Journal of Orthopaedics 16 (2019) 563–568

Contents lists available at ScienceDirect

Journal of Orthopaedics

journal homepage: www.elsevier.com/locate/jor

Should we use dabigatran or aspirin thromboprophylaxis in total hip and knee arthroplasty? A natural experiment

Stephen McHale[1,**], Mark Williams[*], Canice O'Mahony, Michael Hockings

Department of Trauma and Orthopaedics, Torbay and South Devon NHS Foundation Trust, Torbay Hospital, Torquay, TQ2 7AA, UK

ARTICLE INFO

Keywords:
Aspirin
Dabigatran
Thromboprophylaxis
Arthroplasty
Hip
Knee

ABSTRACT

Background: Despite long clinical experience some authorities recommend against the use of aspirin for perioperative VTE prophylaxis and favour alternatives such as dabigatran. A change from Dabigatran to an Aspirin based protocol in a British district general hospital created the conditions of a natural experiment.

Methods: We conducted a single centre, retrospective study of 6-months using a dabigatran based protocol (THA n = 191, TKA n = 155) and 6-months using and aspirin based protocol (THA n = 165, TKA n = 136). Outcomes addressed include: VTE used, VTE events within 90-days, 30-day return to theatre (RTT) rates, and 90-day mortality.

Results: Pre-intervention, the dabigatran prescription rate was 73% (n = 139) and 78% (n = 123) with aspirin prescription post-intervention in 67% (n = 110) and 70% (n = 90) for THA and TKA respectively. We found a similar VTE rate when comparing dabigatran and aspirin groups for THA (2.2% vs. 0%, p = 0.17) and TKA (0.64% vs. 0%, p = 0.32). Similarly, no difference in the RTT rate was seen for THA (0.7% vs.2.7%, p = 0.23) or TKA (1.6% vs. 3.2%, p = 0.38).

Conclusion: No significant differences in safety were found comparing aspirin to dabigatran for VTE prophylaxis for lower limb arthroplasty which, has not been previously reported and represents significant cost saving implications.

1. Introduction

In the United Kingdom and worldwide, hip and knee total joint arthroplasty (TJA) operation rates have grown in recent decades, and this growth is likely to continue.[1,2,3,4] TJA for end-stage hip and knee arthritis is extremely effective both clinically and in terms of cost effectiveness.[5] The complication of a venous thrombo-embolism (VTE), as defined by a deep vein thrombosis (DVT) or pulmonary embolism (PE), despite chemical thrombophrophylaxis occurs in 1.84% and 2.04% of THA and TKA respectively.[6] Near-unanimous consensus exists amongst orthopaedic surgeons that pharmacological thromboprophylaxis is warranted following TJA.[7,8] However high rates of wound complications and increased length of stay associated with the direct oral anticoagulant (DOAC) dabigatran have been observed.[9]

In April 2015, our unit protocol changed from dabigatran to aspirin pharmacoprophylaxis after total hip (THA) and total knee arthroplasty (TKA). We compare VTE and wound related complications rates for THA and TKA, prior to and after this intervention. We hypothesise that, following arthroplasty, patients taking aspirin have similar incidence of VTE and return to theatre (RTT) as patients taking dabigatran.

2. Methods

2.1. Population

The study was approved by the institutional review board prior to commencement. A retrospective study was conducted of patients undergoing THA and TKA between May to November 2013 (THA n = 191, TKA n = 155) and between May to November 2015 (THA n = 165, TKA n = 136). During the earlier period we used a dabigatran based VTE prophylaxis strategy and in the later period we used an aspirin based VTE prophylaxis strategy. A 6-month period was chosen as this was the

[*] Corresponding author.
[**] Corresponding author.
E-mail addresses: stevemchale@hotmail.com, Stephen.mchale@kellogg.ox.ac.uk, stephenmchale@nhs.net (S. McHale), m.williams13@nhs.net (M. Williams), comahony@nhs.net (C. O'Mahony), michael.hockings@nhs.net (M. Hockings).
[1] Present Address: Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, University of Oxford, Botnar Research Centre, Windmill Road, Oxford, UK, OX3 7LD.

https://doi.org/10.1016/j.jor.2019.05.008
Received 7 January 2019; Received in revised form 5 March 2019; Accepted 26 May 2019
Available online 27 May 2019

maximum time span that would allow a 90-day follow up for all patients in the post intervention groups. A 90-day follow up period was chosen to be consistent with previously published studies.[6] Patients were included if they had a primary THA or TKA for any indication during the study periods. As patients were identified through a National Joint Registry (NJR) request, any patients not on the registry were excluded. Retrospective chart review of patient demographic and characteristics was performed to include: implant type, age, gender, American Society of Anasthesiology grade (ASA), Body Mass Index (BMI), previous history of VTE and pharmacological VTE agent used.

