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Original Research

Prescription of Pharmacologic Venous Thromboembolism Prophylaxis Upon Hospital Discharge After Surgery for Lower Limb Fracture—A 3-Center Study in the North-West of England

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ABSTRACT

Purpose: The risk of venous thromboembolism (VTE) after surgery for lower limb trauma may be reduced with pharmacologic prophylaxis upon hospital admission and hospital discharge. To determine the rate and duration of prescription of VTE pharmacologic prophylaxis upon hospital discharge in patients who have surgery for a lower limb fracture.

Methods: Retrospective analysis of patients who had surgery for a lower limb fracture at 3 National Health Trust hospitals in the North-West of England.

Findings: Data from 127 patients were collected. All patients were prescribed pharmacologic VTE prophylaxis upon hospital admission, and 125 (98%) upon discharge, with 91.3% of patients discharged with low-molecular weight heparin. There was substantial variation in the duration of pharmacologic VTE prescription upon hospital discharge, with a median duration of 42 days (interquartile range, 28–42 days; range, 1–84 days). In our cohort, 7 (5.5%) of patients were prescribed VTE prophylaxis for less than 14 days, and 30(23.6%) prescribed for less than 35 days.

Implications: This study reported that pharmacologic prophylaxis for VTE was prescribed for almost all patients upon hospital discharge. However, there was substantial variation in the duration of the prescribed prophylaxis upon hospital discharge, with almost a quarter of patients prescribed less than 35 days. National level prescription guidance for VTE prophylaxis upon hospital discharge may improve consistency within and between centers.

Introduction

Venous thromboembolism (VTE) is a major cause of morbidity and mortality with an annual global incidence of approximately 10 million; more than half of these episodes are triggered by hospital admission, including surgery.[1,2]

The risk of developing life-threatening VTE appears to be higher after orthopedic surgery compared with other types of surgery. In the absence of VTE prophylaxis, the reported overall incidence of deep vein thrombosis (DVT) is in the range of 15% to 40% in general surgical procedures but it is reported as high as 40% to 60% after trauma or orthopedic surgery.[3–5] This is possibly due to a marked reduction in mobility, which commonly follows orthopedic surgery. This is especially true after lower limb surgery when patients may be unable to weight bear on the operated leg.

Venous thromboembolism prophylaxis in orthopedic patients is used to reduce the risk of lower limb morbidity and life-threatening thromboembolic episodes. There is strong evidence for their efficacy in or-

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thopedic patients with 1 study showing more than a 75% reduction in relative risk compared with placebo.[6,7] The National Institute for Health and Care Excellence (NICE) in the United Kingdom recommends screening all surgical patients admitted in hospital for VTE risk and considering pharmacologic prophylaxis with low-molecular-weight heparin (LMWH) or fondaparinux in orthopedic patients over 18 years of age.[8]

Although guidelines are clear for VTE assessment and prevention upon hospital admission, there is less clarity for VTE assessment and prophylaxis at the time of hospital discharge. This may be important as upon discharge some patients may have gained additional VTE risk factors that were not present on admission, such as recent surgery.

As there are no standardized guidelines for VTE assessment and prescription of prophylaxis upon hospital discharge we hypothesized that there would be a wide variation in practice. Our study aim was to assess current practice at 3 UK National Health Service (NHS) orthopedic centers. Understanding this practice is the first step to identify areas that may be improved to enhance patient care.

Patients and Methods

Study Population

Consecutive patients admitted between 2019 and 2021 with isolated lower limb fractures in 3 NHS Hospital Trusts in the North-West of England were included in this study. Exclusion criteria were:

1. Age 18 years or below
2. Admitted on anticoagulant (including direct oral anticoagulants [DOACs] or vitamin K antagonists); patients on antiplatelets were not excluded
3. Nonsurgical management for the lower limb fracture
4. Evidence of thromboembolism (DVTs or pulmonary embolisms [PEs]) on admission or during hospital stay
5. Multiple trauma (defined as having more than 1 fracture and/or other concurrent system injury)
6. Neck of Femur fracture
7. Transfer to tertiary center during admission
8. Known contraindication for pharmacologic VTE prophylaxis at hospital discharge

