**Původní sdělení** | Original research article

# The role of the $CHA_2DS_2$-VASc score as a venous thromboembolism predictor in cancer patients

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SOUHRN

**Cíl:** V poslední době se předmětem zájmu kardiologů stal obor kardioonkologie. Jedním z problémů kardiovaskulární medicíny, s nimiž se lze setkat po stanovení diagnózy karcinomu a během onkologické léčby, je žilní tromboembolická nemoc (venous thromboembolism, VTE). Skóre $CHA_2DS_2$-VASc je skórovací systém, který hodnotí riziko embolie při fibrilaci síní a pomáhá při indikování antikoagulační léčby. V naší studii jsme zkoumali vztah mezi VTE a skóre $CHA_2DS_2$-VASc u pacientů s karcinomem plic.
**Materiál a metoda:** Retrospektivně byly analyzovány údaje 687 pacientů s diagnózou karcinomu plic stanovenou v období mezi 1. červencem 2010 a 15. květnem 2020. Z účasti ve studii bylo vyloučeno 403 pacientů s chirurgickým výkonem v anamnéze v posledním měsíci před stanovením diagnózy VTE, u nichž byla provedena masivní transfuze krve nebo katetrizace centrálním/periferním žilním katétrem na končetině s VTE, případně v jejichž zdravotních záznamech nebyly k dispozici úplné údaje. Do studie tak bylo nakonec zařazeno 96 pacientů s diagnózou VTE a 188 pacientů bez této diagnózy. U obou skupin byly vypočítány hodnoty skóre $CHA_2DS_2$-VASc a skóre v systému podle Khorana.
**Výsledky:** Mezi oběma skupinami pacientů, s diagnózou VTE a bez ní, nebyl významný rozdíl ve věku. Byly nalezeny statisticky významné rozdíly mezi oběma skupinami z hlediska pohlaví, přítomnosti hypertenze a diagnózy cévního onemocnění, a žádný významný rozdíl ve skóre podle Khorana. Skóre $CHA_2DS_2$-VASc bylo významně vyšší ve skupině s diagnózou VTE než ve skupině bez tohoto onemocnění.
**Závěr:** Se zvyšujícími se počty případů karcinomu a možností chemoterapie roste každým dnem i význam kardioonkologie. Skóre $CHA_2DS_2$-VASc, které často používáme v klinické praxi, lze využít jako prediktor rozvoje VTE u onkologických pacientů.



*Keywords:*
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ABSTRACT

**Objective:** Cardiooncology is one of the subjects of interest of cardiology department recently. Venous thromboembolism is one of the cardiovascular problems encountered after cancer diagnosis and during cancer treatment. The $CHA_2DS_2$-VASc score is a score system that determines the risk of embolism in atrial fibrillation and determines the indication for anticoagulant therapy. In our study, we wanted to investigate the relationship between venous thromboembolism and $CHA_2DS_2$-VASc score in patients diagnosed with lung cancer.
**Material and method:** 687 patients diagnosed with lung cancer between 1 July 2010 and 15 May 2020 were analyzed retrospectively. 403 patients who had a surgical history in the last 1 month before the diagnosis of VTE, who received massive transfusion therapy, and who underwent central-peripheral venous catheterization in the extremity with VTE, or who had incomplete data in their files were excluded from the study. As a result, 96 patients with a diagnosis of VTE and 188 patients without a diagnosis of VTE were included in the study. $CHA_2DS_2$-VASc score and Khorana score were calculated in both groups.
**Results:** There was no significant difference in age between the patient groups with and without VTE diagnosis. There was a statistically significant difference between the two groups in terms of gender, hypertension and vascular disease diagnosis. There was no statistically significant difference in both groups in terms of Khorana score. The $CHA_2DS_2$-VASc score was significantly higher in the group diagnosed with VTE compared to the group without VTE.
**Conclusion:** Under the increasing number of cancer cases and chemotherapy options, the importance of cardiooncology is increasing day by day. The $CHA_2DS_2$-VASc score, which we frequently use in clinical practice, can be used as a predictor of venous thromboembolism in cancer patients.

