Survival assessment of warfarin and international normalized ratio exposure in cancer-associated venous thromboembolism: Veterans Affairs healthcare system-based analysis

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Abstract

Venous thromboembolism (VTE) is a common complication among patients with cancer. While randomized clinical trials have established the safety and efficacy of direct oral anticoagulants (DOAC) and low-molecular-weight heparin (LMWH) relative to warfarin for the treatment of cancer-associated thrombosis, emerging evidence suggests that warfarin may be associated with improved overall survival in patients with malignancy. We evaluated survival outcomes among patients with cancer and VTE treated with warfarin compared with other anticoagulants within the Veterans Affairs (VA) Healthcare System and analyzed the association of international normalized ratio (INR) exposure and overall survival. Among 12,298 propensity-matched patients (mean age 69 years; 97% men), warfarin use was associated with a 16% lower risk of mortality compared with other anticoagulants (hazard ratio [HR]=0.84; 95% confidence interval [CI]: 0.80-0.88; P<0.001). Median survival was 1,457 days in the warfarin group *versus* 1,045 days in the non-warfarin group. Survival benefits were consistent across subgroups defined by tumor type, stage, and demographic characteristics. In landmark analyses, the greatest benefit was observed with extended periods in the INR range of 2.5 to 3.0 (HR=0.81; 95% CI: 0.75-0.87). In this population-based cohort study of patients with cancer and VTE, warfarin use was associated with improved survival compared with other anticoagulants. The greatest benefit was observed among patients who maintained an INR between 2.5 and 3.0.

Introduction

Venous thromboembolism (VTE) is a serious and potentially life-threatening condition that poses a significant risk to cancer patients due to the hypercoagulable state induced by malignancy.[1,2] VTE stands as the second leading cause of death in cancer patients.[3,4] Given this significant burden, effective management of cancer associated VTE is crucial. A pivotal clinical trial comparing low molecular weight heparin (LMWH) to warfarin demonstrated a lower risk of recurrent VTE with LMWH; however no survival advantage was observed.[5] The lack of survival benefit with LMWH was attributed to the potential underpowering of these trials to detect small but clinically meaningful reductions in fatal VTE events.

We previously evaluated whether a survival benefit could be observed in larger cohorts. We performed analyses of population-based studies utilizing data from Surveillance, Epidemiology, and End Results (SEER) - Medicare Linked database. Unexpectedly, we observed warfarin use was associated with improved overall survival compared with LMWH or direct oral anticoagulant (DOAC) for the treatment of cancer-associated VTE.[6,7] This novel finding was

consistent across every subgroup including stage, different cancer sites, age, year of diagnosis, and comorbidity burden. These findings lead to an interesting hypothesis that warfarin may provide overall survival advantage over LMWH or DOAC, independent of anticoagulation effectiveness. This survival advantage may be mediated by modification of cancer biology, consistent with multiple preclinical models that have demonstrated that warfarin has anti-neoplastic effects.[8-10] Taken at face value, these could be considered practice changing. The reticent reception of these findings is understandable with a critique being that these observations may be an idiosyncrasy related to the SEER-Medicare database. As such, we sought to explore survival outcomes among patients within the Veterans Affairs (VA) Healthcare System who received warfarin *versus* alternative anticoagulant for the treatment of cancer-associated thrombosis. The VA is the largest integrated health network in the US, consisting of 171 medical centers and 1,113 outpatient clinics. An advantage of the VA database relative to SEER is that it is not limited to a cancer registry but is linked to comprehensive electronic health record (EHR) data, including laboratory results and prescription records. This integration enables a more detailed analysis of the relationship between warfarin dose-intensity - measured by INR levels - and survival outcomes. Based on prior SEER-Medicare findings and preclinical evidence, we hypothesized that warfarin use would be associated with improved overall survival compared with DOAC or LMWH, with the greatest benefit observed among patients who maintained INR values in the higher therapeutic range. While both datasets include cases through 2021, the VA's complete EHR infrastructure allows for a more granular assessment of treatment patterns and longitudinal patient follow-up.

Methods

Study design and cohort selection

We conducted a retrospective cohort study of adult patients receiving care within the VA Healthcare System. The VA's comprehensive infrastructure ensures patients have continuous oncologic care and robust longitudinal follow-up. This study was approved by the VA Boston Research and Development committee as an exempt study before data collection and analysis, with a waiver of informed consent due to the use of existing data, per the Common Rule.

