Black Patients Experience Highest Rates of Cancer-associated Venous Thromboembolism

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Purpose: Cancer patients are at a higher risk of venous thromboembolism (VTE) than the general population. In the general population, blacks are at a higher risk of VTE compared with whites. The influence of race on cancer-associated VTE remains unexplored. We examined whether black cancer patients are at a higher risk of VTE and whether these differences are present in specific cancer types.

Design: A retrospective study was performed in the largest safety net hospital of New England using a cohort of cancer patients characterized by a substantial number of nonwhites.

Results: We identified 16,498 subjects with solid organ and hematologic malignancies from 2004 to 2018. Among them, we found 186 unique incident VTE events, of which the majority of the events accrued within the first 2 years of cancer diagnosis. Overall, blacks showed a 3-fold higher incidence of VTE (1.8%) compared with whites (0.6%; $P < 0.001$). This difference was observed in certain cancer types such as lung, gastric and colorectal. In lung cancer, the odds of developing VTE in blacks was 2.77-times greater than those in white patients (confidence interval, 1.33-5.91; $P = 0.007$). Despite the greater incidence of cancer-associated VTE in blacks, their Khorana risk score of VTE was not higher.

Conclusions: In a diverse cancer cohort, we observed a higher incidence of cancer-associated VTE in blacks compared with patients from other races. This study indicates the consideration of race in the risk assessment of cancer-associated VTE. It could also lead to future mechanistic studies aiming at identifying reasons for differential VTE risk depending on cancer type.

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In the United States, venous thromboembolism (VTE) is responsible for an estimated 300,000 deaths annually.[1] An estimated 20% of these deaths occur among patients with cancer. Several studies have shown that cancer is associated with a 4-fold to 7-fold increased risk of VTE,[2–4] with an absolute risk ranging from 1% to 8%.[5] The incidence of VTE varies with cancer type and tumor burden, and is the highest among patients with pancreatic and gastric cancers.[5–7] Furthermore, patients are at the highest risk in the immediate period after cancer diagnosis. In a population-based study, the adjusted odds ratio for developing VTE in the first 3 months was 53.5 and declined to 14.3 and 3.6 within 1-year and 1 to 3 years period, respectively. Interestingly, the VTE risk persisted over several years and eventually subsided to levels observed in the general population 15 years after cancer diagnosis.[6,8]

The occurrence of VTE in cancer has prognostic significance. Even after adjusting for age, race, and stage, the diagnosis of VTE is associated with reduced overall survival in the first year.[9] Moreover, patients with active cancer have a 52% 10-year cumulative incidence of VTE recurrence, an event that further increases the hazard ratio for death by 3-fold.[4]

Multiple factors have been implicated in the development of VTE in cancer patients. These can be categorized as tumor-related, treatment-related, and patient-related risk factors. Tumor-related and treatment-related risk factors comprise tumor histology, site, stage, and duration as well as treatment with agents, such as tamoxifen, bevacizumab, cisplatin, thalidomide, multitarget tyrosine kinase inhibitors, etc.[6,10–12] Various patient-related factors including age, sex, and comorbidities; such as obesity and cardiovascular disease, are implicated in cancer-associated VTE.[6]

Little attention has been given to the association of race with cancer-associated VTE. Large epidemiological studies have shown that black patients have a significantly higher rate of incident VTE, particularly following a provoking risk factor such as surgery, medical illness and trama.[13,14] The Cardiovascular Health Study (CHS) And Geographic and Race Differences in Stroke Study (REGARDS) showed that black patients were at a significantly higher risk with a hazard ratio 1.81 and 1.62 for VTE compared with other races, respectively.[14] Despite an overwhelming evidence of influence of race on VTE in the general population, race remains an unexplored risk factor in cancer-associated VTE. This knowledge gap is largely driven by composition of the study cohort used in previous studies. It is noteworthy that even the

cohorts used to develop and validate current risk models of cancer-associated VTE, such as the Khorana score, the Protecht or the Vienna Cancer and Thrombosis Study (CATS) scores, either had an undisclosed racial composition or consisted of a disproportionately higher number of whites and conspicuously lacked ethnic minorities.[7,15–17] Collectively, the previous studies were not suited to examine the influence of race on cancer-associated VTE due to their case mix of the cohort.

