Venous Thromboembolism in Hip Fracture Patients: A Subanalysis of the FAITH and HEALTH Trials

David R. W. MacDonald, MRCS (Glas),[a] David Neilly, FRCS Tr & Orth,[a] Prism S. Schneider, MD, FRCSC,[b] Sofia Bzovsky, MSc,[c] Sheila Sprague, PhD,[c,d] Daniel Axelrod, MD, MSc (Cand),[c] Rudolf W. Poolman, MD, PhD,[e] Frede Frihagen, MD,[f] Mohit Bhandari, MD, PhD, FRCSC,[c,d] Marc Swiontkowski, MD,[g] Emil H. Schemitsch, MD, FRCSC,[h] and Iain M. Stevenson, FRCS Tr & Orth[a] on behalf of the FAITH and HEALTH Investigators

Background: The primary objective of this study was to determine the incidence of symptomatic venous thromboembolism (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT), in the hip fracture population. Secondary objectives included determining timing of VTE diagnosis, VTE thromboprophylaxis given, and identifying any factors associated with VTE.

Methods: Using data from the FAITH and HEALTH trials, the incidence of VTE, including DVT and PE, and the timing of VTE were determined. A multivariable Cox regression analysis was used to determine which factors were associated with increased risk of VTE, including age, treatment for comorbidity, thromboprophylaxis, time to surgery, and method of fracture management.

Results: 2520 hip fracture patients were included in the analysis. Sixty-four patients (2.5%) had a VTE [DVT: 36 (1.4%), PE: 28 (1.1%)]. Thirty-five (54.7%) were diagnosed less than 6 weeks postfracture and 29 (45.3%) more than 6 weeks postfracture. One thousand nine hundred ninety-three (79%) patients received thromboprophylaxis preoperatively and 2502 (99%) received thromboprophylaxis postoperatively. The most common method of preoperative (46%) and postoperative (73%) thromboprophylaxis was low molecular weight heparin. Treatment with arthroplasty compared to internal fixation was the only variable associated with increased risk of VTE (hazard ratio 2.67, $P = 0.02$).

Conclusions: The incidence of symptomatic VTE in hip fracture patients recruited to the 2 trials was 2.5%. Although over half of the

Accepted for publication August 11, 2020.

From the [a]Department of Trauma and Orthopaedic Surgery, Aberdeen Royal Infirmary, Aberdeen, United Kingdom; [b]Department of Surgery, University of Calgary, Calgary, Canada; [c]Division of Orthopaedic Surgery, Department of Surgery, McMaster University, Hamilton, ON, Canada; [d]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada; [e]Department of Orthopedic and Trauma Surgery, OLVG, Amsterdam and Leiden University Medical Center, Leiden, the Netherlands; [f]Division of Orthopaedic Surgery, Oslo University Hospital, Oslo, Norway; [g]Department of Orthopaedic Surgery, University of Minnesota, Minneapolis, MN; and [h]Department of Surgery, University of Western Ontario, London, ON, Canada.

The FAITH Study was supported by research grants from the Canadian Institutes of Health Research (MOP-106630 and MCT-87771), National Institutes of Health (1R01AR055267-01A1), Stichting NutsOhra (SNO-T-0602-43), the Netherlands Organisation for Health Research and Development (80-82310-97-11032), and Physicians' Services Incorporated. M. Bhandari was also funded, in part, through the Early Research Award Program, which provided funding for the FAITH study as well as by a Canada Research Chair in Musculoskeletal Trauma, which is unrelated to the FAITH study (McMaster University, Hamilton, ON, Canada). The HEALTH trial was supported by research grants from the Canadian Institutes of Health Research (CIHR) (MCT-90168), National Institutes of Health (NIH) (1UM1AR063386-01), ZorgOnderzoek Nederland-medische wetensehappen (ZonMw) (17088.2503), Sophies Minde Foundation for Orthopaedic Research, McMaster Surgical Associates, and Stryker Orthopaedics. The funding sources had no role in design or conduct of the study; the collection, management, analysis, or interpretation of the data; or the preparation, review, or approval of the manuscript.

