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Full Length Article

Venous thromboembolism incidence, recurrence, and mortality based on Women's Health Initiative data and Medicare claims

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ABSTRACT

Introduction: Our objective was to compare Medicare claims to physician review and adjudication of medical records for identifying venous thromboembolism (VTE), and to assess VTE incidence, recurrence, and mortality in a large national cohort of post-menopausal women followed up to 19 years.
Materials and methods: We used detailed clinical data from the Women's Health Initiative (WHI) linked to Medicare claims. Agreement between data sources was evaluated among 16,003 women during 1993–2010. A claims-based definition was selected to analyze VTE occurrence and impact among 71,267 women during 1993–2012.
Results: Our VTE definition had 83% sensitivity. Positive predictive value was 69% when all records were included, and 94% after limiting Medicare records to those with a WHI hospitalization adjudicated. Annualized VTE incidence was 4.06/1000 person-years (PY), recurrence was 5.30/100 PY, and both rates varied by race/ethnicity. Post-VTE mortality within 1 year was 22.49% from all causes, including 1.01% from pulmonary embolism, 10.40% from cancer, and 11.08% from other causes. Cancer-related VTE compared to non-cancer VTE had significantly ($p < 0.001$) higher recurrence (9.86/100 PY vs. 4.43/100 PY) and mortality from all causes (45.89% vs. 12.28%), but not from pulmonary embolism (0.40% vs. 1.27%).
Conclusions: Medicare claims compared reasonably well to physician adjudication. The combined data sources provided new insights about VTE burden and prognosis in older women.

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1. Introduction

Venous thromboembolic disease (VTE), consisting of deep venous thrombosis (DVT) and pulmonary embolism (PE), has serious health consequences. A report by the U.S. Surgeon General estimated that annually 350,000–600,000 cases of venous thromboembolism (VTE) are diagnosed, and 100,000 or more deaths may be related to the disease [1]. Short term mortality is elevated in acute VTE patients [2–4] and long-term survival in community cohorts has been decreased in some but not other studies [5–7]. Risk of VTE recurrence is substantial [8,9]. Furthermore, complications such as post-thrombotic syndrome and chronic pulmonary hypertension result in lower quality of life [10–14]. Additionally, the costs of VTE have been recently estimated to be $13.5–27.2 billion per year [15].

Between one quarter and one half of incident VTE cases are idiopathic [9,16], which may be associated with a poorer prognosis than VTE provoked by predisposing conditions [6,17]. However, individuals with predisposing conditions, such as extremity trauma [18–21], cancer [10,22–24], surgery [25–28], prolonged immobilization [29–32], as well as treatments such as hormone therapy [33,34] are at greatest risk for VTE. Early detection and effective therapies have been associated with an improvement in the case-fatality rates for PE. Analysis of the National Hospital Discharge Survey (NHDS) suggests that the case fatality rate for PE has fallen from 14% to 7% between 2000 and 2008 [35].

Despite improved survival, older adults, those with comorbidities, and women are at higher risk for fatal events related to VTE [35]. Also, VTE prevalence increases with age and is higher in women than men

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[36]. Given the high burden of VTE in older women, the Women's Health Initiative (WHI) has the potential to be a powerful resource for understanding the natural history and risk factors of VTE. Other studies of VTE epidemiology have often been geographically limited [9,37,38], lacked sufficient sample size to evaluate certain subgroups, or used only administrative data (e.g., insurance claims) which lack clinical detail [39]. The WHI has the benefit of physician-adjudicated assessment of VTE in two rigorous randomized clinical trials of hormone therapy [33,34], which included over 26,000 women nationally. Also, the WHI includes follow-up of a large observational cohort of post-menopausal women who have been extensively characterized with detailed surveys, physical assessments, and laboratory measures. Furthermore, as most of the study participants are eligible for Medicare, a wealth of administrative data can be linked to the WHI data repository. We hypothesized that Medicare claims data would identify VTE with sufficient accuracy to be useful for longitudinal outcome ascertainment in WHI participants, and that the combined data sources would provide new insights about VTE in older women. To address this, we evaluated the agreement between Medicare claims data and physician-adjudicated VTE, and characterized the occurrence and outcome of VTE in post-menopausal women in the WHI.

2. Methods

2.1. Data sources

From 1993 to 1998, the WHI enrolled over 160,000 postmenopausal women in the United States between 50 and 79 years of age into four clinical trials or an observational study and then followed these participants for predefined incident disease events, including VTE. WHI participant data were previously linked to Medicare enrollment data from the U.S. Centers for Medicare & Medicaid Services (CMS). Medicare is the federal health insurance program for elderly persons age 65 years and older, and younger persons with disabilities or end stage renal disease. We included WHI participants who were enrolled in fee-for-service Medicare Parts A and B (i.e., not in a Medicare managed care plan) at the time of their WHI baseline evaluation; thus the included cohort was predominantly age 65 years and older. Women who did not meet these criteria at the time of WHI enrollment, but subsequently met these criteria when they first enrolled in Medicare (e.g., aged in), were also counted beginning at that time. Thus, the included period was the overlapping period when a woman was enrolled in both WHI and Medicare.

