

LEŚKIEWICZ, Michał, DANIEL, Piotr, SKŁADANEK, Justyna, OTREBA, Karina, CIESZKOWSKA, Joanna and CZUPRYŃSKA, Karolina. Risk Factors for Thromboembolism in the Population of Cancer and Hospice Patients. *Journal of Education, Health and Sport*. 2024;72:51119. eISSN 2391-8306.

<https://dx.doi.org/10.12775/JEHS.2024.72.51119>

<https://apcz.umk.pl/JEHS/article/view/51119>

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences). Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu). © The Authors 2024; This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited. The authors declare that there is no conflict of interests regarding the publication of this paper. Received: 21.04.2024. Revised: 10.05.2024. Accepted: 22.05.2024. Published: 26.05.2024.

Risk Factors for Thromboembolism in the Population of Cancer and Hospice Patients

Michał Leśkiewicz, University Clinical Centre of the Medical University of Warsaw, Żwirki i Wigury 63A, 02-091 Warsaw, Poland michal.les13@gmail.com, <https://orcid.org/0009-0000-0890-2672>

Piotr Daniel, National Medical Institute of the Ministry of the Interior and Administration, Wołoska 137, 02-507 Warsaw, Poland <https://orcid.org/0009-0007-3920-2645>, piotr.dan@onet.eu

Justyna Aleksandra Składanek, Doctor Anna Gostyńska Wolski Hospital, Marcina Kasprzaka 17, 01-211 Warsaw, Poland <https://orcid.org/0009-0003-0547-6841>, justyna.skladanek97@gmail.com

Karina Zofia Otręba, University Clinical Centre of the Medical University of Warsaw, Żwirki i Wigury 63A, 02-091 Warsaw, Poland <https://orcid.org/0009-0009-9655-5353>, karina.zofia.otreba@gmail.com

Joanna Cieszkowska, Medical University of Lublin, Aleje Raławickie 1, 20-059 Lublin, Poland <https://orcid.org/0000-0002-4011-1149>, joasia.cieszkowska.99@gmail.com

Karolina Czupryńska, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland <https://orcid.org/0009-0007-8932-2688>, czuprynska.karolina@gmail.com

Abstract

Venous thromboembolism (VTE) is a significant cause of death among palliatively treated patients. So far, numerous studies have been conducted on the general population. As a result, special scales were created to assess the risk of VTE or the probability of its occurrence. Among patients with terminal disease, there are much fewer publications discussing the problem of VTE. Hospice care patients constitute a special group due to their epidemiological structure and accompanying diagnoses. The most common are malignant tumors and heart failure. For this reason, they are particularly vulnerable to VTE events.

This article reviews the literature on risk scales such as The Padua Risk Assessment Scale, Khoran score, Wells scale, PVFS scale and VTE-BLEED scale. We also present risk factors which contribute to the development of the VTE as well as to a more serious course of VTE. We discuss the epidemiological structure of patients, the impact of cancer as well as the chemotherapy used to treat it. We discuss the epidemiological structure of patients, the impact of cancer as well as the chemotherapy used in its treatment. We describe how the presence of a catheter and immobilization contribute to the development of VTE. We focus particularly on scales and risk factors to which a patient with a terminal disease is exposed.

More research is needed in the future to better predict VTE in hospice patients. We hope that this work will increase awareness and encourage researchers to expand knowledge in this area.

Keywords: Venous Thrombosis, Pulmonary Embolism, Venous Thromboembolism, Signs and Symptoms, Prevention and Control

Introduction

Venous thromboembolism (VTE/VTE) is a disease entity that includes in its definition, deep vein thrombosis (DVT) and pulmonary embolism (PE). Although the two diseases differ in clinical presentation, they share risk factors ¹ and pathophysiology. ² The description of the biomechanics of clot formation proposed by Rudolph Virchow in the form of a triad of factors

- slowing the flow, damage to the vascular wall and hypercoagulability of the blood - is still valid. Clots most often form in the veins of the pelvis or lower limbs, from where they can break off and, after passing through the heart, cause pulmonary embolism. Depending on the advancement of the disease - in particular the degree of vascular occlusion, the efficiency of collateral circulation and the patient's general condition, VTE may be symptomatic or asymptomatic.²

