





Original Article

Evaluation of blood loss after early or late release of ischemia in patients undergoing total knee replacement

Marcos George de Souza Leão, 1,* Hugo Alves Paulo de Souza, 2 Yacov Machado Costa Ferreira 2

¹Preceptor of the Medical Residence Program and Attending Physician in the Orthopedics and Traumatology Service, Fundação Hospital Adriano Jorge, Manaus, AM, Brazil.

²Resident Physician in the Medical Residence Program, Orthopedics and Traumatology Service, Fundação Hospital Adriano Jorge, Manaus, AM, Brazil.

Work performed in the Orthopedics and Traumatology Service, Fundação Hospital Adriano Jorge, Manaus AM, Brazil.

ARTICLE INFO

Article history: Received on January 15, 2012 Approved on March 8, 2012

Keywords: Blood loss, surgical Arthroplasty, replacement, knee Ischemia

ABSTRACT

Objective: compare blood loss in 40 patients underwent to unilateral total knee replacement with the release of ischemia before and after skin closure and compressive dressing. Methods: in a prospective randomized study, in 40 patients underwent to total knee replacement, dividing then into two groups: group A in which the ischemia was released before skin closure, allowing bleeding control and group B where the ischemia was released after skin suture and pressure dressing. We compared the results of laboratory tests of serum hemoglobin before surgery and 48 hours postoperatively, the blood volume contained in vacuum suction drain and the transfusions that was necessary. Results: As a result, the post operative serum hemoglobin levels had a mean decrease of 3.57 g/dL in group A and 4.24 g/dL in group B with an average of 0.67g/dL difference between them, statistically insignificant. The observed mean drainage, in the vacuum drain, were 705 mL in group A and 700 mL in group B. The 5ml difference between medians was considered statistically insignificant. The number of patients who received transfusions was four patients in both groups and all received two units of red blood cells. Conclusion: the post operative serum hemoglobin levels, as well as the need of blood transfusion, in the patient underwent to total knee replacement, where the ischemia was released before wound closure, has no statistical effect in comparison with patients where the sutures and bandages were done after the ischemia release. Level of Evidence IB - Individual randomized controlled trial with narrow confidence interval.

© 2013 Sociedade Brasileira de Ortopedia e Traumatologia. Published by Elsevier Editora Ltda. Este é um artigo Open Access sob a licença de CC BY-NC-ND

*Corresponding author at: Fundacao Hospital Adriano Jorge. Avenida Carvalho Leal, 1778. Cachoeirinha, CEP: 69065-000, Manaus, AM. Tel.: (92) 3612-2200.

E-mail: mgsleao@uol.com.br

Introduction

Degenerative osteoarthritis or knee arthrosis is a disease of inflammatory and degenerative nature that causes destruction of the joint cartilage and frequently leads to joint deformity and severe functional incapacity in more advanced cases, with surgical treatment reserved for these patients. Total knee arthroplasty (TKA) is one of the procedures most often performed within orthopedic settings and it presents good and excellent long-term results very consistently. The indications for TKA are based on deviations from the axis, the degree to which joint compartments have been compromised and patients' ages and complaints.

According to Camanho et al., the set of criteria that determine such indications include varus deviation greater than 15°; valgus deviation greater than 10°; femorotibial subluxation in the frontal plane greater than 10 mm; anteriorization of the tibia in relation to the femur on lateral radiographs; and severe compromising of two of the three joint compartments of the knee (medial femorotibial, lateral femorotibial or femoropatellar). There is a consensus regarding the age of 60 years for patients who present severe arthrosis without an indication for osteotomy or unicompartmental arthroplasty. Indication of TKA among patients under the age of 60 years starts to be considered in cases of severe joint destruction, in which other therapeutic processes are inefficient. With advances in the precision of implants, instruments and operative techniques, TKA is being increasingly indicated for this special group of patients.

During TKA, there is considerable blood loss, which increases the morbidity-mortality rates. 1 Certain methods assist in reducing the bleeding, such as use of pneumatic cuffs, minimally invasive surgery and antifibrinolytic substances. 1-3 With the aim of diminishing the number of blood transfusions during TKA, certain precautions for minimizing trans and postoperative bleeding have been described, such as use of pneumatic tourniquets and suction drains, improvement of surgical techniques, use of tranexamic acid, local infusion of norepinephrine, occlusion of the femoral milling orifice using a bone graft femoral, and most recently, placement of gel containing platelets in the operative wound.⁴ Ischemia in TKA provides a cleaner surgical field, makes it easier to place the implants and provides a better interface for the cement.^{5,6} However, use of a tourniquet for periods of more than two hours has been correlated with nerve paralysis, especially of the external popliteal sciatic nerve, and with greater postoperative pain.^{1,7}

The pressure used in the tourniquet needs to be sufficient to stop the bleeding in the surgical field, and the average used is 350 mm Hg. However, if the pressure is excessive, this may increase the postoperative pain. Moreover, there is controversy in the literature regarding the time when the tourniquet should be removed. This can be done during the operation, just after cementing the prosthesis, in order to provide direct hemostasis for the wound, or after suturing and applying the compressive dressing.