An understanding of the influence of race in cancer-associated VTE is increasingly relevant. In the United States, racial minority populations are expected to increase from 83 million in 2000 to 157 million in 2030. This trend will translate into a >100% increase in cancer incidence by 2030.[18] Both VTE-associated mortality and morbidity and the proposed trend of a more racially diverse cancer cohort underscore the public health importance of this question. Also, the question of race and cancer-associated VTE has potential prognostic and therapeutic implications for the individual cancer patient. Should race influence the VTE risk, further studies are warranted to recalibrate the risk predictive models with race as a variable. This could enable precise stratification of the cancer population, so that thromboprophylaxis can be utilized for those patients at highest risk for cancer-associated VTE. To investigate the risk of cancer-associated VTE by race, we conducted a retrospective study in a diverse patient population at the Boston Medical Center (BMC).

PATIENTS AND METHODS

Study Population and Data Collection

This observational study focused on patients diagnosed with cancer between January 2004 and July 2018 at BMC using their electronic health record (EPIC). BMC serves a racially diverse cancer cohort of patients consisting of a similar proportion of white and nonwhites, with the latter group consisting of blacks and other ethnic minorities.[19] The study was conducted after obtaining an approval from the Institutional Review Board of Boston University School of Medicine (H-26367).

The inclusion criteria consisted of all patients diagnosed or treated for solid organ cancers or hematologic malignancies identified through the hospital's tumor registry between January of 2004 and July of 2018. The clinical data elements extracted from the medical record included basic demographics, date of diagnosis, best American Joint Committee on Cancer (AJCC) staging, primary site of the cancer, and tumor histology.

Event Ascertainment and Definitions

Events included thrombosis of deep veins, popliteal, superior vena cava, hepatic vein, portal vein, renal vein, etc., and pulmonary embolism in the context of cancer, and were identified by the review of providers encounter using ICD-9-CM (453.0 to 453.9, 451.1, and 996.74) and ICD-10-CM (I82.0 to I82.499, I82.4Y9, I82.5-599m I82.5Y-I82-5Z, I82.6-I82.729, I82.A-I82.B29, I82.C-I82.C29, and I26.0-I26.99) codes. Cancer-associated VTE was defined as VTE events that occurred any time after the diagnosis of cancer, as done by previous studies.[1,3,4,20] We limited our events till 6 years after cancer diagnosis since most of our patients developed VTE in this time frame.

All the VTE cases were adjudicated independently by 2 physicians using chart review and utilizing ICD codes. To be included in our analysis, objective documentation of the VTE event was required by contrast venography or duplex ultrasonography for suspected DVT, pulmonary angiography, lung scintigraphy, or computed tomography scan for suspected PE. Cases with superficial phlebitis or superficial thrombosis were excluded in our analysis. Date of the exam, type of incident VTE, baseline characteristic, as well as medications such as anticoagulants were obtained by review of hospital medical record. Self-reported race was used for this study. Body mass index was defined as weight in kilograms divided by the square of height in meters at the time of diagnosis of VTE.

Application of VTE Risk Prediction Score

Khorana score was used for determining the VTE risk in patients with cancer-associated VTE.[7] Khorana score was calculated by assigning 1 point each for prechemotherapy platelet count $\geq$350,000/μL, hemoglobin level <10 g/dL or use of red cell growth factors, white blood cells count $\geq$11,000/μL, and body mass index (BMI) $\geq 35\ kg/m^2$. As recommended, we assigned 2 points for the presence of gastric, pancreatic, or brain cancer, which is a "very-high-risk" site of cancer and 1 point for a "high-risk" site of cancer comprised of lung, kidney, lymphoma, or myeloma. Patients with a total of 0 points were considered at low-risk, 1 to 2 points intermediate-risk and ≥ 3 points high-risk for VTE.[7]

Missing Data

No missing data were noted for this analysis in this cohort.