VTE Guidance

In all 3 centers, protocols outlined the need for VTE risk assessment upon hospital admission and prescription of pharmacologic prophylaxis. However, there was no specific requirement for VTE assessment upon hospital discharge. In 1 center, there was guidance for lower limb fractures to continue VTE prophylaxis until mobility no further significantly reduced, while in another center there was guidance to consider stopping thromboprophylaxis if lower limb immobilization continues beyond 42 days. In the third center guidance stated to continue VTE prophylaxis in those cases who immobilization of the lower limb after orthopedic surgery to the lower limb until normal mobility returns or until removal of the plaster. It was also advised to consider discontinuing VTE prophylaxis if immobilization exceeded 42 days. In the third center, guidance also stated that in those with fractures of the lower limb treated with a plaster to prescribe enoxaparin until further review or clinic attendance.

Data Collection

Patients were identified from ward books and hospital databases. Information was extracted from the electronic patient records using a predesigned standardized data collection form. Data collection included patient demographic characteristics (age, sex, and date of admission), reason for admission, nature of surgical intervention, discharge information including type and duration of any VTE prophylaxis, and complications after discharge.

Study Governance

The study had approval of the Research and Development department of one of the centers and the Audit department of 2 of the centers. Data collected were analyzed in an anonymous way. Ethics committee approval was not required.

Statistical Analysis

Descriptive statistics were used to describe demographic characteristics. Categorical variables are presented as frequencies and percentages. Continuous data are presented as mean, median, ranges, and interquartile ranges (IQRs).

Results

Two hundred four consecutive patients admitted with isolated lower limb fractures in 3 NHS Hospital Trusts in the North-West of England were evaluated. In 1 hospital, only ankle fractures were included because of logistical reasons in identifying all lower limb fracture patients. From 204 patients, 127 were included in the final analysis after application of the exclusion criteria (53 did not have surgery, 4 were <18 years old, 9 were admitted on a DOAC or warfarin, 7 because of inadequate information collected, 2 died while in hospital, 1 patient had an upper gastrointestinal bleed, and 1 patient was transferred to a limb reconstruction center for further care) (Figure 1).

Patient Demographic Characteristics

The median age of the 127 participants analyzed was 49 years (IQR, 32–68 years; mean, 50.3 years; range, 18–88 years). There were 74 females and 53 male patients. All patients were admitted for a lower limb fracture (Table 1) and treated surgically. There were 3 periprosthetic fractures, 2 femoral and 1 tibial.

VTE Prophylaxis

Upon hospital admission, all 127 (100%) patients were prescribed pharmacologic VTE prophylaxis with LMWH, either dalteparin or enoxaparin. In our cohort, 125 patients (98%) were discharged from hospital

Table 1
Patient demographic characteristics.

Patient Demographic Characteristic	Median (IQR)	Mean (Range)
Gender, n		
Female	74	
Male	53	
Age (y)	49 (32–68)	50.3 (18–88)
Location of the Fracture	**Number of Patients (%)**	**Description**
Femur	7 (5.5%)	2 periprosthetic
Tibia	30 (23.6%)	3 tibial plateau and 1 periprosthetic
Fibula	4 (3.1%)	
Patella	4 (3.1%)	
Ankle	77 (60.6%)	
Foot	5 (3.9%)	
Details of Surgical Management	**Number of Patients (%)**	
Open reduction and internal fixation	122 (96%)	
Closed reduction and internal fixation	1 (0.79%)	
Closed reduction and external fixation	2 (1.6%)	
Manipulation under anesthesia ± plaster/backslab application	2 (1.6%)	

