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Late Venous Thromboembolism in Survivors of Adolescent and Young Adult Cancer: A Population-Based Study in California

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abstract

Introduction—Venous thromboembolism (VTE), a common complication in cancer patients, occurs more often during the initial phase of treatment. However, information on VTE beyond the first two years after diagnosis ('late VTE') is scarce, particularly in young survivors.

Methods—We examined the risk of, and factors associated with, late VTE among adolescents and young adults (AYA, 15–39 years) diagnosed with cancer (2006–2018) who survived ≥2 years. Data were obtained from the California Cancer Registry linked to hospitalization, emergency department and ambulatory surgery data. We used non-parametric models and Cox proportional hazard regression for analyses.

Results—Among 59,343 survivors, the 10-year cumulative incidence of VTE was 1.93% (CI 1.80–2.07). The hazard of VTE was higher among those who had active cancer, including progression from lower stages to metastatic disease (Hazard Ratio (HR)=10.41, 95% confidence interval (CI): 8.86–12.22), second primary cancer (HR=2.58, CI:2.01–3.31), or metastatic disease at diagnosis (HR=2.38, CI:1.84–3.09). The hazard of late VTE was increased among survivors who underwent hematopoietic cell transplantation, those who received radiotherapy, had a VTE history, public insurance (vs private) or non-Hispanic Black/African American race/ethnicity (vs non-Hispanic White). Patients with leukemias, lymphomas, sarcoma, melanoma, colorectal, breast, and cervical cancers had a higher VTE risk than those with thyroid cancer.

Conclusions—VTE risk remained elevated ≥2 years following cancer diagnosis in AYA survivors. Active cancer is a significant risk factor for VTE. Future studies might determine if late VTE should prompt evaluation for recurrence or second malignancy, if not already known.

Keywords

Adolescents and young adults; cancer; venous thromboembolism; VTE; second cancer; metastatic disease; recurrence

Introduction

Venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and/or pulmonary embolism (PE), is a common complication and one of the leading causes of death in patients with cancer.[1] It has been estimated that approximately 15% of all patients with cancer will develop a VTE during their lifetime.[2] In the US, 5.3% of cancer patients aged 15–24 years had a VTE event identified in the Pediatric Hospital Information System (PHIS) between 2001 and 2008.[3] In Europe, the risk of VTE has been reported to be 9–15 times higher in patients with a history of cancer compared to the general population.[4,5] A study from the United States (US) reported that 4.1% of hospitalized patients diagnosed with cancer developed VTE.[6]

VTE is associated with impaired quality of life and may delay cancer treatment.[7] Cancer-associated VTE is associated with worse survival than cancer without a VTE occurrence.[8] Studies have shown an increasing incidence of VTE among patients with cancer in the last two decades, with risk being higher among patients receiving chemotherapy and those of non-Hispanic (NH) Black/African American race/ethnicity.[6] A European study compared

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the risk of VTE among individuals with and without cancer during 2006–2007 (median age 41 years). Among patients with cancer, the risk of VTE was higher among younger (≤39 years) vs older patients.[5]

It is well-recognized that the incidence rates of VTE are highest during the first 6 months after a cancer diagnosis and decrease over time, likely a result of higher tumor burden at diagnosis and active therapies (surgery, radiation, systemic therapy).[9,10] However, data on VTE beyond the first two years after diagnosis, when most initial therapy has been completed (hereafter referred to as 'late VTE') in cancer survivors is scarce. In addition, few studies in the United States have evaluated long-term medical outcomes, including VTE, in survivors of AYA cancer, a population with among the greatest number of years of life lost due to cancer. Much of the data on late effects come from childhood cancer studies.[11–13] Therefore, we aimed to evaluate the cumulative incidence of late VTE, and factors associated with its occurrence among adolescents and young adults (AYAs) diagnosed with cancer at ages 15–39 years and who survived ≥2 years after cancer diagnosis.

Methods

Data Source and Study Population

The analyses presented here was conducted as part of the VOICE (Valuing Opinions and Insights from Cancer Experience) Study,[14] a research program designed to increase knowledge of the health problems, health care, and life experiences of AYA cancer survivors. The overall research program comprises several data sources, including the California Cancer Registry (CCR), Utah Cancer Registry, Kaiser Permanente Northern and Southern California, and the North Carolina Cancer Information Population Health Resource. Data for this analysis was provided by the CCR linked to the California Department of Health Care Access and Information (HCAI, formerly the Office of Statewide Health Planning and Development). The CCR is one of the country's largest and most diverse registries by race/ethnicity and socioeconomic status (SES), capturing nearly all patients diagnosed with cancer in California. HCAI encompasses hospitalization, emergency department, and ambulatory surgery visits from over 400 non-federal facilities in California.