In the Brazilian literature, there is only one paper regarding red blood cell levels during the early postoperative period (48 hours) or the quantity drained, in relation to deflation of the pneumatic tourniquet before or after closure of the operative wound and placement of the compressive dressing.⁴

The aim of this study was to demonstrate the advantages and disadvantages of removing the ischemia before or after closure of the skin and placement of the compressive dressing in these surgical procedures, with regard to blood losses.

Materials and methods

A prospective randomized study was conducted between January 2009 and July 2010, in which the sample consisted of 40 patients who underwent unilateral TKA. There were 18 male patients (45%) and 22 female patients (55%), with a minimum age of 50 years and maximum of 76 years (mean of 65.38 years). The right side was affected in 57.5% of the cases. The serum hemoglobin level was measured before the surgery and 48 hours after the operation, and the volume contained in the vacuum suction drain was measured at the same time. The patients were divided into two groups: group A (20 knees from 20 patients) and group B (20 knees from 20 patients). In group A, formed by 11 women (55%) and nine men (45%), the ischemia was released before closure of the operative wound, which enabled rigorous control over the bleeding. The mean age in this group was 65.3 years, with a standard deviation of plus or minus 7.41 years. The minimum age in the group was 50 years and the maximum was 75 years. In group B, which like group A was composed of 11 women (55%) and nine men (45%), the ischemia was released after suturing of the skin and application of the compressive dressing. The mean age in this group was 65.45 years, with a standard deviation of plus or minus 6.6 years. The minimum age in this group was 51 years and the maximum was 76 years. The patients were divided between the groups by means of simple random sampling, using sequential numbers, i.e. they were numbered when they were admitted to the hospital. Those who received even numbers were included in group A and those who received odd numbers, in group B.

The criteria for patient exclusion were as follows: presentation of a diagnosis of mild primary knee arthrosis (Ahlback, as modified by Keys < III10-11); insufficient information in the medical records (lack of records of the volume drained and/or absence of pre and postoperative tests); presence of hematological diseases; use of anticoagulant medication; history of TKA revision or previous knee surgery; and presence of secondary degenerative or inflammatory arthropathy. All the patients signed an informed consent statement before being included in the study. The study had previously been assessed and approved by the hospital's ethics committee.

All the procedures were performed by the same surgeon and all of them were done using the same anesthetic technique. Exsanguination of the lower limb to be operated was done by means of elevation for five minutes followed by application of an elastic band and maintenance of ischemia by means of an inflated pneumatic cuff in the proximal region of the thigh, adjusted to 350 mm Hg. The knee was exposed by means of a median skin incision, a deep medial parapatellar retinacular

approach and mid-vastus capsulotomy. This was followed by bone cuts, performed by means of intramedullary guides, both in the femur and in the tibia (the surgeon's preference), and progressive ligament balance, without preservation of the posterior cruciate ligament. Bone plugs were routinely placed in the femoral and tibial canals and the knee was then copiously irrigated with saline solution. Cemented total prostheses (Modular III–MDT) were implanted which was done in association with replacement of the patellar component. Before closing the surgical wound, a vacuum suction drain of 3.2 mm in diameter was placed intra-articularly and in the deep layers of the subcutaneous cellular tissue. None of the surgical procedures lasted for more than 120 minutes. An inguinal-malleolar compressive dressing of Robert-Jones type was applied to all the patients.

Prophylaxis for deep vein thrombosis was administered, and a postoperative rehabilitation protocol was applied, involving active mobilization of the limb starting on the first postoperative day and early walking 48 hours after the operation, if tolerated by the patient. Dabigratan etexilate (110 mg orally) was also administered to all patients, at the dose of one capsule four hours after the operation and then two capsules as a single dose per day, for 10 days. Blood product transfusions were given to patients whose serum hemoglobin level was lower than 9 g/dL when measured 48 hours after the operation, with hemodynamic repercussions.