Statistical Methods

The summary statistics for all cancer patients presenting to BMC between years 2004 and 2018 were obtained from Boston Medical Centre's Tumor Registry and electronic health record EPIC. Summary statistics were presented as mean (with SD) and proportions (with percentage) for continuous and discrete variables, respectively. Groups were compared using student t test for continuous variables and χ^2/Fisher exact test as appropriate for discrete variables. The incidence of VTE for different cancer sites, including lung, breast, prostate, colorectal, and gastric/small intestine were calculated and compared across the 3 race groups using χ^2 analysis or Fisher exact test as appropriate. The difference in time to occurrence of VTE between the 3 race groups was then evaluated. A Kaplan-Meier curve was generated with respect to race and compared using the log-rank test. "Time to VTE" diagnosis was defined as the time between the "Date of cancer diagnosis" and the "Date of VTE diagnosis." As all patients in the cohort being analyzed had cancer-associated VTE, no censoring was necessary. A subcohort of lung cancer patients presenting at BMC between 2004 and 2018 was analyzed to assess for the difference in the incidence of VTE with respect to race. Important variables like age, sex, cancer stage, and anticoagulation status were included in a logistic regression model. Statistical significance was assessed at $P<0.05$ and analyses were performed using R software (Mac v3.4.1).

RESULTS

Race-based Distribution of Different Cancer Types in the Studied Cohort

We identified a total of 16,498 cases with a wide range of solid organ and hematologic malignancies from 2004 to 2018. The demographics and cancer characteristics of the cohort are described in Table 1. Cases had a relatively even sex distribution. Our cancer population had a relative even distribution of white (54%) and nonwhite patients (45.1%). Most of the nonwhite population was composed of blacks (33%),

TABLE 1. Baseline Characteristics of the Total Study Population

	Total, n (%)
Patient, n	16,498
Baseline characteristics	
Sex	
Women	8179 (49.57)
Men	8311 (50.37)
Race	
Blacks	5498 (33.32)
Whites	9060 (54.91)
Others*	1940 (11.75)
Cancer characteristics	
Primary site of cancer	
Respiratory system	2196 (13.30)
Digestive system	2896 (17.60)
Urinary system	1036 (6.30)
Female genital system	863 (5.20)
Breast	2259 (13.70)
Male genital system	2223 (13.50)
Leukemia and lymphoma	908 (5.50)
Skin excluding basal and squamous	509 (3.10)
Oral cavity and pharynx	1041 (6.30)
Brain and other nervous system	447 (2.70)
Myeloma	235 (1.40)
Endocrine system	1,290 (7.80)
Bone and joints, soft tissue	96 (0.60)
Eye and orbit	24 (0.10)
Mesothelioma, Kaposi sarcoma and miscellaneous	475 (2.90)
Stage	
0	935
I	4804
II	3313
III	2153
IV	2820
NA	1929
Unknown†	542

*Including, but not limited to patients of Spanish origin.
†Data not available.
NA indicates not available; NS, nervous system.

followed by patients of Spanish origin, Asians, and others (11%). This case mix provides a desirable cohort composition to specifically examine the role of minority populations in a cancer phenotype, as done previously.[19] The most common sites of cancer were seen in the digestive system, respiratory system, breast, and male genital system. A similar proportion of patients consisted of early stage cancer (stages I) compared with more advanced disease (stage III and stage IV). Cancer stage was not applicable for a total of 1949 cases (11%) cases.

Given that the primary objective of our investigation was to examine the influence of race on certain cancer-associated VTE, we first assessed the race-based distribution of different cancer types in our cohort. Table 2 provides a summary of cancer types stratified by race. Whites had significantly higher prevalence of lung, breast, and prostate cancer, while prostate cancer was the most prevalent in black patients, followed by breast and lung cancer. Leukemia, brain, and kidney cancer showed no significant differences between races.

Incidence of VTE

Of 16,498 cancer patients, a total of 186 patients (1.1%) demonstrated incident VTE event (Table 3). Black cancer patients had a close to 3-fold higher incidence of VTE (1.8%, n = 97) compared with whites (0.6%, n = 52); $P < 0.001$. Patients of race "Others" also had higher incidence of VTE compared with Others (nonblack) (1.9%, n = 37). Overall, we did not observe a statistically significant difference in average age, sex, and BMI across all racial groups. Sixty-five percent of patients with cancer-associated VTE presented with an advanced stage of cancer (stage III and IV). Considering that patients with higher tumor burden (advanced stage of cancer) are at higher risk of VTE, we anticipated greater number of black cancer patients with an advanced cancer stage.[21] However, there was no significant difference in presenting stage across the racial groups (Table 3).

Incidence of VTE at Different Sites and in Relation to Different Cancer Types

We next examined the site of venous thrombosis, VTE recurrence and treatment with anticoagulants in different races (Supplementary Table 1, Supplemental Digital Content 1, http://links.lww.com/AJCO/A313). Femoral and popliteal vein thrombosis was the highest involved site in all the races and no difference was observed in the site of thrombosis among race.

