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Preoperative haemoglobin cut-off values for the prediction of post-operative transfusion in total knee arthroplasty

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Abstract
Purpose The purpose of this study is to determine preoperative haemoglobin cut-off values that could accurately predict post-operative transfusion outcome in patients undergoing primary unilateral total knee arthroplasty (TKA). This will allow surgeons to provide selective preoperative type and screen to only patients at high risk of transfusion.
Methods A total of 1457 patients diagnosed with osteoarthritis and underwent primary unilateral TKA between January 2012 and December 2014 were retrospectively reviewed. Logistic regression analyses were applied to identify factors that could predict transfusion outcome.
Results A total of 37 patients (2.5 %) were transfused post-operatively. Univariate analysis revealed preoperative haemoglobin ($p < 0.001$), age ($p < 0.001$), preoperative haematocrit ($p < 0.001$), and preoperative creatinine ($p < 0.001$) to be significant predictors. In the multivariate analysis with patients dichotomised at 70 years of age, preoperative haemoglobin remained significant with adjusted odds ratio of 0.33. Receiver operating characteristic curve identified the preoperative haemoglobin cut-off values to be 12.4 g/dL (AUC = 0.86, sensitivity = 87.5 %, specificity = 77.2 %) and 12.1 g/dL (AUC = 0.85, sensitivity = 69.2 %, specificity = 87.1 %) for age above and below 70, respectively.
Conclusions The authors recommend preoperative haemoglobin cut-off values of 12.4 g/dL for age above 70 and 12.1 g/dL for age below 70 to be used to predict post-operative transfusion requirements in TKA. To maximise the utilisation of blood resources, the authors recommend that only patients with haemoglobin level below the cut-off should receive routine preoperative type and screen before TKA.
Level of evidence IV.

Keywords Preoperative · Haemoglobin · Total knee arthroplasty · Knee replacement · Transfusion

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Introduction

In the past, total knee arthroplasty (TKA) was associated with substantial intraoperative and post-operative blood loss [28, 29], frequently leading to allogeneic blood transfusion. However, with the advent of tranexamic acid (TXA) treatment in TKA, blood loss and transfusion rates have declined significantly over the last decade [2, 3, 11, 25, 30, 33]. With such low transfusion rates, a routine preoperative type and screen may no longer be mandatory for provision of elective primary TKA [21]. In fact, most patients who are typed and screened will not require a transfusion, which means unnecessary patient burden and costs [31, 32].

Identifying patients at risk for considerable blood loss and the need for blood transfusion is an important step towards establishing an effective blood management strategy for TKA. Several studies have indicated preoperative haemoglobin to be the strongest predictor for post-operative blood transfusion [1, 4–6, 9, 12–20, 22–24, 34], although other predictors such as age [1, 6, 9, 15, 16, 22, 34], weight [1, 12, 19, 20, 24, 34], female gender [9, 16, 34], body mass index (BMI) [9, 16, 23], preoperative creatinine [9], and American Society of Anesthesiologists (ASA) score [4, 16] may also be significant.

The purpose of this study is to determine preoperative haemoglobin cut-off values that could accurately predict post-operative transfusion outcome in patients undergoing primary unilateral TKA. This will allow surgeons to provide selective preoperative type and screen to only patients at high risk of transfusion. The authors hypothesised that there is a specific preoperative haemoglobin cut-off value that can dichotomise patients into high and low risk for transfusion.

Materials and methods

Patients diagnosed with osteoarthritis and underwent primary unilateral TKA by three adult reconstruction surgeons at a tertiary hospital between January 2012 and December 2014 were included in this study. Those who were diagnosed with inflammatory arthritis, posttraumatic arthritis, or pre-existing coagulopathy were excluded from this study. Patients who underwent bilateral TKA or any other concomitant procedure, including removal of hardware, were also excluded.