Palliatively treated patients and oncological patients are particularly vulnerable to VTE³, due to immobilization, chronic inflammatory reactions caused by the neoplasms as well as direct damage to the vascular wall through infiltration and secretion of prothrombotic factors by the neoplasm.⁴

It is estimated that up to one third of hospice patients will develop VTE.⁵ Despite its high actual incidence, VTE is relatively rarely diagnosed in palliative care patients⁶, and is caused by 3 main factors. The first is the fact that most blood clots remain asymptomatic or have few symptoms (swelling of the lower limbs).⁷ The second factor is that the symptoms of VTE are masked by the symptoms of the underlying disease, such as lymphedema of the lower limbs, pleural effusion, pulmonary effusion, and others.^{6, 7}

Risk factors

Venous thromboembolism has well-defined risk factors.^{8 9}The Padua Risk Assessment Scale was created to assess the patient's risk of developing VTE while being hospitalized.¹⁰ Depending on the clinical feature, you can get 3, 2 or 1 point. The score for each predisposing factor is added up and if it is above 3, it indicates a high risk of VTE.

Clinical feature	Points
Active cancer	3
Diagnosed thrombophilia	3
Immobilization (expected to be in bed for at least 3 days)	3
Previous VTE (except superficial vein thrombosis)	3
Recent (< 1 month) injury or surgical procedure	2
Age at least 70 years	1
Heart or respiratory failure	1
Recent myocardial infarction or ischemic stroke	1
Acute infection or rheumatological disease	1
Obesity (BMI = 30 and above)	1
Hormonal treatment	1

Table 1. The Padua Risk Assessment Scale

On the other hand, in patients receiving chemotherapy, the scale determining the risk of VTE is the Khoran score. It is a proven and validated tool for identifying cancer patients at higher risk of venous thromboembolism.^{11,12}

Clinical feature	Points
Platelet count before chemotherapy $\geq 350 \times 10^9/l$	1
Hemoglobin level < 10 g/dL or EPO use	1
Leukocyte count before chemotherapy $> 11 \times 10^9/l$	1
BMI ≥ 35 kg/m ²	1
lung cancer	1
bladder cancer	1
testicular cancer	1
lymphoma	1
reproductive tract cancer	1
pancreatic cancer	2
stomach cancer	2

≤ 0 – low risk

1–2 – intermediate risk

≥ 3 – high risk

Table 2. Khoran score

There are studies that indicate problems with the use of the above scale. In one of them, researchers indicate that the Khorana score does a poor job of distinguishing pancreatic cancer patients at intermediate and high risk of VTE.¹³ U. Pelzer, M. Sinn, J. Stieler, and H. Riess therefore propose replacing the BMI parameter with the fitness status in patients with pancreatic cancer.¹⁴

In patients with lymphoma, thanks to the use of this scale, researchers were able to identify high-risk patients with a low (7%) chance of symptomatic VTE shortly after the examination.

15

Specific risk factors to which hospice care patients are exposed

So far, many high-quality scientific papers have been published on the topic of VTE risk factors for the general population.^{8 9 10} The essence of this problem is different for the

population of patients under palliative care.^{16,17} Therefore, in this part of the publication we will focus on discussing the risk factors to which palliative patients are particularly exposed.

Epidemiological structure of patients

Due to their epidemiological structure, hospice care patients are at high risk of developing VTE.^{18,19} Among the diseases that lead a patient to the stage of palliative care, cancer and cardiovascular diseases come to the fore.^{19,20} According to a study by Johnson et al conducted on a group of hospice patients, cancer patients have a greater chance of developing symptoms indicating VTE (new pleuritic pain, new swelling of the lower limb, or new increasing shortness of breath) (13%) than patients staying in hospice due to diseases such as heart failure (12%) or neurological diseases (4%). Among the study cohort, as many as 24% showed TER (Temporary elevated risk), and 96% THRIFT at a moderate or high level.¹⁸

