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Full Length Article

Home treatment of patients with cancer-associated venous thromboembolism – An evaluation of daily practice

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ABSTRACT

Background: Home treatment of cancer-associated venous thromboembolism (VTE) is challenging due to the high risk of adverse events. While home treatment is quite agreeable to cancer patients, studies evaluating the safety of VTE home treatment in this setting are largely unavailable.

Methods: This was an observational study in patients with cancer-associated VTE. The main outcomes were the proportion of patients treated at home (hospital discharge < 24 h after diagnosis) and the 3-month incidence of VTE-related adverse events (major bleeding, recurrent VTE and/or suspected VTE-related mortality) in patients managed in hospital versus at home.

Results: A total of 183 outpatients were diagnosed with cancer-associated VTE: 69 had deep vein thrombosis (DVT) and 114 had pulmonary embolism (PE ± DVT). Of those, 120 (66%) were treated at home; this was 83% for patients with DVT and 55% for patients with PE (± DVT). The 3-month incidence of any VTE-related adverse event was 13% in those treated at home versus 19% in the hospitalized patients (HR 0.48; 95%CI 0.22–1.1), independent of initial presentation as PE or DVT. All-cause 3-month mortality occurred in 33 patients treated as inpatient (54%) compared to 29 patients treated at home (24%; crude HR 3.1 95%CI 1.9–5.0).

Conclusions: Two-third of patients with cancer-associated VTE - including PE - were selected to start anticoagulant treatment at home. Cancer-associated VTE is associated with high rates of VTE-related adverse events independent of initial in hospital or home treatment. However, home treatment may be a good option for selected patients with cancer-associated DVT or PE.

1. Introduction

Several large trials have shown that home treatment of selected patients with venous thromboembolism (VTE) is feasible and safe due to a low incidence of adverse events [1–11]. In these outpatient management studies, only a small minority of patients with cancer-associated VTE were included. One of the reasons that studies in cancer-associated acute pulmonary embolism (PE) are lacking may be that the current European Society of Cardiology (ESC) algorithm for PE risk stratification - including criteria for home treatment - are based on the simplified PE severity index (sPESI) which categorizes all patients with cancer as 'high risk', implicating that those are considered to be 'non-suitable' for home treatment [12].

In current literature, hardly any study has been performed for home treatment in cancer-associated VTE and those that have been published mainly involved incidentally detected PE [13]. Notably, this subgroup of cancer-associated VTE is very relevant for clinical practice. First, up to one in four patients with VTE has cancer. Second, due to the higher risk of recurrent thrombosis, major bleeding and all-cause mortality than in those without malignancy, management of patients with cancer-associated venous thromboembolism is particularly challenging [14]. Third, the psychosocial advantages and quality-of life (QOL) considerations of home treatment are particularly relevant for cancer patients. Studies in patients with advanced oncological disease for instance showed significant decline in QOL during hospitalization, especially with longer duration of hospitalization [15,16].

Hence, knowledge of the frequency and outcome of home treatment of patients with cancer associated VTE is highly relevant for guiding

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clinical practice. We therefore aimed to evaluate current practice patterns and outcome of in hospital and home treatment of patients with cancer-associated VTE in a Dutch University Hospital.

2. Methods

2.1. Design and patients

In this retrospective study, all consecutive patients diagnosed with cancer-associated VTE in a Dutch academic medical center (Leiden University Medical Center, Leiden, the Netherlands) between December 2015 and July 2018 were identified via the hospitals' administrative system. Active cancer was defined as a diagnosis of cancer that occurred within 6 months before the diagnosis of index VTE (excluding basal-cell or squamous-cell carcinoma of the skin), or any treatment for cancer within the previous 6 months, or recurrent or metastatic cancer [17,18]. Patients were eligible for inclusion if they were 18 years or older and had established acute symptomatic or incidental PE involving subsegmental or more proximal pulmonary arteries confirmed by CTPA, or symptomatic or incidental deep vein thrombosis (DVT) of the upper or lower extremities, involving the popliteal, femoral, iliac, subclavian, axillary or brachial vein or the inferior vena cava, diagnosed by compression ultrasound or CT venography [19]. The only exclusion criterion for this study was age below 18 years. The need for informed consent was waived by the institutional review board of the Leiden University Medical Center due to the retrospective study design. All patients were treated in our hospital for the cancer and the incident VTE. Hence, detailed follow-up data was available until patients died, were considered in remission or were referred back to the general practitioner for end-of-life care.