2.2. Intervention and comparator

The original VTE prophylaxis guideline used dabigatran 220 mg once daily for 28 days after THA, or 10 days after TKA. The doses and durations of dabigatran were as recommended in NICE guideline CG92.[10] The intervention was to change the guideline to enteric coated Aspirin 150 mg once daily for six weeks after both THA and TKA. This dose and duration of Aspirin was chosen as recommended by the American College of Chest Physicians (AACP).[11] Oral pharmacoprophylaxis was started on discharge from hospital.

2.3. Other VTE prophylaxis used

The VTE prophylaxis strategy was multimodal at both time points. Patients were permitted to drink water until being sent to theatre and prescribed intravenous fluid for immediate post-operative hydration. All patients in all groups received foot pumps prior to mobilisation. Mobilisation was on the first postoperative day, or in the afternoon of the day of surgery if the operation took place in the morning. Patients were prescribed dalteparin, a Low Molecular Weight Heparin (LMWH), at 6-h post operation. The dosage of dalteparin was typically 5000 units once daily, but however the dose could be modified according to body mass and renal function. Dalteparin was continued until discharge, which is typically three days post operation. No oral VTE prophylaxis was given whilst on dalteparin. The rational for using dabigatran as an inpatient is that subcutaneous pharmacoprophylaxis avoids problems with perioperative nausea and vomiting, which might interfere with oral alternatives. Patients who were anticoagulated preoperatively, returned to their usual anticoagulant on day-1 post operation. All patients wore graduated compression stockings whilst an inpatient from day-1 post operation. Patients were then discharged on oral VTE prophylaxis. No changes were made to this multimodal VTE prophylaxis strategy other than the switch to aspirin instead of dabigatran on discharge.

2.4. Outcomes

The primary outcome was 90-day clinically significant VTE rate. Secondary outcomes included 90-day all cause mortality, 30-day return to theatre and 30-day readmission rates.

2.5. VTE diagnosis

As is standard UK practice, we do not routinely screen for VTE after THA and TKA. Investigation with duplex ultrasound or Computed Tomography Pulmonary Angiogram (CTPA) are performed for patients presenting with signs and symptoms consistent with DVT or PE. We identified patients who had VTE by review of the Picture Archiving and Communication System (Insignia, Basingstoke, UK), and cross referenced this against a local VTE database held by the hematology department. Patients were considered to have a clinically significant VTE event if a positive venous duplex scan or CTPA was performed within the first 90-days after the operation. The clinical significance of distal DVT or asymptomatic DVT in THA or TKA patients is unclear with little evidence supporting treatment.[12] Furthermore, unexplained deaths within that time period were assumed to be due to PE; this was to remain consistent with previously published work by Ogonda et al.[13]

2.6. 90-Day all-cause mortality and 30-day return to theatre

This data was available through the NJR, which routinely collects this data. This was validated against local electronic records and by contacting the patient's family doctor where necessary. Cause of death was examined. Reason for return to theatre was recorded.

2.7. Analysis

Analysis of all patients regardless of actual prophylaxis given was performed and subgroup analysis comparing patients receiving dabigatran pre-intervention (dabigatran group) and aspirin post-intervention (aspirin group).

2.8. Statistical analysis

The Statistical Package for the Social Sciences (IBM Corp. in Armonk, NY) was used. Statistical analysis was performed on 2 cohorts, THA and TKA, with subgroup analysis of dabigatran and aspirin groups. Categorical data are described using counts and percentages, and compared using chi-square and Fisher's exact test; continuous data are described using means and standard deviations, and compared using unpaired t-tests. The level of statistical significance was set at $p < 0.05$. No a priori sample size calculation was performed as the nature of the study restricted the population size.