Data standardization and variable extraction were performed as previously described (see *Online Supplementary Appendix*).[11,12] VTE was defined as radiographically confirmed symptomatic or incidental pulmonary embolism (PE), proximal or distal lower extremity deep vein thrombosis (LE-DVT), or upper extremity deep vein thrombosis (UE-DVT).[13] Patients with a diagnosis of both cancer and VTE between 2006 and 2021 were eligible for inclusion. Exclusion criteria included lack of follow-up or survival data beyond 30 days post-VTE diagnosis, absence of an anticoagulation prescription within 30 days of the VTE diagnosis, anticoagulation prescription issued more than 30 days prior to VTE, and missing co-variate data. Patients were classified as receiving warfarin if they filled a prescription for warfarin within 30 days of VTE diagnosis and, and as non-warfarin if they filled prescription for non-warfarin anticoagulants (DOAC, LMWH, or direct thrombin inhibitor) in the same window. Cohorts were based on initial qualification on an intention-to-treat basis. Renal failure and liver disease were defined using the Charlson Comorbidity Index via the comorbidity R package. Briefly, the algorithm maps ICD-9 or ICD-10 diagnosis codes to predefined comorbidity categories (e.g., myocardial infarction, diabetes, renal disease, liver disease). In our analysis, we used ICD codes recorded within the 3 years prior to the cancer diagnosis date. Prescription data were captured from the same national pharmacy database for both groups, ensure comparable ascertainment. Similarly, cancer diagnoses were obtained from the VA Cancer Registry and VTE diagnosis from imaging reports for all patients, regardless of treatment group, ensuring uniform outcome definitions and measurement methods. Mortality was captured via death certificate from the National Death Index and linked to VA patient identifiers using the VA Mortality Data Repository. Study size was determined by the total number of eligible VA patients with cancer and VTE during 2006-2021; no apriori sample size calculation was performed given the retrospective design.

Propensity matching

To compare outcomes between patients treated with warfarin and those who were not, we utilized a propensity-score matched retrospective cohort design. A propensity score was generated using a multivariable logistic regression model, incorporating the following co-variates: cancer type, cancer stage, age at VTE diagnosis, sex, race, body mass index (BMI), rurality, time from cancer diagnosis to VTE event, Charlson Comorbidity Index,[14] and VTE type. We used a multivariable logistic regression to estimate the PS and to perform 1:1 nearest matching using a caliper of 0.1 of the propensity score logit.[15] Ultimately, 6,149 patients treated with warfarin were matched to 6,149 patients treated with non-warfarin anticoagulants.

Statistical analysis

Overall survival was compared between warfarin users and non-users in the matched cohort using Cox proportional hazards regression. The predefined INR categories were <1.5, 1.5-2, 2-2.5, 2.5-3, 3-3.5, and >3.5. INR cut points were selected based on established therapeutic ranges with subcategories reflecting clinical convention. For each landmark time, we calculated the cumulative time spent in each INR category, expressed in 90-day increments. See the *Online Supplementary Appendix* for additional methodologic details.

Results

Cohort selection

Between 2006 and 2021, a total of 42,232 adult patients with both cancer and a VTE diagnosis were identified within the VA healthcare system. After applying exclusion criteria (Figure 1), the final cohort consisted of 17,728 patients. These patients were stratified into two cohorts based on their anticoagulation treatment: 10,858 patients were included in the non-warfarin cohort, while 6,880 patients received warfarin within 30 days of their VTE diagnosis. The index date was the initial prescription date of the anticoagulation treatment. Prior to matching, we identified 9,911 patients in the non-warfarin group and 6,222 in the warfarin group with complete data, while 947 and 525, respectively, were excluded due to missing co-variates (*Online Supplementary Table S1*). After propensity score matching on cancer type, cancer stage, age at VTE diagnosis, sex, race, BMI, rurality, time from cancer diagnosis to VTE event, comorbidity score, and VTE type, a total of 6,149 patients were included in both the warfarin and non-warfarin cohorts (*Online Supplementary Figures S1* and *S2*). These variables were selected as potential confounders because they are established determinants of both anticoagulant selection and overall survival in patients with cancer-associated VTE. Among the non-warfarin cohort, 42.4% received direct oral anticoagulants (DOAC), 56.4% were treated with low-molecular-weight heparin (LMWH), and 1.2% received direct thrombin inhibitors (DTI).