We identified all AYAs (15–39 years) diagnosed with primary invasive cancer (except breast, where in situ tumors were also included) in the CCR from 2006 to 2018 who survived ≥2 years after cancer diagnosis. We included 11 common malignancies in AYAs: acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL), melanoma, sarcoma, colorectal cancer (excludes anus cancer), cervical, thyroid, testicular, and breast cancer (invasive and in situ). Topography (anatomic site) and morphology (tumor histology and behavior) were based on the International Classification of Diseases for Oncology, third edition (ICD-O-3),[15] and malignancies were categorized according to Barr et al 2020.[16] Patients without identifiers to link to HCAI (n=8,503) and those with a second cancer within 60 days of diagnosis (n=146) were excluded from the analyses.

The primary outcome was the occurrence of a late VTE ≥2 years after cancer diagnosis. VTE was coded according to International Classification of Diseases, Ninth

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or Tenth Revision, Clinical Modifications (ICD-9-CM/ICD-10-CM) obtained from HCAI (Supplemental Table S1). It was categorized as PE only, PE plus DVT, proximal DVT, distal DVT, lower extremity DVT, or VTE not otherwise specified. Medical visits in the outpatient setting are not captured in HCAI.

VTE occurring prior to the 2-year post-cancer diagnosis landmark (called "History of VTE" for this analysis) was categorized hierarchically as 1) acute VTE event within 2 years after cancer diagnosis or 2) an acute, or history of VTE that was recorded using ICD-9/10 codes documented up to 5 years prior to cancer diagnosis (Supplemental Table S2). Sociodemographic variables were ascertained from the CCR and include age at cancer diagnosis, year of cancer diagnosis, sex, race/ethnicity (NH White, NH Black/African American, Hispanic, NH Asian/Pacific Islander, other/unknown), health insurance (private, public/no insurance, public Medicaid, public Medicare and neighborhood SES[17] (nSES – a combined measure of seven indicators of education, poverty, and unemployment rates at the census block-group level) at time of cancer diagnosis. In the multivariable models, we combined patients with public insurance and no insurance because, in California, patients who receive a cancer diagnosis become eligible for Medicaid.

Clinical variables included initial type(s) of treatment (chemotherapy, radiation, primary surgery, and hematopoietic cell transplant (HCT, classified as 'yes' or 'no/unknown'), cancer stage (based on the American Joint Committee on Cancer classification), and second primary cancer. Additionally, we identified disease progression from lower stages (0–III) to metastatic disease (stage IV) assessed 6 months or later after diagnosis using ICD-9/10 codes from HCAI (Supplemental Table S3). Progression as defined herein also likely encompassed recurrence in those diseases with a high likelihood of initial complete response (e.g., Hodgkin lymphoma, testicular cancer). Because we were not able to ascertain who had a complete response to initial therapy, recurrence cannot be separately defined. Stage classification is not applicable for leukemias. For testicular cancer, stage III is considered distant/metastatic disease. Disease progression and metastatic disease at diagnosis were mutually exclusive, except for patients with NHL, HL, or testicular cancer because these patients often have a complete response to therapy. A case was categorized as having the "presence of active cancer" if there was disease progression, a second primary cancer or metastatic disease at diagnosis (exceptions aforementioned).

Statistical Analysis

Descriptive analyses show the distribution of sociodemographic and clinical characteristics among patients with and without VTE, and the chi-square p-value assessed differences in frequency distribution across all levels of each variable. Patients were followed from 2 years after cancer diagnosis to the VTE date, death, last known contact in the CCR, or end of study (12/31/2020), whichever occurred first. Cumulative incidence between 2–5 years (hereafter referred to as 5-year cumulative incidence) and 2–10 years (hereafter referred to as 10-year cumulative incidence) after cancer diagnosis and associated 95% confidence intervals (CIs) of developing a late VTE were estimated using non-parametric models, accounting for death as a competing risk.[18] To compare cumulative incidence of developing late VTE between patients with and without active cancer (disease progression and second

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cancer), patients with active cancer were matched to 3 patients without active cancer by age at diagnosis (+/− 2 years), year of diagnosis (+/− 2 years), sex, and cancer type. Patients without active cancer also had to be followed for a comparable time from cancer diagnosis to date of progression or second cancer as patients with active cancer. The Gray's test p-value assessed differences in cumulative incidence across the entire study time period.

