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Are Myocardial Infarction and Venous Thromboembolism Associated? Population-Based Case-Control and Cohort Studies

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Abstract

Introduction—Because the association of myocardial infarction (MI) and venous thromboembolism (VTE) is uncertain, we tested MI as a VTE risk factor and VTE as a predictor of MI.

Materials and Methods—Using Rochester Epidemiology Project resources, we identified all Olmsted County, MN residents with objectively-diagnosed incident VTE over the 13-year period, 1988–2000 (n=1311), one to two resident controls per VTE case (n=1511), and all residents with incident MI over the 31-year period, 1979–2010. For VTE cases and controls, we reviewed their complete medical records in the community for VTE and MI risk factors. Using conditional logistic regression we tested MI as a potential VTE risk factor, both unadjusted and after adjusting for VTE risk factors. We also followed VTE cases and controls without prior MI forward in time for incident MI through 12/31/2010, and using Cox proportional hazards modeling, tested VTE as a predictor of MI, both unadjusted and after adjusting for MI risk factors.

Results—The number (%) of MI prior to VTE among cases and controls were 75 (5.7) and 51 (3.4), respectively, and the number (%) of MI after VTE among cases and controls were 58 (4.4) and 77 (5.1), respectively. In univariate analyses, MI was significantly associated with VTE but

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not after adjusting for VTE risk factors. In both univariate and multivariate analyses, VTE (overall or idiopathic) was not a predictor of MI.

Conclusions—MI is not an independent risk factor for VTE, and VTE is not a predictor of MI.

Keywords

epidemiology; myocardial infarction; risk factors; thrombosis; veins

Introduction

Venous thromboembolism (VTE), consisting of deep vein thrombosis (DVT) and its complication, pulmonary embolism (PE), is a relatively common condition that is associated with serious and costly outcomes.[1-3] VTE is predominantly a disease of older age; incidence rates increase exponentially with age for both men and women, and for both DVT and PE.[1, 2] Independent risk factors for VTE include hospitalization for major surgery and for acute medical illness, nursing home confinement, active cancer, trauma, fracture, leg paresis, prolonged immobilization, and among women, pregnancy or the puerperium, oral contraceptives, estrogen and progestin.[1, 2, 4]

VTE and arterial thrombosis historically have been considered as two separate disease entities with distinct pathologies; venous thrombi mainly consist of red blood cells and fibrin while arterial thrombi mainly consist of platelets.[5] Moreover, the risk factors for VTE and arterial thrombosis are also distinctly different. Acute arterial thrombosis is usually due to atherosclerotic plaque rupture such that the risk factors for arterial thrombosis are essentially those for atherosclerosis (i.e., diabetes mellitus, hypertension, tobacco smoking and dyslipidemia).[6] Recent studies suggesting a relationship between VTE and arterial thrombosis, atherosclerosis and atherosclerosis risk factors have reached conflicting conclusions largely due to differing study populations, designs, definitions, measurements and outcomes, diagnostic uncertainty or misclassification, and absent or inadequate adjustment for potential confounding variables.[7] Nevertheless, it is biologically plausible to hypothesize that the same underlying thrombophilia that predisposes to VTE might also predispose to symptomatic arterial thrombosis after rupture of an atherosclerotic plaque. [8-10] We hypothesized that MI is a risk factor for VTE after adjusting for all known major VTE risk factors, and that VTE is a predictor for MI after adjusting for known MI risk factors. We restricted our analyses to MI rather than include other arterial thrombosis manifestations (e.g., ischemic stroke) because the pathophysiology of MI is less heterogeneous. To test our hypotheses, we performed population-based case-control and cohort studies using previously identified inception cohorts consisting of all Olmsted County, MN residents with objectively-diagnosed incident VTE over the 13-year period, 1988-2000, and all Olmsted County residents with objectively-diagnosed incident acute MI over the 32-year period, 1979-2010, as well as previously identified age- and sex-matched non-VTE controls drawn from the same population. In the cohort study, incident VTE cases and matched controls who survived at least one day after the VTE event or index dates, respectively, were followed forward in time for first lifetime MI, death or other loss to follow-up, or 12/31/2010, whichever came first.

