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The incidence of symptomatic venous thromboembolism following hip fractures with or without surgery in Taiwan☆

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ABSTRACT

Background: Information on the incidence of venous thromboembolism (VTE) following hip fractures in Asia is rare. This study will investigate the epidemiology of symptomatic VTE in Taiwanese patients experiencing hip fractures.

Methods and results: We used Taiwan's National Health Insurance Research Database to retrospectively identify patients (≧45 years) who experienced hip fractures from 1998 to 2007 and were followed up for 3 months after the discharge. Logistic regression analysis determined the independent risk factors of symptomatic VTE after the fractures. We identified 134,034 patients (mean age: 76.2 ± 9.7 years; female: 57.8%) who experienced hip fractures, 83.2% of whom underwent hip surgery. The overall pharmacological thromboprophylaxis rate was 2.7%. The mean length of stay was 11.3 ± 7.9 days. The 3-month cumulative incidence of symptomatic VTE was 77 events per 10,000 persons. Multivariate analysis showed that previous DVT, previous PE, varicose veins, cancer, heart failure, renal insufficiency, and older age were independent risk factors of developing VTE.

Conclusions: The incidence of symptomatic VTE after hip fractures is low in Taiwan. Patients rarely received pharmacological thromboprophylaxis following hip fractures. Universal thromboprophylaxis for patients experiencing hip fractures was not necessary in Taiwan, but it should be considered in high-risk populations.

1. Introduction

Overall, hip-fracture incidence significantly increased by 30%, from 49.6 to 64.4 per 10,000 per year from 1996 to 2002 in Taiwan [1]. Because co-morbid medical problems are common in this population, hip fracture easily causes severe morbidity, including heart failure (5%), acute myocardial infarction (1%), and venous thromboembolism (2%) [2]. Additionally, the one-year mortality rate in this population has been reported to be high (10 to 30%) in different countries [3–7]. Major orthopedic surgery, including knee and hip replacement, has been identified as a uniformly high-risk event for VTE [8–9]. The incidence of deep vein thrombosis (DVT) was about 27%, and fatal pulmonary embolism oscillated between 1.4% and 7.5% of patients within 3 months of hip fracture surgery [10]. Thromboembolism prophylaxis reduces the rate of DVT by approximately 60% [11]. Therefore, routine pharmacological thromboprophylaxis is recommended in hip fracture surgery according to the American College of Chest Physicians (ACCP) guideline in 2012 [12]. On the other hand, the American Association of Orthopedic Surgeons (AAOS) suggests the use of pharmacologic agents and/or mechanical compressive devices for the prevention of VTE in patients undergoing elective hip or knee arthroplasty, and who are not at elevated risk beyond that of the surgery itself for VTE or bleeding [13]. For management of hip fractures in the elderly, AAOS recommends that VTE prophylaxis should be used given the significant established risk factors for VTE present in this patient population, including age, presence of hip fracture, major surgery, delays to surgery, and the potential serious consequences of failure to provide prophylaxis in the hip-fracture population [14]. Even though the ACCP guidelines are widely adopted in Western countries and worldwide, pharmacological thromboprophylaxis in Asia is not routine, as the incidence of VTE is generally thought to be low and wound bleeding is a major concern. The aim of our study was to investigate the percentage of pharmacological thromboprophylaxis use and the incidence of symptomatic VTE of patients within 3 months of experiencing hip fractures. Additionally, the secondary objective was to determine risk factors for VTE events among these populations.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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2. Methods

2.1. Database

This study used claims data from the 1997–2007 National Health Insurance Research Database (NHIRD) provided by the National Health Research Institute in Taiwan. The NHIRD includes data on every inpatient admission covered under the NHI program, which has enrolled nearly 99.99% of the Taiwanese population throughout the nation. The databases used in this study included all inpatient and outpatient medical claims between Jan 1, 1997 and Dec 31, 2007. From the databases, we retrieved for each patient the disease diagnosis, prescription drugs, procedures, and surgery incurred during a hospitalization or at an outpatient visit. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

