# The association of incident clot location and the risk of VTE recurrence

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Abstract

# The association of incident clot location and the risk of VTE recurrence

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Recurrent venous thromboembolism (VTE) affects 16-30% of individuals who have experienced an incident VTE event, according to recent population-based studies conducted in the United States. Researchers and healthcare providers have worked to estimate recurrence risk among individuals to assess proper use and duration of anticoagulants and other therapies to prevent recurrence after an incident clot. Among risk estimation methods are risk-scoring systems that include recognized risk factors.

Our study used population-based Group Health Cooperative (GHC) data to evaluate incident clot location on risk of recurrent VTE. Using Cox proportional hazards regression, we compared risk of recurrence among subjects who had distally located incident deep vein thrombosis (DVT) and subjects who had incident pulmonary embolism (PE) with subjects who experienced an incident DVT clot in a proximal location. After adjusting for race, age, sex, BMI, and smoking status, we observed lower risk of recurrence among subjects with distal incident clots (HR 0.44 [95% CI 0.29-0.66]) and pulmonary embolism (HR 0.61 [95% CI 0.50-0.74]) when compared with subjects with incident clots in a proximal location.

This research supports the inclusion of incident clot location as a factor in future recurrence risk scoring systems as well as in general medical practice. Future research may benefit from further evaluation of the idiopathic subgroups and the potential differing risk within them, particularly among subjects with cancer-provoked incident clot, who experienced a higher rate of recurrence than other groups. Additionally, we suggest further differentiation of regions of incident clot location as it relates to recurrence risk, including a more granular evaluation of individual leg veins.

## Introduction

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are the two primary manifestations of venous thromboembolism (VTE), a condition that affects 300,000-600,000 people in the United States annually.[1] Once an individual has experienced an incident VTE, the person is much more likely to experience another.[2] Prior research has provided wide-ranging estimates for VTE recurrence based on study population. The best estimates of community recurrence risk in the U.S. general population come from population-based studies, such as the Heart and Vascular Health and the Olmstead County studies. The Heart and Vascular Health study observed 16% recurrence over an average follow-up of 3.4 years.[3] The Olmstead County study observed a 30.4% recurrence over an average follow-up of 10 years.[5]

Understanding VTE recurrence risk is central to determining the appropriate course of treatment for an individual. Oral anticoagulants, which are commonly used to treat VTE, carry significant risk of morbidity and mortality related to major bleeds and should be administered with close attention to individual need and duration of use.[5] Multivariate risk-assessment scales for VTE recurrence have been built for use in determining appropriate treatment approaches for specific subgroups of VTE patients. These scales include the HERD002 scoring system,[6] the Vienna prediction model,[7] and the DASH score.[8] These risk-rating scoring approaches include demographic and clinical factors such as sex,[6,7] age,[6,8] body mass index (BMI),[6] type of VTE (DVT or PE),[7] presence of abnormal levels of D-dimer,[6,8] use of exogenous estrogens,[8] and the presence of post-thrombotic syndrome[6] (Supplemental Figure 1). Male sex, as well as greater height, BMI, and age, are risk factors for recurrent VTE.[6–11] Those with idiopathic and cancer-related incident VTE are also known to be at greater risk for VTE recurrence.[4,12] Other factors examined in prior research include inferior vena cava (IVC) filter placement, superficial thrombophlebitis, and varicose vein stripping; however these have not been demonstrated to be associated with risk of recurrence.[11,13,14]