Materials and Methods

Study Setting, Population and Designs

Using the longitudinal and population-based resources of the Rochester Epidemiology Project (REP)[11-13] we identified all Olmsted County, MN residents with incident DVT and/or PE over the 35-year period, 1966-2000, and all Olmsted County residents with incident MI over the 32-year period, 1979-2010, as previously described.[14-17] All Olmsted County residents with a first lifetime objectively-diagnosed DVT or PE during the 13-year period, 1988 to 2000, were included in the present study as VTE cases. Olmsted County provides a unique opportunity for investigating the relationship of VTE and MI. Rochester, the county seat, is approximately 80 miles from the nearest major metropolitan area. Mayo Clinic and its two hospitals, together with Olmsted Medical Center (OMC), a second group practice and its hospital, provide essentially all of the medical care delivered to County residents.[12] The REP medical records-linkage system affords access to comprehensive details regarding all medical care provided to all local residents for their entire period of residence in the community. The REP exists because Olmsted County is isolated from other urban centers, because unit patient medical records that combine all inpatient and outpatient data for each resident have been preserved since 1910, and because indexes to diagnoses, surgical procedures and test results have provided access to the patients of interest since 1935. The result is linkage of individual-level medical data from all sources of medical care available to and used by the population of Olmsted County, thus assuring complete ascertainment of all clinically-recognized VTE and MI events (including autopsy-discovered events) and outcomes for the source population over many decades. Indeed, in a comparison to the U.S. Census enumeration for Olmsted County, the REP Census enumeration had excellent validity for every Census year since 1930.[12]

The REP also provides an enumeration of the entire Olmsted County population from which controls can be sampled.[11-13] Using this system, one to two age- ($\pm$ one year) and sex-matched Olmsted County residents who had an episode of medical care within $\pm$ one year of the VTE case event date and whose medical record number was closest to the case's medical record number were selected as controls as previously described.[18-20] Since a patient's medical record number is assigned sequentially and in perpetuity, matching on medical record number assures a similar length of medical history among cases and matched controls. We then performed a case-control study nested within the Olmsted County population, testing MI as a risk factor for VTE. In addition, in a historical cohort (case-control follow-up) study, we followed each Olmsted County resident with incident VTE and their matched control(s) with no prior MI, conditional on surviving at least one day after the VTE event or index date, respectively, forward in time from the onset of incident VTE symptoms or signs to first MI, death or other loss to follow-up, or 12/31/2010, whichever came first, using their complete (inpatient and outpatient) medical records in the community. We tested VTE as a predictor of MI. The study was approved by the Mayo Clinic and OMC Institutional Review Boards.

Measurements

Using explicit criteria, trained and experienced nurse abstractors reviewed all medical records (inpatient and outpatient) in the community[21, 22] for VTE cases and controls who provided consent to review of their medical records for research purposes. All records were reviewed from date first seen by a REP healthcare provider until the earliest of death, date of last medical record follow-up or 2005, as previously described.[18, 19] For cases, data were recorded on the method of diagnosis and type of incident VTE event (DVT, PE or both; chronic thromboembolic pulmonary hypertension). A DVT was categorized as objectively-diagnosed when symptoms or signs of acute DVT were present and the diagnosis was confirmed by venography, compression venous duplex ultrasonography, impedance plethysmography, computed tomographic venography, magnetic resonance imaging or pathology examination of thrombus removed at surgery or autopsy. A PE was categorized as objectively-diagnosed when symptoms and/or signs of acute PE were present and the diagnosis was confirmed by pulmonary angiography, a ventilation/perfusion lung scan interpreted as high probability for PE, computed tomographic pulmonary angiography, magnetic resonance imaging or pathology examination of thrombus removed at surgery or autopsy. Mayo Clinic pathologists performed all autopsy examinations and completed the death certificates of persons dying within Olmsted County during the study period. Death certificate diagnoses of DVT or PE in the absence of objective criteria were not categorized as “objectively-diagnosed” VTE events.

