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ORIGINAL ARTICLE

CARDIAC GENERAL

Blood transfusion after on-pump coronary artery bypass grafting: focus on modifiable risk factors†

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Abstract

OBJECTIVES: Perioperative transfusions are known to increase morbidity and mortality after coronary artery bypass grafting (CABG). The aims of the study were (1) to identify the clinical profile of the patient subset at highest risk from transfusion and (2) to disclose causative relationship and dose-dependency of transfusion on hospital mortality.

METHODS: A prospective observational design was employed on a cohort of 1047 consecutive patients (median age 63.2 ± 9.3, 18.8% female, 30.6% diabetics, 31.9% urgent/emergent, 15.3% with low preoperative left ventricular ejection fraction (LVEF)) who underwent on-pump isolated CABG between January 2004 and December 2007. Univariate and multivariate regression analysis and *post-hoc* risk stratification, by means of propensity scoring and binary segmentation, were adopted.

RESULTS: The following independent risk factors were identified: age, body surface area (BSA), preoperative glomerular filtration rate, preoperative haemoglobin, surgical priority, length of cardiopulmonary bypass, intraoperative haemodilution and early postoperative blood loss. The patient population was stratified in quintiles of transfusional risk, by means of propensity scoring. As to modifiable risk factors, patients in the highest quintiles of risk were those with BSA (< 1.73, preoperative haemoglobin < 12 g/dl, intraoperative haemoglobin < 8.0 g/dl and those undergoing cardiopulmonary bypass > 90). Binary segmentation was performed to avoid any association between red cell transfusion and worse outcomes being causative and dose-dependent. A dose-dependent pattern was disclosed, with patients receiving > 5 units being at highest risk.

CONCLUSIONS: High exposure to blood transfusions may be prevented by preoperative patient stratification and by the close tailoring of management strategies on planning and implementing surgical timing, as well as by cardiopulmonary bypass technique.

Keywords: CABG • Transfusion • Outcomes

INTRODUCTION

Perioperative allogenic blood transfusion is a much-debated practice in the context of myocardial surgical revascularization. Though beneficial to correct low oxygen delivery conditions, it implies several well-known drawbacks [1].

Despite the continuous implementation of guidelines, there is clearly a diffuse lack of acceptance of these recommendations, mainly due to logistical issues, institutional dogma and economic considerations [2]. Perioperative transfusional practice in cardiac surgery is indeed highly heterogeneous, ranging from 50% to 100%, implying that many of these transfusions may have been unnecessary [3].

As authoritatively reported by Ranucci *et al.*, optimization of both red blood cell (RBC) mass and physiological anaemia tolerance and minimization of blood loss constitute the pillars of the newly-developed concept of patient blood management. The factors that guide the decision making in blood management still need to be adequately addressed to resolve whether they should, in fact, influence transfusion decisions [4].

As part of our hospital's continuous quality improvement program, we performed an observational cohort study, designed to survey blood transfusion practice and its effects on outcomes in coronary artery bypass grafting procedures.

METHODS

Study setting and patient sample

The study was conducted at the Department of Cardiothoracic and Respiratory Sciences of the Second University of Naples,

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located in the V. Monaldi Hospital, an affiliated teaching hospital. At our institution, nearly 700 patients annually undergo cardiac surgery and are admitted to a dedicated 12-bed postoperative intensive care unit (ICU). Our hospital operates a continuous quality improvement program structured into a surveillance phase (collection, from individual departments, of data on outcomes and complications) and an intervention phase (modifications of protocols and practices). In our department, information on all operated patients is collected daily, using standardized case report forms. All clinical perioperative data (including demographics, laboratory tests, nature of surgery, blood product transfusions, re-exploration, postoperative complications and lengths of stay in the intensive care unit and in the hospital) are collected routinely. Data are entered into a computer database covering 100 variables, programmed to accept only matching double-entry data falling within pre-specified ranges. All queries are resolved by referring to the patients' original records. Out of 1323 consecutive patients undergoing CABG between January 2004 and December 2007, the study sample comprised of 1047 patients who received no preoperative transfusion and underwent on-pump procedures.

Study design and aims

The present observational study was conceived to identify preoperative and intraoperative patient characteristics predicting a higher risk of RBC transfusion in isolated CABG, in order to reveal factors or practices which might be modified. Having previously found transfusions to be among the factors associated with adverse outcomes of CABG operations, we now aimed to study causative relationships and dose-dependency of transfusions on hospital mortality [5, 6]. The research protocol was approved by the local Ethics and Research Committee, which waived the need for informed consent.

