Thromboprophylaxis Following Hip and Knee Surgery: A Review of Current Practices in a Canadian Tertiary Care Center

Lilia Panamsky, MD, MS[1], Sarah Gomes, MD, MSc[2], Elizabeth McAuley, MD[3], Wilma Hopman, MA,[4,5], Kristen Marosi, MD[1], Siddhartha Srivastava, MD, MSc[1]

[1]Department of Medicine, Division of General Internal Medicine, Queen's University, Kingston, Canada; [2]Department of Family Medicine, University of Toronto, Toronto, Canada; [3]Department of Family Medicine, University of Calgary, Calgary, Canada, Queen's University, Kingston, ON, Canada; [4]Kingston General Hospital Research Institute, Kingston, ON, Canada; [5]Department of Public Health Sciences, Queen's University, Kingston, ON, Canada

Corresponding Author: Lilia Panamsky: lilia.panamsky@queensu.ca

Submitted: 22 November 2021; *Accepted:* 1 January 2022; *Published:* 11 August 2022

DOI: https://doi.org/10.22374/cjgim.v17i3.592

Abstract

Objective: We aimed to describe the current pharmacologic thromboprophylaxis practice after total hip arthroplasty (THA) and total knee arthroplasty (TKA) at a tertiary care center in Canada.

Methods: A retrospective cohort study was conducted on patients following elective arthroplasty or fracture surgery between March 1, 2019 and March 31, 2020. The primary outcome was the rate of use of different antithrombotic medications. Secondary outcomes included duration of antithrombotic therapy, adherence to major international guidelines, 30-day venous thromboembolism (VTE) incidence, and bleeding complications.

Results: Over 98% of patients were prescribed pharmacoprophylaxis in hospital and on discharge. Inpatient VTE prophylaxis was predominantly dalteparin (64.5%) and aspirin (ASA; 34.1%) for THA, and dalteparin (65.5%) and ASA (33.1%) for TKA. Discharge prescriptions had dalteparin (60.2%) and ASA (36.9%) for THA compared to ASA (56.5%), dalteparin (28.2%), and combined dalteparin with ASA (12.3%) for TKA. There was minimal use of direct oral anticoagulants (DOAC) in either type of surgery (<1%). The average total duration of prophylaxis after THA and TKA was 34.7 days (±8.2 days) and 36.6 days (±11.3 days), respectively. The 30-day incidence rate of post-operative VTE was 1.6% and the 30-day bleeding rate was 2.2%.

Conclusion: There was nearly universal prescribing of postoperative VTE prophylaxis and high rate of adherence to international guidelines. There was, however, considerable variability in practice of prescribing, particularly following TKA. Use of DOAC remained negligible in both types of surgeries.

Résumé

Objectif : Cet article vise à décrire la pratique actuelle de la thromboprophylaxie pharmacologique après une arthroplastie totale de la hanche (ATH) et une arthroplastie totale du genou (ATG) dans un centre de soins tertiaires au Canada.

Méthodologie : Une étude de cohorte rétrospective a été réalisée chez des patients ayant subi une arthroplastie ou une opération pour une fracture non urgente entre le 1er mars 2019 et le 31 mars 2020. Le critère d'évaluation principal est la fréquence d'utilisation de différents antithrombotiques. Les critères d'évaluation secondaires sont la durée du traitement antithrombotique, l'observance des principales lignes directrices internationales, l'incidence de la thromboembolie veineuse (TEV) à 30 jours et les complications hémorragiques.
Résultats : Plus de 98 % des patients se sont fait prescrire une pharmacoprophylaxie à l'hôpital et à leur sortie. Les médicaments administrés en prophylaxie contre la TEV à l'hôpital sont surtout la daltéparine (64,5 %) et l'acide acétylsalicylique (AAS) (34,1 %) pour l'ATH et la daltéparine (65,5 %) et l'AAS (33,1 %) pour l'ATG. Les médicaments prescrits à la sortie de l'hôpital sont la daltéparine (60,2 %) et l'AAS (36,9 %) pour l'ATH, tandis que pour l'ATG, il s'agit de l'AAS (56,5 %), de la daltéparine seule ou en combinaison (28,2 %), puis de l'AAS (12,3 %). L'utilisation d'anticoagulants oraux directs (AOD) est minime dans les deux types d'intervention chirurgicale (< 1 %). La durée totale moyenne de la prophylaxie après l'ATH est de 34,7 jours (± 8,2 jours) et de 36,6 jours (± 11,3 jours) après l'ATG. Le taux d'incidence de la TEV postopératoire à 30 jours est de 1,6 % et le taux d'hémorragie à 30 jours est de 2,2 %.
Conclusion : La prescription de médicaments contre la TEV en prophylaxie est presque universelle et le taux d'observance des lignes directrices internationales est élevé. Toutefois, la variabilité est considérable en ce qui concerne les pratiques de prescription, particulièrement après l'ATG. L'utilisation d'AOD demeure négligeable dans les deux types d'intervention chirurgicale.

