

Re-exploration for Hemorrhage Following Open Heart Surgery Differentiation on the Causes of Bleeding and the Impact on Patient Outcomes

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Objectives: To differentiate surgical bleeding requiring re-exploration from postoperative coagulopathy and determine the differences in patient outcomes.

Methods: This was a retrospective chart review of 2,263 adult patients undergoing elective and emergency open heart procedures encompassing coronary artery bypass, valvular, and a combined procedure to determine the impact of source of bleeding leading to re-exploration.

Results: Eighty-two patients (3.6%) required re-exploration. Sixty-six percent had surgical bleeding; the remaining 34% were coagulopathic. Postoperative coagulopathy was associated with preoperative heparin use (37% vs. 19.9% for controls $p < 0.05$). Re-operative procedures combined bypass/ valve ($p < 0.001$) and prolonged cardiopulmonary bypass and aortic cross-clamp times ($p < 0.05$) were more prevalent in the coagulopathy group. Postoperative inotrope use was increased in patients who were re-explored ($p < 0.001$), as were cardiac, pulmonary, renal and abdominal complications ($p < 0.001$), and in all cases those patients with medically related bleeding had worse acute outcomes than the group with surgical causes for re-exploration. The hospital stay was prolonged for both patients with surgical bleeding (23.5 days) and patients with coagulopathy (27.1 days) compared to patients not undergoing re-exploration for bleeding (12.0 days, $p < 0.001$). Survival was 91.3% for patients with surgical bleeding, 87.5% for patients with coagulopathy, and 98.0% for all others ($p < 0.01$).

Conclusions: Severe postoperative hemorrhage is associated with significant morbidity and increased mortality. Postoperative hospital stay, morbidity, and mortality were significantly worse in patients suffering from coagulopathy when compared to those patients with hemorrhage from surgical causes. (*Ann Thorac Cardiovasc Surg* 2001; 7: 352–7)

Key words: heart, surgery, hemorrhage, outcomes

Introduction

Postoperative bleeding is a concern for all patients undergoing cardiac surgery. In patients exposed to cardiopulmonary bypass, bleeding following surgery is excessive in up to twelve percent of patients, in whom subsequent re-exploration is required.¹⁻¹² Several studies have evaluated the impact of postoperative bleeding on acute

patient outcomes.¹³⁻¹⁶ The primary weakness in these prior studies, some of which involved large patient populations, is the lack of differentiation of two different patient populations; those with bleeding from surgical causes with mild coagulation defects and those that have severe coagulopathy without a specific surgical source. The purpose of this study was to characterize the causes of bleeding in patients with hemorrhage that required re-exploration and assess the impact on patient outcomes from the different causes of bleeding.

Materials and Methods

Patient population and study variables

2,263 patients that had undergone elective and emergent cardiac operations by five surgeons over a five year pe-

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Received February 19, 2001; accepted for publication May 4, 2001.

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riod were evaluated. All cases were conducted with cardiopulmonary bypass. The data was gathered through a retrospective chart review. Reliability of data retrieval was assessed by an additional internal review. The patient characteristics evaluated included: age, ejection fraction, gender, procedure, heparin dose, body surface area, cardiopulmonary bypass time, aortic cross clamp time, preoperative renal function, preoperative anticoagulant medications, preoperative intra-aortic balloon pump use, protamine sulfate dose, prior open heart procedures, postoperative inotropic support, postoperative blood loss, transfusions, postoperative hospital stay, complications, and mortality. Postoperative morbidity was recorded according to the classifications used in the Appendix. Transfusion practices including whole blood, packed red blood cells, fresh frozen plasma, platelets, and cryoprecipitate were recorded for each group. In general a red blood cell transfusion was administered for hematocrits below 24% in patients without co-morbidities or hemodynamic compromise. Patients were categorized as having had surgical bleeding, if at the time of re-exploration, a specific site was identified which was controlled by surgical means and eliminated 80% of the chest tube output. Surgically controlled bleeding was defined as the applications of sutures, electrical cautery or a fibrin sealant to one or more specific sites of bleeding, which were subsequently controlled. Heparin was discontinued prior to transport to the operating room. Coumadin was routinely discontinued 5 days prior to the procedure. Patients on aspirin continued their medication until the day of surgery. Chest tube drainage was assessed at 18 to 24 hours. To be considered as having required inotropic support the levels of inotropic drugs were: dopamine >5 ug/kg/min, epinephrine >0.05 ng/kg/min, norepinephrine >0.05 ng/kg/min, dolbutamine >5 ug/kg/min, amrinone >1 ug/kg/min.

