Challenges in managing venous thromboembolism: insights into cancer- and COVID-19-associated thrombosis

Kaptein, F.H.J.

CHAPTER 3

Discharge from the emergency department and outpatient clinic in cancer patients with acute symptomatic and incidental pulmonary embolism: a multicenter retrospective cohort study

Noori A.M. Guman*, Fleur H.J. Kaptein*, Susan B. Lohle, Albert T.A. Mairuhu, Frederikus A. Klok, Menno V. Huisman, Pieter W. Kamphuisen, Nick van Es
**Both authors contributed equally.*

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ABSTRACT

Background: It is unclear how often cancer patients with acute pulmonary embolism (PE) are discharged from the emergency department (ED) or outpatient clinic and whether direct discharge is safe. We assessed treatment setting and early safety outcomes in cancer patients with acute symptomatic and incidental PE.

Methods: Cancer patients diagnosed with PE at the ED or outpatient clinic between August 2017 and May 2021 were included in Four Cities VTE Cancer, a Dutch multicenter retrospective cohort study. The main outcome was direct discharge versus hospitalization. Safety outcomes were cumulative 14-day mortality and PE-related readmission incidences.

Results: We included 602 patients (median age 71 years; 49.5% female) of whom 285 (47.3%) were discharged directly and 317 (52.7%) were hospitalized. The cumulative 14-day mortality incidence was 0.7% (95% CI, 0.1-2.4%) in patients discharged directly and 9.0% (95% CI, 6.2-12.5%) in those hospitalized. The cumulative 14-day PE-related readmission incidence was 1.8% (95% CI, 0.7-3.9%) and 1.4% (95% CI, 0.5-3.3%) in directly discharged and hospitalized patients, respectively. Of the 220 patients with incidental PE, 180 (81.8%) were discharged directly compared to 105 of 382 (27.5%) patients with symptomatic PE (P<0.001). Mortality and readmission incidences in symptomatic and incidental PE were consistent with the main analysis.

Conclusions: About 28% and 82% of cancer patients with symptomatic or incidental PE, respectively, were discharged directly, with low 14-day mortality and PE-related readmission incidences. These data underline the need for PE risk stratification in oncological populations and suggest that clinicians successfully identify a proportion of patients in whom direct discharge is safe.

INTRODUCTION

Pulmonary embolism (PE) is a common complication in patients with cancer resulting in significant morbidity and mortality.[1] The incidence of PE in the 6 months after cancer diagnosis ranges from 0.5% to 4.7%[2], depending on cancer type, stage, anticancer treatment, and other comorbidities.[2,3] Advances in diagnostic strategies have led to an increased incidence of cancer-associated PE, in particular due to high-sensitivity CT-scanning with increased spatial resolution and increased use of CT-scanning.[4,5] Nowadays, almost half of all PE are detected incidentally on CT-scans performed for other reasons than suspected PE, and many of these patients are asymptomatic.[4]

Risk stratification of patients with PE is recommended to guide management, including decisions on direct discharge from the emergency department (ED) or outpatient clinic and initial hospitalization. In hemodynamically stable PE patients without right ventricular (RV) dysfunction and no other reason for hospitalization, the current European Society of Cardiology (ESC) guideline[6] suggests that direct discharge is safe in those with a low Pulmonary Embolism Severity Index (PESI)[7] or simplified PESI[8], or no Hestia criteria[9] (**Supplementary Table 1**). However, since sPESI includes cancer as a risk item, no cancer patients are selected for direct discharge. PESI also includes cancer, but additional risk factors are needed to be classified as high risk. The Hestia criteria allow to consider cancer as a risk item based on the item *'Medical or social reason for treatment in the hospital for >24 hours (infection, malignancy, or no support system)'*, but leave room for considering direct discharge for this patient group.

It is unclear how cancer patients diagnosed with acute PE are managed in clinical practice and whether direct discharge is safe for these patients. In this study, we retrospectively assessed management (i.e. direct discharge vs. hospitalization) and early safety outcomes in patients with cancer-associated PE in Dutch practice, with a focus on symptomatic and incidental PE.