Baseline characteristics

The demographic and clinical characteristics of the patients were similar in the two groups, with standardized mean differences (SMD) less than 0.1 for all matched variables (Table 1; *Online Supplementary Figure S1*). The most common cancer types in both cohorts were prostate (33.0% *vs*. 33.9%, respectively), lung (15.0% *vs*. 15.3%), and gastrointestinal cancers (16.1% *vs*. 15.2%). The mean age at the time of VTE diagnosis was 69 years (±9.3 in the non-warfarin cohort and ±9.7 in the warfarin cohort). Sex distribution was predominantly male in both cohorts (97.0% *vs*. 96.9%, respectively). The racial composition was largely White (74.1% in non-warfarin *vs*. 73.6% in warfarin cohorts). Time from cancer diagnosis to VTE and comorbidity scores were also similar between the groups. And many of the patients had acute pulmonary embolism (46.5% in the non-warfarin cohort *vs*. 45.3% in the warfarin cohort).

Primary outcome

The survival analysis (Figure 2) demonstrates that patients treated with warfarin experienced a significantly greater survival probability compared to those not treated with warfarin. The hazard ratio (HR) for the warfarin group of 0.84 (95% confidence interval [CI]: 0.80-0.88), indicating a 16% risk reduction in the risk of death (P<0.001). The median survival time was 1,457 days for the warfarin cohort, compared to 1,045 days for the non-warfarin cohort. In landmark analyses for patients surviving at least 60 or

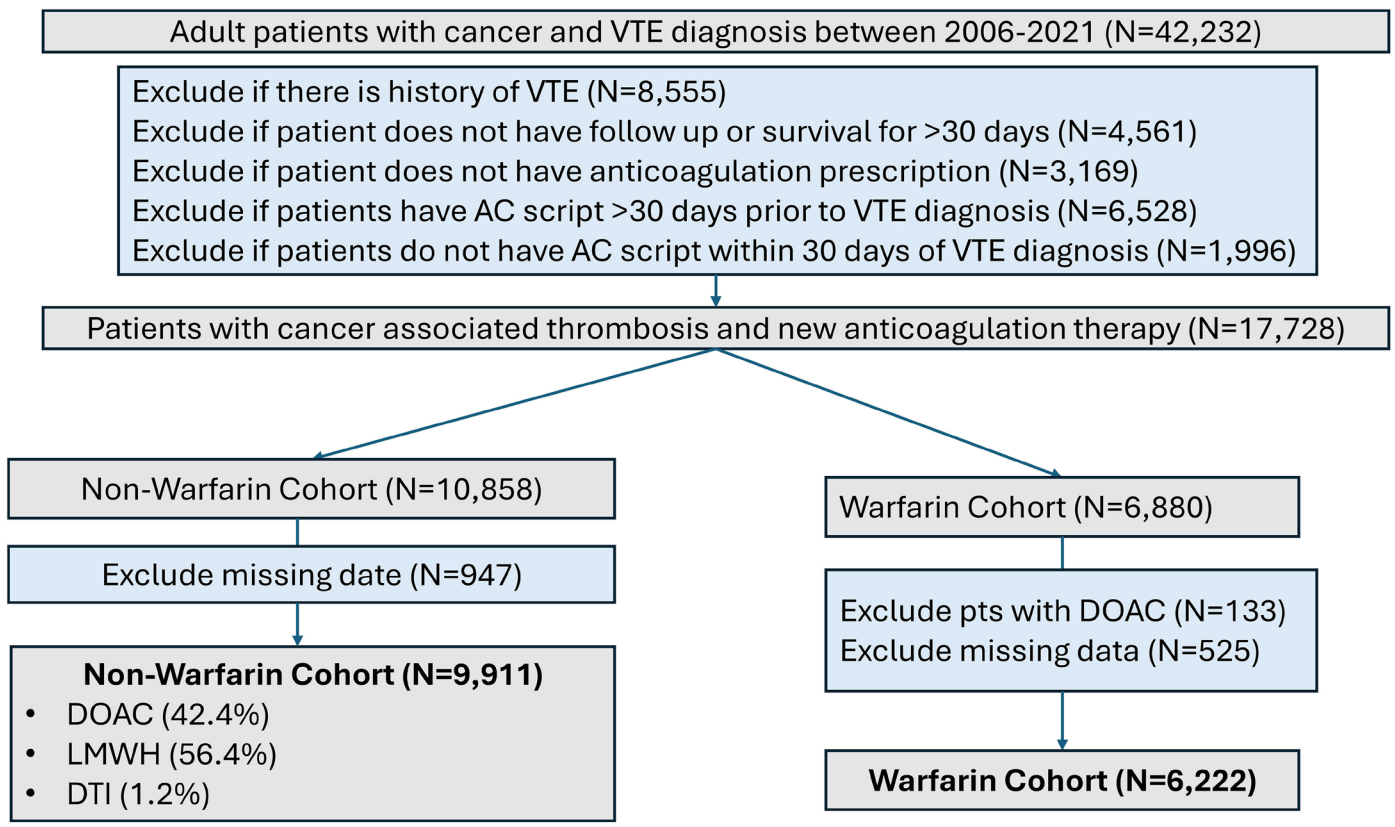


Figure 1. Patient selection and exclusion in cohort selection. A total of 42,232 individuals with a venous thromboembolism (VTE) diagnosis between 2006 and 2021 were identified from the cancer registry. After the application of exclusion criteria, the final cohort consistent of 17,729 individuals. This cohort was divided into the non-warfarin or warfarin cohort based on the type of anticoagulation used within the first 30 days of VTE diagnosis. AC: anticoagulation; DOAC: direct oral anticoagulation; LMWH: low molecular weight heparin; DTI: direct thrombin inhibitor.