We used multivariable Cox proportional hazards regression, accounting for death as a competing risk, to investigate the association of late VTE with sociodemographic and clinical factors. All variables in Table 1 were based on prior studies and clinical relevance[19,20] and were evaluated in univariable (Supplemental Table S4) and multivariable analyses. HCT, second primary cancer, and disease progression were analyzed as time-dependent variables. The proportional hazard assumption was tested by using the Schoenfeld Residuals test.[21] Chemotherapy violated the proportional hazard assumption; therefore, it was included as stratification variable in the model. Thyroid cancer was selected as the reference for cancer site as it was the most common cancer and has a 5-year survival in AYAs over 90%. Results are reported as hazard ratio (HR) and corresponding 95% confidence interval (CI). All p-values were two-sided. Results with p-values <0.05 were considered statistically significance. All analyses were conducted using SAS version 9.4 software. This study was approved by the California Committee for the Protection of Human Subjects and Kaiser Permanente Northern California Institutional Review Board under single IRB provisions for the VOICE Study.

Results

Of 59,343 AYA cancer survivors included in the analyses, 64.2% were female and median age at diagnosis was 32 years (Table 1). With a median follow-up of 7.4 years (range 2.0–15.0 after cancer diagnosis), 927 patients (1.6%) developed a late VTE. In univariate analysis, patients who had a late VTE were more likely to have been diagnosed with metastatic disease (16.4%) than patients who did not develop a VTE (7.2%). Compared to patients without a VTE, patients with a VTE were more likely to have had a second primary cancer (11.4% vs 3.9%) or disease progression (49.2% vs 7.6%). Patients with late VTE were also more likely that their non-VTE counterparts to have received chemotherapy (65.5% vs 41.5%), radiation (39.3% vs 30.9%) and HCT (9.7% vs 3.2%), and to have had a history of VTE within 2 years of cancer diagnosis (11.5% vs 1.3%) or before cancer diagnosis (1.9% vs 0.3%). In addition, late VTE were more frequent in AYAs diagnosed with cancer in the earlier period (2006–2011 vs 2012–2018), among AYAs of NH Black/African American or Hispanic race/ethnicity, those who had public/no health insurance at diagnosis and resided in the lowest SES neighborhoods.

The majority of patients with late VTE had PE alone (48%) or PE with DVT (11%) (Figure 1). Overall cumulative incidences at 5- and 10-years were 1.1% and 1.9%, respectively (Table 2). The highest 10-year cumulative incidences were observed among patients with sarcoma and colorectal cancer (4.0% each), leukemias (ALL, 3.8% and AML, 3.3%), and cervical cancer (3.7%). A higher 10-year cumulative incidence of VTE was found among patients with metastatic disease at diagnosis (4.3%) than those diagnosed at lower stages (1.7%). Supplemental Figure S1 compared cumulative incidence curves of patients with

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and without disease progression and second cancer. Patients with a history of VTE within 2 years after diagnosis or 5 years prior to diagnosis (15.7% and 12.5%, respectively) had a 10-year cumulative incidence of VTE higher than those without a prior VTE (1.7%). Among treatment exposures, the highest incidence of late VTE was observed in patients who underwent a HCT (5.5%). Older AYAs (30–39 vs 15–29 years), those of NH Black/African American or Hispanic race/ethnicity (vs NH Whites and NH Asians/ Pacific Islanders), AYAs living in low or middle nSES (vs high) neighborhoods, those with public/no insurance (vs private) had a greater incidence of late VTE. There was no difference in cumulative incidence of VTE by sex.

In a multivariable model, compared to thyroid cancer survivors, higher hazards of late VTE were observed in survivors of ALL (HR=5.7, CI:3.3–10.1), AML (HR=5.6, CI:3.1–9.9), cervical cancer (HR=3.5, CI:2.4–5.0), sarcoma (HR=3.4, CI:2.4–4.9), colorectal (HR=3.1, CI:2.1–4.5), invasive breast cancer (HR=2.3, CI:1.6–3.2), NHL (HR=2.1, CI:1.3–3.3), HL (HR=1.8, CI:1.1–2.9), and melanoma (HR=1.8, CI:1.2–2.6), with no difference for in situ breast and testicular cancer (Figure 2). Among treatment exposures, patients who received a HCT (HR=1.5, CI 1.1–2.0) or radiation (HR=1.3, CI: 1.1–1.5) were more likely to develop a late VTE than those who did not receive each of those treatments, respectively. Metastatic disease at diagnosis (HR=2.4, CI:1.8–3.1), disease progression (HR=10.4, CI:8.9–12.2), second primary cancer (HR=2.6, CI:2.0–3.3), and history of VTE (within 2 years of diagnosis (HR=4.2, CI:3.3–5.3) or prior to cancer diagnosis (HR=7.0, CI:4.1–11.8)) were associated with higher hazards of late VTE. In addition, patients of NH Black/African American (vs NH White, HR=1.4, CI:1.1–1.7) and those with public health insurance (vs private, HR=1.5, CI:1.3–1.7) were more likely to experience a late VTE. No associations were found by age at diagnosis, sex, year of diagnosis, or nSES.

