

# Factors that influence blood loss and need for transfusion following total knee arthroplasty

Achilleas Boutsiadis<sup>1</sup>, Ryan Jacob Reynolds<sup>2</sup>, Mo Saffarini<sup>2</sup>, Jean-Claude Panisset<sup>1</sup>

<sup>1</sup>Department of Orthopaedic Surgery, Centre Osteoarticulaire des Cèdres, Grenoble, France; <sup>2</sup>Medical Technology, ReSurg SA, Nyon, Switzerland  
*Contributions:* (I) Conception and design: A Boutsiadis, M Saffarini, JC Panisset; (II) Administrative support: A Boutsiadis, M Saffarini, JC Panisset; (III) Provision of study materials or patients: A Boutsiadis, JC Panisset; (IV) Collection and assembly of data: A Boutsiadis, JC Panisset; (V) Data analysis and interpretation: RJ Reynolds, M Saffarini; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.  
*Correspondence to:* Mo Saffarini, MEng. Medical Technology, ReSurg S.A., Chemin de la Vuarpillière 35, 1260 Nyon, Switzerland.  
Email: journals@resurg.eu.

**Background:** Blood loss during total knee arthroplasty (TKA) remains a concern, as many patients require blood transfusions, which increase risks of allergic reactions, disease transmission, and thromboembolisms. The purpose was to determine factors associated with blood loss and need for transfusion in patients receiving routine TKA.

**Methods:** The authors prospectively analyzed 150 consecutive uncemented TKAs for age, gender, body mass index (BMI), anticoagulant medication, type of anesthesia, tranexamic acid (TXA) administration, tourniquet inflation, drain placement, pre- and post-operative Haemoglobin (Hb) level (g/dL), and whether transfusion was necessary. Univariable and multivariable regression analyses were performed to identify factors associated with Hb loss and need for transfusion with significance level set at P value < 0.05.

**Results:** The cohort comprised 92 women and 58 men, aged 69.5 ± 8.9 years. The mean Hb loss was 3.7 ± 1.3 g/dL. The 20 patients (13%) who had transfusions also had lower preoperative Hb (12.6 ± 1.2 g/dL) compared to the remaining patients (14.3 ± 1.2 g/dL). Hb loss was significantly associated with preoperative Hb, TXA, and gender, but multivariable regression identified gender as a confounder and indicated that TXA reduced Hb loss by 0.92 g/dL. Multivariable regression revealed the need for transfusion was only significantly associated with preoperative Hb and indicated that a decrease of preoperative Hb by 1 g/dL nearly quadrupled the chances of needing transfusion.

**Conclusions:** Hb loss was significantly associated with preoperative Hb levels and use of TXA, while the need for transfusion was only associated with preoperative Hb levels. These findings could help identify patients at risk for blood transfusions. Level of evidence: level III, prospective case series.

**Keywords:** Total knee arthroplasty (TKA); blood loss; transfusion; tranexamic acid (TXA); anticoagulants; Hb level

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## Introduction

Blood loss during total knee arthroplasty (TKA) remains a concern, as 18% to 67% of patients require blood transfusion following their operation (1-3). Allogenic transfusions increase risks of allergic reactions, hemolytic reaction, 30-day mortality, disease transmission, surgical-

site infection, periprosthetic infections, and venous thromboembolisms (4-8). For these reasons, several measures have been introduced and evaluated to limit blood loss during and following TKA, including the use of tourniquets, autologous blood transfusion, drain clamping or retransfusion drains, computer assisted surgery, hypotensive anesthesia, and patient-specific instruments, as

well as various pharmaceuticals (2,9-12).

The efficacy and drawbacks of these blood management strategies are frequently debated. While erythropoietin (11,13) and antifibrinolytic drugs such as tranexamic acid (TXA) (14-20) are known to be effective with limited side effects, fibrinogen and fibrin sealants were recently found ineffective (21,22), despite disagreement with earlier studies (23). Likewise, the use of tourniquets reduced blood loss intraoperatively, but not postoperatively, hence a diminished net effect, as well as risks of bruising, neurovascular injury, and metabolic disturbance (24,25). Most other solutions such as drain clamping, computer assisted surgery, and patient-specific instruments demonstrated little or no benefit (2,9,12).