By convention, early release from ischemia was defined as release done before doing the suturing and applying the dressings, in which the knee was compressed for 10 minutes and hemostasis was carefully achieved; and late release was defined as release done after doing the suturing and applying the Robert-Jones compressive dressing to the operated limb.

The Minitab 15 and R 2.9.1 statistical software were used for the descriptive analyses and tests on the values obtained.

Results

Using the estimated overall population, the sample size was calculated by means of the formula for estimating proportions for finite N12 (Fig. 1).

In this case, an estimated proportion \hat{p} of 50% was used, to obtain the largest and smallest samples possible, with a 5% margin of error and 95% confidence interval.

The sample size obtained was 45 patients. It was decided to increase the sample by 10%, in order to compensate for possible losses, thus obtaining a final number of 49 patients. However, there were fewer occurrences of cases of unilateral TKA over the study period than had been expected. Therefore, all the cases of this type that were attended over the study period and which fitted within the criteria were included in this study, thus totaling 40 patients.

Tables 1 to 5 show the data relating to the values for groups A and B, regarding serum hemoglobin levels and blood losses through the suction drain (Fig. 2).

The values for the groups were close to the means for the pre and postoperative hemoglobin levels. Thus, the means for the decreases in hemoglobin levels in the groups also had values that were close to each other. The mean for group B was

slightly higher, thus firstly indicating that the group in which the ischemia was released after suturing the skin and applying the compressive dressing had slightly higher blood loss.

Student's t test was applied in order to investigate whether there was any difference in the mean decreases in hemoglobin levels in groups A and B, as shown in Table 6. The *p* value obtained in the test was not significant. However, there was statistical evidence that there was no significant difference between the means decreases in hemoglobin in groups A and B (Fig. 3).

The mean values for the two groups were very close to each other, and the values for the difference in hemoglobin levels observed in group B were within the interval of values of group A, distributed almost symmetrically, with lower variability. The confidence intervals also illustrate the test result well. The interval generated included zero, thus meaning that the difference in the means was zero at some moment and showing that the means were equal.

The means for blood drainage were then compared (Fig. 4). The mean blood volume drained in group B was greater, but the difference in relation to group A was small. This firstly indicates that group B required greater blood drainage. Because the data on the blood volumes drained in the groups was not normally distributed, the Mann-Whitney test was used for comparing the means, i.e. the nonparametric alternative to Student's t test, which compares the medians of the two populations (Table 7).

The p value obtained in the test was not significant. Thus, the statistical evidence showed that there was no significant difference between the medians of the blood volumes drained in groups A and B (Fig. 5). The medians in the two groups were practically equal and the intervals of values were close to each other, with positive asymmetry in group A and distribution of data within the interval similar to that of group B.

The serum hemoglobin levels showed a mean decrease of 3.57 g/dL in group A and 4.24 g/dL in group B, and there was a

$$n = \frac{Z^{2}.\hat{p}.\hat{q}.N}{d^{2}(N-1)+Z^{2}.\hat{p}.\hat{q}}$$

Fig. 1 -Estimated formula for sampling.

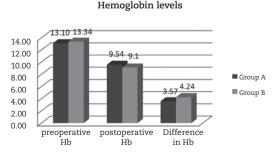


Fig. 2 - Mean hemoglobin levels in groups A and B in g/dL.

Table 1 - Descriptive measurements on the groups analyzed.										
Variables	Me	ean	Med	lian	Standard	deviation	Mini	mum	Maxii	num
	Α	В	A	В	A	В	A	В	A	В
Age	65.3	65.5	-	-	7.4	6.6	50.0	51.0	75.0	76.0
Preoperative Hb	13.1	13.3	13.2	13.5	0.8	0.9	12.0	12.0	14.6	14.9
Postoperative Hb	9.5	9.1	9.5	8.1	1.6	1.1	7.0	7.0	12.2	10.6
Volume drained	749.5	761.0	705.0	700.0	205.8	228.8	500.0	530.0	1,150.0	1,250.0

Hb group A Hb group B

Fig. 3 - Decreases in hemoglobin levels in groups A and B.

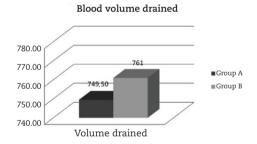


Fig. 4 - Mean blood volumes drained in groups A and B in mL.

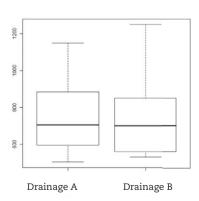


Fig. 5 - Blood volume drained in groups A and B.

