

Original Article

## Prevalence and incidence of deep venous thrombosis and pulmonary embolism in 2 regions in Turkey (A sub-analysis of CAT-TR study)

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### Abstract

**Aim:** Venous thromboembolism (VTE) is a relatively common public health problem. In addition to increasing mortality due to complications, it also causes an increase in the cost of the country's economy and loss of labor due to the morbidity it creates. Considering that the recurrence of VTE is a common condition, the importance of this disease for the society increases even more. Although we have come a long way in treatment and follow-up, we see that VTE and its related complications maintain their place as a significant risk factor in the society at increasing rates.

**Material and Methods:** This is an additional analysis of a multicentral, retrospective descriptive study, CAT-TR (Assessment of Patient Characteristic in Cancer Associated Venous Thrombosis in Turkey). The aim of the CAT-TR study was to evaluate patient characteristic and treatment patterns of cancer-induced VTE in Turkey. This article aims to evaluate the incidence and prevalence of cancer-induced VTE in two regions of Turkey between January 01, 2016 and December 31, 2019.

**Results:** In our study, the 4-year prevalence of Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE) in Central Anatolia and Marmara was 86.43, 103.56 and 105.68, 98.04 per 100.000 people, respectively. The cumulative incidence of cancer-related VTE in the Central Anatolian and Marmara populations is 17.22 and 6.71 per 100.000 people, respectively.

**Conclusion:** The values we found in the prevalence and incidence study of VTE will be very valuable in terms of being a reference for us in the treatment and prevention of the disease. We believe that this study will shed light on new studies for diseases that may cause VTE in larger populations and strategies to be followed in prevention.

**Keywords:** Deep vein thrombosis, deep venous thrombosis, pulmonary embolisms pulmonary thromboembolism, thromboembolism, venous

### CITATION

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## INTRODUCTION

Considering the articles stating that symptomatic DVT can be seen in an average of 145 people and PE in an average of 69 people in a population of 100.000 people at least once in a lifetime [1], we can predict that this rate will be much higher in the presence of concomitant diseases. In these studies, this rate is much higher especially in cancer patients, but this rate can vary considerably according to the cancer type, stage, treatment and other accompanying conditions [1].

If VTE is not diagnosed or treated, it can cause long-term complications and morbidity due to post-thrombotic syndrome and recurrent VTE. Besides morbidity, the most important complication is mortality. In a study covering six European countries, the mortality rate associated with DVT, PE, and VTE was reported to be 465,715, 295,982, and 370,012 per year, respectively [2].

The incidence of cancer-associated Venous Thromboembolism (CAT) can vary greatly depending on the site of the primary tumor. Many studies have shown an increased risk of CAT in pancreatic, lung, brain, stomach, and ovarian cancers [1]. Age, drugs used in chemotherapy, and accompanying comorbidities can be listed among the factors that cause CAT formation other than primary cancer. Advanced stage of cancer obviously increases the risk of VTE, and the presence of metastasis has the highest risk of VTE [3].

## MATERIAL AND METHODS

This is an additional analysis of a multicentral, retrospective descriptive study, CAT-TR. The approval of the ethics committee was taken from Başkent University Non-interventional Clinical Research Ethics Committee (Date: 04.11.2020, Number: 20/118). The aim of CAT-TR study was to evaluate the data obtained in