Our epidemiologic study examined the impact of physical location of an incident VTE on the risk of recurrence. At this time, location of the incident clot has not been incorporated into multivariate VTE recurrence risk assessment scales aside from the Vienna Prediction Model,[7] though prior research suggests that inclusion of this factor may improve estimates of individual recurrence risk. Prior studies have found VTE recurrence to be lower among those in whom the incident DVT occurred in a distal location compared with those in whom the incident clot occurred in a proximal location[15,16] and another study found no statistical difference by incident clot location.[14] Other studies have demonstrated the adverse effects of unnecessary treatment and presently help inform decisions surrounding anticoagulant use for the lowest-risk patients, particularly those with isolated incident distal DVT.[17] To date, most of the literature for VTE recurrence and its risk factors have relied primarily on data from patients being treated at specialty centers for anti-coagulation and not necessarily including patients seen in the general population with treatment by primary care physicians.[6,7,18] In this study, we describe the rate and risk of recurrence in a population-based study of incident VTE and examine the relative risk of recurrence by traditional risk factors as well as the location of the incident clot.

We evaluated the relationship between incident clot location and risk of recurrent VTE. Based on prior literature, we expected proximal incident clots to carry a greater risk of recurrence compared with distal incident clots, but individuals with PE incident events to have similar risk to that of those with proximal incident clots. We also evaluated location-based recurrence risk by idiopathic status and anticipated there may be statistical difference between our three idiopathic subgroups: unprovoked, cancer-related provoked, and non-cancer provoked.

## Methods

### *Setting and Design*

To address the aims of the study, we used an incident VTE inception cohort that was followed for recurrence from the Heart and Vascular Health (HVH) Venous Thrombosis study, a population-based case-control study set within Group Health Cooperative (GHC), now Kaiser Permanente Washington (KPW), in Western Washington State.[3] The Cooperative was an integrated healthcare delivery system in which members received virtually all their care within the unified GHC system. For the HVH study, trained medical record abstractors reviewed the complete health record (outpatient, inpatient, provider notes, laboratory measures, pharmacy records) to obtain study data prior to the incident event and through follow-up; telephone interviews were also conducted on surviving participants. The HVH Venous Thrombosis study and subsequent analyses have been approved by the GHC/KPW institutional review board.

### *Cohort of Incident VTE*

Subjects included in this analysis were cases from a case-control study of VTE, details of which have been published previously.[19,20] These cases included men aged 30-89 years and women aged 18-89 years who suffered an incident VTE from January 2002 through December 2014. All subjects were members of GHC at the time of their incident VTE. Incident VTE was identified using electronic health records and each case was reviewed by a trained abstractor to confirm the presence of an incident VTE. Qualifying events required confirmatory imaging including Doppler or duplex ultrasound, computed tomography, pulmonary angiography, or ventilation-perfusion scan, or supporting clinical evidence of an incident VTE with a physician diagnosis.[19,20] Ninety-eight percent of qualifying event included imaging[3]. We included all confirmed diagnoses of VTE including those with recent cancer and both provoked and

unprovoked events. Excluded from our study were GHC members with upper-extremity DVT and those who died on the day of the incident VTE, had no follow-up in the GHC record, or had been pregnant in the year prior to the incident event.

Incident DVT location was identified using imaging information and categorized as distal or proximal. Distal clots are those in the leg that extended only to the peroneal, fibular, anterior or posterior tibial, and muscular veins. Proximal clots are those which extended beyond the distal location to include the popliteal, deep femoral and femoral veins, iliac veins, as well as the vena cava. Incident events were also categorized by their presumed etiology: unprovoked, provoked, and cancer-related. Unprovoked incident events are those in which there was no known risk factor present. Provoked incident events are those in which the VTE was related to a known transient or persistent non-cancer risk factor that included inpatient surgery, hospitalization, or fracture within the preceding 30 days or current use of oral estrogen hormone therapy or oral contraceptives. Cancer-related are those provoked by a prevalent cancer or cancer treatment at the time of incident VTE or in the 2 years prior.

*Recurrent VTE*

The full health record of GHC members with an incident VTE were reviewed by trained abstractors to identify recurrences from the time of their incident event through December 2014 (end of follow-up), death, or separation from GHC. Recurrent events were defined as detection of a clot in a new location any time after the incident event or clots occurring in the same location 14 or more days after the incident event. Qualifying recurrent events required both physician diagnosis and supporting imaging; symptoms alone were not sufficient to qualify as a recurrent VTE. The date of the recurrent VTE was defined as the diagnosis date.