2.2. Study design

For calculating the percentage of pharmacological thromboprophylaxis in patients experiencing hip fractures and the 3-month cumulative incidences of VTE, we identified from the above-mentioned NHIRD 134,034 adult patients who were hospitalized for hip fracture between Jan 1, 1998 and Sep. 30, 2007. (Fig. 1) That admission for hip fracture was defined as the index hospitalization. Patients who were ≥45 years of age with the discharge codes of International Classification of Disease-Clinical Modification, ninth revision (ICD-9-CM) 820.x were all included. These patients had been followed for 3 months after the index hospitalization, and data were censored at the date of the VTE event, the date of death, or the end of the follow-up period. The exclusion criteria included (1) patients who stayed in the hospital for longer than 60 days and (2) incomplete electronic medical records. To avoid underestimation of fatal events from pulmonary embolism, patients who were hospitalized and died within 3 days without obvious etiologies were enrolled and regarded as fatal pulmonary embolism possibly related to procedure.

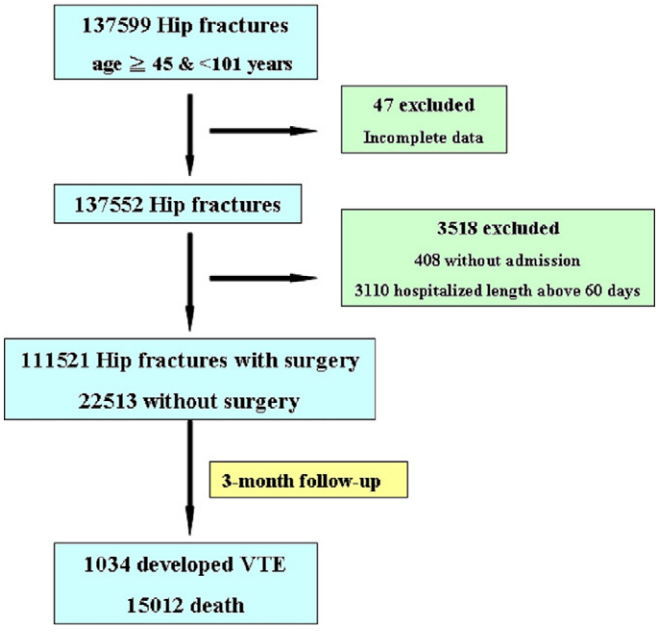

Fig. 1. The flow diagram of the population-based retrospective cohort study.

2.3. Comorbid diseases and potential risk factors of VTE

For each patient, we retrieved the comorbidities for VTE from both the inpatient and outpatient claims databases for one year before and during the index hospitalization. The comorbidities were recorded using ICD-9-CM codes. (Supplement 1) History of VTE was defined as being hospitalized or diagnosed at an outpatient clinic with VTE before the index hospitalization. Chronic lung disease included emphysema, chronic bronchitis, bronchiectasis, other obstructive pulmonary disease, and chronic respiratory failure. For neurological diseases, we only recorded serious illness, including stroke or other central and peripheral nervous disease associated with extremity paresis or paralysis.

2.4. Exposure to drugs

We used prescription records to ascertain the status of drug use. In Taiwan, anticoagulant drugs included warfarin, unfractionated heparin, and low molecular-weight heparin (LMWH). The new oral anticoagulant drugs, such as rivaroxaban and dalbigatran were not available until 2013. Pharmacological thromboprophylaxis was defined as the new administration of any of the anticoagulant drugs during the index hospitalization. In this study, the presence of other drugs of interest, including statins, antiplatelet agents, and analgesics, was recorded only if they were documented within one month preceding the index hospitalization. The antiplatelet agents included aspirin, ticlopidine, and clopidogrel. The analgesic agents included opioids and non-steroidal anti-inflammatory drugs (NSAIDs). Hormone therapy included the use of estrogen and/or progesterone in hormone replacement therapy and oral contraceptives.

