Predictive Factors for Blood Transfusion after Total Knee Arthroplasty*

Fatores preditivos de hemotransfusão após artroplastia total de joelho

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Abstract

Objectives The present paper aims to (1) verify the incidence and volume of blood transfusion among patients undergoing unilateral cemented total knee arthroplasty (TKA) in a single Brazilian reference center; (2) identify pre and perioperative variables to determine subjects with higher risk (i.e., predictive factors) for blood transfusion within 48 hours following surgery; (3) estimate the risk of blood transfusion during the first 48 hours after the procedure.

Methods The initial sample consisted of all patients undergoing TKA from August 2010 to August 2013. After applying the exclusion criteria, 234 patients aged 30 to 83 years old and diagnosed with primary or secondary osteoarthritis due to rheumatoid arthritis remained in the study.

Results Preoperative hemoglobin levels $\leq$ 12.3 g/dL and ischemia time $\geq$ 87 minutes were independent predictors for post-TKA blood transfusion, with a relative risk of 2.48 and 1.78, respectively. Approximately half of the TKA patients (51.3%) presenting these two variables required a blood transfusion.

Conclusion The incidence of post-TKA blood transfusion was 33.7%. On average, each transfused patient received 480 mL of packed red blood cells. Preoperative hemoglobin levels $\leq$ 12.3 g/dL ($p < 0.001$) and ischemia time $\geq$ 87 minutes ($p < 0.047$) were independent predictors for blood transfusion in TKA using a pneumatic cuff, with a relative risk of 2.48 and 1.78, respectively. Age, gender, diagnosis, or body mass index were not considered independent predictors for the need for blood transfusion up to 48 hours after the procedure.

Keywords
- arthroplasty, replacement, knee
- blood transfusion
- osteoarthritis, knee

Resumo

Objetivos O presente estudo teve como objetivos (1) verificar a incidência e o volume de transfusão sanguínea entre os pacientes submetidos à artroplastia total do joelho

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(ATJ) unilateral cimentada em um único centro de referência nacional; (2) identificar variáveis pré e perioperatórias que nos permitam identificar os indivíduos sob maior risco (fatores preditores) quanto à necessidade de transfusão sanguínea nas 48 horas subsequentes à realização da cirurgia; (3) estimar o risco de transfusão sanguínea durante as primeiras 48 horas após o procedimento.

Métodos A amostra inicial foi constituída por todos os pacientes submetidos à ATJ entre agosto de 2010 e agosto de 2013. Após aplicação dos critérios de exclusão, permaneceram no estudo 234 pacientes com idade entre 30 e 83 anos, portadores de osteoartrose primária ou secundária a artrite reumatoide.

Resultados A análise dos resultados mostrou que valores de hemoglobina pré-operatória $\leq$ 12,3 g/dL e tempo de isquemia $\geq$ 87 minutos são preditores independentes para hemotransfusão após ATJ, com risco relativo de 2,48 e 1,78, respectivamente. Aproximadamente metade dos pacientes (51,3%) submetidos a ATJ com essas duas variáveis necessitaram de hemotransfusão.

Conclusão A incidência de transfusão sanguínea após ATJ foi de 33,7%. Em média, cada paciente foi transfundido com 480 mL de concentrado de hemácias. Concentração de hemoglobina pré-operatória $\leq$ 12,3 g/dL ($p < 0,001$) e tempo de isquemia $\geq$ 87 minutos ($p < 0,047$) foram preditores independentes para hemotransfusão em ATJ sob uso de manguito pneumático, com risco relativo de 2,48 e 1,78, respectivamente. A idade, o gênero, diagnóstico ou índice de massa corpórea não foram considerados preditores independentes para a necessidade de hemotransfusão até 48 horas após o procedimento de artroplastia.

Palavras-chave
- artroplastia do joelho
- transfusão de sangue
- osteoartrite do joelho

Introduction

Total knee arthroplasty (TKA) is often associated with visible, significant blood loss, possibly exceeding 1,500 mL.[1] In addition, such volume losses are also underestimated, because they disregard blood leakage to traumatized soft tissues, hematoma formation in joint cavity, and hemolysis. About 80% of this occult bleeding occurs within 24 hours and correspond to up to 50% of the actual total blood loss.[1–3]

Volume losses of such magnitude usually result in blood transfusion requirement in 7.1 to 67% of patients.[4–9] Although the incidence of blood transfusion-related complications has decreased in recent decades, this is not a risk-free procedure.[8–12] Allogeneic blood transfusion is also associated with an increased risk of postsurgical infection when orthopedic implants are used. This evidence, however, remains inconclusive and needs further studies.[10–17]

Therefore, prior identification of patients with a higher risk of receiving a blood transfusion after TKA can help change pre, intra, and postoperative care.[7]

As such, the present study aims to: (1) determine blood transfusion incidence and volume among patients undergoing unilateral cemented TKA in a single center; (2) identify predictive factors regarding the need for blood transfusion within 48 hours following TKA; (3) estimate the risk of blood transfusion during the first 48 hours after the procedure.