Cancer

It is well documented in the literature that cancer is a risk factor for VTE.²¹ The first mention of an increased incidence of thrombosis among cancer patients appeared as early as 1865.²² The increased risk of VTE results from the activity of cancer cells. There is an increase in the secretion of tissue thrombocystin by cancer cells, which, in combination with coagulation proteases in the plasma, activates the coagulation cascade. Other phenomena include the invasion of cancer cells into the vessel lumen or the penetration of cancer cells into the circulatory system.^{23 24} Moreover, some cancers predispose to the development of VTE. Patients with cancer of the pancreas, stomach, kidney, bladder, endometrium and lung have the highest risk.^{25,26} A study by Chew et al on a large group of oncology patients showed that when metastases occur, the risk increases many times over (20 times more in the case of melanoma, 9 times more in the case of bladder cancer, 5-6 times more in the case of endometrial cancer). Moreover, among the study group of patients, the incidence rate was higher during the first year of follow-up than during the second year in all cancers except pancreatic cancer without metastases. There was no relationship between gender and the occurrence of VTE. Moreover, a higher risk of incidence was observed among black patients with uterine cancer and a lower risk among patients with lung cancer and non-Hodgkin's lymphoma than among Caucasian patients.²⁵

Chemotherapy-related VTE.

Side effects of treatment for oncology patients are also important. Chemotherapy increases the risk of VTE. ²⁷⁻²⁹ Previous meta-analyses have shown that patients receiving cisplatin or bevacizumab have a higher risk of VTE compared to patients receiving chemotherapy without these drugs.^{30,31}

Khorana et al in their study showed that upper gastrointestinal cancer, breast cancer and lymphomas are associated with a higher risk of developing VTE in patients undergoing chemotherapy. There was no relationship between the risk of VTE and the chemotherapy cycle, but a correlation was observed between VTE events and the level of platelets. Patients with high PLT values (350,000/mm³) before starting chemotherapy are at greater risk than patients with lower values of this parameter throughout the treatment period. Moreover, a statistically insignificant increase in the risk of morbidity was demonstrated among patients with an ECOG score of 2 or greater. Patients with a hemoglobin level below 10g/dL and those receiving blood cell growth factors during the first cycle of chemotherapy had a statistically significant increased risk.³²

Catheter in a peripheral vein

Another risk factor a palliative patient is exposed is a catheter in a peripheral or central vein.
^{33,34}

In their study on a group of 2,227 patients with cancer and a peripheral venous catheter, Wang et al identified the following risk factors: male gender, age over 65, platelet level over 9.5 thousand/mm³, Hb<13g/dl, D Dimer >0.5mg/L, APTT<25s, lung or gastrointestinal cancer, presence of any infection, smoking, use of cisplatin, carboplatin, vincristine, paclitaxel, long-term catheter use.³⁵

Cardiovascular disease

Cardiovascular diseases, next to cancer, are the most common diseases of palliative medicine patients. ^{19,20} Among them, heart failure occurs most often. Patients suffering from this disease have an increased predisposition to prothrombotic states, including all three elements of Vichow's triad. Flow disturbances are caused by poor contractility and abnormal blood flow through the ventricles, resulting in low cardiac output. ³⁶

In the course of heart failure, abnormalities in the structure of the endothelium have also been demonstrated. The secretion of nitric oxide from endothelial cells is reduced, which causes the

activation of monocytes and platelets, which, by adhering to the endothelium, increase the risk of thromboembolism.³⁷ The last element of Virchow's triad is an increase in the concentration of prothrombotic blood elements. Compared to a healthy person, patients with heart failure have increased levels of beta-tromboglobulin, D-Dimers and thrombin-antithrombin III complexes. The above results indicate increased activation of platelets, thrombin and plasma fibrinolytic activity. Importantly, patients with more severe heart failure recorded results indicating a more severe prothrombotic process.³⁸