Keywords: thromboprophylaxis; athroplasty; VTE

Introduction

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are considered as two of the highest risk surgeries for the development of postoperative venous thromboembolism (VTE). Without any thromboprophylaxis, the rate of symptomatic cases of VTE is 3–10%.[1–4] With pharmacologic prophylaxis, the rate of symptomatic VTE decreases to 0.3–2.7%; this is predominantly occurring patients after discharge from hospital.[5–10] Studies in the past 5 years have calculated even lower rate of VTE, that is, between 0.5% and 1%, which could be likely due to higher adherence and longer duration of chemoprophylaxis.[9,10] Although the risk of VTE is highest in the first few postoperative days, it remains elevated for at least 6 weeks because of ongoing physiologic changes, including hypercoagulable state and reduced flow of blood.[11]

Postoperative thromboembolism prophylaxis with pharmacologic measures has become the standard of care following joint arthroplasty. However, there is variability among international guidelines regarding optimal choice of pharmacologic agent.[12,13] Furthermore, the most popular guidelines are outdated and have not incorporated results of major research into the use of direct oral anticoagulants (DOACs) and aspirin (ASA). The American Association of Orthopaedic Surgery (AAOS) guidelines of 2007 recommended 325-mg ASA twice daily for 4 weeks;[14] however, AAOS update of 2011 removed specific recommendations and simply recommended pharmacologic agents and/or mechanical compression devices.[15] The American Society of Chest Physicians (ACCP) guidelines, last updated in 2012, preferentially recommended low molecular weight heparin (LMWH) over all other options, but also recommended the use of warfarin, fondaparinux, or ASA as an alternative to no prophylaxis. The recommended duration was for a minimum period of 10–14 days and maximum of up to 35 days.[4] The newest guidelines that of the American Society of Hematology (ASH) were published in December 2019. The ASH guidelines incorporated newer data that demonstrated that both DOACs and ASA are safe and effective alternatives to LMWH.[16–18] The ASH guidelines suggested either anticoagulants, preferably DOAC or LMWH, or ASA.[19] Wide variation in guidelines is reflected in clinical practice, with heterogenous prescription practices between and even within individual centers. For example, a retrospective study conducted in Australia from 2014 found that LMWH followed by ASA was most commonly prescribed[20] whereas a more recent study conducted in the United

Kingdom has found that a DOAC with or without LMWH followed by ASA with or without LMWH were prescribed most commonly.[21]

The present study aimed to explore the current practice of thromboprophylaxis after THA and TKA as well as occurrence of VTE at a tertiary care center in Canada to determine the types of antithrombotic therapies prescribed, and their duration and adherence to guidelines.

Methods

A retrospective cohort study was conducted consecutively on 855 patients admitted to hospital following THA or TKA at Kingston Health Sciences Centre (KHSC) between March 1, 2019 and March 31, 2020. This timeframe was chosen in order to avoid delay in surgery because of the COVID-19 pandemic.

The included patients were aged 18 years or older and had undergone joint arthroplasty at KHSC. The included surgeries were primary elective THA or TKA, hemiarthroplasties, joint repairs and revisions, and joint fracture surgeries. Fractures were included due to the known high risk of VTE, particularly after hip fracture surgery.[22,23]

Patients were excluded if they had previously taken anticoagulant for a different indication (e.g., atrial fibrillation), or had developed another indication for anticoagulation during their hospital stay (e.g., atrial fibrillation or acute coronary syndrome). Patients on single antiplatelet therapy were included but those on dual antiplatelet therapy were excluded from this study. Patients who were hospitalized for more than 30 days were also excluded from the study. In the case of multiple surgeries on the same patient, only the first surgery was included.