90-days post VTE, differences in survival remained apparent (*Online Supplementary Figure S3*).

Subgroup analysis

To explore the heterogeneity of warfarin's effect on overall survival, we conducted a comprehensive subgroup analysis (Figure 3), stratified by cancer type, stage, year range, and VTE subtype. This analysis revealed important insights into the populations most likely to benefit from warfarin therapy.

Prostate cancer patients (N=4,114) had the most pronounced benefit from warfarin, with a HR of 0.73 (95% CI: 0.67-0.81). Gastrointestinal cancer patients (N=1,921) also showed improved survival (HR=0.83; 95% CI: 0.75-0.92). However, no significant effect was observed in lung cancer (N=1,860) (HR=0.92; 95% CI: 0.83-1.03) or hematologic malignancies (N=1,174) (HR=0.98; 95% CI: 0.84-1.14).

Warfarin associated survival benefit for patients with early-stage cancer (N=8,561) (HR= 0.87; 95% CI: 0.82-0.93) rather than advanced-stage cancer (N=1,949) (HR=0.96; 95% CI: 0.86-1.06). The survival benefit of warfarin was observed in both earlier cohort entailing 2006 through 2013 (N=5,642) with a HR of 0.67 (95% CI: 0.63-0.72), as well as more contemporary cohort between 2014 and 2021 (N=6,656) with a HR of 0.82 (95% CI: 0.76-0.88). Survival improvement was noted even when restricting enrollment to patients who survived at least 60 or 90 days following VTE (*Online Supplementary Figure S3*).

Landmark analysis of international normalized ratio status and survival

To evaluate the potential impact of warfarin dosing on long-term survival, we conducted a landmark analysis of survival outcomes across different INR ranges (<1.5, 1.5-2.0, 2-2.5, 2.5-3.0, 3.0-3.5, and >3.5) among patients actively prescribed warfarin. INR measurements were validated by confirming concurrent warfarin prescriptions, with no prescription lapse exceeding 90 days at the time of INR sampling. The analysis was performed at 1-year, 3-year, and 5-year after VTE diagnosis to evaluate the association between INR status and survival over time.

Our findings demonstrated that patients maintaining a therapeutic INR range of 2.5-3 experienced the most favorable survival outcomes (Table 2). At 1 year, every 90 days spent in the INR 2.5-3 range was associated with a HR of 0.81 (95% CI: 0.75-0.87), indicating a significant survival benefit. This survival advantage persisted at 3 years (HR=0.89; 95% CI: 0.84-0.94) and 5 years (HR=0.94, 95% CI: 0.89-1.00).

In contrast, patients with INR levels between 2-2.5 showed no substantial survival benefit, with HR of 0.96 (95% CI: 0.91-1.01) at 1 year, 0.99 (95% CI: 0.95-1.03) at 3 years, and 0.99 (95% CI: 0.95-1.03) at 5 years. Notably, INR values falling below 2 or exceeding 3 were associated with worse survival outcomes.

Table 1. Demographic and clinical characteristics of study cohort at baseline after propensity score matching.