2.2. Study objectives

No specific decision tools for selecting patient with DVT for home treatment exist, and current guidelines do not make notion of a different policy on this issue between patients with cancer-associated DVT and other DVT. Patients with PE were routinely selected for home management according to the Hestia criteria, as described in the hospitals protocol for VTE management. According to the Hestia criteria, and in contrast to the ESC guidelines, patients with cancer-associated PE could be eligible for home treatment [12]. Our hypothesis therefore was that most patients with DVT were treated at home and that risk stratification by the Hestia criteria would allow for home treatment of a relevant number of PE patients as well. The primary objectives of the this study were to assess i) the proportion of outpatients diagnosed with VTE who were treated at home and ii) the 3-month incidence of a composite of VTE-related adverse events (major bleeding, recurrent VTE and/or suspected VTE-related mortality) in patients managed in hospital versus at home. The latter was to evaluate the natural course after initial therapy management, but not to compare in- and outpatient management of cancer-associated VTE.

We planned subgroup analyses for cancer-associated PE and DVT separately, and for incidental VTE. Secondary outcomes were i) the number and timing of PE-related re-admissions during a 3-month follow-up period after the index VTE diagnosis and ii) overall 3-month mortality.

2.3. Study definitions

Home management was defined as hospital discharge < 24 h after diagnosis of VTE. Major bleeding was defined as any bleeding resulting in death, symptomatic bleeding in a critical organ (intracranial, intra spinal, intraocular, retroperitoneal, intra articular and pericardial bleeding and muscle bleeding resulting in compartment syndrome) or symptomatic bleeding resulting in a decrease in the hemoglobin concentration of at least 2 g/dl or resulting in the transfusion of at least two packs of red blood cells [20]. Recurrent VTE was defined as a new intraluminal filling defect on computed tomographic pulmonary angiography, confirmation of a new PE at autopsy or a new intraluminal filling defect on computed tomographic angiography in other venous beds. Recurrent lower extremity DVT was defined as new non-compressibility by ultrasonography or as an increase in vein diameter under maximal compression, as measured in the abnormal venous segment, indicating an increase in thrombus diameter (≥ 4 mm), or by a positive signal on magnetic resonance direct thrombus imaging (DTI) indicative of fresh thrombus in the proximal veins of the leg [19,21,22]. VTE-related mortality was defined as death within 7 days of PE diagnosis, PE confirmed as cause of death during autopsy, or sudden unexpected death with no other explanation. VTE-related readmission was defined as any unscheduled outpatient visit, emergency room visit or readmission in hospital due to VTE-related problems, i.e. thoracic pain, dyspnea (without other explanation than PE), major bleeding, clinically relevant non-major bleeding or due to recurrent VTE within a 3 month follow-up. All events were adjudicated by 2 independent experts who were unaware of the initial management decision (in hospital or home treatment).

2.4. Statistical analysis

For the presentation of the baseline characteristics, categorical data are presented as percentages or as proportion and continuous variables as means with standard deviation (SD). The main outcomes of the study are expressed by frequency with corresponding 95% confidence interval (95%CI) or cumulative incidence calculated from Kaplan Meier analysis. Crude Cox regression analysis was used to compare the rate of adverse events between patients treated at home and those admitted to the hospital. SPSS version 25.0.0 (SPSS, IBM) was used to perform all analyses.

3. Results

3.1. Study patients

Between December 2015 and July 2018, 706 consecutive patients were diagnosed with VTE in our hospital, of whom 228 were diagnosed with cancer-associated VTE (32%). In this group with cancer-associated VTE, 183 patients were diagnosed as outpatient: 114 patients with PE (± DVT) and 69 with DVT. Of the PE diagnoses, 30 were incidental (26%) versus none of the DVT diagnoses. Table 1 summarizes the baseline characteristics of the study patients. Their mean age was 62 years (SD 13) and 63 years (SD 14) for patients treated at home or in-hospital, respectively. Slightly more patients who were hospitalized (77%) than those treated at home (63%) had recurrent or metastatic cancer. The vast majority was treated with LMWH (n = 128; 70%), while 23 (13%) patients were treated primarily with vitamin K antagonists (after a short course of LMWH) and 30 (16%) with direct oral anticoagulants.