Discussion

Our study is among the first population-based study to consider the risk of late VTE in AYA cancer survivors. While it is well-known that VTE risk is higher during the first 12 months after cancer diagnosis and decreases over time,[9,10] our study extends prior work to describe VTE risk >2 years after cancer diagnosis. Notably, we observed that patients with active cancer (metastatic disease at diagnosis, progression from lower stages to metastatic disease or second primary cancer) had a considerably higher risk of late VTE. Our study also identified factors associated with higher risk of late VTE, including NH Black/African American race/ethnicity, public health insurance, treatment exposures (including HCT), select primary cancer sites, and prior VTE.

A prior history of VTE was a strong predictor of late VTE in AYA cancer patients. The associations were apparent whether the VTE occurred within 2 years after diagnosis or in the 5 years before cancer diagnosis. Our results are consistent with previous reports that found that patients with cancer and a history of VTE prior to cancer diagnosis had a 6–7 fold increased risk of a cancer-associated VTE compared with those without a VTE history.[22–24] We also found that AYAs with presence of active cancer ^{3}2 years after diagnosis had a high risk of late VTE, which may have implications for thromboprophylaxis. For example, the markedly increased risk we found after controlling for sociodemographic and clinical

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factors (HR=10.4), may warrant pharmacological thromboprophylaxis for patients with cancer progression, especially if there was a prior history of cancer-associated thrombosis.

Consistent with prior studies,[25,26] we found that patients who underwent HCT were more likely to develop VTE than those who did not receive this treatment. For example, a single-institution study[25] evaluated the incidence of VTE in patients who underwent allogeneic HCT during 2002–2013. With a median follow-up of 4 years, 8.3% of HCT recipients developed VTE, which was associated with increased non-relapse mortality. Acute and chronic graft-versus-host disease and a prior VTE history were independent risk factors for VTE. Another study examined late incidence of VTE in patients ages ≥18 years who underwent autologous HCT during 1974–2010 for a hematologic malignancy and survived ≥2 years. With a median follow-up of 9.8 years, the cumulative incidence of VTE at 5 years and 10 years after diagnosis was 3.9% and 6.1%, respectively. Survivors of HCT had a 2.6-fold greater risk of developing VTE compared to their siblings.[26] These findings highlight the need for identifying HCT survivors who are at high risk of VTE and may benefit from thromboprophylaxis.

In addition to HCT, we found a higher risk of VTE among patients who received radiation therapy. Although radiation therapy is not generally considered a risk factor for VTE, there have been some reports suggesting prothrombotic effects of radiotherapy.[27] While we were unable to evaluate the influence of chemotherapy in the multivariable model, our study revealed a higher cumulative incidence of late VTE among patients who received chemotherapy, which is consistent with previous studies.[7,28–30] We did not find an association between late VTE and primary surgery, consistent with the concept of surgery being a transient provoking factor.[31]

Our study revealed disparities in late VTE by sociodemographic factors. We found that, compared with NH Whites, NH Blacks/African Americans had a higher risk of late VTE while NH Asians/Pacific Islander survivors had a decreased risk. These findings are consistent with our prior study, also based on CCR data but with all age groups, which revealed racial disparities in incident VTE.[19] Pulmonary embolism emerged as a primary determinant of racial/ethnic disparity. Possible factors associated with a higher risk of VTE among NH Black/African American patients compared with NH Whites patients include a higher level of Factor VIII[32] and lower receipt of thromboprophylaxis among NH Black/African American patients.[33] Whether these factors contributed to the higher risk of late VTE that we observed in NH Black/African American AYA cancer survivors is unknown. As the VOICE Study includes participation by researchers at Kaiser Permanente (which provides health care to over 20% of the California population), it may be possible to examine the contribution of receipt of thromboprophylaxis or other treatments to VTE risk in future analyses.