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## Introduction

Cardiooncology is one of the subjects of interest of cardiology department recently. With the increase in the number of patients receiving chemotherapy and the use of new chemotherapy agents, the relationship between cancer and chemotherapy and the cardiovascular system has begun to be investigated more frequently. Ventricular dysfunction, development of coronary artery disease, arrhythmia, and hypertension are some of the side effects encountered during cancer treatment.[1] In addition, vascular endothelial dysfunction due to vascular endothelial dysfunction caused by vasoactive peptides and cytokines released in cancer tissue cause thrombus formation.[2] Therefore, another cardiovascular pathology seen in cancer patients is venous thromboembolism. The scoring system that predicts embolism in atrial fibrillation (AF) patients and indicates an indication for anticoagulant therapy is the $CHA_2DS_2$-VASc score.[3] CHA2DS2-VASc score is one of the most frequently used scores in clinical practice. In this study, we wanted to investigate the predictive value of $CHA_2DS_2$-VASc score, which is an embolism predictor in patients with AF, for venous thromboembolism in lung cancer patients.

## Methods

Patients who were diagnosed with lung cancer in our hospital between July 1, 2010 and May 15, 2020 and had regular controls for at least 6 months were screened retrospectively. 284 patients with complete data for the study in their files were included in the study. The patients were grouped as with and without venous thromboembolism. Patients who had deep vein thrombosis and/or pulmonary embolism after being diagnosed with lung cancer were accepted under the diagnosis of venous thromboembolism. There were 96 patients with a diagnosis of VTE and 188 patients without a diagnosis of VTE. Patients who underwent surgery in the last 1 month and received massive transfusion prior to VTE diagnosis were not included in the study. There was no central-peripheral venous catheterization in patients with venous thromboembolism. When calculating the $CHA_2DS_2$-VASc score, congestive heart failure (1 point), hypertension (1 point), age ≥75 (2 points), diabetes (1 point), stroke (2 points), vascular disease (previous myocardial infarction, history of coronary revascularization, such as a history of peripheral artery disease) (1 point), age range 65–74 (1 point), and female gender (1 point for women 65 and above) were used. In addition, the Khorana score, which indicates the risk status for venous thromboembolism in cancer patients, was also calculated for both groups. In Khorana score; 2 points for very high risk cancers (stomach, pancreas), 1 point for high risk cancers (lung, gynecological, genitourinary), 1 point for hemoglobin <10 g/dL or red cell growth factor use, pre-chemotherapy leukocyte >11 × $10^9$/L, 1 point for >350 × $10^9$/L before chemotherapy and 1 point for body mass index >35 kg/$m^2$ were calculated. For Khorana score, 0 points were considered a low risk, 1–2 points as a medium risk, <2 points as a very high risk.

## Statistics

SPSS for Windows version 23.0 (SPSS Inc., IL, USA) was used for statistical analysis. The normal distribution analysis of the data was interpreted with the values of Skewness and Kurtosis. Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as percentages. Continuous data were compared using Student's t test. Categorical data were compared using the chi-square test. Pearson's correlation coefficient was used for correlation analysis. A value of $p$ <0.05 was considered statistically significant. Multiple logistic regression analysis was used with all of the predetermined factors $p$ <0.25 in the univariate analysis. Statistical significance was accepted as $p$ <0.05 in multivariate analysis.

## Results

The average age of the study population is 62.45±9.19 years. The number of female patients included in the study was 44 (15.5%). The mean follow-up period after diagnosis of cancer was 30.56±21.82 months. There was no significant difference in age between the patient groups with and without VTE diagnosis. There was a statistically significant difference between the two groups in terms of gender, hypertension, and diagnosis of vascular disease (Table 1). There was no statistically significant difference in both groups in terms of Khorana score. The CHADVASC score was significantly higher in the group diagnosed with VTE than in the group without VTE. In regression analyzes in which the variables of the $CHA_2DS_2$-VASc score were evaluated individually and multiplely, gender, heart failure, hypertension, diabetes, stroke, and a history of vascular disease were found to be associated with venous thromboembolism in lung cancer patients (Table 2).

**Table 1 – Clinical characteristics of the study group patients**

| | Without VTE n = 188 | With VTE n = 96 | $p$-value |
|---|---|---|---|
| Age (years) | 62.35±8.52 | 62.66±10.43 | 0.788 |
| Gender<br>Female<br>Male | <br>14 (7.4%)<br>174 (92.6%) | <br>30 (31.3%)<br>66 (68.7%) | <0.001 |
| Heart failure | 3 (1.6%) | 4 (4.2%) | 0.186 |
| Hypertension | 38 (20.2%) | 31 (32.3%) | 0.025 |
| Diabetes mellitus | 30 (16.0) | 21 (21.9%) | 0.219 |
| Stroke | 8 (4.3%) | 1 (1.0%) | 0.144 |
| Vascular disease | 27 (14.4%) | 24 (25.0%) | 0.027 |
| Khorana score<br>Intermediate<br>High | <br>163 (86.7%)<br>25 (13.3%) | <br>80 (83.3%)<br>16 (16.7%) | 0.445 |
| $CHA_2DS_2$-VASc score | 1.02±1.23 | 1.46±1.77 | 0.015 |

VTE – venous thromboembolism.