P. S. Schneider reports editorial or governing board for the Canadian Journal of Surgery, board or committee member for the Canadian Orthopaedic Association, paid presenter/speaker for Stryker, and paid presenter/speaker for Synthes, outside the submitted work. S. Sprague reports editorial or governing board for BMS Women's Health, employment from Global Research Solutions Inc., and employment from McMaster University, outside the submitted work. R. W. Poolman reports board or committee member for the Dutch Orthopaedic Association, research support from Lima, and research support from Link Orthopaedics, outside the submitted work. F. Frihagen reports personal fees from Amgen Co, personal fees from Smith & Nephew, personal fees from Synthes, and personal fees from Zimmer, outside the submitted work. M. Bhandari reports research support from Acumed, LLC, research support from Aphria, research support from Ferring Pharmaceuticals, research support and personal fees from Pendopharma, and research support and personal fees from Sanofi-Aventis, outside the submitted work. M. Swiontkowski reports board or committee member for the American Orthopaedic Association, consultant to the Minnesota Board of Medical Practice, editorial or governing board and publishing royalties, financial or material support for the Journal of Bone and Joint Surgery—American, publishing royalties, financial or material support from Saunders/Mosby-Elsevier, and publishing royalties, financial or material support from Wolters Kluwer Health—Lippincott Williams & Wilkins, outside the submitted work. E. H. Schemitsch reports personal fees from Acumed, LLC, personal fees from Amgen Co, research support from Biocomposites, board or committee member for the Canadian Orthopaedic Association, personal fees from DePuy, board or committee member for the Hip Society, board or committee member for the International Society for Fracture Repair, personal fees from ITS, editorial or governing board for the Journal of Orthopaedic Trauma, board or committee member for the Orthopaedic Trauma Association, editorial or governing board for the Orthopaedic Trauma Association International, board or committee member for the Osteosynthesis and Trauma Care Foundation, personal fees from Pentopharm, personal fees from Sanofi-Aventis, personal fees from Saunders/Mosby-Elsevier, personal fees from Smith & Nephew, personal fees from Springer, personal fees from Stryker, personal fees from Swemac, and personal fees from Zimmer, outside the submitted work. The remaining authors report no conflict of interest.

Reprints: Iain M. Stevenson, FRCS Tr & Orth, Department of Trauma and Orthopaedic Surgery, Aberdeen Royal Infirmary, Aberdeen, United Kingdom AB25 2ZN (e-mail: iainstevenson@nhs.net).

DOI: 10.1097/BOT.0000000000001939

cases were diagnosed within 6 weeks of fracture, VTE is still prevalent after this period. The majority of patients received thromboprophylaxis. Treatment with arthroplasty rather than fixation was associated with increased incidence of VTE.

Key Words: femoral neck fracture, venous thromboembolism, pulmonary embolism, deep vein thrombosis

Level of Evidence: Therapeutic Level II. See Instructions for Authors for a complete description of levels of evidence.

(*J Orthop Trauma* 2020;34:S70–S75)

INTRODUCTION

Venous thromboembolism (VTE), which comprises deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common cause of morbidity and mortality in hip fracture patients.[1] Although most cases are asymptomatic, in the absence of thromboprophylaxis, postoperative VTE rates of up to 80% have been reported.[2] Symptomatic VTE is less common, particularly when thromboprophylaxis is used. In the presence of thromboprophylaxis, the incidence of symptomatic postoperative DVT and PE has been reported from 1.18%–6% and 0.25%–4.6%, respectively.[3–6]

Symptomatic VTE is most often diagnosed within the first 30 days after hip fracture,[7,8] but patients may be at increased risk for up to 1 year after surgery.[9] VTE is also commonly present before surgery in hip fracture patients, although this is usually asymptomatic.[10–12] A number of factors have been associated with an increased risk of VTE in hip fracture patients including delay to surgery, extracapsular fracture pattern, and pulmonary disease.[8,10,13] The increased risk of VTE after hip fracture is well recognized and VTE prevention is emphasized by many organizations including the National Institute for Health and Clinical Excellence (NICE),[14] the Scottish Intercollegiate Guidelines Network, and American College of Chest Physicians.[14–16] These bodies recommend different combinations of chemical and mechanical VTE prophylaxis, but all agree that VTE prophylaxis should be instituted for hip fracture patients.