Table 2 - Descriptive measurements on the hemoglobin levels in group A in g/dL.						
Mean	Median	SD	Min	Max		
13.10	13.15	0.78	12	14.60		
9.54	9.45	1.58	7	12.20		
	Mean 13.10	Mean Median 13.10 13.15	Mean Median SD 13.10 13.15 0.78	Mean Median SD Min 13.10 13.15 0.78 12		

	Table 3 - Descriptive measurements on the blood volume drained in group A in mL.							
Variables	Mean	Median	SD	Min	Max			
Blood drainage	749.5	705	205.8	500	1,150			

Table 4 - Descriptive measurements on the hemoglobin levels in group B in g/dL.						
Variables	Mean	Median	SD	Min	Max	
Preoperative Hb	13.34	13.45	0.89	12	14.9	
Postoperative Hb	9.10	8.10	1.14	7	10.6	

Table 5 - Descriptive measurements on the blood volume drained in group B in mL.						
Variables	Mean	Median	SD	Min	Max	
Blood drainage	761	700	228.8	530	1,250	

Table 6 - Student's t test for the mean hemoglobin levels in g/dL.						
Variables	Mean value	p-value	Confidence interval			
ΔНВ А	3.57	0.2321	(-1.7736; 0.4436)			
ΔНВ В	4.24	0.2321	(-1.7730, 0.4430)			

Table 7 - Medians for blood volumes drained in groups
A and B in mL.

Variables	Mean value	p-value	Confidence interval
Volume drained A	705	0.9892	(-120; 109.9)
Volume drained B	700		(1, 2000)

difference of 0.67 g/dL between the means. This was considered to be statistically non-significant (p = 0.2321), with a confidence interval from -1.7736 to 0.4436. The median for the drainage observed was 705 mL in group A and 700 mL in group B. The difference of 5 mL between the medians was considered to be statistically non-significant (p = 0.9892). The number of patients who received transfusions was four in each group and all of them received the same quantity (two units of red cell concentrate), which was not considered to be statistically significant.

A single patient in group A presented a complication, with evolution to superficial infection of the surgical wound seven days after the first operation. Mechanical-surgical cleaning was performed and antibiotic therapy was administered. No thromboembolic events such as deep vein thrombosis and/or pulmonary embolism, proven clinically or through laboratory tests, were observed.

Discussion

Use of a pneumatic tourniquet in TKA makes it possible for the operative field to be blood-free, which facilitates soft-tissue dissection and bone-cutting and improves the cementation of the prosthesis. However, there are divergences of opinion regarding the time to remove the tourniquet, with a view to preserving the blood stock.

The first study comparing the two methods was conducted by Newman et al., ¹³ on 80 patients who underwent cemented TKA. These authors reported that there was less blood loss when the tourniquet was removed after suturing and applying the dressing. On the other hand, in a non-randomized study, Page et al. ¹⁴ reported that better results were obtained among patients in whom the ischemia was released during the operation in order to achieve direct hemostasis, since there was a possibility of lesions in larger vessels that could not be ascertained during the operation and hence the possibility of bleeding of the wound despite applying a compressive dressing. Despite the reduction in bleeding that was found, all of their patients received transfusions. Since then, several studies have been published with discordant results. ⁴

Abdel-Salam and Eyres⁵ did not find any difference in the duration of the operation or in blood loss when they compared use or nonuse of a tourniquet. However, they noted that there was lower postoperative pain among patients in whom a

tourniquet had not been used. Release of the ischemia before closing the wound does not have any benefit if the blood loss and need for transfusion is considered. 15-17 Schuh et al. 18 found the same results but observed that there was a greater number of cases of deep vein thrombosis in the group in which the ischemia had not been released before closure in order to perform rigorous hemostasis. Pre-closure release did not interfere with the postoperative bleeding, thus justifying earlier release of the ischemia with the aim of ascertaining the integrity of the blood vessels and controlling any severe hemorrhaging. 19

Releasing the tourniquet after closure of the wound diminished the operative blood loss and there was greater possibility of reinfusion of the postoperative drained blood.²⁰ This has the result of reducing the use of blood banks, which diminishes the risk of infection and the length of stay in hospital,^{21,23} as well as reducing the transmission of infectious diseases. In the same way, patients with preoperative hemoglobin levels lower than 13 g/dL have higher incidence of postoperative blood transfusion.²² Recent studies have demonstrated that there are no statistically significant differences between immediate opening of the suction drain or doing this more than one hour after the end of the procedure.^{23,24}