Characteristics	Non-Warfarin cohort N=6,149	Warfarin cohort N=6,149
Cancer type, N (%)		
Prostate	2,029 (33.0)	2,085 (33.9)
Gastrointestinal	987 (16.1)	934 (15.2)
Lung	921 (15.0)	939 (15.3)
Genitourinary	669 (10.9)	654 (10.6)
Head and neck	352 (5.7)	345 (5.6)
Hepatobiliary	249 (4.0)	255 (4.1)
Lymphoid	245 (4.0)	235 (3.8)
Skin	199 (3.2)	194 (3.2)
Multiple myeloma	172 (2.8)	178 (2.9)
Myeloid malignancy	171 (2.8)	173 (2.8)
Breast	86 (1.4)	88 (1.4)
Brain	49 (0.8)	50 (0.8)
Gynecological	20 (0.3)	19 (0.3)
Cancer stage, N (%)		
Unknown	926 (15.1)	862 (14.0)
1	1,414 (23.0)	1,283 (20.9)
2	1,828 (29.7)	2,201 (35.8)
3	921 (15.0)	914 (14.9)
4	1,060 (17.2)	889 (14.5)
Age at VTE, years, mean (SD)	69 (±9.3)	69 (±9.7)
Sex, N (%)		
Female	182 (3.0)	190 (3.1)
Male	5,967 (97.0)	5,959 (96.9)
Race, N (%)		
White	4,556 (74.1)	4,528 (73.6)
Black Or African American	1,452 (23.6)	1,475 (24.0)
Native Hawaiian or Other Pacific Islander	45 (0.7)	46 (0.7)
Unknown	49 (0.8)	50 (0.8)
American Indian or Alaska Native	41 (0.7)	43 (0.7)
Asian	6 (0.1)	7 (0.1)
BMI, kg/m^2, mean (SD)	31 (±6.2)	31 (±6.5)
Renal failure, N (%)	607 (9.9)	629 (10.2)
Liver disease, N (%)	642 (10.4)	514 (8.4)
Rurality, N (%)		
Highly rural	88 (1.4)	82 (1.3)
Rural	2,015 (32.8)	2,000 (32.5)
Urban	4,046 (65.8)	4,067 (66.1)
Time from cancer diagnosis to VTE, days, mean (SD)	1,100 (±1,300)	1,100 (±1,200)
Comorbidity score, mean (SD)	3.9 (±8.2)	3.9 (±7.6)
VAFI, mean (SD)	0.16 (±0.09)	0.15 (±0.09)
VTE type, N (%)		
Acute LE-DVT	2,261 (36.8)	2,288 (37.2)
Acute PE	2,861 (46.5)	2,785 (45.3)
Acute UE-DVT	1,027 (16.7)	1,076 (17.5)

BMI: body mass index; GI: gastrointestinal; GU: genitourinary; GYN: gynecologic, HBP: hepatobiliary and pancreatic; HN: head and neck; LE-DVT: lower extremity deep vein thrombosis; MM: multiple myeloma; PE: pulmonary embolism; UE-DVT: upper extremity deep vein thrombosis; VAFI: Veterans Affairs frailty index; VTE: venous thromboembolism; SD: standard deviation.

Discussion

The findings of this study contribute to a growing body of literature suggesting that warfarin may offer a survival advantage for cancer patients with VTE when compared to other anticoagulants.[6,7,16] In this large, population-based cohort of patients treated within the VA Healthcare System, we observed that warfarin use was associated with a significant 16% reduction in mortality risk compared to other anticoagulants. The survival advantage persisted even after adjusting for known confounders, such as age, cancer type, stage, and comorbidities.

These findings corroborate the prior unexpected SEER findings.[6,7] Similarly, a prior Finnish study that included over 6,000 men with cancer, use of warfarin was associated with improved survival relative to other anticoagulants.[17] Another population-based study demonstrated a significantly lower incidence of cancer among individuals receiving warfarin compared with non-users (incidence rate ratio 0.84; 95% CI: 0.82-0.86).[16] While our results align with earlier research, this analysis uniquely leverages the VA's extensive and integrated dataset, ensuring comprehensive follow-up and minimizing loss to follow-up - a common limitation in other cohort studies. The VA database has complete individual level medical record and administrative data including demographics, laboratory data, comorbidity burden, and prescription data. This comprehensive dataset allowed us to consider as many confounding variables as possible to build the best model to assess the difference in survival. Similarly, the VA is a single-payer healthcare system which minimizes the likelihood of missing data.

The observed survival benefit of warfarin is particularly striking given the context of modern anticoagulation practices. Contemporary clinical guidelines have increasingly favored DOAC due to their ease of use and established efficacy in preventing VTE recurrence.[18] However, despite these shifts in practice, these findings suggest that vitamin K antagonism may confer additional survival benefits that extend beyond its anticoagulant properties; one proposed mechanism is the inhibition of tumor-specific pathways, such as the Axl receptor tyrosine kinase.[19]

Our landmark analysis further revealed that the survival benefit of warfarin was predominantly observed within the therapeutic INR range of 2.0-3.0, with a more pronounced benefit in the higher sub-range of 2.5-3.0 compared to the lower range of 2.0-2.5. For every 30 days spent within the