Patient medical records, including preanesthetic report, operative report, and discharge summary, were reviewed. Baseline information regarding age of the patient, gender, calculated Charlson Comorbidity Index (CCI), VTE risk factors,[22] antiplatelet use, type of anesthesia, length of stay, and name of surgeon was extracted from the patient medical record, and documented. Use of any pharmacologic therapy thromboprophylaxis was recorded, including the type, dose, and duration of antithrombotic medication. Information was collected regarding 30- and 60-day emergency department visits and readmission rates.

The primary outcome was the rate of use of different antithrombotic medications. Secondary outcomes included the duration of antithrombotic therapy, VTE incidence within 30 and 60 days of surgery, bleeding complications within 30 and 60 days of surgery, and difference in prophylaxis of hip and knee arthroplasty.

Descriptive statistical analysis was performed using SPSS version 27. The underlying distributions of continuous data were assessed with the Shapiro–Wilk test, and nonparametric tests were applied as per requirement. An independent sample *t*-test was used to compare variable mean values. Differences between groups were compared using the Chi-squared test, and $P < 0.05$ and a two-tailed output were considered as statistically significant. Ethical approval was obtained from Queen's University Health Sciences Research Ethics Board (HSREB).

Results

A total of 855 patients were included in the study, of which 50.1% (n = 428) underwent THA, and 49.9% (n = 427) underwent TKA. Patient demographics are presented in Table 1. The median age was 68.0 years with a slight female predominance (55.1%). The median body mass index (BMI) was 31. In all, 443 patients had general anesthesia and 412 had spinal anesthesia. Spinal anesthesia was used in 191 THA and 221 TKA, and general anesthesia was used in 237 THA and 206 TKA. Spinal anaesthesia was more probably used ($P = 0.037$) in patients undergoing TKA than THA.

A total of 120 patients (14%) had additional moderate or strong risk factors for VTE documented in their preoperative assessment or discharge summary.[22] Risk factors included active cancer (469/855; 5.4%), prior VTE (29/855; 3.4%), paralytic stroke (22/855; 2.6%), congestive heart failure (19/855; 2.2%), central line access during hospital admission (9/855; 1.1%), and respiratory failure during admission (0.58%; 5/855). Seven patients (0.82%) had multiple risk factors documented, 21 patients (2.5%) had a bleeding history documented in their preoperative clinical note or dictation summary.

Inpatient thromboprophylaxis

A total of 849 patients were admitted to hospital following their surgery, while six were discharged on the same day and not included in the inpatient statistics. Of the patients who remained in hospital, 99.5% (845/849) received pharmacologic prophylaxis. Four patients did not receive prophylaxis because of a documented history of bleeding disorder or an active bleed while in hospital.

The most prescribed inpatient VTE prophylaxis was LMWH (dalteparin) (550/845; 65.0%), followed by ASA

Table 1. Demographics and baseline characteristics of patients

	Total knee arthroplasty (n = 427)	Total hip arthroplasty (n = 428)	Total (n = 855)
Age, median (IQR) in years	68 (61–76)	69 (59–78)	68 (61–76)
Female, No. (%)	242 (56.7%)	229 (53.5%)	471 (55.1%)
Charlson comorbidity index, mean (SD)	0.15 (±0.5)	0.18 (±0.6)	0.16 (±0.53)
BMI, median (IQR)	31 (27–36)	29 (25–34)	31 (27–36)
Elective joint replacement, No. (%)	417 (97.7%)	330 (77.1%)	747 (87.4%)
Fractures, No. (%)	10 (2.3%)	98 (22.9%)	108 (12.6%)
Length of stay in days, median (IQR)	4 (2–8)	3 (2–6)	4 (2–8)
Anti-platelet use prior to surgery, No. (%)	100 (23.4%)	74 (17.3%)	175 (20.4%)
ASA	88 (20.6%)	65 (15.2%)	153 (17.9%)
Clopidogrel	12 (2.8%)	9 (2.1%)	21 (2.5%)
Anesthesia type			
Spinal	221 (51.8%)	191 (44.6%)	412 (48.2%)
General	206 (48.2%)	237 (55.4%)	443 (51.2%)
VTE risk factors			
Respiratory failure	2 (0.5%)	3 (0.7%)	5 (0.6%)
Active cancer	15 (3.5%)	31 (7.2%)	46 (5.4%)
Congestive heart failure	14 (3.3%)	5 (11.7%)	19 (2.2%)
Stroke	13 (3.0%)	9 (2.1%)	22 (2.6%)
Prior VTE	13 (3.0%)	16 (3.7%)	29 (3.4%)
Bleeding history	9 (2.1%)	12 (2.8%)	21 (2.5%)
Central venous line insertion	4 (0.9%)	4 (0.9%)	8 (9.4%)
Total	70 (16.3%)	80 (2.9%)	150 (17.5%)

IQR, interquartile range; VTE, venous thromboembolism; ASA, aspirin.