3.2. Primary outcome

Of all 183 outpatients with cancer-associated VTE 120 (66%) were treated at home; this was 83% for patients with DVT and 55% for patients with PE with or without DVT. For the patients treated as inpatients, the mean admission duration was 8.2 days (± 7.9 days). Reasons for admission are shown in Table 2.

VTE-related mortality within 3-months occurred in 2 patients treated at home (1.7%) and in 5 patients initially treated in hospital (7.9%; crude hazard ratio [HR] 0.32; 95% confidence interval [CI] 0.06–1.6; Table 3a). Four patients (3.3%) experienced symptomatic recurrent VTE during follow-up in the group treated at home versus 6 initially hospitalized patients (9.5%; crude HR 0.33; 95%CI 0.09–1.2). The details of diagnosis and management of the VTE recurrences are

Table 1
Baseline characteristics at diagnosis of cancer-associated VTE.

	Home treatment (n = 120)	Initially hospitalized (n = 63)
Age, mean (SD)	62 (13)	63.2 (14)
Male sex, no (%)	66 (55)	30 (49)
Previous venous thromboembolism — no. (%)	23 (19)	12 (20)
Weight in kg, mean (SD)	81 (17)	80 (20)
Body Mass Index, mean (SD)	26 (5.0)	26 (4.9)
Creatinine clearance < 60 ml/min — no. (%)	18 (15)	10 (16)
Platelet count below 100,000 per μl — no. (%)	10 (8.3)	4 (6.6)
Qualifying diagnosis of VTE — no. (%)		
PE with or without DVT	63 (53)	49 (80)
DVT only	57 (48)	12 (20)
Incidental PE no. (%)	21 (18)	8 (13)
Most proximal location of PE — no. (%)		
Central PE	21 (18)	26 (43)
Segmental PE	33 (28)	17 (28)
Subsegmental PE[a]	10 (8.3)	6 (9.8)
Primary site of malignancy no. — no. (%)		
Breast	7 (5.8)	3 (4.9)
Upper gastrointestinal	20 (17)	7 (12)
Lower gastrointestinal	6 (5.0)	2 (3.3)
Lung	5 (4.2)	11 (18)
Genitourinary tract	35 (29)	16 (26)
Brain	7 (5.8)	7 (12)
Heamatological	11 (9.2)	5 (8.2)
Skin (excl squamous/basal)	12 (10)	5 (8.2)
Other	13 (11)	5 (8.2)
Recurrent or metastatic cancer — no. (%)	76 (63)	47 (77)
Receiving systemic anti-cancer therapy[b]	63 (53)	30 (49)

Abbreviation: SD, standard deviation; VTE, venous thromboembolism; DVT, Deep vein thrombosis; PE, pulmonary embolism.
[a] Eight cases of isolated subsegmental pulmonary embolism were included.
[b] Systemic chemotherapy, immunotherapy or hormonal therapy.

Table 2
Reasons for hospitalization according to Hestia criteria (n = 61).

Reasons for hospital admission	Frequency	Proportion
1. Hemodynamically unstable	12	19.7%
2. Active bleeding or high bleeding risk	1	1.6%
3. > 24 h oxygen supply	22	36.1%
4. Diagnosis during anticoagulant treatment	5	8.2%
5. Need for intravenous pain medication > 24 h	2	3.3%
6. Renal failure (clearance < 30 ml/min)	4	1.7%
7. Severe liver impairment	1	1.6%
8. Heparin induced thrombocytopenia	1	1.6%
9. Medical or social reasons	27	44.3%
Concomitant infection	6	
Need for further diagnostic tests	4	
Social reasons	10	
(Oncological) surgery	3	
Need for non-intravenous pain medication	2	
Unknown	2	

provided in Table 4. None of the recurrent VTE events were fatal, six were incidental findings and five occurred within the first month after the index VTE was diagnosed.