Conduct of operation

Anesthetic preparation of patients involved invasive monitoring followed by a narcotic based anesthetic prior to cardiopulmonary bypass. A loading dose of heparin was administered intravenously at 300 units per kilogram. The ACT was maintained greater than 400 seconds during cardiopulmonary bypass with additional heparin as necessary. Roller pumps and membrane oxygenators were used in all cases. The cardiopulmonary bypass circuit was primed with two liters of crystalloid. Intra-operatively, red blood cell salvage was accomplished by using standard scavenging and re-infusion techniques, a Cell

Saver (Haemonetics, Braintree, MA), and hemoconcentration was used in all cases. Myocardial preservation was maintained by intermittent cold blood cardioplegia. All patients were exposed to moderate hemodilution (Hematocrit 19-24%) and hypothermia (34-25°C) with re-warming to temperatures above 35°C. After cardiopulmonary bypass was discontinued, protamine sulfate was administered in a 1:1 ratio with administered heparin (1 mg per 1 unit). If the activated clotting time (ACT) remained elevated following the initial dose of protamine, an additional dose of 50 mg was given.

Criterion for re-exploration

The decision for re-exploration was based on both the rate of postoperative bleeding and the accumulated volume, as has been previously established.¹⁷⁾ In general, patients were explored for bleeding at a rate of 200 ml/hr for over a 4 hour period or for a sudden increase in bleeding after the first two hours.

Statistics

All information was gathered following appropriate Institutional Review Board approval. Hospital mortality was defined as death during the same admission regardless of duration or cause. Group comparisons were made for categorical variables with the Fisher's exact test and for continuous variables with ANOVA, Turkey's post-hoc and Student's t tests. A p value less than 0.05 was considered statistically significant. For convenience, values less than 0.001 were reported at the 0.001 level.

Results

Bleeding characteristics

Of the 2,263 patients studied, 82 (3.6%) patients were re-explored for excessive postoperative hemorrhage. In 55 (66%), a surgical source of bleeding was identified. The most common sites for postoperative bleeding were the side branches of bypass grafts and the chest wall, primarily from the internal mammary artery harvest bed. (Fig. 1)

Patient characteristics

There was a trend toward a greater exposure to preoperative coumadin (3.7%) and thrombolytic therapy (7.2%) in the coagulopathic group, but not at statistically significant levels (p=0.2, p=0.16 respectively). Preoperative heparin usage was more frequent in patients with a postoperative coagulopathy at borderline levels (37% vs.

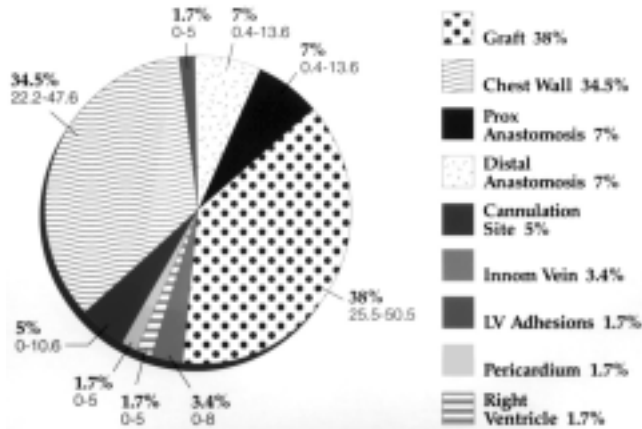


Fig. 1. Surgical sources of bleeding found at exploration.

19.9% controls, $p=0.053$). Prolonged aortic cross-clamp time, extended cardiopulmonary bypass time, re-operative procedures, and coronary artery bypass with associated valve procedures were accompanied by a greater incidence of postoperative coagulopathy ($p=0.001$ for all).