3. Results

For the THA cohort, baseline demographics were similar pre and post-intervention (Table 1). More hybrid THA (18.8%, n = 36 vs. 36.4%, n = 60), and fewer cemented or cementless THA were performed post-intervention. This reflects the trends presented in the National Joint Registry Annual Report in 2016.[14] The mean ASA for THA pre-intervention was 2.4 ± 0.6 and 2.2 ± 0.5 post-intervention ($p = 0.02$). For the TKA cohort baseline demographics were similar pre and post-intervention (Table 1). For THA, 72.8% (n = 139) received dabigatran pre-intervention and 66.7% (n = 110) aspirin post-intervention ($p < 0.001$). 77.8% (n = 123) of TKA patients used dabigatran pre-intervention and, 69.3% (n = 95) of patients used aspirin post-intervention ($p < 0.001$). Comparable numbers of CTPA and venous duplex scans were performed for both THA and TKA patients ($p = 0.72$ and $p = 0.21$). The primary outcome for both THA and TKA demonstrated no difference in VTE events rate within 90 days. Furthermore, there was no statistically significant difference in the RTT rate, and 90-day mortality in either the THA or TKA groups (Table 2).

The characteristics of the dabigatran and aspirin subgroups were comparable for all variables, apart from implant type used in THA (Table 3). In the THA subgroup analysis the 90-day VTE rate was 2.2% (n = 3) for the dabigatran group and 0% in the aspirin group ($p = 0.17$). The 30-day RTT rate for THA was 0.7% (n = 1) in the dabigatran group and 2.7% (n = 3) in the aspirin group ($p = 0.23$). The 30-day readmission rate was similar between groups (Table 4). One patient on aspirin was readmitted with a gastrointestinal perforation. This was secondary to small bowel obstruction due to pre-existing intestinal adhesions. The 90-day mortality rate for THA was similar in both groups. The 90-day VTE rate for TKA was 1.6% (n = 2) in the dabigatran group and 0% in the aspirin group ($p = 0.32$). The 30-day return to theatre for was 1.6% (n = 2) in the dabigatran group and 3.2% (n = 3) in the aspirin group ($p = 0.38$). The 30-day readmission rate was highly similar between groups (Table 4). There was no significant difference in the 90-day mortality rate for TKA).

Table 1
Characteristics of patients with THA and TKA before and after change in VTE policy.

	Total Hip Arthroplasty			Total Knee Arthroplasty		
	Pre-intervention (n = 192)	Post-intervention (n = 165)	P value	Pre-intervention (n = 158)	Post- intervention (n = 137)	P value
Type (%)						
Cement	134 (69.8)	95 (57.6)	< 0.001	155 (98.1)	137 (100)	0.25
Hybrid	36 (18.8)	60 (36.4)		3 (1.9)	0	
No cement	22 (11.4)	10 (6.0)		0	0	
Mean Age ± SD (range)	72.7 yr ± 11.4	72.2 yr ± 10.7	0.66	72.3 yr ± 10.4	71.9 yr ± 9.1	0.67
Gender (%)						
Male	75 (39.1)	65 (39.4)	0.95	69 (43.7)	58 (42.3)	0.82
Female	117 (60.9)	100 (60.6)		89 (56.3)	79 (58.7)	
Mean ASA ± SD	2.4 ± 0.6	2.2 ± 0.5	0.02	2.4 ± 0.6	2.3 ± 0.5	0.11
Mean BMI ± SD	28.4 ± 6.1	28.9 ± 5.9	0.86	30.4 ± 7.8	31.5 ± 7.0	0.39
Previous VTE (%)						
Yes	6 (3.1)	5 (3.0)	1.0	1	2	0.6
No	186 (96.9)	160 (97.0)		157	135	

4. Discussion

This study describes a natural experiment comparing the use of aspirin and dabigatran for VTE pharmacoprophylaxis. No clear differences were seen between treatments. Regarding the primary outcome of 90-day VTE no patient treated with aspirin had a clinically significant VTE. Due to the low frequency of outcomes events, this study lacks statistical power. Post hoc power calculations suggest that we achieved 50% power to identify a difference with α set at 0.05. The study size was restricted by the period passed since the intervention. However, there is little published evidence directly comparing dabigatran and aspirin, and this study found no clinically significant differences between agents, in the context of a multimodal VTE prophylaxis strategy.

