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Original Article

Associations between preoperative anaemia and hospital costs following major abdominal surgery: cohort study

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Abstract

Background: Determining the cost-effectiveness and sustainability of patient blood management programmes relies on quantifying the economic burden of preoperative anaemia. This retrospective cohort study aimed to evaluate the hospital costs attributable to preoperative anaemia in patients undergoing major abdominal surgery.

Methods: Patients who underwent major abdominal surgery between 2010 and 2018 were included. The association between preoperative patient haemoglobin (Hb) concentration and hospital costs was evaluated by curve estimation based on the least-square method. The in-hospital cost of index admission was calculated using an activity-based costing methodology. Multivariable regression analysis and propensity score matching were used to estimate the effects of Hb concentration on variables related directly to hospital costs.

Results: A total of 1286 patients were included. The median overall cost was US $18 476 (i.q.r.13 784–27 880), and 568 patients (44.2 per cent) had a Hb level below 13.0 g/dl. Patients with a preoperative Hb level below 9.0 g/dl had total hospital costs that were 50.6 (95 per cent c.i. 14.1 to 98.9) per cent higher than those for patients with a preoperative Hb level of 9.0–13.0 g/dl ($P < 0.001$), 72.5 (30.6 to 128.0) per cent higher than costs for patients with a Hb concentration of 13.1–15.0 g/dl ($P < 0.001$), and 62.4 (21.8 to 116.7) per cent higher than those for patients with a Hb level greater than 15.0 g/dl ($P < 0.001$). Multivariable general linear modelling showed that packed red blood cell (PRBC) transfusions were a principal cost driver in patients with a Hb concentration below 9.0 g/dl.

Conclusion: Patients with the lowest Hb concentration incurred the highest hospital costs, which were strongly associated with increased PRBC transfusions. Costs and possible complications may be decreased by treating preoperative anaemia, particularly more severe anaemia.

Introduction

Preoperative anaemia is independently associated with an increased risk of postoperative morbidity and mortality as well as greater healthcare expenditure[1–3]. This increased risk generates a substantial health burden by increasing the requirement for allogeneic packed red blood cell (PRBC) transfusion, the need for ICU admission, and the duration of hospital stay[1,4,5]. To mitigate these effects, multidisciplinary perioperative patient blood management programmes have been developed to optimize patient haemoglobin (Hb) concentration before surgery[6]. To justify the expense and prove the sustainability of such programmes, they must be cost-effective.

There are limited studies exploring the relationship between preoperative anaemia and the drivers of increased hospital costs. A deeper understanding of these associations will be of use to healthcare decision-makers in driving the pursuit of more efficient preoperative care for patients with anaemia, and improving the use of financial, logistical, and workforce resources. Therefore, to address this knowledge gap, a detailed cost analysis of patients with preoperative anaemia undergoing major abdominal surgery was conducted. The hypothesis was that increasing severity of preoperative anaemia would be associated independently with adverse patient outcomes and higher total hospital costs.

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Methods

After ethics approval had been obtained (20/Austin/04), a single-centre, retrospective cohort study was undertaken using data from an Australian university hospital. Cost and outcome data were collected from the financial costing and medical records of patients undergoing major abdominal surgery between July 2010 and June 2018. The study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12620000177954).

Three types of subspecialty procedures were selected *a priori*, each of which is associated with significant patient morbidity: pancreatoduodenectomy[7], major colorectal resection[8,9], and liver resection[10]. Adult patients aged 18 years or more, who underwent surgery lasting more than 2 h and who required at least one overnight hospital stay were included.

Primary outcome

The primary outcome was the association between total hospital costs and preoperative anaemia. Costs were estimated by examining the relationship between Hb concentration and total hospital costs, and by investigating the association between such costs and four Hb categories: less than 9.0, 9.0–13.0, 13.1–15.0, and more than 15.0 g/dl.

Secondary outcomes

Relationships between Hb level and prespecified hospital cost drivers that directly influence hospital costs were also assessed. These drivers included duration of operation, allogeneic PRBC transfusion, number of PRBC units transfused, number of patients admitted to ICU after surgery, duration of ICU admission for patients requiring intensive care, duration of hospital stay, readmission within 30 days after discharge, costs incurred during readmission within 30 days after discharge, development of complications, number of complications per patient, and severity of complication. All patients underwent preoperative optimization of Hb and blood glucose levels according to national management guidelines[6,11]. All operations were performed by consultant hepatobiliary–pancreatic and colorectal surgeons.

Definitions

Preoperative anaemia was prespecified using a non-gendered definition of Hb level below13.0 g/dl. This definition encompasses both the WHO definition of anaemia for men (Hb below 13.0 g/dl)[12,13] and borderline anaemia for women (Hb less than 13.0 g/dl), which has been reported to be physiologically suboptimal in this population[14–16] and is associated with increased duration of hospital stay, fewer days alive out of hospital, and an increased incidence of complications following surgery[17].

Definitions of postoperative complications followed European Perioperative Clinical Outcomes definitions[18]. Complications were graded using the Clavien–Dindo classification system[19]. Patients were stratified by their most severe complication and by the total number of complications recorded. Duration of hospital stay was calculated as the number of days between completion of surgery and hospital discharge. Readmissions were defined as any unplanned admission within 30 days after discharge.

Data collected

Demographic data collected included: age, sex, BMI, ASA classification[20], Charlson Co-morbidity Index (CCI) score[21], principal diagnosis, presence of malignancy, and history of chemotherapy within the 3 months before surgery. Preoperative laboratory results collected included: Hb, serum creatinine, bilirubin and albumin concentrations, and estimated glomerular filtration rate (eGFR). Perioperative data collected included: type of surgery, emergency operation schedule, duration of operation, concomitant procedures, and duration of ICU admission. Clinical variables included: counts of allogeneic intraoperative and postoperative PRBC transfusion, number of surgical complications, and severity of complications. All data were obtained from the hospital clinical information system (Cerner®; Cerner Systems, Kansas City, Missouri, USA).