MATERIALS AND METHODS

Study design and patients

We performed the Four Cities VTE Cancer study, a retrospective multicenter cohort study in two academic and two non-academic Dutch hospitals: Amsterdam University Medical Centers (Amsterdam UMC), Leiden University Medical Center (LUMC), Tergooi Medical Center (Tergooi MC), and Haga Hospital. Based on the local protocols for PE management, the Hestia criteria were endorsed in the latter three, whereas the Amsterdam UMC protocol endorsed sPESI. Ambulatory patients diagnosed with radiologically confirmed symptomatic or incidental PE between August 1, 2017 and May 1, 2021 in the presence of active cancer, other than non-melanoma skin cancer, were included. Active cancer was defined as measurable disease

(i.e. based on laboratory biomarkers, signs on imaging, or pathology confirmation) or any cancer treatment in the preceding 6 months. Patients who died on the date of PE diagnosis, visited the hospital for a second opinion, or were diagnosed with PE in a non-participating center were excluded. Patients were identified based on ICD-10 and diagnosis treatment combination codes, and unstructured data from radiologic reports using CTcue software version 4.6.2 (CTcue B.V., Amsterdam, the Netherlands). CTcue is a text-mining tool, which enables users to search and extract pseudonymized patient data from electronic patient data. The full CTcue searching strategy is provided in **Supplementary Table 2**. Eligibility for this study of each patient identified was confirmed by manual patient chart review.

The study was declared exempted from the Medical Research Involving Human Subjects Act (WMO) and was approved by the Independent Review Boards (IRB). As per the IRB's request, patients from the Amsterdam UMC and Tergooi MC, who were not registered to be death, were given the opportunity to object against inclusion within four weeks after being notified; no additional consent was required in the other centers. This study adheres to the STROBE statement for reporting on observational studies (**Supplementary Table 3**).

Data collection, study outcomes and follow-up

Clinical, laboratory, and imaging data were collected by manual review of electronic patient records. Patients were followed from the day of PE diagnosis until death or last date of contact with the hospital. A modified sPESI was calculated at baseline, including heart rate >100 beats per minute (bpm), and a modified PESI score was calculated in which all patients were considered not having an altered mental status, as data on heart rate >110 bpm and mental status were not collected. The individual Hestia criteria could not be evaluated, since these data were not systematically collected. The main outcome was direct discharge versus hospitalization. Direct discharge was defined as discharge from the ED or outpatient clinic, or, after an incidental PE diagnosis, as evaluation by telephone only followed by home treatment. Safety outcomes were all-cause mortality and PE-related readmission. PE-related readmission was defined as a hospital admission after discharge related to worsening PE symptoms (e.g. dyspnea or hemodynamic deterioration) or anticoagulant-related bleeding. Secondary outcomes were cause of death at the discretion of the physician and length of hospital stay.

Statistical analysis

Standard descriptive statistics were used to compare characteristics of patients who were discharged directly and those hospitalized. The continuous variable of the estimated glomerular filtration was categorized according to the Kidney Disease: Improving Global Outcomes (KDIGO) classification for chronic kidney disease. Vital parameters were categorized based on the lower and/or the upper limits of normal. The cumulative 14-day mortality and PE-related readmission incidences were evaluated

in Kaplan-Meier analyses. A 14-day observation period was chosen, assuming that deaths within this period were potentially related to PE and deaths beyond the 14 days were foremost caused by the ongoing cancer. Patients were censored at loss to follow-up or at the end of the observation period, and for the PE-related readmissions, at death, whichever occurred first. The lost to follow-up date was defined as the last date of contact with the hospital in those not registered to be death. Subgroup analyses were performed in patients from academic and non-academic hospitals and in those with symptomatic and incidental PE, as we assumed the management strategy could be different for these groups of patients. Additional analyses were performed to evaluate cumulative 14-day mortality and PE-related readmission incidences in patients discharged early (hospitalization <2 days) and those hospitalized ≥2 days.