Due to the continued high transfusion rates and the compounding effect of risk factors, Noticewala *et al.* (26) examined 31 factors to determine variables associated with blood loss and need for transfusion. Their multivariable analysis concluded that age, preoperative haemoglobin (Hb), and surgical time were significant factors in predicting the need for transfusion, though they did not consider the use of TXA (26).

The purpose of this study was, therefore, to determine patient factors (age, gender, BMI, anticoagulant use, preoperative Hb) and surgical factors (tourniquet, TXA, drain, and type of anesthesia) associated with blood loss and need for transfusion in a consecutive series of TKA performed by a single surgeon. The clinical relevance of this study is the findings could help identify patients at increased risk of blood loss and need for transfusion.

## Methods

The authors prospectively enrolled 151 consecutive patients that underwent TKA for tibiofemoral osteoarthritis (OA) between April 2015 and January 2016. All patients were operated through a standard medial parapatellar approach by an experienced surgeon using uncemented tibial and femoral components as well as a cemented patellar button (T-KAPS, X.NOV, Hericourt, France). One patient was excluded due to a hematological disorder (myeloma).

For the remaining 150 patients, the following information was documented: age, gender, body mass index (BMI), and detailed medical history. In addition, the following perioperative parameters were recorded:

- (I) Anticoagulant drugs (yes/no), such as Clopidogrel, Aspirin and non-steroidal anti-inflammatory drugs (NSAIDs), which were stopped 1 week prior to surgery (n=39);
- (II) Type of anesthesia (regional/general);
- (III) TXA administration (yes/no), followed a standard protocol of a bolus dose of 15 mg/kg three minutes after starting anesthesia, and a continuous perfusion of 1 mg/kg/h during the operation. Patients were contraindicated by prothrombotic conditions or previous thromboembolic events including deep vein thrombosis (DVT) (n=17), pulmonary embolism (n=2), myocardial infarction (n=5), stroke (n=7), coronary artery stent (n=14), or bypass graft (n=4);
- (IV) Tourniquet inflation (yes/no), depended on the patient arterial pressure, use of anticoagulants, and whether TXA was administered;
- (V) Drain placement (yes/no), used to prevent swelling in patients with excessive intra-operative bleeding. The drain had negative suction for one hour and was removed after 24 hours;
- (VI) Preoperative Hb (g/dL) level, collected two or three days before the operation, during preoperative assessment;
- (VII) Postoperative Hb (g/dL) level, collected during routine postoperative assessments;
- (VIII) Hb loss (g/dL), calculated as the difference between preoperative Hb level and the lowest recorded postoperative Hb level;
- (IX) Blood transfusion (yes/no), administrated in accordance with established ASA guidelines (n=20) (27).

Postoperatively, all patients received low molecular weight heparin (LMWH) as a thrombosis prophylaxis and NSAIDs were avoided. The presence of DVT was evaluated for all patients through routine ultrasonography (Triplex) of both lower limbs at 48 hours and 5 days. The ethical review board of our hospital approved this study (IRB# 2015-01).

## Statistical analysis

Statistical analyses were performed using R version 3.3.3 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were used to summarize the data. For non-Gaussian quantitative data, between group differences were evaluated using Wilcoxon rank sum tests (Mann Whitney U test). Categorical data were analyzed using Pearson chi-square tests or Fisher's exact tests. Univariable and multivariable linear (Hb loss) and ordinal (transfusions) regression analyses were performed to identify factors

**Table 1** Patient demographics

Patient specifics	Cohort (n=150)
Age	69.5±8.9 (50.0–91.0)
BMI (kg/m <sup>2</sup> )	28.5±5.1 (17.9–45.4)
Preoperative Hb (g/dL)	14.0±1.3 (10.2–17.8)
Male gender	58 (38.7%)
Preoperative anticoagulants	39 (26.0%)

**Table 2** Descriptive surgical results

Intraoperative observations	Cohort (n=150)
Surgery	
Tourniquet	45 (30%)
Type of anesthesia	
Regional	100 (67%)
General	50 (33%)
Surgical drain	44 (29%)
TXA	101 (67%)
Transfusion	20 (13%)
Complications	
Hb loss (g/dL)	3.7±1.3 (0.9–7.7)
DVT	15 (10%)
Infection	1 (0.7%)

TXA, tranexamic acid; Hb, hemoglobin; DVT, deep vein thrombosis.

associated with outcomes. The factors considered were patient age, BMI, preoperative Hb, gender, anticoagulant use, tourniquet use, type of anesthesia, drain use, and TXA administration.