A total of 1470 patients met the study criteria and were retrospectively reviewed. Patients' factors such as preoperative haemoglobin, preoperative haematocrit, preoperative creatinine, and BMI were recorded to an accuracy of one decimal place, while age was recorded to the nearest whole number. There were 13 patients with missing preoperative haemoglobin values; therefore, they were excluded from subsequent statistical analyses. They all had no transfusion.

All surgeries were performed using the standard medial parapatellar quadriceps-splitting approach with the patella everted and under tourniquet control at 300 mmHg. The distal femur was prepared using an intramedullary rod, and an autologous bone plug was used to close the femoral medullary cavity. The proximal tibia was prepared using an extramedullary jig. All patients had cemented implants from DePuy Synthes PFC® Sigma® Knee System (Warsaw, IN, USA) or Zimmer® NexGen® Knee Replacement System (Warsaw, IN, USA). After cementing of implants but before the closure of retinaculum, all patients received topical TXA intraoperatively. No intravenous TXA was given and surgical drains were not used. The tourniquet was released after standard wound closure and bulking dressing had been applied. Postoperatively, a standard thromboembolic prophylaxis protocol was followed. Pneumatic calf pumps were given until ambulation. Subcutaneous Clexane 40 mg once daily (Sanofi, Paris, France) was given to all patients on the first post-operative day and continued until discharge from hospital.

The hospital's blood transfusion protocol was adhered to, with a haemoglobin level of less than 8.0 g/dL [7, 8, 35, 36] considered the transfusion trigger for all ages. For patients presenting with anaemic symptoms or any anaemia-related organ dysfunctions, the transfusion trigger was less than 9.0 g/dL. Allogeneic blood was used in all instances.

This study was approved by the hospital's ethics committee (CIRB: 2015/2133) and carried out in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed consent was obtained from the patients.

Statistical analysis

Statistical analysis was carried out using SPSS® 19.0 (IBM, Armonk, NY, USA). In the univariate analysis, t test was used to compare the difference in the quantitative variables between transfusion and non-transfusion groups, while Chi-square test/Fisher's exact test was used for categorical variables. Variables found to display a statistically significant relationship were included in the multivariate regression analysis. Adjusted odds ratios and 95 % confidence interval (CI) were presented. Age was further categorised at a cut-off of 70 years of age, and each dichotomous group was evaluated on the independent influence of preoperative haemoglobin on transfusion outcome. Receiver operating characteristic (ROC) curve was constructed to determine the preoperative haemoglobin cut-off values through finding a mathematical balance between sensitivity and specificity. The area under the ROC curve was calculated to quantify the performance of the model. Statistical significance was defined as a p value of ≤ 0.05.

Power analysis was done prior to the conduct of this study. The authors aimed for a moderately predictive area under the ROC curve of 0.8 to be detected under power of 0.80 and type I error of 0.05. Based on the observation of overall transfusion of 2.5 %, the minimum required sample size would be 312 wherein 8 were transfused.

Results

The final study cohort consisted of 1457 patients divided into 586 patients (40 %) with age above 70 and 871 patients (60 %) with age below 70, of which 24 patients (4 %) and 13 patients (2 %) were transfused for each respective age group.

The univariate association between each independent variable and the status of post-operative transfusion was assessed (Table 1). Variables identified to be statistically significant include preoperative haemoglobin ($p < 0.001$), age ($p < 0.001$), preoperative haematocrit ($p < 0.001$), and preoperative creatinine ($p < 0.001$). However, no relationship was found between the need for transfusion and gender, BMI, and ASA score (all n.s.). When transfusion rate

