ORIGINAL ARTICLE

Peri-operative blood transfusion increases length of hospital stay and number of postoperative complications in non-cardiac surgical patients

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Objectives To test the hypothesis that blood transfusion alone was a significant risk factor for in-hospital morbidity in non-cardiac patients.

Design Propensity analysis.

Setting University teaching hospital, Hong Kong.

Patients Consecutive non-cardiac patients seen in our department from 2006 to early 2009 who underwent a major procedure under general or spinal anaesthesia were included. Propensity analysis was performed to neutralise the confounding effects of preoperative variables and identify the true effects of transfusions on surgical outcomes.

Main outcome measures Receipt of intra-operative and postoperative blood transfusion was established and the difference in proportions between patients who did and did not receive donor blood tested for mortality, overall morbidity, individual complications, and number of adverse events.

Results Transfused patients were significantly older and sicker, more likely to be male, to have lower haemoglobin values and undergo longer and more emergency surgical procedures than those not receiving a transfusion. Blood transfusion was predictive of length of postoperative hospital stay and number of complications before discharge. The amount of transfused blood was predictive of in-hospital mortality, with an odds ratio of 1.4 for each unit of blood received. The risk of a surgical wound infection was almost doubled when the patient had received a blood transfusion.

Conclusion After controlling for the factors associated with an increased likelihood for receiving a blood transfusion, the actual transfusion was predictive of a slower and more eventful postoperative recovery with associated costs to both the patient and health services.

Key words
Blood component transfusion; General surgery; Infection; Morbidity; Risk factors

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Introduction

Transfusion of donor blood undoubtedly saves the lives of haemorrhaging or anaemic individuals and patients needing rapid oxygen delivery or peri-operative blood replacement. Reduction in mortality, however, may come at the cost of a higher rate of infections, transfusion reactions, receipt of contaminated red blood cells, compromised immunity, and tissue destruction.[1,2] Aside from these relatively uncommon problems, there may be errors in ordering, preparation, or administration of blood products.

Outcome of medical care may also be negatively impacted by blood transfusion. Studies in intensive care patients have established that lower transfusion rates are associated with less in-hospital deaths, fewer myocardial infarctions, less episodes of pulmonary oedema, and fewer patients developing respiratory distress.[3] Transfusion has been identified as an independent risk factor for postoperative bacterial infection, surgical site infection, and post-injury multiple organ failure.[4-6] In separate cohorts of patients with cardiac disease, blood transfusion was associated with significantly longer hospital stays, higher rates of multi-system organ failure and greater mortality, especially in patients who received 4 units or more.[7,8] The adverse effects did not appear to differ when leukocyte-depleted blood was compared with usual allogenic blood.[9]

替非心臟手術病人進行圍術期輸血會增加留院時間及術後併發症

目的 測試輸血本身是否非心臟手術病人留院罹病的一項重要風險因子。

設計 傾向分析。

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患者 研究對象包括於2006年至2009年初，所有進行大型非心臟手術及全身或脊髓麻醉的病人。我們進行傾向分析以減低術前變數的干擾影響，及探討輸血對術後結果的真正影響。

主要結果測量 確定病人是否在術中或術後接受輸血，並比較接受輸血和沒有接受輸血病人的死亡率、總罹病率、併發症和產生不良反應的數目。

結果 與沒有接受輸血的病人比較，接受輸血的病人年紀較大、病況較嚴重、男性居多、血紅蛋白濃度較低、手術時間較長及較緊急。輸血是病人留院時間及出院前併發症數目的預測因子。輸血量亦是住院死亡率的預測因子，比數比為每單位輸血量1.4。接受輸血的病人，其手術傷口受感染的風險增加幾乎一倍。

結論 在控制其他增加輸血機會的因素下，輸血是病人術後康復速度較慢及較多不良反應的預測因子，使病人及醫護服務的成本增加。

We recently reported that in cardiac patients, blood transfusion was a significant predictor of morbidity, with an odds ratio of 3.8 for the development of a surgical site infection.[10] However, the complex relationship between blood transfusion, the presenting illness, and haemoglobin and haematocrit levels precludes assumptions of causality.

The aim of this audit was to establish the rate of blood transfusion associated with different non-cardiac surgical procedures and thence to use propensity analysis to test the hypothesis that blood transfusion alone was a significant risk factor for in-hospital morbidity in non-cardiac patients undergoing a range of surgical procedures.