All statistical analyses were performed using R software version 4.2.1 for statistical computing (R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org/), using packages 'tableone', 'survival', and 'survminer'. A P-value smaller than 0.05 was considered to indicate statistical significance.

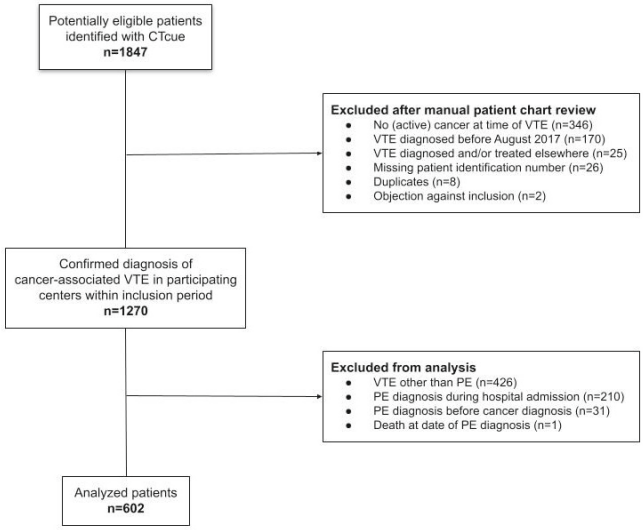
RESULTS

A total of 1,847 patients were identified with the CTcue search, of whom 1,270 (68.8%) met the criteria for cancer-associated VTE (**Figure 1**). Of these, 426 (33.5%) were excluded as they had VTE other than PE, 210 (16.5%) were already admitted at the time of PE diagnosis, 31 (2.4%) were diagnosed with PE before cancer diagnosis, and one (0.1%) died on the date of PE diagnosis. The remaining 602 (47.4%) cancer patients with acute PE at the ED or outpatient clinic were included. The median age was 68 years (interquartile range [IQR], 58-74), and 49.5% (n=298) were female. The most common cancer types were gastrointestinal (n=192, 31.9%), lung (n=96, 15.9%), and genitourinary (n=84, 14.0%); 62.8% (n=344) had distant metastasis. The median time between cancer diagnosis and PE was 3.8 months (IQR, 1.3-12.7). At 14 days follow-up, 16 (2.7%) patients were lost to follow-up, 30 (5.0%) died and nine (1.5%) were readmitted; reasons for readmission were worsening PE-related symptoms (n=4) and bleeding (n=5).

Overall, 285 patients (47.3%) were discharged directly and 317 (52.7%) were hospitalized (see **Table 1** for baseline characteristics). The main reasons for hospitalization are shown in **Supplementary Table 4**; reasons were PE-related in 230 (72.6%), cancer-related in 39 (12.3%), and other or unknown in 48 (15.1%). The median duration of hospitalization was 4 days (IQR, 2-7). Variables associated with direct discharge were younger age, ECOG performance status 0-1, incidental PE, and absence of cardiopulmonary comorbidities, abnormal vital measurements, leukocytosis, chronic kidney dysfunction, and elevated cardiac biomarkers. The proportion of patients discharged directly was consistent over the years of inclusion. About 57% of cancer patients from an academic hospital were discharged directly compared to 34% of

patients in the non-academic hospitals (P<0.001). Baseline characteristics of patients from academic and non-academic hospitals are summarized in **Supplementary Table 5**; notable differences were observed in the proportions with incidental PE (44.0% vs. 26.6%; P<0.001) and subsegmental PE only (37.7% vs. 7.4%; P<0.001).

Figure 1. Study flow diagram



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

Two directly discharged patients died within 14 days (cumulative mortality 0.7%, 95% CI, 0.1-2.4), none was judged PE-related. Of those hospitalized, 27 died within 14 days (cumulative mortality 9.0%, 95% CI, 6.2-12.5); one death was caused by PE. The cumulative 14-day PE-related readmission incidence was 1.8% (95% CI, 0.7-3.9; n=5) in directly discharged patients and 1.4% (95% CI, 0.5-3.3; n=4) in hospitalized patients. Characteristics of patients who were discharged directly and died or were readmitted within 14 days are provided in **Table 2**.