In their meta-analysis of 530,641 patients with heart failure, Xu et al showed that patients with chronic heart failure have a higher risk of VTE than patients with acute heart failure, which is explained by a potentially reversible cause in the second group.³⁹, while a study by Ota et al among hospitalized patients with congestive heart failure showed that the incidence of deep vein thrombosis was higher among NYHA 4 patients than among patients scoring 2 or 3 on this scale.⁴⁰

Immobilization

Immobilization for at least three days is a strong risk factor according to the Padua scale.⁴¹ Hospice care patients, due to their condition, often achieve an ECOG score of 4, which means spending the entire day in bed. Previous studies on groups of several thousand hospice patients have shown that 85% of patients without cancer, 75% of patients with cancer, and over 70% of all patients achieve 3 or 4 points on the ECOG scale.^{42 43}

Scales

To diagnose deep vein thrombosis, we use a combination of appropriate scales (which are a clinical assessment of the probability of thrombosis) and additional tests such as D-dimer concentration and an ultrasound compression test. Examples of scales used to diagnose VTE will be discussed below.

Wells scale

This is a scale used to assess the clinical probability of DVT.

Features	Score (points)
Active cancer (treatment within last 6 months or palliative)	1
Calf swelling >3 cm compared to the other leg	1
Recently bedridden \geq 3 days,	1
Collateral (nonvaricose) superficial veins present	1
Entire leg swollen	1
Localized tenderness along the deep venous system	1
Pitting edema, confined to symptomatic leg	1
Paralysis, paresis, or recent plaster immobilization of the lower extremity	1
Alternative diagnosis at least as likely	-2

≤ 0 – low risk

1–2 – moderate risk

≥ 3 – high risk

Table 3 Wells scale

As can be seen from the table above, palliative patients can easily obtain a higher number of points, which increases the likelihood of deep vein thrombosis. However, as shown by G. J. Geersing et al, the use of this scale in patients with malignant tumors is less effective in excluding thrombosis. Additionally, in the same study, it is recommended to use a modified scale where an additional point is added for a history of DVT in patients with a history of deep vein thrombosis.⁴⁴

PVFS scale

This is a scale that allows us to assess the functioning of a patient after an episode of thrombosis. It contains 5 categories of functional limitations and a separate category D if the patient died before evaluation. Thanks to this scale, we can better select appropriate rehabilitation and medical activities to the patient's condition and needs.

In a cohort study, the use of this scale captured differences between groups of patients over and under 70 years of age.⁴⁵ This indicates a reduced ability of the older people to recover and increases the need for care and assistance in this group of patients.

PVFS scale grade + description	Description
0 No functional limitations	No symptoms, pain, or anxiety.
1 Negligible functional limitations	All usual duties/activities at home or at work can be carried out at the same level of intensity, despite some symptoms, pain, or anxiety.
2 Slight functional limitations	Usual duties/activities at home or at work are carried out at a lower level of intensity or are occasionally avoided due to symptoms, pain, or anxiety.
3 Moderate functional limitations	Usual duties/activities at home or at work have been structurally modified (reduced) due to symptoms, pain, or anxiety.
4 Severe functional limitations	Assistance needed in activities of daily living due to symptoms, pain, or anxiety: nursing care and attention are required.
D Death	

Table 4 PVFS scale

VTE-BLEED scale

By using this score, the risk of serious or clinically significant bleeding after day 30 of anticoagulation can be estimated among patients with VTE.^{46,47} As the table shows, having

only a malignant tumor indicates an increased risk of bleeding, which makes treatment with anticoagulants particularly difficult in this group of patients.

Clinical feature	Score
Active cancer	2
Male patient with uncontrolled hypertension	1
Anemia	1.5
History of bleeding	1.5
Renal dysfunction (creatinine clearance 30-60 mL/min)	1.5
Age \geq 60 years	1.5

Table 5 VTE-BLEED scale

Reaching a total of 2 points or more indicates a high risk of bleeding.

Conclusions

Venous thromboembolism is a significant diagnostic and therapeutic problem in patients undergoing palliative treatment. Due to their diseases, hospice patients are at high risk of thrombosis. The greatest difficulty is the lack of an adequate number of scientific studies conducted on this group of patients, which means that there are no appropriate guidelines for diagnostics and treatment. Therefore, doctors most often use VTE risk scales validated in cancer. We hope that thanks to the development of research, scales intended for hospice patients will appear in the future.