Surgical and clinical care

All procedures were performed by the same three senior surgeons throughout the study period. Details of surgical strategy and postoperative care are extensively reported elsewhere [5–7]. Aprotinin was never used for bleeding prevention, since it is not approved in Italy. Tranexamic acid was given preoperatively to patients on dual anti-platelet therapy (a bolus dose of 15 mg/kg i.v. before surgery, followed by 10 mg/kg/h intraoperative infusion, 2 mg/kg added to the pump prime). Heparinization was managed throughout the operation by both heparin blood level and activated coagulation time (ACT) monitoring. The heparin loading dose was 300–400 IU/kg with a target ACT of at least 400 s. Given the lack of definite scientific evidence supporting the use of cell savers and the inherent cost of the devices in our centre, an intraoperative autologous blood salvage method was used only in patients with preoperative anaemia or ongoing dual anti-platelet therapy [4]. A specific perioperative transfusion algorithm was applied: patients received two packed red cells units before cardiopulmonary bypass (CPB) whenever the preoperative haematocrit value was below 30% and they received two or more packed red cells units during CPB in case of excessive haemodilution (haematocrit value below 22%). After CPB, the patients received packed red cells in order to maintain a haematocrit value greater than 25%. This target value was increased according to clinical condition—specifically to haemodynamic status, need for inotropic support and the age of the patient. Fresh frozen plasma was not used before the patient reached the ICU. Platelets were usually not transfused, except in patients reaching the operating room under a full dose of ticlopidine or clopidogrel and demonstrating severe postoperative bleeding. Such protocol complies largely with those adopted in major centres carrying out these procedures. Severe bleeding was defined as follows: i) drainage of more than 500 ml during the 1st h, ii) more than 400 ml during each of the first 2 h, iii) more than 300 ml during each of the first 3 h, or iv) more than 1000 ml in total in the first 4 h.

Baseline data and clinical outcomes

All definitions were established as part of the original study design. The incidence of cardiac surgery-associated acute kidney injury (CSA-AKI) was investigated according to 'risk injury failure loss end-stage kidney disease' (RIFLE) criteria [8]. The change in kidney function was based on plasma creatinine concentration and defined as the difference between baseline concentration and the highest concentration during the stay in ICU.

Preoperative glomerular filtration rate (GFR) and nadir GFR during ICU stay were calculated with the Modification of Diet in Renal Disease equation:

$$\text{estimated GFR} = 186 \times \text{plasma creatinine level [in mg/dl]}^{-1.154} \times (\text{age [in years]})^{-0.203}$$

For women, the product of this equation was multiplied by a correction factor of 0.742 [9]. Cardiac morbidity was defined as the occurrence of myocardial infarction and/or heart failure. The diagnosis of myocardial infarction required either the development of new Q-waves, or new persistent ST-segment or T-wave changes associated with an elevation of CK-MB isoenzyme values, or autopsy evidence of acute myocardial infarction. The diagnosis of heart failure required either the use of a ventricular assist device or the use of continuous inotropic support for at least 24 h. Intra-aortic balloon-pump (IABP) usage was considered as a variable *per se*, rather than as a criterion for heart failure definition, since it was also implanted in cases of refractory angina or high-risk arrhythmia without pump deficit. Deep sternal wound infections were defined according to Cardiac Diagnostic Centre criteria as described previously [7]. Respiratory complications were defined as mechanical ventilation > 48 h and/or need for tracheotomy. Fatality (hospital mortality) was defined as any death occurring after surgery and during the index hospitalization.

Statistical analysis

Bivariate analysis (using the $\chi 2$ statistic for categorical variables and the '*t*-test' or Wilcoxon sum-rank test for normally and non-normally distributed continuous variables, respectively) was used to identify significant preoperative and intraoperative factors associated with transfusion requirements in the general surgical population, using as dependent variable a dichotomous variable reflecting the prevalence of transfused patients. Transfusion practice to which risk factors were correlated, was defined as the transfusion of two or more units of red cells. Variables that were