Methods

Two years ago, prospective data registries for audit purposes were instituted in our department for specific major surgical procedures within the specialties of colorectal, vascular, head and neck, thyroid, thoracic, liver, and cardiac surgeries. Missing data audits are routinely performed to ensure quality. Demographic, medical, disease-specific, operative and outcome variables, along with hospital stay parameters, were available for analysis from each of these registers. A range of intra-operative and postoperative complications was available on request. For this study, data from common fields were merged.

Patients included in this study were consecutive non-cardiac cases seen in our department from 2006 to early 2009, who underwent a major procedure under general or spinal anaesthesia.

The frequency of intra-operative and postoperative blood transfusions was established for each surgical subspecialty and descriptive analyses were performed. Data were checked for normality of distribution and the difference in proportions between patients who did and did not receive donor blood was tested for mortality, overall morbidity, individual complications, and number of adverse events. Between-group comparisons were also made for hospital stay parameters.

Since the likelihood of blood transfusions may be influenced by preoperative variables and the discretion of different surgeons, propensity analysis was performed to neutralise these confounders and identify the true effects of transfusions on operative outcomes. This technique was described by Rao et al[8] when evaluating the association between blood transfusions and clinical outcomes in a group of cardiac patients. Propensity testing was selected for use in the analysis because outcome data were non-experimental and the differences being investigated were between patients with heterogeneous characteristics. We wished to reduce such biases by controlling for preoperative variables known to influence the likelihood of an individual patient receiving a blood transfusion.

Preoperative variables that were associated with transfusions on univariate analysis and found to be significant at a P value of less than 0.1 were entered into a backward logistic regression. The regression equation was used to calculate propensity scores for each patient. Scores ranged from 0 to 1 and indicated each patient's likelihood of being transfused given their individual preoperative variables. Two approaches were made for the propensity analysis. First, each transfused patient was matched to a unique non-transfused patient with identical or similar propensity scores, and analysis was performed among this subgroup of patients. Second, the entire sample was tested with propensity scores directly included in the multivariate analyses. Inclusion of the scores in the regression statistically controls the propensity effects. Variables were considered significant if the P value was less than 0.05.

Results

There were 712 data sets from the subspecialties of colorectal (n=386), head and neck (54), liver (99), thyroid (86), and vascular (87) surgeries. For comparison there were also 522 cardiac surgery data sets. Of the non-cardiac patients, 62% were male.

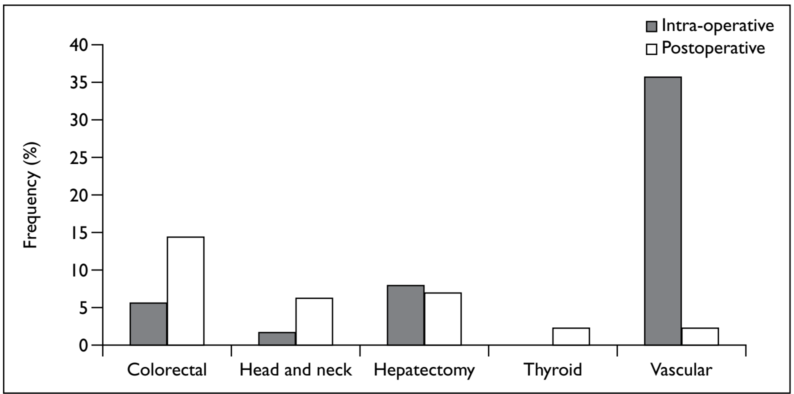

FIG. Blood transfusions at different time-points in patients undergoing non-cardiac surgery

TABLE 1. Demographic and peri-operative features in non-cardiac surgical patients who were transfused and not transfused

Demographic and peri-operative data*	Transfused (n=118)	Not transfused (n=594)	P value
Median (IQR) age (years)	72 (59-79)	65 (54-75)	<0.001
Age >70 years	53%	36%	0.001
Age >80 years	19%	10%	0.004
ASA grading >2	40%	20%	<0.001
Male gender	74%	60%	0.004
Median (IQR) preoperative haemoglobin level (g/L)	100 (81-121)	125 (108-138)	<0.001
Median (IQR) operating time (mins)	195 (150-296)	180 (140-240)	0.002
Emergency	48%	32%	0.012

* IQR denotes interquartile range, and ASA American Society of Anesthesiologists

TABLE 2. Comparison of outcome variables in non-cardiac surgical patients who were transfused and not transfused