For Olmsted County residents meeting our criteria for objectively-diagnosed DVT or PE and matched controls, the study nurses also collected data from the medical record on date of incident event (cases) or index episode of care (controls); patient age at incident event (cases) or index episode of care (controls); sex; patient location at incident event onset (cases) or index episode of care (controls) (four categories, defined as community-dwelling, confined to a hospital, community-dwelling but hospitalized in the previous 92 days, or confined to a nursing home [including chronic rehabilitation facility]); body mass index (BMI; kg/m²); tobacco use (current, former, never); active cancer (recent tumor burden without curative surgery, chemotherapy, or radiotherapy, excluding non-melanoma skin cancer); serious neurologic disease with leg paresis (stroke or other disease affecting the nervous system with associated leg paresis, or acute stroke with leg paresis requiring hospitalization within the previous three months); any surgery requiring general, spinal, or epidural anesthesia; trauma/fracture resulting in hospital admission (major fracture or severe soft tissue injury); prior superficial vein thrombosis; varicose veins (varicose veins, or treated varicose veins [injection sclerotherapy or stripping]); oral, intramuscular or subcutaneous hormone therapy (estrogen; progestin); and for women: pregnancy or three months postpartum at the time of the incident event; oral contraceptive use; and gynecologic surgery. We also collected data on ambulatory blood glucose (value, date of assay, and fasting status); diabetes mellitus therapy (drug[s], date of therapy); physician diagnosis of diabetes mellitus; hyperlipidemia; lipid-lowering medication therapy (statin and non-statin); hypertension; and warfarin anticoagulation. Chemotherapy, serious neurologic disease, all surgery variables, anesthesia, trauma/fracture, central vein catheterization, lipid-lowering medication, pregnancy or recent delivery of newborn, oral contraceptive use and hormone therapy had to have been documented in the three months prior to the incident VTE event

for cases or the index episode of medical care for controls. Active cancer had to have been documented in the three months prior to or three months after the incident VTE event. Diabetes mellitus, tobacco use, hyperlipidemia, hypertension, prior superficial vein thrombosis, varicose veins and permanent transvenous pacemaker could be documented any time prior to the incident event. Body mass index was based on the most recent height and weight measurements prior to the incident VTE event (cases) or index episode of care (controls). If either height or weight was missing (n=38), the value was imputed based on case status and 10-year age group (mean value was used). Diabetes mellitus was defined as any ambulatory blood glucose value ≥ 140 mg/dL (excluding gestational diabetes), [23-25] and/or use of anti-diabetic drug therapy.

We also identified all Olmsted County residents admitted to Olmsted County hospitals with possible MI from 1979 to 2010 as previously described.[16, 17, 26] We reviewed the complete medical records in the community for all patients with International Classification of Diseases, Ninth Revision, Clinical Modification (**ICD-9-CM**), code 410 (acute MI), a 50% random sample of patients with code 411 (other ischemic heart disease) from 1987 to 1998, a 10% random sample of events with code 411 from 1999 to 2002, and a 100% sample of events with code 411 from 2003 to 2010; additional ICD-9 CM codes were not included because they were low-yield.[27] We used standard algorithms to verify the diagnosis of MI on the basis of the presence of 2 out of 3 of the following: cardiac pain, elevated biomarkers, or electrocardiographic (ECG) changes.[27-29] Biomarkers included CK and CK-MB until 2000 and troponin thereafter. Case reviews were performed to ensure that alternative causes of biomarker elevation were considered. Troponin T, creatine kinase, and creatine kinase-MB were measured with a sandwich electrochemiluminescence immunoassay system on an Elecsys 2010 analyzer (Roche Diagnostics, Indianapolis, Indiana) in the laboratories of the Department of Medicine and Pathology at the Mayo Clinic. We coded 3 ECGs per episode by using the Minnesota Code Modular ECG Analysis System.[30]

