

Venous Thromboembolism Risk Assessment Among Ambulatory Cancer Patients: Demographic Study and Doctor's Adherence to Guidelines

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ABSTRACT

Background: Cancer-associated thrombosis (CAT) is the second cause of death for cancer patients. National Comprehensive Cancer Network (NCCN) guidelines recommend assessing CAT risk for all ambulatory cancer patients by Khorana score and prescribing thromboprophylaxis for high-risk patients. Unfortunately, clinical practice in many countries fails to apply this guideline effectively.

Objectives: To determine the level of venous thromboembolism (VTE) risk among ambulatory cancer patients and the oncologists' role in prescribing thromboprophylaxis to high-risk patients in Al-Diwaniyah Teaching Hospital, Al-Qadisiyah, Iraq.

Materials and methods: A cross-sectional study was conducted from September to October 2023 in the Oncology Center at Al-Diwaniyah Teaching Hospital, Al-Qadisiyah, Iraq. The oncologist's role in prescribing thromboprophylaxis for newly diagnosed ambulatory cancer patients visiting the oncology center was assessed after calculating the thrombosis risk score using the validated Khorana score.

Results: A 49 patients newly diagnosed with cancer were enrolled in the study. Most of the participants were females with a normal body weight. Breast cancer was the most common cancer type among study participants. Regarding the risk of VTE, eight (16.3%) participants had a high risk, 24 (48%) had a moderate risk, and 17 (36%) had a low risk. All of the study participants regardless of their thrombosis risk were not prescribed thromboprophylaxis by oncologists.

Conclusion: Most newly diagnosed ambulatory cancer patients had moderate to high risk of VTE. Oncologists did not prescribe thromboprophylaxis to any of these patients. Therefore, we recommended that all oncologists must be adherent to NCCN thromboprophylaxis guidelines.

Keywords: Cancer-associated thrombosis (CAT); Khorana score; Thromboprophylaxis

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INTRODUCTION

Cancer is a devastating disease characterized by the uncontrolled growth and survival of abnormally transformed cells [1, 2]. Significant morbidity and mortality can be associated with it, making it a leading cause of death worldwide. Cancer-associated thrombosis (CAT) is a major health problem for patients with cancer [3]. CAT ranks second as a cause of death for cancer

patients [4] because it is associated with worsened survival, morbidity, the need for hospitalization, and potential delay or interruption of systemic therapy for cancer [5]. Meanwhile, CAT often develops in 8% of cancer patients within a year of their malignancy diagnosis or disease progression [6, 7]. People who use newer systemic treatments for cancer, such as immunotherapy, anti-angiogenic agents, multitargeted tyrosine kinase inhibitors, and immunomodulatory drug combinations, also have a higher risk of venous thromboembolism (VTE) [5]. In cancer patients, VTE prediction often involves the use of risk assessment models or scores. There are many scoring systems, such as Khorana, PROTECHT, Vienna CATS, and CONKO scores. All of these scores are based on the presence of specific clinical and laboratory factors [8]. The total score

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determines the risk category of the patient, ranging from low to high risk, and thromboprophylaxis is necessary for those with high-risk [9]. A systematic review found that anticoagulant prophylaxis significantly reduced the risk of symptomatic VTE by about half among ambulatory cancer patients [10]. Additionally, research found that CAT prevention is a cost-effective method for ambulatory cancer patients at high risk of thrombosis [11]. Therefore, the current guidelines recommend assessing CAT risk among all ambulatory cancer patients using the validated Khorana score and prescribing thromboprophylaxis for high-risk patients (Khorana score ≥ 2) [12].

Unfortunately, in clinical practice, NCCN recommendations for CAT assessment and prevention are poorly followed, as shown in a recent study conducted in Turkey [13], a neighboring country to Iraq. Therefore, the current study aimed to determine the level of VTE risk among ambulatory cancer patients and the oncologists' role in prescribing thromboprophylaxis to high-risk patients in Al-Diwaniyah Teaching Hospital, Al-Qadisiyah, Iraq.

