The influence of tourniquet use and operative time on the incidence of deep vein thrombosis in total knee arthroplasty

Arnaldo José Hernandez,1 Adriano Marques de Almeida,1 Edmar Fávaro,II Guilherme Turola Sguizzato1

1Faculdade de Medicina da Universidade de São Paulo, Department of Orthopedics and Traumatology São Paulo/SP, Brazil. II Hospital Santa Casa de São Paulo, São Paulo/SP, Brazil.

OBJECTIVE: To evaluate the association between tourniquet and total operative time during total knee arthroplasty and the occurrence of deep vein thrombosis.

METHODS: Seventy-eight consecutive patients from our institution underwent cemented total knee arthroplasty for degenerative knee disorders. The pneumatic tourniquet time and total operative time were recorded in minutes. Four categories were established for total tourniquet time: <60, 61 to 90, 91 to 120, and >120 minutes. Three categories were defined for operative time: <120, 121 to 150, and >150 minutes. Between 7 and 12 days after surgery, the patients underwent ascending venography to evaluate the presence of distal or proximal deep vein thrombosis. We evaluated the association between the tourniquet time and total operative time and the occurrence of deep vein thrombosis after total knee arthroplasty.

RESULTS: In total, 33 cases (42.3%) were positive for deep vein thrombosis; 13 (16.7%) cases involved the proximal type. We found no statistically significant difference in tourniquet time or operative time between patients with or without deep vein thrombosis. We did observe a higher frequency of proximal deep vein thrombosis in patients who underwent surgery lasting longer than 120 minutes. The mean total operative time was also higher in patients with proximal deep vein thrombosis. The tourniquet time did not significantly differ in these patients.

CONCLUSION: We concluded that surgery lasting longer than 120 minutes increases the risk of proximal deep vein thrombosis.

KEYWORDS: Deep Vein Thrombosis; Prophylaxis; Thromboembolism; Tourniquet; Knee Prosthesis.

INTRODUCTION

The induction of deep vein thrombosis (DVT) following total knee arthroplasties (TKAs) and total hip arthroplasties is frequently studied (1), although DVT also results from other knee procedures (2). Despite the importance of and interest in this problem, most researchers studying DVT generally focus on postoperative prophylaxis. Surprisingly, few studies have investigated the isolated risk factors for DVT associated with TKA. Although controversy exists regarding the role of TKA alone as a risk factor for DVT (3–7), some researchers believe that bone manipulation, reaming of the medullary canal, and the operative time are relevant risk factors for DVT (8,9). Another important and controversial factor related to TKA is the use of surgical tourniquets. Although all of these factors are mentioned in the literature, operative time has received little attention as an isolated risk factor for DVT in TKA.

We used ascending venography (AV) to determine the presence of proximal and distal DVT after TKA and evaluated the association between tourniquet time and TKA operative time and the occurrence of DVT.

PATIENTS AND METHODS

Seventy-eight consecutive patients from our institution underwent cemented TKA for degenerative knee disorders. Of the 78 patients, 78.2% were women and 21.8% were men, with an average age of 65.1 years (range, 31–88 years; SD, 11.5 years). Osteoarthrosis was the diagnosis in 74.4% of the cases, rheumatoid arthritis in 21.8%, and other disorders in the remaining 3.8%.

All total knee arthroplasties were performed with the same technique. An intramedullary guide was used for distal femoral osteotomy. An extramedullary guide was
used for proximal tibial osteotomy. We recorded the total pneumatic tourniquet time and total operative time in minutes. In all cases, the use of a tourniquet was interrupted for hemostasis after the implant was cemented and before wound closure. Four categories were established for total tourniquet time: <60, 61 to 90, 91 to 120, and >120 minutes. The total operative time was consistently defined as the time from the initial incision to the last suture stitch made to close the incision. Three categories were defined for operative time: <120, 121 to 150, and >150 minutes. Only two patients (3.1%) were administered a general anesthetic; all other patients received a spinal block. All patients received DVT prophylaxis with oral anticoagulants for 12 days, with an international normalized ratio maintained at approximately 2.5 (range, 2.0–3.0) in all cases (10).

