



Original article

Postoperative thromboprophylaxis does not reduce the incidence of thromboembolic events after ACL reconstruction



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ABSTRACT

Introduction: Anterior cruciate ligament (ACL) reconstructive surgery is one of the most common ligament-related surgeries performed in France. The French Society of Anesthesia & Intensive Care Medicine (SFAR) recommends the systematic use of low-molecular weight heparin postoperatively to prevent venous thromboembolisms (VTE). However, these recommendations differ from one country to another; several national societies do not recommend them. To specify the benefits of such a treatment, we did a retrospective case-control study to evaluate the incidence of symptomatic VTE after ACL reconstruction.

Hypothesis We hypothesized that the rate of symptomatic VTE would be the same, whether a course of postoperative anticoagulants is prescribed or not.

Methods: This was a retrospective, multicenter, multi-surgeon study. Of the four participating surgeons, two never prescribed thromboprophylaxis after surgery while the other two always prescribed a 10-day course of low-molecular weight heparin. All patients who underwent primary ACL reconstruction using an autologous graft between the 1st of January 2019 and the 15th of February 2020 were included. The 535 patients who had undergone ACL reconstruction were divided into two groups: (Group 1) 279 patients in the group without anticoagulants; 96% received a four-strand semi-tendinosus graft (ST4) and 4% received a quadriceps tendon (QT) graft; the mean age of these patients was 30 years (14–58); 41% of them were women and 22% of them were smokers; the mean body mass index was 24.4 (18–37); the mean tourniquet time was 37 minutes. (Group 2) 256 patients in the group with anticoagulants; 81% received a semi-tendinosus/gracilis graft, 15% received a ST4 and 4% a QT; the mean age of these patients was 29 years (14–60); 38% of them were women and 21% of them were smokers; the mean body mass index was 25.0 (18–38); the mean tourniquet time was 34 minutes. The two groups were comparable in all respects except for the type of graft used. All patients were contacted at a minimum interval of 3 months after their surgery, by telephone. Doppler ultrasonography was done solely when a VTE was suspected.

Results: In the group without anticoagulants, 249 of 279 patients were contacted, while in the group with anticoagulants, 221 of 256 were contacted. The two groups were comparable in terms of age, gender ratio, tourniquet time, body mass index and proportion of smokers. Two cases of deep vein thrombosis (all in the calf region) were found in each group with no associated pulmonary embolism. There was no difference between groups in the VTE rate.

Discussion: Our hypothesis was confirmed since the incidence of symptomatic VTE was the same whether postoperative anticoagulants were prescribed or not. The incidence of symptomatic VTE after ACL reconstruction was identical whether thromboprophylaxis was used or not. This casts doubt on the need for postoperative thromboprophylaxis, especially in younger patients who do not have risk factors, and brings into question whether the recommendations in France should be changed.

Level of Evidence: III (retrospective case-control study).

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1. Introduction

The number of anterior cruciate ligament (ACL) tears has increased over the past 20 years. Reconstruction is recommended in young patients and athletes. In 2006, the French National Authority for Health (HAS) documented 35,500 ACL reconstructions procedures with a 10% increase in 1 year [1].

Venous thromboembolism (VTE) is a rare but feared complication after ACL reconstruction surgery. Studies analyzing registers of symptomatic VTE after ACL surgery report an incidence of 0.16% to 0.53% [2–5] while studies analyzing the incidence of asymptomatic VTE report a rate between 9% and 14% [6–10].

Thromboprophylaxis is the current practice in France after this surgery. In 2005, the French Society of Anesthesia & Intensive Care Medicine (SFAR), which has published a good practice guide in this area [11], did not recommend the systematic use of low-molecular weight heparin (LMWH) given the low risk of VTE after ACL surgery. Instead, it recommended preventative anticoagulant treatment only if one or more risk factors for VTE were present. But when these guidelines were updated in 2011, this surgery was considered moderate risk, thus it was recommended that LMWH be prescribed to every patient after ACL reconstruction surgery [12]. The incidence of VTE varies amongst studies, along with alternative conclusions about the use of thromboprophylaxis. The same goes for national-level recommendations in other countries [13]. Moreover, postoperative drugs used to prevent clots have a non-negligible cost and may be associated with specific complications, such as hematomas, heparin-induced thrombocytopenia, bleeding, etc.

