VALUE IN HEALTH REGIONAL ISSUES 6C (2015) 73–79

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Economic Burden of Venous Thromboembolism in Patients Undergoing Major Abdominal Surgery

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ABSTRACT

Background: Venous thromboembolism (VTE) is a serious complication that arises after major abdominal surgery. VTE poses risks of negative outcomes and health care burden. The literature on the cost of VTE in Japanese surgical patients, however, is scarce. **Objective:** This study was conducted to investigate the economic consequences of VTE in Japanese patients with major abdominal surgery, using a hospital claims database. **Methods:** This is a retrospective, matched cohort study. Patients who had a VTE event up to 90 days after their first major abdominal surgery and initiated warfarin or heparin within 1 day of VTE diagnosis with continued treatment for more than 4 weeks were matched with controls for surgery type, hospital, and date of surgery ± 6 months in a 1:2 scheme. The primary outcome was 90-day costs associated with major abdominal surgery. The secondary outcomes were 6-month total costs, average length of initial inpatient stay, and cost of initial inpatient stay. **Results:** The 90-day cumulative incidence of VTE was 4.89%. The development of a VTE event in patients undergoing major abdominal surgery resulted in a 1.5-fold increase in the length of hospitalization and a 2.8-fold increase in total costs 90 days after the surgery. Total costs further increased to 3.4-fold at 6 months. Overall, costs incurred in patients with VTE are on average much higher than in patients without VTE throughout 6-month postsurgery. **Conclusions:** The preventive care for VTE using more effective prophylactic treatment is recommended to reduce the economic burden associated with major abdominal surgery.

Keywords: cost, incidence, Japan, major abdominal surgery, VTE.

Introduction

Venous thromboembolism (VTE), defined as either deep vein thrombosis (DVT) or pulmonary embolism (PE), is a serious, common complication that arises after major abdominal surgery. It can occur in patients as a result of prolonged immobilization, impairment of venous function, or impairment of endogenous anticoagulant or fibrinolytic systems [1]. Recurrent VTE and postthrombotic syndrome are both serious sequelae of DVT, and postthrombotic syndrome may further cause persistent symptoms such as chronic edema, dermatitis, ambulatory venous hypertension, and venous ulceration [1,2]. Postthrombotic syndrome is characterized by swelling, pain, and discomfort that are typically most pronounced at the end of the day and are aggravated by standing and walking [3]. PE is a major cause of sudden death after surgery and is manifested by clinical symptoms including dyspnea, chest pain, and syncope [4].

In Japan, the incidence of clinical PE after general surgery was reported to be 0.33% [5]. The mortality rate of patients with PE was 31%, and fatal PE was reported in 0.08% of the surgical population [5]. In addition, evidence suggests that in some patients, the risk of developing VTE may persist for several weeks after a triggering event such as a major abdominal surgery [6].

Although the occurrence of VTE has been reported to be relatively low in the Asian population, its incidence has increased rapidly in the past decade in Japan to 0.02% of total births and 0.08% of total gynecological operations in Japan between 1991 and 2000 [7]. The number of PE cases in obstetrics and gynecology was reported to have increased by 6.5-fold over the past 10 years. One more recent study reported the incidence of postoperative

Conflict of interest: Masato Sakon, Takao Kobayashi, Hiroshi Kobayashi, Toru Shimazui, and Norimasa Seo received advisory board fees from Sanofi K.K. Izuru Miyoshi is an employee of Sanofi K.K.

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2212-1099$36.00 – see front matter

http://dx.doi.org/10.1016/j.vhri.2015.03.017

VTE in patients without chemical thromborphylaxis to be 7.7% in Japan [8]. The incidence of VTE was also observed in 24.3% of the 173 Japanese patients undergoing open major laparotomy [9], which was slightly more but comparable to that of the Caucasian patient population undergoing general or gynecologic surgery (15%–19%) [9–11]. Furthermore, besides the increasingly similar VTE incidence in Asian and Western populations, the literature suggests that patients in both regions may share the same risk factors and VTE disease pattern [12].

VTE brings serious risks of negative outcomes to patients after major surgery [1]. Its recurrence and complications also pose an enormous burden on health care resources for its management [13]. The age-adjusted mortality rate of patients with PE has increased rapidly in the last 50 years in Japan [14]. Risk factors for developing postoperative VTE include age over 40 years, obesity, and stage III/IV cancer [1,12,15], and patients with gynecological cancer undergoing major abdominal surgery demonstrated a 14-fold greater probability of developing PE than did patients with benign disease ($P < 0.001$) [16]. In addition, pharmacologic thromboprophylaxis including low-molecular-weight heparin (LMWH) is associated with an increased incidence of postoperative bleeding complications that can be life-threatening [16].