Disclosure

Author's contribution:

Analysis and Preliminary Research: **Piotr Daniel**

Planning and Designing: **Karina Otręba**

Writing and Editing: **Michał Leśkiewicz**

Data Analysis: **Karolina Czupryńska**

Scientific Verification **Joanna Cieszkowska**

Summary and Conclusions: **Justyna Składanek**

All authors have read and agreed with the published version of the manuscript.

Financing statement: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflict of interest: The authors deny any conflict of interest.

References

1. Bruni-Fitzgerald KR. Venous thromboembolism: An overview. *Journal of Vascular Nursing*. 2015;33(3). doi:10.1016/j.jvn.2015.02.001
2. Phillippe HM. Overview of venous thromboembolism. *Am J Manag Care*. 2017;23(20).
3. Costa J, Araújo A. Cancer-Related Venous Thromboembolism: From Pathogenesis to Risk Assessment. *Semin Thromb Hemost*. 2021;47(6). doi:10.1055/s-0040-1718926
4. Eichinger S. Cancer associated thrombosis: Risk factors and outcomes. *Thromb Res*. 2016;140. doi:10.1016/S0049-3848(16)30092-5
5. Heit JA, Silverstein MD, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Risk factors for deep vein thrombosis and pulmonary embolism: A population-based case-control study. *Arch Intern Med*. 2002;160(6):809-815. doi:10.1001/archinte.160.6.809
6. Noble S. The challenges of managing cancer related venous thromboembolism in the palliative care setting. *Postgrad Med J*. 2007;83(985). doi:10.1136/pgmj.2007.061622

7. Alhamadh MS, Alanazi RB, Alqirnas MQ, et al. The burden and predictors of venous thromboembolic diseases in patients with multiple primary malignancies. *Cancer Rep.* 2023;6(3). doi:10.1002/cnr2.1742
8. Anderson FA, Spencer FA. Risk Factors for Venous Thromboembolism. *Circulation.* 2003;107(23_suppl_1). doi:10.1161/01.CIR.0000078469.07362.E6
9. Rogers MAM, Levine DA, Blumberg N, Flanders SA, Chopra V, Langa KM. Triggers of Hospitalization for Venous Thromboembolism. *Circulation.* 2012;125(17):2092-2099. doi:10.1161/CIRCULATIONAHA.111.084467
10. BARBAR S, NOVENTA F, ROSSETTO V, et al. A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score. *Journal of Thrombosis and Haemostasis.* 2010;8(11):2450-2457. doi:10.1111/j.1538-7836.2010.04044.x
11. Dutia M, White RH, Wun T. Risk assessment models for cancer-associated venous thromboembolism. *Cancer.* 2012;118(14):3468-3476. doi:10.1002/CNCR.26597
12. Lyman GH, Bohlke K, Falanga A. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. *J Oncol Pract.* 2015;11(3):e442-e444. doi:10.1200/JOP.2015.004473
13. van Es N, Franke VF, Middeldorp S, Wilmink JW, Büller HR. The Khorana score for the prediction of venous thromboembolism in patients with pancreatic cancer. *Thromb Res.* 2017;150:30-32. doi:10.1016/J.THROMRES.2016.12.013
14. Pelzer U, Sinn M, Stieler J, Riess H. Primäre medikamentöse Thromboembolieprophylaxe bei ambulanten Patienten mit fortgeschrittenem Pankreaskarzinom unter Chemotherapie? *DMW - Deutsche Medizinische Wochenschrift.* 2013;138(41):2084-2088. doi:10.1055/S-0033-1349608
15. Antic D, Milic N, Nikolovski S, et al. Development and validation of multivariable predictive model for thromboembolic events in lymphoma patients. *Am J Hematol.* 2016;91(10):1014-1019. doi:10.1002/AJH.24466
16. Zabrocka E, Sierko E. Thromboprophylaxis in the End-of-Life Cancer Care: The Update. *Cancers (Basel).* 2020;12(3):600. doi:10.3390/cancers12030600
17. Noble S. Venous thromboembolism and palliative care. *Clinical Medicine.* 2019;19(4):315-318. doi:10.7861/clinmedicine.19-4-315