Material and Methods

After approval by the Research Ethics Committee of the institution, we performed a retrospective evaluation of medical records from all patients undergoing cemented unilateral TKA by two surgeons between August 2010 and August 2013.

Patients undergoing unicompartmental knee arthroplasty (UKA), UKA conversion to TKA, bilateral surgery or TKA revision, and those with coagulopathies or under preoperative anticoagulant therapy were excluded from the sample. No patient donated blood prior to the surgery.

The study included both male and female patients, aged 30 to 83 years old, diagnosed with primary osteoarthritis (OA) or rheumatoid arthritis (RA). All procedures were performed through a medial parapatellar approach after spinal anesthesia with peripheral sciatic and femoral nerve block. The surgeries were performed under a 300 mm Hg pressure ischemia applied before incision. After cementing the P. F. C. Sigma Knee System (DePuy-Synthes Companies, Warsaw, IN, USA) implants with posterior stabilization and pa + tellar replacement, the ischemia was released for hemostasis with a monopolar electrocautery alone. No hemostatic drugs were administered. A single 4.8-mm drain was used in all patients for 24 hours. Antimicrobial prophylaxis was performed with cefazolin (2 g, intravenously during anesthetic induction) and sustained for 24 hours (1 g, intravenous, every 8 hours). Deep vein thrombosis was prevented with low molecular weight heparin (Clexane Sanofi-Avenitis, Sao Paulo, SP, Brazil) subcutaneously administered in a single daily dose of 40 mg, starting 12 hours within surgery, and sustained for 10 days.

The following preoperative variables were surveyed: gender, age, diagnosis, body mass index (BMI) according to the World Health Organization (WHO) criteria from 2000, surgical risk according to the American Society of Anesthesiology (ASA) criteria and hemoglobin (Hb) level measured 24 hours

before surgery. Ischemia time was assessed intraoperatively. In the immediate postoperative period, determined as the first 48 hours following surgery, the lowest Hb level and the total volume of transfused allogeneic blood products were recorded.

The need for allogeneic blood transfusion during surgery was determined by the anesthesiologist, who did not play a role in this study. The postoperative blood transfusion requirement was determined by the assistant team as per the proper protocol adopted by the institution, which states that patients with Hb level greater than 10 g/dL do not need it. Blood transfusion is recommended for patients with Hb levels between 6 and 7 g/dL. For Hb values between 7 and 10 g/dL, the decision is individually tailored. Next, patients were divided into two groups, according to the need for blood products transfusion: the transfused group (T group, n = 79) and non-transfused group (nT group, $n = 155$).

Statistical Analysis

Kolmogorov-Smirnov and Shapiro-Wilks normality tests were applied to ascertain the normal distribution of a variable.

The existence of a significant relationship between the studied variables and post-TKA blood transfusion requirement were evaluated by the following methods: (1) Student *t*-test for numerical data comparison and Mann-Whitney test for independent samples; (2) inferential analysis using the Spearman correlation coefficient to determine the degree of association between hemoglobin level range (ΔHb), ischemia time, and transfused volume; (3) χ^2 or Fisher exact test for categorical data comparison; and (4) logistic regression analysis to assess the simultaneous influence of predictor variables. The variable-selecting process was stepwise forward at a 5% level.

A receiver operator characteristic (ROC) curve determined the accuracy of the model in predicting blood transfusion requirement. This graphical representation is built with sensitivity/specificity fractions at several cutoff points for each variable, illustrating system performance and its discrimination threshold. In addition, the ROC curve allows the identification of the best cutoff point.

Statistically significant differences were determined by *p*-values < 0.05. All calculations were performed by an independent statistician, using SAS version 6.11 statistical software (SAS Institute, Inc., Cary, NC, USA).

