Cancer Associated Thrombosis Training

Risk Assessment Scores

Version 3.0, August 2024

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This project has been supported by an un-restricted, hands-off education grant from Bayer Plc. Bayer has had no involvement whatsoever in any part of the project.

Contents

1. Introduction

Classifying prognosis in cancer associated thrombosis (CAT) is important as patients with thromboembolic events deemed low risk might be managed as outpatients or granted early discharge, thus reducing costs and patient burden. Patients classified as higher risk should receive close monitoring and treatment where necessary.

The standard of care remains to treat all cancer patients with a PE or DVT irrespective of the manner of the diagnosis. Outpatient care is commonly used however, there is little evidence to support outpatient approaches and, even with current guidelines for management of cancer patients with CAT, care is usually based on individual clinical expertise. In this context, risk assessment scores are useful in assisting clinical decisions.

A good risk assessment score is based on variables that are easy to obtain, easy to use and has potential implications for clinical management.

Using risk assessment scores and clinical decision rules to assist in decision making can pose problems, not least because the score must be suitable for the type of CAT being assessed. Furthermore, complications such as bleeding risk and patient co-morbidities must be considered alongside the results of the scores. It is therefore important to recognise that while risk assessment scores are a handy tool for healthcare professionals (HCPs), decisions must be made at the discretion of the HCP with the individual patient in mind.

In this booklet, a selection of currently available risk assessment scores has been suggested for use in different types of CAT:

- suspected pulmonary embolism (PE),
- incidental PE (IPE),
- deep vein thrombosis (DVT),
- venous thromboembolism (VTE) recurrence and,
- bleeding risk.

2. Hestia Criteria for Outpatient Pulmonary Embolism Treatment

for Suspected / Diagnosed Pulmonary Embolism

When to use:
Use in haemodynamically stable patients with acute pulmonary embolism (PE) being managed as outpatients.

Why to use:

- Hestia Criteria safely triages patients for outpatient management.
- Easily applied in a clinical setting at the bedside.
- Associated with decreased length of stay and lower costs.
- Associated with fewer in-hospital complications.

Important to note:

- Predictions are only a guide and decisions should be taken at the discretion of the attending physician.
- Not all patients deemed low risk will have acute life threatening complications and not all require inpatient management. This tool only helps identify those who are low risk and does not necessarily predict those who are high risk.
- This tool is not cancer specific.

The Hestia Criteria were first derived in 297 patients with acute PE across 12 hospitals in The Netherlands between 2008 and 2010. The study aimed to evaluate the efficacy and safety of outpatient treatment according to predefined criteria [1]. It was found that patients with PE selected for outpatient treatment with predefined criteria can be treated with anticoagulants on an outpatient basis.

VTE recurred in 2% of patients, with the upper limit of the confidence interval reaching 4.3%, which is lower than the predefined limit of 7%. None of the recurrences was fatal. None of the patients experienced a recurrent VTE event within seven days of the initial event, a period that equals the average duration of hospital admission for PE.

The Hestia Criteria have since been validated in multiple studies [2-5].

Hestia Criteria Online Tool:

https://www.mdcalc.com/calc/3918/hestia-criteria-outpatient-pulmonary-embolism-treatment

Table 1: The Hestia Criteria:

Criteria
Hemodynamically unstable sBP <100 mmHg and HR >100, needing ICU care, or by clinician judgment
Thrombolysis or embolectomy needed For reasons other than hemodynamic instability
Active bleeding or high risk for bleeding GI bleeding or surgery ≤2 weeks ago, stroke ≤1 month ago, bleeding disorder or platelet count <75 × 10^9/L, uncontrolled HTN (sBP >180 or dBP >110), or by clinician judgment
>24 hrs on supplemental oxygen required to maintain SaO_2 >90%
PE diagnosed while on anticoagulation
Severe pain needing IV pain medication required >24 hr
Medical or social reason for admission >24 hr (infection, malignancy, no support system)
Creatinine clearance <30 mL/min by Cockcroft-Gault
Severe liver impairment By clinician judgment
Pregnant
Documented history of heparin-induced thrombocytopenia (HIT)
Score
An answer of 'No' = 0 **An answer of 'Yes' = +1** **If ≥1 present, patient is not eligible for outpatient management by Hestia Criteria.**

References

1. Zondag W, Mos IC, Creemers-Schild D. et al.; Hestia Study Investigators. Outpatient treatment in patients with acute pulmonary embolism: the Hestia Study. J Thromb Haemost. 2011 Aug;9(8):1500-7.