2.5. Study outcome

The primary study outcome was the incidence of symptomatic VTE (defined as thrombophlebitis, deep vein thrombosis, or pulmonary embolism). The secondary study outcome was the composite of VTE and overall mortality within the 3-month follow-up. In our study, symptomatic VTE was identified from the inpatient and outpatient claims database by an ICD9-CM code of 451.1×; 451.2; 451.83; 453.1; 453.2; 453.4; 453.8; 453.9; 415.1×. To avoid misdiagnoses, we selected inpatients who met the following criteria: (1) the discharge diagnosis was thrombophlebitis, DVT or PE; (2) the patient must have received a course of subcutaneous or intravenous anticoagulation therapy with unfractionated heparin or surgical thrombectomy during hospitalization and continued oral warfarin therapy after discharge; and (3) the length of stay was at least 3 days, unless the patient died. We also selected outpatients who met the following criteria: (1) the principle diagnosis was DVT or thrombophlebitis and (2) the patient must have received a course of subcutaneous anticoagulation therapy with LMWH and continued oral warfarin therapy. The same criteria were used in previous studies that investigated VTE risk in Taiwan [15–17].

2.6. Statistical analysis

Demographic data were expressed as means (±SD) or percentages. The cumulative incidence of VTE was determined within 3 months of hip fracture between Jan. 1, 1998, and Sep. 30, 2007. Outcomes were categorized as occurring during the hospitalization or after discharge with follow-up admission to an acute-care facility with a principal diagnosis of VTE. The primary outcomes were a principal or secondary diagnosis of VTE within 3 months (91 days) of the day of index hospitalization. We also calculated the cumulative rates of the secondary outcomes (VTE and all-cause mortality) within 3 months after the index hospitalization. For subgroup analysis, we calculated separately the incidence of primary and secondary outcomes following the fracture. The potential risk factors of VTE after the hip fracture were evaluated by COX proportional hazards regression analyses. Univariate analysis was

performed to screen potential variables for inclusion in the final multivariate model. Variables that were significant at the p ≦ 0.1 level in the univariate analysis were included in the multivariate analysis. Variables significant at the $p < 0.05$ level in the Wald chi-square test in the final multivariate analysis were regarded as independent risk factors. We assessed the robustness of our results based on the different lengths of hospital stay (down to 21 days) and repeated all the same analyses, including COX proportional hazards regression analyses, for evaluating the predicting factors of VTE following the fractures. The hazard ratio and associated 95% CI for the various potential risk factors were calculated. We used SAS statistical software (version 9.1; SAS Institute Inc., Cary, NC) for the claims data conversion and analysis.

3. Results

3.1. Baseline characteristics and pharmacological thromboprophylaxis rate

Of the total 134,034 hospitalized patients (≧45 years) experiencing hip fractures between Jan. 1998 and Sep. 2007, the mean age (±SD) was 76.2 (±9.7) years old. The percentage of fractures of the femoral neck was 60.6% and of the trochanter was 39.4%. Among these patients, 77,449 (57.8%) were women and 111,521 (83.2%) received hip surgery. The mean length of hospitalization was 11.3 (±7.9) days. Within one month before surgery, 22,419 (16.7%) patients received antiplatelet agents and 79,068 (59.0%) received non-steroidal anti-inflammatory drugs. The crude thromboprophylaxis rate was 2.7%, including subcutaneous or intravenous anticoagulant therapy (2.68%) and oral warfarin (0.12%). There were significantly higher percentages of co-morbid diseases in patients with new VTE events compared with those without new VTE events. However, we did not observe a significant difference in thromboprophylaxis rate between these two groups. (Table 1).