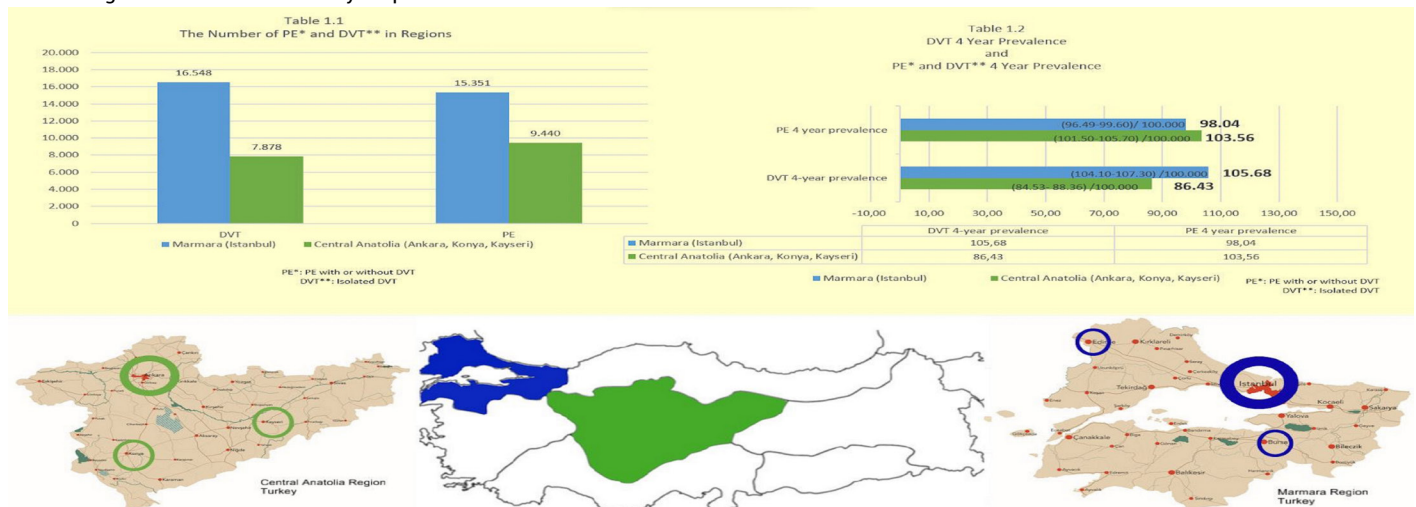
the cancer induced VTE in Turkey between January 01, 2016 and December 31, 2019. Data from CTA-TR total DVT and PE studies were collected in 2 regions and data from 8 centers and 2 regions were utilized; Central Anatolia and Marmara Region were used to estimate DVT and PE prevalence. In our study, Marmara and Central Anatolia regions, which are the two densest regions in terms of population density, were included in the study. Thus, the aim was to reach a general point of view from these regions that make up almost half of the Turkish population.

We included all eligible patients with a diagnosis of proximal lower-limb DVT and/or PE between January 1, 2016 and December 31, 2019 and diagnosis of any cancer. Data were retrieved from electronic health record systems of hospitals by searching respective ICD codes and/or physical patient files. VTE was determined by using respective codes of I26 and I80 – I82 of ICD-10. Descriptive statistics were used to define mean, standard deviation, minimum, median and maximum continuous variables. Frequency and percentage values were calculated for the descriptive statistics of categorical variables. Analyses were performed using MedCalc Statistical Software version 12.7.7 (MedCalc Software, Ostend, Belgium; <http://www.medcalc.org>; 2013).

## RESULTS

The study included 49.217 patients diagnosed with and followed for VTE between 2016 and 2019 from 2 regions, Central Anatolia (Ankara, Konya, Kayseri) and Marmara (İstanbul). 24.426 patients were diagnosed with DVT and 24.791 were diagnosed with PE. The regional distribution and 4-year prevalence of DVT and PE are shown in Table 1. In the two regions where the study was conducted, the incidence of VTE according to population density was found to be similar in the Marmara region and Central Anatolia region ( $P>0.05$ , 0.12 vs. 0.13, respectively).