2. Zondag W, Vingerhoets LM, Durian MF. et al.; Hestia Study Investigators. Hestia criteria can safely select patients with pulmonary embolism for outpatient treatment irrespective of right ventricular function. J Thromb Haemost. 2013 Apr;11(4):686-92.

3. Beam DM, Kahler ZP, Kline JA. Immediate Discharge and Home Treatment With Rivaroxaban of Low-risk Venous Thromboembolism Diagnosed in Two U.S. Emergency Departments: A One-year Preplanned Analysis. Acad Emerg Med. 2015 Jul;22(7):788-95. doi: 10.1111/acem.12711. Epub 2015 Jun 25.

4. den Exter PL, Zondag W, Klok FA. et al.; Vesta Study Investigators *. Efficacy and Safety of Outpatient Treatment Based on the Hestia Clinical Decision Rule with or without N-Terminal Pro-Brain Natriuretic Peptide Testing in Patients with Acute Pulmonary Embolism. A Randomized Clinical Trial. Am J Respir Crit Care Med. 2016 Oct 15;194(8):998-1006. doi: 10.1164/rccm.201512-2494OC. PMID: 27030891.

5. Weeda ER, Kohn CG, Peacock WF, Fermann GJ, Crivera C, Schein JR, Coleman CI. External Validation of the Hestia Criteria for Identifying Acute Pulmonary Embolism Patients at Low Risk of Early Mortality. Clin Appl Thromb Hemost. 2017 Oct;23(7):769-774.

3. HULL Score

for Unsuspected / Incidental Pulmonary Embolism

When to use:

- Adults (≥18 years)
- The patient has active cancer, is receiving adjuvant treatment, or is on long-term surveillance for cancer.
- Pulmonary embolism diagnosis is made on a CT scheduled to assess tumour response, surveillance or for other reasons.
- **The patient is ambulatory being managed in an outpatient setting.**

When not to use:

- The incidental PE is found on a CT scan done in an acutely unwell patient in the inpatient setting.

Why to use:

- The objective of this tool is to classify cancer patients with PE who are safe to be managed as outpatients.

Important to note:

- Predictions are only a guide and decisions should be taken at the discretion of the attending physician.

At Hull University Teaching Hospitals NHS Trust (HUTH), a simple prognostic score was developed to stratify early and medium term mortality outcomes of ambulatory patients with cancer and an unsuspected or incidental PE (IPE). The HULL Score considers IPE-specific symptoms as a self-reported variable and performance status (PS) at the time of IPE diagnosis to provide a more accurate risk assessment [3].

In the HUTH patient cohort, the HULL score was used to effectively stratify the 30-day (3.4%, n = 8), 3 month (15%, n = 35) and 6 month (31%, n = 72) mortality [3].

PS is measured using the ECOG/World Health Organisation Performance Status (ECOG/WHO PS) classification [4].

This simple prognostic score based on patient reported clinical factors (symptom assessment and contemporaneously assessed PS) can be used to easily and reliably stratify the mortality outcomes of cancer patients with IPE.

Table 2: The HULL Score.

Variable	Categories	Points
New or worsening symptoms	Yes	1
	No	0
Performance Status	0	0
	1/2	2
	3/4	3
Scoring:		
• Low Risk: 0 • Intermediate Risk: 1 – 2 • High Risk: 3 – 4		

References

3. Bozas G, Jeffery N, Ramanujam-Venkatachala D, Avery G, Stephens A, Moss H, et al. Prognostic assessment for patients with cancer and incidental pulmonary embolism. Thromb J. 2018;16:8.

4. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. American journal of clinical oncology. 1982;5(6):649-55.

4. Villalta Scale

for Post-thrombotic Syndrome

When to use:

- Patients with signs and symptoms related to lower extremity deep vein thrombosis (e.g. swelling, discoloration, ulceration) and clinical suspicion for post-thrombotic syndrome.
- Patients with a predicted long actuarial survival (e.g. adjuvant treatment).

Why to use:

- Post-thrombotic syndrome can be seen in up to half of patients with lower extremity deep vein thrombosis within 2 years. This risk assessment score both diagnoses and grades severity of post-thrombotic syndrome.

Important to note:

- Venous ulceration indicates severe post-thrombotic syndrome and automatically confers a score of ≥15.
- Diagnosis of post-thrombotic syndrome should be deferred until after the acute DVT phase has passed (3 - 6 months).
- Predictions are only a guide and decisions should be taken at the discretion of the attending physician.

The Villalta Scale stratifies severity of post-thrombotic syndrome (PTS) for patients with lower limb deep vein thrombosis (DVT) [5, 6]. The Villalta Scale is often used in a modified version to diagnose PTS in paediatric cancer patients [7, 8].