Table 1: Characteristics at time of pulmonary embolism diagnosis

	Direct discharge N=285	Hospitalization N=317	P-value
Age in years, median [IQR]	66 [56, 73]	69 [60, 75]	0.001*
Female sex, n (%)	139 (48.8)	159 (50.2)	0.80
ECOG performance status ≥2, n/N (%)	53/278 (19.1)	110/310 (35.5)	<0.001¶
Cardiovascular disease, n (%)	30 (10.5)	69 (21.8)	<0.001±
COPD requiring medication, n (%)	9 (3.2)	41 (12.9)	<0.001*
Hospitalization >3 days in the preceding 4 weeks, n (%)	16 (5.6)	57 (18.0)	<0.001*
Ongoing anticoagulant treatment, n/N (%)	13/284 (4.6)	13 (4.1)	0.93
Cancer type, n (%)	-	-	0.01±
Gastrointestinal	113 (39.6)	79 (24.9)	<0.001±
Lung	34 (11.9)	62 (19.6)	0.02±
Genitourinary	42 (14.7)	42 (13.2)	0.68
Gynecological	29 (10.2)	37 (11.7)	0.65
Hematological	22 (7.7)	31 (9.8)	0.46
Breast	17 (6.0)	31 (9.8)	0.12
Other or multiple primary tumors	28 (9.8)	35 (11.0)	0.84
Distant metastases, n/N (%)	166/263 (63.1)	178/285 (62.5)	0.94
Type of PE, n (%)	-	-	<0.001
Incidental	180 (63.2)	40 (12.6)	-
Symptomatic	105 (36.8)	277 (87.4)	-
PE location, n/N (%)	-	-	0.44
Segmental or more proximal	181/251 (72.1)	212/281 (75.4)	-
Subsegmental only	70/251 (27.9)	69/281 (24.6)	-
Symptoms§, n/N (%)	119/275 (43.3)	260/316 (82.3)	<0.001±
Abnormal vitals‡, n/N (%)	47/118 (39.8)	205/285 (70.9)	<0.001
Modified sPESI score ≥2, n/N (%)	75/151 (49.7)	227/311 (73.0)	<0.001*
Modified PESI score ≥86, n/N (%)	87/100 (87.0)	255/263 (97.0)	0.001*
Hemoglobin level in mmol/L, median [IQR]	7.4 [6.5, 8.2]	7.5 [6.5, 8.4]	0.49
Leukocyte count x10^9/L, median [IQR]	7.2 [5.4, 9.9]	9.7 [7.3, 13.2]	<0.001
Platelet count x10^9/L, median [IQR]	231 [177, 323]	235 [177, 320]	0.99
eGFR, n/N (%)	-	-	0.14*
≥60 ml/min	168/215 (78.1)	213/307 (69.4)	0.03*
45-59 ml/min	32/215 (14.9)	63/307 (20.5)	0.13
30-44 ml/min	13/215 (6.0)	19/307 (6.2)	1.00
<30 ml/min	2/215 (0.9)	12/307 (3.9)	0.07
Alanine aminotransferase in U/L, median [IQR]	23 [17, 35]	24 [16, 45]	0.37
Elevated cardiac troponins, n/N (%)	3/20 (15.0)	58/79 (73.4)	<0.001*