Analyses of the data from the FAITH (Fixation using Alternative Implants for the Treatment of Hip fractures) and the HEALTH (Hip fracture evaluations with Alternatives of Total Hip Arthroplasty vs. Hemiarthroplasty) trials both independently and combined were performed.[17,18] The primary objective was to determine the incidence of symptomatic VTE, including DVT and PE, in the population of hip fracture patients included in these studies. Secondary objectives were to determine the timing of VTE diagnosis, determine the proportion of patients receiving VTE prophylaxis and the type of prophylaxis given, describe the differences in patients who suffered a VTE and those who did not, and to determine which factors were associated with VTE.

METHODS

In this preplanned study, we analyzed the data from the 1079-patient FAITH and the 1441-patient HEALTH trials to determine the incidence of symptomatic VTE, including DVT and PE, in this population of 2520 hip fracture patients. In both studies, incidence of symptomatic VTE was recorded as a secondary outcome during inpatient stay and when participants returned for follow-up (either in person or through telephone) at 1 and 10 weeks, and at 6, 9, 12, 18, and 24 months after surgery. This allowed for both incidence of VTE in this population and the timing of VTE diagnosis to be determined and presented as frequencies and percentages.

In both studies, the baseline characteristics of all patients included were recorded, including age, sex, body mass index, prefracture living setting, prefracture functional status, American Society of Anesthesiologists (ASA) classification, and comorbidity. This allowed us to describe the characteristics of patients who suffered a VTE and the characteristics of patients who did not. The preoperative and postoperative VTE prophylaxis given for each patient was also recorded, allowing us to determine the proportion of patients receiving VTE prophylaxis and the type of VTE prophylaxis given. Method of fracture management and time from injury to surgery were also recorded in each trial. We used descriptive statistics to summarize these results (frequencies and percentages for categorical variables and means and ranges for continuous variables).

A multivariable Cox regression analysis was used to determine which factors were associated with increased risk of symptomatic VTE including: age, treatment for comorbidity (yes vs. no), thromboprophylaxis (medical vs. nonmedical), time from injury to surgery, and method of fracture management (arthroplasty vs. internal fixation). Factors were selected based on biological rationale, previous literature, and expert opinion. Statistical analysis was conducted using R (version 3.6.1, R Foundation for Statistical Computing, Vienna, Austria). Results were presented as hazard ratios (HRs), 95% confidence intervals (CIs), and *P*-values. A *P*-value of less than 0.05 was considered to be statistically significant.

RESULTS

In the FAITH trial, 1079 patients were randomized to treatment. At 24 months, 923 patients were alive, and complete follow-up was achieved for 844 (91%).[17] In the HEALTH trial, 1441 patients were randomized to treatment.[18] At 24 months, 1243 patients were alive, and complete follow-up was achieved for 1058 (85.1%).

Within the FAITH trial, 17 cases of VTE were recorded (1.6%) and 47 cases of VTE were recorded within the HEALTH trial (3.3%), resulting in a total of 64 cases of symptomatic VTE across the 2520 hip fracture patients from both studies and an incidence of VTE of 2.5%. The baseline characteristics of patients who suffered a VTE and those who did not suffer a VTE are summarized in Table 1.

In the FAITH trial, 12 cases of DVT were recorded (1.1%) with 24 cases of DVT in the HEALTH trial (1.7%). In total, 36 cases of symptomatic DVT were recorded across the 2520 hip fracture patients from both studies giving an incidence of symptomatic DVT of 1.4%. The FAITH trial recorded 5 cases of PE (0.5%) and 23 cases of PE were