IQR = interquartile range

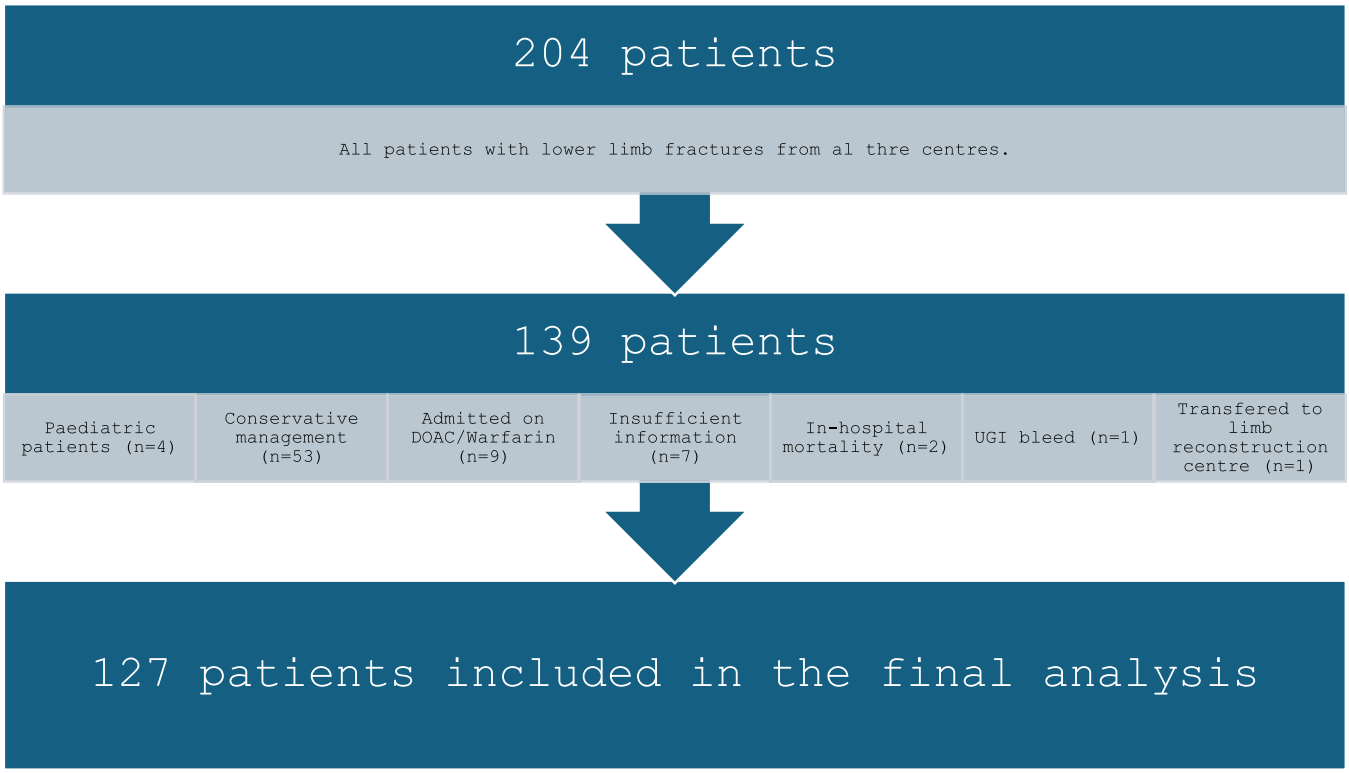

Figure 1. Flowchart showing study participants. DOAC = direct oral anticoagulant; UGI = upper gastrointestinal.

Table 2
Distribution of the type of pharmacologic VTE prophylaxis prescribed upon hospital discharge.

Pharmacologic VTE Prophylaxis at Hospital Discharge	Number of Patients (%)
LMWH	116 (91.3%) a. Dalteparin (n = 59) b. Enoxaparin (n = 39) c. Unspecified (n = 18)
Rivaroxaban	8 (6.3%)
Aspirin	1 (0.78%)
Nil	2 (2%)

LMWH = low-molecular-weight heparin; VTE = venous thromboembolism.

Table 3
Number of patients based on duration of VTE prophylaxis and fracture location.