An ascending venography, for which the patients provided informed consent, was performed between 7 and 12 days after surgery after discharge from the hospital. The study end point was defined based on the execution of bilateral AV. The AV was performed by a specialist in vascular radiology. The technique applied was performed essentially as described by Rabinov and Paulin (11). The presence of clinically manifested DVT and/or pulmonary embolism was also considered. The clinical manifestations of DVT were defined as follows: greater edema of the affected lower limb than would be expected for the procedure, intense pain on palpation of the calf, and pain on passive dorsiflexion of the foot. An AV finding that was considered to be positive for DVT was the presence of blood clots in the vein lumens (Figure 1). DVTs were characterized as occurring on the operated side, on the contralateral side or bilaterally and were classified as proximal or distal DVT.

We used the chi-squared test for the comparison of qualitative variables between groups. For the quantitative variables, we used Levene’s test to determine the homogeneity of variances and the Kolmogorov-Smirnov test to determine the normality of the distribution. In cases in which both conditions were met, the averages of both groups were compared using Student’s t-test. A level of significance of 5% was adopted in the analyses. The statistical program used was SPSS (SPSS for Windows, release 6.0, SPSS Inc., Chicago, IL, USA).

RESULTS

We found that 45 patients (57.7%) had negative bilateral AV, and 33 (42.3%) had DVT. Thirteen patients (16.7%) had a proximal DVT. We compared the patients with DVT with those without DVT. We also compared the cases with proximal DVT with the cases involving distal DVT and the cases with normal findings on AV.

The baseline characteristics of our patients are summarized in Table 1. We observed that patients with DVT were older than patients without DVT (62.9 ± 12.3 vs 68.2 ± 9.7 years, respectively; p = 0.04). When we compared only the patients with proximal DVT with the other patients, we found no difference in age between the groups (64.3 ± 12.0 vs 69.2 ± 7.8 years, respectively; p = 0.2). We also observed that osteoarthritis was the most frequent diagnosis and was found in almost 90% of patients with DVT.

The total population did not demonstrate any statically significant differences in tourniquet or total operative time based on the presence or absence of DVT, as shown in Table 2. Considering only patients with proximal DVT, we found no significant difference in tourniquet time (p = 0.08). For total operative time, we observed a significant difference between the groups, with a higher frequency of proximal DVT in patients with an operative time that was longer than 120 minutes (p = 0.05) (Table 3). Patients with proximal DVT also had a higher mean operative time (146.9 ± 20.4 vs 127.9 ± 22.4 min, respectively; p = 0.01) (Table 4).

DISCUSSION

The systematic reviews of DVT in TKA almost exclusively address therapeutic alternatives for this condition (12–15); few reviews address the risk factors. We believe that undergoing TKA is itself a risk factor for DVT (3–5,12,16,17). One of the few reports that contradict this hypothesis is a report by Fowkes et al. (18), which addresses the general aspects of the incidence of DVT, reporting it as approximately 10,000 persons/year in the general population. Bhandari et al. (19) warned that the inherent limitations of those studies and the lack of attention to other risk factors render these reports of limited value. Gross et al. (20) noted that studies on DVT prophylaxis have demonstrated a low incidence of DVT complications after total hip arthroplasty and TKA, which is far below the incidences that were initially reported in venography studies conducted to detect asymptomatic DVT. Improving the techniques used in perioperative orthopedic care should reduce thromboembolic complications, regardless of prophylaxis. According to Bergqvist et al.
Although many authors accept the possibility of DVT with these procedures, others no longer consider this complication to be a serious problem (21,22). Some authors believe that mechanical prophylaxis, even with limited resources, is adequate in all cases of TKA (23–25), whereas others believe that pharmacologic prophylaxis in arthroplasty is indicated in select cases according to the individual risk for DVT (26). We agree with the view of Haas et al. (14); although there is no ideal prophylaxis, a multimodal approach that combines pharmacologic therapy with mechanical prophylaxis has proven to be safe and effective.

The number of studies that clearly define the risk factors for DVT in TKA remains small. Surgical and orthopedic aspects, such as the duration of tourniquet use and operative time, are not identified as risk factors by some authors (6,7).

The frequency of DVT observed in TKA varies from 20.3% to 84%, regardless of prophylaxis. In the proximal form of DVT, these values range from 4.4% to 20% (6,27–30). In our study, we observed only one case of clinical DVT, which made statistical analysis unfeasible. Although most studies report small numbers of patients with symptomatic DVT, Wang et al. (28) observed this clinical phenomenon in up to 70% of cases. There were no cases of pulmonary embolism in the present study. The frequency of pulmonary embolism has been reported to be low, varying between 0 and 20% (31,32), but most studies have reported that the frequency is approximately 1% (6,33,34). In our analyses, we only considered cases of general DVT and proximal DVT, which were specifically studied because these forms are considered to potentially have more severe complications (30,35,36).