Warfarin and heparin are used as common prophylaxis treatments to prevent VTE. According to the Japan guideline for prophylaxis and treatment of VTE [17], standard treatment includes unfractionated heparin followed by warfarin for at least 3 months for patients with reversible risk factors. Treatment can also be administered for a longer time when there are no apparent risk factors or when patients have cancer or recurrent VTE [17].

Although several studies have investigated the cost associated with VTE in Western countries, there is a paucity of literature describing the true costs associated with VTE after major abdominal surgery in Japan [18–21]. The present study investigated the incidence and economic consequences of having a VTE event after major abdominal surgery, using electronic hospital medical records.

Methods

Data Source

Data were obtained from the database developed by Medical Data Vision, Inc., an electronic hospital claims database containing hospital medical records from hospitals across Japan. The database contains health insurance claims for about 1 million patients since 2003 [22], providing a large number of patient samples needed to evaluate the incidence of clinical VTE. Anonymous information including patient background, disease, medications, tests, surgeries, and diagnosis procedure combination claims is included in this database [22]. Data were extracted on all major abdominal surgeries in the time frame between January 1, 2003, and October 31, 2009, to ensure an adequate number of events given the expected low incidence.

Study Subjects

A major abdominal surgery was defined as a principal procedure of gastrointestinal surgery, urological surgery, and male and female genitourinary surgery and was identified using receipt codes, which are standardized codes used by the Ministry of Health, Labour and Welfare for electronic claims processing. These codes were associated with 68 *International Classification of Diseases, Ninth Revision, Clinical Modification* codes. Patients who underwent the defined major abdominal surgery comprised the primary population for the analysis. Patients who were aged 18 years or older and had at least 3 months data before the index surgery and 3 to 6 months postsurgery follow-up available were included in the analysis. Patients who underwent more than one of these procedures during the same inpatient admission were excluded.

VTE Cases

The Japanese guideline for prophylaxis and treatment of VTE suggests that unfractionated heparin followed by warfarin may be used for the treatment of VTE and/or prevention of VTE before the surgery or immediately after the surgery, depending on the risk of VTE [17]. Given that prophylactic treatment cannot be prescribed without an associated diagnostic code, utilizing only the administration of unfractionated heparin or warfarin would result in an excessively high false-positive VTE rate. Therefore, candidate VTE cases were grouped into PE (using receipt codes equivalent to the *International Classification of Diseases, Tenth Revision* code I269) or DVT (*International Classification of Diseases, Tenth Revision* code equivalence: I801, I802, and I803). After being identified by PE and DVT codes, patients were considered potential cases if they had a DVT or PE diagnosis code up to 90 days after their first major abdominal surgery. Patients were also required to have no VTE diagnosis from 90 to 7 days before surgery to reduce the risk of patients with prior VTE being included. In addition, those patients who received anticoagulants up to 1 week before surgery or immediately after surgery as prophylaxis may not be true VTE candidates despite the diagnosis code. Thus, it is possible for the identified VTE code to be from prior VTE, and it would not be considered as a potential postoperative VTE case. Therefore, additional criteria that require warfarin or heparin to be initiated within 1 day of VTE diagnosis (to account for a delay in data entry) and patients to receive an anticoagulant for more than 28 days were added. Those patients who used an anticoagulant for 28 days or less were assumed to be on prophylaxis treatment only and were thus excluded. In addition to the criteria mentioned above, patients with an inferior vena cava filter placement (receipt codes equivalent to the *International Classification of Diseases, Ninth Revision, Clinical Modification* code of 38.7) within 128 days of surgery were assumed to have a PE. The very strict criteria of inclusion were intentionally used here to ensure that all included cases were credible VTE cases and to avoid the risk of reporting false incidence or costs resulting from false VTE cases.

Matched Controls

Identified cases were matched to control cases on a 1:2 matching scheme. Cases were matched on the basis of same surgery type, at the same hospital, and a date of surgery ± 6 months. Because of anticipated limited sample sizes, age and sex were not included in the matching process. These criteria were expected to reduce the impact of treatment practice changes that may influence the costs and resource utilization associated with surgery and the treatment of complications, including VTE.

To make sure patients' eligibility for the analysis, it was ensured that the patients' primary point of contact for clinical care was the matched hospital. If the patient attended the hospital only for a surgery and received treatment for postdischarge VTE elsewhere, neither the comprehensive treatment costs for the "episode of care" for the surgical intervention nor the possible postdischarge occurrence of VTE was captured. Therefore, all patients with at least one additional visit during the 6-month period after surgery were included.

Pharmacoeconomic Analyses

The primary outcome measure was 90-day costs associated with major abdominal surgery. Secondary outcomes included total 6-