The results should be interpreted with some caution, as the observational nature of the study may introduce bias. Specifically, after the guideline change to aspirin a small proportion of patients continued to be prescribed dabigatran. It is possible that surgeons were identifying patients who they perceived to be at high risk and prescribed them dabigatran instead of aspirin. However, it should be noted that patents treated with aspirin included high risk patients such as those undergoing THR for metastatic disease. It should also be noted that the only two VTE events to occur in 2015 patients were both in patients receiving warfarin, which they were prescribed long term pre-operatively. We strongly recommend that all patients have a personalised risk assessment, and that surgeons choose a VTE prophylaxis strategy in that context. It is important to emphasise the multimodal nature of our VTE prophylaxis strategy, and that anaesthetic and mechanical elements play in important role in preventing VTE. All of our patients receive in-hospital dalteparin, typically in the first 3 days post operation, and so this study provides no evidence for the immediate use of aspirin as sole

Table 2
Outcomes of patients with THA and TKA before and after change in VTE policy.

	Total Hip Arthroplasty			Total Knee Arthroplasty		
	Pre-intervention (n = 191)	Post- intervention (n = 165)	P value	Pre- intervention (n = 158)	Post- intervention (n = 137)	P value
VTE agent (%)						
Aspirin	2 (1.0)	110 (66.7)		0	95 (69.3)	
Dabigatran	139 (72.8)	20 (12.1)		123 (77.8)	20 (14.6)	
None	27 (14.1)	8 (4.8)		13 (8.2)	3 (2.2)	
Warfarin	22 (11.5)	12 (7.3)		16 (10.1)	12 (8.8)	
LMWH	1 (0.5)	11 (6.7)		3 (1.9)	4 (2.9)	
Rivaroxiban	0	3 (1.8)		1 (0.6)	1 (0.7)	
VTE investigations within 90 days (%)						
Venous duplex	15 (7.9)	12 (7.3)	0.21	7 (4.4)	8 (5.8)	0.72
CTPA	7 (3.7)	1 (0.6)		5 (3.2)	8 (5.8)	
All VTE[a] events within 90 days (%)	3 (1.6)	0	0.15	3 (1.9)	2 (1.5)	0.57
DVT[b] (%)	3 (1.6)			0 (0)	0	
PE[c] (%)	0			3 (1.9)	2 (1.5)	
RTT[d] within 30 days (%)	3 (1.6)	4 (2.4)	0.42	2 (1.2)	4 (2.9)	0.28
	1 DSSI[e]	2 DSSI[e]		1 DSSI[e]	1 DSSI[e]	
	1 Haematoma evacuation	2 SSSI[f]		1 Wound Problem	1 SSSI	
	1 Dislocation				2 Wound problem	
Mortality 90 days (%)	3 (1.6)	0	0.15	2 (1.2)	1 (0.7)	0.55
Readmission within 30 days (%)	4 (2.1)	5 (3.0)	0.74	8 (5.1)	6 (4.4)	1.0
	2 DSSI	2 DSSI		2 DSSI	2 DSSI	
	1 Wound problem	2 SSSI		3 Wound Problem	1 Wound Problem	
	1 Dislocation	1 Perforation		1 Pain	2 Pain	
				1 SSSI	1 SSSI	
				1 PE		

[a] VTE, venous thromboembolism.
[b] DVT, deep-vein thrombosis.
[c] PE, pulmonary embolism.
[d] RTT, return-to theatre.
[e] DSSI, Deep Surgical site infection.
[f] SSSI, Superficial surgical site infection.

Table 3
Characteristics of patients in dabigatran 2013 and aspirin 2015 groups THA and TKA cohorts.

	Total Hip Arthroplasty			Total Knee arthroplasty		
	Dabigatran (n = 139)	Aspirin (n = 110)	P value	Dabigatran (n = 123)	Aspirin (n = 95)	P value
Type (%)						
Cement		47 (42.7)	< 0.01	120 (97.5)	95 (100)	0.26
Hybrid		56 (50.9)		3 (2.5)	0	
No cement		7 (6.4)		0	0	
Mean Age ± SD	71.8 ± 11.1	70.4 ± 11.1	0.54	71.5 ± 10.8	71.5 ± 9.4	0.97
Gender (%)						
Male	52 (37.4)	43 (39.1)	0.79	53 (43.1)	38 (40)	0.68
Female	87 (62.6)	67 (60.9)		70 (56.9)	57 (60)	
Mean ASA ± SD	2.3 ± 0.6	2.1 ± 0.5	0.43	2.3 ± 0.6	2.3 ± 0.5	0.21
Mean BMI ± SD	26.3 ± 9.7	27.3 ± 8.5	0.28	30.2 ± 8.3	31.5 ± 6.6	0.4
Previous VTE (%)						
Yes	2 (1.4)	2 (1.8)	1.0	1 (0.8)	0	1.0
No	137 (98.6)	108 (98.2)		122 (99.2)	95 (100)	