AYA cancer survivors with public insurance had a higher risk of late VTE than those privately insured. A previous study which evaluated the prevalence of VTE following oncologic surgery found that patients with public insurance, particularly Medicaid, had the highest risk of VTE, followed by uninsured patients and those with Medicare.[34] These disparities may be partially explained by advanced cancer stage at diagnosis[30] and reduced

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access to high-volume/high-quality healthcare, where VTE thromboprophylaxis may be implemented, as well as prompt VTE diagnosis and treatment.[35,36]

Our study used comprehensive cancer registry and hospitalization, emergency department and ambulatory surgery data from the most populous US state, which also has the largest socioeconomic and racial/ethnic diversity among its population. However, we acknowledge several limitations. First, we did not have information on VTE that was diagnosed and treated exclusively in the outpatient setting. Thus, we likely underestimated the incidence of late VTE. Similarly, we could have underestimated the prevalence of active cancer in patients who received second-line therapy in the entirely outpatient setting. Second, we did not have detailed treatment information (drug, dose, duration) or data on thromboprophylaxis. Third, we used ICD-9/10 codes to ascertain VTE. Although some studies suggested inaccuracies in the use of ICD coding for VTE, White et al have shown a high predictive value using an algorithm with more specific codes[37] as we have used here. Likewise, we used ICD-9/10 codes to ascertain disease progression and would miss evidence of progression that was not coded and only present in progress notes.

Conclusions

To our knowledge, this is the first population-based study in the US to show the cumulative incidence and risk factors associated with VTE occurrence beyond initial treatment completion in AYA cancer survivors. Our findings show that active cancer is a strong risk factor for late VTE in long-term cancer survivors. With the possible exception of HCT, other initial therapeutic modalities and risk factors were associated with lower cumulative incidence and hazard of late VTE than active cancer. This suggests that late VTE might prompt assessment for active cancer in those who are not known to have recurrence and/or disease progression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Risk of VTE persists after cancer treatment in adolescents and young adults.
- Hematopoietic cell transplant, prior VTE, and active cancer are VTE risk factors.
- Black race/ethnicity and public insurance are associated with increased VTE risk.
- If not already known, late VTE may prompt second cancer or recurrence evaluation.

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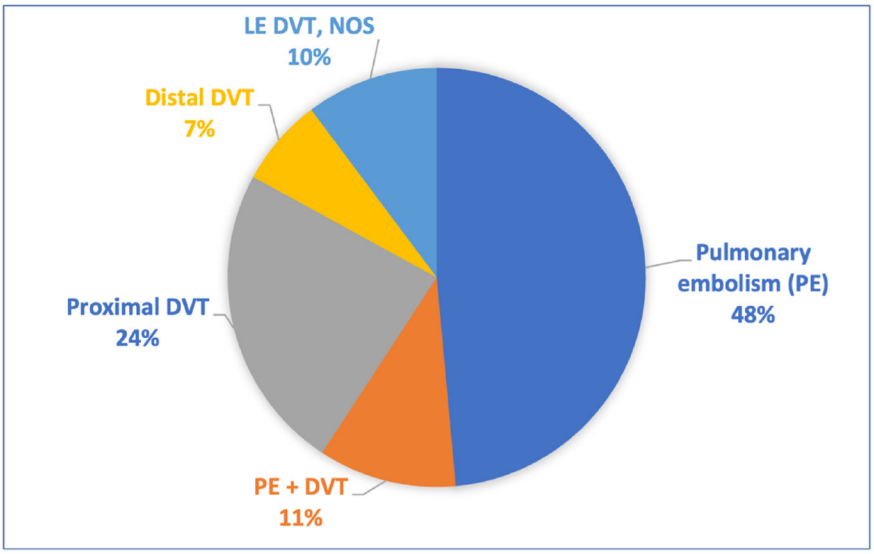

Figure 1.

Distribution of late VTE location in adolescents and young adults diagnosed with cancer during 2006–2018 in California. Abbreviations: DVT, deep venous thrombosis; LE, lower extremity; NOS, not otherwise specified.