During the study period major bleeding was more frequently observed in patients treated at home: 10 patients (8.3%) versus 1 patient (1.6%, crude HR 5.2; 95%CI 0.67–41). The details of diagnosis and management of the major bleedings are provided in Table 5. Of all 11 major bleedings, none occurred during the initial 8 days (mean duration of hospitalization of initially admitted patients) and most occurred after 14 days (82%). Two were fatal (18%), one bleed occurred with concomitant use of aspirin and one bleed occurred in presence of a mild thrombocytopenia. The cumulative incidence of major bleeding in both groups started to divert after day 20 of follow-up (Fig. 1).

The 3-month incidence of any VTE-related adverse event was 13% in those treated at home versus 19% in the initially hospitalized patients (crude HR 0.48; 95%CI 0.22–1.1; Table 3a, Fig. 1). Results of the subgroup analysis for cancer-associated PE and DVT separately, are shown in Tables 3b and 3c. Comparable hazard ratios were observed for a 3-month incidence of any VTE-related adverse event with either cancer-associated PE or cancer-associated DVT. We also performed sensitivity analyses after excluding 8 patients with isolated subsegmental pulmonary embolism and found comparable hazard ratios (data not shown).

In the subgroup analysis of incidental PE, 21 (70%) were treated at home. The 3-month incidence of any VTE-related adverse event was 14% in those treated at home versus 13% in the hospitalized patients (crude HR 1.5; 95%CI 0.14–16.5; Table 6).

3.3. Secondary outcome

Of all initially hospitalized patients, there were no relevant readmissions due to PE related complications within the 3-month follow-up, whereas 16 patients in the group treated at home were re-admitted (13%). Mean duration until readmission was 30 days (SD 20). Reasons for readmission are shown in Table 7, and consisted mainly of major bleeding complications. Notably, 22 (35%) of all initially hospitalized patients died during the index hospitalization or were discharged for palliative end-of-life care with a no-return policy.

All-cause 3-month mortality occurred in 33 patients treated as inpatient (54%) compared to 29 patients treated at home (24%; crude HR 3.1 95%CI 1.9–5.0).

4. Discussion

In our cohort, two-thirds of patients with cancer-associated VTE were selected to start anticoagulant treatment at home: 83% of patients with cancer-associated DVT and 55% of patients with cancer-associated PE. Overall, rates of adverse events were high, independent of initial in hospital or home treatment. For patients treated at home, adverse events consisted mostly of major bleeding events, occurring beyond the first 14 days after diagnosis. Reasons for initial admission and rates of VTE-related readmission in our study were comparable to those reported in non-cancer VTE patients [5,7]. The observed higher rate of overall mortality in the patients who were initially admitted can be explained by a more advanced tumor stage. The observed higher rate of

Table 3a
VTE-related adverse events in cancer-associated VTE.

	Home treatment (n = 120)	Initially hospitalized (n = 63)	HR	95% CI
1. Suspected VTE-related mortality	N = 2	N = 5	0.32	(0.06–1.6)
2. Major bleeding	N = 10	N = 1	5.2	(0.67–41)
3. Recurrent VTE	N = 4	N = 6	0.33	(0.09–1.2)
4. Composite outcome	N = 16	N = 12	0.48	(0.22–1.1)

Abbreviations: PE, pulmonary embolism; VTE, venous thromboembolism; HR, Hazard ratio; CI confidence interval.