Of 186 cases treated with anticoagulants, 57% of patients were treated with heparin or heparin derivate, 12% received Warfarin at some point and 8% were on Direct-Acting Oral Anticoagulants (DOACs). We found no significant difference between VTE site and the use of anticoagulants across all races. Similarly, the incidence of VTE recurrence across all races was not significantly different.

We subsequently, examined whether there were racial differences in the incidence of VTE in specific cancer types (Table 4). Intriguingly, we found that the incidence of VTE was twice as high in the black lung cancer population compared with white. We additionally found that the VTE incidence was significantly higher in the black population with lung cancer, gastric/small intestine and colorectal cancer, although no such difference was noted in the other cancer types.

Cumulative Incidence of VTE

The time of VTE event was examined over a period of 6 years (Supplementary Fig. 1, Supplemental Digital Content 1, http://links.lww.com/AJCO/A313). Of 186 incident VTE events, 70% were observed within the first year after diagnosis of cancer, which was consistent with data from previous studies.[1,3,4,20] We then examined the cumulative incidence of VTE, which showed statistically significant differences between the 3 races ($P = 0.039$) (Fig. 1). Further comparison between only black and white cancer patients showed a greater significant difference in the cumulative incidence of VTE events over time ($P = 0.023$). However, the occurrence of VTE at different time intervals did not differ in the 3 races (Supplementary Table 2, Supplemental Digital Content 1, http://links.lww.com/AJCO/A313). For example, in the first 6 months after cancer diagnosis, 25 VTE events (48%) of total 52 VTE occurred in white patients, while 60 events (61%) of total 97 events occurred in black cancer patients ($P = 0.148$). By the end of first year, this difference reduced between blacks and white patients. At the end of 1 year of cancer diagnosis, 32 events (61%) of a total 52 VTE events occurred in white patients and similarly 63 events (65%) in a total of 97 VTE occurred in black cancer patients. The third racial group (Others) likewise experienced the highest incidence of VTE within the first 6 months after diagnosis of cancer (64%), and the overall cumulative incidence of VTE was significantly different compared with whites ($P = 0.033$).

TABLE 2. Cancer Type Prevalence of Study Population By Race

	Whites	Blacks	*P*	Other†	*P*
Patient, n (%)	9060 (54.9)	5498 (33.3)		1940 (11.8)	
Primary site of cancer, n (prevalence %)			<0.001		<0.001
Lung and bronchus	1212 (13.4)	566 (10.3)	<0.001	142 (7.3)	<0.001
Colon and rectum	619 (6.8)	489 (8.8)	<0.001	121 (6.2)	0.368
Stomach and small intestine	235 (2.6)	211 (3.8)	<0.001	59 (3.0)	0.302
Breast	1021 (11.3)	918 (16.7)	<0.001	320 (16.5)	<0.001
Prostate	928 (10.2)	928 (16.8)	<0.001	256 (13.2)	<0.001
Leukemia and lymphoma	514 (5.7)	272 (4.9)	0.066	122 (6.3)	0.317
Oral cavity and pharynx	776 (8.6)	159 (2.9)	<0.001	106 (5.5)	<0.001
Brain and other NS	227 (2.5)	137 (2.5)	1.000	83 (4.2)	<0.001
Kidney and renal pelvis	328 (3.6)	196 (3.6)	0.900	68 (3.5)	0.857
Others	3200 (35.3)	1622 (29.5)	<0.001	663 (34.2)	0.351

P-values compare cancer prevalence in blacks versus whites and others versus whites.
†Including, but not limited to patients of Spanish origin.
NS indicates nervous system.

Odds of Developing Cancer-associated VTE in Lung Cancer Patients

We generated a logistic regression model to examine the odds of developing cancer-associated VTE with respect to race. This model was developed for patients with lung cancer, given that this cancer type had the highest events of VTE (33/186 total events). Our results showed that compared with the white cancer patients, blacks had a 2.77-times higher odds of developing VTE (confidence interval, 1.33-5.91; $P=0.007$) (Table 5) even after adjusting for age, sex, cancer stage and use of antithrombotic medications. Although the Others had 2.27-fold higher risk of developing VTE (confidence interval 0.51-7.33) compared with whites, it did not reach a statistical significance ($P=0.166$).