Table 2. Characteristics of inpatient VTE prophylaxis

	Total knee arthroplasty (n = 423)	Total hip arthroplasty (n = 422)	Total (n = 845)
Apixaban	0.2% (1/423)	0.2% (1/422)	0.2% (2/845)
ASA	33.1% (140/423)	34.1% (144/422)	33.6% (284/845)
Clopidogrel	0.9% (4/423)	0.9% (4/422)	0.9% (8/845)
Dalteparin	65.5% (277/423)	64.5% (272/422)	65.0% (549/845)
Dual antiplatelet (ASA + clopidogrel	0.2% (1/423)	0%	0.1% (1/845)
Warfarin	0% (0/423)	0.2% (1/422)	0.1% (1/845)
None	0.2% (1/423)	0.7% (3/422)	4 (0.5%)

ASA, aspirin.

(284/845; 33.6%). Details concerning inpatient prophylaxis are presented in Table 2. There was no statistically significant difference in the rate of inpatient VTE prophylaxis in TKA versus THA (P = 0.896).

Thromboprophylaxis at discharge

Out of 855 patients, 842 (98.5%) were discharged from hospital with antithrombotic medication, although 11 of these discharged patients had a therapeutic dose of anticoagulant medication because of a new inpatient diagnosis of VTE. Four patients did not receive outpatient prophylaxis: three of these because of a history of bleeding disorder and one because of an active bleed in hospital. Data were lacking for eight patients for different reasons, including transfer to another facility, leaving hospital against medical advice, or no prescription documented in the discharge summary.

Table 3. Characteristics of VTE prophylaxis at time of discharge

	Knee arthroplasty (n = 422)	Hip arthroplasty (n = 420)	Total (n = 842)
Apixaban	0.2% (1/422)	0.2% (1/420)	0.2% (2/842)
ASA	56.4% (238/422)	36.9% (155/420)	46.7% (393/842)
Clopidogrel	0.9% (4/422)	0.9% (4/420)	0.9% (8/842)
Combination			
Dalteparin + ASA	12.3% (52/422)	0.2% (1/420)	6.3% (53/842)
Rivaroxaban + ASA	0.2% (1/422)	0%	0.1% (1/842)
Dalteparin	28.2% (119/422)	60.2% (253/420)	44.2% (372/842)
Rivaroxaban	0%	0.2% (1/420)	0.1% (1/842)
Warfarin	0%	0.2% (1/420)	0.1% (1/842)
Full dose of anticoagulation for VTE	1.7% (7/422)	0.9% (4/420)	1.3% (11/842)

ASA, aspirin; VTE, venous thromboembolism.

Table 4. Duration of pharmacologic VTE prophylaxis by thromboprophylaxis and type of surgery

	Total knee arthroplasty median duration (IQR) in days	Total hip arthroplasty median duration (IQR) in days	Total Median duration (IQR) in days
Apixaban (n = 2)	40 (N/A)	36 (N/A)	38 (N/a)
ASA (n = 389)	44 (2)	44 (2)	44 (2)
Dalteparin + ASA (n = 53)	41.5 (14)	29 (N/A)	41 (14)
Dalteparin (n = 367)	17 (14)	28 (1)	28 (1)
Rivaroxaban + ASA (n = 1)	28 (N/A)	N/A	28 (N/A)
Rivaroxaban (n = 1)	N/A	44 (N/A)	44 (N/A)
Warfarin (n = 1)	N/A	63 (N/A)	63 (N/A)
Total (n = 814)	43 (16)	30 (15)	42 (16)

ASA, aspirin; IQR, interquartile range.

Patients undergoing TKA were more likely to be prescribed ASA and a combination of dalteparin and ASA compared to patients undergoing THA ($P < 0.001$).