**Table 1.** Regional distribution and 4-year prevalence of DVT\*\* and PE\*



The prevalence and rates are given with 95% confidence intervals

\*PE with or without DVT

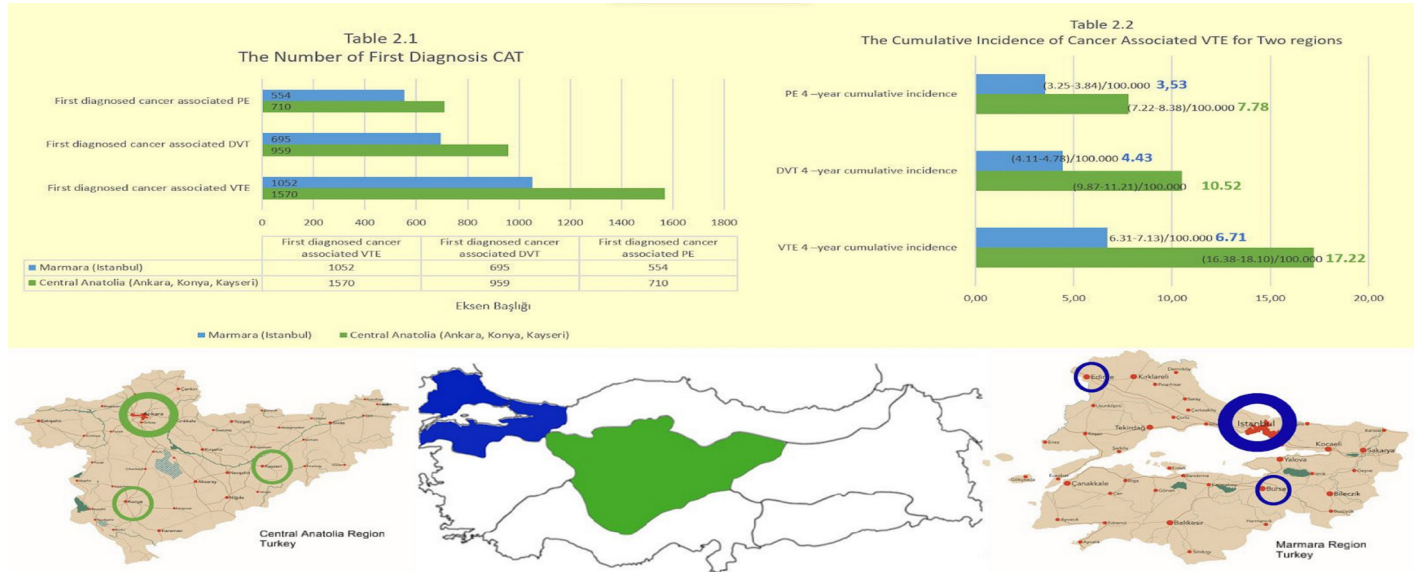
\*\* Isolated DVT

Lung cancer was the most common cancer type (29.7%), followed by colon cancer (8.6%) and breast cancer with (6.8%). 70.3% of the patients were at advanced stage (Stage 4). Chemotherapy±targeted therapy was administered to 469 (65.7

%) patients at the time of onset.

In the evaluation of two regions, we found that 2622 patients were diagnosed with cancer-induced VTE. The cumulative incidence of cancer-associated VTE in these regions are shown in Table 2.

**Table 2.** The cumulative incidence of cancer associated VTE for two regions



The incidence rates are given with 95% confidence intervals

\*PE with or without DVT \*\* Isolated DVT

## DISCUSSION

While the annual incidence of venous thrombosis in the general population was reported as 0.1%, this rate increased 5 times in cancer patients and was stated as 0.5% [4].

In our study, the prevalence of DVT and PE in the Marmara region was 86.43 and 103.56 per 100,000 people, respectively, while the prevalence of DVT and PE in the central Anatolian region was 105.68 and 98.04 per 100,000 people, respectively. In studies of people of European descent, the annual incidence of VTE varies from 104 to 183 per 100,000 people [5,6]. Studies with an annual incidence rate of PE with and without DVT of 29 to 78 per 100,000 have found an annual incidence rate of patients with only DVT without PE to be between 45 and 117 per 100,000 per year [7,8].

In a study of the UK population with ten-year follow-up, 35,373 VTE patients were included and the overall incidence rate of VTE per 100,000 per year was found to be 131.5 (95% CI, 130.2–132.9) [9].