Patient outcomes

As expected, blood product utilization was significantly elevated in both bleeding groups. The average amount of blood products used for those patients not re-explored for bleeding was 1.83 ± 3.1 u PRBC, 0.49 ± 1.6 u FFP and 1.49 ± 4.4 u platelets. The blood product usage increased approximately five-fold in the patients with postoperative bleeding from surgical causes. In those patients with postoperative coagulopathy, blood product usage was increased ten times.

Postoperative inotrope use in the intensive care unit (ICU) demonstrated a trend paralleling the blood product use (Fig. 2). Of the patients not requiring re-exploration, 8.6% were on dopamine, 12.4% on epinephrine, 10.7% on norepinephrine and 1.1% on amrinone. Inotropic support was required more frequently in patients re-explored for bleeding. (Dopamine surgical 18.5%, medical 29.6%, $p=0.003$, epinephrine surgical 38%, medical 37%, $p=0.001$, norepinephrine surgical 32.0%, medical 41%, $p=0.001$, amrinone 7.4%, $p=0.001$, $p=0.002$).

The impact of postoperative bleeding on patient outcomes is demonstrated in Fig. 3. Morbidity was increased in multiple organ systems in both the medical and surgical bleeding groups. One-half (53.7% surgical, 55.6% medical) of the patients in the bleeding groups had pulmonary complications as compared to 23% of patients not explored for postoperative bleeding ($p=0.001$). Re-

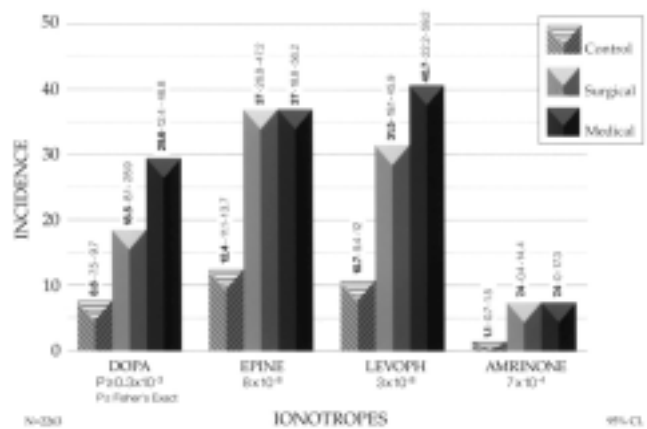


Fig. 2. Postoperative inotrope use related to postoperative hemorrhage. The control group did not require re-exploration and are compared to patients found to have surgically related bleeding and coagulopathies.

nal insufficiency occurred in 27.8% of patients with surgical bleeding and 25.9% of patients with medical postoperative bleeding which compared to 5.5% of those not re-explored ($p=0.001$). Cardiac complications occurred in 6.7% of the non-bleeding group. The frequency of cardiac complications was increased to 24.1% in patients with surgical bleeding and 51.9% of the patients in the medically related bleeding group ($p=0.007$, and $p=0.001$). Abdominal complications were also increased in the bleeding groups. Only 3.3% of patients not requiring re-exploration suffered an abdominal complication. Fifteen percent (15.2%) of the surgical bleeding group and 16.7% of those patients with coagulopathies suffered abdominal complications ($p=0.001$ for both). In the surgical bleeding group, there was an increased percentage of postoperative neurological complications (26.1% versus 4.1% in controls, $p=0.001$) and arrhythmic events (62.9 versus 41.8 in controls, $p=0.002$).

The increased postoperative morbidity from bleeding was reflected in a significantly increased length of stay in the bleeding groups (23.6 days surgical and 27.1 days medical) as compared to those not re-explored (12.0 days, $p=0.001$) (Fig. 4). The mortality was also higher in the bleeding groups (8.7% surgical and 12.5% medical) versus those not re-explored (2% $p=0.001$) (Fig. 4).