Costs were calculated from the day of index operation until the day of discharge. Raw costing data were obtained from the institution's clinical informatics and costing centre. Hospital costs were calculated using an activity-based costing methodology. All costs were adjusted to 30 June 2019 values based on the Australian end of fiscal quarter consumer price index, as reported by the Australian Tax Office[22]. Costs were then converted to US dollars (US $) based on the market rate on 30 June 2019[23]. All dollar values shown in this study are in US $.

Statistical analysis

For statistical analysis, SPSS® for Windows® version 23.0 (IBM, Armonk, New York, USA) and R version 3.5.2 (R Development Core Team, Vienna, Austria) were used. Data were coded with numerical values, and names of variables were encrypted to blind the variables' characteristics to the statistician. Data are presented as mean(s.d.), median (i.q.r.) or the number of patients with percentage for descriptive statistics. Estimated values are described with 95 per cent confidence intervals. Statistical results are shown with *P* values and corresponding effect sizes. Two-sided $P < 0.050$ was considered statistically significant.

Before statistical analysis, normality was assessed for continuous variables using a normal quantile–quantile plot. For skewed distributions, transformation using logarithmic or exponential scales was applied, and normality was re-evaluated. If normality was violated after transformation, non-parametric statistical methods were applied for that variable. Extreme values were identified based on 1.5-fold of the interquartile range and then compared with the original values from the data source. If any extreme value could not be reconciled by interrogating the clinical notes and context of the value, they were replaced using the Winsorization method.

Variables with a missing rate of greater than 5 per cent were identified and evaluated to determine whether the missing values occurred at random. In such cases, the multiple imputation method was planned using the mice and missMDA packages in R[24,25]. Otherwise, statistical analysis was undertaken as a complete-case analysis. Parametric statistical methods were used only for continuous numerical variables that satisfied the normality assumption; otherwise, non-parametric methods were applied. For parametric statistical purposes, the homogeneity of variance assumption was also evaluated if required.

Statistical analysis was conducted in three stages. First, the unadjusted relationship between Hb concentration and hospital cost was investigated. For crude visualization of the relationship between Hb level and hospital costs, curve estimation based on the least-square method was evaluated for linear, quadratic, and cubic models. According to the curve-fit results and physiologically accepted criteria, Hb concentration was divided into the four prespecified categories described above. ANOVA was used to confirm hospital cost differences between the four Hb categories.

Second, the factors related to Hb concentration and hospital cost were identified among patient factors and hospital cost drivers using correlation analysis. Patient factors that correlated

significantly with hospital cost were reserved for the independent variables of a multiple linear regression analysis, and hospital cost drivers correlating with Hb level were reserved for dependent variables of a multivariable general linear model.

Finally, the adjusted hospital cost drivers that were affected by Hb concentration were characterized. This step was performed in the following order: identification of patient factors that were related causally to hospital cost; creation of matched data based on these factors; and confirmation of the adjusted effect of Hb level on cost drivers with the matched data. Multiple linear regression analysis was used to sort the factors, among patient factors, related to hospital cost.

A stepwise selection method was applied to determine the relevant regression coefficient for multiple linear regression modelling. All categorical variables with more than three levels were transformed into dummy variables. Residuals were evaluated by means of the Durbin–Watson statistical test and standardized residual plots, including all partial plots. Pearson's correlation coefficient (r) with 95 per cent confidence intervals, collinearity diagnostics with the condition index and variance proportion, and variance inflation factor were used to assess collinearity between the selected variables. A constant was included during estimation to compensate for the unknown effect. To enhance the robustness of estimates, bootstrapping was applied to the final regression model with 1000 bootstrap samples, and the simple random sampling method was applied to estimate the 95 per cent confidence interval of percentile type.

The matched data were constructed with propensity scores to obtain the adjusted effect of Hb concentration on hospital cost drivers. For propensity score matching, the nearest-neighbour matching without the caliper method was applied. Hb concentration was used as a dependent variable for estimating the propensity score. Patient factors selected in the final multiple linear regression model were used as independent variables, given that they could directly affect the drivers of total hospital cost. Matched quality was assessed using standardized differences with a criterion of 0.1, a propensity score distribution graph, and a standardized differences density plot check. Using matched data, the adjusted effects of Hb concentration on the drivers of total hospital cost were evaluated using a multivariable general linear model. For multivariable general linear modelling, the multivariable normal distribution assumption was tested using the mshapiro.test function in the mvnormtest package in R[26]. Box's M test was used to test the homogeneity of co-variance matrices. Multicollinearity was tested with Pearson's correlation analysis between dependent variables.

Results

There were 1314 eligible patients; 28 were excluded owing to incorrect surgical procedure or duplication of data, leaving 1286 patients for statistical analysis (*Fig. 1*).

Extreme outliers were observed in the following variables: duration of hospital stay (3.5 per cent of data), duration of ICU admission (4.0 per cent), serum creatinine concentration (1.4 per cent), total bilirubin concentration (2.1 per cent), operating time (4.6 per cent), and total hospital cost (8.2 per cent). All values were justified with appropriate clinical reasons, and no values were replaced. The variables were treated with log transformation or categorized as described below.

There were four variables with missing values exceeding 5 per cent. These were serum bilirubin (23.6 per cent), albumin (18.6 per cent), and creatinine (6.8 per cent) concentrations, and eGFR (17.9 per cent). These laboratory tests were not performed as there was no clinical indication to necessitate these as part of standard clinical care. Missing patterns for the missing variables were evaluated with t tests, which established that these missing data occurred at random; accordingly, missing values were imputed as planned. After imputation, the quality of imputation was found to be adequate upon cross-validation. After checking for outliers, testing missing values and testing for normality, log transformation was applied to the following variables: operating time, duration of stay, duration of ICU admission, and costs incurred during readmission within 30 days after discharge. ASA classification, and serum creatinine, bilirubin and albumin concentrations were categorized into two levels. Demographic data and a summary of all data collected are shown in *Table 1*. Overall, the Hb concentration was below 13.0 g/dl in 568 patients and 13.0 g/dl or more in 718 patients.