Results

Allogeneic Blood Transfusion Incidence and Volume

The initial sample consisted of 237 patients. After excluding 3 patients for hemophilia, 234 patients remained in the study, with a mean age of 66.6 ± 9.1 years old (range, 30 to 83 years old). Of this total, 81.6% (191/234) were women. As for diagnosis, 83.8% (196/234) had idiopathic OA and 16.2% (38/234) had RA.

The incidence of post-TKA blood transfusion was 33.7% (79/234). On average, each patient was transfused with 480 mL (1.6 units) of packed red blood cells. About half (50.6%) of the transfused patients received a total of 600 mL of blood products, while 35 (44.3%) subjects required 300 mL, and only 5.1% (4/79) of the patients needed more than 2 units of blood products.

Table 1 Patients characteristics and clinical numerical variables ($n = 234$)

	T group ($n = 79$)	nT group ($n = 155$)	*p*-value
Age*	67.6 ± 9.3	66.1 ± 9.0	0.23
Gender**			
Male	10 (12.7%)	33 (21.3%)	0.10
Female	69 (87.3%)	122 (78.7%)	
Diagnosis**			
RA	10 (12.7%)	28 (18.5%)	0.25
OA	69 (87.3%)	123 (81.5%)	
BMI (kg/m^2)*	30 ± 5.4	30.2 ± 5.3	0.71
ASA**			
1	3	11	0.49
2	75	139	
3	1	5	

Abbreviations: RA, rheumatoid arthritis; ASA, American Society of Anesthesiology; BMI, body mass index; OA, osteoarthrosis.
Numerical data expressed as mean ± standard deviation values. Categorical data expressed as frequency and percentage values.
T Group= received postoperative blood transfusion, nT Group= received no postoperative blood transfusion.
*Student's *t*-test for independent samples or Mann-Whitney test.
**χ^2 or Fisher exact test.

►**Table 1** summarizes the general characteristics of patients allocated to the T (transfused) and nT (non-transfused) groups. There was no difference between groups regarding age, gender, diagnosis, BMI, and surgical risk according to the ASA score (►**Table 1**).

Predictive Factors for Allogeneic Blood Transfusion Requirement

Univariate analysis of clinical and surgical parameters revealed that post-TKA blood transfusion requirement was related to pre- and postoperative low hemoglobin levels. In addition, transfused patients were subjected to a longer ischemia time ($p < 0.0014$). Other variables, such as diagnosis, gender, age, BMI, and ASA-based surgical risk, were not related to the need for postoperative blood transfusion (►**Tables 2** and **3**).

Both male and female patients from the T group presented significantly lower pre- and postoperative Hb levels when compared to the nT Group. Similarly, the Hb level range (absolute and relative ΔHb) was significantly higher in comparison to both male and female subjects from the nT group (►**Table 4**).

In transfused patients (T group), considering the pre and postoperative Hb level ranges (ΔHb), there was a significant correlation between absolute ΔHb ($r_s = 0.18$; $p = 0.006$) and relative ΔHb ($r_s = 0.17$; $p = 0.007$) with ischemia time.

Table 2 Univariate analysis of numerical parameters ($n = 234$)

Variable	T group ($n = 79$)		nT group ($n = 155$)		p-value[a]
Age (years old)	67.6 ± 9.3	(40–83)	66.1 ± 9.0	(30–82)	0.23
BMI (kg/m^2)	30.0 ± 5.4	(20.8–44.9)	30.2 ± 5.3	(15.0–43.8)	0.71
Ischemia time (minutes)	94.5 ± 21.0	(50–150)	87.0 ± 20.2	(40–135)	0.0014

T group= received postoperative blood transfusion, nT Group= received no postoperative blood transfusion. Data expressed as mean ± standard deviation values; range is showed within parenthesis.
[a]Student *t*-test for independent samples.

Table 3 Univariate analysis of categorical parameters

Variable	T group ($n = 79$)		nT group ($n = 155$)		p-value[a]
Gender					
Male	10	12.7%	33	21.3%	0.10
Female	69	87.3	122	78.7	
Diagnosis					
OA	69	87.3	122	78.7	0.25
RA	10	12.7	33	21.3	
Surgical Risk					
ASA 1	3	3.9	11	7.1	0.49
ASA 2	74	94.9	139	89.7	
ASA 3	1	1.3	5	3.2	

Abbreviations: RA, Rheumatoid Arthritis; OA, osteoarthrosis.
T group= received postoperative blood transfusion, nT Group= received no postoperative blood transfusion.
[a]χ^2 or Fisher exact test.