3.2. Clinical outcomes

During the 3-month follow-up after surgery, the overall cumulative incidence of symptomatic VTE (n = 1034) was 77 events per 10,000 persons, which included 72.3% deep vein thrombosis, 22.3% pulmonary embolism, and 5.4% coexisting deep vein thrombosis and pulmonary embolism. Of these events, 215 (20.8%) happened during the hospitalization while 819 (79.2%) had VTE after discharge. Among patients with new VTE after discharge, most events (n = 748, 91.3%) occurred within 21 days, with a median time of diagnosis of 13.9 days after discharge.

The overall incidence of VTE was 76 events per 10,000 persons in men and 78 events per 10,000 persons in women. In women, the incidence drastically increased from 36 events per 10,000 persons in those younger than 55 years to 80 events per 10,000 persons in those over 75 years. We found a similar trend in men: the incidence increased from 51 events per 10,000 persons in those younger than 55 years to 90 events per 10,000 persons in those over 75 years (Fig. 2). In subgroup analysis, we found that the overall cumulative rate of VTE events within 3 months after surgery was 735 events per 10,000 persons in patients with previous DVT, 622 events per 10,000 persons with previous PE, 397 events per 10,000 persons with varicose veins, 148 events per 10,000 persons with heart failure, and 111 events per 10,000 persons with cancer (Fig. 3). The overall cumulative rate of VTE in other disease-specific populations was 93 events per 10,000 persons with chronic lung diseases, 80 events per 10,000 persons with diabetes mellitus, 107 events per 10,000 persons with coronary heart disease, and 111 events per 10,000 persons with renal insufficiency. The cumulative VTE incidence in patients undergoing hip surgery was lower than those not receiving surgery (74 vs 95 events per 10,000 persons, p = 0.001). The overall cumulative mortality rate was 8.3% (n = 11,125) up to 3 months after surgery. Patients with history of PE (19.6%), cancer (15.2%), heart failure (14.8%), coronary artery disease (11.2%), and varicose veins (10.8%) had higher mortality rates than overall populations of the study. (Fig. 3).

3.3. Predictors for venous thromboembolism

Potential VTE risk factors were prior DVT (0.4%), prior PE (0.1%), malignancy (7.3%), serious neurologic disease (33.2%), heart failure (16.4%), and varicose veins (0.7%). Univariate analysis showed that

Table 1
Overall clinical characteristics of hip fracture patients from Jan. 1998 to Sep. 2007.

Characteristics	Overall N = 134,034	VTE N = 1034	Non-VTE N = 133,000	p value
Mean age (±SD), years	76.2 ± 9.7	76.9 ± 9.0	76.2 ± 9.7	0.016
Female	77,449 (57.8)	604 (58.4)	76,845 (57.8)	0.681
History of DVT	490 (0.4)	36 (3.5)	454 (0.3)	<0.001
History of PE	193 (0.1)	12 (1.2)	181 (0.1)	<0.001
Cancer	9791 (7.3)	109 (10.5)	9682 (7.3)	<0.001
Hypertension	86,293 (64.4)	744 (72.0)	85,549 (64.3)	<0.001
Heart failure	22,034 (16.4)	326 (31.5)	21,708 (16.3)	<0.001
Coronary artery disease	43,239 (32.3)	461 (44.6)	42,778 (32.2)	0.025
Renal insufficiency	26,207 (19.6)	290 (28)	25,917 (19.5)	<0.001
Chronic lung disease	50,467 (37.7)	470 (45.5)	49,997 (37.6)	0.294
Diabetes mellitus	46,265 (34.5)	370 (35.8)	45,895 (34.5)	0.393
Stroke[a]	29,485 (22.0)	243 (23.5)	29,242 (22.0)	0.243
Neurologic disease[b]	44,524 (33.2)	363 (35.1)	44,161(33.2)	0.196
Varicose vein	932 (0.7)	37 (3.6)	895 (0.7)	<0.001
Statin use	2656 (2.0)	34 (2.5)	2622 (2.9)	0.606
Antiplatelet use	22,419 (16.7)	260 (19.4)	22,159 (12.3)	<0.001
NSAID use	79,068 (59.0)	523 (50.6)	78,543 (59.1)	<0.001
Thromboprophylaxis[c]	3665 (2.7)	5 (2.5)	3660 (2.8)	0.575
Fracture types				
Femoral neck	81,257 (60.6)	581 (56.2)	80,676 (60.7)	0.004
Trochanter	52,777 (39.4)	453 (43.8)	52,324 (39.3)	0.004
Hip surgery	111,521 (83.2)	820 (79.3)	110,701 (83.2)	0.001
Length of hospital stay, days	11.3 ± 7.9	12.9 ± 9.5	11.3 ± 7.9	<0.001