**Table 2 – Regression analysis of variables in the $CHA_2DS_2$-VASc score in lung cancer patients**

| | Univariate regression analysis | | | Multivariate regression analysis | | |
|---|---|---|---|---|---|---|
| | Odd ratio | CI (95%) | *p*-value | Odds ratio | CI (95%) | *p*-value |
| Age | 1.004 | 0.997–1.031 | 0.787 | – | – | – |
| Gender | 5.649 | 2.820–11.317 | <0.001 | 5.501 | 2.690–11.249 | <0.001 |
| Heart failure | 2.681 | 0.588–12.231 | 0.203 | 1.250 | 0.206–7.595 | 0.809 |
| Hypertension | 1.883 | 1.079–3.284 | 0.026 | 1.514 | 0.782–2.931 | 0.218 |
| Diabetes mellitus | 1.475 | 0.792–2.746 | 0.221 | 1.086 | 0.514–2.294 | 0.829 |
| Stroke | 0.237 | 0.029–1.922 | 0.178 | 0.177 | 0.020–1.576 | 0.121 |
| Vascular disease | 1.988 | 1.073–3.680 | 0.029 | 2.016 | 0.953–4.263 | 0.067 |

## Discussion

The effects of these changes on cardiovascular system have recently begun to attract more attention, along with advances in cancer tests, frequent updates in pathological diagnoses, and new chemotherapy and radiotherapy treatment options. Conditions such as left ventricular dysfunction, coronary artery disease, pericardial involvement, hypertension, and arrhythmia are cardiotoxicity conditions that occur after cancer diagnosis, especially with chemotherapy and radiotherapy.[1,4,5] In addition, cancer diagnosis increases the risk of venous thromboembolism independent of all risk factors for venous thromboembolism.[6–8] Patients with lung cancer are also prone to hypercoagulation and thromboembolism. Both hypercoagulability due to primary cancer tissue and endothelial damage due to chemotherapies may predispose to venous thromboembolism. In addition, central catheters, cancer-induced immobility or cancer surgery also predispose to VTE.

The $CHA_2DS_2$-VASc score is a scoring system for atrial fibrillation patients to indication for anticoagulant therapy to prevent embolic complications. The higher the score, the higher the risk of embolic complications. It is one of the most frequently used scores in cardiology clinical practice. There are some studies in the literature investigating the relationship between cardiovascular system diseases and $CHA_2DS_2$-VASc score.[9–11] The relationships between this $CHA_2DS_2$-VASc score and stent thrombosis prediction, mortality prediction in patients with heart failure, and development of atrial fibrillation in patients with acute coronary syndrome have been revealed. When we consider the pathophysiology of thromboembolism, we thought that this score could predict venous thromboembolism in cancer patients. Considering the patient groups with and without VTE in our study, the $CHA_2DS_2$-VASc score was statistically significantly higher in the group with VTE. Considering single and multiple regression analyses, all variables other than "age", one of the variables that constitute the $CHA_2DS_2$-VASc score, predispose patients to venous thromboembolism in patients with lung cancer.

The Khorana score used for venous thromboembolism prophylaxis in cancer patients was also calculated for the patient groups in the study.[12] Since the patient group was lung cancer patients, the risk status was at least moderate for the patient groups. There was no statistically significant difference in Khorana score between the two groups. Despite this result in our study, the significant difference in the $CHA_2DS_2$-VASc score in both groups may indicate that additional scores in terms of VTE should be evaluated and the $CHA_2DS_2$-VASc score can be used in this regard. In addition, our study may have brought a perspective on the fact that a single risk scoring system may not be sufficient in determining the risk group in cancer types such as lung cancer that have a tendency to thromboembolism.

Cancer pathology, which is limited to lung cancer patients due to the patient population in the hospital we work in, can be considered a limitation for the study. Although the study is retrospective, the lack of data loss thanks to regular follow-up of cancer patients and keeping their files systematically increases the reliability of the study.

## Conclusion

With increasing number of cancer cases and chemotherapy options, the importance of cardiooncology is increasing day by day. The $CHA_2DS_2$-VASc score, which we frequently use in clinical practice, can be used as a predictor of venous thromboembolism in cancer patients.

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