not linearly related were also mathematically transformed, categorized along appropriate cut points or converted into multiple dichotomous variables. The logistical fit of each continuous variable was examined and dichotomization was performed by choosing, as a cutoff, the value that indicated a transfusional risk greater than the median risk of the overall population. A propensity score for the likelihood of receiving RBC transfusion was calculated for each patient using multivariable logistic regression with forward selection. Only significant variables at bivariate analysis ($P \leq 0.05$) were included in the model. A good predictive performance (area under the receiving-operator curve = 0.86, 95% CI 0.83–0.88) was demonstrated for the model, as shown in Figure 1. The propensity score was divided in quintiles of risk and the resulting five groups of patients were compared in terms of outcomes and clinical characteristics. Bivariate analysis was used for measurement of outcomes. Finally, binary segmentation analysis through a classification tree was employed to assess causality and the dose-response relationship of transfusions on hospital mortality. Along with EuroSCORE-derived determinants of death, a dummy dichotomous variable was generated, reflecting the total incidence of postoperative complications that necessitated transfusional practice. Such a dummy variable was forced at the first step of the analysis in order to reduce the collinearity between i) the drawbacks of the critical clinical profiles triggering transfusion and ii) drawbacks of transfusion *per se*. Data are expressed as mean ± SD for continuous variables and as percentages for categorical variables. All statistical analyses were performed with SPSS 17.0 software (SPSS Inc, Chicago, Ill).

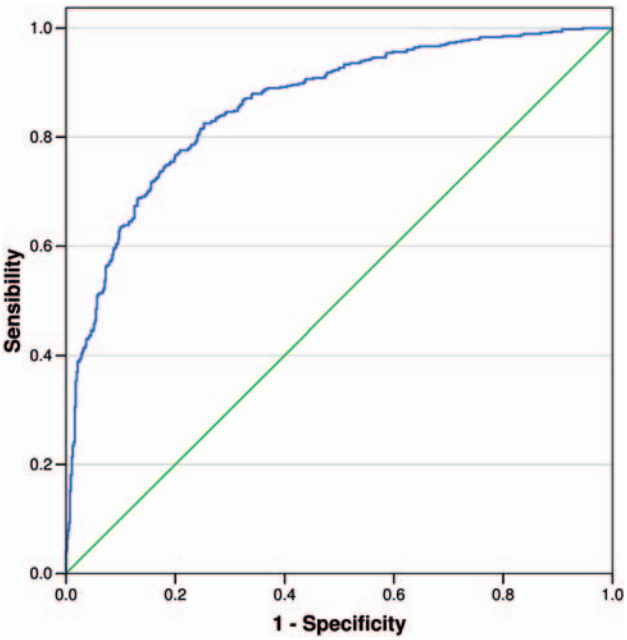

Figure 1: Receiving-operator curve (ROC) of the Logistic model for blood transfusion. AUC = 0.86 (95%CI 0.83–0.88).

RESULTS

Study samples features

Study sample features are reported in Tables 1–3 along with results of univariate analysis for transfusion predictors. Transfusion of ≥2 RBC units was performed in 45.9% of the patients with a mean of 2.5 ± 2.9 RBC units per patients. In particular, 37.4% of the transfused patients received 2 units; 18.1%, 3 units; 16%, 4 units; 8.1%, 5 units and 20.4%, >5 units.

Predictors of RBC transfusion at multivariate analysis

Independent predictors are reported in Table 4.

Patient stratifications in quintiles according to propensity score

Table 5 reports features of patients after resampling in quintiles of risk through propensity score. Table 6 reports outcomes in these quintiles. Patients in the highest quintile were those who were transfused with 52.2% of all RBC units. Hospital mortality (RR = 15.3) and morbidity (acute kidney injury [RR = 8.3], respiratory complications [RR = 9] and cardiac complications [RR = 44])

Table 1: Preoperative Characteristics

Baseline characteristics	Study population (n = 1047)	Non-transfused (n = 566)	Transfused (n = 481)	P
Age (years)	63.2 ± 9.3	60.9 ± 8.8	65.9 ± 9.4	<0.0001
Body Surface Area (m^2)	1.84 ± 0.16	1.9 ± 0.15	1.79 ± 0.15	<0.0001
Female Sex (%)	18.8%	9%	30.4%	<0.0001
Diabetes mellitus (type I or II) (%)	30.6%	30%	31.2%	0.513
Hypertension (%)	70.1%	69.8%	70.5%	0.80
COPD (%)	13.7%	12.7%	14.8%	0.34
Hypercholesterolemia (%)	41.4%	41.5%	41.4%	0.65
LVEF < 35% (%)	15.3%	13.4%	17.5%	0.07
Preoperative haemoglobin (mean ± SD; g/dl)	13.4 ± 1.7	14.1 ± 1.3	12.6 ± 1.8	<0.001
Baseline eGFR (ml/min/1.73 m^2)	79.6 ± 23	84 ± 21	74.5 ± 23	<0.0001
Preoperative medications (%)				
Warfarin (within 5 d of surgery)	0.7%	0.4%	1%	0.17
Acetylsalicylic acid (within 5 d of surgery)	45.2%	44.8%	45.6%	0.79
Clopidogrel (within 5 d of surgery)	14.2%	13.5%	15.1%	0.46