Statistical Analyses

We performed two sets of analyses. In the first set of analyses, we tested MI for an association with VTE using conditional logistic regression. In univariate analyses, we tested MI as well as other previously identified independent VTE risk factors (i.e., BMI, current or recent hospitalization within the previous 92 days with and without surgery, nursing home confinement, trauma or fracture, active cancer, neurologic disease with leg paresis, prior superficial vein thrombosis, varicose veins, and among women, pregnancy or the postpartum period, oral contraceptives and hormone therapy)[18] as well as transfemoral catheterization, hyperlipidemia, lipid-lowering medication and VTE prophylaxis for an association with VTE. We also tested MI for an independent association with VTE in a multivariable model, adjusting for patient age, BMI and all characteristics with a univariate p-value ≤ 0.15 level. In the second set of analyses, we tested VTE as a potential predictor of MI using Cox proportional hazards (**PH**) modeling. We estimated the cumulative incidence of MI after the VTE event and index date among cases and controls, respectively, conditional on surviving one day after the event (cases) or index (controls) date, using the Kaplan-Meier product limit method, and tested for a significant difference in time-to MI

using the log rank test. We tested patient age, sex and BMI, diabetes mellitus, tobacco smoking, hyperlipidemia, lipid-lowering medication, hypertension, warfarin and VTE as potential predictors of incident MI using univariate and multivariate Cox PH modeling. Warfarin anticoagulation was tested as a time-dependent variable. A two-tailed alpha level of 0.05 was used for all statistical analyses. Analyses were conducted in SAS version 9.3 (SAS Institute, Cary, NC).

Results

Over the 13-year study time frame, 1988-2000, 1400 residents of Olmsted County developed a first lifetime DVT and/or PE; of these, 1311 (93.3%) were objectively-diagnosed. Of the objectively-diagnosed VTE events, 726 (55.6%) occurred in women. The distribution of VTE events by event type was 410 (56.5%) DVT alone, 314 (43.3%) PE with or without DVT, and 2 (0.3%) chronic thromboembolic pulmonary hypertension. The mean $\pm$ SD ages of the cases (n=1311) and matched controls (n=1511) were 65.0 ± 19.0 and 64.6 ± 18.9 years, respectively, and did not differ significantly. Of the 1311 objectively-diagnosed VTE cases, 134 (10.2%) were diagnosed at autopsy (127 were PE). The overall mean $\pm$ SD duration of prior medical record documentation was 36.3 ± 20.8 and 36.2 ± 20.9 years, respectively, for cases and controls.

The demographic and baseline characteristics among VTE cases and controls are shown in Table 1. Among the VTE cases and controls, 75 (5.7%) and 51 (3.4%) had an incident MI prior to the VTE event or index date, respectively. In univariate analyses of baseline characteristics as potential risk factors for incident VTE, increasing patient BMI, hospitalization for major surgery or acute medical illness, nursing home confinement, active cancer, neurological disease with leg paresis, transfemoral catheterization, trauma/fracture, prior superficial vein thrombosis, VTE prophylaxis and MI, and among women, pregnancy or the postpartum period, oral contraceptives and hormone therapy were associated with a significantly increased odds of VTE, while lipid-lowering medication was associated with a significantly reduced odds of VTE; hyperlipidemia was not associated with VTE (Table 2). After adjusting for hospitalization for major surgery or medical illness, and for nursing home confinement, MI remained marginally associated with VTE (OR=1.64; 95% CI: 1.05, 2.57); 98% of the 602 cases with hospitalization within 93 days prior to the incident VTE event were hospitalized for an indication other than MI. However, in a multivariable model adjusting for all characteristics identified as univariate risk factors for VTE, MI was not significantly associated with VTE (Table 2).

Among the 1177 VTE cases and 1495 controls who survived at least one day after the event (cases) or index (controls) date and had no prior MI, 58 (4.9%) and 77 (5.2%) developed an incident MI, respectively, over 8,826 and 11,596 person-years of follow-up for cases and controls, respectively. The median (interquartile range) duration of followup for VTE cases and controls was 7.3 (1.3, 12.3) and 7.5 (5.1, 10.4) years, respectively. The cumulative incidence of MI among VTE cases and controls did not differ significantly (log-rank $p=0.41$; Figure 1) In univariate Cox proportional hazards analyses, increasing patient age, diabetes mellitus, hypertension and hyperlipidemia were associated with a significantly increased hazard of MI, while patient sex, tobacco smoking and lipid-lowering medication were

marginally associated; VTE was not associated with an increased hazard of MI, and female sex and warfarin anticoagulation were marginally associated with a reduced hazard (Table 3). In the multivariable model, increasing patient age, patient sex and diabetes mellitus were associated with an increased hazard of MI, and female sex was associated with a reduced hazard of MI; VTE was not a predictor of MI (Table 3). In a similar multivariable model, idiopathic VTE (n=278 [21.2%]) also was not a predictor of MI (HR=0.84, 95%CI: 0.47, 1.52; p=0.57).