The score is comprised of symptoms (pain, cramps, feeling of heaviness, paraesthesia, pruritus) and clinical signs (pretibial oedema, skin induration, hyperpigmentation, redness, venous ectasia, pain on calf compression, venous ulcer) of DVT [Table 3] which are classified on a point system [Table 4].

Villalta Scale Online Tool:

https://www.mdcalc.com/calc/10125/villalta-score-post-thrombotic-syndrome-pts

Table 3: The Villalta Scale.

Symptoms	Score
Pain	Absent 0 Mild +1 Moderate +2 Severe +3
Cramps	Absent 0 Mild +1 Moderate +2 Severe +3
Heaviness	Absent 0 Mild +1 Moderate +2 Severe +3
Paraesthesia	Absent 0 Mild +1 Moderate +2 Severe +3
Pruritis	Absent 0 Mild +1 Moderate +2 Severe +3
Clinical Signs	**Score**
Pretibial oedema	Absent 0 Mild +1 Moderate +2 Severe +3
Skin induration	Absent 0 Mild +1 Moderate +2 Severe +3
Hyperpigmentation	Absent 0 Mild +1 Moderate +2 Severe +3
Redness	Absent 0 Mild +1 Moderate +2 Severe +3
Venous ectasia	Absent 0 Mild +1 Moderate +2 Severe +3
Pain on calf impression	Absent 0 Mild +1 Moderate +2 Severe +3
Venous ulcer	Absent Present If venous ulcer is present and score is <15, then 15 points total are assigned.

Table 4: Interpretation of the Villalta Scale.

Villalta Scale Score	PTS diagnosis	PTS severity
0 - 4	Absent	-
5 - 9	Present	Mild
10 - 14		Moderate
≥15, or presence of venous ulcer		Severe

References

5. Villalta S BP, Picciolo A, Lensing AWA, Prins MH, Prandoni P. Assessment of validity and reproducibility of a clinical scale for the post-thrombotic syndrome. Haemostasis. 1994;24(1 Supplement):158a.

6. Kahn SR. Measurement properties of the Villalta scale to define and classify the severity of the post-thrombotic syndrome. Journal of thrombosis and haemostasis: JTH. 2009;7(5):884-8.

7. Betensky M, Goldenberg NA. Post-thrombotic syndrome in children. Thrombosis research. 2018;164:129-35.

8. Polen E, Weintraub M, Stoffer C, Jaffe DH, Burger A, Revel-Vilk S. Post-thrombotic syndrome after central venous catheter removal in childhood cancer survivors: A prospective cohort study. Pediatric Blood & Cancer. 2015;62(2):285-90.

5. Ottawa Score

for Venous Thromboembolism Recurrence

When to use:

- Patients with active cancer who are receiving anticoagulant treatment for CAT and are at risk of recurrent VTE.

Why to use:

- To determine whether patients with CAT are at low risk or at high risk of recurrent thromboembolic complications.

Important to note:

- Predictions are only a guide and decisions should be taken at the discretion of the attending physician.

The Ottawa Score is a prediction rule used to stratify CAT patients at a low, intermediate or high risk of recurrent venous thromboembolism (VTE) within the first six months of anticoagulation. The risk of recurrent VTE among cancer patients with VTE is not homogeneous, and the Ottawa score is capable of differentiating those patients who are at high risk of recurrent VTE from those at low risk of recurrence.

Independently validated in a cohort of 419 cancer patients with VTE (defined as PE, DVT or both), risks of recurrent VTE during anticoagulant treatment were 12% for patients with low clinical probability (score: less than or equal to -1), 43% for those with intermediate clinical probability (score: 0), and 44% for those with high clinical probability (score: ≥ 1) [9].

A recent meta-analysis of the Ottawa Score in its original and modified versions has further validated its accuracy in the risk stratification of recurrent VTE in CAT patients [10].

The Ottawa score is composed of 5 variables: female sex (+1), lung cancer (+1), and previous DVT (+1) each give one point. Breast cancer (-1) and cancer stage I and II (-1) each give a negative point. A score ≤0 is associated with a low risk of recurrent VTE.

References

9. den Exter PL, Kooiman J, Huisman MV. Validation of the Ottawa prognostic score for the prediction of recurrent venous thromboembolism in patients with cancer-associated thrombosis. Journal of thrombosis and haemostasis : JTH. 2013;11(5):998-1000.

10. Delluc A, Miranda S, Exter PD, Louzada M, Alatri A, Ahn S, et al. Accuracy of the Ottawa score in risk stratification of recurrent venous thromboembolism in patients with cancer-associated venous thromboembolism: a systematic review and meta-analysis. Haematologica. 2020;105(5):1436-42.

