures during surgery (p = 0.013) and the use of aprotinin perioperatively (p < 0.001) all contributed significantly towards decreasing the postoperative blood loss.

The regression equation is as follows:

Blood loss (ml) in 12 h = 1391.69 − 132.50(gender) − 8.26(core body temperature in °C) − 12.74(BMI) − platelet count(0.933) − 7.9(monocyte%) − 117.49(aprotinin) [gender = 1 for male or gender = 2 for female; platelet count as × 10^9 l⁻¹ if platelet count >160 × 10^9 l⁻¹; aprotinin = 0 if not used and aprotinin = 1 if used].

4. Discussion

4.1. Findings of study

In our study, we observed that the monocytosis that occurred after surgery was more pronounced with off-pump surgery than with on-pump coronary surgery. It is well appreciated in the literature that off-pump surgery is associated with less postoperative bleeding [8]. The contribution of monocytes to postoperative bleeding may potentially play a role in this difference in postoperative bleeding as we observed that both circulating platelet and

Variable Coefficient p-value 95% confidence interval

Female gender −132.50 <0.001 −178.82 to −86.18
BMI −12.74 <0.001 16.96 to −8.52
Platelet count if >160 × 10^9 l⁻¹ −0.933 <0.001 1.31 to 0.55
Monocyte% count −7.90 0.012 14.08 to −1.72
Core temperature −8.26 0.013 −14.78 to −1.73
Use of aprotinin −117.49 <0.001 −158.83 to −76.16
sequelae such as amaurosis fugax and other forms of transient ischaemic attack (TIAs) towards the end of the first postoperative week. The presence of significantly higher numbers of pro-thrombotic platelet—monocyte aggregates in patients with TIAs or stroke has previously been demonstrated in a non-surgical setting [17]. Interestingly, previous studies have demonstrated that the presence of circulating PMCs immediately postoperatively can act as a predictor of lower limb graft occlusion within the first six months following peripheral vascular surgery [18].

In agreement with earlier work, our study confirms that aprotinin decreases postoperative blood loss. This is thought to be in-part mediated by its anti-fibrinolytic affect. However, our group recently demonstrated that aprotinin also decreases thrombin-induced activation of platelets, whilst not inhibiting platelet aggregation induced by collagen and ADP [19]. Peak monocyte—platelet conjugate formation has been shown to be significantly reduced by aprotinin [20] and may protect both platelets and monocytes from activation by thrombin generated during cardiopulmonary bypass, allowing more effective haemostasis at the sites of surgical trauma postoperatively.

4.2. Potential impact of results on current practice

Leucocyte-depleting filters used in cardiac surgery have been shown to bind monocytes and platelets [21]. We observe platelet—monocyte conjugate formation to be at its lowest at 2 h after discontinuation of bypass, coinciding with the immediate postoperative period during which both platelet counts and function are depleted. The use of leucocyte depleting filters is likely to activate and entrap, and further decrease platelets and monocytes and PMCs, thereby reducing their availability for postoperative haemostasis [22]. Thus, it may be that they are best avoided in patients with preoperative risk factors likely to contribute to a higher risk of postoperative bleeding.

4.3. Potential future clinical use of results

In patients having postoperative bleeding diatheses not controlled by standard strategies for the management of patients having postoperative bleeding diatheses not controlled by standard measures.

4.4. Weaknesses of the study

Despite the monocyte count influencing postoperative blood loss, the absolute volume decrease appears small in relation to the contribution made by the platelet count. Nonetheless this interaction has not been studied previously. The monocytic mechanisms underlying these observations remain unclear, but do not appear to relate to monocyte TF up-regulation. Further mechanisms that may play a role will need to be addressed by a study entirely dedicated towards unravelling these processes. A further weakness is that the influence on postoperative bleeding seen in the study relates only to on-pump coronary surgery. We have mapped the response in off-pump surgery, but do not have the data to extrapolate the findings to postoperative blood loss in off-pump surgery.

The results of this study are clearly of a preliminary nature into platelet—monocyte behaviour after on-pump coronary surgery and we hope will stimulate further investigation.

Acknowledgement

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References


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