Discussion

We hypothesized that the same underlying thrombophilia(s) that predispose to VTE might also predispose to “augmented” thrombosis at the site of atherosclerotic coronary artery plaque rupture and lead to symptomatic acute MI. In support of this hypothesis, case-control studies of young women (18 to 44 years of age) found the Factor V Leiden (*F5* rs6025) and prothrombin G20210A (*F2* rs1799963) mutations were associated with a 2.4- and 4-fold increased risk of myocardial infarction, respectively; women carriers who were current smokers were at highest MI risk.[8] In another study, Factor V Leiden was found in 12 percent of young patients (mean age 44 years) with MI and normal coronary angiography, in 4.5 percent of age- and sex-matched patients with MI and significant coronary artery disease (odds ratio 2.6, $p = 0.01$), and 5 percent of normal controls (odds ratio 2.9, $p = 0.01$).[10]

We found that univariately, MI was significantly associated with VTE in our case-control study. The strength of this association was markedly attenuated after adjustment for three major VTE risk factors: hospitalization for surgery or acute medical illness, and nursing home confinement. This finding suggests that similar to diabetes mellitus, MI is only indirectly associated with VTE through the MI hospitalization.[1] In support of this conclusion, a large case-control study of residents of North Jutland and Aarhus Counties, Denmark found that prior hospitalization for MI was significantly associated with VTE in the three months after the MI but not in the 4-60 months after MI, suggesting that the MI hospitalization was the VTE risk factor rather than the MI itself.[31] In our study, MI was not associated with VTE after controlling for other characteristics univariately associated with VTE, illustrating the need to control for all VTE risk factors. Previous case-control studies that found an association of asymptomatic atherosclerosis (i.e., carotid artery plaque, coronary artery calcification) failed to adequately control for all VTE risk factors.[32, 33] Furthermore, a cross sectional study could not establish an association of coronary artery thrombosis with VTE at autopsy,[34] and three large cohort studies could not confirm asymptomatic carotid artery plaque or increased intima-media thickness as predictors of VTE.[35-37]

In our cohort study, incident VTE was not a predictor of MI, either univariately or in a multivariate model that adjusted for atherosclerosis risk factors and warfarin anticoagulation; in a similar model, idiopathic VTE also was not a predictor of MI. Previous cohort studies that identified VTE as a predictor of MI were limited by potential diagnostic uncertainty or misclassification and inability to reliably separate incident from recurrent events due to use of administrative data (i.e., hospital discharge diagnoses codes),[38-40] small number of outcome events,[21, 22] absent or inadequate adjustment for potential

confounding variables,[38, 41, 42] lack of an appropriate non-VTE comparison group,[43, 44] failure to construct a multivariate model limited to MI as the sole outcome,[40, 43-45] and significant study heterogeneity.[46]

Our study had several important strengths. We avoided referral bias and tested the entire spectrum of VTE and MI occurring in the community by including all objectively-diagnosed incident VTE and MI cases from a well-defined geographic area, including rapidly-fatal and non-hospitalized VTE events. We avoided diagnostic uncertainty or misclassification by ascertaining acute incident VTE and MI cases based on application of strict criteria after careful review of the complete provider-linked medical records rather than rely on administrative diagnosis codes. We insured a comparable VTE control group by performing a population-based study where both cases and controls were residents from the same community with similar lifetime access to medical care. We adjusted for all important risk factors for VTE and for MI including the effect of warfarin anticoagulation therapy, and constructed a multivariate model including VTE as a potential predictor with MI as the sole outcome.