Absolute ΔHb ($r_s = 0.24$; $p = 0.0002$) and relative ΔHb ($r_s = 0.35$; $p = 0.0001$) were significantly correlated with the final volume of transfused blood products when pre and postoperative Hb level ranges were considered. There was also a significant correlation ($r_s = 0.16$; $p = 0.013$) between ischemia time and the volume of transfused blood products.

In addition, ischemia time was related to a higher drop in absolute and relative Hb values. Reduced Hb levels and ischemia time were directly related to a higher volume of transfused blood products in TKA perioperative period.

A subsequent multivariate logistic regression analysis assessed the simultaneous influence of predictor variables on the need for blood transfusion. This evaluation confirmed the preoperative Hb level ($p < 0.0001$) and ischemia time as independent predictive factors for postoperative blood transfusion requirement. Other variables did not present a significant independent contribution at a 5% level.

Receiver operator characteristic curves for Hb levels and ischemia time identified the cutoff value for post-TKA blood transfusion as preoperative Hb levels ≤ 12.3 g/dL. This test presented 62.0% sensitivity and 61.9% specificity. For ischemia time, the cutoff value was ≥ 87 minutes, with 62.0% sensitivity and 51.6% specificity (►**Figure 1**).

At logistic regression after cutoff values identification, preoperative Hb levels ≤ 12.3 g/dL ($p < 0.001$) and ischemia time ≥ 87 minutes ($p < 0.047$) were independent predictors for blood transfusion in TKA using a pneumatic cuff, with respective relative risk values of 2.48 and 1.78.

Table 4 Hemoglobin (Hb) levels and range (Δ) according to gender-stratified transfusion

Variable	T group		nT group		p-value[a]
Male gender	$n = 10$		$n = 33$		
Preoperative Hb (g/dL)	12.9 ± 0.7	(11.8–14.1)	13.8 ± 1.4	(11.2–16.7)	0.046
Postoperative Hb (g/dL)	8.0 ± 1.1	(6.7–10)	9.9 ± 1.5	(7.3–14.2)	0.0007
Δ Hb (g/dL)[1]	5.0 ± 1.1	(6.7–3)	4.0 ± 1.3	(6.7–1.1)	0.033
Δ Hb (%)[2]	38.3 ± 8.0	(50–24)	28.7 ± 8.7	(48–9.4)	0.003
Female gender	n = 69		n = 122		
Preoperative Hb (g/dL)	11.9 ± 1.3	(9.3–14.8)	12.4 ± 1.2	(8.7–16.1)	0.002
Postoperative Hb (g/dL)	7.8 ± 1.0	(5.8–10.9)	9.1 ± 1.4	(6.1–12.3)	0.0001
Δ Hb (g/dL)[1]	4.1 ± 1.6	(7.4–1.3)	3.3 ± 1.4	(8.2–1.1)	0.0005
Δ Hb (%)[2]	34.0 ± 10.5	(54–12.7)	26.5 ± 9.8	(51–9.1)	0.0001

Abbreviation: Hb, hemoglobin.
T group = received postoperative blood transfusion, nT Group= received no postoperative blood transfusion. Data expressed as mean ± standard deviation values; range is showed within parenthesis.
[1]Absolute Δ = preoperative Hb – postoperative Hb.
[2]Relative Δ (%) = absolute Δ / preoperative Hb *100.
[a]Student *t*-test for independent samples.