6. HAS-BLED Score

for Bleeding Risk

When to use:

- In patients with VTE to predict the risk of a bleeding event while being anticoagulated.

Why to use:

- The risk for major bleeding as calculated by the HAS-BLED Score can be used to guide the decision of the benefit of anticoagulation vs the risks.
- The HAS-BLED Score can guide the decision to start anticoagulation in patients with CAT.

Important to note:

- Bleeding risk stratification scores should not be used to withhold treatment.
- The risk score can be used to identify patients for monitoring or modified therapeutic approaches as well as identification of some modifiable risk factors (e.g., blood pressure, medication use).
- Predictions are only a guide and decisions should be taken at the discretion of the attending physician.

The HAS-BLED Score was developed to assess the 1-year risk of major bleeding (intracranial, hospitalisation, haemoglobin decrease >2 g/L, and/or transfusion) for atrial fibrillation patients receiving anticoagulation [11].

A further study showed that HAS-BLED has high predictive validity for bleeding events in VTE patients receiving anticoagulation and that cancer, a strong independent risk factor for bleeding, can be included in field B of the risk score [12] [Table 5].

Though risk categories are not defined in the HAS-BLED Score, in a cancer cohort an increase from score 3 to score 4 was statistically significant for all bleeds and major bleeds [12] and so a score ≥4 should be considered ‘high risk’ in the cancer population.

Importantly, a classification of high risk should be used to “flag up” patients for additional review and follow-up. The management of reversible bleeding risk factors (and the HAS-BLED score contains most of the more common modifiable bleeding risk factors) should be performed in all patients. The designation of high bleeding risk is not necessarily intended for the withholding of anticoagulation treatment and this decision should be made at the discretion of the HCP.

HAS-BLED Score Online Tool:

https://www.mdcalc.com/calc/807/has-bled-score-major-bleeding-risk

Table 5: The HAS-BLED Score.

Letter	Clinical Characteristic	Points Awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding history or predisposition (e.g. cancer)	1
L	Labile International Normalized Ratio	1
E	Elderly (>65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2

References

11. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest. 2010;138(5):1093-100.

12. Brown JD, Goodin AJ, Lip GYH, Adams VR. Risk Stratification for Bleeding Complications in Patients With Venous Thromboembolism: Application of the HAS-BLED Bleeding Score During the First 6 Months of Anticoagulant Treatment. Journal of the American Heart Association. 2018;7(6):e007901.

7. Post-VTE Functional Status (PVFS) Scale

Functional limitations after CAT are prevalent after both DVT and PE, occurring in up to 50% of patients. These post-VTE experiences of anxiety, pain, discomfort, breathlessness and exercise intolerance are associated with a decreased quality of life, higher risk of depressive disorders, unemployment and increased use of healthcare resources.

Current diagnostic and prognostic scores, such as those above, focus on the presence of signs and symptoms of recurrent VTE or PTS rather than establishing the impact on daily activities and general wellbeing. The Post-VTE Functional Status (PVFS) scale was created to better capture the heterogeneity of post VTE syndromes [Table 6] [13, 14].

The PVFS covers the entire spectrum of functional outcomes ranging from no symptoms to death. It focuses on both limitations in usual activity as well as changes in lifestyle. The scale is not meant to replace current diagnostic or prognostic scores for post-VTE syndromes, but to be used as an outcome measure to evaluate the overall consequences of VTE on functional status.

The PVFS scale is to be assessed during a short, structured interview with the patient, either by phone or within clinic, and categorises the level of physical functioning with reference to pre-CAT activities. The authors suggest that the post-VTE functional status scale is assessed at the moment of hospital discharge and after 90 days following a VTE diagnosis [13], with optional pre-CAT PVFS scale score taken, if possible.

Table 6: The Adjusted Post-VTE Functional Status (PVFS) scale

Scale Category		Description
0	No functional limitations	All usual duties/activities at home or at work can be carried out at the same level of intensity. Symptoms, pain and anxiety are absent.
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	Some 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	Death occurred before the scheduled assessment.

A full manual on how to use the PVFS scale can be found at:
https://www.thrombosisresearch.com/article/S0049-3848(20)30102-X/fulltext

References

13. Klok FA, Barco S, Siegerink B. Measuring functional limitations after venous thromboembolism: A call to action. Thrombosis research. 2019;178:59-62.

14. Boon GJAM, Barco S, Bertoletti L, Ghanima W, Huisman MV, Kahn SR, et al. Measuring functional limitations after venous thromboembolism: Optimization of the post-vte functional status (pvfs) scale. Thrombosis research. 2020;190:45-51.