## Results

The cohort comprised 92 women and 58 men, aged 69.5±8.9 years (*Table 1*). Regional anesthesia was administered in 100 patients (67%), the tourniquet was inflated in 45 (30%), TXA was administered in 101 patients (67%), the drain was used in 44 (29%), and a transfusion was necessary in 20 (13%) (*Table 2*). DVT developed in 7 of the 101 patients (7%) who received TXA compared to 8 of the 49 patients (16%) who did not receive TXA ( $P=0.116$ ). The mean Hb loss was 3.7±1.3 g/dL.

Univariable regression revealed that Hb loss was significantly associated with: preoperative Hb ( $P<0.001$ ), TXA ( $P=0.029$ ), and gender ( $P<0.001$ ) (*Table 3*). Multivariable regression clarified that Hb loss was directly associated with preoperative Hb ( $P<0.001$ ), TXA ( $P<0.001$ ), and drain placement ( $P=0.044$ ), but not with gender (n.s.). Adjusting for confounding variables, an increase of preoperative Hb by 1 g/dL was found to increase Hb loss by 0.37 g/dL, while use of TXA was found to reduce Hb loss by 0.92 g/dL (*Figure 1*).

Univariable regression revealed that the need for transfusion was significantly associated with: age ( $P=0.041$ ), anticoagulants ( $P<0.001$ ), preoperative Hb ( $P<0.001$ ), and TXA ( $P<0.001$ ) (*Table 4*). Multivariable regression clarified that the need for transfusion was only directly associated with preoperative Hb ( $P<0.001$ ). Adjusting for confounding variables, a decrease of preoperative Hb by 1 g/dL nearly quadrupled the chances of needing transfusion. In fact, patients that needed transfusions had preoperative Hb of 12.6±1.2 (median 12.7; range, 10.2–14.6) compared to 14.3±1.2 (median 14.2; range, 11.4–17.8) for patients that did not need transfusions (*Figure 2*).

## Discussion

The most important finding from this consecutive series of TKA was that, accounting for confounding variables, the need for blood transfusion was only associated with patient preoperative Hb levels. Furthermore, the total Hb loss was significantly associated with preoperative Hb levels (direct relationship) as well as TXA administration (inverse relationship).

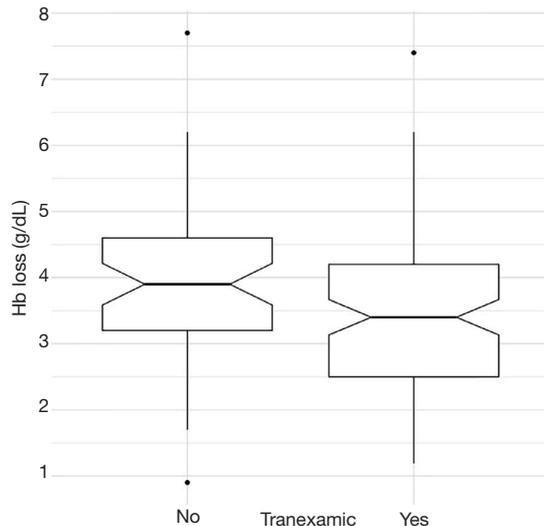
The purpose of this study was to determine patient and surgical factors associated with blood loss and need for transfusion in a consecutive series of TKA performed by a single surgeon. Our findings are in agreement with several studies that reported how preoperative Hb is significantly associated with blood loss and the need for transfusion (26,28–32). In particular, Noticewala *et al.* (26) evaluated the association of 31 factors with blood loss and need for transfusion during TKA. After adjusting for confounding variables, they found age, preoperative Hb, and surgical time to have significant effect, though they did not consider the use of TXA (26). Also, routine arthroplasty has a reported Hb loss of 3.8 g/dL, which is comparable to the 3.7 g/dL observed in the present study (33).