Duration of VTE Prophylaxis on Discharge	Total Number of Patients (%) by Fracture Location			
	Ankle	Tibia	Foot	Other
Not prescribed	0	0	0	2 (1.6%)
<35 d	19 (14.8%)	11 (8.6%)	0	7 (5.5%)
>35 d	58 (45.3%)	19 (14.8%)	5 (3.9%)	6 (4.7%)

VTE = venous thromboembolism.

Table 4
Duration of VTE prophylaxis upon discharge based on NHS center.

NHS Center Examined	Mean (d) VTE Length on Discharge (Range)	Median (d) VTE Length on Discharge (IQR)
Center 1	33 (1–55)	42 (26–42)
Center 2	40 (12–42)	42 (42–42)
Center 3	36 (14–84)	42 (28–42)

IQR = interquartile range; VTE = venous thromboembolism; NHS = National Health Service.

Table 5
Complications/substantial events during follow-up period.

Complication/Substantial Event	Number of Patients (%)
DVT confirmed with Doppler US	1 (0.78%)
Wound healing problems	1 (0.78%)
Wound infection requiring hospital admission	3 (2.4%)
Removal of fixation device	5 (3.9%)
Ulceration over the Achilles tendon	1 (0.78%)
Complex regional pain syndrome	1 (0.78%)
Death due to a cause unrelated to VTE	1 (0.78%)
Allergic reaction to dalteparin	2 (1.6%) 1—switched to enoxaparin 1—prophylaxis discontinued in clinic

DVT = deep vein thrombosis; US = ultrasound; VTE = venous thromboembolism.

with pharmacologic VTE prophylaxis, mainly LMWH (Table 2). Two patients (2%) had no pharmacologic prophylaxis prescribed at discharge with no obvious justification as determined by review of their medical records. Both had an open reduction and internal fixation (ORIF) for a femoral fracture in the same center.

The median duration of prescribed pharmacologic prophylaxis upon discharge was 42 days (IQR, 28–42 days; mean, 35.6 days; range, 1–84 days). In the cohort examined, 7 (5.5%) patients had VTE prophylaxis prescribed for <14 days, 30 (23.6%) for less than 35 days, and 88 (69.2%) for more than 35 days (Tables 3 and 4, Figure 2 summarize the duration of VTE prophylaxis upon hospital admission and discharge).

Follow-up Complications

Several complications/substantial events occurred within 6 months of follow-up (Table 5). No bleeding adverse effects were identified. One patient developed an ultrasound-confirmed DVT that was diagnosed on day 43 after discharge. The patient had been discharged with 42 days of enoxaparin after an ORIF of an ankle fracture.