It is also important to address potential limitations of our study. This investigation was limited to a single geographical region, Olmsted County, which is predominantly white of non-Hispanic ancestry. The age and sex distribution of Olmsted County residents is similar to that of the U.S. white population although the median income and level of education for Olmsted County residents are higher than for the U.S. white population.[22, 47] While no geographic area is representative of all others, the under representation of minorities and relatively few providers may compromise the generalizability of our findings to other racial and ethnic groups and different healthcare environments. With our VTE case-control sample size, we had 90% power to detect an OR=2.3 for an association of MI with VTE. Similarly, with our cohort sample size and VTE case and matched control follow-up durations of over 8,800 and 11,500 person-years, respectively, we had 90% power to detect a HR=1.8 for VTE as a predictor of MI. Thus, it is possible that we missed significant associations of smaller magnitude.

In conclusion, in this population-based study, although MI was univariately associated with VTE, this association was markedly attenuated after controlling for hospitalization and nursing home confinement, indicating that MI is an indirect risk factor for VTE due to the MI hospitalization. After controlling for all important VTE risk factors, MI was not associated with VTE, and VTE was not a predictor of MI.

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Highlights

- VTE and MI historically have been considered as two separate disease entities.
- Studies suggesting VTE and MI are associated reached conflicting conclusions.
- We found that MI was not a VTE risk factor, and VTE was not a predictor of MI.
- We had 90% power to detect an association of MI with VTE at OR=2.3, and VTE as a predictor of MI at HR=1.8.
- It is possible that we missed significant associations of smaller magnitude.

Figure 1.

Cumulative Incidence of Acute Myocardial Infarction among Olmsted County, MN Residents with Incident Deep Vein Thrombosis and/or Pulmonary Embolism Over the 13-year Period, 1988-2000, and Age-, Sex- and Index Date-Matched Olmsted County Resident Controls Followed To 12/31/2010

Table 1
Demographic and Baseline Characteristics among Olmsted County Residents with Incident Deep Vein Thrombosis and/or Pulmonary Embolism, 1988-2000, and Age-, Sex- and Venous Thromboembolism Index Date-Matched Olmsted County Resident Controls

Characteristic	Cases n=1311	Controls n=1511
Patient age, mean $\pm$ SD, median (range)	65.0 $\pm$ 19.0, 68.3 (0.02-103.7)	64.6 $\pm$ 18.9, 67.5 (0-102.7)
Patient sex, % female	55	55
Body mass index (kg/m ²), mean $\pm$ SD, median (range)	28.0 $\pm$ 7.0, 27.1 (6.3-72.3)	27.7 $\pm$ 5.3, 26.0 (12.6-53.2)
Hospitalization, with surgery, n (%)	325 (24.8)	40 (2.7)
Hospitalization, acute medical illness, n (%)	277 (21.1)	98 (6.5)
Nursing home confinement, n (%)	165 (12.6)	100 (6.6)
Trauma/fracture, n (%)	162 (12.4)	43 (2.9)
Active cancer, n (%)	324 (24.7)	47 (3.1)
Neurologic disease with leg paresis, n (%)	95 (7.3)	13 (0.9)
Superficial vein thrombosis, n (%)	201 (15.3)	84 (5.7)
Pregnancy or postpartum, n (%)	24 (1.8)	10 (0.7)
Oral contraceptives, n (%)	60 (4.6)	38 (2.5)
Estrogen alone, n (%)	111 (9.6)	124 (8.2)
Progestin alone, n (%)	99 (7.6)	57 (3.7)
Non-contraceptive estrogen plus progestin, n (%)	165 (12.6)	133 (8.8)
Myocardial infarction prior to VTE or index, n (%)	75 (5.7)	51 (3.4)
Diabetes mellitus, n (%)	144 (11.3)	66 (4.7)
Tobacco smoking, n (%)		
Current or former	678 (51.7)	746 (49.4)
Never	633 (48.3)	765 (50.6)
Hyperlipidemia, n (%)	429 (32.7)	528 (34.9)
Lipid-lowering medication, n (%)	95 (7.3)	145 (9.6)
Statin medication, n (%)	69 (5.3)	107 (7.1)
Non-statin medication, n (%)	33 (2.5)	48 (3.2)
Transfemoral procedure, n (%)	86 (6.6)	16 (1.1)
VTE prophylaxis, n (%)	301 (23)	59 (3.9)

Table 2

Univariate and Multivariate Analyses of Baseline Characteristics as Potential Risk Factors for Incident Deep Vein Thrombosis and/or Pulmonary Embolism among Olmsted County, MN Residents, 1988-2000.