MATERIALS AND METHODS

Study design

A cross-sectional pilot study was conducted from 18 September to 18 October 2023 in the Oncology Center at Al-Diwaniyah Teaching Hospital, Al-Qadisiyah, Iraq. This center is the only one caring for cancer patients in the Al-Diwaniyah Governorate. The physician's role in prescribing thromboprophylaxis for newly diagnosed ambulatory cancer patients visiting the oncology center was assessed after calculating the thrombosis risk score using the validated Khorana score, which can be calculated based on 5 criteria: The site of primary cancer, platelet count level, white blood cell (WBC) count, and body mass index (BMI) (Table 1). Patients with total scores of ≥ 3 were stratified as having a high thrombosis risk; those with scores of 1–2 were considered to have a moderate risk, and those scoring zero were considered to have a low risk [9].

The College of Pharmacy, University of Baghdad's Ethical Committee approved the current study (Reference number: RECAUBCP10620238 on 10/6/2023).

Table 1. Calculation of Khorana score.

| Parameters | Score |
|---|----------|
| Site of primary cancer | |
| Very high risk tumors (like pancreas and stomach tumors). | 2 |
| High-risk tumors (like lymphoma, lung, testicular, gynecological, and bladder). | 1 |
| All other sites. | 0 |
| Platelets count (Prechemotherapy) $[\geq 350 \times 10^9/L]$. | 1 |
| Hemoglobin level (Prechemotherapy) $[\leq 10 \text{ g/dL}]$ or use of erythropoiesis-stimulating agents (ESAs). | 1 |
| Leukocyte count (Prechemotherapy) $[\geq 11 \times 10^9/L]$. | 1 |
| Body mass index $(\geq 35 \text{ kg/m}^2)$. | 1 |
| Risk category | |
| High risk | ≥ 3 |
| Moderate risk | 1–2 |
| Low risk | 0 |

Study sample

A total of 725 cancer patients visited the center during the study period. Adult non-hospitalized (ambulatory) cancer patients who are newly diagnosed to have cancer were considered eligible to participate in this study. Only 62 patients met the study inclusion criteria. Patients with hematological malignancies, except lymphoma, and those who refused to undergo blood testing were excluded from the study. The study included only 51 patients after applying the exclusion criteria, with 11 patients excluded for various reasons. All of the eligible patients ($n = 51$) were informed about the study objectives, and only 49 signed the informed consent and were thus included in this study (Figure 1).

Data collection

To assess thrombosis risk, the patient's age, gender, and site of cancer were directly obtained from the patient's medical sheet. A 3 ml blood specimen was obtained from each participant to measure the WBC and platelet count. In addition, all enrolled patients were requested to measure their height and weight. BMI was calculated by dividing weight (per Kg)/ height (per square meter). Those with a BMI of 18.5–24.9 kg/m^2 were considered to have normal body weight, those with BMI $< 18.5 \text{ kg/m}^2$ were considered to be thin, and those with a BMI $\geq 30 \text{ kg/m}^2$ were considered to be obese [14]. All of the above data were recorded in a data collection sheet and then transferred to Excel sheet.

Statistical analysis

Data input was done using Microsoft Excel 2010. Data analysis was done using Statistical Package for the Social Sciences (SPSS) version 17. Categorical variables were presented as numbers and percentages. While continuous variables were presented as mean \pm standard deviation. The Chi-square test was used to test the significance among categorical variables. A P-value of less than 0.05 was considered a statistically significant difference.

RESULTS

Most participating patients in this study were non-elderly females with a normal body weight (BMI of 18.5–24.9 kg/m^2). Breast cancer was the most common type of cancer among study participants (22%). Table 2 provides further details.

Around half of the patients were at moderate risk (Figure 2).

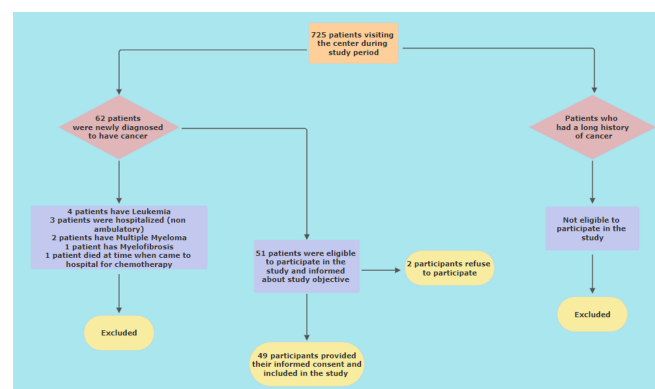


Figure 1. Flow chart of study participants.