18. Johnson MJ, McMillan B, Fairhurst C, et al. Primary thromboprophylaxis in hospices: the association between risk of venous thromboembolism and development of symptoms. *J Pain Symptom Manage*. 2014;48(1):56-64. doi:10.1016/J.JPAINSYMMAN.2013.08.016
19. Loosen SH, Krieg S, Eschrich J, et al. The Landscape of Outpatient Palliative Care in Germany: Results from a Retrospective Analysis of 14,792 Patients. *Int J Environ Res Public Health*. 2022;19(22). doi:10.3390/IJERPH192214885
20. World Health Organization, Palliative care, World Health Organization (2020). <https://www.who.int/news-room/fact-sheets/detail/palliative-care#:~:text=Each%20year%2C%20an%20estimated%2040,palliative%20care%20currently%20receive%20it.>
21. Gade IL, Brækkan SK, Næss IA, et al. The impact of initial cancer stage on the incidence of venous thromboembolism: the Scandinavian Thrombosis and Cancer (STAC) Cohort. *Journal of Thrombosis and Haemostasis*. 2017;15(8):1567-1575. doi:10.1111/jth.13752
22. A. Trousseau. *Clinique Médicale de l'Hôtel-Dieu de Paris / Par A. Trousseau*.
23. Nuttall GAM. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice, 5th Ed*.
24. Rak J, Yu JL, Luyendyk J, Mackman N. Oncogenes, Trousseau Syndrome, and Cancer-Related Changes in the Coagulome of Mice and Humans. *Cancer Res*. 2006;66(22):10643-10646. doi:10.1158/0008-5472.CAN-06-2350
25. Chew HK, Wun T, Harvey D, Zhou H, White RH. Incidence of Venous Thromboembolism and Its Effect on Survival Among Patients With Common Cancers. *Arch Intern Med*. 2006;166(4):458. doi:10.1001/archinte.166.4.458
26. Stein PD, Beemath A, Meyers FA, Skaf E, Sanchez J, Olson RE. Incidence of Venous Thromboembolism in Patients Hospitalized with Cancer. *Am J Med*. 2006;119(1):60-68. doi:10.1016/j.amjmed.2005.06.058
27. Kabbinavar F, Hurwitz HI, Fehrenbacher L, et al. Phase II, randomized trial comparing bevacizumab plus fluorouracil (FU)/leucovorin (LV) with FU/LV alone in patients with metastatic colorectal cancer. *J Clin Oncol*. 2003;21(1):60-65. doi:10.1200/JCO.2003.10.066
28. Kuenen BC, Levi M, Meijers JCM, et al. Potential role of platelets in endothelial damage observed during treatment with cisplatin, gemcitabine, and the angiogenesis inhibitor SU5416. *J Clin Oncol*. 2003;21(11):2192-2198. doi:10.1200/JCO.2003.08.046
29. Cavo M, Zamagni E, Cellini C, et al. Deep-vein thrombosis in patients with multiple myeloma receiving first-line thalidomide-dexamethasone therapy. *Blood*. 2002;100(6):2272-2273. doi:10.1182/BLOOD-2002-06-1674