Characteristic	Univariate		Multivariate	
	Odds Ratio (95% CI)	Wald P-value	Odds Ratio (95% CI)	Wald P-value
Patient age	1.13 (0.96, 1.34)	0.15	1.25 (0.97, 1.62)	0.09
Body mass index	1.04 (1.03, 1.06)	<0.001	1.07 (1.04, 1.09)	<0.0001
Hospitalization for major surgery	13.29 (8.96, 19.71)	<0.001	12.30 (7.60, 19.93)	<0.0001
Hospitalization for acute medical illness	3.62 (2.81, 4.66)	<0.001	4.36 (2.97, 6.41)	<0.0001
Nursing home confinement	2.25 (1.66, 3.05)	<0.001	4.76 (2.99, 7.57)	<0.0001
Active cancer	9.50 (6.78, 13.33)	<0.001	10.46 (6.81, 16.06)	<0.0001
Neurological disease with leg paresis	9.20 (4.92, 17.22)	<0.001	7.22 (3.29, 15.85)	<0.0001
Transfemoral catheterization	6.38 (3.67, 11.07)	<0.001	1.56 (0.73, 3.33)	0.25
Trauma/fracture	4.58 (3.22, 6.51)	<0.001	3.45 (2.10, 5.66)	<0.0001
Superficial vein thrombosis	3.09 (2.35, 4.08)	<0.001	3.64 (2.49, 5.31)	<0.0001
Acute myocardial infarction	1.84 (1.25, 2.71)	0.002	1.25 (0.70, 2.24)	0.46
Hyperlipidemia	0.92 (0.78, 1.08)	0.3	0.96 (0.73, 1.24)	0.73
Lipid-lowering medication	0.74 (0.56, 0.98)	0.036	1.86 (0.34, 10.15)	0.48
Statin medication	0.75 (0.55, 1.04)	0.082	0.34 (0.07, 1.98)	0.25
Non-statin lipid-lowering medication	0.76 (0.48, 1.21)	0.25	0.42 (0.09, 1.99)	0.27
Prophylaxis	7.37 (5.32, 10.20)	<0.001	1.74 (1.14, 2.65)	0.01
Among women:				
Pregnancy or postpartum	3.36 (1.42, 7.95)	0.006	3.81 (1.75, 8.28)	0.0007
Oral contraceptives	2.69 (1.44, 4.67)	<0.001	4.47 (1.40, 14.3)	0.012
Hormone therapy	1.57 (1.16, 2.12)	0.003	1.73 (1.14, 2.63)	0.01

Table 3

Univariate and Multivariate Analyses of Baseline Characteristics as Potential Predictors of Myocardial Infarction among Olmsted County, MN Residents with Incident Deep Vein Thrombosis and/or Pulmonary Embolism, 1988-2000.

Characteristic	Univariate		Multivariate	
	Hazard Ratio (95% CI)	P-Value	Hazard Ratio (95% CI)	P-Value
Patient age	1.05 (1.04, 1.07)	<0.0001	1.06 (1.04-1.07)	<0.0001
Female sex	0.73 (0.52, 1.02)	0.06	0.63 (0.44-0.90)	0.01
Body mass index	1.01 (0.98, 1.04)	0.45	1.01 (0.97-1.04)	0.67
Diabetes mellitus	2.97 (1.78, 4.96)	<0.0001	2.25 (1.32-3.83)	0.003
Tobacco smoking	1.19 (0.99, 1.43)	0.06	1.12 (0.93-1.34)	0.22
Hypertension	1.98 (1.41, 2.80)	<0.0001	1.15 (0.80-1.65)	0.46
Hyperlipidemia	1.64 (1.17, 2.30)	0.005	1.31 (0.90-1.91)	0.17
Lipid-lowering medication	1.58 (0.95, 2.64)	0.08	0.98 (0.56-1.72)	0.94
Venous thromboembolism	0.86 (0.62, 1.22)	0.40	1.02 (0.70-1.46)	0.94
Warfarin anticoagulation	0.57 (0.27, 1.24)	0.16	0.51 (0.24-1.13)	0.10