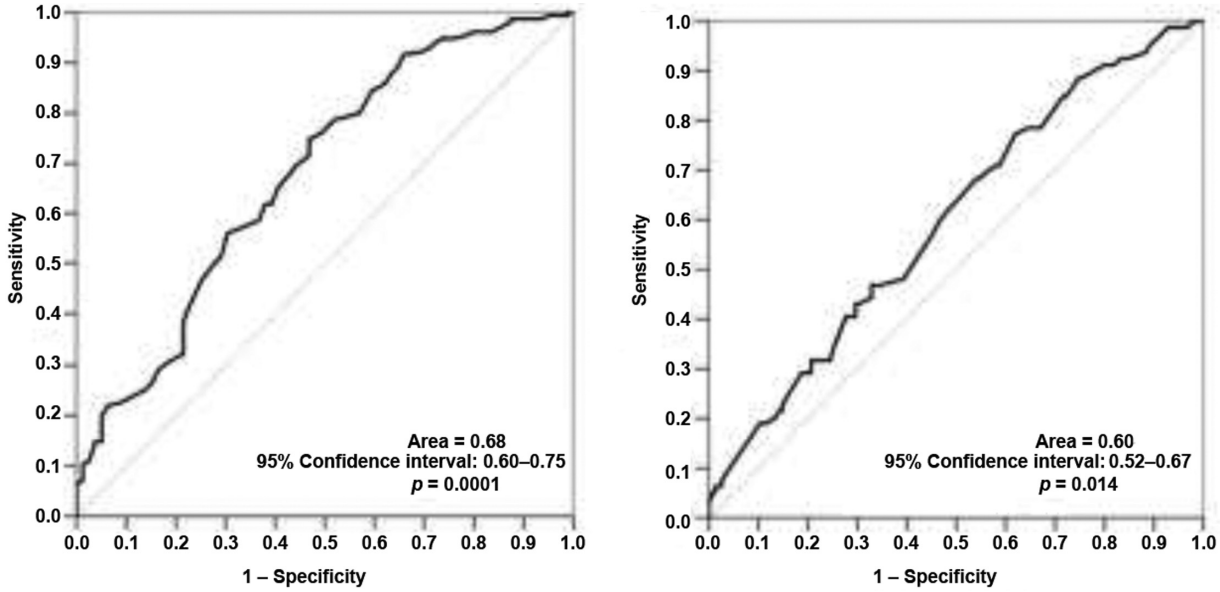

Fig. 1 Global accuracy according to the receiver operator characteristic curve for preoperative hemoglobin value (**A**) and ischemia time (**B**) for blood transfusion after total knee arthroplasty under ischemia with a pneumatic cuff.

Risk of Post-TKA Allogeneic Blood Transfusion

Based on the logistic regression model, the probability of a patient undergoing TKA requiring blood transfusion within 48 hours after the procedure is calculated using the following formula:

$$\mathrm{Pr_{est}\ (hemotransfusão)} = \frac{e^{3{,}7596 - (0{,}5178 \times \text{Hb pré em g/dL}) + (0{,}0211 \times \text{tempo de cirurgia min})}}{1 + e^{3{,}7596 - (0{,}5178 \times \text{Hb pré em g/dL}) + (0{,}0211 \times \text{tempo cirurgia min})}}$$

►**Table 5** presents the estimated probability of transfusion according to the relevant parameters.

Discussion

The present study is a cross-sectional evaluation of 234 patients undergoing TKA demonstrating that preoperative Hb levels ≤12.3 g/dL and ischemia times ≥ 87 minutes are independent predictors for postprocedural blood transfusion.

Even though TKA surgeries are usually associated with high total blood loss, the literature reports widely variable blood transfusion rates. In our sample, transfusion was performed in 33.7% of the patients within 48 hours after surgery. Although this result is similar to those described in a large series,[9] the adoption of conservative institutional criteria for blood transfusion may reduce this rate. Ballantyne et al.[17] identified a reduction in the incidence of blood transfusion after unilateral TKA from 31 to 11.9% after adopting a more rigorous institutional protocol, in which blood transfusion was indicated only in patients with postoperative Hb levels < 8.5 g/dL or those with acute anemia symptoms.

Table 5 Estimated probability of blood transfusion according to the logistic model

Preoperative hemoglobin level ≤ 12.3 g/dL	Ischemia time ≥ 87 minutes	Estimated probability (%)	95% Confidence interval
No	No	19.3	12.4–28.9
No	Yes	29.9	20.8–40.8
Yes	No	37.2	26.4–49.4
Yes	Yes	51.3	40.0–62.6

Predictive models to identify patients most likely to need postoperative blood transfusion are essential for the rational management of blood components.[7] As such, we sought to assess pre and perioperative variables in the Brazilian population that would allow the identification of subjects at higher risk for requiring blood transfusion within 48 hours after TKA.

The most consistent independent predictor of postoperative blood transfusion requirement was a preoperative hemoglobin level up to 12.3 g/dL. Based on this value, the relative risk of transfusion was 2.48, therefore suggesting that patients with this Hb level are 2.48 times more likely to require a blood transfusion after undergoing TKA compared to subjects with higher levels. Salido et al.[18] also identified a preoperative Hb level below 13 g/dL as a blood transfusion predictor in patients undergoing total hip arthroplasty (THA) or TKA, with a relative risk similar to the one observed by us (2.51). The percentage of patients within this range of preoperative Hb values that received blood transfusions (69%) was also similar to the value detected in our series (62%). Similar results were noted by Guerin et al.,[19] who identified a 4-fold higher risk of transfusion in patients with preoperative Hb levels < 13 g/dL; in addition, this risk was exacerbated in both ASA 3 and 4 patients.[9]

In our study, another independent predictive factor for blood transfusion was ischemia time ≥ 87 minutes, resulting in a relative risk of 1.78. Noticewala et al.[20] showed that total

surgical time alone (and not ischemia time) is an independent predictive factor for post-TKA blood transfusion requirement. Although Salido et al.[18] reported that a surgical time of 91.1 minutes was associated with a greater need for blood transfusion, this finding has not been confirmed as an independent predictive factor.