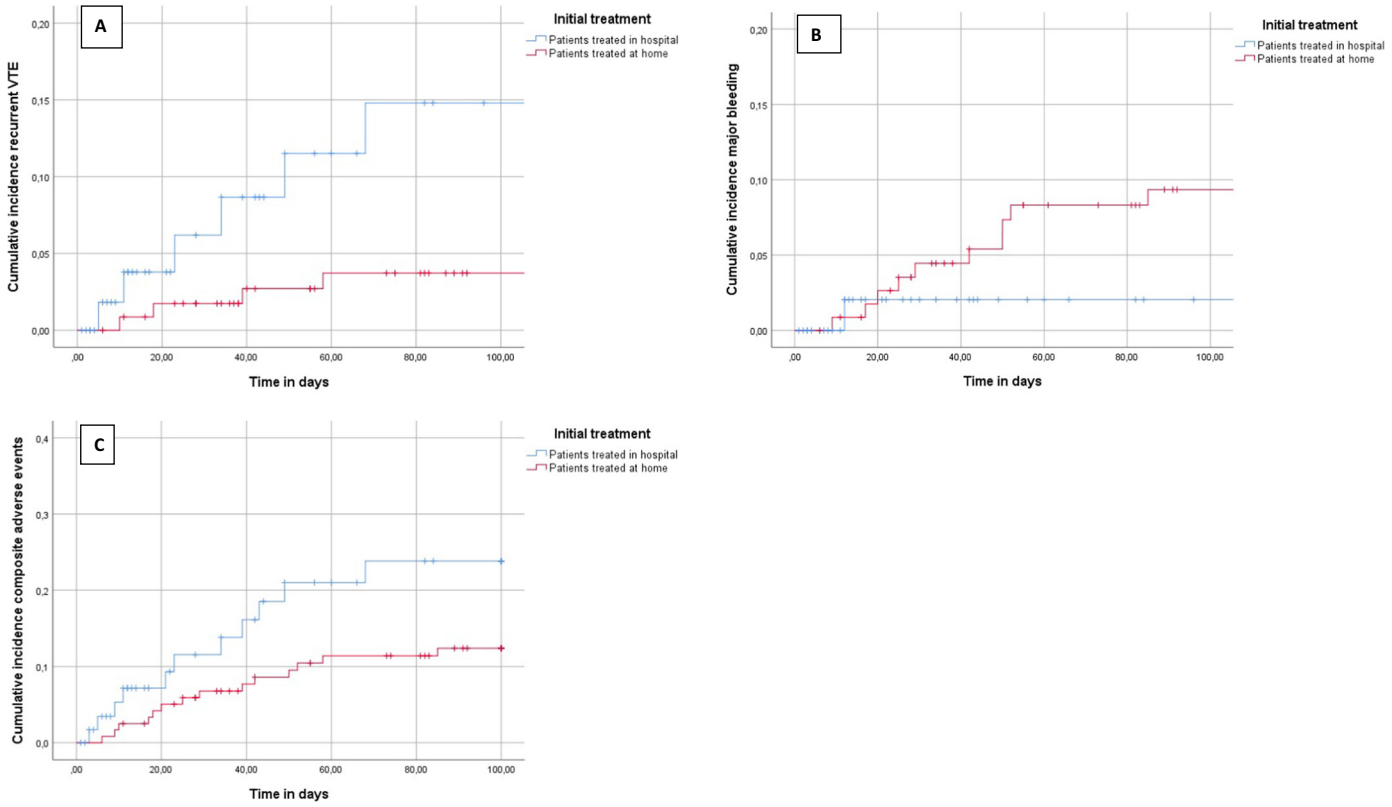

Fig. 1. Shown are the cumulative incidence of recurrent VTE within a 3 month period (A), the Kaplan-Meier estimate for major bleeding within a 3 month period (B) and the cumulative composite 3-month outcome of any adverse VTE event (C).

Table 3b
Subgroup analysis: VTE-related adverse events with cancer-associated PE as initial diagnosis.

	Home treatment (n = 63)	Initially hospitalized (*n* = 51)	HR	95% CI
1. Suspected VTE-related mortality	*N* = 1	*N* = 5	0.27	(0.03–2.3)
2. Major bleeding	*N* = 3	*N* = 0	∞	∞
3. Recurrent VTE	*N* = 2	*N* = 3	0.52	(0.09–3.1)
4. Composite outcome	*N* = 6	*N* = 8	0.38	(0.12–1.1)

Abbreviations: PE, pulmonary embolism; VTE, venous thromboembolism; HR, Hazard ratio; CI confidence interval.

Table 3c
Subgroup analysis: VTE-related adverse events with cancer-associated DVT as initial diagnosis.

	Home treatment (*n* = 57)	Initially hospitalized (*n* = 12)	HR	95% CI
1. Suspected VTE-related mortality	*N* = 1	*N* = 0	∞	∞
2. Major bleeding	*N* = 7	*N* = 1	1.5	(0.19–12)
3. Recurrent VTE	*N* = 2	*N* = 3	0.13	(0.02–0.76)
4. Composite outcome	*N* = 10	*N* = 4	0.42	(0.11–1.6)

Abbreviations: DVT, deep venous thrombosis; VTE, venous thromboembolism; HR, Hazard ratio; CI confidence interval.

