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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.

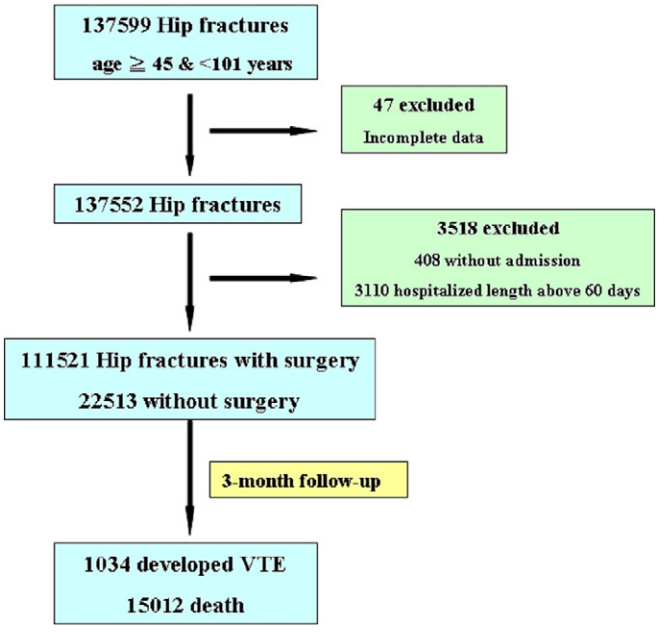

Fig. 1. The flow diagram of the population-based retrospective cohort study.

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