*Covariates*

Covariate details were collected from the health record and the telephone interview, for those who completed it. Age was defined as the subject's age at the time of the incident VTE event. Race was by self-report; in the absence of self-report, this information was collected from the health record. Race was categorized as white, black, or other; we could not define these categories further due to small numbers of other races. Smoking status was also by self-report or from the health record; smoking status was based on the participant's smoking status at the time of their incident VTE event and was categorized as never a smoker, a former smoker, or a current smoker. Body mass index (weight[kg]/height[m]$^2$) was calculated using the most recent height and weight at the time of the incident event.

*Analyses*

Each participant entered into the follow-up study on the date of their incident VTE event and contributed person-time while he or she was at risk for a recurrent event. We calculated unadjusted recurrence rates stratified on key characteristics including incident clot location, sex, age, and etiology group. To illustrate recurrence burden, a cumulative incidence plot was created displaying the proportion of subjects experiencing a recurrent event over time based on the location of the incident clot.

We used Cox proportional hazards regression to describe the association of incident clot location on risk of recurrence while adjusting for potential confounding factors. Time zero for the date of the incident event and a participant's time at risk was calculated through a first recurrence or through death, withdrawal from GHC, or December 2014, which ever came first. Incident clot location was categorized two ways. The primary categorization created three groups: distal without concomitant PE; proximal without concomitant PE (reference); and PE

with or with diagnosed DVT. Those with only record of DVT but unknown clot location made up a small proportion of our population and were independently compared to our reference group. The secondary categorization included six comparison groups: distal without concomitant PE, proximal without concomitant PE (reference), DVT with unknown site and no concomitant PE, proximal with concomitant PE, distal with concomitant PE, and DVT with unknown site and concomitant PE.

Adjustments were made for variables identified *a priori* to control for potential confounding and index event bias; these included age (linear), sex (binary), BMI (linear), race (index variables for black and other), and smoking (index variables for former and current). Few participants were omitted from adjusted analyses due to missingness relating to smoking history and BMI and these cumulatively made up less than 1%.

We tested for effect modification of incident event location by idiopathic status using a likelihood ratio test. Due to small numbers, we combined the provoked idiopathic subgroups and compared provoked versus unprovoked status.

**Results**

Our data included 2844 participants with an incident VTE, from which we excluded those with upper-extremity DVT (n=56), those who died on the day of the incident clot or otherwise had no follow-up (n=22), and those who had been pregnant the year prior (n=23). Analyses were conducted on the remaining 2,743 participants.

Table 1 provides participant characteristics, stratified by the primary recurrence location classification. Among all participants, there were slightly more women in our population than men and the majority of subjects are white. At the time of their incident VTE and entry into the cohort, the mean age of the population was 65.7 years and the mean BMI was 30.2. Mean

follow-up time was 3.4 years, and 16.3% (n=448) of our study population experienced a recurrent VTE. Among those with information on incident DVT without a PE (n=1,266), 936 (73.9%) were proximal, 232 (18.3%) were distal, and 98 (7.7%) had no identified location. 1,477 participants had a PE, among whom 505(34.2%) had concomitant DVT. Characteristics of our population appear generally similar across our comparison groups. Anticoagulant use was high among all groups, ranging from 92.9% to 99.2% (Table 1). Unprovoked events constituted the largest group across all location categories.

The overall average recurrence rate was 4.9 events per 100 person-years (Table 2) and estimates ranged from 2.8 event per 100 person-years for distal DVTs to 6.7 events per 100 person-years for proximal DVTs. Estimated cumulative probabilities at 1 and 5 years were 8.5% and 25.5% for those with proximal incident clots, 5.1% and 12.4% for those with distal incident clots and 5.4 and 15.2% for subjects with PE. Recurrence rates varied by idiopathic subgroups.