Table 2. Demographic and clinical characteristics of the 49 participants.*

| | | |
|------------------------------|-----------------------------|---------------|
| Age (in years) | Mean ± SD | 60.53 ± 13.58 |
| | < 65 years | 27 |
| | ≥ 65 years | 22 |
| Gender | Male | 22 |
| | Female | 27 |
| Height | Mean ± SD | 162.39 ± 7.63 |
| Weight | Mean ± SD | 71.12 ± 18.46 |
| Body mass index (BMI) | Mean ± SD | 26.97 ± 6.92 |
| | < 18.5 kg/m ² | 3 |
| | 18.5–24.9 kg/m ² | 17 |
| | 25–29.9 kg/m ² | 16 |
| White blood cell (WBC) count | Mean ± SD | 8.43 ± 4.62 |
| | | |
| Platelet count | Mean ± SD | 261.38 ± 93.4 |
| Type of cancer | Breast | 11 |
| | Lung | 7 |
| | Bladder | 8 |
| | Gastric | 4 |
| | Pancreatic | 3 |
| | Prostate | 2 |
| | Lymphoma | 2 |
| | Colorectal | 2 |
| | Others* | 10 |

* Brain, thyroid, appendiceal, adrenocortical, oropharyngeal, and soft tissue sarcoma.

Among participants aged 65 years and older, there are 15 patients (68.2%) with moderate risk. Conversely, among participants younger than 65 years, 51.9% were categorized as low risk. There was a statistically significant difference between age and the risk of thrombosis (P-value = 0.017). The gender analysis revealed a 54.5% moderate risk distribution among male participants. While female participants exhibited

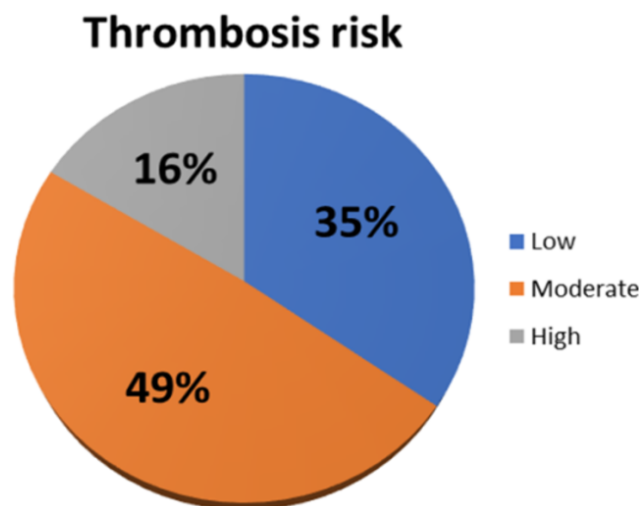


Figure 2. Thrombosis risk among study participants according to Khorana risk score.

44.4% moderate risk distribution. There was no statistically significant difference (P-value = 0.616) between sex and risk of thrombosis (Table 3).

Oncologists did not prescribe thromboprophylaxis to any of the participating patients, regardless of their thrombosis risk.

DISCUSSION

VTE is a highly prevalent and potentially fatal disease. Many risk factors have been associated with VTE, like obesity, hormone use and immobility, but cancer is the most risk factor for such condition. Approximately 20% of cancer patients will experience VTE at some stage [15]. VTE is the second-most common cause of cancer death, second only to cancer itself. The study’s main outcome is that oncologists do not prescribe thromboprophylaxis to high-risk cancer patients.

The current study revealed that the mean age of diagnosing cancer among study participants was about 60 years, which is somewhat less than the average age of cancer incidence in the world [16]. However, the significant increase in cancer incidence among adolescents and young adults in Middle Eastern countries like Iraq [17] somewhat predicts this finding.