Data related to the surgical procedure itself are always important to orthopedists. The most optimal moment at which the surgical technique can be evaluated and modified for the patient’s benefit is during the operation. The type of anesthesia used is certainly one of the most frequently evaluated topics in the literature, although some doubts remain regarding the effects of anesthesia type on DVT incidence. Researchers have studied epidural block alone versus general anesthesia, and most data suggest that epidural block should be protective against DVT (29,37–40). However, in a recent article, Macfarlane et al. (41) questioned these results. Evaluating anesthesia in isolation was not the objective of our study. The high frequency of spinal blocks in the present study (96.9%) can be attributed to the routines of the anesthesia service. Thus, it was not possible to detect the influence of the type of anesthesia on the occurrence of DVT.

Table 1 - Patient baseline characteristics.

| Variable          | Population | Without DVT | With DVT | p-value |
|-------------------|------------|-------------|----------|---------|
| Gender            | Male       | 17 (21.8)   | 11 (24.4)| 6 (18.2)| 0.51    |
|                   | Female     | 61 (78.2)   | 34 (75.6)| 27 (81.8)|        |
| Age (Mean [range])| 65.1 (31-88)| 62.9 (31-88)| 68.2(39-82)|       | 0.04*   |
| Ethnic group      | White      | 56 (71.8)   | 30 (66.7)| 26 (78.8)|        |
|                   | Black      | 14 (17.9)   | 11 (24.4)| 3 (9.1) | 0.21    |
|                   | Other      | 8 (10.3)    | 4 (8.9)  | 4 (12.1)|         |
| Diagnosis         | Osteoarthritis | 58 (74.4)  | 29 (64.4)| 29 (87.9)|        |
|                   | Rheumatoid arthritis | 17 (21.8)  | 14 (31.1)| 3 (9.1) | 0.05*   |
|                   | Other      | 3 (3.8)     | 2 (4.4)  | 1 (3.0) |         |
| BMI (Mean [range])| 29.2 (18.5-48.3) | 29.2 (18.5-41.4)| 29.3 (21-48.3)|       | 0.95    |

Table 2 - The population distribution based on tourniquet (n = 74) and operative times (n = 78) and a comparative analysis of patients with and without DVT.

| Variable          | No. of Patients (%) | p-value |
|-------------------|---------------------|---------|
| Tourniquet time (min) |                     |         |
| <120              | 6 (8.1)             | 3 (7.0) | 3 (9.7) | 0.19 |
| 61–90             | 33 (44.6)           | 21 (48.8)| 12 (38.7)| |
| 91–120            | 32 (43.2)           | 19 (44.2)| 13 (41.9)|         |
| 121–150           | 3 (4.1)             | ---     | 3 (9.7) |         |
| Surgery time (min) |                     |         |
| <120              | 24 (31.1)           | 16 (35.6)| 8 (24.2) | 0.56 |
| 121–150           | 43 (53.8)           | 23 (51.1)| 20 (60.6)|         |
| >150              | 11 (14.1)           | 6 (13.3) | 5 (15.2) |         |

Table 3 - The population distribution by tourniquet (n = 74) and operative times (n = 78) and a comparative analysis of patients with and without proximal DVT.

| Variable          | No. of Patients (%) | p-value |
|-------------------|---------------------|---------|
| Tourniquet time (min) |                     |         |
| <120              | 5 (8.1)             | 1 (8.3) | 0.08 |
| 61–90             | 27 (43.5)           | 6 (50.0) |        |
| 91–120            | 29 (46.8)           | 3 (25.0) |         |
| 121–150           | 1 (1.6)             | 2 (16.7) |         |
| Surgery time (min) |                     |         |
| <120              | 23 (35.4)           | 1 (7.7) | 0.05* |
| 121–150           | 35 (53.8)           | 8 (61.5) |         |
| >150              | 7 (10.8)            | 4 (30.8) |         |

Chi-squared test; *significant value.

DVT, deep vein thrombosis.
Despite our conviction concerning the link between operative time and DVT, which was confirmed by our findings, we do not recommend rushing the surgical procedure in an attempt to shorten it because other equally severe problems, such as poor component alignment, poor ligament balance, and unsatisfactory homeostasis, may develop. We believe that the most effective way to shorten surgery is detailed planning, discipline, and familiarization of the surgical team with the surgical instruments. We should note that our institution is a training center for large numbers of medical residents, who perform many TKAs.