Cumulative incidence graphs show proximal DVT having the greatest cumulative recurrence at nearly all time points over the 10-year period and distal DVT experiencing the lowest cumulative recurrence over time (Figures 1-3).

Among all incident events in adjusted Cox regression models (Table 3), we observed those with incident clots in a distal location had less than half the risk of recurrence compared with those with incident proximal clots, (HR 0.44 [95% CI 0.29-0.66]). The adjusted hazard ratio comparing subjects with incident PE to those with proximal incident DVT clots showed a similar relationship (HR 0.61 [95% CI 0.50-0.74]). When stratifying by idiopathic status (Table 4), adjusted hazard ratios for distal compared with proximal incident clots were 0.35 (95% CI 0.19-0.63), 0.57 (0.27-1.21), and 0.68 (0.29-1.62) for those categorized as having unprovoked, provoked, and cancer-related incident VTE, respectively. After combining cancer-related and provoked subgroups, a likelihood ratio test did not indicate effect modification by idiopathic subgroup (p=0.79) on the relative risk of a distal compared with proximal event. Adjusted hazard ratios for PE versus

compared with proximal clot location were similar across idiopathic subgroups: 0.65 (95% CI 0.51-0.84), 0.60 (0.38-0.94), and 0.55 (0.35-0.86) for those categorized as having unprovoked, provoked, and cancer-related incident VTE, respectively.

Secondary groupings of clot location are presented in Table 5. Compared with participants with a proximal DVT and no PE, the relative risk of those with a PE and a proximal DVT was closer to 1.0 than the relative risk of those with a PE and distal DVT. Relative risks of those with an unknown DVT location were similar to the reference group.

**Table 1.** Study population demographic and clinical characteristics by location of incident VTE event

| | **Full population (n=2,743)** | **Stratified by Location of Incident VTE Event** | | | |
|---|---|---|---|---|---|
| | | **Proximal DVT without PE (n=936, 32.1%)** | **Distal DVT without PE (n=232, 8.5%)** | **Unknown DVT Location without PE (n=98)** | **Pulmonary Embolism with or without DVT (n=1,477, 53.9%)** |
| Female, n (%) | 1,519 (55.4%) | 492 (52.6%) | 121 (52.2%) | 62 (63.3%) | 844 (57.1%) |
| | | | | | |
| Ancestry: European, n (%) | 2,463 (89.8%) | 851 (90.9%) | 217 (93.5%) | 83 (84.7%) | 1,312 (88.8%) |
| Ancestry: African American, n (%) | 138 (5.0%) | 31 (3.3%) | 4 (1.7%) | 10 (10.2%) | 93 (6.3%) |
| Ancestry: Other/Unknown, n (%) | 142 (5.18%) | 54 (5.8%) | 11 (4.7%) | 5 (5.1%) | 72 (4.9%) |
| | | | | | |
| Mean age, yrs (SD) | 65.7 (14.8) | 65.2 (14.8) | 61.1 (14.3) | 68.0 (14.7) | 66.7 (14.8) |
| | | | | | |
| Mean BMI, kg $m^{-2}$ (SD) | 30.2 (7.7) | 29.3 (6.7) | 30.6 (6.4) | 30.6 (8.1) | 30.7 (8.3) |
| | | | | | |
| Mean height, in (SD) | 67.2 (3.9) | 67.3 (4.2) | 67.5 (3.8) | 66.4 (4.1) | 67.1 (3.8) |
| | | | | | |
| Anticoagulant use within 30 days of incident VT, n (%) | 2,673 (97.5%) | 928 (99.2%) | 219 (94.4%) | 91 (92.9%) | 1,435 (97.2%) |
| | | | | | |
| Current Smoker, n (%) | 232 (8.5%) | 103 (11.1%) | 19 (8.2%) | 4 (4.1%) | 106 (7.2%) |
| Former Smoker, n (%) | 1,204 (44.1%) | 381 (41.0%) | 102 (44.0%) | 40 (40.8%) | 681 (46.3%) |
| Never Smoked, n (%) | 1,294 (47.4%) | 445 (47.9%) | 111 (47.9%) | 54 (55.1%) | 684 (46.5%) |
| | | | | | |
| DVT only, n (%) | 1,266 (46.2%) | 936 (100%) | 232 (100%) | 98 (100%) | - |
| PE only, n (%) | 972 (35.4%) | - | - | - | 972 (65.8%) |
| Both, n (%) | 505 (18.4%) | - | - | - | 505 (34.2%) |
| | | | | 43 (43.9%) | 710 (40.1%) |
| Unprovoked, n (%) | 1,393 (50.8%) | 527 (56.3%) | 113 (48.7%) | 20 (20.4%) | 426 (28.8%) |