Table 2: Surgical and Perioperative Hb/Hct variables

Surgical and perioperative Hb/Hct variables	Study population (n = 1047)	Non transfused (n = 566)	Transfused (n = 481)	P
Emergent surgery (%)	7.4%	4.6%	10.6%	<0.001
Urgent surgery (%)	24.5%	20.3%	29.5%	<0.001
Redo surgery (%)	1.0%	0.9%	1%	0.80
Distal anastomosis n°	2.66 ± 0.84	2.6 ± 0.8	2.8 ± 0.8	<0.0001
CPB duration (min)	83.9 ± 33.2	77.2 ± 27.6	91.8 ± 37.5	<0.0001
Aortic × clamp duration (min)	44.9 ± 20.2	42.3 ± 18.2	48.1 ± 22	<0.0001
Indexed CPB flow (L min^{-1} m^{-2})	2.37 ± 0.2	2.4 ± 0.23	2.4 ± 0.17	0.44
Hb, preoperative (g/dl)	13.42 ± 1.69	14 ± 1.3	12.6 ± 1.8	<0.0001
Hb, lowest during CPB (g/dl)	8.8 ± 1.3	9.4 ± 1.1	8.1 ± 1.1	<0.0001
DO_2, lowest during CPB (ml min^{-1} m^{-2})	297.6 ± 49	315 ± 46	276 ± 42	<0.0001
Chest drains (ml/24 h)	720 ± 363	660 ± 267	790 ± 440	<0.0001
Resternotomy for bleeding (%)	2.4%	0%	5.2%	0.0001

Table 3: Outcomes

Outcomes	Study population (n = 1047)	Non transfused (n = 566)	Transfused (n = 481)	P
Cardiac Complications (%)	7.3%	2.8%	12.5%	<0.0001
Peak eGFR (ml/min/1.73 m^2)	64.2 ± 31.6	68.9 ± 17	58.8 ± 42	<0.0001
AKI 50%	5.4%	1.2%	10.4%	<0.0001
CVVH (%)	3.4%	0.4%	7.1%	<0.0001
Prolonged ventilation (>24 h) (%)	3.2%	1.2%	5.6%	<0.0001
Stroke (%)	1.9%	0.9%	3.1%	0.008
Deep sternal wound infection (%)	1.5%	1.6%	1.5%	0.86
ICU stay (days)	3.2 ± 3.9	2.5 ± 1.4	4.2 ± 5.5	<0.0001
Hospital stay (days)	8.07 ± 4.7	7.2 ± 2.5	9.1 ± 6.4	<0.0001
Hospital death (%)	3.9%	0.5%	7.9%	<0.0001

AKI: Acute Kidney Injury with eGFR loss>50%.
CVVH: continuous veno-venous haemofiltration.

Table 4: Determinants of transfusion

Transfusion	β	OR	95% CI	P
Age	0.021	1.02	1.001–1.041	0.035
BSA	−2.6	0.08	0.024–0.24	<0.0001
Baseline eGFR	−0.013	0.99	0.98–0.99	0.002
Emergent surgery	1.01	2.76	1.46–5.2	0.002
Urgent surgery	0.57	1.78	1.2–2.6	0.004
CPB duration	0.014	1.01	1.01–1.02	<0.0001
Hb, preoperative (g/dl)	−0.42	0.66	0.58–0.74	<0.0001
Hb, lowest during CPB(g/dl)	−0.70	0.50	0.42–0.59	<0.0001
Chest drains (ml/24 h)	0.002	1.002	1.002–1.003	<0.0001

significantly increased in the highest quintile of risk, with strong a correlation with the extent of transfusional requirements.

Binary segmentation

Figure 2 reports results of binary segmentation through classification tree on hospital mortality. The disclosed association of RBC transfusion with fatality may be qualified as a causality relationship with a dose-dependent pattern.