Data are presented as number (percentages).
p value compared with VTE and non-VTE groups using Student's t test or χ^2 test.
VTE = venous thromboembolism; DVT = deep vein thrombosis; PE = pulmonary embolism.
[a] Stroke includes ischemic and hemorrhagic stroke.
[b] Neurologic disease means stroke or other central and peripheral nervous disease with associated extremity paresis or paralysis.
[c] Thromboprophylaxis means in-hospital use of unfractionated heparin, low molecular weight heparin, or warfarin.

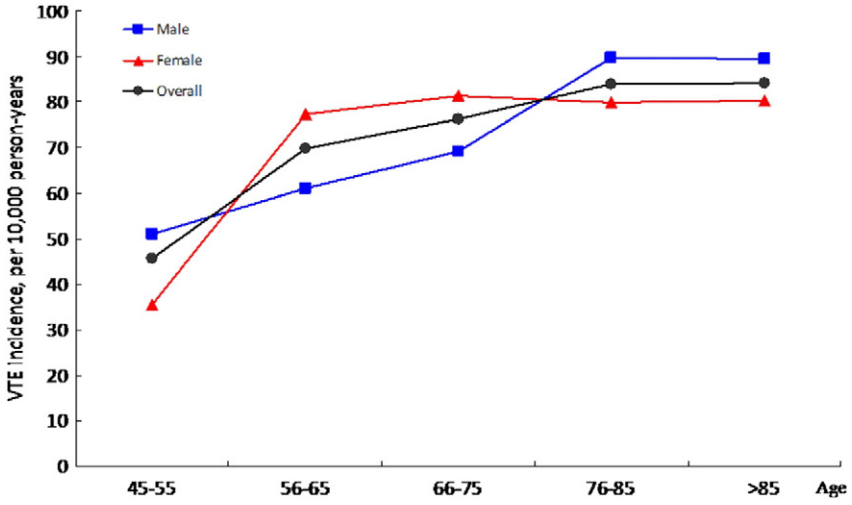

Fig. 2. The incidence of venous thromboembolism among various age and gender groups in Taiwan from 1998 to 2007.

there were significantly higher percentages of underlying diseases, such as history of VTE, cancer, cardiovascular diseases, renal insufficiency, serious neurologic diseases, and varicose veins, in patients with new VTE events than those without VTE events (Table 1). In primary analysis, several baseline characteristics and potential risk factors were compared between the VTE and non-VTE groups by COX proportional hazards regression analyses (Table 2). Although the VTE incidence in patients undergoing hip surgery was lower than in patients who did not undergo surgery, hip surgery was not an independent risk factor of VTE occurrence after using hazards regression analyses. We thought that patients who did not receive surgery had more complex comorbid diseases than those who received surgery. Therefore, lower VTE incidence in patients undergoing surgery may be due to less complex underlying diseases. (Supplement 2) In our study, previous DVT (hazard ratio (HR) 8.62, 95% confidence interval (CI) 5.95–12.66), previous PE (HR 4.59, 95% CI 2.41–8.77), varicose veins (HR 5.01, 95% CI 3.56–6.99) malignant neoplasm (HR 1.42, 95% CI 1.16–1.74), heart failure (HR 1.87, 95% CI 1.62–2.16), renal insufficiency (HR 1.29, 95% CI 1.12–1.49), and older age (HR 1.08, 95% CI 1.02–1.16) were independent risk factors for developing VTE (Table 2).