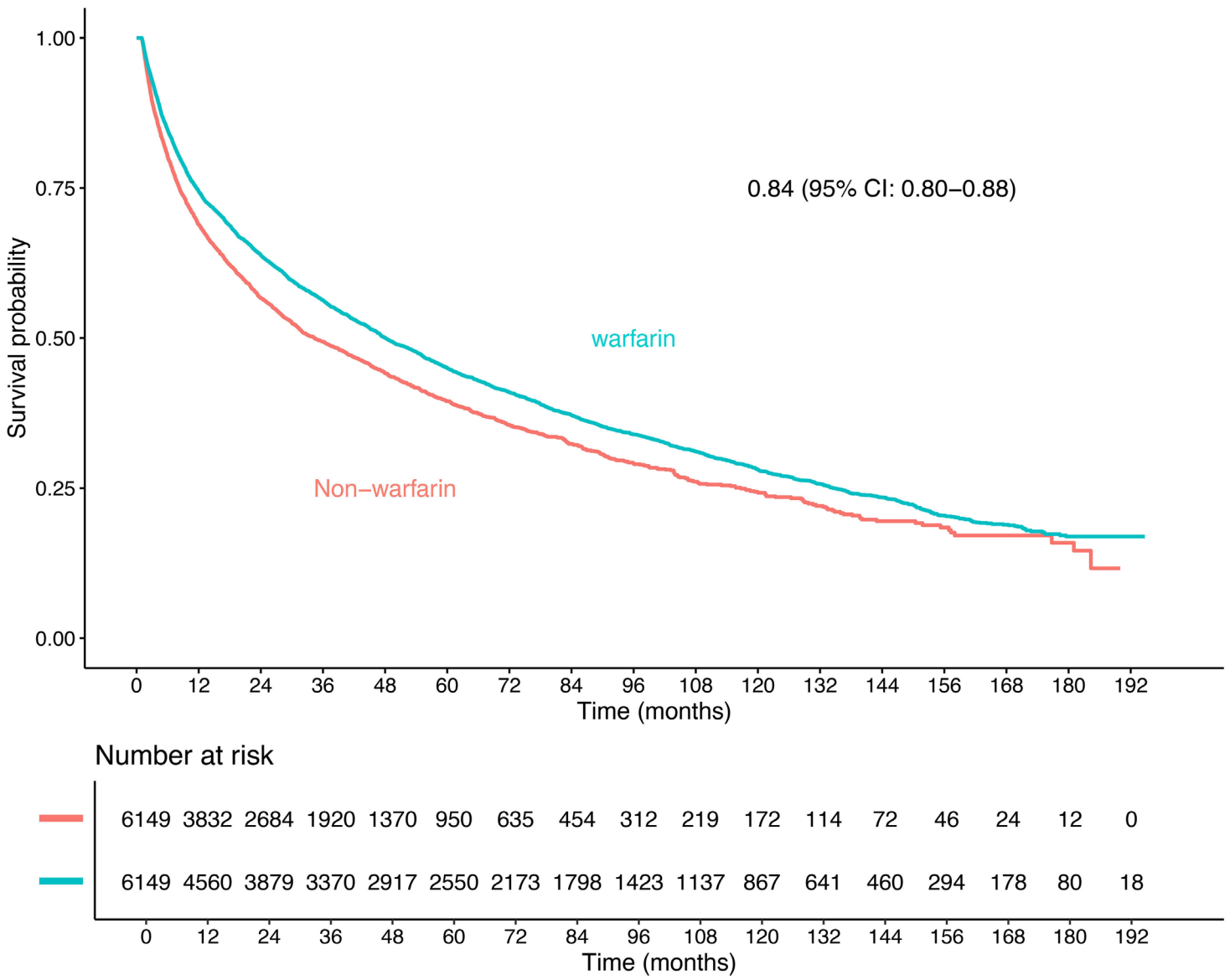


Figure 2. Overall survival of warfarin compared to the non-warfarin in the matched cohort. Hazard ratios, confidence intervals (CI), and *P* values were derived from Cox proportional hazard ratio with bootstrapping with 1,000 iterations (N=12,298). Median survival for the non-warfarin cohort was 1,045 days and the median survival for warfarin cohort was 1,457 days.