| | | | | | |
|---|---|---|---|---|---|
| Provoked, non-cancer-related, n (%) | 716 (26.1%) | 189 (20.2%) | 81 (34.9%) | 35 (35.7%) | 341 (23.1%) |
| Provoked, cancer-related, n (%) | 634 (23.1%) | 220 (23.5%) | 38 (16.4%) | | |
| | | | | 17 (17.4%) | 197 (13.3%) |
| Recurrent events, n (%) | 448 (16.3%) | 207 (22.1%) | 27 (11.6%) | | |

SD, standard deviation; yrs, years; BMI, body mass index; In, inches; VTE, venous thromboembolism; DVT, deep vein thrombosis; PE, pulmonary embolism

**Table 2.** Recurrence rates by participant characteristic

| | Person-years of follow-up | Events | Recurrence Rate |
|---|---|---|---|
| Full Population | 9232 | 448 | 4.9/100 person-years |
| Location of Incident DVT | | | |
| Proximal DVT | 3104 | 207 | 6.7/100 person-years |
| Distal DVT | 962 | 27 | 2.8/100 person-years |
| Pulmonary Embolism | 4929 | 197 | 4.0/100 person-years |
| Sex | | | |
| Male | 4070 | 220 | 5.4/100 person-years |
| Female | 5162 | 228 | 4.4/100 person-years |
| Age Groups | | | |
| <50 | 1420 | 58 | 4.1/100 person-years |
| 50-65 | 3144 | 160 | 5.1/100 person-years |
| >65 | 4668 | 230 | 4.9/100 person-years |
| Idiopathic Subgroups | | | |
| Unprovoked | 5320 | 266 | 5.0/100 person-years |
| Provoked | 2912 | 94 | 3.2/100 person-years |
| Cancer-related | 1001 | 88 | 8.8/100 person-years |

**Table 3.** Unadjusted and adjusted hazard ratios comparing VTE recurrence by distal or proximal incident clot location

| | HR (95% CI), Unadjusted | | | | HR (95% CI), adjusted for age, sex, BMI, race, smoking* | | | |
|---|---|---|---|---|---|---|---|---|
| Primary Categorization | Proximal DVT without PE | Distal DVT without PE | Pulmonary Embolism | Unknown DVT Location without PE | Proximal DVT without PE | Distal DVT without PE | Pulmonary Embolism | Unknown DVT Location without PE |
| Recurrent events/incident events | *207/936* | *27/232* | *197/1477* | 17/98 | *207/924* | *27/231* | *197/1462* | *17/97* |
| | ***1.00 (ref)*** | 0.43 (0.29-0.65) | 0.61 (0.50-0.74) | 1.05 (0.64-1.73) | ***1.00 (ref)*** | 0.44 (0.29-0.66) | 0.61 (0.50-0.74) | 1.04 (0.63-1.71) |
| | | *P<0.001* | *P<0.001* | *P=0.835* | | *P<0.001* | *P<0.001* | *P=0.878* |

*Some subjects dropped from adjusted analyses due to missingness in BMI and smoking fields. Total missing makes up <1%.