VTE-related mortality in the inpatient group can be explained by more severe PE, with a higher prevalence of patients in shock or requiring oxygen therapy. These differences in patients treated at home or in hospital are easily explained by application of the Hestia criteria, selecting lower-risk PE patients eligible for home treatment.

While the higher risk of recurrent VTE and overall mortality in patients who were initially admitted to the hospital was expected considering the more advanced stages of disease of these patients, we did not anticipate the higher risk of major bleeding in patients treated at home. Since the increased risk evolved long after duration of hospitalization of the admitted patients and the majority of bleeding occurred at the cancer site (gastrointestinal tract, urogenital tract or central nervous system) without evidence of supratherapeutic anticoagulant treatment (e.g. incorrect dose, renal insufficiency), we do not think that these bleedings could have been prevented by initial hospitalization. They rather occurred in patients with a very different bleeding risk profile than patients who were initially admitted. Also, the observed higher risk of major bleeding may have been overestimated by competing risk of death. Patients treated at home had a mean time at risk of 82 days compared to 58 days for those who were initially hospitalized (mean difference 24.3; 95%CI 15.7–32.9). Also, one third of initially hospitalized patients were discharged with a no-return policy, which may have caused underreporting of adverse events and by all means, prevented readmissions.

Home treatment in general is currently widely applied in patients with DVT but reserved for selected PE patients at low risk of adverse

Table 4
Details of adjudicated recurrent VTE events.

Pt	Sex	Age	Initial treatment	Incidental or symptomatic VTE finding	Days after index VTE	Specification
No. 1	M	79	At home	Incidental	10 days	Progressive renal vein thrombosis and PE after PE diagnosis during LMWH treatment adequate anti-Xa level (> 2.00 IU/ml) in patient with advanced melanoma. Due to concomitant CRNMB, the anticoagulant treatment remained unchanged.
No. 2	F	76	In hospital	Symptomatic	10 days	Progressive thrombus load in external iliac vein compared to 10 days earlier during LMWH treatment in patient with vulvar carcinoma. LWMH dosage was increased with 17%.
No. 3	F	28	In hospital	Incidental	15 days	New bilateral PE after initial diagnosis of DVT during argatroban treatment (APTT 81.7), (HIT test positive) in patient with advanced cervical carcinoma. No systemic anti-cancer treatment possible due to the condition of the patient.
No. 4	F	41	At home	Incidental	18 days	Incidental PE after initial diagnosis of DVT during edoxaban treatment in patient with advanced colorectal carcinoma treated with palliative chemotherapy. No change made.
No. 5	M	73	In hospital	Symptomatic	23 days	New PE after initial diagnosis of DVT during LMWH treatment with adequate anti-Xa level (1.48 IU/ml) in patient with advanced non-small cell lung cancer. No change in therapy was made.
No. 6.	M	65	In hospital	Symptomatic	34 days	New symptomatic DVT after initial diagnosis of PE during VKA treatment in patient with progressive MDS treated with lenalidomide. VKA was stopped and LWMH started.
No. 7	F	66	At home	Incidental	39 days	Progressive thrombus in superior vena cava after initial diagnosis under VKA treatment (no INR available) in patient with progressive endometrial cancer. No change in treatment made. Palliative treatment started two weeks later
No. 8	F	65	In hospital	Symptomatic	49 days	New symptomatic DVT, several days after temporary stop of LMWH for diagnostic procedure in patient with diffuse large cell B cell lymphoma. LMWH treatment was restarted.
No. 9	M	77	In hospital	Incidental	68 days	Progressive DVT in the inferior vena cava during LMWH treatment with adequate anti-Xa levels (1.67 IU/ml) in patient with progressive melanoma. Treatment was not changed.
No. 10	M	76	At home	Incidental	58 days	New incidental PE after initial diagnosis of DVT during LMWH treatment in patient with SCLC. LWMH dosage was increased with 25%.