Given the lack of scientific proof about the benefits of using post-operative anti-thrombotic or anticoagulant drugs on the incidence of symptomatic VTE, we aimed to determine the VTE rate in a population of patients who did not receive thromboprophylaxis after ACL reconstruction and compare it to a control group who received preventative anticoagulants. To specify the benefits of such a treatment, we did a retrospective case-control study to evaluate the incidence of symptomatic VTE after ACL reconstruction with a minimum 3 months' follow-up. We hypothesized that the incidence of symptomatic VTE was the same in both groups.

2. Patients and methods

2.1. Study design

This was a longitudinal, retrospective, multi-surgeon and multicenter study done in France (Clinique des Cèdres, Cornebarrieu; Clinique Médipôle, Cabestany; Clinique Aguiléra, Biarritz). All patients who underwent primary ACL reconstruction between the 1st of January 2019 and the 15th of February 2020 by one of four surgeons were included and contacted by telephone at a minimum of 3 months post-surgery. The group without anticoagulants was compared to the group with anticoagulants, which was the control group. The anticoagulant prescribed was enoxaparin (Lovenox™, Sanofi-Aventis, Paris, France) as one injection of 4000 IU daily for 10 days.

2.2. Surgical techniques and postoperative care

The operations were done under general anesthesia combined with a nerve block of the adductor canal with a tourniquet inflated to between 250 and 300 mmHg. Three different surgical techniques were used, depending on the surgeon. The grafts used were either the gracilis plus semi-tendinosus (STG), four-strand semi-tendinosus (ST4) or quadriceps tendon with bone block (QT). All patients were provided with immediate postoperative

cryo-compression therapy [14] and were operated in the context of an outpatient procedure. Weight-bearing was allowed immediately postoperatively using crutches until the ability to lock the knee had been regained.

2.3. Assessment methods

The following patient demographics were collected: age, sex, body mass index (BMI) and smoking status. The patients who were on anticoagulants before the operation or had a history of VTE were excluded from the study. The patients who could not be contacted by telephone were considered as lost to follow-up.

The patients were either contacted by telephone or queried during the 6-month postoperative visit. Three standardized questions were asked:

- Did you undergo a Doppler ultrasonography to look for a deep vein thrombosis (DVT) during the 3 months following your operation?
- Did you have a DVT or pulmonary embolism (which could migrate as a blood clot in a vein) during the 3 months following your knee operation?
- If yes, did you have to take anticoagulants, which ones, and for how long?

2.4. Statistical analysis

Qualitative variables were compared between groups with a Fisher exact test, given the expected values based on an independence hypothesis. Quantitative variables were compared between groups using Student's *t* test if the data were normally distributed and the variances were homogeneous. If the variances were not equal between groups, we used Student's *t* test for unequal variances. If the distribution was not normal, a Wilcoxon test was used instead. A *p* value of less than 0.05 was considered as statistically significant.

3. Results

The two groups were comparable in all respects except for the type of graft used (Table 1). During the inclusion period in the group without anticoagulants, 279 patients underwent primary ACL reconstruction and 2 patients were excluded because of a history of DVT (they were prescribed thromboprophylaxis post-operatively). Twenty-eight patients could not be contacted again and were considered lost to follow-up (10%). In all, 249 patients completed the questionnaire: 221 by telephone and 28 during an in-person follow-up visit. Five patients (including two VTE) underwent an ultrasonography because of a suspected DVT.

In the group with anticoagulants, 256 patients underwent primary ACL reconstruction. None were excluded. Twenty-five patients could not be contacted again and were considered lost to follow-up (14%). In all, 221 patients completed the questionnaire: 179 by telephone and 42 during an in-person follow-up visit. Eight patients (including two VTE) underwent an ultrasonography because of a suspected DVT.

In each group, 2 DVTs occurred in the calf area that required curative anticoagulant treatment (Fig. 1). There was no statistically significant difference between groups.

4. Discussion

The main finding of this study is that the rate of symptomatic VTE was comparable between the two groups, thus confirming our hypothesis. Of the four patients who suffered a DVT, the only

Table 1
Comparison of groups.

	Control group with anticoagulants (N = 221)	Study group without anticoagulants (N = 249)	p
Mean age	29.35 (14–60)	29.96 (14–58)	NS
Sex	85 women (38.5%)	102 women (41%)	NS
Smoker	51 (21.3%)	56 (22.5%)	NS
Body mass index	24.96 (17.7– 38.3)	24.36 (18–37.2)	NS
Tourniquet time (minutes)	34.5 (22–90)	37 (23–95)	NS
Number of DVTs	2 (0.9%)	2 (0.8%)	NS
STG	179	0	< 0.05
ST4	34	240	< 0.05
QT	8	9	NS

NS: not significant, STG: semitendinosus plus gracilis, ST4: four-strand semitendinosus, QT: quadriceps tendon.