Duration of VTE prophylaxis

The median duration of total VTE prophylaxis, including inpatient and outpatient prophylaxis, was 42 days, with a range of 13–63 days. TKA had significantly longer total duration of therapy compared to THA (median duration 42 vs. 30 days; $P < 0.001$). Table 4 illustrates the average duration based on type of antithrombotic medication prescribed at the time of discharge.

Of 814 patients, 11 patients were discharged with their home dose of antiplatelets (three patients with ASA, and eight with clopidogrel) and the duration was documented as "indefinite" and excluded from the statistics. Reasons for the missing data (concerning 12 patients) included transfer to another facility, leaving against medical advice, or incomplete documentation (prescription not documented in the discharge summary).

Adherence to current guidelines

For the patients who received inpatient thromboprophylaxis, 100% adherence to the AAOS 2011 guidelines was monitored. Regarding the ACCP 2012 guidelines, a 99.1% adherence rate was observed, with only eight patients prescribed clopidogrel monotherapy not adhering to the guidelines. Regarding the Thrombosis Canada 2018 guidelines, 99.1% adherence rate was observed. This was largely due to the high rate of ASA use, which is not currently endorsed by the Thrombosis Canada 2018 guidelines. Finally, a 98.9% adherence rate was found to the ASH 2019 guidelines, with only nine patients (eight on clopidogrel monotherapy, and one on warfarin) not adhering to the guidelines. Slightly over half of the patients (422/814) were prescribed antithrombotic therapy as prophylaxis for more than 35 days; this was longer than that recommended in the ACCP and Thrombosis Canada guidelines but adhered to the ASH 2019 recommendations for extended prophylaxis.

Rate of VTE and bleeding

The 30-day VTE event rate was 1.6% (14/855), and the 60-day event rate was 1.75% (15/855). There were 11 instances of pulmonary embolism (PE) and four of deep venous thrombosis (DVT). There was no significant difference between rate of VTE following THA (6/428) versus TKA (9/427) (P = 0.450). The post-surgical occurrence of VTE was observed within 4 days (median value; IQR, 2–8 days).

All instances of PE were confirmed with computed tomography pulmonary angiography or ventilation perfusion scan, except for one case, which occurred intraoperatively and was confirmed with echocardiography. Three of the four cases of DVT were confirmed with ultrasonography, and one case was treated empirically following equivocal doppler ultrasound findings. Eleven events occurred in the inpatient setting and four occurred following discharge. In all, 14 patients (93%) received dalteparin as inpatient prophylaxis and one patient received ASA. One death occurred due to PE but none because of DVT.

The 30-day bleeding event rate was 2.2% (19/855). The 60-day bleeding event rate was the same as all bleeds occurred within 30 days. Six of these bleeds occurred in hospital, while 13 occurred following discharge. The post-surgical bleeding occurred within 3 days (median number; IQR, 1.25–11.75). The most frequent bleeding occurred from the surgical site (13/19; 68.4%), followed by upper gastrointestinal bleeding (4/19; 21.0%), lower gastrointestinal bleeding (1/19; 5.2%), and hematuria (1/19, 5.2%).

Discussion

Our study demonstrates the prescribing habits following THA and TKA at a tertiary care center in Canada. For over a decade, pharmacologic thromboprophylaxis has been considered as a standard of care following joint arthroplasty, and is recommended in all recent guidelines. The high rate of VTE prophylaxis (>99% during inpatient care and >98% on discharge prescriptions) is significantly more than the worldwide adherence rate of 62% calculated by a meta-analysis of examining studies between 2004 and 2014;[24] however, the value is consistent with the adherence rates calculated in an American review examining joint arthroplasties between 2014 and 2016.[25]

We found that one-third of patients in the inpatient setting and nearly half of patients at time of discharge were prescribed ASA monotherapy as prophylaxis. Although this is not a part of Thrombosis Canada guidelines, it is the recommendation of all major international guidelines, including AAOS, ACCP, and ASH guidelines. Moreover, this is consistent with other recent real-world data demonstrating high proportion of use of ASA.[25] Use of DOAC in our study was considerably lower than observed in other recent retrospective cohort studies.[21] Reasons for the low proportion of DOAC use may include preference of local surgeon, prohibitive kidney function, or a lack of an updated AAOS guideline.