Our analysis had two stages. In the first stage, we aimed to identify a useful coding algorithm for ascertaining VTE in Medicare claims data by comparison with WHI data as the reference. The WHI subset used for this was the cohort of women who participated in the Hormone Trials because VTE was systematically adjudicated only in this group. We randomly split this cohort and used half as a training set to evaluate a number of possible coding algorithms, and the other half as a test set to validate performance of a selected algorithm. In the second stage, we used the selected coding algorithm to define VTE, in order to examine the epidemiology of this condition among the remainder of the WHI cohort (the Observational Study [40] and Dietary Modification Trial [41] participants who were not also enrolled in the Hormone Trials).

2.2. Outcome ascertainment and definitions

In the WHI, annual or semi-annual survey questionnaires requested participants to report all hospitalizations, including DVT and PE. These reports triggered a centralized process of medical record review by physician adjudicators. At study inception, DVT and PE events were ascertained only from hospital medical records. Subsequently, outpatient reports of DVT were also adjudicated. The first self-report of outpatient DVT was captured in 2001. WHI included only lower extremity, pelvis, or inferior vena cava DVT and PE as adjudicated outcomes. The diagnosis of DVT was based on having the diagnosis listed on the hospital discharge summary and/or positive findings on a diagnostic test (venogram, impedance plethysmography, isotope scan, Doppler duplex, ultrasound, or other non-invasive test), while a diagnosis of PE was based on positive results of any one or combination of 1) hospital discharge summary, 2) high probability ventilation-perfusion scan, 3) pulmonary angiogram, 4) CT angiogram or spiral CT, 5) diagnosis of DVT with signs/symptoms suggestive of PE, or 6) other documentation (e.g., autopsy). If a participant had died or was unable to respond, a proxy report of hospitalizations from a pre-identified contact was requested. Death certificates, autopsy reports, and linkage with data from the National Death Index were used in addition to available medical records to adjudicate the cause of death.

For Medicare data, hospital claims with a discharge diagnosis code for a VTE in any position (one principal and up to nine secondary diagnosis codes may be recorded) were identified in the Medicare Provider Analysis and Review (MedPAR) files. We used International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) discharge diagnosis codes to define PE (415.11, 415.19) and DVT (453.40, 453.41, 453.42, 453.8). To define an incident VTE event, we used the first occurrence of any of these codes. This set of codes, which we defined as algorithm Z1, was based on a modification from a published study [42] and our first stage analysis. Other coding algorithms (described in Appendix A, available online) were evaluated including some that incorporated data from the Medicare carrier file (e.g., physician claims) and institutional outpatient file.

2.3. Agreement analysis

In the first stage analysis, which used data from 1993 to 2010, we compared agreement between WHI and Medicare data for VTE using a person-based analysis. A total of 16,003 women were included, randomly split into training ($n = 8001$) and test ($n = 8002$) data sets. A participant was counted as having VTE in both WHI and Medicare data if she had VTE in the respective data source anytime during the overlapping period of WHI and Medicare enrollment. We defined WHI adjudicated outcomes as the reference standard and calculated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of VTE diagnoses within Medicare data. We also assessed agreement using a kappa statistic and evaluated reasons for disagreement.

To better evaluate the performance of the Medicare data in comparison to adjudicated medical records, we performed additional analyses that excluded events that were not informative with respect to the Medicare data (e.g., no medical record was available to evaluate whether the Medicare event was a true or false event), as done in other WHI and Medicare data comparisons [43–45].

We evaluated a number of coding algorithms in the training data set; algorithms Z1–Z6 are described in Appendix A (available online). The coding algorithm selected for further use based on the best performance and implementation characteristics (algorithm Z1) was then evaluated in the test data set.

2.4. Incidence, recurrence and mortality

In the second stage analysis, which used data from 1993 to 2012, we used the selected Medicare coding algorithm (Z1) to define VTE, and evaluated incidence, recurrence and mortality for VTE among 71,267 other participants in the WHI cohort who met the Medicare criteria. Person-time analysis was performed with WHI participants contributing time once they were enrolled in fee-for-service Medicare Parts A and B. Person-time accrued until a participant had a VTE, died, no longer met the Medicare inclusion criteria, chose not to participate in either of two WHI extension studies, was lost to WHI follow-up, or until December 31, 2012. Incidence was defined as first VTE event (PE or DVT) during the included person-time. Women who at baseline