DISCUSSION

Optimization of patient blood management in the CABG context requires identification of predictors of blood loss and transfusion

Table 5: Stratification in quintiles through propensity score

	1st Quintile (210 pts)	2nd Quintile (209 pts)	3rd Quintile (209 pts)	4th Quintile (210 pts)	5th Quintile (209 pts)	*P*
Age	55.7 ± 8	61.7 ± 8	63.8 ± 8	66.4 ± 8.5	68.4 ± 8.9	<0.0001
BSA	1.99 ± 0.14	1.87 ± 0.13	1.83 ± 0.12	1.78 ± 0.12	1.73 ± 0.15	<0.0001
Baseline eGFR	89.8 ± 24	84.6 ± 17	80 ± 20	75.7 ± 22	67.9 ± 24	<0.0001
Emergent surgery	2.4%	2.4%	6.2%	10%	15.8%	<0.0001
Urgent surgery	14.8%	23.9%	26.3%	21.9%	35.9%	<0.0001
CPB duration	69.4 ± 22	77 ± 28	83 ± 30	88 ± 32	101 ± 41	<0.0001
Hb, preoperative (g/dl)	14.4 ± 1.3	14 ± 1.3	13.4 ± 1.5	12.9 ± 1.7	12.3 ± 1.6	<0.0001
Hb, lowest on-pump (g/dl)	10.2 ± 0.9	9.3 ± 0.8	8.7 ± 0.9	8.2 ± 1	7.6 ± 1	<0.0001
Chest Drains (ml/24 h)	630 ± 233	651 ± 226	700 ± 281	756 ± 350	863 ± 565	<0.0001

Table 6: Outcomes according to propensity score quintiles

	1st Quintile (210 pts)	2nd Quintile (209 pts)	3rd Quintile (209 pts)	4th Quintile (210 pts)	5th Quintile (209 pts)	*P*
Overall Blood Units	0.32 ± 0.9 (95% CI 0.2–0.45)	0.72 ± 1.3 (95% CI 0.55–0.9)	1.4 ± 1.6 (95% CI 1.2–1.6)	2.45 ± 1.9 (95% CI 2.18–2.71)	5.35 ± 4.1 (95% CI 4.8–5.9)	<0.0001
Intraoperative Blood Units	0.07 ± 0.41 (95% CI 0.02–0.13)	0.13 ± 0.5 (95% CI 0.06–0.2)	0.42 ± 0.95 (95% CI 0.3–0.55)	1.0 ± 1.3 (95% CI 0.84–1.2)	2.4 ± 2.0 (95% CI 2.1–2.7)	<0.0001
FFP Units	0.6 ± 1.5 (95% CI 0.4–0.8)	0.8 ± 2.2 (95% CI 0.5–1.1)	1.2 ± 2.3 (95% CI 0.9–1.5)	1.6 ± 2.6 (95% CI 1.2–1.9)	3.6 ± 5.2 (95% CI 2.9–4.3)	<0.0001
PLT Units	0.8 ± 2.3 (95% CI 0.5–1.1)	0.9 ± 2.7 (95% CI 0.5–1.3)	1.2 ± 2.7 (95% CI 0.8–1.6)	1.7 ± 3.3 (95% CI 1.3–2.1)	3.4 ± 6.6 (95% CI 2.5–4.3)	<0.0001
Hospital mortality	0%	0.5%	1.9%	1.9%	15.3%	<0.0001
AKI 50%	1.9%	0.5%	3.8%	5.2%	15.8%	<0.0001
CVVH	0%	0%	1.9%	1.4%	13.9%	<0.0001
Cardiac Compl.	0.5%	3.8%	4.8%	5.2%	22%	<0.0001
IABP	0.5%	1.9%	6.2%	9.5%	26.3%	<0.0001
Pulmon. Compl.	1%	0.5%	1.4%	4.3%	9.1%	<0.0001
Stroke	0%	0.5%	1.9%	2.9%	4.3%	0.008

requirements, aiming to create tailored preoperative management algorithms. In order to derive clinical parameters that might be extrapolated and useful to the international heart surgery community, appropriate model-building standards have to be employed in the study design. As reported by Shehata and associates [10], standards affecting quality of the studies in this field are:

(1) Appropriate, fully characterized study sample (size, isolated vs combined surgical procedures, primary vs redo, mixed surgical priority)
(2) Clear definition of transfusion practice to which risk factors were correlated (i.e. overall blood products vs red cell only transfusions, along with any transfusion vs a pre-specified cut-off units value)
(3) Study design (retrospective vs prospective data collection)
(4) Unbiased, controlled inclusion of all preoperative, intraoperative and postoperative data that are known to date, to influence transfusional practice
(5) Full elucidation of the principles of surgical and perioperative care, with accurate details on adherence to institutional transfusion algorithms and 'guidelines'
(6) Validated definition of outcomes events
(7) Adoption of multiple *ad hoc* statistical tools in order to both rule out independent predictors of transfusions and to study the effects of such practice on outcomes, overcoming the confounding effects of those critical states that simultaneously signal red cell administration and directly affect target events.

The present prospective single-centre observational trial aimed to reveal preoperative predictors of packed red cell transfusions through regression logistic analysis. Eight predictors emerged: age, body surface area, preoperative glomerular filtration rate, preoperative haemoglobin, surgical priority, length of cardiopulmonary bypass, intraoperative haemodilution and early postoperative blood loss. Propensity matching for red cell transfusion allowed stratification of patient population in quintile of risks. Patients in the highest quintile of risk—a subset that accounted for more than 50% of overall blood usage (1118 units out of 2142 assigned)—were those who also experienced the highest rates of postoperative complications. In order to eliminate the possibility that any significant statistical association between red cell transfusion and worse outcomes was causative—and in case a dose-response pattern might be implied—a binary segmentation analysis through classification tree was performed. A dose

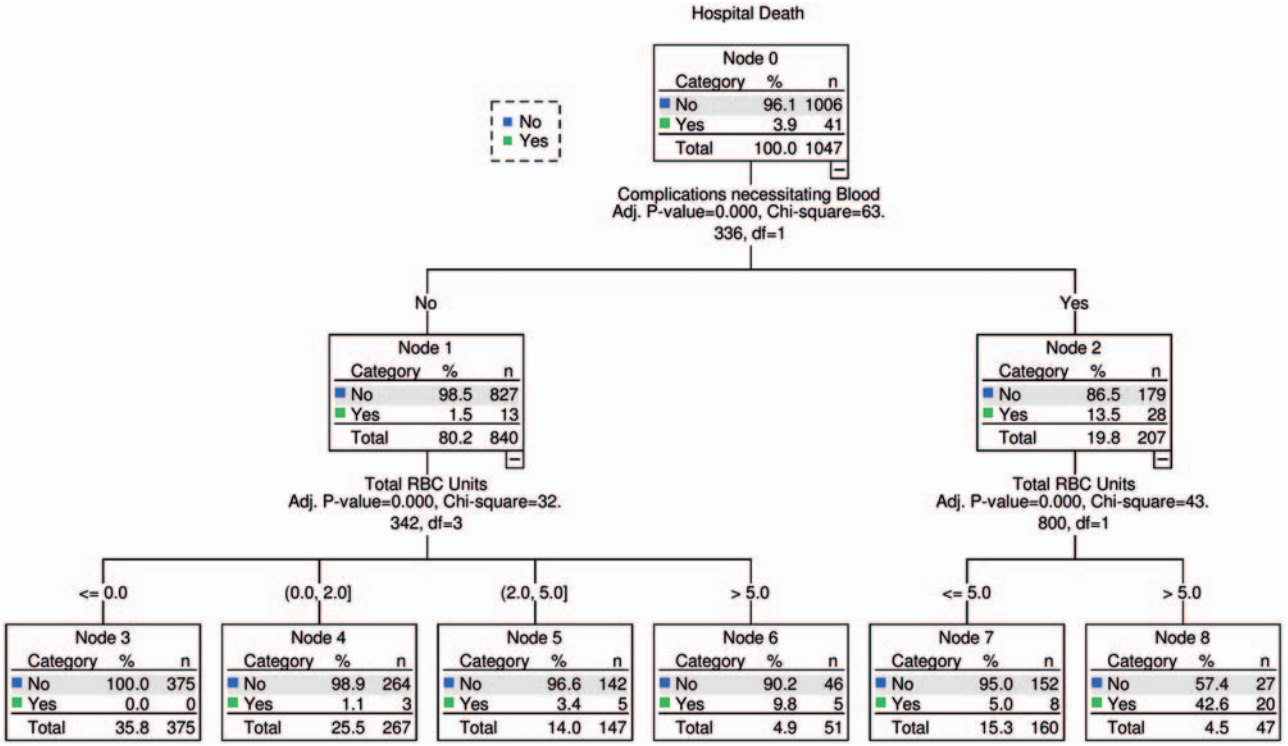

Figure 2: Binary logistic analysis for hospital death.