Abbreviations: Pt, Patient; VTE, venous thromboembolism; F, female; M, male; DVT, deep venous thrombosis; CRNMB, clinically relevant non-major bleeding; APTT, activated partial thromboplastin time; HIT, heparin induced thrombocytopenia; LMWH, low molecular weight heparin; VKA vitamin K antagonists; MDS, myelodysplastic syndrome; SCLC, small cell lung cancer; NMCRB, non-major clinically relevant bleeding.

Table 5
Details of adjudicated major bleeding events.

Patient	Sex	Age	Initial treatment	Time after index VTE	Specification
No. 1	M	69	At home	9 days	Upper GI bleeding requiring transfusion during LMWH treatment in patient with gastric cancer, LMWH treatment was discontinued.
No. 2	F	76	In hospital	12 days	Decrease in the hemoglobin concentration > 2 g/dl and transfusion required because of limited bleeding from inguinal wound during LMWH treatment in patient with vulvar carcinoma. Because of concomitant symptomatic progressive DVT, LMWH dosage was increased with 17%.
No. 3	M	66	At home	17 days	Hemodynamically important and ultimately fatal upper GI bleeding in patient with advanced esophageal cancer, LMWH treatment was discontinued.
No. 4	M	87	At home	20 days	Macroscopic hematuria after luxated indwelling catheter requiring transfusion during LMWH treatment in patient with prostate cancer. Treatment remained unchanged.
No. 5	M	41	At home	25 days	Decrease in the hemoglobin concentration > 2 g/dl due to post-operative bleed on site of pancreatic anastomosis during LMWH treatment in patient with pancreatic cancer operated with curative intent.
No. 6	F	61	At home	29 days	Intracerebral bleeding during LMWH treatment in patient with advanced glioblastoma. LMWH continued in prophylactic dosage.
No. 7	M	81	At home	42 days	Upper GI bleeding requiring transfusion during LMWH treatment in patient with advanced melanoma. LMWH treatment was discontinued.
No. 8.	M	79	At home	50 days	Intramuscular bleeding with decrease in the hemoglobin concentration > 2 g/dl, during therapy with aspirin 100 mg once daily and LMWH in patient with advanced melanoma Both drugs were temporary stopped.
No. 9	M	59	At home	50 days	Intracerebral bleed during LMWH treatment in patient with advanced renal cell carcinoma with cerebral metastasis, complicated by focal epileptic insults. Therapeutic LMWH was stopped and the next day continued in prophylactic dosage.
No. 10	M	62	At home	52 days	Persistent haematuria resulting in decrease of hemoglobin concentration > 2 g/dl during LMWH treatment in patient with progressive Large cell anaplastic T-cell Lymphoma. LMWH treatment was temporarily discontinued and restarted the next day in a prophylactic dosage.
No. 11	M	41	At home	85 days	Fatal intracerebral bleed during LMWH treatment in patient with cerebral metastasized melanoma, resulting in start terminal palliative treatment. Mild thrombocytopenia $116*10^9$/l at moment of bleeding.

Abbreviations: VTE, venous thromboembolism; F, female; M, male; DVT, deep venous thrombosis; LMWH, low molecular weight heparin; GI, gastrointestinal.

Table 6
VTE-related adverse events in incidental cancer-associated VTE.

	Home treatment (n = 21)	Initially hospitalized (n = 8)	HR	95% CI
1. Suspected VTE-related mortality	N = 2	N = 1	1.5	0.14–16.5
2. Major bleeding	N = 0	N = 0	–	–
3. Recurrent VTE	N = 1	N = 0	∞	∞
4. Composite outcome	N = 3	N = 1	1.5[a]	0.14-16.5

Abbreviations: PE, pulmonary embolism; VTE, venous thromboembolism; HR, Hazard ratio; CI confidence interval.
[a] Two adverse events were scored in one patient.

Table 7
Reasons of readmission in cancer-associated VTE.