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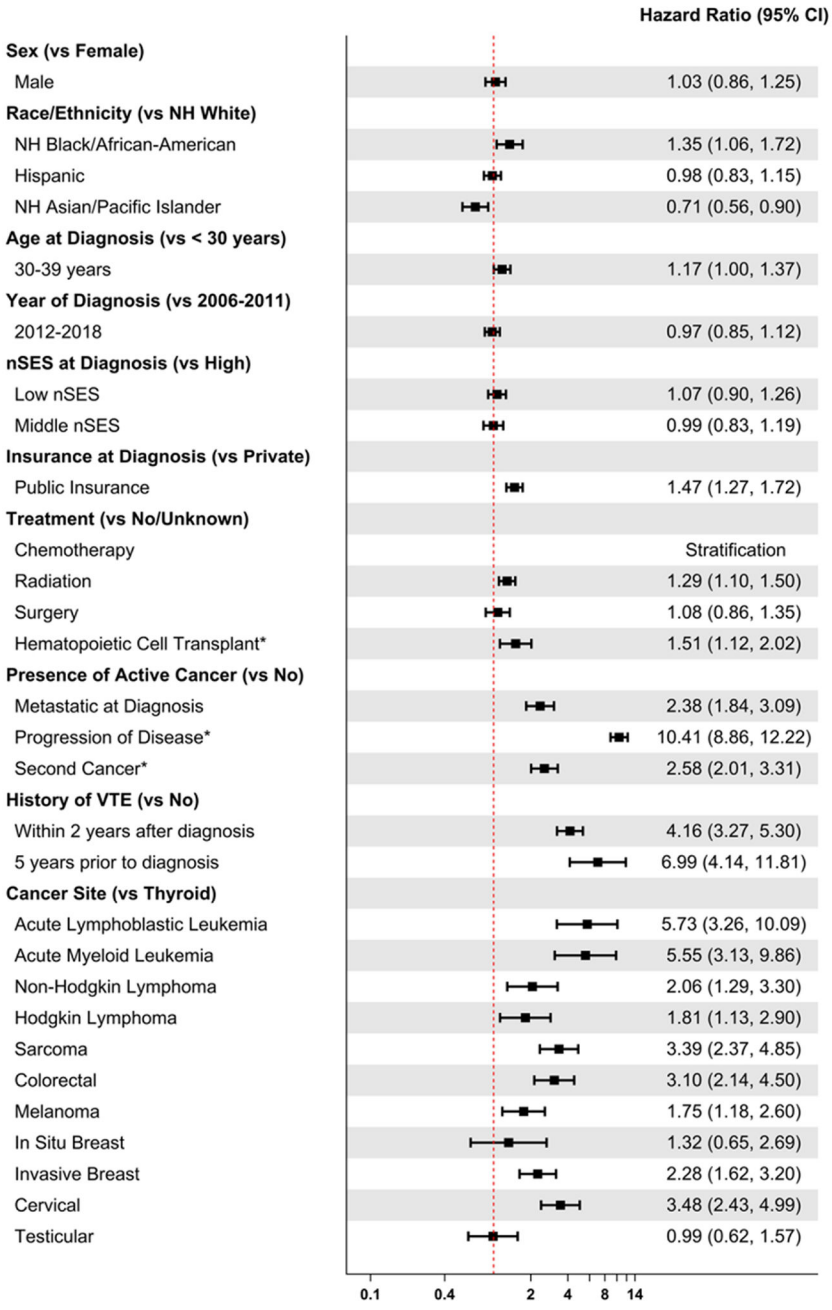

Figure 2.

Relation of venous thromboembolism to sociodemographic and clinical factors among adolescents and young adults with cancer, 2006–2018, California

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Table 1:

Characteristics of adolescents and young adults with cancer in California, by venous thromboembolism status (VTE), 2006–2018

Characteristics	Total cohort N (%)	Acute VTE N (%)	No Acute VTE N (%)	P-value[#]
Total	59343 (100)	927 (1.6)	58416 (98.4)	
Patient Characteristics				
Sex				0.440
Female	38094 (64.2)	584 (63.0)	37510 (64.2)	
Male	21249 (35.8)	343 (37.0)	20906 (35.8)	
Race/ethnicity				<.0001
Non-Hispanic White	28465 (48.0)	399 (43.1)	28066 (48.1)	
Non-Hispanic Black/African American	2849 (4.8)	94 (10.1)	2755 (4.7)	
Hispanic	18745 (31.6)	335 (36.1)	18410 (31.5)	
Non-Hispanic Asian/Pacific Islander	7618 (12.8)	84 (9.1)	7534 (12.9)	
Other/unknown	1666 (2.8)	15 (1.6)	1651 (2.8)	
Age at cancer diagnosis, years				0.160
15–19	3769 (6.4)	52 (5.6)	3717 (6.4)	
20–29	17979 (30.3)	260 (28.1)	17719 (30.3)	
30–39	37595 (63.4)	615 (66.3)	36980 (63.3)	
Year of cancer diagnosis				<.0001
2006–2011	28609 (48.2)	565 (61.0)	28044 (48.0)	
2012–2018	30734 (51.8)	362 (39.0)	30372 (52.0)	
NSES at cancer diagnosis				<.0001
High	25911 (43.7)	335 (36.1)	25576 (43.8)	
Middle	12376 (20.9)	195 (21.0)	12181 (20.9)	
Low	19666 (33.1)	386 (41.7)	19280 (33.0)	
Unknown	1390 (2.3)	11 (1.2)	1379 (2.43	
Health insurance at cancer diagnosis				<.0001
Private/military	44802 (75.5)	549 (59.2)	44253 (75.8)	
Public/Medicaid/Medicare	11113 (18.7)	328 (35.4)	10785 (18.4)	
Uninsured	1238 (2.1)	23 (2.5)	1215 (2.1)	
Unknown	2190 (3.7)	27 (2.9)	2163 (3.7)	
Treatment				
Chemotherapy				<.0001
Yes	24872 (41.9)	607 (65.5)	24265 (41.5)	
No	33942 (57.2)	305 (32.9)	33637 (57.6)	
Unknown	529 (0.9)	15 (1.6)	514 (0.9)	
Radiotherapy				<.0001
Yes	18428 (31.1)	364 (39.3)	18064 (30.9)	
No	40854 (68.8)	561 (60.5)	40293 (69.0)	
Unknown	61 (0.1)	2 (0.2)	59 (0.1)	
Surgery of primary site				0.0011