Some studies have reported that there is greater bleeding when uncemented prostheses are used, in comparison with cemented prostheses. Use of orthopedic cement diminishes bleeding in TKA because of its mechanical properties on bone cuts, along with the chemical and thermal properties of the cementation. Another factor reported in the literature that might influence blood losses in TKA is early rehabilitation programs. This comes about particularly through using apparatus for continuous passive movement, which has been correlated with increased postoperative bleeding.⁴ The patients studied did not use continuous passive movement. The rehabilitation program was started early on, but with active exercises done by the patients themselves, which went as far as the pain threshold. Early rehabilitation is important for avoiding joint stiffness, improving circulatory conditions and preventing thromboembolism.

Only four patients of this series (10%) underwent blood transfusion, which is discordant with the descriptions in the literature that we researched, in which the number of transfusions is higher. However, these studies did not present any pre-established criteria for carrying out.

Tranexamic acid acts by inhibiting activation of the fibrinolytic system at the start of the coagulation cascade, which results in lower blood loss. It can be used topically without any noteworthy systemic effects. ²⁶ There is concern regarding the fact that this inhibition may cause an increase in thromboembolic events. ^{27,28}

In the conventional technique, use of an autologous bone plug extracted from bone cuts would diminish the postoperative bleeding,²⁹ although some studies in the literature do not support this measure.³⁰

In this light, and even given all of the controversy that the present topic might generate, the data obtained from the sample and their results were absolutely coherent with the literature. The approaches of early or later release of ischemia are for the surgeon to determine.

Conclusions

TKA is a universally accepted procedure that is performed to treat degenerative disorders of the knee, with consistently good and excellent long-term results. However, it is not a procedure that is free from complications. Among these is the great blood loss that makes it necessary to use blood products.

With the aims of avoiding increased blood losses, achieving greater precision in bone-cutting, improving the soft-tissue balance and increasing the cemented interface, many surgeons choose to work with a blood-free field, through inducing ischemia using a tourniquet at the root of the thigh of the limb to be operated.

From the statistical analysis, it was found and concluded that releasing the ischemia before closing the operative wound does not have any significant effect on the blood loss through the suction drain or on the postoperative serum hemoglobin levels, in comparison with ending the ischemia after doing the suturing and applying the dressings. Thus, this remains a matter for the surgeon's discretion and experience.

Conflicts of interest

The authors declare that there was no conflict of interests in conducting this study.

REFERENCES

- Camanho GL, Oliv R, Camanho LF. Artroplastia total de joelho em pacientes idosos portadores de osteoartrose. Rev Bras Ort. 1998;33:274-71.
- Lotke PA, Faralli VJ, Orenstein EM, Ecker ML. Blood loss after total knee replacement: effects of tourniquet release and continuous passive motion. J Bone Joint Surg Am. 1991;73(7):1037-40.
- Levy O, Martinowitz U, Oran A, Tauber C, Horoszowski H. The
 use of fibrin tissue adhesive to reduce blood loss and the
 need for blood transfusion after total knee arthroplasty. A
 prospective, randomized, multicenter study. J Bone Joint Surg
 Am. 1999;81(11):1580-8.
- Vasconcelos JW, Vasconcelos GA. Avaliação da perda sanguínea na artroplastia total do joelho com e sem soltura do torniquete. Acta Ortop Bras. 2011;19(1):32-6.
- 5. Abdel-Salam A, Eyres KS. Effects of tourniquet during total knee arthroplasty: a prospective randomized study. J Bone Joint Surg Br. 1995;77(2):250-3.
- Wakankar HM, Nicholl JE, Koka R, D'Arcy JC. The tourniquet in total knee arthroplasty: a prospective, randomized study. J Bone Joint Surg Br. 1999;81(1):30-3.
- Christodoulou AG, Ploumis, AL, Terzidis IP, Chantzidis P, Metsovitis SR. The role of timing of tourniquet release and cementing on perioperative blood loss in total knee replacement. Knee. 2004;11(4):313-7.