TABLE 1. Characteristics of Patients Who had a VTE

Variable	No VTE, N = 2456	VTE, N = 64
Age, mean (SD)	75.7 (10.8)	77.3 (10.0)
Sex, n (%)		
Male	829 (33.9)	24 (37.5)
Female	1617 (66.1)	40 (62.5)
Body mass index, mean (SD)	24.8 (4.7)	25.4 (5.0)
Prefracture living setting, n (%)		
Institutionalized	116 (4.7)	2 (3.1)
Not institutionalized	2340 (95.3)	62 (96.9)
Prefracture functional status, n (%)		
Use of aid	581 (23.7)	19 (29.7)
Independent ambulator	1875 (76.3)	45 (70.3)
ASA classification, n (%)		
Class I/II	1302 (53.0)	34 (53.1)
Class III/IV/V	1154 (47.0)	30 (46.9)
Receiving treatment for major comorbidities, n (%)		
Osteopenia	34 (1.4)	0 (0.0)
Osteoporosis	129 (5.3)	9 (14.1)
Lung disease	316 (12.9)	7 (10.9)
Diabetes	328 (13.4)	10 (15.6)
Ulcers or stomach disease	213 (8.7)	8 (12.5)
Kidney disease	112 (4.6)	5 (7.8)
Anemia or other blood disease	109 (4.4)	6 (9.4)
Depression	259 (10.6)	5 (7.8)
Cancer	117 (4.8)	4 (6.3)
Osteoarthritis, degenerative arthritis	204 (8.3)	3 (4.7)
Back pain	178 (7.3)	3 (4.7)
Rheumatoid arthritis	47 (1.9)	6 (9.4)
Heart disease	644 (26.2)	11 (17.2)
High blood pressure	1192 (48.5)	31 (48.4)
Method of fracture management, n (%)		
Internal fixation	1062 (43.2)	17 (26.6)
Arthroplasty	1394 (56.8)	47 (73.4)
Preoperative thromboprophylaxis, n (%)*		
Medical only		
Heparin	143 (5.8)	2 (3.1)
Warfarin	68 (2.8)	0 (0.0)
DOAC/other oral	47 (1.9)	1 (1.6)
acetylsalicylic acid	16 (0.7)	0 (0.0)
LMWH	1120 (45.6)	32 (50.0)
Mechanical only	433 (17.6)	9 (14.1)
Medical and mechanical		
Heparin and mechanical	23 (0.9)	0 (0.0)
Warfarin and mechanical	10 (0.4)	1 (1.6)
DOAC/other oral and mechanical	3 (0.1)	0 (0.0)
acetylsalicylic acid and mechanical	2 (0.1)	0 (0.0)
LMWH and mechanical	67 (2.7)	1 (2.9)
None	509 (20.7)	18 (28.1)
Postoperative thromboprophylaxis, n (%)*		
Medical only		
Heparin	158 (6.4)	3 (4.7)
Warfarin	95 (3.9)	2 (3.1)
DOAC/other oral	91 (3.7)	3 (4.7)
acetylsalicylic acid	25 (1.0)	0 (0.0)
LMWH	1804 (73.5)	51 (79.7)
Mechanical only	81 (3.3)	0 (0.0)
Medical and mechanical		
Heparin and mechanical	25 (1.0)	0 (0.0)
Warfarin and mechanical	37 (1.5)	1 (1.6)
DOAC/other oral and mechanical	13 (0.5)	0 (0.0)
acetylsalicylic acid and mechanical	23 (0.9)	0 (0.0)
LMWH and mechanical	175 (7.1)	6 (9.4)
None	14 (0.6)	0 (0.0)
Time from injury to surgery, mean (SD) (hours)	52.0 (75.6)	40.1 (31.8)

*In some cases, more than one type of thromboprophylaxis was used.

ASA, American Society of Anesthesiologists; DOAC, direct oral anticoagulants; LMWH, low-molecular-weight heparin; SD, standard deviation; VTE, venous thromboembolism.

recorded in the HEALTH trial (1.6%). A total of 28 cases of PE were recorded across the 2520 hip fracture patients from both studies giving an incidence of PE of 1.1%.

The timing of VTE diagnosis is summarized in Table 2. Across both studies, 3 (4.7%) cases of VTE were diagnosed presurgery and 61 (95.3%) were diagnosed postsurgery. Of VTE cases, 22 (34.4%) were diagnosed prehospital discharge and 42 (65.6%) were diagnosed posthospital discharge. Overall, 35 (54.7%) cases of VTE were diagnosed less than 6 weeks postfracture and 29 (45.3%) were diagnosed more than 6 weeks postfracture.

The proportion of patients given VTE prophylaxis and the type of prophylaxis used are summarized in Table 3. Across both studies, 1993 patients (79.3%) received thromboprophylaxis preoperatively and 2502 (99.4%) received thromboprophylaxis postoperatively. The most common methods of preoperative thromboprophylaxis were low molecular weight heparin (LMWH) (46.0%) and mechanical prophylaxis (18.0%). The most common method of postoperative thromboprophylaxis was LMWH (73.0%).