Primary outcome

The unadjusted relationship between Hb concentration and total hospital cost is shown in *Fig. 2a*. The relationship between hospital cost and Hb concentration was different in patients with a level below 13.0 g/dl compared with those with level of 13.0 g/dl or higher. Hospital costs increased as Hb concentration decreased for patients with a level below 13.0 g/dl, but increased as Hb concentration increased in patients with a level of 13.0 g/dl or more (quadratic model: $R^2 = 0.022$, $F(2,1283) = 14.744$, $P < 0.001$). The median overall cost per patient was $18 476 (i.q.r. 13 784–27 880). It was $26 486 (21 116–49 960) for a haemoglobin concentration below 9.0 g/dl, $19 906 (14 031–31 124) for 9.0–13.0 g/dl, $17 137 (12 889–25 196) for 13.0–15.0 g/dl, and $17 722 (13 902–25 548) for over 15.0 g/dl ($F(3, 1282) = 11.508$, $P < 0.001$, $\eta^2 = 0.026$). For patients with a haemoglobin concentration below 9.0 g/dl, total hospital costs were 50.6 (95 per cent c.i. 14.1 to 98.9) per cent higher than those for patients with a Hb level of 9.0–13.0 g/dl ($P < 0.001$), 72.5 (30.6 to 128.0) per cent higher than those for patients with a Hb level of 13.0–15.0 g/dl ($P < 0.001$), and 62.4 (21.8 to 116.7) per cent higher than costs among patients with a Hb level exceeding 15.0 g/dl ($P < 0.001$) (*Fig. 2b*).

Secondary outcomes

According to the fitted curve (*Fig. 2a*), the lowest hospital cost in the log scale was close to 13.0 g/dl Hb. With this intuitive information, the secondary outcomes analysis was performed based on the demarcation of Hb concentration below 13.0 *versus* 13.0 g/dl and above.

Patients with a haemoglobin concentration below 13.0 g/dl

Overall, 568 patients had a Hb level below 13.0 g/dl. A number of associations were observed between patient factors (*Table 2*) and total hospital cost drivers (*Table 3*) and Hb concentration. Of these, PRBC transfusion requirement and the number of PRBC units transfused were significantly associated with both Hb and total hospital cost. A moderate correlation was observed between total hospital costs and both allogeneic transfusions (Spearman's $\rho = 0.471$, $P < 0.001$) and units of PRBC transfused (Pearson's $r = 0.618$, $P < 0.001$). Duration of ICU admission (Pearson's $r = 0.706$, $P < 0.001$), number of complications per patient (Pearson's $r = 0.647$, $P < 0.001$), severity of complications according to the Clavien–Dindo classification (Spearman's $\rho = 0.608$, $P < 0.001$), ASA classification (Spearman's $\rho = 0.230$, $P < 0.001$), and hypoalbuminaemia (Spearman's $\rho = 0.211$, $P < 0.001$) correlated weakly to moderately with hospital costs.

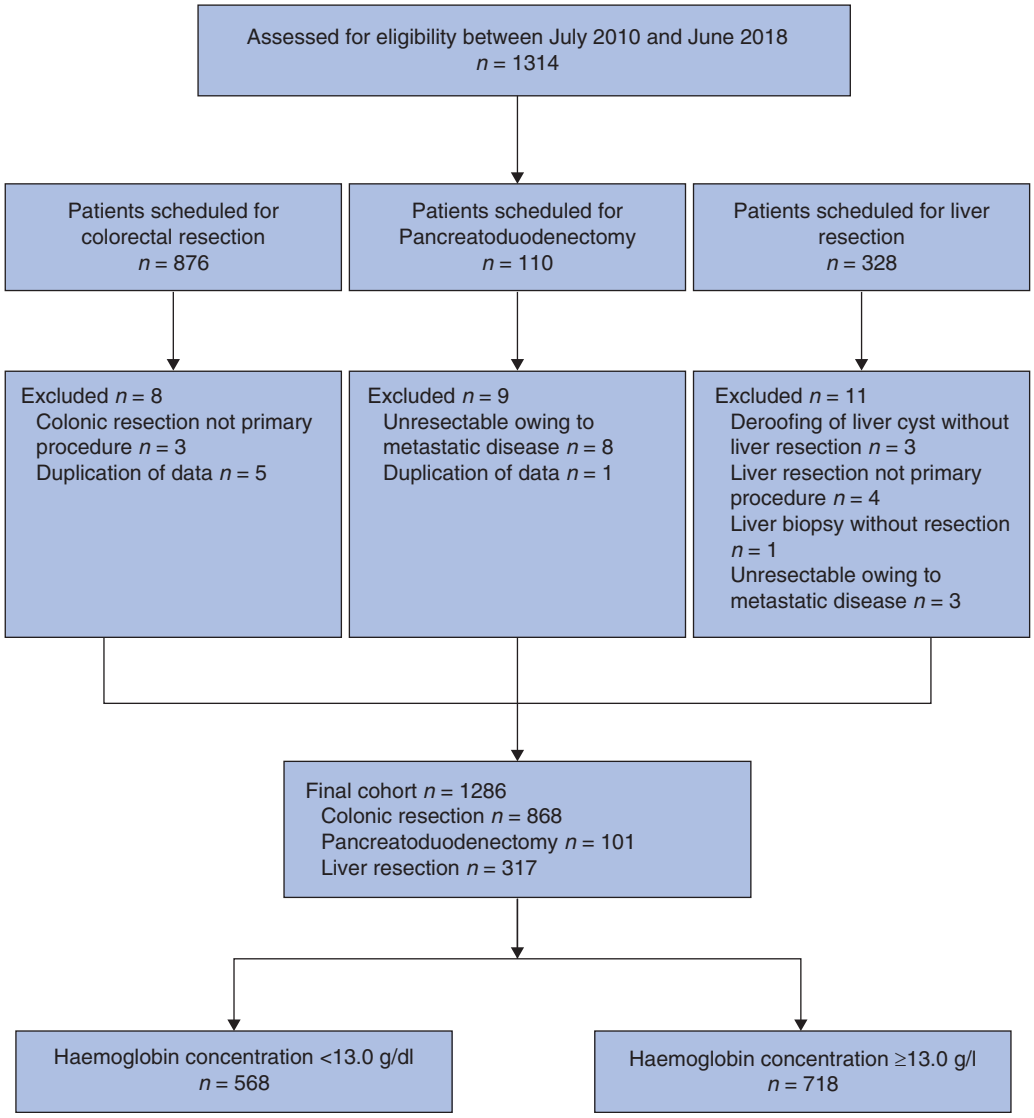

Fig. 1 Study flow diagram

All these variables were also statistically correlated with Hb concentration, but did not achieve a statistically significant linear relationship.