response pattern emerged, irrespective of the complexity of the postoperative course, with transfusion of more than five red cell units as the strongest predictor. With regard to results of the regression analysis on transfusion predictors, this study adds to the literature evidence as recently reviewed [4, 10]. Three predictors deserve brief consideration: age, baseline estimated GFR and preoperative anaemia that, to a variable extent, are frequently clustered together. Published data support the notion that older patients and those with comorbidity are transfused more frequently: whether they are more likely to develop complications associated with anaemia as opposed to transfusion is far from clear. A significant association of anaemia with increased perioperative and long-term morbidity and mortality has been reported in cardiac surgery [6, 11]. Whether anaemia is a risk factor for adverse outcomes or a marker of disease remains unaddressed and the present study is unable to support any further evidence. Causes of preoperative anaemia should be routinely investigated, at least in elective cases, even though the implementation of pharmacological interventions to increase red cell mass remains poorly addressed. Indeed, the use of preoperative erythropoietin plus iron, given several days before cardiac operation, as suggested by recently-released guidelines, must be considered 'off label' and incompletely studied. The potential for thrombotic complications in patients with unstable angina—and economic considerations—significantly limits the clinical relevance of such an approach. Similarly, uncertainty persists over how to maximize the benefits of CABG in patients with chronic kidney disease (CKD) because perioperative mortality and morbidity strictly relate to the CKD stage; but long-term outcomes in hospital survivors are favourable [12, 13]. Since CKD is known to impair erythrocytosis, is associated with preoperative anaemia and may increase risks of postoperative bleeding, transfusion thresholds and requirements are likely to differ in this patient subset. These observations certainly portend specific blood management algorithms but also indicate the need for better preoperative risk-stratification of CKD patients prior to CABG, as advocated by Charytan and associates [13]. Indeed, patients with the highest predicted risk of mortality should be better treated by medical therapy. Clustering of BSA with intraoperative haemoglobin concentration, length of cardiopulmonary bypass and, to some extent, with early postoperative blood loss strongly advocates the implementation and widespread adoption of 'mini-CPB', that is, associated with a 60% reduction in blood transfusion [14]. Larger trials are warranted but such an approach should be implemented, at least in the high-risk patients' subset.

Finally, as far as the causality relationship linking blood transfusion to fatality is concerned, binary segmentation analysis in this study foretells of such a pattern. Elucidation of the mechanism by which red blood cell units result in organ injury is still an area of uncertainty and a topic for further study.

Study overview

Several study limitations should be considered for a thorough data interpretation. First the single-centre setting, though guaranteeing a uniform process of care with special emphasis on transfusion triggers, closely reflects the influence of specific standards of clinical practice and a unique patient population, which may have led to one-sided results not readily transferable to other patient populations. However, in this study the inclusion of all consecutive patients admitted for CABG surgery, prospective data-mining through the hospital's quality assurance program and correctness of statistical tools in balancing for 'confounders' make results objective and transferable.

The present cohort includes both 'redo' and high-priority procedures that, given their peculiar risk profile, are often excluded by other studies on this topic. Inclusion of these subsets is intended to reproduce a real-world setting and has enhanced the chances of extrapolating these findings to other experiences. There is some evidence that the relationship between transfusion and adverse outcomes is affected by donor blood processing (leukodepletion) and storage duration [4, 15]. Our study lacks any information about length of RBC storage. Hints on the effects of leukodepletion have been reported by these authors elsewhere [9].

CONCLUSIONS

The need for RBC transfusion in isolated CABG can be predicted preoperatively. Patient stratification can help in identifying the patient subsets more worthy of being targeted by management modifications and close tailoring of preventive strategies may reduce blood transfusion. The relation of transfusional practice to adverse events appears causative and dose-dependent in both high- and low-risk CABG patients.

Conflict of interest: none declared.

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APPENDIX. CONFERENCE DISCUSSION

Dr I. Modrau *(Arhus, Denmark)*: I have two questions for you. The first question is that many of the risk factors you identified in your study were well-known from the STS guidelines. Surprisingly, you couldn't confirm aspirin and clopidogrel to be independent risk factors for transfusion. Do you have any explanation for that?