The results of the multivariable Cox regression analysis are summarized in Table 4. Advancing age, receiving treatment for a comorbidity, type of postoperative thromboprophylaxis, and increased time from injury to surgery were not associated with an increased incidence of symptomatic VTE ($P > 0.05$). However, surgical treatment with arthroplasty was associated with an increased incidence of symptomatic VTE within 24 months of hip fracture compared to surgical treatment with internal fixation (HR 2.21, $P = 0.02$). Total hip arthroplasty and hemiarthroplasty versus internal

TABLE 2. Timing of VTE in FAITH and HEALTH

Weeks From Hip Fracture	FAITH, N = 17	HEALTH, N = 47	Overall, N = 64
Presurgery, n (%)	0 (0.0)	3 (6.4)	3 (4.7)
Postsurgery, n (%)	17 (100.0)	44 (93.6)	61 (95.3)
Prehospital discharge, n (%)	3 (17.6)	19 (40.4)	22 (34.4)
Posthospital discharge, n (%)	14 (82.4)	28 (59.6)	42 (65.6)
<6 wk postfracture, n (%)	8 (47.0)	27 (57.5)	35 (54.7)
≥6 wk postfracture, n (%)	9 (53.0)	20 (42.5)	29 (45.3)

fixation were associated with a 2.67 and 1.77 times increase in VTE, respectively.

DISCUSSION

This sub-analysis of data from the FAITH and HEALTH trials demonstrates that the incidence of symptomatic VTE in hip fracture patients included in these trials is 2.5%, with the overall combined incidence of symptomatic DVT being 1.4%. The FAITH trial recorded 5 cases of PE (0.5%) and 23 cases of PE were recorded in the HEALTH trial (1.6%). Although over half of cases were diagnosed within 6 weeks of the fracture, VTE is still prevalent after this period. The majority of patients received thromboprophylaxis before and after surgery with LMWH given alone being the most common type of VTE

TABLE 3. VTE Prophylaxis in FAITH and HEALTH

	FAITH, N = 1079	HEALTH, N = 1441	Overall, N = 2520
Preoperative thromboprophylaxis, n (%)*			
Medical only			
Heparin	73 (6.8)	72 (5.0)	145 (5.7)
Warfarin	37 (3.4)	31 (2.2)	68 (2.7)
DOAC/other oral	29 (2.7)	21 (1.5)	50 (2.0)
ASA	3 (0.3)	10 (0.7)	13 (0.5)
LMWH	506 (46.9)	663 (46.0)	1169 (46.0)
Mechanical only	280 (25.9)	177 (12.3)	457 (18.0)
Medical and mechanical			
Heparin and mechanical	16 (1.5)	7 (0.5)	23 (0.9)
Warfarin and mechanical	5 (0.5)	6 (0.4)	11 (0.4)
DOAC/other oral and	2 (0.2)	1 (0.1)	3 (0.1)
Mechanical			
ASA and mechanical	0 (0.0)	2 (0.2)	0 (0.0)
LMWH and mechanical	41 (3.8)	27 (1.9)	2 (0.1)
None	106 (9.8)	421 (29.2)	527 (20.7)
Postoperative thromboprophylaxis, n (%)*			
Medical only			
Heparin	85 (7.9)	76 (5.3)	161 (6.3)
Warfarin	39 (3.6)	58 (4.0)	97 (3.8)
DOAC/other oral	52 (4.8)	29 (2.0)	81 (3.2)
ASA	11 (1.0)	14 (1.0)	25 (1.0)
LMWH	733 (67.9)	1122 (77.9)	1855 (73.0)
Mechanical only	40 (3.7)	41 (2.9)	81 (3.2)
Medical and mechanical			
Heparin and mechanical	18 (1.7)	7 (0.5)	25 (1.0)
Warfarin and mechanical	10 (0.9)	28 (1.9)	38 (1.5)
DOAC/other oral and mechanical	6 (0.6)	7 (0.5)	13 (0.5)
ASA and mechanical	6 (0.6)	17 (1.2)	23 (0.9)
LMWH and mechanical	120 (11.1)	61 (4.2)	181 (7.2)
None	5 (0.5)	9 (0.6)	14 (0.6)

*In some cases, more than one type of thromboprophylaxis was used.
ASA, acetylsalicylic acid; DOAC, direct oral anticoagulants; LMWH, low-molecular-weight heparin; VTE, venous thromboembolism.