Total hospital costs were 50.6 (95 per cent c.i. 14.1 to 98.9) per cent higher in patients with a Hb concentration less than 9.0 g/dl compared with patients with a level of 9.0–13.0 g/dl ($P < 0.001$). The highest total hospital costs occurred in patients who underwent pancreatic surgery. These patients incurred a 95 (65 to 137) per cent increase in hospital costs compared with those undergoing other types of operation ($P < 0.001$). The second highest hospital costs occurred in patients with a Hb level below 9.0 g/dl. For these patients, total hospital costs increased by 31 (5 to 66) per cent compared with those for patients with a level of 9.0 g/dl or higher ($P = 0.024$). ASA grade greater than II, increased serum creatinine concentration, hypoalbuminaemia, and emergency surgery were other factors associated with higher hospital costs, increasing them by 25 (14 to 37) per cent ($P < 0.001$), 18 (4 to 34) per cent ($P = 0.006$), 16 (5 to 28) per cent ($P = 0.004$), and 13 (2 to 28) per cent ($P = 0.025$) respectively.

There was a significant association between costs and operating time, number of PRBC transfusions, duration of ICU admission, duration of hospital stay, cost incurred during readmission, and the number and severity of complications as a group, in relation to Hb concentration (Hb 9.0–13.0 *versus* less than 9.0 g/dl: $F(7, 60) = 2.199$, $P = 0.047$, partial $\eta^2 = 0.204$, for propensity score-matched data) (*Fig. 3*). Among these, the number of PRBC units transfused was significantly influenced by Hb level ($F(1, 566) = 48.244$, $P < 0.001$, partial $\eta^2 = 0.079$) (*Fig. 3b*).

Patients with a haemoglobin concentration of 13.0 g/dl and higher

Overall, 718 patients had a Hb concentration of 13.0 g/dl or higher. Associations between patient factors and total hospital cost drivers, and Hb and total hospital cost are shown in *Tables 2* and *3* respectively. Duration of hospital stay (Pearson's $r = 0.718$, $P < 0.001$), number of complications per patient (Spearman's $\rho = 0.621$, $P < 0.001$), operating time (Pearson's $r = 0.526$, $P < 0.001$), and duration of ICU admission (Pearson's $r = 0.510$, $P < 0.001$) correlated moderately with total hospital cost. Among these variables that correlated with total hospital costs, none had a significant relationship with Hb concentration. Sex correlated significantly with Hb level (Spearman's $\rho = -0.269$, $P < 0.001$), and CCI score with both Hb concentration exceeding 15.0 g/dl (Spearman's $\rho = -0.093$, $P = 0.013$) and total hospital cost

Table 1 Demographic, biochemical, and clinical data for patients undergoing surgery

	No. of patients* (*n* = 1286)
Age (years)†	63.0 (14.3)
Sex ratio (M : F)	693 : 593
BMI (kg/m^2)†	27.3(5.6)
ASA physical status classification	
I–II	548 (42.6)
III–V	738 (57.4)
Charlson Co-morbidity Index score‡	6 (4–8)
Haemoglobin (g/dl)†	13.10 (1.97)
Preoperative anaemia	568 (44.2)
Increased creatinine (> 110 μmol/l for men, > 90 μmol/l for women)	156 (12.1)
Hypoalbuminaemia (< 35 g/l)	443 (34.4)
Type of surgery	
Colorectal	868 (67.5)
Liver	317 (24.7)
Pancreatic	101 (7.9)
Emergency operation	270 (21.0)
Operating time (min)‡	268 (204–338)
Allogeneic PRBC transfusion	237 (18.4)
Amount of PRBCs in patients who received transfusion during admission (units)‡	2.0 (1.0–4.0; 1–30)
No. of patients with postoperative ICU admission	564 (43.9)
Duration of ICU admission for patients requiring ICU (h)‡	18 (14–45)
Duration of hospital stay (days)‡	8 (6–13)
Readmission within 30 days after discharge	180 (14.0)
Costs incurred during readmission (US $)‡	5993 (2365–13 037)
No. of patients who experienced a complication	918 (71.4)
No. of complications per patient‡	1 (0–3)
No. of complications for patients experiencing a complication	2 (1–4)
Clavien–Dindo classification of complications	
I	288 (22.4)
II	420 (32.7)
II	72 (5.6)
IV	113 (8.8)
V	25 (1.9)

* With percentages in parentheses unless indicated otherwise; values are †mean(s.d.) and ‡median (i.q.r.; range). PRBC, packed red blood cell.