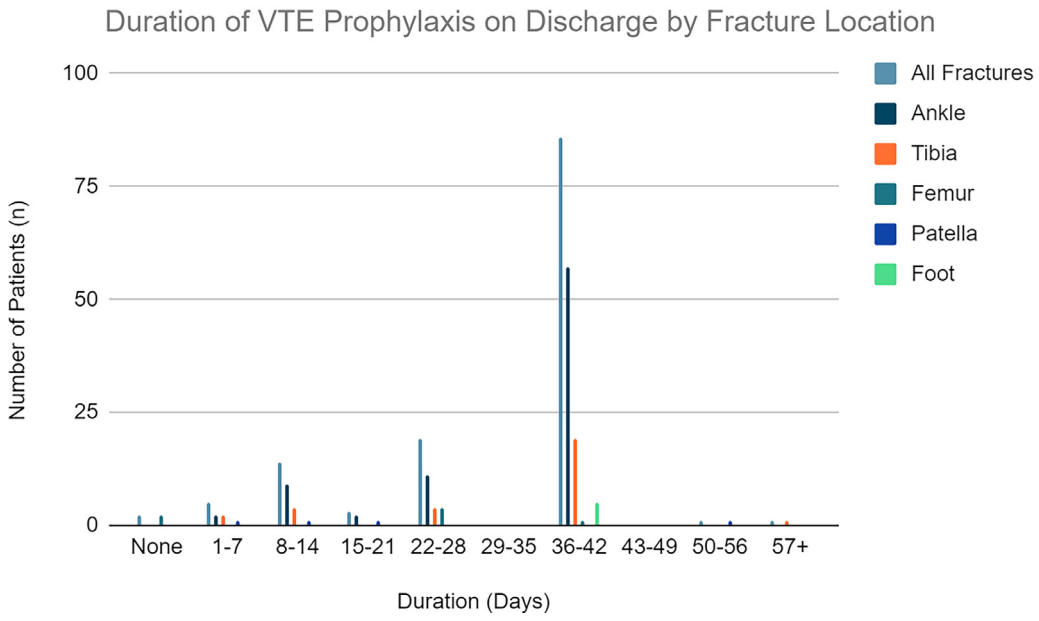

Figure 2. Duration of venous thromboembolism (VTE) prophylaxis on discharge—overall and by fracture location.

Discussion

Before our study we hypothesized that in the absence of clear guidelines for the prescription of VTE prophylaxis upon hospital discharge there may be inconsistency of practice and our study findings prove this hypothesis. Our data demonstrate that most patients who underwent surgery for a lower limb fracture were prescribed pharmacologic VTE prophylaxis upon hospital discharge but there was substantial variation in the duration of this prophylaxis both within and between centers. We noted that upon hospital discharge 2 patients received no VTE prophylaxis at all, almost a quarter of patients (23.6%) were prescribed less than 35 days of VTE prophylaxis, and 5.5% less than 14 days. By contrast, all patients in our cohort were assessed for risk and prescribed pharmacologic VTE prophylaxis upon hospital admission, which suggests that all were considered at risk of VTE and had no contraindications to anticoagulation.

One previous study[9] characterized the timing of DVT and PE after ORIF of closed ankle fractures in a cohort of 17,318 patients. They reported that the median day of diagnosis for DVT was 17 days (IQR, 10–22 days; middle 80%, 3–27 days) and for PE was 10 days (IQR, 3–21 days; middle 80%, 0–27 days). Another similar study[10] looked at the timing of VTE in 298,886 patients with isolated foot or ankle fractures. In that cohort 1661 (0.56%) had VTE in the 90 days after fracture with 27.3% occurring in the first 7 days, 49.8% in the first 21 days, but with approximately 50% occurring later than 21 days, with the rate of occurrence increasing for the duration of the study follow-up. A relationship between missed prophylactic enoxaparin doses and an increase in VTE rates in trauma patients has also been described.[11]

Hence, as there is evidence that a substantial proportion of VTE occurs at a late stage after a lower limb fracture, rather than in the immediate postfracture period, prolonged VTE prophylaxis seems logical for this patient population. In keeping with this evidence, NICE guidelines emphasize the significance of adequate VTE prophylaxis and advise pharmacologic prophylaxis in lower limb fractures up to 42 days.[8] Considering this guidance and the available evidence it seems likely the patients in our study who received either no VTE prophylaxis or prophylaxis for a short duration were undertreated.

We recognize that our study was designed with the primary outcome goal of determining current practice and heterogenicity between hospitals, not to determine the reasons for any practice variations. Our data show that for the prescription of VTE prophylaxis upon discharge there was inconsistency of practice between 3 separate hospitals. One possibility is that each patient in the study was in fact appropriately prescribed VTE prophylaxis and the differences we found are a manifestation of different patient groups at each center. Given the similar patient demographic characteristics at each hospital this seems unlikely, and furthermore, we believe our findings would more likely than not be replicated across other similar UK hospitals, but also across hospitals at an international level. Our findings are in line with those of the UK Foot and Ankle Thrombo-Embolism Audit,[12,13] which looked at the variation in anticoagulation prescribed in foot and ankle surgery in the United Kingdom, both elective and trauma. In that multicenter study, 11,363 patients were available for analysis and it was shown that 11 chemical anticoagulants were used, with the most common chemical anticoagulation prescribed being LMWH. Of the cohort's patients, 32.71% received no chemical prophylaxis. There was also substantial variation in the duration of prophylaxis, which for LMWH was median 6 weeks (mean, 4.82 weeks; 95% CI, 4.77–4.87). Ninety-nine VTE cases were recorded (incidence, 0.87%), with an associated mortality of 0.03%. Higher American Society of Anesthesiologists grade and the type of foot and ankle procedure performed were the strongest predictors for VTE. Along similar lines, in a clinical vignette survey using hypothetical orthopedic trauma patients, O'Hara et al[14] assessed the VTE prophylaxis prescription patterns for patients with orthopedic trauma of 287 surgeons and advanced practice providers across the United States. The median VTE prophylaxis duration prescribed at discharge was 30 days for both enoxaparin (IQR, 28–20 days) and aspirin (IQR, 28–42 days).