We conclude that a total operative time of >120 minutes, which is generally sufficient for a careful procedure in the majority of TKAs, increases the risk of proximal DVT, and although our findings were not statistically significant, a tourniquet time of >90 minutes should be considered as a possible risk factor for proximal DVT.

**AUTHOR CONTRIBUTIONS**

Hernandez AJ was the main author and researcher and performed patient and data evaluation, the statistical analyses, and manuscript writing. Almeida AM and Favaro E were involved in data analysis and manuscript writing. Sguizzato GT performed patient evaluations and collected data.

**REFERENCES**

1. Bergqvist D, Bergentz SE, Fredin H. Thromboembolism in orthopaedic surgery. Acta Orthop Scand. 1984;55(3):247-50.
2. Stringer MD, Steadman CA, Hedges AR, Thomas EM, Morley TR, Kakkar VV. Deep vein thrombosis after elective knee surgery. An incidence study in 312 patients. J Bone Joint Surg Br. 1989;71(3):492-7.
3. Caprini JA, Arcelus JJ, Reyna JJ. Effective risk stratification of surgical and nonsurgical patients for venous thromboembolic disease. Semin Hematol. 2001;38(2 Suppl 5):12-9.
4. Geerts WH, Heit JA, Clagett GP, Pineo GF, Colwell CW, Anderson FA Jr et al. Prevention of venous thromboembolism. Chest. 2001;119(1 Suppl):132S-55.
5. Haas S. Prevention of venous thromboembolism: recommendations based on the International Consensus and the American College of Chest Physicians Sixth Consensus Conference on Antithrombotic Therapy. Clin Appl Thromb Hemost. 2001;7:317-7, http://dx.doi.org/10.1177/10760 29601007003001.
6. Stulberg BN, Issall JN, Williams GW, Ghelman B. Deep-vein thrombosis following total knee replacement. An analysis of six hundred and thirty-eight arthroplasties. J Bone Joint Surg Am. 1984;66(2):194-201.
7. Kim YH, Kim VE. Factors leading to low incidence of deep vein thrombosis after cemenless and cemented total knee arthroplasty. Clin Orthop Relat Res. 1991(191):19-24.
8. Haas S. Managing the risk of venous thromboembolism in orthopedics: concluding remarks. Orthopedics. 1997;20(Suppl):26-7.
9. Zaw HM, Osborne IC, Pettit PN, Cohen AT. Risk factors for venous thromboembolism in orthopedic surgery. Isr Med Assoc J. 2002;4(11):1040- 2.
10. Geerts W, Heit J, Clagett J, et al. Prevention of venous thromboembolism. Chest. 2001;119(Suppl 1):1325-1755.
11. Rabinov K, Paulin S, Roentgen diagnosis of venous thrombosis in the leg. Arch Surg. 1972;104(2):134-44, http://dx.doi.org/10.1001/archsurg.1972. 0418002014004.
12. Brookenthal KR, Freedman KB, Lotke PA, Fitzgerald RH, Lonner JH. A meta-analysis of thromboembolic prophylaxis in total knee arthroplasty. J Arthroplasty. 2001;16(3):293-300, http://dx.doi.org/10.1054/artj.2001. 21499.
13. Pellegrini VD Jr, Sharrock NE, Paiement GD, Morris R, Warwick DJ. Venous thromboembolic disease after total hip and knee arthroplasty: current perspectives in a regulated environment. Instr Course Lect. 2008;57:637-61.
14. Johanson NA, Lachiewicz PF, Lieberman JR, Lotke PA, Parvizi J, Pellegrini V. et al. Prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty. J Am Acad Orthop Surg. 2009;17(3):183-96.
15. Haas SB, Barrack RL, Westrich G. Venous thromboembolic disease after total hip and knee arthroplasty. Instr Course Lect. 2009;58:781-93.
16. Westrich GH, Haas SB, Mosca P, Peterson M. Meta-analysis of thromboembolic prophylaxis after total knee arthroplasty. J Bone Joint Surg Br. 2000;82(6):795-800, http://dx.doi.org/10.1302/0301-620X.82B6. 9869.