Discussion

Preoperative and operative risk characteristics predictive of postoperative bleeding

Our study demonstrated that excessive postoperative bleeding is from surgical sources in the majority of pa-

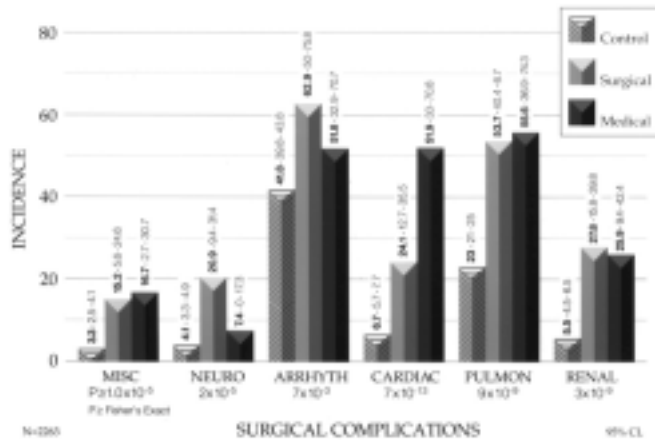


Fig. 3. Organ system complications related to postoperative hemorrhage. Control group without excessive bleeding compared to surgical bleeders and patients with coagulopathy.

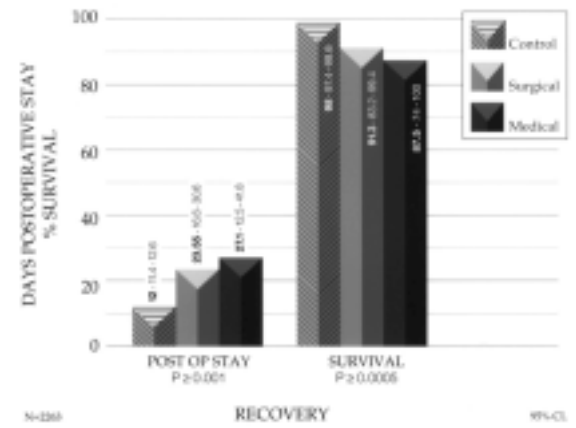


Fig. 4. Recovery postoperative stay and survival related to those patients without significant postoperative hemorrhage as compared to those with a surgical and medical source of bleeding.

tients (67%), which agrees with a recent study by Unsworth-White (at 67%).¹³ In prior studies, surgical causes of bleeding necessitating re-exploration were found to range from 35-100%.^{3-9,14,18-23} Our study demonstrated that the most common sites of surgical bleeding were located in primarily two categories: the chest wall (internal mammary artery bed) and the side branches of bypass grafts.

Our study was able to identify high-risk patient groups for postoperative coagulopathy but not for surgical bleeding. The patients at risk for coagulopathy included those patients with complex and/or prolonged procedures, those exposed to preoperative anticoagulants and to a lesser extent patients with a preoperatively elevated PT and ACT. Moulton et al. demonstrated that age, renal insufficiency, procedures other than coronary bypass, and prolonged bypass time were preoperative predictors of the need for reexploration.¹⁵ Grover's review of the Society of Thoracic Surgeons (STS) and Veterans Affairs (VA) databases which was included in the discussion of Moulton's study, identified renal failure-dialysis, prior heart surgery, emergency and urgent surgery, congestive heart failure/shock, severe angina, age, procedures other than coronary bypass and chronic steroid use as risk factors for reexploration.¹⁵ Studies by Verska et al.²⁴ and Despotis et al.²⁵ demonstrated similar results. Dacey et al.¹⁶ identified increased age, decreased body size, time on cardiopulmonary bypass, number of distal anastomoses and intra-operative insertion of an intra-aortic balloon pump as risk factors for reexploration. On the subject of preoperative anticoagulant exposure, Torosain et al.²⁶ and Sethi et al documented increased postopera-

tive bleeding with preoperative aspirin and coumadin as did our study. Our study showed preoperative heparin use to be significantly increased in the coagulopathy group in contrast to a prior study.

One could argue that if the majority of postoperative bleeding which necessitates re-exploration is from surgical causes then preoperative risk factors should be of limited predictive value as they are related to re-exploration. The apparent discrepancy may be explicable by two points. First, a source of bleeding is a surgical problem depending on the size of vascular defect and the adequacy of the coagulation system of the patient. All of the risk factors noted from the studies listed above can be associated with events that contribute to the coagulopathy that is associated with open heart surgery. Following this line of reasoning, the studies that have identified these risk factors for re-exploration through multivariate analysis may have enunciated a failure to identify and treat the coagulopathy component of the bleeding diathesis following surgery. The implication is that fewer patients would have required re-exploration with better identification and treatment schemes for postoperative coagulopathy.