To fully understand the influence of these factors on the prescription of VTE prophylaxis upon hospital discharge further studies are needed. However, we speculate that the reasons for this are likely to be multifactorial but may include:

- Lack of standardized VTE risk assessment and prescription protocols specific to the time of hospital discharge. In the absence of such guidelines, training, experience, local custom, and practice may influence decisions about VTE prophylaxis.
- Difficulty predicting the progress of mobilization after discharge and therefore the need of VTE prophylaxis. This may be compounded by the prescription of a short duration of VTE prophylaxis in the expectation of a further assessment in a follow-up clinic, which may then be overlooked.

- Hospital discharge summaries and prescription are commonly performed by less experienced doctors, or by out of hours on-call duty doctors, and sometimes by nonmedical staff. These staff may not be fully aware of the postsurgery immobilization protocols or likely mobilization progress associated with various fractures.

Given the reported rates of VTE after lower limb trauma and surgery adequate prophylaxis is important. The wide variation of prescribing patterns within and between centers, which were located only a few miles apart, highlights the need for further guidance and a VTE risk assessment upon discharge. One consideration may be to discharge patients with the NICE recommended duration of prophylaxis (of 42 days) and advise them to consider stopping when they return to normal mobility. Prescription of an adequate duration of VTE prophylaxis may not influence patient related factors such as compliance but will be a positive step forward.[15] It is indeed of note that the 1 patient in our study who developed DVT was diagnosed on day 43 after being discharged with 42 days of VTE prophylaxis. Hence, VTE prophylaxis does not aim to abolish, but to reduce the risk of VTE, which is in line with previous findings.[16] Furthermore, guidance as to the type of prophylaxis will be useful given the plethora of agents that may be used, including unfractionated heparin, LMWH, antiplatelet agents such as aspirin, vitamin K antagonists such as warfarin, and DOACs.[16] In addition, although LMWH is commonly used, there is evidence that different LMWH agents may vary in their pharmacologic properties both with regards to efficacy but also side effects.[17]

We realize that our study has limitations. These include the retrospective collection of data from medical records, with the inherent limitations that retrospective studies confer such as reliance on documentation and nonstandardized way of documentation. In addition there was variation of sample size and exact patient diagnosis between different centers. Furthermore, the overall sample size examined was small with only 127 patients included in the final analysis. Nevertheless, we feel that the inclusion of 3 centers make our results reliable and noticeable.

Conclusions

Venous thromboembolism prophylaxis is now considered an integral part of improving long term outcomes in patients with lower limb trauma. Our study suggests poor consistency of VTE prophylaxis prescription upon hospital discharge for these patients. National level prescription guidance for VTE prophylaxis upon hospital discharge may improve consistency within and between centers.

Declaration of competing interest

None.

CRediT authorship contribution statement

Fatima Kayali: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Hritik Nautiyal:** Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Jonathan Topping:** Writing – review & editing, Writing – original draft, Data curation. **Chea Tze Ong:** Writing – review & editing, Data curation. **Emadeldin M. Ahmed:** Writing – review & editing, Data curation. **Martin Sharrock:** Writing – review & editing, Supervision, Data curation. **Jenny Oakley:** Writing – review & editing, Resources, Methodology. **Makaram Srinivasan:** Writing – review & editing, Supervision. **Kuntal Patel:** Writing – review & editing, Supervision. **Amit Shah:** Writing – review & editing. **Paul M. Sutton:** Writing – review & editing, Writing – original draft. **Charalambos P. Charalambous:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

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