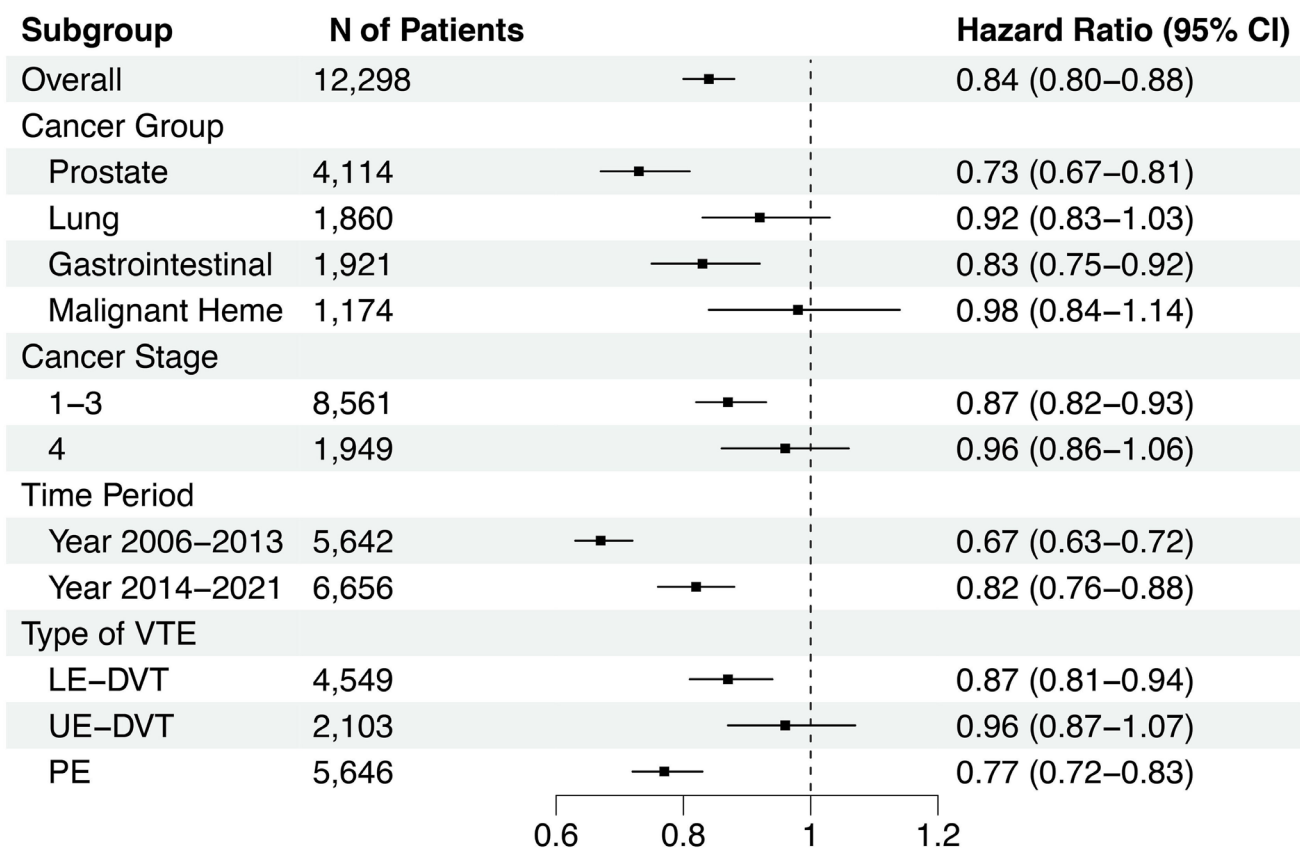


Figure 3. Subgroups analysis of overall survival. A cox proportional hazard ratio with bootstrapping was used to estimate the overall survival between the warfarin cohort and the non-warfarin cohort, across the largest cancer subtypes and cancer stages. Malignant Heme cohort comprised of multiple myeloma, lymphoid malignancies, and myeloid malignancies. CI: confidence interval; VTE: venous thromboembolism; LE-DVT: lower extremity deep vein thrombosis; PE: pulmonary embolism; UE-DVT: upper extremity deep vein thrombosis.

INR range of 2.5-3.0 in year 1, there was an approximate 20% improvement in overall survival at year 1, an effect that persisted up to 3 years later. This finding suggests a dose-dependent association with survival within the therapeutic INR window. Although it could be argued that the observed survival advantage is primarily due to enhanced anticoagulation and reduced thrombotic events, previous studies have reported similar risks of ischemic stroke or recurrent VTE across therapeutic 2.0 to 3.0 INR values.[20-22] Notably, there is an apparent survival benefit in non-cancer patients within a lower therapeutic INR (between 2-2.5) compared with higher therapeutic INR as observed in our cancer cohort.[20] Preclinical studies have provided further support for this hypothesis by demonstrating anti-neoplastic effects of warfarin, offering a plausible biological explanation for our findings.[8-10] In a prior randomized trial conducted in the 1970's at the VA, 431 patients with various tumors and stages including lung, prostate, colorectal, and head and neck cancer were randomized to warfarin or no anticoagulant.[23] The mean prothrombin time for the treated cohort was 17.6 seconds compared with 11.6 seconds in the control cohort which translates to an approximate mean INR of 1.5 in the therapeutic arm. In that study there was an improvement in overall survival in the subgroup of patients with small cell carcinoma treated with warfarin but not the other malignancies; an effect likely impacted not only by INR intensity but heterogeneity of cohorts including diagnoses, stage at enrollment and duration of treatment.