Table 1 Patient demographics and preoperative factors

Preoperative factor	Total	Transfusion	Non-transfusion	*P* value
Mean age (years) (SD)	67.5 (7.9)	72.9 (6.1)	67.3 (7.9)	<0.001
Age ≥70 (*n*, %)	595 (40.5)	24 (64.9)	571 (39.8)	0.002
Age <70 (*n*, %)	875 (59.5)	13 (35.1)	862 (60.2)	
Gender (male) (*n*, %)	317 (21.6)	5 (13.5)	312 (21.8)	n.s.
Gender (female) (*n*, %)	1153 (78.4)	32 (86.5)	1121 (78.2)	
Mean BMI (SD)	27.7 (4.7)	26.6 (5.0)	27.7 (4.6)	n.s.
ASA 1 (*n*, %)	113 (7.7)	0	113 (7.9)	n.s.
ASA 2 (*n*, %)	1131 (75.5)	28 (75.7)	1103 (75.5)	
ASA 3 (*n*, %)	226 (15.4)	9 (24.3)	217 (15.1)	
Mean preoperative haemoglobin (SD)	13.3 (1.3)	11.3 (1.4)	13.3 (1.3)	<0.001
Mean preoperative haematocrit (SD)	39.9 (3.6)	34.1 (3.7)	40.0 (3.5)	<0.001
Mean preoperative creatinine (SD)	70.7 (29.3)	106.5 (102.7)	69.8 (24.1)	<0.001

Table 2 Multivariate regression analysis: preoperative haemoglobin level and age

Preoperative factor	Adjusted OR	Lower 95 % CI	Upper 95 % CI	*P* value
Preoperative haemoglobin	0.31	0.23	0.41	<0.001
Age	1.10	1.05	1.16	<0.001

Table 3 Multivariate regression analysis: preoperative haemoglobin level and dichotomous age

Preoperative factor	Adjusted OR	Lower 95 % CI	Upper 95 % CI	*P* value
Preoperative haemoglobin	0.33	0.24	0.43	<0.001
Age <70 relative to age ≥70	0.40	0.18	0.84	0.021

was compared between two different age groups of above and below 70, the difference was found to be significant ($p = 0.002$).

Preoperative haemoglobin level and age were included in the multivariate regression analysis (Table 2), and both were revealed to be significant variables, with adjusted odds ratio of 0.31 (95 % CI 0.23–0.41, $p < 0.001$) and 1.10 (95 % CI 1.05–1.16, $p < 0.001$), respectively. When age was dichotomised at a cut-off of 70 years of age (Table 3), it was found that preoperative haemoglobin level remains statistically significant with adjusted odds ratio of 0.33 (95 % CI 0.24–0.43, $p < 0.001$).

Receiver operating characteristic (ROC) curves were constructed to show the relationship between true positive and false positive when using preoperative haemoglobin level to predict transfusion. The preoperative haemoglobin cut-off values were determined to be 12.4 g/dL for age above 70 and 12.1 g/dL for age below 70 at maximal Youden index, associated with area under the ROC curve of 0.86 (95 % CI 0.78–0.93) (Fig. 1) and 0.85 (95 % CI 0.74–0.96) (Fig. 2), respectively. The sensitivity, specificity, positive predictive