Secondly, in your title you focus on modifiable risk factors for blood transfusion. In the conclusion of your article, it's the main message that patient stratification and tailoring of the surgical treatment could prevent excess blood transfusion in your patients. I could not find this issue addressed in your article, neither in the methods nor in the results. I would like to ask what allows you to draw this conclusion.

Dr De Santo: As to the first question, we found no impact of clopidogrel or aspirin. It is our routine practice to not refrain from aspirin in patients that are undergoing CABG surgery. All the patients are usually on aspirin in daily practice today and we ask for 5 days weaning off from clopidogrel. And when you operate on patients that are weaned off—with the aid of thromboelastography intraoperatively and postoperatively—usually you do not have problem.

As to the modification, if you have patient characteristics that you can't modify because they belong to the clinical presentation, what you can modify is the way that you stratify your patients and the way you try to treat them. There is no one dressing fitting all the patients. After this study, we moved to different management strategies. Sicker patients are treated with less invasive CPB techniques and most of the patients have been shifted to OPCAB [off-pump coronary artery bypass] surgery. Also, we have tried to implement perioperative strategies to improve renal function because this is one of the main aspects. What leaves us unsatisfied is the treatment of perioperative anaemia. We had different causes of perioperative anaemia in our series. We had perioperative anaemia due to chronic disease, which is strictly related to older age and renal impairment. And we also had blood loss during catheterization for the coronary artery evaluations. But most of the patients in the fifth quintile of risk were urgent or emergent—nearly 50%—so we were not able to do anything in this setting.

In the other patients, we tried to improve the red blood cell mass before the operation. But this is not completely satisfactory in our experience, because you can't safely use erythropoietin which may cause thrombosis in this subset of patients. So we are just trying iron supplement and other kinds of medication and wait for the operation. The modification is not on the patients; the patient has his own features. The modification is in the way you can look at the patient, perioperatively stratify the risk of the patient, and address the operation. You have to be flexible.

Dr M. Uva *(Lisbon, Portugal)*: And how do you address that?

Dr De Santo: As I said, we have been looking at reducing the amount of priming and using retrograde priming. And in the latest experience we are also using mini-CPB and we have considerably increased the number of patients done off-pump.

Dr R. Arora *(Winnipeg, MB, Canada)*: You've highlighted the risk factors, as others have in the past, with the addition of propensity analysis. However, at the end of the day we know who is at risk but we still don't know the reasons why they're transfused. We don't really know what the individual practices are when they got to the ICU or the postoperative environment that may

influence transfusion. And I think that's the issue with what is missing in most of these studies that have been done in the past; we can identify who but we don't know the reasons why. And I think that's something, as we move forward as a group, where we have to have a better understanding. What are the therapeutic endpoints we're trying to achieve with blood transfusions? So the preoperative risks are one factor but don't necessarily tell the whole story. Do you have any comments in that regard?

Dr De Santo: I didn't get your question, sorry.

Dr Arora: You've identified the risk factors but not why we're transfusing them. We know what the risks are but we don't know why we're transfusing them. Someone has a low BSA or an urgent status: what therapeutic endpoint are we trying to achieve by transfusing them? How does that affect patient outcome? And that's the second half of the equation we don't know yet.

Dr De Santo: I'm sorry, I didn't get it. But if you refer to the transfusion algorithm...

Dr Arora: I'll try again. A question that was asked in the earlier talk was, what was the trigger for transfusion? So the similar thing is, we know the risk factors but we don't really know why we're transfusing. What's the trigger? Is it simply a number? And what is the clinical endpoint of that number? What effect does that create?

Dr Uva: 'What is the aim of transfusion?' in other words.

Dr Arora: Correct. So we know the risks, but what are we trying to achieve by transfusing?

Dr De Santo: It is not always based on numbers. When you set an algorithm for transfusion, you set the parameters that have to be in your mind and trigger your transfusion. But the final decision on transfusion is not only based on numbers but also on the status of the patient, the oxygen delivery of the patient. You may control this under the CPB, but you may also control this during the first day in the ICU with invasive measures, even though there is no evidence in the literature that oxygen delivery, rather the haemoglobin parameters, may better prescribe transfusion. So this is a tricky argument. Because even though you have a fixed algorithm, anyhow there is room to allow for a medical judgment because is not just a bell and you prompt the transfusion.