TABLE 4. Association Between Thromboprophylaxis and VTE Incidence Post Internal Fixation or Arthroplasty Surgery (N = 2,231, 56 Events)*

Variable	HR (95% CI)	*P*
Age (y)	0.99 (0.97–1.03)	0.94
Receiving treatment for a comorbidity yes vs. no	1.46 (0.76–2.78)	0.25
Postoperative thromboprophylaxis medical vs. not medical	1.27 (0.54–2.97)	0.58
Time from injury to surgery (h)	0.99 (0.986–1.002)	0.11
Method of fracture management arthroplasty vs. internal fixation	2.21 (1.15–4.26)	0.02
Method of fracture management		
Total hip arthroplasty vs. internal fixation	2.67 (1.33–5.38)	0.006
Hemiarthroplasty vs. internal fixation	1.77 (0.84–3.74)	0.14

*Patients with VTE occurring before the initial surgery were excluded from this analysis.
CI, confidence interval; HR, hazard ratio; OR, odds ratio.

prophylaxis given preoperatively and postoperatively. Treatment with arthroplasty rather than fixation was the only factor analyzed that was associated with increased incidence of symptomatic VTE in this population.

The incidence of symptomatic VTE from the FAITH and HEALTH trials is comparable to the incidences reported in other large studies. The ESCORTE study was a multicenter cohort study of 6860 hip fracture patients, 98% of whom received VTE prophylaxis with LMWH.[5] The authors reported a VTE incidence of 1.34% at 3 months of follow-up, with a 1.09% incidence of DVT and 0.25% incidence of PE. The Pulmonary Embolism Prevention trial was a multicenter randomized controlled trial comparing VTE thromboprophylaxis with aspirin or placebo, in addition to other thromboprophylaxis thought necessary in hip fracture patients.[3] In the 6679 patients assigned aspirin, the authors reported a VTE incidence of 1.6% at 35 days of follow-up, with a 1% incidence of DVT and 0.7% incidence of PE. McNamara et al[8] conducted a single-center cohort study of 5300 hip fracture patients, all of whom received thromboprophylaxis with heparin. The authors reported a 2.2% incidence of symptomatic VTE at 1-year follow-up, with a 1.5% incidence of DVT and 0.7% incidence of PE.

Although the majority (55%) of symptomatic VTE occurred within 6 weeks of hip fracture in the current study, a significant percentage occurred after this period. This is in keeping with the results of other large studies. Bjørnarå et al conducted a single-center cohort study of 2420 hip fracture patients with 6 months of follow-up.[7] Thirty-six patients had a symptomatic DVT. The median time to diagnosis was 24 days (range 3–150 days). Thirty-nine patients had a symptomatic PE. The median time to diagnosis was 17 days (range 1–173 days). McNamara et al[8] reported a mean time to VTE presentation of 24 days (range 3–91 days). Mean time to DVT presentation was 25 days (range 4–91 days) and mean time to PE presentation was 20 days (range 3–81 days). Eighty-five percent of VTE events occurred within 5 weeks of fracture, but patients presented up to 13 weeks after the injury. Despite the majority of cases presenting within the first 6 weeks in the current study, VTE was still prevalent after this period with 45% of cases presenting after 6 weeks. Pedersen et al[9] conducted a cohort study from the Danish Health registry comparing 110,563 hip fracture patients to a cohort of 552,774 people from the general population.bib9 The adjusted HR of VTE among hip fracture patients was highest during the first 30 days after hip fracture (HR = 17.29, 95% CI: 14.74–20.28), but remained elevated during 31–365 days after hip fracture (HR = 2.13, 95% CI: 1.95–2.32). Although this prolonged increased risk of VTE is consistent with this current study, our results suggest that risk may be greater than previously demonstrated.