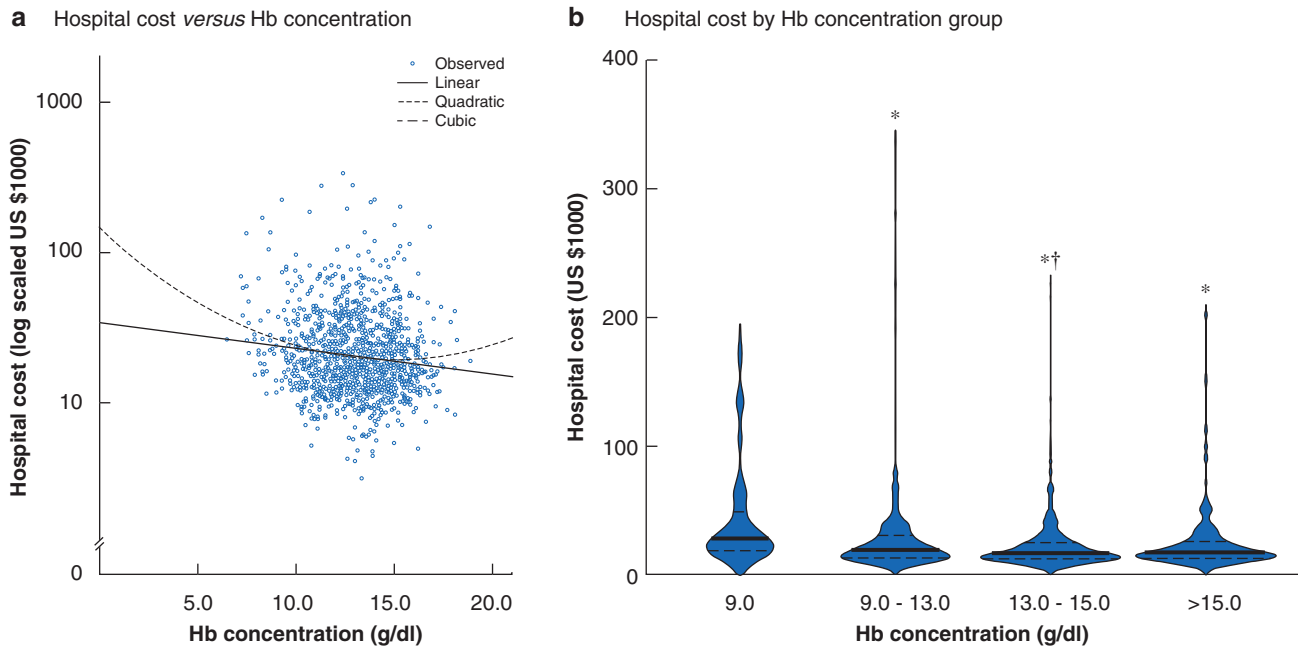

Fig. 2 Relationship between unadjusted hospital cost and haemoglobin concentration

a Curve-fit modelling of hospital cost *versus* haemoglobin (Hb) concentration with quadratic model. $R^2 = 0.022$, $F(2,1283) = 14.744$, $P < 0.001$; estimated model: log costs = 0.004 × $(Hb)^2$ + –0.119 × Hb + 5.167 ($P = 0.001$, $P = 0.003$, $P<0.001$ for the coefficients of $(Hb)^2$,Hb and constant). **b** Total hospital costs for each prespecified level of Hb. Data are presented as median and interquartile range. Data are presented as median (solid line) and interquartile range (dashed line). The width of each curve indicates the approximated data frequency in the corresponding region. *$P <$ 0.050 *versus* below 9.0 g/dl, †$P <$ 0.050 *versus* 9.0–13.0 g/dl (ANOVA with log-transformed hospital cost ($F(3,1282) = 11.508$, $P <$ 0.001, $\eta^2 = 0.026$).

Table 2 Correlation analysis between patient factors and haemoglobin concentration and total hospital costs

	No. of patients	Hb concentration		Total hospital costs	
		Coefficient	P	Coefficient	P
Age (years)					
Hb < 13.0 g/dl	568	–0.004	0.917	0.001	0.974
Hb ≥ 13.0 g/dl	718	–0.068	0.071	0.105	0.005
Sex (F)					
Hb < 13.0 g/dl	568	–0.037	0.376	–0.044	0.295
Hb ≥ 13.0 g/dl	718	–0.269	< 0.001	–0.052	0.166
BMI (kg/m^2)					
Hb < 13.0 g/dl	568	–0.057	0.176	–0.010	0.811
Hb ≥ 13.0 g/dl	718	0.027	0.467	0.028	0.461
ASA (I–II, III–V)					
Hb < 13.0 g/dl	568	0.119	0.004	0.230	< 0.001
Hb ≥ 13.0 g/dl	718	–0.004	0.919	0.200	< 0.001
Charlson Co-morbidity Index					
Hb < 13.0 g/dl	568	0.026	0.534	–0.004	0.920
Hb ≥ 13.0 g/dl	718	–0.093	0.013	0.108	0.004
Hb concentration					
Hb < 13.0 g/dl	568	–	–	0.147	< 0.001
Hb ≥ 13.0 g/dl	718	–	–	0.046	0.219
Increased creatinine concentration*					
Hb < 13.0 g/dl	568	0.128	0.002	0.126	0.003
Hb ≥ 13.0 g/dl	718	–0.078	0.036	0.007	0.846
Hypoalbuminaemia†					
Hb < 13.0 g/dl	568	0.146	< 0.001	0.211	< 0.001
Hb ≥ 13.0 g/dl	718	–0.073	0.052	0.106	0.005
Type of surgery (colorectal/liver/pancreatic resection)					
Hb < 13.0 g/dl	568	–0.078	0.063	0.177	< 0.001
Hb ≥ 13.0 g/dl	718	0.017	0.641	0.227	< 0.001
Emergency operation					
Hb < 13.0 g/dl	568	0.108	0.01	0.141	0.001
Hb ≥ 13.0 g/dl	718	–0.016	0.663	–0.039	0.298

* Above 110 μmol/l for men, above 90 μmol/l for women. †Below 35 g/l. Coefficient, correlation coefficient; Hb, haemoglobin. Pearson's correlation analysis was used for continuous variables, and Spearman's rank correlation analysis for categorical variables.

(Pearson's $r = 0.108$, $P = 0.004$); however, the relationships were not linear.

The median hospital cost per patient was $17 137 (i.q.r. 12 889–25 196) for those with a Hb concentration of 13.0–15.0 g/dl and $17 722 (13 902–25 548) for those with a level exceeding 15.0 g/dl (effect size 6.2 (95 per cent c.i. –6.0 to 20.3) per cent; $P = 1.000$). Among patient factors that correlated with hospital cost, the most significant risk factor for higher hospital costs was pancreatic resection, which increased total hospital costs by 114.8 (95 per cent c.i. 79.5 to 156.4) per cent ($P < 0.001$). A Hb level exceeding 15.0 g/dl increased costs by 9.6 (1.4 to 18.9) per cent ($P = 0.025$). Other drivers of increased hospital costs included an ASA grade greater than II (15.3 (6.4 to 25.0) per cent; $P < 0.001$), hypoalbuminaemia (13.0 (1.6 to 28.2) per cent; $P = 0.035$) and CCI score (1.9 (0.5 to 3.0) per cent; $P = 0.013$) (*Table 3*). There were no significant effects on hospital costs observed for the set of dependent variables as a group in relation to Hb ($F(7, 705) = 0.382$, $P = 0.913$, partial $\eta^2 = 0.004$, for propensity score-matched data) (*Fig. 4*).