Outcome variable*	Transfused (n=118)	Not transfused (n=594)	P value
Intra-operative complications	10%	2%	<0.001
Median volume of blood loss (mL)	150 (20-500)	30 (0-121)	<0.001
Median (IQR) postoperative length of hospital stay (days)	13 (8-20)	8 (6-11)	<0.001
Morbidity during hospital stay	77%	33%	<0.001
Rate of wound infection	31%	15%	<0.001
Mean (SD) number of postoperative complications	1.55 (1.4)	0.56 (1.0)	<0.001
Mortality	7%	1%	<0.001

* IQR denotes interquartile range, and SD standard deviation

Patients ranged in age from 16 to 94 years with a mean age of 64 (standard deviation [SD], 14.0) years. Patients younger than 40 years comprised 4.8% of cases and those aged above 70 and 80 years accounted for 39% and 11% of the cases, respectively. Approximately 71% of surgeries were non-emergency procedures. All of the colorectal, hepatectomy, and head and neck surgeries were performed for cancer; overall 79% of the procedures addressed malignancy. The remaining surgeries were vascular procedures or thyroid resections that proved non-malignant.

The Figure summarises the proportion of patients in each subspecialty who received donor blood during and after surgery. In total, 62 (8.7%) of the non-cardiac surgical patients received an intra-operative blood transfusion. By contrast, 50% of cardiac surgical patients received blood during their surgery. For the subspecialties, the point prevalence of intra-operative transfusion was: colorectal 5.5%, head and neck 1.7%, liver disease 8.1%, thyroid 0%, and vascular 35.6%. Postoperative blood transfusion was noted in 10% of non-cardiac patients and in 29.5% following cardiac procedures. When considered by subspecialty, 14.5% of colorectal, 7.1% of hepatectomy, 5.8% of head and neck, 3.4% of vascular, and 2.4% of thyroid patients received a blood transfusion in the postoperative period.

As can be seen from Table 1, transfused patients were significantly older and sicker, more likely to be male, had lower haemoglobin values, and had longer and more emergency surgical procedures. The only type of surgery associated with receipt of a transfusion was vascular (r=0.191; P<0.001). Table 2 shows that transfused patients demonstrated significantly more adverse surgical outcomes and longer hospital stay than those not transfused.

Propensity scoring in non-cardiac patients identified low levels of preoperative haemoglobin, male gender, and American Society of Anesthesiologists (ASA) grading greater than 2 as being significant preoperative predictors of a peri-operative blood transfusion. The propensity score equation was $1 / (1 + e^{-z})$ where z=0.843 – 0.294 (preoperative haemoglobin level) + 0.846 (male) + 0.652 (ASA grading >2). The presence of diabetes, a high body mass index, and a history of smoking were not significantly associated with having received a blood transfusion.

Regression analyses for individual outcomes are shown in Table 3. Receipt of a blood transfusion was predictive of the duration of the postoperative hospitalisation and of the number of complications before discharge. The amount of transfused blood was predictive of in-hospital mortality, with an odds ratio (OR) of 1.4 for each unit of blood received. The risk of a surgical wound infection was almost doubled when the patient had received a blood transfusion.

Discussion

This study has shown that older, male patients with significant multi-system disease were more at risk of receiving a blood transfusion than others. After controlling for the factors associated with an increased likelihood of receiving donor blood, transfusion in non-cardiac patients was significantly associated with a slower and more eventful recovery.

These findings provide a benchmark of transfusion practice for the various subspecialties within our department. Teams are now well placed to collect real-time transfusion data that quantify which blood product was used, at what time-point in the peri-operative process, how many units were used, and the storage age of the blood. Whilst these variables appear straight forward, we observed that documentation of the use of one or more of six possible blood products, presented in non-uniform quantities by a cross-section of professionals, was problematic. Standardisation and documentation of transfusion details are necessary before the practice can be fully evaluated.

The issue of transfusion is complex and considerations will vary according to clinical presentation and procedural details. Whilst each surgical team can respond specifically, attention should be directed at the findings from our propensity analysis. The only modifiable predictor of peri-operative transfusion in our non-cardiac population was a low preoperative haemoglobin value. This variable is open to interpretation with some clinicians considering a haemoglobin level of 75 g/L to be acceptable whilst others might transfuse at 100 g/L. Furthermore, in some situations, such as emergency vascular surgery, it is impossible to impact haemoglobin levels until after surgical repair of bleeding vessels. The fact that each additional 1 unit of transfusion carries a nearly 1.5-time risk for death whilst in hospital warrants close attention. Clear guidelines for each specialty could be useful for new or junior team members, allow transparency of practice, and provide a safeguard for patients.