National Institute for Health and Clinical Excellence (NICE, UK), Scottish Intercollegiate Guidelines Network, and American College of Chest Physicians guidance documents recommend preoperative medical VTE prophylaxis with heparin unless contraindication exists, in addition to preoperative mechanical VTE prophylaxis for patients with hip fractures.[14–16] These guidelines also recommend postoperative VTE prophylaxis with heparin, unless contraindication exists, in addition to mechanical VTE prophylaxis until the patient's mobility is no longer significantly reduced. In our subanalysis, 61.3% of patients received preoperative medical thromboprophylaxis, most commonly with LMWH (46.1%), and 23.1% of patients received preoperative mechanical prophylaxis. 96.2% of patients received medical VTE prophylaxis postoperatively, most commonly with LMWH (80.2%), and 11% received postoperative mechanical prophylaxis. The lower rate of preoperative medical VTE prophylaxis may be partially due to early surgery preventing the use of anticoagulants, but our study suggests that mechanical VTE prophylaxis is often not used preoperatively or postoperatively despite advice from available guidelines. The use of mechanical VTE prophylaxis has been suggested to confer additional benefit when used with medical prophylaxis and this is an area of practice that may be improved.[19]

Regression analysis in this study demonstrated that age was not associated with VTE incidence. This is consistent with analyses performed by McNamara et al and the ESCORTE study, both of which showed that age was not associated with postoperative symptomatic VTE.[5,8] In addition, a regression analysis by Shin et al[11] demonstrated that age was not associated with preoperative DVT diagnosed by multidetector CT venography. Our analysis also demonstrated that patient comorbidity was not associated with VTE incidence. The analysis by Shin et al also showed that many comorbidities including diabetes, hypertension, and cardiac disease were not associated with VTE, but suggested that pulmonary disease was associated with increased risk of VTE. Our analysis demonstrated that time from injury to surgery was not associated with increased risk of VTE. Although there is limited evidence investigating the effect of time to surgery on postoperative VTE, several studies have suggested that delay increases the risk of preoperative VTE.[10,20]

Our regression analysis demonstrated that treatment with arthroplasty as opposed to fixation was associated with an over 2-fold increased incidence of VTE, and that this increased risk was greater with total hip arthroplasty than hemiarthroplasty. No published studies have previously compared VTE incidence for arthroplasty and fixation as surgical treatments for a femoral neck fracture. Analyses by McNamara et al. and Shin et al demonstrated that intertrochanteric and subtrochanteric fracture patterns were associated with increased incidence of postoperative VTE compared to femoral neck fractures.[8,11] Although this may suggest that fixation increases postoperative VTE incidence, these studies are not directly comparable to our study of femoral neck fractures only.

The main strength of our subanalysis is that our data are sourced from 2 large-scale international studies, which both had broad inclusion criteria with recruitment from a large number of hospitals in diverse health care systems. These results are therefore more likely to give a realistic picture of symptomatic VTE in hip fracture patients. Although the use of imaging to screen patients may identify many more cases of VTE, our study used symptomatic VTE as its outcome, which we believe makes our results more clinically relevant to patients and current practice in most health care systems.

A limitation of our subanalysis is the loss of patients over the 24 months of follow-up in both studies. However, the loss to follow-up in both studies was consistent with or better than other trials including hip fracture patients.[21] Both studies also had unavoidable heterogeneity of variables such as patient positioning, surgical exposure, use of traction, type of anesthetic and physiotherapy and rehabilitation protocols, which may have affected results.

In conclusion, the incidence of symptomatic VTE in the hip fracture patients recruited to the FAITH and HEALTH trials was 2.5%. Although over half of cases were diagnosed within 6 weeks of surgery, VTE was still prevalent after this period with 45% of patients presenting after 6 weeks. The majority of patients received thromboprophylaxis before and after surgery, but mechanical prophylaxis was not commonly used. Although several factors were examined, only treatment with arthroplasty rather than fixation was associated with increased incidence of VTE.

The high incidence of symptomatic VTE over 6 weeks after surgery and the increased VTE risk with arthroplasty seen in our study have not been previously described. These results should be considered to guide future clinical decision making in hip fracture patients.

ACKNOWLEDGMENTS

The authors thank the FAITH and HEALTH Investigators (http://links.lww.com/JOT/B230).