pharmacoprophylaxis. However, our overall PE rates were similar to those described by Ogonda et al. in a cohort of 11,459 patients who received only aspirin pharmacoprophylaxis.[13]

VTE is an uncommon event after THA and TKA and fatal PE is particularly uncommon. We identified one fatal PE in 652 patients undergoing THA and TKA. This was an assumed PE clinically diagnosed without imaging in an ASA-3, 89-year-old man who was post TKA and receiving dabigatran prophylaxis. It is possible that there was an alternative cause of death. Nevertheless, we identified no possible fatal PE in patients receiving aspirin thromboprophylaxis.

We found that the crude RTT rate was higher in the aspirin groups than in the dabigatran groups, however this did not reach statistical significance. Of the 14 patients readmitted with wound complications, equal numbers had been prescribed dabigatran and aspirin. Previous studies have demonstrated prolonged wound ooze and length of stay in patients receiving dabigatran rather than LMWH followed by aspirin.[9,15,16] Gill et al. reported a higher rate of RTT for dabigatran than aspirin, however their numbers were small and not statistically significant.[17] This issue requires further study.

One patient on aspirin was readmitted with a gastrointestinal perforation. Given that this was secondary to small bowel obstruction due to pre-existing adhesions, we judge that the contribution of aspirin to this complication was minimal. Feldstein et al. observed a rate of gastrointestinal bleeding of 0.9% when using aspirin for VTE prophylaxis.[18] Our finding of one gastrointestinal adverse event in 205 patients equates to a rate of 0.49%. We routinely use enteric coated aspirin in our unit and this may help to reduce gastrointestinal adverse events.

The American Academy of Orthopaedic Surgeons guidelines, published in 2011 was unable to recommend for or against specific pharmacoprophylaxis after TJA.[19] In 2012, the ACCP issued the 9th edition of its guidelines on antithrombotic therapy and prevention of VTE.[11] They recommend TJA patients receive one of nine prophylactic regimens, of which aspirin is one, for at least 35 days postoperatively in the outpatient period. Unsurprisingly, large variations in clinical practice exist, reflecting surgeons' differing assessment of the efficacy, safety and cost-effectiveness associated with each agent.[7]

The National Institute for Health and Care Excellence (NICE) clinical guidance 92, last updated in 2015, is discordant with the ACCP guidelines. Aspirin is not recommended and, dabigatran, fondaparinux sodium, LMWH, rivaroxiban, or UFH are advised.[10] Bozic et al. conducted a multicentre study of 93,840 patients undergoing TKA receiving various pharmacoprophylaxis. They found aspirin use was

Table 4
Outcomes in dabigatran 2013 and aspirin 2015 groups for THR and TKR cohorts.

	Total Hip Arthroplasty			Total Knee Arthroplasty		
	Dabigatran (n = 139)	Aspirin (n = 110)	P Value	Dabigatran (n = 123)	Aspirin (n = 95)	P Value
VTE investigations within 90 days (%)						
Venous duplex	13 (9.4)	7 (6.4)	0.53	6 (4.9)	4 (4.2)	0.50
CTPA	3 (2.2)	0		3 (2.4)	4 (4.2)	
All VTE[a] events within 90 days (%)	3 (2.2)	0	0.17	2 (1.6)	0	0.32
DVT[b] (%)	3			0	0	
PE[c] Fatal (%)	0			1 (0.8)	0	
PE Non-Fatal (%)				1 (0.8)	0	
RTT[d] within 30 days (%)	1 (0.7)	3 (2.7)	0.23	2 (1.6)	3 (3.2)	0.38
	1 DSSI[e]	1 DSSI		1 DSSI	2 DSSI	
		2 SSSI[f]		1 Wound Problem	1 Wound Problem	
Mortality 90 days (%)	1 (0.7)	0	0.56	2 (1.6)	0	0.32
Readmission within 30 days (%)	2 (1.4)	4 (3.6)	0.41	7 (5.7)	6 (6.3)	1.0
	2 DSSI	1 DSSI		2 DSSI	2 DSSI	
		2 SSSI		3 Wound Problem	1 Wound Problem	
		1 GI perforation		1 Pain	2 Pain	
				1 PE	1 SSSI	