In our study, both ASA use and the combination of LMWH followed by ASA were significantly higher in TKA than in THA. The reason for this is unclear and requires further investigations. Studies have shown that the risk for proximal DVT is reportedly higher and longer following THA compared to TKA;[26,27] therefore, this difference could be the reason that surgeons are not comfortable with ASA in the THA setting.

The 30-day VTE rate in our study (1.6%) was slightly higher compared to the most recent studies, where VTE rates were 0.5–1%.[9,10] A possible explanation for this could be the inclusion of fractures in our data set, as they accounted for 0.5% (4/855) of VTEs.

Strengths of the present study include the inclusion of both elective procedures and fractures to obtain an accurate real-world picture of prescribing practices. We also compared prescribing habits and a variety of guideline recommendations to identify similarities and discrepancies that arise from variation in practice.

Weaknesses of the study include its reliance on electronic medical records, which may have incomplete data, including data on the use of pneumatic compression devices during hospital stay. There was also a lack of data on patient compliance following discharge. Information on post-discharge VTE and bleeding events was based on emergency room or inpatient data of 30- and 60-day postoperative period, and it does not account for patients who may have visited their primary care center or other hospitals. Event rates may therefore be underestimated. Finally, as this is a single center study, the generalizability of the results is limited. However, as ours is the region's main tertiary care center for THA and TKA, the proportion of thromboprophylaxis may be similar to other academic tertiary care centers in Canada.

Conclusion

This study demonstrates that a Canadian academic tertiary care center has high rates of pharmacologic prophylaxis

among patients undergoing THA and TKA, high rates of adherence to international guidelines, including ACCP and ASH, and a predilection for extended prophylaxis. There is a higher proportion of ASA use following TKA than THA, which remained unexplained but could be due to higher risk of proximal DVT following THA. Use of DOAC in both THA and TKA remains negligible. The future studies are required to further understand individual thromboprophylaxis preferences.