Khorana Risk Score

Khorana score is widely used in clinical practice to predict the risk of cancer-associated VTE before the initiation of chemotherapy. A higher Khorana score corresponds with higher risk of VTE. In view of a significantly higher incidence of VTE events in the black cancer population compared with whites, we posited that the black cancer patients with VTE will have higher Khorana score compared with whites. A distribution of Khorana score from 0 to 5 was compared between 3 races. The results showed that the white cancer patients clustered around a score of 1 and had a Khorana risk score of 1 in significantly higher number of patients compared with the Blacks ($P=0.015$) and Others ($P=0.004$) (Supplementary Table 2, Supplemental Digital Content 1, http://links.lww.com/AJCO/A313). However, the majority of black cancer patients had a lower Khorana score in the range of 1 to 2. In the strata with higher Khorana risk score, there was no difference in the number of black and white patients. A similar result was noted for Others.

DISCUSSION

In a cohort characterized by a comparable proportion of whites and nonwhite cancer patients, we observed a 3-fold higher incidence of VTE in black cancer patients compared with white cancer patients. Contrary to our expectation, the applied Khorana risk score to our study population could not predict a higher VTE risk, despite higher incidence of cancer-associated VTE in black cancer patients. This underscores the potential limitation of current risk predictive models due to lack of generalizability to minority populations. Hence, this study addresses a previously underappreciated component of racial differences in cancer-associated VTE.

The development of VTE is complex and various potential explanations for higher VTE occurrence in blacks might exist. Previous studies have shown that VTE risk is higher in patients

TABLE 3. Clinical Characteristics of Cancer Patients With VTE (n = 186) (Incidence 1.1% of Total Cancer Patients)

	Total	Whites	Blacks	*P*	Other*	*P*
Patient, n (%)	186 (100)	52 (27.96)	97 (52.15)		37 (19.89)	
Incidence of VTE (%)	186/16498 (1.1)	52/9060 (0.6)	97/5498 (1.8)	<0.001	37/1940 (1.9)	<0.001
Age, mean (SD) (y)	63.65 (13.03)	62.38 (12.86)	65.79 (13.25)	0.133	59.66 (11.74)	0.318
Sex, n (%)				0.515		0.982
Men	105 (56.5)	31 (59.6)	51 (52.6)		23 (62.2)	
Women	81 (43.5)	21 (40.4)	46 (47.4)		14 (37.8)	
BMI (SD)	26.73 (7.20)	27.91 (6.88)	26.04 (7.6)	0.144	26.88 (6.49)	0.117
Stage, n (%)				0.592		0.433
I	15 (8.1)	6 (11.5)	7 (7.2)	0.416	2 (5.4)	0.594
II	33 (17.7)	11 (21.2)	17 (17.5)	0.533	5 (13.5)	0.629
III	38 (20.4)	11 (21.2)	21 (21.6)	0.670	6 (16.2)	0.825
IV	83 (44.6)	18 (34.6)	45 (46.4)	0.330	20 (54.1)	0.168
NA	17 (9.1)	6 (11.5)	4 (4.1)	0.557	4 (10.8)	1.000

P-values compare characteristics of patients with cancer-associated VTE in blacks versus whites and others versus whites.
*Including, but not limited to patients of Spanish origin.
BMI indicates body mass index; NA, not available; VTE, venous thromboembolism.

TABLE 4. Analysis of Cancer-associated VTE Stratified by Race and Primary site, n = 186

	Incidence of VTE Per Cancer Type				
Primary Site	**Whites**	**Blacks**	***P***	**Others†**	***P***
Lung, n/N (%)	13/1212 (1.07)	17/566 (3.0)	0.006	3/142 (2.1)	0.231*
Gastric/small intestine, n/N (%)	0/235 (0)	6/211 (2.84)	0.011*	2/59 (3.39)	0.039*
Colon and rectum, n/N (%)	6/667 (0.9)	14/512 (2.73)	0.028	2/126 (1.59)	0.750*
Breast, n/N (%)	4/1021 (0.39)	10/918 (1.1)	0.123	3/320 (0.94)	0.368*

P-values compare incidence of VTE in blacks and others versus whites.
**P*-value obtained using Fisher's exact test.
†Including, but not limited to patients of Spanish origin.
VTE indicates venous thromboembolism.

with metastatic cancer.[3,4,20] However, in the current study we did not find black cancer patients have a higher stage of cancer at presentation than white patients. Well known patient-related factors, including age, sex, and BMI did not seem to play a role in our study population, given that we could not detect significant difference across race. Interestingly, none of the black cancer patients carried an underlying diagnosis of sickle cell trait or sickle cell disease, which is a known risk factor for VTE. Furthermore, there was no significant difference in utilization of anticoagulants between blacks and whites. While it is not possible to rule out all potential confounders in this study, the data in this body of work points to other potential factors imparting a higher risk of cancer-associated VTE in black patients.