**Table 4.** Unadjusted and adjusted hazard of recurrent clot by location of incident clot, by idiopathic status.

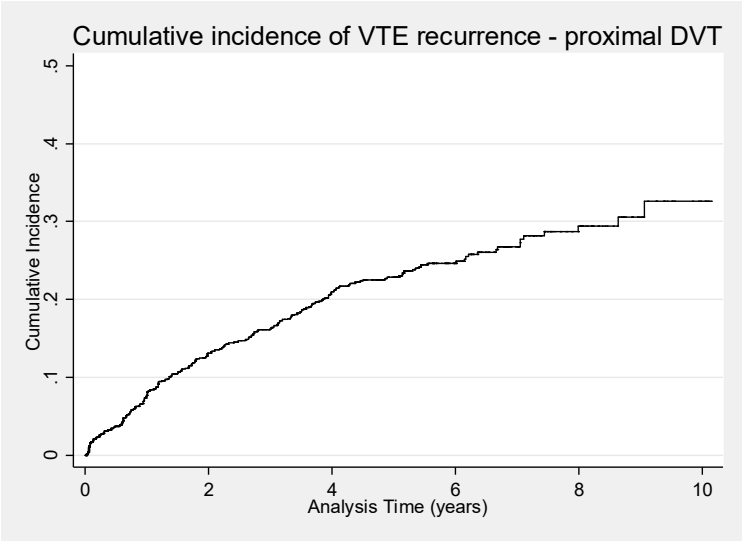
| | HR (95% CI), Unadjusted | | | | HR (95% CI), adjusted for age, sex, BMI*, race, smoking* | | | |
|---|---|---|---|---|---|---|---|---|
| Stratified Analyses | Proximal DVT without PE (reference) | Distal DVT without PE | Unknown DVT Location without PE | PE | Proximal DVT without PE (reference) | Distal DVT without PE | Unknown DVT Location without PE | PE |
| Unprovoked incident VTE | *132/189* | *12/81* | *4/20* | *114/426* | *132/189* | *12/81* | *4/20* | *114/426* |
| | ***1.00 (ref)*** | 0.38 (0.21-0.68) | *1.27 (0.45-3.59)* | 0.66 (0.51-0.84) | ***1.00 (ref)*** | 0.35 (0.19-0.63) | 0.93 (0.31-2.71) | 0.65 (0.51-0.84) |
| | | *p<0.001* | *P=0.656* | *p<0.001* | | *p<0.001* | *p=0.884* | *p<0.001* |
| Provoked incident VTE | *32/527* | *9/113* | *8/43* | *49/710* | *32/523* | *9/113* | *8/43* | *49/708* |
| | ***1.00 (ref)*** | 0.56 (0.27-1.18) | *0.86 (0.42-1.76)* | 0.65 (0.41-1.01) | ***1.00 (ref)*** | 0.57 (0.27-1.21) | 0.86 (0.42-1.76) | 0.60 (0.38-0.94) |
| | | *p=0.128* | *P=0.685* | *p=0.056* | | *p=0.140* | *p=0.677* | *p=0.026* |
| Cancer-related incident VTE | *43/220* | *6/38* | *5/35* | *34/341* | *43/220* | *6/38* | *5/35* | *34/340* |
| | ***1.00 (ref)*** | 0.64 (0.27-1.51) | *1.30 (0.51-3.30)* | 0.55 (0.35-0.86) | ***1.00 (ref)*** | 0.68 (0.29-1.62) | 1.18 (0.45-3.09) | 0.55 (0.35-0.86) |
| | | *p=0.308* | *p=0.583* | *p=0.009* | | *p=0.387* | *p=0.744* | *p=0.010* |