---

**Table 4 - Analysis of patients with proximal DVT and patients without proximal DVT by tourniquet (n = 74) and operative times (n = 78) and a comparison of means.**

| Variable                  | No. of Patients (%) | p-value |
|---------------------------|---------------------|---------|
| Tourniquet time (min)     |                     |         |
| µ ± SD Range              |                     |         |
| µ ± SD                    |                     |         |
| Surgery time (min)        |                     |         |
| µ ± SD Range              |                     |         |

Chi-squared test, *significant value.

DVT, deep vein thrombosis; µ, mean; SD, standard deviation.
17. Eikelboom JW, Quinlan DJ, Douketis JD. Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials. Lancet. 2001;358(9275):9-15, http://dx.doi.org/10.1016/S0140-6736(00)05249-1.

18. Fowkes FJ, Price JP, Fowkes FG. Incidence of diagnosed deep vein thrombosis in the general population: systematic review. Eur J Vasc Endovasc Surg. 2003;25(1):1-5, http://dx.doi.org/10.1016/j.ejvs.2002.1778.

19. Bhandari M, Morrow F, Kulkarni AV, Tornetta P3rd. Meta-analyses in orthopaedic surgery: A systematic review of their methodologies. J Bone Joint Surg Am. 2001;83A(1):15-24.

20. Gross M, Anderson DR, Nagpal S, O’Brien B. Venous thromboembolism prophylaxis after total hip or knee arthroplasty: a survey of Canadian orthopaedic surgeons. Can J Surg. 1999;42(4):437-61.

21. McNally MA, Mollan RA. Venous thromboembolism and orthopaedic surgery. J Bone Joint Surg Br. 1993;75(4):517-9.

22. Prentice CR. Thromboprophylaxis in elective orthopaedic surgery—what is the purpose? J Bone Joint Surg Br. 1997;79(6):889-90, http://dx.doi.org/10.1302/0301-620X.79B6.8449.

23. Sarmiento A, Goswami AD. Thromboembolic prophylaxis with use of aspirin, exercise, and graded elastic stockings or intermittent compression devices in patients managed with total hip arthroplasty. J Bone Joint Surg Am. 1999;81A(3):339-46.

24. Goldberg A. Prevention of deep-vein thrombosis after total knee replacement. J Bone Joint Surg Br. 2000;82(2):304-5.

25. Lotke PA, Ecker ML, Alavi A, Berkowitz H. Indications for the treatment of deep vein thrombosis following total knee replacement. J Bone Joint Surg Am. 1984;66(2):202-8.

26. Gillespie W, Murray D, Gregg PJ, Warwick D. Risks and benefits of prophylaxis against venous thromboembolism in orthopaedic surgery. J Bone Joint Surg Br. 2000;82(4):479-90, http://dx.doi.org/10.1302/0301-620X.82B4.10452.

27. Hirsh J. Prevention of venous thrombosis in patients undergoing major orthopaedic surgical procedures. Acta Chir Scand. 1990(Suppl):536:30-5.

28. Wang CJ, Wang JW, Chen LM, Chen HS, Yang BY, Cheng SM. Deep vein thrombosis after total knee arthroplasty. J Formos Med Assoc. 2000;99(11):848-53.

29. Francis CW, Berkowitz SD, Comp PC, Lieberman JR, Ginsberg JS, Paiement G, et al. Comparison of similagatran with warfarin for the prevention of venous thromboembolism after total knee replacement. N Engl J Med. 2003;349(18):1703-12, http://dx.doi.org/10.1056/NEJMoa035162.

30. Nathan SB, Am MA, Thiagarajan P, Das De S. The incidence of proximal deep vein thrombosis following total knee arthroplasty in an Asian population: a Doppler ultrasound study. J Orthop Surg (Hong Kong). 2003;11(2):184-9.

31. Sudhir A, Saini A, Horikawa K, Yamakawa T, Shi D, Uchida A. The incidence of deep vein thrombosis after hip and knee arthroplasties in Japanese patients: a prospective study. J Orthop Surg (Hong Kong). 2003;11(2):174-7.

32. Della Valle CJ, Steiger DJ, Di Cesare PE. Thromboembolism after hip and knee arthroplasty: diagnosis and treatment. J Am Acad Orthop Surg. 1998;6(6):327-36.

33. Khaw FM, Moran CG, Pinder IM, Smith SR. The incidence of fatal pulmonary embolism after knee replacement with no prophylactic anticoagulation. J Bone Joint Surg Br. 1993;75(6):940-1.