The percentages of clinical morbidities did not change appreciably when we redefined the length of hospital stay shortening it to 21 days. (Supplement 3) As expected, the results of predictors for fracture-related VTE were virtually unchanged when we performed multivariate logistic regression analysis (Table 2).

4. Discussion

Nowadays, it is almost impossible to conduct a nationwide population-based cohort study to observe the natural course of VTE among hip-fracture patients awaiting surgery with a rather low rate of pharmacological thromboprophylaxis in Western countries because pharmacological thromboprophylaxis would be routinely given in these populations. This study was a 10-year nationwide population-based observational cohort study to estimate the pharmacological thromboprophylaxis rate in patients experiencing hip fractures and the incidence of symptomatic VTE within a 3-month follow-up. The main findings were as follows: (1) the rate of pharmacological thromboprophylaxis was very low (2.7%) in these patients; (2) among the 134,034 patients, the 3-month cumulative incidence of symptomatic VTE following hip fractures was only 77 events per 10,000 persons; (3) previous VTE, malignancy, heart failure, varicose veins, and chronic kidney disease were associated with higher risks of VTE occurrence following hip fractures; (4) most VTE events (79.2%) occurred after discharge, with a median time of 13.9 days between discharge and diagnosis.

VTE is a major public health concern in Western countries. The estimated annual incidence is 71 to 133 cases per 100,000 persons [18–20]. DVT is one of the principal causes of perioperative morbidity and mortality in hip fracture patients. Without thromboembolism prophylaxis, the prevalence of venography-detected proximal DVT rises to 27% of

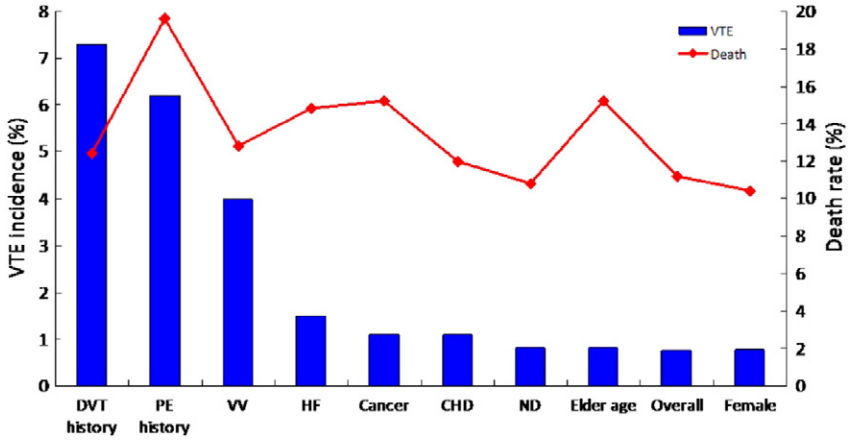

Fig. 3. Cumulative incidences of VTE admission and/or deaths among different patient groups following hip fractures. DVT denotes deep vein thrombosis; PE, pulmonary embolism; HF, heart failure; ND, neurologic disorder with extremity paralysis or paresis; VV, varicose veins; CAD, coronary artery disease.