The current study’s results indicate that females were more likely than males to receive a cancer diagnosis. This gender difference in cancer incidence is different from that detected in developed countries; meanwhile, it was detected in developing countries due to the social vulnerability of females in those countries (i.e., poorer diet and reproductive risks) [18]. In addition, a high prevalence of breast cancer in Iraq, which is a predominant cancer in females [19], may be responsible for this higher incidence of cancer among participating women. The present study showed that most newly diagnosed patients with cancer were either obese or overweight. This finding is highly reasonable since obesity increases the risk of developing cancer as shown by a recent review study by Pati and colleagues [20].

According to the findings in the current study, the most common cancer among study participants was breast cancer. This finding is consistent with WHO data for the most common types of cancer in Iraq [21].

After stratifying study participants using the Khorana risk score, only a minority (16%) of participants were classified as having a high risk of VTE. This finding was very close to that obtained by a recent retrospective study that included Korean cancer patients in which most of them had either low or moderate risk of thrombosis [22]. Meanwhile, our study found that elderly cancer patients had a higher risk score than younger patients. A similar finding was detected by Douce and colleagues among cancer patients who visited ambulatory cancer clinic at the University of Vermont Medical Center (UVMCC), in which younger individuals had a significantly lower Khorana score [23].

However, the current study discovered that oncologists did not prescribe prophylactic anticoagulants to any patients at high risk of VTE. Other Middle East countries like Turkey [13] and Lebanon [24] also showed poor adherence to recommended guidelines for prescribing thromboprophylaxis for cancer patients at high risk of thrombosis. There are some possible reasons behind the inadequate thromboprophylaxis for cancer patients in the current study, including the limited awareness of oncologists about the thrombosis risk among ambulatory cancer patients [25] and the limited use of risk scores in clinical practice [26]. Therefore, enhancing oncolo-

Table 3. The level of venous thromboembolism risk according to participants' demographics.

| Variable | Low risk N (%) | Moderate risk N (%) | High risk N (%) | Total N (%) | P-value |
|--------------|----------------|---------------------|-----------------|-------------|---------|
| Age per year | | | | | 0.017 |
| ≥ 65 | 3 (13.6) | 15 (68.2) | 4 (18.2) | 22 (44.9) | |
| < 65 | 14 (51.9) | 9 (33.3) | 4 (14.8) | 27 (55.1) | |
| Total | 17 (34.7) | 24 (49) | 8 (16.3) | 49 (100) | |
| Gender | | | | | 0.616 |
| Male | 6 (27.3) | 12 (54.5) | 4 (18.2) | 22 (44.9) | |
| Females | 11 (40.7) | 12 (44.4) | 4 (14.8) | 27 (55.1) | |
| Total | 17 (34.7) | 24 (49) | 8 (16.3) | 49 (100) | |

gists' awareness and motivation to use risk scores in stratifying thrombosis risk for ambulatory cancer patients is mandatory.

The main limitation of the present study is its focus on a single oncology center in a single Iraqi governorate, which is also the only oncology center in the Al-Qadisiyah governorate. Therefore, we strongly recommend conducting a larger study to evaluate the adherence of Iraqi oncologists to thromboprophylaxis guidelines in other Iraqi governorates.

CONCLUSION

A significant number of recently diagnosed ambulatory cancer patients in Al-Diwaniyah Teaching Hospital had a moderate to high risk of developing VTE. Oncologists did not prescribe thromboprophylaxis for any of these individuals. We advise all oncologists to strictly follow the NCCN guidelines for thromboprophylaxis to achieve the best possible patient outcome.

ETHICAL DECLARATIONS

Acknowledgements

None.

Ethics Approval and Consent to Participate

The Ethical Committee at the College of Pharmacy, University of Baghdad, Baghdad, Iraq (reference number: RE-CAUBCP10620238) approved the study on 10/6/2023. We asked participants to participate based on their willingness. We informed them about the study's objectives, their confidentiality, and the use of the data solely for research purposes.

Consent for Publication

Not applicable (no individual personal data included).

Availability of Data and Material

Data generated during this study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that there is no conflict of interest.

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Authors' Contributions

Study conception and design: Michael EM. Literature search: Tariq MA. Data acquisition: Tariq MA. Data analysis and interpretation: Michael EM. Manuscript preparation: Tariq MA. Manuscript editing and review: Michael EM. Both authors read and approved the final version of the manuscript.

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