- 8. Ishii Y, Matsuda Y. Effect of tourniquet pressure on perioperative blood loss associated with cementless total knee arthroplasty. J Arthroplasty. 2005;20(3):325-9.
- Barwell NJ, Anderson G, Hassan A, Rawlings I. The effects of early tourniquet release during total knee arthroplasty: a prospective randomized double-blind study. J Bone Joint Surg Br. 1997;79(2):265-8.
- Ahlback S. Osteoarthrosis of the knee. A radiographic investigation. Acta Radiol Diagn (Stockh). 1968;(Suppl 277):72-7.
- Keyes GW, Carr AJ, Miller RK, Goodfellow JW. The radiographic classification of medial gonarthrosis. Correlation with operation methods in 200 knees. Acta Orthop Scand. 1992;63(5):497-501.
- 12. Bolfarine H, Bussab WO. Elementos de amostragem. São Paulo: ABE/Projeto Fisher, 2005.
- 13. Newman JH, Jackson JP, Waugh W. Timing of tourniquet removal after knee replacement. J R Soc Med. 1979;72(7):492-3.
- 14. Page MH, Shepard BD, Harrisson JM. Reduction of blood loss in knee arthroplasty. Aust NZ J Surg. 1984;54(2):141-4.
- Burkart BC, Bourne RB, Rorabeck CH, Kirk PG, Nott L. The efficacy of tourniquet release in blood conservation after total knee arthroplasty. Clin Orthop Rel Res. 1994;(299):147-52.
- Widman J, Isacson J. Surgical hemostasis after tourniquet release does not reduce blood loss in knee replacement: a prospective randomized study of 81 patients. Acta Orthop Scand. 1999;70(3):268-70.
- Hersekli MA, Akpinar S, Ozkoc G, Ozalay M, Uysal M, Cesur N, Tandogan RN. The timing of tourniquet release and its influence on blood loss after total knee arthroplasty. Int Orthop. 2004;28(3):138-41.
- Schuh A, Hausel M, Salminen S. Effect of tourniquet use on blood loss in total knee arthroplasty. Zentralbl Chir. 2003;128(10):866-70.
- Mencia-Barrio R, Sanchez-Herraez S, Alonso-Barrio JA, Sanchez-Lazaro J, Betegon-Nicolas JC, Fernandez-Hernandez O. Eficacia de la hemostasia tras retirada del torniquete en la artroplastia de rodilla. Rev Ortopedia Traumatol. 2005;49(5):341-5.
- Newman JH, Bowers M, Murphy J. The clinical advantage of autologous transfusion: a randomized, controlled study after knee replacement. J Bone Joint Surg Br. 1997;79(4):630-2.
- 21. Majkowsk RS, Currie IC, Newman JH. Postoperative collection and reinfusion of autologous blood in total knee arthroplasty. Ann R Coll Surg Engl. 1991;73(6):381-4.
- 22. Keating EM, Meding JB, Faris PM, Ritter MA. Predictors of transfusion risk in elective knee surgery. Clin Orthop Relat Res. 1998;(357):50-9.
- 23. Vandenbussche E, Duranthon LD, Couturier M, Podhorz L, Augereau B. The effect of tourniquet use in total knee arthroplasty. Int Orthop. 2002;26(5):306-9.
- 24. Kiely N, Hockings M, Gambhir A. Does temporary clamping of drains following knee arthroplasty reduce blood loss? A randomized controlled trial. Knee. 2001;(4):325-7.
- 25. Rosencher N, Kerkkamp HE, Macheras G, Munuera LM, Menichella G, Barton DM et al. Orthopedic surgery transfusion hemoglobin european overview (Ostheo) study: blood management in elective knee and hip arthroplasty in Europe. Transfusion. 2003;43(4):459-69.
- Wong J, Abrishami A, El Beheiry H, Mahomed NN, Davey Jr, Gandhi R et al. Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: a randomized controlled trial. J Bonde Joint Surg. 2010;92(15):2505-13.

- 27. Cid J, Lozano M. Tranexamic acid reduces allogeneic red cell transfusions in patients undergoing total knee arthroplasty: result of a meta-analysis of randomized controlled trials. transfusion. 2005;45(8):1302-7.
- 28. Orpen NM, Little C, Walker G, Crawfurd E. Tranexamic acid reduces early post-operative blood loss after total knee arthroplasty: a prospective randomized controlled trial of 29 patients. Knee. 2006;13(2):106-10.
- 29. Ko PS, Tio MK, Tang YK, Tsang WL, Lam JJ. Sealing the intramedullary femoral canal with autologous bone plug in total knee arthroplasty. J Arthroplasty. 2003;18(1):6-9.
- 30. Demey G, Servien E, Pinaroli A, Lustig S, Selmi TAS, Neyret P. The influence of femoral cementing on perioperative blood loss in total knee arthroplasty: a prospective randomized study. J Bone Joint Surg. 2010;92(3):536-41.