Table 2
Results of COX proportional hazards regression analyses of potential risk factors of symptomatic venous thromboembolism.[a]

Variables	Primary analysis Hazard ratio (95% CI), p value	Additional analysis[a] Hazard ratio (95% CI), P value
Deep vein thrombosis history	8.62 (5.95–12.66), <0.001	7.83 (5.17–11.85), <0.001
Pulmonary embolism history	4.59 (2.41–8.77), <0.001	4.65 (2.28–9.52), <0.001
Cancer	1.42 (1.16–1.74), 0.001	1.44 (1.16–1.79), 0.001
Varicose veins	5.01 (3.56–6.99), <0.001	4.59 (3.18–6.62), <0.001
Heart failure	1.87 (1.62–2.16), 0.029	1.95 (1.67–2.27), <0.001
Renal insufficiency	1.29 (1.12–1.49), <0.001	1.38 (1.18–1.61), <0.001
Age	1.08 (1.02–1.18), 0.005	1.03 (1.01–1.16), 0.006
[*]Neurologic disease	1.01 (0.88–1.16), 0.892	1.02 (0.87–1.21), 0.875
Hypertension	1.14 (0.99–1.32), 0.072	1.08 (0.92–1.26), 0.340
Hip surgery	0.98 (0.84–1.15), 0.833	1.04 (0.87–1.25), 0.664
Coronary artery disease	1.13 (0.68–1.49), 0.894	1.09 (0.72–1.56), 0.879
Pharmacological VTE prophylaxis	0.81 (0.55–1.21), 0.304	0.85 (0.67–1.23), 0.487

[*] Neurologic disease means stroke or other central and peripheral nervous disease with associated extremity paresis or palalysis.
[a] We repeated COX proportional hazards regression analyses based on the different lengths of hospital stay (down to 21 days).

patients and the incidence of fatal pulmonary embolism oscillates between 1.4% to 7.5% within 3 months of hip-fracture surgery [10]. Thromboembolism prophylaxis reduces the rate of DVT by approximately 60% [11]. The AAOS guidelines for the prevention of VTE in patients undergoing hip or knee surgery conflict with ACCP guidelines [21,22]. Both guidelines accepted that the most important goal of thromboprophylaxis in patients undergoing hip fracture surgery is to prevent PE. The ACCP guidelines included asymptomatic and symptomatic DVT detected by venography as a measure of the efficacy of thromboprophylaxis, whereas the AAOS did not regard DVT as a valid indicator because the link between DVT and PE was unproven. However, these studies were mostly conducted among Caucasian populations. The incidence of VTE in Taiwan and other Asian countries is much lower than in Western countries [15,23–25], even though pharmacological thromboprophylaxis is not yet a routine practice in Asia, even in high-risk surgical situations [16,26–30]. Particularly, our previous nationwide population-based study shows that the crude incidence of VTE is only 15.9 cases per 100,000 persons [15]. In addition, our serial studies found out that the pharmacological thromboprophylaxis rate was 2.2–3.0% and the 3-month cumulative incidence of symptomatic VTE was 0.41–0.46% in patients undergoing major orthopedic surgery [16,17]. In the SMART study [29–30], the pharmacological thromboprophylaxis rate was only 3.6% in patients undergoing major orthopedic surgery. Although the incidence of asymptomatic VTE was 35.6% during the hospitalization, the incidence of symptomatic VTE and sudden death within a one-month follow-up was only 1.5%. We could not obtain the asymptomatic VTE incidence rate in our populations, but the all-cause mortality in our study (8.3%) was at the lower end as compared with previous ones (8–20% at 3 months) [31–33]. Based on the SMART and our study, it is very likely that most asymptomatic VTE events developing after major orthopedic surgery regress spontaneously in Asian patients without pharmacological intervention. Our results support the viewpoint of the AAOS guidelines that the link between DVT and PE is uncertain in these populations.

We observed the time course of developing symptomatic VTE in hip fracture patients. Among patients who developed symptomatic VTE, 20.8% occurred during hospitalization and 79.2% had VTE after discharge. Among patients with new VTE after discharge, most events (91.3%) occurred within 21 days, with a median time of diagnosis of 13.9 days after discharge. Although the incidence of symptomatic VTE was much lower in Taiwan than in Western countries, the time course of developing symptomatic VTE in these populations was very similar. White and colleagues reported that the median time of diagnosis of symptomatic VTE was about 17 days in patients undergoing major hip surgery [34]. These findings suggest that orthopedic surgeons should be aware of patients' signs of VTE within 2–3 weeks after discharge and, in high-risk Taiwanese patients experiencing hip fractures, the use of pharmacological thromboprophylaxis should be extended from the hospital stay to at least 2 weeks after discharge.