REFERENCES

1. Todd C, Freeman C, Camilleri-Ferrante C, et al. Differences in mortality after fracture of hip: the East Anglian audit. *BMJ* 1995;310:904–908.
2. Geerts WH, Code KI, Jay RM, et al. A prospective study of venous thromboembolism after major trauma. *N Engl J Med.* 1994;331:1601–1606.
3. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: pulmonary Embolism Prevention (PEP) trial. *Lancet.* 2002; 355:1295–1302.
4. Eriksson BI, Lassen MR. PENTasaccharide in HIp-FRActure Surgery Plus Investigators. Duration of prophylaxis against venous thromboembolism with fondaparinux after hip fracture surgery: a multicentre, randomized, placebo-controlled, double blind study. *Arch Intern Med.* 2003; 163:1337–1342.
5. Rosencher N, Vielpeau C, Emmerich J, et al. Venous thromboembolism and mortality after hip fracture surgery: the ESCORTE study. *J Thromb Haemost.* 2005;3:2006–2014.
6. Westrich GH, Rana AJ, Terry MA, et al. Thrombpembolic disease prophylaxis in patients with hip fracture: a multimodal approach. *J Orthop Trauma.* 2005;19:234–240.
7. Bjornara BT, Gudmundsen TE, Dahl OE. Frequency and timing of clinical venous thromboembolism after major joint surgery. *J Bone Joint Surg Br.* 2006;88:386–391.
8. McNamara I, Sharma A, Prevost T, et al. Symptomatic venous thromboembolism following a hip fracture: incidence and risk factors in 5300 patients. *Acta Orthop.* 2009;80:687–692.
9. Pedersen AB, Ehrenstein V, Szepligeti SK, et al. Excess risk of venous thromboembolism in hip fracture patients and the prognostic impact of comorbidity. *Osteoporos Int.* 2017;28:3421–3430.
10. Smith EB, Parvizi J, Purtill JJ. Delayed surgery for patients with femur and hip fractures-risk of deep venous thrombosis. *J Trauma.* 2011;70: E113–E116.
11. Shin WC, Woo SH, Lee SJ, et al. Preoperative prevalence of and risk factors for venous thromboembolism in patients with a hip fracture: an indirect multidetector CT venography study. *J Bone Joint Surg Am.* 2016;98:2089–2095.
12. Xia ZN, Xiao K, Zhu W, et al. Risk assessment and management of preoperative venous thromboembolism following femoral neck fracture. *J Orthop Surg Res.* 2018;13:291.
13. Shin WC, Lee SM, Suh KT. Recent Updates in the diagnosis and prevention of venous thromboembolisms in patients with a hip fracture. *Hip Pelvis.* 2017;29:159–167.
14. National Institute for Health and Clinical Excellence. *Venous Thromboembolism: Reducing the Risk of Venous Thromboembolism (Deep Vein Thrombosis and Pulmonary Embolism) in Patients Admitted to Hospital. Clinical Guideline 92 [Internet]*. London, United Kingdom: National Institute for Health and Clinical Excellence; 2015. Available at: https://pubmed.ncbi.nlm.nih.gov/23346611/. Accessed February 23, 2020.
15. Scottish Intercollegiate Guidelines Network. *Management of Hip Fracture in Older People: A National Clinical Guideline [Internet]*. Edinburgh, United Kingdom: Scottish Intercollegiate Guidelines Network; 2009. Available at: https://pdf4pro.com/view/part-of-nhs-quality-improvement-scotland-67a27.html. Accessed February 13, 2020.
16. 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:e278S–e325S.
17. Fixation using Alternative Implants for the Treatment of Hip fractures (FAITH) Investigators. Fracture fixation in the operative management of hip fractures (FAITH): an international, multicentre, randomised controlled trial. *Lancet.* 2017;389:1519–1527.
18. HEALTH Investigators. Total hip arthroplasty or hemiarthroplasty for hip fracture. *N Engl J Med.* 2019;381:2199–2208.
19. Nam JH, Kim DH, Yoo JH, et al. Does preoperative mechanical prophylaxis have additional benefits in preventing postoperative venous thromboembolism in elderly patients with hip fracture?—retrospective case-control study. *PLoS One.* 2017;12:e0187337.
20. Hefley FG Jr, Nelson CL, Puskarich-May CL. Effect of delayed admission to the hospital on the preoperative prevalence of deep-vein thrombosis associated with fractures about the hip. *J Bone Joint Surg Am.* 1996;78:581–583.
21. Bhandari M, Devereaux PJ, Swiontkowski MF, et al. Internal fixation compared with arthroplasty for displaced fractures of the femoral neck. A meta-analysis. *J Bone Joint Surg Am.* 2003;85-A:1673–1681.