The pathophysiology of excessive mediastinal bleeding and re-exploration

Several large studies have delineated the significant impact that re-exploration for bleeding has on patient outcomes.^{13-16,19,27,28} These studies documented a high rate of occurrence of renal failure, prolonged ventilation, ARDS, sepsis, arrhythmias, prolonged hospital stay, and death in those patient groups requiring re-exploration.

These results are consistent with prior studies documenting renal and respiratory complications and increased mortality for similar patients.^{19,27,28} In trying to understand the cause for these adverse outcomes, Moulton et al. evaluated the amount of bleeding and blood product use with acute morbidity. This study demonstrated substantial increases in morbidity with re-exploration with limited blood loss or with excessive transfusions with or without re-exploration. Our study demonstrated similar increases in morbidity and mortality when compared to the studies previously mentioned. Pulmonary, renal, and abdominal complications were increased in both bleeding groups. However, a difference that was clarified by our study was that the patients that were bleeding from coagulopathies, bled to a greater extent, were exposed to greater amounts of inotropes with alpha effects and had a greater incidence of low output syndrome than the patients with surgical bleeding. This was further reflected in longer hospital stays and an increased mortality rate. This may be enunciating the deleterious effects of prolonged periods of high doses of inotropes and hemodynamic instability, which often accompany excessive mediastinal bleeding related to coagulopathy. The pulmonary, renal and miscellaneous complications (which include infections) were comparatively elevated in both the surgical and medical bleeding groups that were re-explored when compared to controls. These results may reflect transfusion-related morbidity, which is often evidenced by greater injury to these organ systems.

Conclusions

Reiterating our initial premise, since all patients bleed following open-heart surgery how do we lessen the deleterious impact of severe postoperative hemorrhage and improve patient outcomes. The data from this study clearly supports preventing significant postoperative bleeding by utilizing prophylactic treatment protocols. For those patients at high-risk for postoperative bleeding, pro-coagulants such as amikar or aprotinin should be used. Our study demonstrated that all patients requiring re-exploration experienced poorer acute outcomes when compared to those not requiring re-exploration and that those patient suffering from severe coagulopathies demonstrated the worst acute outcomes in all areas. Should patients clinically appear to be coagulopathic following protamine reversal, FFP, platelet transfusions and fibrin glue should be administered in the operating room prior to chest closure. This approach is focused on

the most expedient process to verify significant control of the coagulopathy. For patients in the ICU with unexpectedly high chest tube output, the goal should be to normalize the patient coagulation profiles within 4 hours. Should bleeding still be significant with a normal coagulation profile, the patient should be re-explored. Our study supports an aggressive treatment approach aimed at avoiding hemodynamic compromise, inotropic exposure and excessive transfusion volume with the associated negative ramifications on patient outcomes.

Appendix

Clinical definitions

Neurological of complications: Stroke documented by changes in a physical exam lasting greater than 24 hours and/or evidence of new head CT findings.

Cardiac-low output syndrome: Cardiac index less than 2.0 for 24 hours or patients requiring inotropic support for 24 hours or more.

Pulmonary: Development of acute respiratory distress syndrome which was defined as bilateral pulmonary infiltrates, hypoxia (P02≤100 on 50%) +/- high pulmonary artery pressures (greater than 50 mmHg systolic). Ventilator dependence not related to pneumonia for 48 hours. Renal: Renal compromise was defined as a creatinine increase of 2x baseline or anuria or requiring dialysis. Arrhythmias: Atrial fibrillation new onset requiring treatment. Ventricular tachycardia – greater than 6 beats requiring treatment. Ventricular fibrillation.

Abdominal-gastrointestinal bleeding: Requiring transfusion or endoscopic intervention or surgery. Pancreatitis was defined as abdominal pain, nausea with amylase elevation. +/- Edema on CT. Ileus was defined as nausea/vomiting without amylase elevation, decreased bowel sounds +/- radiographic findings, evidence of intestinal fluid collection after day 3.

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