Both Hatzidakis *et al.* (31) and later Guerin *et al.* (30) reported that patients undergoing lower extremity total

**Table 3** Regression analysis of Hb loss (g/dL)

Variable	Univariable			Multivariable		
	Regression coefficient	95% CI	P value	Regression coefficient	95% CI	P value
Continuous <sup>1</sup>						
Age (years)	0.0	(0.0 to 0.0)	0.145	0.0	(0.0 to 0.0)	0.177
BMI (kg/m <sup>2</sup> )	0.0	(-0.1 to 0.0)	0.328	0.0	(-0.1 to 0.0)	0.113
Preoperative Hb (g/dL)	0.4	(0.2 to 0.5)	<0.001	0.4	(0.2 to 0.6)	<0.001
Categorical <sup>2</sup>						
Gender (male vs. female)	0.7	(0.3 to 1.1)	<0.001	0.2	(-0.3 to 0.7)	0.398
Anticoagulant (yes vs. no)	0.1	(-0.4 to 0.6)	0.693	0.0	(-0.5 to 0.5)	0.907
Tourniquet (yes vs. no)	0.0	(-0.5 to 0.4)	0.842	0.0	(-0.4 to 0.4)	0.991
Anesthesia (regional vs. general)	-0.3	(-0.8 to 0.1)	0.166	-0.1	(-0.5 to 0.3)	0.710
Drain placement (yes vs. no)	0.3	(-0.2 to 0.7)	0.246	0.4	(0.0 to 0.8)	0.044
TXA (yes vs. no)	-0.5	(-0.9 to 0.1)	0.029	-0.9	(-1.4 to 0.4)	<0.001

<sup>1</sup>, Regression coefficient represents the expected difference in Hb loss for an increase of the independent variable by one unit; <sup>2</sup>, Regression coefficient represents the expected difference in Hb loss for the specified binary category. BMI, body mass index; Hb, hemoglobin; TXA, tranexamic acid.

**Figure 1** Haemoglobin (Hb) loss in patients that did or did not receive tranexamic acid (TXA).

joint arthroplasty with preoperative Hb levels <13 g/dL were 4 (31) to 5.6 (30) times more likely to need transfusion relative to those with Hb levels >15 g/dL. Furthermore, Salido *et al.* (34) advocated that patients with preoperative Hb >15 g/dL rarely need blood transfusion. Similarly, our

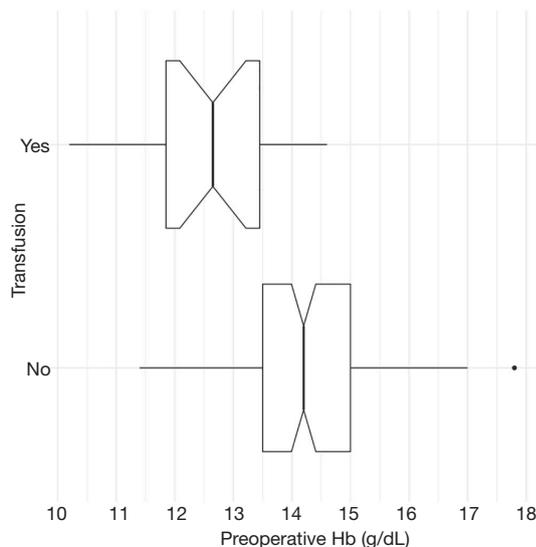
data revealed that patients who needed transfusions had preoperative Hb of  $12.6 \pm 1.2$  compared to  $14.3 \pm 1.2$  for patients that did not need transfusions, and multivariable regression indicated that a decrease of preoperative Hb by 1 g/dL nearly quadrupled the chances of needing transfusion. Several blood management algorithms use preoperative Hb levels to predict the need for transfusion, and were found effective in limiting transfusion (11,26,35). However, Kapadia *et al.* (36) conclude that these algorithms need to be evaluated further by prospective randomized studies.

Our findings also confirmed that TXA significantly reduced blood loss without increasing the incidence of thromboembolism (17,37). Review articles focusing on the prediction of blood transfusion after joint arthroplasty concluded that drugs intended to reduce blood loss, such as TXA, have significantly lowered the need for transfusion (15,16,32,38-40). However, these drugs are simply one part of the solution required to limit bleeding and transfusion rates (32,40). For instance, we have evidence that the surgical drain increased blood loss. Therefore, when a drain is placed, retransfusion drains (41,42) or drain clamping techniques (2) should be considered in order to reduce blood loss.