[a] VTE, venous thromboembolism.
[b] DVT, deep-vein thrombosis.
[c] PE, pulmonary embolism.
[d] RTT, return-to theatre.
[e] DSSI, Deep Surgical site infection.
[f] SSSI, Superficial surgical site infection.

associated with no differences in risk of bleeding, infection, or mortality and to have lower odds for VTE compared with warfarin and comparable odds to LMWH.[20] This study pre-dates the trials which compared dabigatran with enoxaparin after TKA and THA.[21,22,23,24]

We acknowledge that this study has several limitations. This is a retrospective study with inherent bias associated with such methodology, therefore appropriate judgment should be used in interpreting the results. Higher level evidence could be obtained by performing a randomised trial of aspirin and dabigatran. A post hoc power calculation suggests that to detect a 1% difference in 90-day VTE rate at 80% power and with α set at 0.05, would require 3414 patients for TKA and 5446 for THA. Given that only one out of eight VTE events identified in this study was fatal, it is questionable whether this would amount to a clinically meaningful difference. Certainly, such a trial would be expensive and difficult to conduct and would leave questions as to how aspirin compares to other available DOACs. Given that it is likely that both arms would have relatively low rates of VTE, and very low rates of fatal PE, it may be reasonable to form a judgment based on pre-existing trials and observational studies. In this context, we believe that aspirin is a reasonable choice of pharmacoprophylaxis as part of a multimodal strategy.

The results of this study support our continued use of aspirin as part of a multimodal VTE prophylaxis protocol. Adoption of an aspirin based multimodal VTE prophylaxis protocol has the potential to generate substantial economic savings for orthopaedic departments without adversely affecting clinical outcomes.

5. Conclusions

No significant differences in safety were found comparing aspirin to dabigatran for VTE prophylaxis for hip and knee arthroplasty and represents significant cost saving implications.

Statement of location of where the work was performed

All work was performed at Torbay Hospital, Torquay, UK, TQ2 7AA. All authors are current or former employees of Torbay and South Devon NHS Foundation Trust, of which Torbay Hospital forms a constituent part.

Institutional review board approval

This study was approved by the Torbay and South Devon NHS Foundation Trust Clinical Audit and Effectiveness Group prior to commencement.

Data

All data generated or analysed during this study are included in this published article.

Compliance with ethical standards

Funding

No funding received.

Conflict of Interest

No conflicts of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Acknowledgements

We thank Rachel Hardcastle-Jones and other staff of the Torbay Clinical Effectiveness Department for providing administrative support.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jor.2019.05.008.