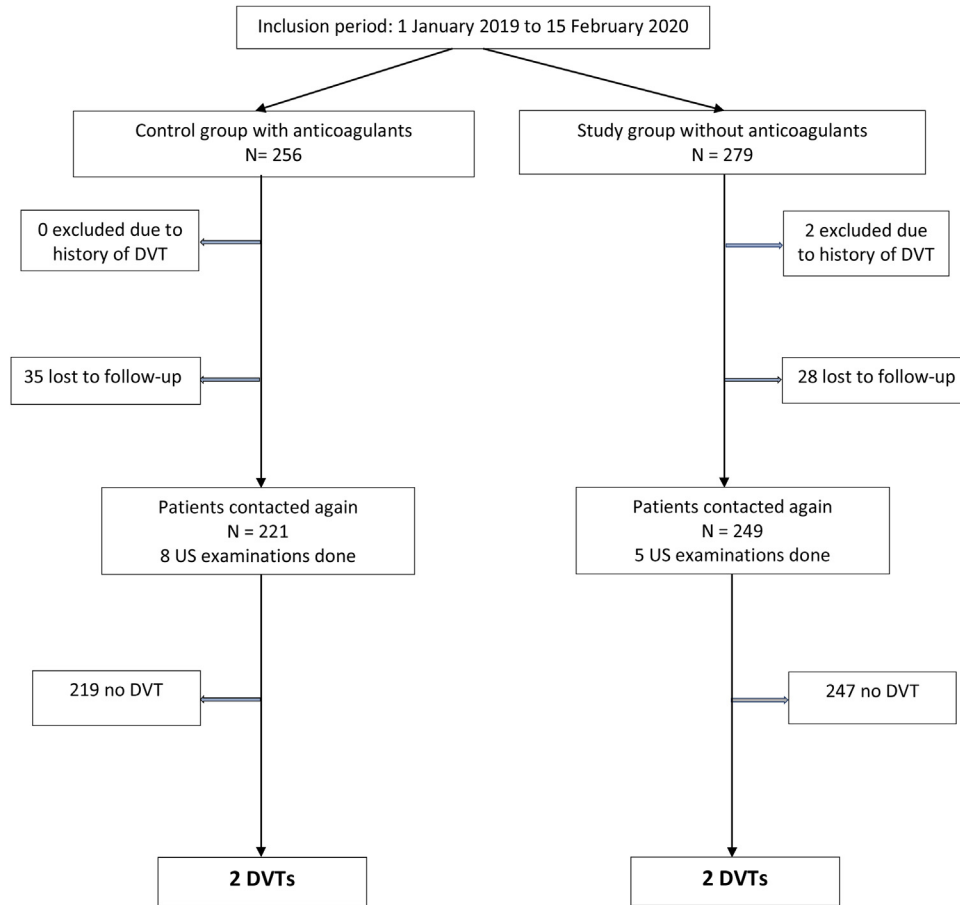


Fig. 1. Study design (US: ultrasound imaging).

common factor was that their body mass index was above 26 (Tables 2 and 3).

Articles reporting the rate of symptomatic VTE demonstrate similar findings. Schmitz et al. [5] looked at the Swedish registry over a 7-year period and identified 26,014 ACL reconstruction procedures. Of these, 9425 had thromboprophylaxis (LMWH or newer direct oral anticoagulants). They found an 0.4% incidence of symptomatic DVT overall with no difference between those who received thromboprophylaxis and those who did not. Gaskill et al. [4] found a rate of 0.5% for 16,558 procedures over a 6-year period (16,411 without anticoagulants and 147 with anticoagulants). Maletis et al. [15] looked at 16,192 patients and found that 0.2% suffered a symptomatic VTE, while Jameson et al. [2] reported an incidence of 0.4% over a 2-year period based on 13,941 patients in the British registry. The latter two studies did not specify whether thromboprophylaxis was used or not.

Table 2
Information about patients who suffered a DVT in the control (with anticoagulants) group.