Data from this study demonstrated that transfused non-cardiac surgical patients were likely to experience one more complication during their recovery and to stay in hospital 4.1 days longer than those not transfused. The low level of variance we were able to explain for length of hospital stay (ie R^2 of only 13.6%) denotes that other variables not identified in this study are of equal or greater importance to the speed of recovery. Such factors as destination after discharge can artificially extend the apparent hospital stay. A patient who lives alone may stay longer before being safely discharged than an individual returning to a family.

Surgical site infection has previously been reported to be associated with intra-operative blood transfusion, with the infection rate increasing incrementally with each unit of blood transfused.[7,11-16] This adverse effect was greater if the blood had been in storage for 21 days or more.[12] The numbers

TABLE 3. Regression analyses of outcome variables: (a) postoperative duration of hospital stay, (b) morbidity during hospitalisation, (c) wound infection, (d) number of postoperative complications, and (e) in-hospital mortality
ASA denotes American Society of Anesthesiologists, HCT haematocrit, OR odds ratio, and CI confidence interval

(a) Postoperative duration of hospital stay

Variable	β	P value
Constant	1.019	0.568
Emergency	3.004	<0.001
Age	0.095	0.001
ASA grading >2	3.989	0.001
Transfusion (binary)	4.086	0.002
R^2	0.136	

Other variables included in the regression: male gender, smoking history, surgery duration, blood loss, transfusion amount, and transfusion propensity score

(b) Morbidity during hospitalisation

Variable	β	P value	OR	95% CI
Constant	-2.169	0.240		
Age	0.034	0.000	1.035	1.018-1.052
Emergency	0.829	0.000	2.291	1.476-3.555
ASA grading >2	1.048	0.015	2.851	1.229-6.616
Diabetes	0.500	0.041	1.649	1.020-2.665

Other variables included in the regression: male gender, preoperative haemoglobin level, preoperative HCT level, malignancy, surgery duration, intra-operative complications, blood loss, transfusion (binary), transfusion amount, and transfusion propensity score

(c) Wound infection

Variable	β	P value	OR	95% CI
Constant	-2.573	0.000		
Emergency	0.647	0.011	1.910	1.163-3.136
Transfusion (binary)	0.649	0.024	1.915	1.087-3.371
Colorectal	0.765	0.065	2.150	0.952-4.853
ASA grading >2	0.502	0.072	1.652	0.957-2.853

Other variables included in the regression: age, preoperative HCT level, blood loss, amount transfused, and transfusion propensity score

(d) Number of postoperative complications

Variable	β	P value
Constant	0.750	0.360
Age	0.013	<0.001
Emergency	0.476	<0.001
Transfusion (binary)	0.968	<0.001
Diabetes	0.378	0.002
Transfusion amount	0.066	0.013
R^2	0.258	

Other variables included in the regression: male gender, ASA grading >2, preoperative haemoglobin level, preoperative HCT level, malignancy, blood loss, and transfusion propensity score

(e) In-hospital mortality

Variable	β	P value	OR	95% CI
Constant	-11.304	0.002		
Transfusion amount	0.332	0.031	1.394	1.031-1.886
Age	0.094	0.052	1.098	0.999-1.207

Other variables included in the regression: male gender, emergency, malignancy, ASA grading >2, blood loss, transfusion (binary), and transfusion propensity score of patients in our study were too small to allow comparison of transfusion risk when blood was given during surgery versus in the postoperative phase. One would need to recalculate separate propensity scores in order to identify at which time-point transfusion was more problematic.

Thus, we were restricted to showing that transfused patients had a 1.9 times greater risk of developing a post-surgical wound infection than those not transfused. Numerous variables contribute to infections, for example, appropriate peri-operative antibiotic cover, clean or contaminated surgical procedures, aseptic techniques, glycaemic dysfunction and immune system integrity. Since our data sets did not contain all these items for each subspecialty, the regression model presented does not fully explain the variance in wound infection.

Each surgical subspecialty has unique secondary endpoints and markers of recovery. Accordingly, we acknowledge a limitation of this study that the number of outcome variables which could be combined across a heterogeneous population was limited. Our process of prospective comprehensive real-time outcome data collection is maturing and once cohorts within each specialty are sizeable enough to support analysis, disease-specific investigation of transfusion effects will be conducted.

The value of this study lies in surgical teams scrutinising their own transfusion practices and ensuring that there are clear documenting requirements to facilitate audit of current practice, along with adequate work-up options for patients with a high propensity for receiving a transfusion. Guidelines favouring a restrictive rather than inclusive blood transfusion strategy should be considered.

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