References

1. Falbrede I, Widmer M, Kurtz S, Schneidmüller D, Dudda M, Röder C. *Utilization Rates of Lower Extremity Prostheses in Germany and Switzerland: A Comparison of the Years 2005-2008.* vol. 40. 2011; 2011:793–801 no. 9.
2. Ravi B, Croxford R, Reichmann WM, Losina E, Katz JN, Hawker GA. The changing demographics of total joint arthroplasty recipients in the United States and Ontario from 2001 to 2007. *Best Pract Res Clin Rheumatol.* 2012;26(5):637–647.
3. Kurtz S, Ong K, Lau E, Mowat F, halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J. Bone. Joint. Surger. American.* April 2007;89(4):780–785.
4. Culliford D, Maskell J, Judge A, et al. Future projections of total hip and knee arthroplasty in the UK: results from the UK Clinical Practice Research Datalink. *Osteoarthritis Cartilage.* April 2015;23(4):594–600.
5. Jenkins PJ, Clement ND, Hamilton DF, Gaston P, Patton JT, Howie CR. Predicting the cost-effectiveness of total hip and knee replacement: a health economic analysis. *Bone. Joint. J.* 2013 Jan;95-B(1):115–121.
6. Jameson SS, Bottle A, Malviya A, Muller SD, Reed MR. The impact of national guidelines for the prophylaxis of venous thromboembolism on the complications of arthroplasty of the lower limb. *Bone Joint J.* 2010;92-B(1):123–129.
7. Anderson FA, Huang W, Friedman RJ. Prevention of venous thromboembolism after hip or knee arthroplasty: findings from a 2008 survey of US orthopedic surgeons. *J Arthroplast.* 2012;27:659–666.
8. Hass SB, Barrack RL, Westruck G. Venous thrombo- embolic disease after total hip and knee arthroplasty. *J Bone Joint Surg Am.* 2008;90:2764–2780.
9. Bloch BV, Patel V, Best AJ. Thromboprophylaxis with dabigatran leads to an increased incidence of wound leakage and an increased length of stay after total joint replacement. *Bone Joint Lett J.* Jan 2014;96:122–126 no. B (1).
10. National Institute for Clinical Excellence. *Venous Thromboembolism: Reducing the Risk for Patients in Hospital . Clinical Guideline [CG92].* June 2015; June 2015 Published date: January 2010 Last updated.
11. Falck-Ytter Y, Francis CW, Johanson NA. 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;14.
12. Righini M. Is it worth diagnosing and treating distal deep vein thrombosis? No. *J Thromb Haemost.* 2007;5:55–59.
13. Ogonda L, Hill J, Doran E, Dennison J, Stevenson M, Beverland D. Aspirin for thromboprophylaxis after primary lower limb arthroplasty: early thromboembolic events and 90 day mortality in 11,459 patients. *Bone Joint J.* 2016;98-B(3).
14. *14th Annual Report. National Joint Registry: National Joint Registry for England, Wales and Northern Ireland.* 2017; 2017.
15. Wilson DG, Poole WE, Chauhan SK, Rogers BA. Systematic review of aspirin for thromboprophylaxis in modern elective total hip and knee arthroplasty. *Bone Joint Lett J.* 2016;98-B(8):1056–1061.
16. Aquilina AL, Brunton LR, Whitehouse MR, Sullivan N, Blom AW. Direct throm- bin inhibitor (DTI) vs. aspirin in primary total hip and knee replacement using wound ooze as the primary outcome measure. A prospective cohort study. *Hip Int.* 2012;22:22–27.
17. Gill SK, Theodorides A, Smith N. Wound problems following hip arthroplasty before and after the introduction of a direct thrombin inhibitor for thromboprophy- laxis. *Hip Int.* 2011;21:678–683.
18. Feldstein MJ, Low SL, Chen AF, Woodward LA, Hozack WJ. A comparison of two dosing regimens of ASA following total hip and knee arthroplasties. *J Arthroplast.* Sep 2017;32(9S):157–161.
19. Mont MA, Jacobs JJ, Boggio LN. Preventing venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty. *J Am Acad Orthop Surg.* 2011;19:768–776.
20. Bozic KJ, Vail TP, Pekow PS, Maselli JH, Lindenauer PK, Auerbach AD. Does aspirin have a role in venous thromboembolism prophylaxis in total knee arthroplasty patients? *J Arthroplast.* 2010;25:1053–1060.
21. Eriksson BI, Dahl OE, Rosencher N. Oral dabigatran etexilate vs. subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee

replacement: the RE-MODEL randomized trial. *J Thromb Haemost.* 2007;5:2178–2185.
22. Eriksson BI, Dahl OE, Rosencher N, et al. Dabigatran etexilate versus enoxaparin for prevention of venous thromboembolism after total hip replacement: a randomised, double-blind, non-inferiority trial. *The Lancet.* 2007;370:949–956.
23. Eriksson BI, Dahl OE, Huo MH. *Oral Dabigatran versus Enoxaparin for Thromboprophylaxis after Primary Total Hip Arthroplasty (RE-NOVATE II*): A Randomised, Double-Blind, Non-inferiority Trial.* vol. 105. 2011; 2011:721–729.
24. Ginsberg JS, Davidson BL, Committee RM. Oral thrombin inhibitor dabigatran etexilate vs North American enoxaparin regimen for prevention of venous thromboembolism after knee arthroplasty surgery. *J Arthroplast.* 2009;24:1–9.