Prasad et al.[3] confirmed a greater need for post-TKA blood transfusion in patients with RA. However, Ogbemudia et al.[21] identified low Hb level as a predictive factor for transfusion in patients with RA. In our study, similarly to Noticewala et al.,[20] RA was not an independent predictive factor. However, as also noted by Ogbemudia et al.,[21] low Hb levels in these patients was a risk factor for postoperative blood transfusion.

Hart et al.[6] reported age as an independent predictor, with a 10.2-fold increase in the risk of transfusion for each decade of life. Our results did not confirm the relationship between age and post-TKA transfusion requirement.

The patient's gender and age were not independent predictors for post-TKA blood transfusion. Although our female subjects usually had lower Hb levels, consistent with the findings of Ogbemudia et al.[21], there was no relationship between gender and transfusion requirement.

Another frequently investigated parameter is BMI. Lower BMI values are associated with lower[13,14] or higher[22] transfusion requirement. Salido et al.[18] described body weight as an independent predictor for postoperative blood transfusion requirement, with a relative risk of 1.05. In RA patients, BMI was associated with a greater need for blood transfusion.[21] Similarly to Bong et al.,[23] we did not observe a relationship between BMI and the need for postoperative transfusion.

The literature points to a consensus that patients presenting an ASA score greater than 2 often require transfusion,[6,7,9,11,15] demonstrating that, compared to subjects with ASA 1 and 2 scores, those with ASA 3 and 4 scores have a 3-fold higher independent risk for postoperative blood transfusion. We did not observe a relationship between surgical risk (ASA) and the need for blood transfusion, which can be explained by the reduced number of ASA 3 or 4 participants.

Preoperative identification of patients most likely needing a post-TKA blood transfusion is pivotal in the Brazilian public health scenario. Thus, we developed a model to estimate the relative risk of blood transfusion requirement. A ROC curve was constructed to determine the accuracy of this model in predicting which patients were at higher transfusion risk after TKA. The discriminatory power of our model, estimated by the Hb ROC curve (area under the curve [AUC], 0.68), although regular, presented statistical significance with 62.0% sensitivity and 61.9% specificity. In the ROC curve for ischemia time (AUC, 0.60), the predictive power of our equation was low, but it presented statistical significance, with 62.0% sensitivity and 51.6% specificity. Other predictive models under similar conditions showed greater discriminatory power than our equation, with an AUC value of 0.74[22] or 0.99[24] and 71%[22] or 90% sensitivity.[18] However, the specificity of this last report (52.5%) was similar to the one found in our study (51.6%).[20]

We believe, however, that before using the equation in the decision-making process, it is important to validate it in other institutions for possible mode adjustments.

Our study has some limitations. Despite the existence of clinical and laboratory parameters in the transfusion protocol, the view of specialists (anesthesiologists, intensivists, clinicians, and surgeons) may have specified the transfusion indication in some patients, which is a limitation of this work. Another important limitation refers to the non-performance of sample calculation; nevertheless, we believe that the fact that our sample consists of an expressive number of patients from a single tertiary reference center in the treatment of highly complex orthopedic diseases gives relevance to our findings. Still, we emphasize the need for additional prospective studies to corroborate our results and guide the most appropriate treatment for patients in preoperative TKA programming with Hb levels < 12.3 g/dL. Likewise, effective measures are required to reduce bleeding in patients submitted to surgeries with an ischemia time > 87 minutes.

Conclusion

The incidence of post-TKA blood transfusion was 33.7%. On average, each transfused patient received 480 mL of packed red blood cells.

Preoperative hemoglobin levels ≤ 12.3 g/dL ($p < 0.001$) and ischemia time ≥ 87 minutes ($p < 0.047$) were independent predictors for blood transfusion in TKA using a pneumatic cuff, with a relative risk of 2.48 and 1.78, respectively.

Age, gender, diagnosis, or BMI were not considered independent predictors for the need for blood transfusion up to 48 hours after the procedure.

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Conflict of Interests

The authors declare that there is no conflict of interests.

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