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Characteristics	Total cohort N (%)	Acute VTE N (%)	No Acute VTE N (%)	P-value[#]
Yes	48772 (82.2)	720 (77.7)	48052 (82.3)	
No	10548 (17.8)	207 (22.3)	10341 (17.7)	
Unknown	23 (0.0)		23 (0.0)	
Hematopoietic cell transplant				<.0001
Yes	1949 (3.3)	90 (9.7)	1859 (3.2)	
No	57394 (96.7)	837 (90.3)	56557 (96.8)	
Presence of Active Cancer				
Stage at diagnosis[*]				<.0001
In situ	1351 (2.3)	9 (1.0)	1342 (2.3)	
Stage I	30636 (51.6)	241 (26.0)	30395 (52.0)	
Stage II	11160 (18.8)	198 (21.4)	10962 (18.8)	
Stage III	5833 (9.8)	190 (20.5)	5643 (9.7)	
Stage IV (Metastatic)[^]	4373 (5.7)	152 (16.4)	4221 (7.2)	
Unknown	3783 (6.4)	77 (8.3)	3706 (6.3)	
Not applicable[*]	2207 (3.7)	60 (6.5)	2147 (3.7)	
Second primary cancer				<.0001
Yes	2412 (4.1)	106 (11.4)	2306 (3.9)	
No	56931 (95.9)	821 (88.6)	56110 (96.1)	
Disease progression				<.0001
Yes	4867 (8.2)	456 (49.2)	4411 (7.6)	
No	54476 (91.8)	471 (50.8)	54005 (92.4)	
History of VTE				<.0001
Acute VTE in 2 years after cancer diagnosis	884 (1.5)	107 (11.5)	777 (1.3)	
VTE prior to cancer diagnosis	185 (0.3)	18 (1.9)	167 (0.3)	
No history of VTE	58274 (98.2)	802 (86.6)	57472 (98.4)	
Cancer site				<.0001
Acute lymphoblastic leukemia	1139 (1.9)	33 (3.5)	1106 (1.9)	
Acute myeloid leukemia	1068 (1.8)	27 (2.9)	1041 (1.8)	
Non-Hodgkin lymphoma	3930 (6.6)	56 (6.0)	3874 (6.6)	
Hodgkin lymphoma	4284 (7.2)	47 (5.1)	4237 (7.3)	
Thyroid	12208 (20.6)	55 (5.9)	12153 (20.8)	
Sarcoma	3285 (5.5)	112 (12.1)	3173 (5.4)	
Colorectal[&]	3555 (6.0)	109 (11.8)	3446 (5.9)	
Melanoma	6356 (10.7)	60 (6.5)	6296 (10.8)	
Breast	11405 (19.2)	226 (24.4)	11179 (19.1)	
In Situ Breast	1351 (2.3)	9 (1.0)	1342 (2.3)	
Cervical	3198 (5.4)	96 (10.4)	3102 (5.3)	
Testicular	7564 (12.8)	97 (10.4)	7467 (12.8)	

Abbreviation: nSES, neighborhood socioeconomic status

[^] Metastatic includes Stage III for testicular cancer

[*] No stage classification for leukemias.

[&] Colorectal excludes anus cancer.

[#] Chi-square test p-value reflects differences in frequency distribution across all levels of each variable.

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Table 2.