**Table 4** Regression analysis of need for transfusion

Variable	Univariable			Multivariable		
	OR	95% CI	P value <sup>1</sup>	OR	95% CI	P value <sup>2</sup>
<b>Continuous<sup>1</sup></b>						
Age (years)	1.1	(1.0–1.1)	0.041	1.0	(0.9–1.1)	0.918
BMI (kg/m <sup>2</sup> )	1.0	(0.9–1.1)	0.795	1.0	(0.9–1.1)	0.760
Preoperative Hb (g/dL)	0.3	(0.1–0.4)	<0.001	0.3	(0.1–0.5)	<0.001
<b>Categorical<sup>2</sup></b>						
Gender (male vs. female)	0.4	(0.1–1.0)	0.075	1.4	(0.3–6.7)	0.676
Anticoagulant (yes vs. no)	5.8	(2.2–16.0)	<0.001	2.1	(0.6–7.9)	0.249
Tourniquet (yes vs. no)	1.7	(0.6–4.4)	0.298	0.7	(0.1–2.8)	0.607
Anesthesia (regional vs. general)	0.7	(0.3–2.0)	0.498	1.3	(0.4–5.4)	0.660
Drain placement (yes vs. no)	0.4	(0.1–1.2)	0.142	0.4	(0.1–1.5)	0.195
TXA (yes vs. no)	0.2	(0.1–0.4)	<0.001	0.3	(0.1–1.2)	0.084

<sup>1</sup>, odds ratio of needing transfusion for an increase of the independent variable by one unit; <sup>2</sup>, odds ratio of needing transfusion for the specified binary category. OR, odds ratio; BMI, body mass index; Hb, hemoglobin; TXA, tranexamic acid.



**Figure 2** Pre-operative haemoglobin (Hb) levels in patients that did or did not require blood transfusions.

Blood management strategies are often debated. While TXA is known to be effective, patients with thromboembolic events and conditions often contraindicate its administration (35,40). Topical application of TXA is perhaps as effective as intravenous administration, and is not contraindicated (35,43–45). Erythropoietin is an effective

means of increasing preoperative Hb, but may not be cost effective (13). Autologous blood transfusion may also not be cost effective, but it has been recommended for anemic patients as long as sufficient time is permitted to replenish red blood cells (46–49). A common reason for anemia is iron deficiency, which can be corrected by intravenous or oral iron supplement (35,36). Intravenous infusion is expected to improve Hb by 1 g/dL over 10 days (35). However the effectiveness of iron supplementation in reducing the need for transfusion is controversial (36). Previous studies showed that the use of tourniquets does not significantly reduce blood loss due to the slight increase in blood loss postoperatively (9,24,25). Use of tourniquet also has risks of bruising, neurovascular injury, and metabolic disturbance (9,25). Also, computer assisted surgery and patient-specific instruments aid in surgery, though they have limited effect on reducing blood loss (9). Further research should be done on pharmaceuticals, devices, and other measures to determine the best solutions to managing blood loss and the need for transfusion.

The present study has a number of limitations typical of non-comparative observational studies. Firstly, TXA was administered in all patients unless contraindicated by prothrombotic conditions or previous thromboembolic events. While TXA was found to significantly reduce blood loss, it is not certain whether this observation is directly

related to the use of TXA or to the contra-indications for its use. Secondly, type of anesthesia, tourniquet inflation and drain placement depended upon several subjective factors, which could induce bias. Thirdly, the relatively small number of transfusions (n=20) may not have enabled detection of all associated factors. The main strength of the study is that it analyzed multiple factors that could influence blood loss and the need for transfusion in the routine practice of a single surgeon using the same implant and surgical technique.

## Conclusions

The findings of this study confirm that, accounting for confounding variables, the need for blood transfusions during our routine TKA procedures depends primarily on patients' preoperative Hb levels. TXA significantly reduces blood loss but did not directly influence the need for transfusion. These findings could help identify patients at risks of excessive blood loss and need for transfusions, to ensure the necessary measures are taken to limit blood loss.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The ethical review board of our hospital approved this study (IRB# 2015-01).

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