Likewise, previous studies showed that prior VTE [35], female gender [34], age over 70 years [19,36], body mass index (BMI) over 25 [37], and longer duration of immobilization [38] are important risk factors for development of symptomatic VTE among patients undergoing major arthroplasty. In the current study, we identified some similar risk factors of VTE following hip fracture surgery, such as prior VTE and older age. We also identified varicose veins, heart failure, cancer, and renal insufficiency as risk factors of VTE. Although we have observed lower risk of VTE occurrence in patients receiving hip surgery than those without hip surgery, we found that the hip surgery itself did not increase the risk of VTE in these populations because patients undergoing surgery were younger and had lower percentages of co-morbidities than those without surgery. The complexity of underlying diseases determined the risk of VTE. The proportion of patients who received pharmacological prophylaxis was only 2.7% in this study. A beneficial effect of pharmacological thromboprophylaxis was not observed. We attributed this neutral effect of pharmacological thromboprophylaxis to the small sample size of patients who received the prevention and the non-selective population without other risk factors. Further randomized controlled study is warranted to examine the effect of pharmacological thromboprophylaxis in Taiwanese hip-fracture patients with other identified VTE risk factors.

Our findings have several clinical implications for Asian populations. First, although the rate of pharmacological thromboprophylaxis was very low in hip fracture patients in Taiwan, symptomatic VTE rarely developed. One prospective Asian study (SMART study) showed that the pharmacological thromboprophylaxis rate was only 3.6% in patients undergoing major orthopedic surgery, but the incidence of VTE and sudden death at a month's follow-up was only 1.5% [29,30]. However, our findings suggest that adequate pharmacological thromboprophylaxis around hip fractures in high-risk populations, especially those with VTE history, may reduce new VTE events. Most VTE events develop within 3 weeks after the discharge; therefore, patients should be educated to become mobile as soon as possible and surgeons should be alert if persistent swelling of the compromised extremity suggests deep vein thrombosis.

There are several limitations in the present investigation. First, the healthcare claims data inherently contains potential disease misclassification bias. However, the auditing mechanism conducted by the Bureau of National Health Insurance would help to minimize the diagnostic uncertainty and misclassification in claims databases. Second, whether the patient received pneumatic compression after the surgery was indeterminate. Third, the true incidence of VTE following hip fractures in Taiwan may be underestimated because some patients with PE may die suddenly without accurate diagnosis and some symptomatic VTE patients may be treated as surgery-related leg edema. To avoid underestimating fatal pulmonary embolism, we also calculated the all-cause mortality within 3 months after the discharge. Given the 3-month mortality rate was 8.3% and similar to previous Western studies, the bias should be low. Finally, surgical procedure time, smoking history, and body mass index were not available in the databases.

In conclusion, the rate of pharmacological thromboprophylaxis is very low in Taiwan, which may be related to the low incidence of symptomatic VTE after hip fractures. Although universal pharmacological thromboprophylaxis is not recommended generally in Taiwan, it should be considered in high-risk populations that include a history of VTE, malignancy, heart failure, varicose veins, and chronic kidney disease.

Authorship

CH Lee initiated and designed the study, prepared the data, conducted the analysis and interpretation, and wrote the first draft of the paper.

LJ Lin contributed to the development of the protocol, design, analysis, and interpretation, and to reviewing the paper. CL Cheng contributed to the design of the study, writing the protocol, interpreting results, and drafting the article. TC Lin undertook the data processing and statistical analysis. YH Kao Yang and CY Yang coordinated the execution of the study, established the strategy of data processing of the claims data, and participated in the manuscript preparation. All authors have approved the final draft.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ctrsc.2015.10.001.

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