	Control group with anticoagulants	
	Patient 1	Patient 2
Age	15 years	45 years
Sex	Female	Male
Body mass index	26.4 kg/m ²	27.8 kg/m ²
Smoker	Yes	No
Time after surgery	1 month	1 month
Graft used	STG	STG
Other data		Arthroscopic lavage at D10 for infected hematoma (6 weeks treatment with ofloxacin + rifampicin)

STG: semitendinosus with gracilis.

Table 3
Information about patients who suffered a DVT in the study (without anticoagulants) group.

	Study group without anticoagulants	
	Patient 1	Patient 2
Age	23 years	28 years
Sex	Male	Female
Body mass index	26.8 kg/m ²	28.8 kg/m ²
Smoker	No	Yes
Time after surgery	1 month	3 months
Graft used	ST4	ST4
Other data		Concurrent use of oral contraceptives

Three registry studies with very large cohorts all found the same statistically significant risk factor: patient age. The age threshold was 35 years for Gaskill et al. [4], while it was 40 years for Schmitz et al. [5] and Jameson et al. [2]. Oshiba et al. [16] found age above 30 years to be a risk factor in a retrospective study of 256 patients. However, in the current study the two patients in the group without anticoagulants who suffered a VTE were less than 30 years of age.

While registry studies with a large number of patients do not support systematic use of thromboprophylaxis after ACL reconstruction, several studies have proven that thromboprophylaxis prevents VTE. A meta-analysis of randomized prospective studies (LMWH versus placebo or no treatment) with more than 4000 patients showed that taking LMWH reduced the risk of VTE by 77%, without increasing the risk of bleeding-related complications [17]. In another prospective randomized study [18], one group of 72 patients received LMWH injections for 20 days while another group of 68 patients received a placebo injection for 20 days; both groups had received LMWH for 3–8 days after surgery. There were 28 VTE in the placebo group versus only 2 VTE in the LMWH group (no pulmonary embolism in either group). There were 13 minor bleeding complications in the LMWH group and 10 in the placebo group (no difference).

In a study by Batailler et al. [19] comparing two lateral tenodesis techniques, there were four hematomas and two DVTs in 82 patients, although the authors did not specify whether thromboprophylaxis had been used. Jameson et al. [2] and Maletis et al. [15] did not report the rate of major bleeding events in their registry studies looking at complications after ACL surgery. Panisset et al. [20] reported that 6% of patients (22/592) suffered major bleeding events, with 1 patient requiring surgical drainage. They did not specify which type of post-surgical anticoagulant treatment had been used. Lefèvre et al. [21] found 32 hematomas in 1206 patients who received LMWH but did not specify the surgical revision rate. Lastly, Rousseau et al. [22] did a prospective study of 958 patients specifically considering complications after primary ACL reconstruction. There were 22 hematomas (3%), of which 13 (1.4%) required surgical revision. Once again, we do not know if thromboprophylaxis had been prescribed postoperatively.

These contradictory results contribute to the uncertainty surrounding this topic. In a study of the current practices of 142 US surgeons, Keller et al. [23] found that approximately half did not use any thromboprophylaxis while more than 95% of the other half prescribed aspirin only, which is a far cry from our practices in France. Also, the American College of Chest Physicians [24] does not recommend using thromboprophylaxis for knee arthroscopy, although they do not differentiate between simple arthroscopy procedures and arthroscopic ACL reconstruction. The SFAR does make a distinction by recommending against thromboprophylaxis for simple arthroscopy procedures while recommending LMWH for ACL reconstructive procedures (without specifying the length of treatment). These disparities in the recommendations are a concern and require a wider consensus.

Since 2019, various scientific experts, including the SFAR, recommend that patients take aspirin after undergoing hip or knee arthroplasty. Several studies in this context have shown that aspirin is effective at preventing VTE, especially in the context of rapid recovery protocols [25–31]. Thus, it would be prudent to determine the benefits of using aspirin instead of LMWH after ACL surgery.

Our study has several limitations: first, it was retrospective and most of the data was collected over the phone. However, given the recent nature of the surgery and the young population, the risk of recall bias is minimal. Second, we did not do routine ultrasonography screening during the first months after surgery to look for a DVT; however, like most current studies on this topic, we based our analysis on symptomatic VTE events. Lastly, this study was done at multiple hospitals with four different surgeons, thus the groups were not comparable in the type of graft used for the ACL reconstruction. However, there is currently no evidence that the type of graft used impacts the risk of VTE.