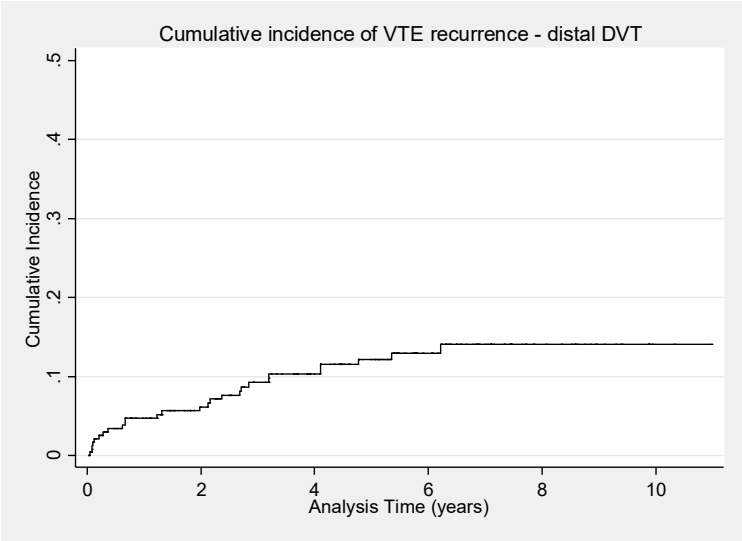
*Some subjects dropped from adjusted analyses due to missingness in BMI and smoking fields. Total missing makes up <1%.

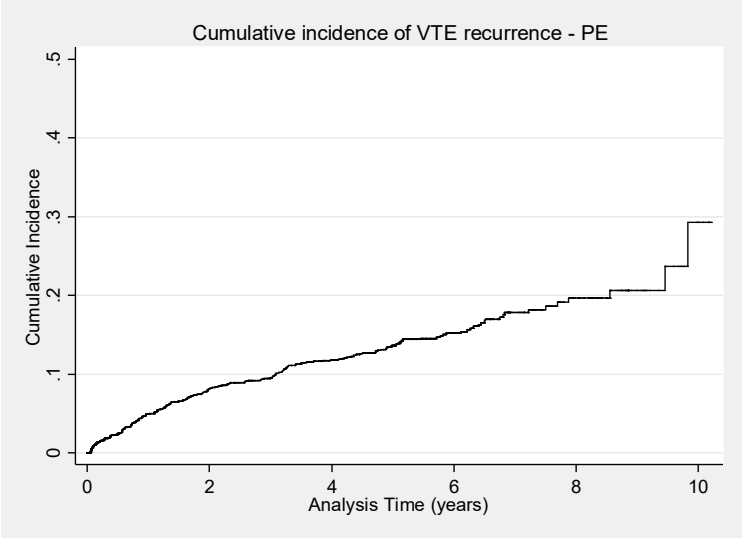
**Table 5.** Hazard of VTE recurrence by incident clot location

| HR (95% CI), adjusted for age, sex, BMI, race, smoking* | | | | | |
|---|---|---|---|---|---|
| Proximal DVT (without PE) (reference) | Distal DVT (without PE) | Unknown DVT site (without PE) | Proximal DVT with PE | Distal DVT with PE | Unknown DVT Location (with PE) |
| 207/924 | 27/231 | *17/97* | 57/317 | *10/78* | 16/108 |
| ***1.00 (ref)*** | 0.44 (0.29-0.66) | 1.03 (0.63-1.71) | 0.82 (0.61-1.10) | 0.48 (0.25-0.90) | 0.89 (0.53-1.49) |
| | *p<0.001* | *p=0.878* | *p=0.178* | *p<0.023* | p=0.656 |

*Some subjects dropped from adjusted analyses due to missingness in BMI and smoking fields. Total missing makes up <1%.




**Figures 1-3.** Cumulative incidence plots of cumulative incidence of VTE recurrence over time, by incident clot location.