Discussion

Worsening anaemia was independently associated with higher hospital cost, and a significant relationship between the severity of anaemia and hospital cost was identified. Anaemic patients with a Hb concentration below 9.0 g/dl incurred the highest costs, with an increase in health expenditure of between 50.6 and 72.5 per cent. Type of surgery, higher ASA grade and CCI scores, and emergency surgery were other factors strongly correlated with an increase in total hospital costs. Moreover, Hb concentration had a significant association with several variables that were independently associated with increased costs, although these additional contributions were small. The principal driver for higher total hospital costs in patients with a Hb level below 9.0 g/dl was the cost associated with higher PRBC transfusion rates. In addition, a Hb concentration under 9.0 g/dl was independently associated with more complications per patient, a greater severity of complications, and longer duration of ICU stay and hospital stay; these factors all moderately correlated with increased total hospital costs.

Feng and colleagues[27] found that preoperative anaemia, defined as anaemia based on a haematocrit below 39.0 per cent (approximating Hb level less than 13.0 g/dl) was associated with a 14.0 per cent relative increase in total hospital cost compared with that for non-anaemic patients. In addition to anaemia, the authors reported that increases in hospital cost may also be a consequence of other cost drivers, such as longer hospital stay, poor functional status, high ASA grade, and thrombocytopaenia, rather than PRBC transfusion rates alone[27]. Gani *et al.*[28] reported that increased hospital costs were associated with men, younger age, insurance status, preoperative co-morbidity, and the development of postoperative complications. In line with these conclusions, the present study found that escalating severity of anaemia correlated independently with escalating cost.

Similar to other cost–outcome analyses[29,30], it was observed that anaemic patients were more likely to receive allogeneic PRBC transfusions, a factor independently and strongly associated with increased hospital cost. Other investigators[31] have also reported that allogeneic blood transfusions correlate strongly with increased duration of hospital stay, higher rates of

Table 3 Correlation analysis between total hospital cost drivers and Hb and total hospital costs

	Hb concentration		Total hospital costs	
	Coefficient	P	Coefficient	P
Operating time (h)				
Hb < 13.0 g/dl	–0.073	0.083	0.251	< 0.001
Hb ≥ 13.0 g/dl	–0.023	0.531	0.526	< 0.001
Allogeneic PRBC transfusion				
Hb < 13.0 g/dl	0.269	< 0.001	0.471	< 0.001
Hb ≥ 13.0 g/dl	–0.019	0.610	0.374	< 0.001
No. of PRBCs transfused				
Hb < 13.0 g/dl	0.277	< 0.001	0.618	< 0.001
Hb ≥ 13.0 g/dl	–0.019	0.617	0.438	< 0.001
No. of patients with postoperative ICU admission				
Hb < 13.0 g/dl	0.080	0.058	0.574	< 0.001
Hb ≥ 13.0 g/dl	–0.012	0.745	0.469	< 0.001
Duration of ICU admission time for patients requiring ICU (h)				
Hb < 13.0 g/dl	0.113	< 0.001	0.706	< 0.001
Hb ≥ 13.0 g/dl	–0.006	0.882	0.51	< 0.001
Duration of hospital stay (days)				
Hb < 13.0 g/dl	0.126	0.003	0.568	< 0.001
Hb ≥ 13.0 g/dl	–0.017	0.659	0.718	< 0.001
Readmission within 30 days after discharge				
Hb < 13.0 g/dl	0.036	0.398	0.249	< 0.001
Hb ≥ 13.0 g/dl	–0.046	0.214	0.219	< 0.001
Costs incurred during readmission (US $)				
Hb < 13.0 g/dl	0.042	0.317	0.251	< 0.001
Hb ≥ 13.0 g/dl	–0.040	0.287	0.232	< 0.001
Patients who experienced complication				
Hb < 13.0 g/dl	0.082	0.051	0.399	< 0.001
Hb ≥ 13.0 g/dl	–0.005	0.895	0.363	< 0.001
No. of complications per patient				
Hb < 13.0 g/dl	0.103	0.014	0.647	< 0.001
Hb ≥ 13.0 g/dl	0.007	0.854	0.621	< 0.001
Clavien–Dindo classification				
Hb < 13.0 g/dl	0.122	0.004	0.608	< 0.001
Hb ≥ 13.0 g/dl	0.038	0.310	0.489	< 0.001

Hb, haemoglobin; coefficient, correlation coefficient; PRBC, packed red blood cell. Pearson's correlation analysis was used for continuous variables, and Spearman's rank correlation analysis for categorical variables.

complications, and increased risk of death. LaPar and co-workers[32] showed that reductions in intraoperative and postoperative blood transfusions were associated with a reduced incidence of adverse postoperative events and healthcare costs.

Research has consistently demonstrated that a low Hb concentration correlates strongly with poorer patient outcomes and more complications[3,33,34], findings that are aligned with the present results. Specifically, patients who experienced a higher incidence and severity of complications imposed a greater cost on hospitals[9]; it is therefore plausible that preoperative anaemia may drive up hospital costs through increased patient complications. However, few studies have investigated the direct relationship between varying preoperative Hb level and hospital cost. In a large prospective study, Baron *et al.*[33] reported higher rates of in-hospital mortality, ICU admission, and use of ICU resources with increasing severity of anaemia; however, quantitative cost analysis of resource consumption was not performed. In a large cohort study[35], preoperative anaemia was associated with increased duration of hospital stay and higher subsequent hospital costs following elective surgery. Duration of hospital stay also correlated positively with severity of anaemia. However, the study focused exclusively on patients who underwent total knee arthroplasty, which may limit comparability with the current cohort. In a cohort of patients undergoing colorectal surgery, Leichtle and colleagues[2] showed a dose–response relationship between severity of anaemia and duration of hospital stay.