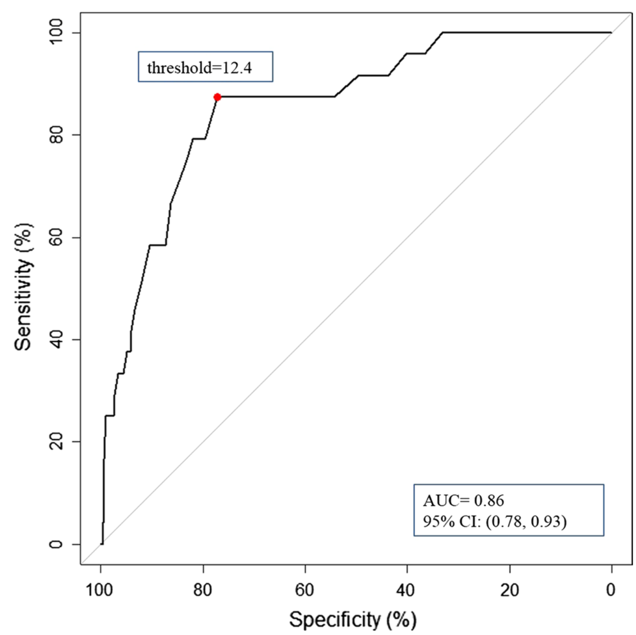

Fig. 1 Receiver operating characteristic curve for age above 70

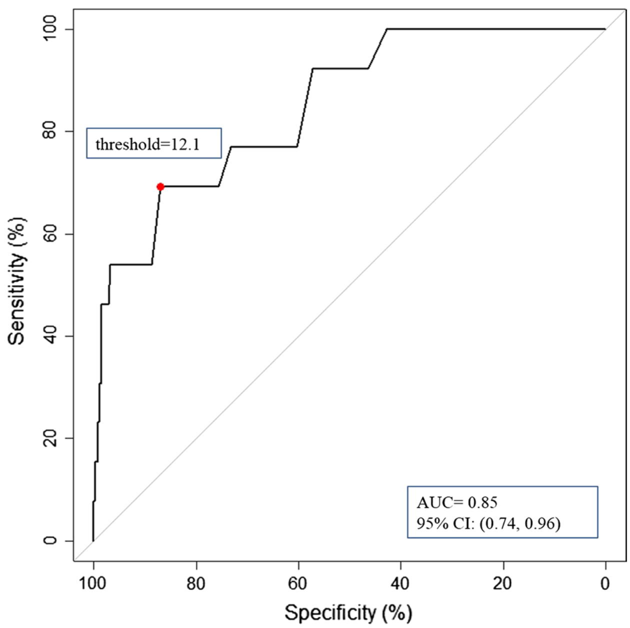

Fig. 2 Receiver operating characteristic curve for age below 70

value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR−) at preoperative haemoglobin values of 12.4 and 12.1 g/dL are shown in Table 4. A flowchart incorporating age and the corresponding preoperative haemoglobin cut-off values is shown in Fig. 3, indicating the rate of transfusion for the different preoperative risk factor combinations ($p < 0.001$).

Discussion

The most important finding of this study was that the authors have identified the preoperative haemoglobin cut-off values that can accurately predict transfusion outcome for the different age groups undergoing TKA. Patients above the age of 70 and with preoperative haemoglobin above 12.4 g/dL, as well as patients below the age of 70 and with preoperative haemoglobin above 12.1 g/dL, have low risk of transfusion with transfusion rates of 0.7 and 0.5 %, respectively.

Previous studies have emphasised that preoperative haemoglobin level is the strongest predictor for post-operative blood transfusion in TKA [1, 4–6, 9, 12–20, 22–24, 34]. Nevertheless, there is little information on what the optimal cut-off value should be. Basora et al. [4] identified the threshold for low preoperative haemoglobin level to be 13.0 g/dL, below which the odds of being transfused increased 3.7-fold for each 1.0 g/dL decrease in the haemoglobin level. Similarly, Salido et al. [24] reported that the risk of transfusion in patients with preoperative haemoglobin <13.0 g/dL was 4 times greater than that in patients with preoperative haemoglobin between 13.0 and 15.0 g/dL, and 15.3 times greater than that in patients with preoperative haemoglobin above 15.0 g/dL. A recent study by Goyal et al. [14] suggested that there should be discretionary evaluation of post-operative haemoglobin for patients with preoperative haemoglobin above 12.0 g/dL as only 0.5 % of these patients required a transfusion. Another

Table 4 Sensitivity, specificity, predictive values, and likelihood ratios at preoperative haemoglobin values of 12.4 and 12.1 g/dL

Haemoglobin (g/dL)	Sensitivity %	Specificity %	PPV %	NPV %	LR+	LR−
12.4	87.5	77.2	14.1	99.3	3.84	0.16
12.1	69.2	87.1	7.5	99.5	5.35	0.35