In the study of White et al. investigating the difference in the incidence of VTE in different regions in the United States, it was stated that VTE rates may vary in people from different ethnic origins [10]. These results were supported by different studies and it was stated that VTE could show heterogeneity in the same population [11]. These results indicate that the variability of

ethnicity, genetic factors, and environmental factors within the population has a heterogeneous basis for VTE. These results led to the conclusion that major and minor factors are affecting the incidence of VTE.

Mahajan et al. evaluated patients who were first diagnosed with cancer between 2005 and 2017 and included patients diagnosed with thirteen common cancer types. They determined that the 12-month cumulative incidence of patients with CAT was 1% in prostate and breast cancer, and this rate increased up to 10% in pancreatic cancer. They reported that the 12-month cumulative incidence (95% cumulative incidence) of these thirteen cancer types was between 1-10% [3].

In our study, cancer associated cumulative incidence of VTE in Central Anatolia and Marmara populations are 17.22 and 6.71 per 100,000 people, respectively. Many studies have reported that the risk of cancer-induced VTE is reduced by the prophylactic use of anticoagulants in high-risk cancer patients under chemotherapy treatment [12,13].

Similar to our study, in a study conducted in the United Kingdom, 83,203 cancer patients and 577,207 control patients were included in the study. Newly developed VTE was diagnosed in 3,352 cancer patients and 6,353 of the control patients. When cancer patients were evaluated, the annual absolute rate of VTE was found to be 13.9 per 1000 subjects (95% confidence interval

[CI] 13.4-14.4). The study also listed the factors associated with cancer-induced VTE as the location of cancer, age, and time of diagnosis. The similar incidence of cancer-induced VTE in these results helped us to emphasize the importance of VTE in cancer disease once again [14]. In a meta-analysis by Freesia Horst et al. of 38 studies investigating one of eight cancer types, it was stated that the overall annual risk of VTE ranged from 7 to 23 per 1000 and was 13 on average (95% cumulative incidence). As the common point of these studies, it was emphasized that patients with pancreatic, brain, and lung cancers are in the highest-risk group. Although these rates are high in some cancer types, the average incidence of VTE includes similar results with our study for Turkey [15].

In a study involving 27.479 patients in the United States, cancer patients who were started on chemotherapy were included in the study. In this study, not all types of cancer were included in the study, but the overall incidence of VTE after 3.5 months after the start of chemotherapy for all cancer types was between 4.6% and 11.6% (mean 7.3%), depending on the location of cancer. When this rate was evaluated as 12 months, it was observed that it increased between 9.8% and 21.3% (mean 13.5%) [16]. In the Prophylaxis of Thromboembolism during Chemotherapy (PROTECHT) study, 1150 patients under chemotherapy were included in the study, thromboembolic events were seen in 2.0% of patients receiving anticoagulants, compared to 3.9% in the placebo group. Thus, it has been reported that anticoagulant therapy reduces the incidence of thromboembolic events in patients with locally grown or metastasized cancer [17]. Among the reasons for the difference in incidence in many retrospective studies may be the statistically significant difference in incidentally asymptomatic VTE patients diagnosed during standard cancer staging in clinical studies [18].

The incidence of cancer-induced VTE found in our study in the whole population has a very prominent place in the prevalence of VTE. This showed that cancer-related VTE should be prioritized for all VTEs.

## CONCLUSION

VTE is an important complication of cancer and the most important cause of morbidity and mortality. Considering the prevalence of VTE, we thought that a larger database can be created by evaluating all regions in Turkey. In addition, revealing the prevalence of VTE will facilitate the assessment of the effects of the disease in the whole population. Statistical follow-up of cancer-related VTE in the population will be valuable not only for cancer patients, but also for understanding and monitoring the importance of cancer-related VTE in the entire population.

**Ethics Committee Approval:** The approval of the ethics committee was taken from Başkent University Non-interventional

Clinical Research Ethics Committee (Date: 04.11.2020, Number: 20/118).

**Patient Consent for Publication:** This is a retrospective descriptive study.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** All authors contributed equally to the article.

**Conflict of Interest:** The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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