The present study highlights the financial implications of varying preoperative Hb concentration, and the findings can be used to develop cost-effective treatment protocols and up-to-date patient blood management guidelines. In this study, 44.2 per cent of patients were anaemic, a value similar to that in previous studies[1,27]. The findings provide detailed cost data that demonstrate the rising costs for patients with a Hb level below 9.0 g/dl, and support the proactive treatment of these patients to reduce total hospital costs and reduce the incidence of complications. Health economic analysis has suggested a significant saving per care episode where parenteral iron is administered before operation[36]. This recommendation is similar to that of others[37,38], who estimated that targeting a Hb concentration below 10.5 g/dl was the most cost-effective treatment approach for anaemia.

The cost-effectiveness of treating preoperative anaemia was also investigated by Calvet *et al.*[39], who demonstrated that ferric carboxymaltose, compared with iron sucrose and oral iron, was the most cost-effective treatment for iron deficiency anaemia in patients with colorectal disease. However, the study did not directly quantify the cost of hospitalization, opting instead to use predefined costs in the analysis. Consequently, surgical costs and postoperative complication costs, which are variables closely related to preoperative anaemia, were excluded from the analysis. These alternative treatments may confer an increased risk of postoperative morbidity and higher hospital costs if applied incorrectly[40].

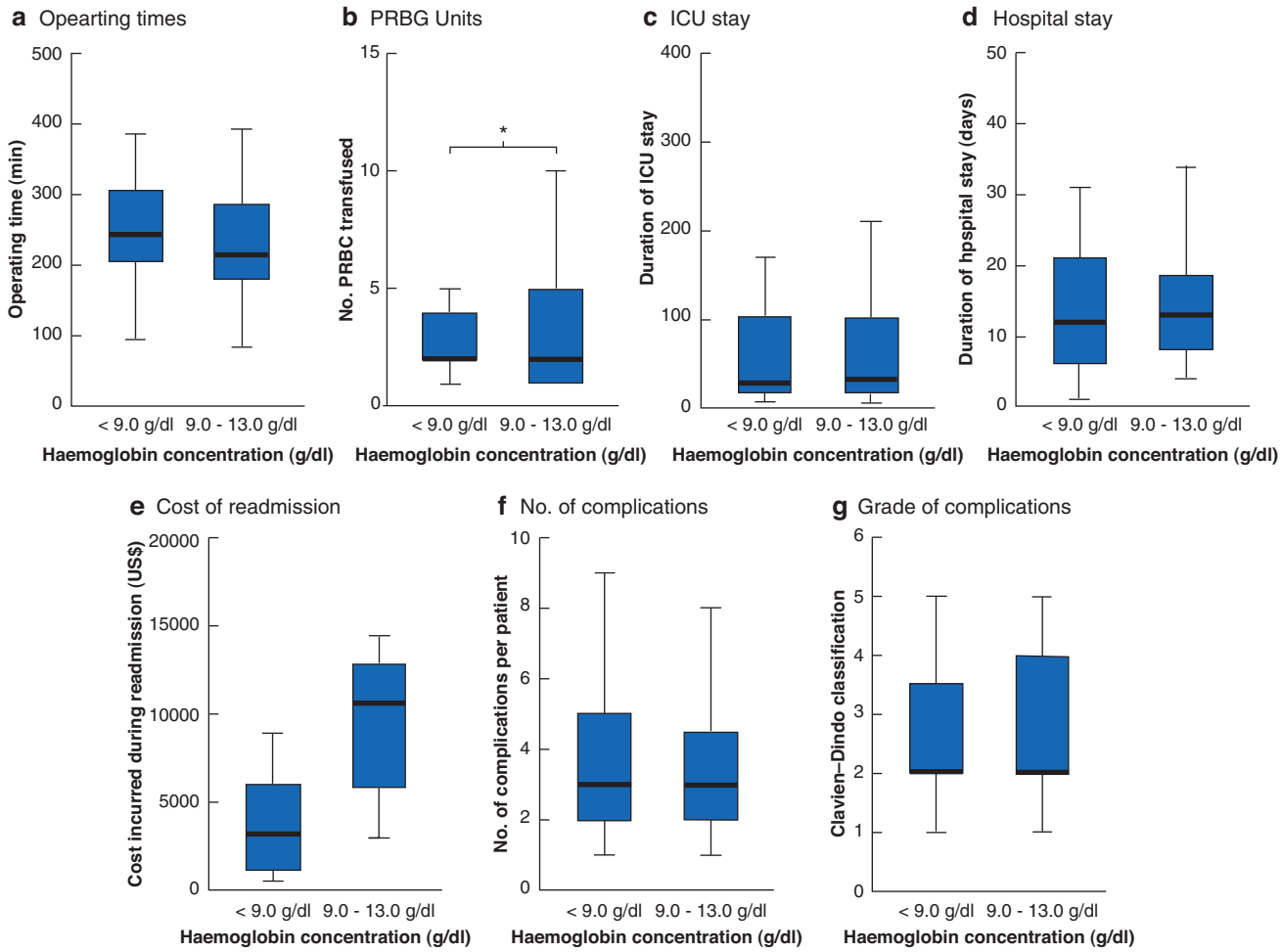

Fig. 3 Effect of haemoglobin on cost drivers in patients with a haemoglobin concentration under 13.0 g/dl

a operating time, **b** number of packed red blood cell (PRBC) units transfused, **c** duration of ICU stay, **d** duration of hospital stay, **e** cost incurred during readmission, **f** number of complications per patient, and **g** Clavien–Dindo classification. Median values (bold line), interquartile range (box), and range (error bars) are shown. All listed variables had a significant adjusted effect on cost as a group ($F(7,60) = 2.199$, $P = 0.047$, partial $\eta^2 = 0.204$ for propensity score matched data). The units of PRBC transfusion accounted the different effect of the haemoglobin concentration on cost ($F(1,566)=48.244$, $P < 0.001$, partial $\eta^2=0.079$). *: indicates $P < 0.05$ by multivariate general linear model with matched data..

The present study had several strengths. First, it was performed with a large patient sample and across three different surgical procedures, providing a robust assessment of the financial and clinical associations of preoperative anaemia across diverse patient populations. Second, by stratifying patients according to severity of anaemia, the relationship between hospital cost and Hb concentration could be evaluated. Third, the large patient sample permitted propensity score matching to adjust for a diverse set of potentially confounding variables related to the patient's status, which may have otherwise affected variables directly related to hospital cost. This allowed a more direct evaluation of the putative effect of Hb level on variables related directly to hospital cost.