34. Mantilla CB, Horlocker TT, Schroeder DR, Berry DJ, Brown DL. Frequency of myocardial infarction, pulmonary embolism, deep venous thrombosis, and death following primary hip or knee arthroplasty. Anesthesiology. 2002;96(5):1140-6.

35. Mitchell D, Friedman RJ, Baker DJ3rd, Cooke JE, Darcy MD, Miller MC3rd. Prevention of thromboembolic disease following total knee arthroplasty. Epiludus versus general anesthesia. Clin Orthop Relat Res. 1991(269):109-12.

36. Leclerc J, Geerts WH, Desjardins L, Laflamme GH, L’Esperance B, Demers C, et al. Prevention of venous thromboembolism after knee arthroplasty. A randomized, double-blind trial comparing enoxaparin with warfarin. Ann Intern Med. 1996;124(7):619-26.

37. Nielsen PT, Jorgensen LN, Albrecht-Beste E, Leffers AM, Rasmussen LS. Lower thrombosis risk with epidural blockade in knee arthroplasty. Acta Orthop Scand. 1990;61(1):29-31.

38. Sharrock NE, Haas SB, Harpget MJ, Urquhart B, Insall JN, Scuderi G. Effects of epidural anesthesia on the incidence of deep-vein thrombosis after total knee arthroplasty. J Bone Joint Surg Am. 1991;73(6):502-6.

39. Shirrock NE, Go G, Williams-Russo P, Haas SB, Harpel PC. Comparison of extradural and general anesthesia on the fibrinolytic response to total knee arthroplasty. Br J Anaesth. 1997;79(1):29-34, http://dx.doi.org/10.1093/bja/79.1.29.

40. Hollihann MW, Wieczorek KS, Smart M, Durieux ME. Epidural anesthesia prevents hypercoagulation in patients undergoing major orthopedic surgery. Reg Anesth Pain Med. 2001;26(3):215-22.

41. Macfarlane AJ, Prasad GA, Chan VW, Brull R. Does regional anesthesia improve outcome after total knee arthroplasty? Clin Orthop Relat Res. 2009;467(9):2379-402, http://dx.doi.org/10.1007/s11999-008-0666-9.

42. Wilson JS, Miranda A, Johnson BL, Shames ML, Back MR, Randyk DF. Vascular injuries associated with elective orthopedic procedures. Ann Vasc Surg. 2003;17(6):641-4, http://dx.doi.org/10.1016/s1091-3077(03)0074-2.

43. Wauke K, Nagashima M, Kato N, Ogawa R, Yoshino S. Comparative study between thromboembolism and total knee arthroplasty with or without tourniquet in rheumatoid arthritis patients. Arch Orthop Trauma Surg. 2002;122(8):442-6.

44. Wanakarar IM, Nicholl JE, Koka R, D’Arcy JC. The tourniquet in total knee arthroplasty. A prospective, randomised study. J Bone Joint Surg Br. 1999;81(1):30-3, http://dx.doi.org/10.1302/0301-620X.81B1.8971.

45. Schlu A, Hausel M, Salmen H. Effect of tourniquet use on blood loss in total knee arthroplasty). Zentralbl Chir. 2003;128(10):866-70.

46. Christodoulou AG, Ploumis AL, Terzidis IP, Chantzidis P, Metsovitis SR, Nikiforos DG. The role of timing of tourniquet release and cementing on perioperative blood loss in total knee replacement. Knee. 2004;11(4):313-9, http://dx.doi.org/10.1053/j.knee.2003.09.005.

47. Aglietti P, Baldini A, Vena LM, Abbate R, Fedi S, Falciani M. Effect of tourniquet use on activation of coagulation in total knee replacement. Anesthesiology. 2002;96(5):1140-6.

48. Abdel-Salam A, Eyres KS. Effects of tourniquet during total knee arthroplasty. A prospective randomised study. J Bone Joint Surg Br. 1995;77(2):250-3.

49. Portney L, Watkins M. Foundations of clinical research. 3rd ed. N: Pearson Prentice Hall; 2009.p.277-300

50. Markovic-Deni L, Zivkovic K, Lesic A, et al. Risk factors and distribution of symptomatic venous thromboembolism in total hip and knee replacements: prospective study. Int Orthop. 2012;36(6):1299-305, http://dx.doi.org/10.1007/s00264-011-1466-5.