Table 2. Landmark analysis of international normalized ratio ranges and survival outcomes in warfarin-treated cancer patients.

INR range	1 year (95% CI)	3 year HR (95% CI)	5 year HR (95% CI)
<1.5	1.06 (1.01-1.10)	1.07 (1.02-1.12)	1.07 (1.00-1.13)
1.5-2	1.09 (1.01-1.18)	1.20 (1.13-1.27)	1.15 (1.09-1.21)
2-2.5	0.96 (0.91-1.01)	0.99 (0.95-1.03)	0.99 (0.95-1.03)
2.5-3	0.81 (0.75-0.87)	0.89 (0.84-0.94)	0.94 (0.89-1.00)
3-3.5	0.99 (0.89-1.11)	1.08 (0.98-1.19)	0.99 (0.89-1.10)
>3.5	1.19 (1.06-1.32)	1.04 (0.98-1.12)	1.00 (0.94-1.06)

The duration for which patients in the warfarin cohort remained in each of the predefined international normalized ratio (INR) categories was calculated, including no warfarin, <1.5, 1.5-2, 2-2.5, 2.5-3, 3-3.5, and >3.5. Landmark analyses were performed with index dates set at 1, 3, and 5 years after completion of anticoagulation treatment, and survival analysis was conducted using Cox proportional hazards regression models to evaluate the association between INR control and long-term survival outcomes. CI: confidence interval; HR: hazard ratio.

While our study provides strong evidence supporting the use of warfarin, it is not without limitations. The retrospective design inherently carries risks of unmeasured confounding, despite propensity score matching. In particular, confounding by indication is possible given the shift in practice from warfarin to LMWH after clinical trial

data in 2003 showing reduced recurrent VTE. Residual unmeasured confounders (e.g., socioeconomic status, performance status) could have biased results in either direction, though the magnitude is uncertain. While the median VA Frailty Index were similar between the two groups, we do not have data on relative chemotherapy intensity or palliative intent status of the patients. To address the issue of immortal time bias (i.e., patients needed to survive PE and transition to warfarin) inclusion mandated survival of at least 30 days as well as landmark analyses at 60 and 90 days post incident VTE (*Online Supplementary Figure S3*). The VA population is 97% male and older (age ~70 years), potentially limiting generalizability to broader cancer populations. Improved survival was apparent between INR ranges of 2.5-3.0 but we cannot exclude the possibility that improved INR control was due to improved health status rather than a causal effect. We also do not have information regarding cause-specific death to determine whether the measured survival advantage was due to a reduction in cardiovascular outcomes rather than cancer progression. And although we have access to prescription filling data, we cannot confirm that the patient was adherent to the anticoagulation medications which could be considered in the subgroup of patients with worse outcomes and subtherapeutic INR. Future prospective studies are warranted to confirm these findings and to elucidate the mechanisms underlying the potential anti-cancer effects of warfarin.

In conclusion, what was initially considered an observation is further bolstered by this analysis of outcomes within the VA Healthcare System indicating a significant survival advantage for warfarin over other anticoagulants in cancer-associated VTE. These findings highlight the potential for warfarin as a dual-purpose antithrombotic, both as an anticoagulant and a potential disease modifier. Considering the risk of thrombosis in patients with cancer receiving chemotherapy and observed survival benefit, the next step would be randomized trial of primary prophylaxis with warfarin that is powered for survival.

Disclosures

JIZ discloses data safety monitoring boards at Sanofi and CSL Behring; consultancy for Perceptive, Incyte, Bristol Myers Squibb (BMS), Regeneron, and Novartis. RP discloses consultancy for Merck Research, and Sanofi; travel honoraria from Octapharma. All other authors have no conflicts of interest to disclose.

Contributions

Study designed by JIZ, JR, JL, RP, and NF. Data analyses and interpretation by all authors. Manuscript authored by JR, JL, RP, NF, and JIZ. All authors had full access to all study data and take full responsibility for the accuracy of the data and full authority over submission preparation and submission.

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Data-sharing statement

Due to US Department of Veterans Affairs (VA) regulations and our ethics agreements, the analytic datasets used for this study are not permitted to leave the VA firewall without a Data Use Agreement. This limitation is consistent with other studies based on VA data. However, VA data are made freely available to researchers with an approved VA study protocol. For more information, please visit https://www.virec.research.va.gov or contact the VA Information Resource Center at VIReC@va.gov.

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