The study also had some limitations. First, all patients were sampled from a single tertiary facility, which may have influenced the external validity of the results. However, much of the perioperative care is similar to that of other tertiary centres within a developed healthcare system. Second, this was a retrospective study of electronic medical records. However, the rigorous protocol applied to the collection, recording, and analysis of patient data helped to minimize the potential biases in outcomes. It was not possible to accurately quantify the cause of anaemia (such as iron deficiency anaemia *versus* anaemia of inflammation) as data regarding ferritin levels and total iron saturation were missing for over 50 per cent of patients. The independent effect of year of surgery or individual surgeons on costs was not evaluated, although this was not the intent of the study. However, all patients underwent a comprehensive enhanced recovery programme after surgery that was unchanged during the observation period; moreover, all patients were operated on by the same group of specialist surgeons throughout the entire study interval. Finally, preoperative and community-related costs were not investigated, and follow-up beyond 30 days after surgery was not conducted, which may be associated with significant economic and clinical patient outcomes.

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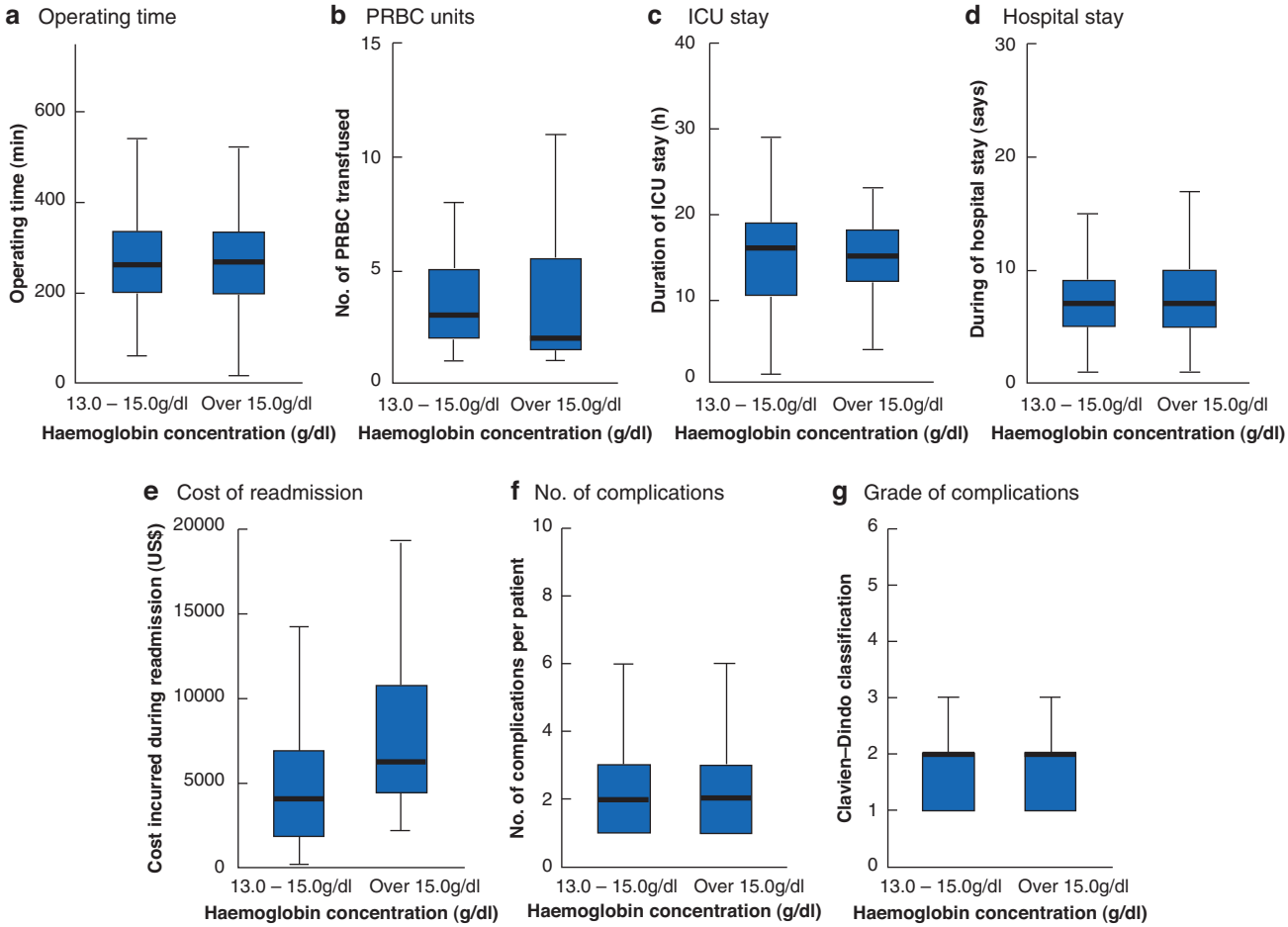

Fig. 4 Effect of haemoglobin on cost drivers in patients with a haemoglobin concentration of 13.0 g/dl and higher

a operating time, **b** number of packed red blood cells (PRBC) units transfused, **c** duration of ICU stay, **d** duration of hospital stay, **e** cost incurred during readmission, **f** number of complications per patient, and **g** Clavien–Dindo classification. Median values (bold line), interquartile range (box), and range (error bars) are shown. There was no significant adjusted effect on hospital costs ($F(7,705) = 0.382$, $P = 0.913$, partial $\eta^2 = 0.004$). Multivariate general linear modeling with matched data.

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The authors are willing to make their data, analytical methods, and study materials available to other researchers. These are available from the corresponding author on reasonable request. This research was preregistered with a statistical analysis plan (7 Jan 2020) when submitted for ethics approval (approval date 29 January 2020). The preregistered statistical analysis plan is available from the Australian New Zealand Clinical Trials Registry (https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=379040&isReview=true). There have been no changes to the statistical analysis plan.

Disclosure. The authors declare no conflict of interest financial or otherwise. Additionally, there are no potential commercial or equity conflicts of interests to declare in relation to this study.

Supplementary material

Supplementary material is available at *BJS Open* online.

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