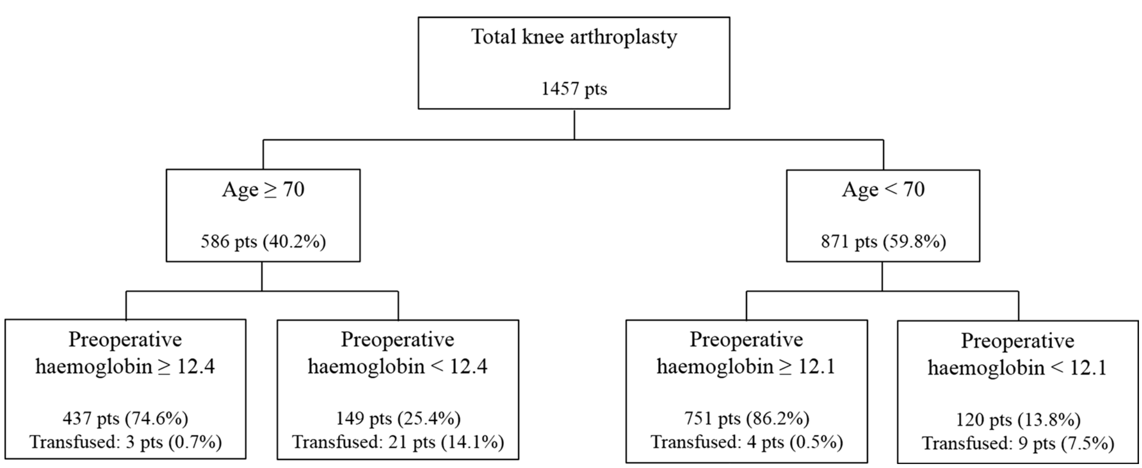

Fig. 3 Flowchart indicating rate of transfusion for the different preoperative risk factor combinations of age and haemoglobin cut-off values

study by Ahmed et al. [1] also took 12.0 g/dL to be the cut-off for low preoperative haemoglobin level.

The results in this study are largely consistent with the findings in the literature, with preoperative haemoglobin of 12.4 and 12.1 g/dL identified as the cut-off values. The accuracy of these values in predicting transfusion risk had been validated using ROC curve analysis, yielding areas under the curve of 0.86 and 0.85, respectively. A slight inconsistency was reported in studies by Fujimoto et al. [10] and Schwab et al. [26, 27], which cited preoperative haemoglobin of 11.0 g/dL as a key level to predict transfusion risk.

The determination of preoperative haemoglobin cut-off values would allow surgeons to identify at-risk patients and modify preoperative, intraoperative, and post-operative planning in an effort to reduce incidence of transfusion. More importantly, surgeons would be able to provide selective preoperative type and screen to only patients at high risk of transfusion. This would have important clinical and economic benefits, allowing the maximum utilisation of blood resources.

In the authors' opinions, it is more convenient to apply a cut-off value rather than a prediction model with complex equation in the clinical setting. Another strength of this study is the large number of patients available for analysis. This is especially important to ensure that the study is adequately powered, with good area under the curve for the ROC curve.

There are limitations to this study. Firstly, only preoperative factors were evaluated in the regression analyses, leaving out intraoperative factors such as the duration of surgery. Longer operation time [9, 22] has been associated with higher rate of blood transfusion in TKA. Nevertheless, the focus of this study was to identify factors that could accurately predict transfusion outcome preoperatively so that an individualised decision to type and screen patients could be made. Inclusion of intraoperative predictors into the analysis defeats this purpose. Secondly, there are inherent selections and observer biases as the patients are recruited from a single hospital. Future multicentre trials will be required to reduce these biases. Thirdly, the design of this study is retrospective in nature although the data are collected prospectively. However, conducting a randomised controlled trial will be impractical based on the sample size involved.

Conclusion

In summary, the results of this study demonstrate that preoperative haemoglobin level and age were consistent predictors for allogeneic blood transfusion after TKA. The calculated preoperative haemoglobin cut-off values are statistically accurate in predicting post-operative transfusion outcome. Therefore, the authors recommend preoperative haemoglobin cut-off values of 12.4 g/dL for age above 70 and 12.1 g/dL for age below 70 to be used to predict transfusion requirements after TKA. Only patients with haemoglobin level below the cut-off should receive routine preoperative type and screen.

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Compliance with ethical standards

Conflict of Interest The authors have no conflict of interest to declare.

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