## D**iscussion**

Our analyses used prospectively documented, population-based cohort data to evaluate the relationship between incident clot location and risk of recurrence. Participants with incident proximal DVT, who did not experience a PE as part of the incident event, were at a greater risk of recurrent VTE than other incident clot location-based groups with which they were compared. The relative risk of recurrence was less than half among subjects with distal incident clots when compared with those with proximal incident clots. When compared with the group with proximal incident DVT, subjects with PE (with or without concomitant DVT) also had a lower risk of recurrence. When assessing VTE recurrence by location and idiopathic subgroups, we observed heterogeneity of recurrence rates across subgroups, however, we were unable to detect any effect modification by etiology of incident event, possibly due to insufficient statistical power.

### *Strengths and Limitations*

Our study benefitted from high-quality objective data prospectively documented by medical professionals and later extracted for the HVH study by trained data abstractors. Our analyses were well-powered for our primary analyses and missingness was low due to complete data collection by the HVH chart abstractors. This population-based cohort included nearly all VTE events among GHC members during the inception period, including those that were cancer-related and both unprovoked and provoked. To maximize generalizability, we applied few exclusions.

A limitation to our analyses was the large proportion of the study population that was without documentation of incident DVT location. Approximately 35% of our population had record of a PE event only, and thus no information on the DVT that was the source of the PE. Also, we are

unable to account for all possible confounders that may exist due to risk factor differentially associated with distal and proximal incident clots. For example, individual behavior of subjects such as sedentary occupations, that may impact the location and recurrence of an incident clot.

*Clinical Relevance*

Our analyses of population-based data generally agree with existing literature, which indicates that risk differs by clot location among those without a PE. Including incident clot location as a factor in recurrence risk-scales may improve the ability of these scales to determine appropriate course and duration of treatment for individuals who have had an incident VTE.

*Recommendations*

Future analyses may seek to further validate existing risk-scoring systems as well as look more closely at some associations we detected in our analyses. Specifically, it may be useful to further examine recurrence risk variance within the cancer-related subgroup, as the recurrence rate estimate was much higher among this group. Also, further characterization of the PE group would be valuable in understanding why their recurrence risk was less than that of the reference group, a finding that we had not anticipated.

**Summary**

Our analyses of a population-based sample of incident VTE provide evidence that those with incident clots in a distal location as well as those with PE are at a lesser risk of recurrence compared with those with incident clots in a proximal location. This finding held even after

adjusting the way groups were defined. Incident clot location may be a valuable marker for recurrence risk and should be considered for use in future risk-assessment models.

**Supplemental Figure 1.** Adapted from *Risk of Recurrent Venous Thromboembolism After an Initial Episode : Risk Stratification and Implications for Long-term Treatment* Agrawal & Kim, 2019

| Scoring system | Risk factor/criteria | Interpretation/outcome |
|---|---|---|
| HERDOO2 scoring system | 1. Female gender (pre-requisite)<br>2. Post-thrombotic syndrome—1<br>a. Hyperpigmentation<br>b. Edema<br>c. Redness of leg<br>3. D-dimer ≥ 250 μg/ml on anticoagulation—1<br>4. Obesity BMI ≥ 30–1<br>5. Old age (age ≥ 65)—1 | Identify low-risk females with score of 0 or 1 that may discontinue anticoagulation after 6 months |
| Vienna prediction model | 1. Gender (male—higher risk)<br>2. Type of VTE (PE > proximal DVT > distal DVT—risk of recurrence)<br>3. D-dimer after discontinuation of AC (higher value = higher risk) | Nomogram calculator—https://cemsiis.meduniwien.ac.at/en/kb/science-research/software/clinical-software/recurrent-vte/ |
| DASH score | 1. D-dimer abnormal—2<br>2. Age < 50–1<br>3. Sex/gender—male 1<br>4. Hormone-associated—(− 2) | Quantitative risk assessment based on score—< 5% recurrence risk for scores ≤ 1 |

*VTE* venous thromboembolism, *DVT* deep vein thrombosis, *PE* pulmonary embolus

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