Five- and 10-year cumulative incidence of venous thromboembolism in adolescents and young adults with cancer, California, 2006–2018

Characteristics	5-year CMI % (95% CI)^	10-year CMI % (95% CI)^
Overall	1.09 (1.00–1.18)	1.93 (1.80–2.07)
Sex		
Female	1.06 (0.96–1.18)	1.91 (1.75–2.08)
Male	1.13 (0.99–1.29)	1.97 (1.76–2.21)
Race/ethnicity #		
Non-Hispanic White	0.90 (0.79–1.03)	1.73 (1.55–1.91)
Non-Hispanic Black/African American	2.51 (1.95–3.18)	3.94 (3.16–4.83)
Hispanic	1.32 (1.15–1.50)	2.29 (2.04–2.57)
Non-Hispanic Asian/Pacific Islander	0.75 (0.57–0.98)	1.28 (1.01–1.61)
Age at diagnosis, years		
15–29	1.02 (0.89–1.17)	1.70 (1.50–1.91)
30–39	1.13 (1.02–1.24)	2.07 (1.90–2.25)
Year at diagnosis		
2006–2011	1.00 (0.89–1.12)	1.81 (1.65–1.97)
2012–2018	1.18 (1.05–1.32)	-
Neighborhood socioeconomic status at diagnosis #		
Low	1.53 (1.36–1.73)	2.46 (2.21–2.74)
Middle	1.06 (0.88–1.26)	1.96 (1.68–2.28)
High	0.81 (0.70–0.93)	1.60 (1.42–1.79)
Health insurance at diagnosis #		
Private/military	0.83 (0.75–0.93)	1.52 (1.39–1.66)
Public/uninsurance	2.07 (1.81–2.35)	3.57 (3.19–3.99)
Chemotherapy		
Yes	1.86 (1.69–2.05)	2.98 (2.73–3.24)
No/Unknown	0.53 (0.46–0.62)	1.19 (1.05–1.34)
Radiotherapy		
Yes	1.46 (1.29–1.65)	2.29 (2.05–2.56)
No/Unknown	0.92 (0.82–1.02)	1.76 (1.61–1.93)
Surgery of primary site		
Yes	0.99 (0.90–1.09)	1.83 (1.69–1.98)
No/Unknown	1.54 (1.31–1.81)	2.43 (2.09–2.80)
Hematopoietic cell transplant		
Yes	3.42 (2.64–4.34)	5.50 (4.39–6.79)
No/Unknown	1.01 (0.92–1.10)	1.81 (1.68–1.94)
Stage at diagnosis # *		
Non-metastatic	0.90 (0.82–0.99)	1.67 (1.54–1.81)
Metastatic	2.99 (2.43–3.65)	4.34 (3.60–5.19)

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Characteristics	5-year CMI % (95% CI)^	10-year CMI % (95% CI)^
History of VTE		
Acute VTE within 2 years of cancer diagnosis	11.36 (9.22–13.75)	15.69 (12.84–18.80)
VTE 5 years prior to cancer	7.74 (4.31–12.45)	12.46 (7.19–19.23)
No history of VTE	0.92 (0.84–1.00)	1.71 (1.58–1.84)
Cancer site		
Acute lymphoblastic leukemia	2.41 (1.59–3.52)	3.81 (2.61–5.36)
Acute myeloid leukemia	1.94 (1.21–2.95)	3.29 (2.18–4.76)
Non-Hodgkin lymphoma	0.82 (0.56–1.17)	1.55 (1.12–2.08)
Hodgkin lymphoma	0.72 (0.49–1.02)	1.30 (0.94–1.76)
Thyroid	0.23 (0.15–0.34)	0.62 (0.46–0.82)
Sarcoma	2.40 (1.89–2.99)	4.02 (3.28–4.88)
Colorectal&	2.61 (2.09–3.22)	4.04 (3.31–4.88)
Melanoma	0.48 (0.33–0.68)	1.14 (0.86–1.48)
Breast	1.39 (1.18–1.64)	2.47 (2.14–2.84)
In Situ Breast	0.32 (0.11–0.78)	0.74 (0.32–1.53)
Cervical	2.36 (1.85–2.96)	3.71 (2.99–4.54)
Testicular	0.92 (0.71–1.17)	1.64 (1.32–2.03)

Abbreviations: VTE, venous thromboembolism CMI, cumulative incidence; CI, confidence interval.

^Gray's test p-values were used to assess differences in cumulative incidence for each variable across the entire study time period. Except for sex, all p-values were significant ($p < 0.05$).

*No stage classification for leukemias.

&Colorectal excludes anus cancer.

#Unknown categories not shown.