5. Conclusion

The risk of symptomatic VTE after arthroscopic ACL reconstruction without thromboprophylaxis was similar to the risk when preventative anticoagulation therapy was used. These findings may prompt scientific societies to re-evaluate the recommendations on thromboprophylaxis after ACL reconstruction in France.

Disclosure of interest

X.B.I. declares that he has no competing interest.

X.C. received royalties from FH Orthopedics and received payments from Microport Orthopedics but declares that he has no competing interest.

B.V. received payments from SERF but declares that he has no competing interest.

J.M. is Associate Editor for Orthopaedics & Traumatology: Surgery & Research but declares that he has no competing interest.

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Author contributions

XBI designed the study and wrote the article. XC and BV designed the study and provided critical revisions of the article. JM designed the study and wrote the article.

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References

- [1] HAS. Prise en charge thérapeutique des lésions méniscales et des lésions isolées du ligament croisé antérieur chez l'adulte; 2008 [Access on 04/08/2020] <https://www.has-sante.fr/jcms/c.680973/fr/prise-encharge-therapeutique-des-lesions-meniscales-et-des-lesions-isolees-du-ligament-croiseantérieur-du-genou-chez-l-adulte>.
- [2] Jameson SS, Downen D, K-James P, Serrano-Pedraza I, Reed MR, Deehan D. Complications following ACL reconstruction in the English NHS. *Knee* 2012;19:14–9.
- [3] Krych AJ, Sousa PL, Morgan JA, Levy BA, Stuart MJ, Dahm DL. Incidence and risk factor analysis of symptomatic venous thromboembolism after knee arthroscopy. *Arthroscopy* 2015;33:2112–218.
- [4] Gaskill T, Pullen M, Bryant B, Sicignano N, Evans AM, Demaio M. The prevalence of symptomatic deep venous thrombosis and pulmonary embolism after anterior cruciate ligament reconstruction. *Am J Sports Med* 2015;43:2714–9.