Recent studies have uncovered genetic risk factors of VTE in the general population and few were noted in blacks patients.[22–25] These studies suggested potential associations between VTE and polymorphisms in genes related to the anticoagulation and fibrinolytic systems, as well as to the factors associated with the coagulation cascade such as EPCR, F11, FGG, CYP4V2, SERPINC1, and GP6 and Factor XI.[22–24] Thrombophilia Study (LETS) and the Multiple Environmental and Genetic Assessment of Risk Factors for Venous Thrombosis (MEGA) study Factors for Venous Thrombosis (MEGA study) have recently identified 2 common single nucleotide polymorphism such as rs2289252 and rs2036914 associated with VTE. Hernandez et al[25] identified single nucleotide polymorphism on chromosome 20 (rs2144940, rs2567617, and rs1998081) that associated with the increased risk of VTE by 2.3-fold. These polymorphisms reduced the expression of thrombomodulin (*THBD*), an inhibitor of thrombin and an anticoagulant protein. These risk variants were found in higher frequency among populations of African descent (> 20%) compared with other ethnic groups (< 10%) explaining in part higher incidence of VTE in black patients. All of these studies suggest racial-based changes in the delicate balance between the procoagulants and anticoagulants factors influencing the risk of VTE in the general population. Such studies are needed to probe the genetic risk factors contributing to the racial disparity in cancer-associated VTE.

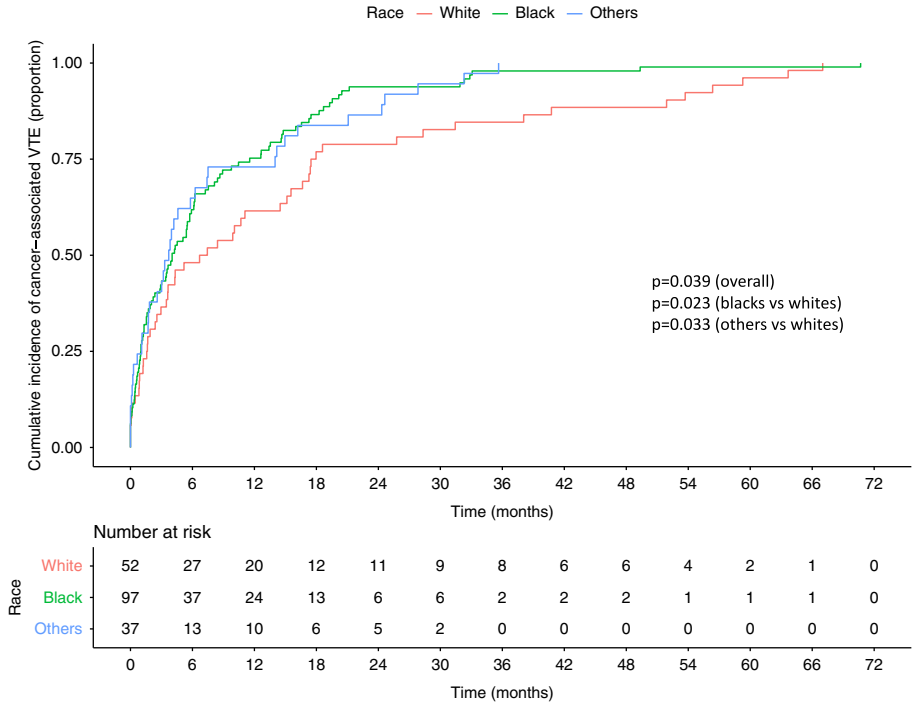

FIGURE 1. Cumulative incidence of venous thromboembolism (VTE) in patients with cancer from different races is shown. The patients at risk of VTE are shown at the bottom of the graph corresponding to every time point.