References

1. Warwick D, Williams MH, Bannister GC. Death and thromboembolic disease after total hip replacement. A series of 1162 cases with no routine chemical prophylaxis. J Bone Joint Surg. 1995 Jan;77(1):6–10. PMID: 7822397.
2. Warwick DJ, Whitehouse S. Symptomatic venous thromboembolism after total knee replacement. J Bone Jt Surg B. 1997;79(5):780–6. http://dx.doi.org/10.1302/0301-620X.79B5.7761
3. Geerts WH, Heit JA, Clagett GP, et al. Prevention of venous thromboembolism. Chest. 2009;119(1):132S–75S.
4. 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. http://dx.doi.org/10.1378/chest.11-2404
5. 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(14):1525–31. http://dx.doi.org/10.1001/archinte.158.14.1525
6. Bjørnarå BT, Gudmundsen TE, Dahl OE. Frequency and timming of clinical venous thromboembolism after major joint surgery. J Bone Jt Surg B. 2006;88(3):386–91. http://dx.doi.org/10.1302/0301-620X.88B3.17207
7. Pedersen AB, Sorensen HT, Mehnert F, Overgaard S, Johnsen SP. Risk factors for venous thromboembolism in patients undergoing total hip replacement and receiving routine thromboprophylaxis. J Bone Jt Surg A. 2010;92(12):2156–64. http://dx.doi.org/10.2106/JBJS.I.00882
8. Lapidus LJ, Ponzer S, Pettersson H, De Bri E. Symptomatic venous thromboembolism and mortality in orthopaedic surgery—An observational study of 45 968 consecutive procedures. BMC Musculoskelet Disord. 2013 Jun;14:177. http://dx.doi.org/10.1186/1471-2474-14-177
9. Shahi A, Bradbury TL, Guild GN, Saleh UH, Ghanem E, Oliashirazi A. What are the incidence and risk factors of in-hospital mortality after venous thromboembolism events in total hip and knee arthroplasty patients? Arthroplast Today. 2018;4(3):343–7. http://dx.doi.org/10.1016/j.artd.2018.02.014
10. Warren JA, Sundaram K, Anis HK, Kamath AF, Higuera CA, Piuzzi NS. Have venous thromboembolism rates decreased in total hip and knee arthroplasty? J Arthroplasty. 2020;35(1):259–64. http://dx.doi.org/10.1016/j.arth.2019.08.049
11. Warwick D, Rosencher N. The "critical thrombosis period" in major orthopedic surgery: When to start and when to stop prophylaxis. Clin Appl Thromb. 2010;16(4):394–405. http://dx.doi.org/10.1177/1076029609355151
12. Flevas DA, Megaloikonomos PD, Dimopoulos L, Mitsiokapa E, Koulouvaris P, Mavrogenis AF. Thromboembolism prophylaxis in orthopaedics: An update. EFORT Open Rev. 2018;3(4):136–48. http://dx.doi.org/10.1302/2058-5241.3.170018
13. Lieberman JR, Pensak MJ. Prevention of venous thromboembolic disease after total hip and knee arthroplasty. J Bone Jt Surg A. 2013;95(19):1801–11. http://dx.doi.org/10.2106/JBJS.L.01328
14. Johanson NA, Lachiewicz PF, Lieberman JR, et al. AAOS clinical practice guideline summary: Prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty rent. J Am Acad Orthop Surg. 2009;17(3):183–96. http://dx.doi.org/10.2106/JBJS.I.00364
15. Goodman S. American Academy of Orthopaedic Surgeons. Preventing venous thromboembolic disease in patients undergoing elective total hip and knee arthroplasty: Evidence-based guideline and evidence report. J Bone Joint Surg Am. 2012 April;94(8):673–4. http://dx.doi.org/10.2106/jbjs.9408edit
16. Turpie AG, Lassen MR, Davidson BL, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty (RECORD4): A randomised trial. Lancet. 2009;373(9676):1673–80. http://dx.doi.org/10.1016/S0140-6736(09)60734-0
17. Lassen MR, Ageno W, Borris LC, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. N Engl J Med. 2008;358:2776–86. http://dx.doi.org/10.1056/NEJMoa076016
18. Eriksson BI, Borris LC, Friedman RJ, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthoplasty. N Engl J Med. 2008;358(26):2765–75. http://dx.doi.org/10.1056/NEJMoa0800374
19. Anderson DR, Morgano GP, Bennett C, et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: Prevention of venous thromboembolism in surgical hospitalized patients. Blood Adv. 2019;3(23):3898–944. http://dx.doi.org/10.1182/bloodadvances.2019000975
20. Pow RE, Vale PR. Thromboprophylaxis in patients undergoing total hip and knee arthroplasty: A review of current practices in an Australian teaching hospital. Intern Med J. 2015;45(3):293–9. http://dx.doi.org/10.1111/imj.12675
21. Todd F, Yeomans D, Whitehouse MR, Matharu GS. Does venous thromboembolism prophylaxis affect the risk of venous thromboembolism and adverse events following primary hip and knee replacement? A retrospective cohort study. *J Orthop.* 2021;25(March):301–4. http://dx.doi.org/10.1016/j.jor.2021.05.030
22. Anderson FA, Spencer FA. Risk factors for venous thromboembolism. Circulation. 2003 Jun;107(23 Suppl. 1):19–6. http://dx.doi.org/10.1161/01.CIR.0000078469.07362.E6

23. McNamara I, Sharma A, Prevost T, Parker M. Symptomatic venous thromboembolism following a hip fracture incidence and risk factors in 5,300 patients. *Acta Orthop.* 2009;80(6):687–92. http://dx.doi.org/10.3109/17453670903448273
24. Farfan M, Bautista M, Bonilla G, Rojas J, Llinás A, Navas J. Worldwide adherence to ACCP guidelines for thromboprophylaxis after major orthopedic surgery: A systematic review of the literature and meta-analysis. Thromb Res. 2016;141:163–70. http://dx.doi.org/10.1016/j.thromres.2016.03.029
25. Runner RP, Shau DN, Staley CA, Roberson JR. Utilization patterns, efficacy, and complications of venous thromboembolism prophylaxis strategies in revision hip and knee arthroplasty as reported by American Board of Orthopedic Surgery Part II Candidates. J Arthroplasty. 2021 Jul;36(7): 2364–70. http://dx.doi.org/10.1016/j.arth.2021.01.072
26. Fisher WD. Impact of venous thromboembolism on clinical management and therapy after hip and knee arthroplasty. Can J Surg. 2011;54(5):344–51. http://dx.doi.org/10.1503/cjs.007310
27. Mula V, Parikh S, Suresh S, Bottle A, Loeffler M, Alam M. Venous thromboembolism rates after hip and knee arthroplasty and hip fractures. BMC Musculoskelet Disord. 2020;21(1):1–7. http://dx.doi.org/10.1186/s12891-020-3100-4