	Frequency	Percent	(Mean) Time until readmission (in days)
1. Thoracic pain	1	6.7	6
2. Dyspnea (without any other explanation than PE)	1	6.7	2
3. Thoracic pain and dyspnea	1	6.7	34
3. Major bleeding	7	47	32
4. Clinically relevant non-major bleeding	2	13	16
5. Recurrent VTE	3	20	50

Abbreviations: PE, pulmonary embolism; VTE, venous thromboembolism.

events. Several studies have demonstrated evident benefits of home treatment of VTE: improved quality of life and patient satisfaction, less use of medical resources and lower healthcare costs [23–25]. Concerns or barriers preventing home treatment are mostly based on fear of early complications, i.e. recurrent VTE, major bleeding and VTE-related mortality [12]. Therefore, the main goals of hospital admission are preventing these early complications as well as observing patients with high risk of bleeding, renal insufficiency, managing other comorbidities and providing support if home circumstances are not appropriate, i.e. oxygen therapy or intravenous analgesia.

These same goals, when deciding on initial treatment, undoubtedly do apply to cancer patients with VTE as well. Because the risk of early mortality in cancer patients with VTE is inherently high, the ESC guideline strongly suggests to hospitalize all patients with PE and cancer. However, should the initial treatment in patients with cancer be only based on the risk of 30-day mortality? In our view, maximizing QOL should be equally important to preventing adverse events. Studies in patients with advanced oncological disease showed significant decline in QOL during hospitalization, especially with longer duration of hospital stay [15,16]. For example, in patients with hematological cancer, the percentage of patients with symptoms of depression more than doubled after hospitalization, with an accompanied increase in fatigue and a clinically significant drop in mean QOL scores [26]. Hence, as initial hospitalization likely does not prevent cancer-associated mortality, we always consider and discuss the possibility of home treatment in all patients in our practice. Notably, the higher incidence of VTE-related readmissions in patients treated at home observed in our study should be taken into account when making the final management decision.

Strong points of our study include the novelty of our data, the completeness of follow-up and the lack of exclusion criteria compared to clinical trials that often exclude patients with the highest risk of bleeding and other adverse outcome. Moreover, all outcomes were adjudicated by independent experts. Main limitation of this study is the retrospective and monocentric design. Therefore, external validity of our findings remains to be proven. However, the comparable rates of adverse events and mortality of our study with the published literature suggest that our results may be widely applicable [17,18]. Of note, as there is no standardized definition for PE-related death, it remains challenging to adjudicate this particular endpoint [27]. All-cause mortality is no good alternative in our cohort of patients with active malignancy because of the intrinsic high mortality rate. We consider the definition we used, i.e. death within 7 days of PE diagnosis, PE confirmed as cause of death during autopsy, or sudden unexpected death with no other explanation, to be fairly sensitive, with a low risk of underestimating the rate of complications in VTE patients treated at home. Furthermore, it is uncertain whether every recurrent incidental PE event was a true recurrence in those who were initially diagnosed with DVT, because no baseline CTPA was performed to exclude for the presence of asymptomatic PE. Lastly, since we did not perform a randomized controlled trial, we cannot judge if home treatment of patients with cancer-associated VTE is better or worse than hospitalization. Because of the inherent differences between the patients treated at home or hospitalized, we specifically chose not to perform multivariate analysis to compare the two treatment strategies but to apply crude comparisons to show the natural course of home treatment in the perspective of patients hospitalized for any reason.

In conclusion, two-thirds of patients with cancer-associated VTE were selected to start anticoagulant treatment at home. Cancer-associated VTE is associated with high rates of overall VTE-related adverse events both in hospitalized patients and in patients treated at home. The vast majority of adverse events in the patients treated at home occurring beyond the first weeks of follow-up. Based on our findings, home treatment may be a good option for selected patients with cancer-associated DVT and/or PE.

Authorship statement

Stephan V. Hendriks Contributed to concept and design of the study, analyzed and interpreted the data, and drafted the manuscript

Menno V. Huisman Contributed to concept and design of the study, analyzed and interpreted the data, reviewed the manuscript and provided important intellectual content

Jeroen C.J. Eikenboom reviewed the manuscript and provided important intellectual content

Jaap Fogteloo reviewed the manuscript and provided important intellectual content

Hans Gelderblom reviewed the manuscript and provided important intellectual content

Felix J.M. van der Meer reviewed the manuscript and provided important intellectual content

Wilhelmina J.E. Stenger analyzed and interpreted the data and provided important intellectual content.

Arie J. Verschoor analyzed and interpreted the data, and reviewed the manuscript and provided important intellectual content

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