TABLE 5. Logistic Regression Model of Occurrence of Cancer-associated Venous Thromboembolism (VTE) in Lung Cancer Patients at Boston Medical Center (Lung Cancer Patients = 1935, Cancer-associated VTE Patients = 33)

Variables	Estimate	95% CI	*P*
Intercept	0.004	0.0004-0.047	< 0.001
Race 2 (blacks)	2.77	1.33-5.91	0.007
Race 3 (others)	2.27	0.51-7.33	0.21
Stage late (3+4)	1.39	0.68-3.02	0.38
Age	1.01	0.98-1.05	0.45
Sex (F)	0.835	0.40-1.68	0.43
Anticoagulation (yes)	0.651	0.19-1.69	0.62

The estimate and 95% CI are exponentiated values after running the logistic regression model.

CI indicates confidence interval; F, female.

Prognostic Impact

Occurrence of a VTE event in a cancer patient augurs a bad prognosis and adds to morbidity and health care cost. Accurate assessment of a prior risk of VTE in these patients is imperative. Currently, available predictive risk scores of VTE, such as Khorana and its modifications Protecht or CATS scores were derived from a limited number of diverse cancer patients, and included only a handful of variables. Thus, their ability to capture staggering variability in cancer-related VTE risk is suboptimal.[7,17,26–28] To date, most studies including randomized clinical trials in the area of cancer-associated VTE lacked a racially and ethnically diverse population, in particular, black patients. Furthermore, prospective validation studies for the most used predictive models for cancer-associated VTE were conducted on a cohort of a predominantly white population.[7,15,17] As a result, the current risk score cannot be directly extrapolated to the minority cohorts. This contention is additionally supported by our results that showed that black cancer patients did not show a higher Khorana risk score (Supplementary Table 2, Supplemental Digital Content 1, http://links.lww.com/AJCO/A313) compared with whites, despite having a higher incidence of VTE in them. On the other hand, there was a significantly higher number of white cancer patients with lower risk score (Khorana score 1), consistent with a lower incidence of VTE in them. As most of the VTE risk scores were developed in whites,[7,15,17] it stands to reason that the risk score may perform well in patients with characteristics similar to the study participants from whom the score was developed. However, the current analysis suggests consideration of race in the risk assessment of VTE in cancer.

In general, an important rationale to predict the risk accurately is to assist in therapeutic decisions. For example, it is conceivable that an accurate prediction of cancer-associated VTE risk will help to identify those patients with cancer who are at higher risk for VTE and, thus, institution of thromboprophylaxis in such a cohort may tilt the balance in favor of prevention of thrombosis rather than the risk of bleeding. More work is needed to robustly improve the accuracy of such models with parameters such as race that influence the occurrence of cancer-associated VTE.

Our cohort represents an urban population in the United States characterized by a large number of black and Hispanic patients. This cohort composition provided a unique opportunity to examine the differences of various clinical phenotypes within different racial and ethnic groups in our cancer population.[19] This is a retrospective study based on chart review and extended back to 2004. The overall incidence of cancer-associated VTE in our cohort was 1.12%, which is at the lower end of cancer-associated VTE reported in the previous studies.[2–5] Several factors might explain this phenomenon including the design of the study and availability of advanced techniques for diagnosing VTE in recent years. Our center has a large catchment area of patients referred from different hospitals. Differences in their referral patterns and loss of patients into these systems may also contribute to the observed incidence in this study.

We observed higher incidence of cancer-associated VTE in blacks with specific cancer types. It is likely that this result may be due to the presence of sufficient number of cases in those specific cancer types. Future larger studies will evaluate generalizability of this observation in other cancer types. Given the number of VTE events in lung cancer, our logistic regression model could include only four variables. Studies in larger cohorts with greater number of VTE events will allow examination of more confounders. In keeping with any retrospective study, the current investigation has limitations with regards to reliance on discharge codes for VTE events and self-identification of race.[29] Nonetheless, these results highlight the need for larger multicenter studies to examine the generalizability of this finding.

In conclusion, this study suggests that race may play a significant role in the development of cancer-associated VTE. Further studies are warranted to confirm these findings. The integration of race into treatment algorithms for anticoagulation in cancer patients may further optimize risk-predictive models and more accurately stratify the risk of cancer-associated VTE. Finally, our study also lays the ground for mechanistic cause-and-effect inquiries related to intricate associations of specific cancers with VTE in blacks.

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