- [5] Kraus Schmitz J, Lindgren V, Janarv P-M, Forssblad M, Stalman. Deep venous thrombosis and pulmonary embolism after anterior cruciate ligament reconstruction. *Bone Joint J* 2019;10134–40.
- [6] White RH, Romano PS, Zhou H, Rodrigo J, Bargar W. Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty. *Arch Intern Med* 1998;158:1525–31.
- [7] Grady-Benson JC, Oishi CS, Hanson PB, Colwell Jr CW, Otis SM, et al. Postoperative surveillance for deep venous thrombosis with duplex ultrasonography after total knee arthroplasty. *J Bone Joint Surg Am* 1994;76:1649–57.
- [8] Struijk-Mulder MC, Ettema HB, Verheyen CC, Buller HR. Deep vein thrombosis after arthroscopic anterior cruciate ligament reconstruction: a prospective cohort study of 100 patients. *Arthroscopy* 2013;29:1211–6.
- [9] Ye S, Dongyang C, Zhihong X, Dongquan S, Jin D, et al. The incidence of deep venous thrombosis after arthroscopically anterior cruciate ligament reconstruction. *Arthroscopy* 2013;29:742–7.
- [10] Dong J, Wang X, Men X, Wang X, Zheng X, Gao S. Incidence of deep venous thrombosis in Chinese patients undergoing arthroscopic knee surgery for cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2015;23:3540–4.
- [11] Mismetti P, Zufferey P, Pernod G, Baylot, Estebe JP, et al. Thromboprophylaxis in orthopedic surgery and traumatology. *Ann Fr Anesth Reanim* 2005;24:871–89.
- [12] Samama CM, Gafsou B, Jeandel T, Laporte S, Steib A, et al. French Society of Anaesthesia and Intensive Care. Guidelines on perioperative venous thromboembolism prophylaxis. Update 2011. Short text. *Ann Fr Anesth Reanim* 2011;30:947–51.
- [13] Struijk-Mulder MC, Ettema HB, Verheyen CC, Buller HR. Comparing consensus guidelines on thromboprophylaxis in orthopedic surgery. *J Thromb Haemost* 2010;8:678–83.
- [14] Murgier J, Cassard X. Cryotherapy with dynamic intermittent compression for analgesia after anterior cruciate ligament reconstruction. Preliminary study. *Orthop Traumatol Surg Res* 2014;100:309–12.
- [15] Maletis GB, Inacio MCS, Funahashi TT. Analysis of 16192 anterior cruciate ligament reconstructions from a community-based registry. *Am J Sports Med* 2013;41:2090–8.
- [16] Oshiba H, Nawata M, Morioka S, Momose T, Maeda T, Nakatsuchi Y. The incidence and risk factor of deep venous thrombosis after arthroscopically assisted anterior cruciate ligament reconstruction. *J Orthop Sci* 2020;25:477–80.
- [17] Zhu J, Jiang H, Marshall B, Li J, Tang X. Low-molecular-weight heparin for the prevention of venous thromboembolism in patients undergoing knee arthroscopic surgery and anterior cruciate ligament reconstruction: a meta-analysis of randomized controlled trials. *Am J Sports Med* 2019;47:1994–2002.
- [18] Marlovits S, Striessnig G, Schuster R, et al. Extended-duration thromboprophylaxis with enoxaparin after arthroscopic surgery of the anterior cruciate ligament: a prospective, randomized, placebo-controlled study. *Arthroscopy* 2007;23:696–702.
- [19] Batailler C, Lustig S, Reynaud O, Neyret P, Servien E. Complications and revision surgeries in two extra-articular tenodesis techniques associated to anterior cruciate ligament reconstruction. A case-control study. *Orthop Traumatol Surg Res* 2018;104:197–201.
- [20] Panisset JC, Pailhé R, Schlatterer B, Sigwalt L, Sonnery-Cottet B, et al. Short-term complications in intra- and extra-articular anterior cruciate ligament reconstruction. Comparison with the literature on isolated intra-articular reconstruction. A multicenter study by the French Arthroscopy Society. *Orthop Traumatol Surg Res* 2017;103(8S):S231–6.
- [21] Lefevre N, Servien E, Colombet P, Cournapeau J, Dalmay F, et al. French prospective multicenter comparative assessment of ambulatory surgery feasibility in anterior cruciate ligament reconstruction. *Orthop Traumatol Surg Res* 2016;102(8S):S257–63.
- [22] Rousseau R, Labruyere C, Kajetanek C, Deschamps O, Makridis KG, Djian P. Complications after anterior cruciate ligament reconstruction and their relation to the type of graft: a prospective study of 958 cases. *Am J Sports Med* 2019;47:2543–9.
- [23] Keller RA, Moutzourous V, Dines JS, Bush-Joseph CA, Limpisvasti O. Deep venous thrombosis prophylaxis in anterior cruciate ligament reconstructive surgery: what is the current state of practice? *Sports Health* 2018;10:156–9.
- [24] Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141(2 Suppl.):e278S–325S.
- [25] Vendittoli PA, Pellei K, Desmeules F, Massé V, Loubert C, et al. Enhanced recovery short-stay hip and knee joint replacement program improves patients outcomes while reducing hospital costs. *Orthop Traumatol Surg Res* 2019;105:1237–43.
- [26] Cassard X, Garnault V, Corin B, Claverie D, Murgier J. Outpatient total knee arthroplasty: readmission and complication rates on day 30 in 61 patients. *Orthop Traumatol Surg Res* 2018;104:967–70.
- [27] Matharu GS, Kunutsor SK, Judge A, Blom AW, Whitehouse MR. Clinical effectiveness and safety of aspirin for venous thromboembolism prophylaxis after total hip and knee replacement: a systematic review and meta-analysis of randomized clinical trials. *JAMA Intern Med* 2020;180:376–84.
- [28] Baumgartner C, Maselli J, Auerbach AD, Fang MC. Aspirin compared with anticoagulation to prevent venous thromboembolism after knee or hip arthroplasty: a large retrospective cohort study. *J Gen Intern Med* 2019;34:2038–46.
- [29] Ghosh A, Best AJ, Rudge SJ, Chatterji U. Clinical effectiveness of aspirin as multimodal thromboprophylaxis in primary total hip and knee arthroplasty: a review of 6078 cases. *J Arthroplasty* 2019;34:1359–63.
- [30] Rondon AJ, Shohat N, Tan TL, Goswami K, Huang RC, Parvizi J. The use of aspirin for prophylaxis against venous thromboembolism decreases mortality following primary total joint arthroplasty. *J Bone Joint Surg Am* 2019;101:504–13.
- [31] Farey JE, An VVG, Sidhu V, Karunaratne S, Harris IA. Aspirin versus enoxaparin for the initial prevention of venous thromboembolism following elective arthroplasty of the hip or knee: A systematic review and meta-analysis. *Orthop Traumatol Surg Res* 2021;107, <http://dx.doi.org/10.1016/j.otsr.2020.04.002> [In press].