30. Seng S, Liu Z, Chiu SK, et al. Risk of Venous Thromboembolism in Patients With Cancer Treated With Cisplatin: A Systematic Review and Meta-Analysis. *Journal of Clinical Oncology*. 2012;30(35):4416-4426. doi:10.1200/JCO.2012.42.4358
31. Nalluri SR, Chu D, Keresztes R, Zhu X, Wu S. Risk of Venous Thromboembolism With the Angiogenesis Inhibitor Bevacizumab in Cancer Patients. *JAMA*. 2008;300(19):2277. doi:10.1001/jama.2008.656
32. Khorana AA, Francis CW, Culakova E, Lyman GH. Risk factors for chemotherapy-associated venous thromboembolism in a prospective observational study. *Cancer*. 2005;104(12):2822-2829. doi:10.1002/cncr.21496
33. Citla Sridhar D, Abou-Ismael MY, Ahuja SP. Central venous catheter-related thrombosis in children and adults. *Thromb Res*. 2020;187:103-112. doi:10.1016/j.thromres.2020.01.017
34. Kucher N. Deep-Vein Thrombosis of the Upper Extremities. *New England Journal of Medicine*. 2011;364(9):861-869. doi:10.1056/NEJMcp1008740
35. Wang P, He L, Yuan Q, et al. Risk factors for peripherally inserted central catheter-related venous thrombosis in adult patients with cancer. *Thromb J*. 2024;22(1):6. doi:10.1186/s12959-023-00574-4
36. Gregory Y. H. Lip MFCRGM. Does Heart Failure Confer A Hypercoagulable State? Virchow's Triad Revisited. *J Am Coll Cardiol*. 1999;33(5):1424-1426. doi:10.1016/S0735-1097(99)00033-9
37. Sbarouni E, Bradshaw A, Andreotti F, Tuddenham E, Oakley CM, Cleland JGF. Relationship between hemostatic abnormalities and neuroendocrine activity in heart failure. *Am Heart J*. 1994;127(3):607-612. doi:10.1016/0002-8703(94)90670-X
38. JAFRI SM, OZAWA T, MAMMEN E, LEVINE TB, JOHNSON C, GOLDSTEIN S. Platelet function, thrombin and fibrinolytic activity in patients with heart failure. *Eur Heart J*. 1993;14(2):205-212. doi:10.1093/eurheartj/14.2.205
39. Xu T, Huang Y, Liu Z, et al. Heart Failure Is Associated with Increased Risk of Long-Term Venous Thromboembolism. *Korean Circ J*. 2021;51(9):766. doi:10.4070/kcj.2021.0213
40. Ota S, Yamada N, Tsuji A, Ishikura K, Nakamura M, Ito M. Incidence and Clinical Predictors of Deep Vein Thrombosis in Patients Hospitalized With Heart Failure in Japan. *Circulation Journal*. 2009;73(8):1513-1517. doi:10.1253/circj.CJ-08-0990
41. BARBAR S, NOVENTA F, ROSSETTO V, et al. A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua

- Prediction Score. *Journal of Thrombosis and Haemostasis*. 2010;8(11):2450-2457. doi:10.1111/j.1538-7836.2010.04044.x
42. Ostgathe C, Alt-Epping B, Golla H, et al. Non-cancer patients in specialized palliative care in Germany: What are the problems? *Palliat Med*. 2011;25(2):148-152. doi:10.1177/0269216310385370
 43. Ostgathe C, Gaertner J, Kotterba M, et al. Differential palliative care issues in patients with primary and secondary brain tumours. *Supportive Care in Cancer*. 2010;18(9):1157-1163. doi:10.1007/s00520-009-0735-y
 44. Geersing GJ, Zuithoff NPA, Kearon C, et al. Exclusion of deep vein thrombosis using the Wells rule in clinically important subgroups: individual patient data meta-analysis. *BMJ*. 2014;348. doi:10.1136/BMJ.G1340
 45. Steiner D, Nopp S, Weber B, et al. The post-VTE functional status scale for assessment of functional limitations in patients with venous thromboembolism: Construct validity and responsiveness in a prospective cohort study. *Thromb Res*. 2023;221:1-6. doi:10.1016/J.THROMRES.2022.11.006
 46. Klok FA, Hösel V, Clemens A, et al. Prediction of bleeding events in patients with venous thromboembolism on stable anticoagulation treatment. *Eur Respir J*. 2016;48(5):1369-1376. doi:10.1183/13993003.00280-2016
 47. Badescu M, Ciocoiu M, Badulescu O, et al. Prediction of bleeding events using the VTE-BLEED risk score in patients with venous thromboembolism receiving anticoagulant therapy (Review). *Exp Ther Med*. 2021;22(5). doi:10.3892/ETM.2021.10779