Table 1: Continued

	Direct discharge N=285	Hospitalization N=317	P-value
NT- proBNP in pg/mL, median [IQR]	174 [108, 349]	478 [148, 2325]	0.003*
D-dimer in µg/mL, median [IQR]	3.4 [1.4, 7.1]	5.9 [3.6, 8.5]	<0.001*
Signs of RV dysfunction, n/N (%)	12/175 (6.9)	74/273 (27.1)	<0.001
Therapeutic treatment, n (%)	-	-	0.60
DOAC	132 (46.3)	148 (46.7)	-
LMWH	136 (47.7)	153 (48.3)	-
Other	17 (6.0)	16 (5.1)	-
Year of PE diagnosis, n (%)	-	-	0.97
2017	23 (8.1)	27 (8.5)	-
2018	82 (28.8)	83 (26.2)	-
2019	65 (22.8)	76 (24.0)	-
2020	82 (28.8)	94 (29.7)	-
2021	33 (11.6)	37 (11.7)	-
Academic hospitals, n (%)	197 (69.1)	146 (46.1)	<0.001
Non-academic hospitals, n (%)	88 (30.9)	171 (53.9)	<0.001

Abbreviations: COPD, chronic obstructive pulmonary disease; DOAC, direct oral anticoagulant; ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate based on the MDRD equation; IQR, interquartile range; LMWH, low-molecular-weight heparin; NT-proBNP, N-terminal pro b-type natriuretic peptide; PE, pulmonary embolism; PESI, Pulmonary Embolism Severity Index; RV, right ventricular; sPESI, simplified Pulmonary Embolism Severity Index.

* After stratification on type of PE, these variables were only significantly different in symptomatic PE patients.

¶ After stratification on type of PE, these variables were only significantly different in incidental PE patients.

± Not significantly different after stratification on type of PE.

§ Symptoms included chest pain, dyspnea or syncope.

‡ Abnormal vital measurements included heart rate >100 bpm, systolic blood pressure <90 mmHg, respiratory rate >20/min, peripheral oxygen saturation <90%, and temperature <36°C or >38°C.

Symptomatic versus incidental pulmonary embolism

PE was symptomatic in 382 (63.5%) patients and detected incidentally in 220 (36.5%). Incidental PE led to a face-to-face evaluation in 149 (67.7%) patients, and was followed by a telephone visit only in 71 (32.3%); baseline characteristics of these subgroups are shown in **Supplementary Table 6**. In the group of patients with incidental PE, 81.8% (n=180), was discharged directly, compared to 27.5% (n=105) of symptomatic PE patients (P<0.001). Hospitalization was more often driven by other medical or social indications in patients with incidental, compared to those with symptomatic PE (54.2% vs. 24.0%; P<0.001). Baseline characteristics stratified by type of PE are shown in **Supplementary Table 7**. Cumulative 14-day mortality and PE-related readmission incidences in incidental and symptomatic PE patients were comparable to the main analysis (**Figure 2**).

Table 2. Characteristics of directly discharged patients who died or were readmitted within 14 days

	Most likely cause/reason	Sex, age in years	ECOG	Known CVD	Cancer type	Cancer stage	Type of PE	Type of visit	PE location	PE symptoms; Abnormal vitals	sPESI/PESI	D-dimer in ug/mL	RV dysfunction	Elevated cardiac troponin levels	ALAT in U/L	Hemoglobin level in mmol/L	Leukocytes x10^9/L	Platelets x10^9/L	eGFR in ml/min
Death 1	Malignancy	Male, 59	1	No	Genito-urinary	Distant metastases	Inc.	Telephone	More proximal	No; NR	NR	NR	No	NR	62	6.1	8.3	221	78
Death 2	Malignancy	Male, 56	1	No	Gastro-intestinal	Distant metastases	Inc.	Face-to-face	More proximal	NR	NR	NR	NR	NR	NR	7.3	18.1	296	NR
Readm. 1	Worsening dyspnea	Female, 65	1	No	Gastro-intestinal	Distant metastases	Symp.	Face-to-face	More proximal	Yes	1/95	5	No	NR	42	6.9	12.5	188	>90
Readm. 2	Fever, hypoxemia, coughing	Female, 72	0	Yes	Genito-urinary	Localized disease	Symp.	Face-to-face	Sub-segmental	Yes; heart rate >100 bpm	3/142	1.8	No	Yes	20	6.7	9.9	424	75
Readm. 3	Dyspnea and dizziness	Male, 68	1	Yes	Gastro-intestinal	Locoregional metastases	Symp.	Face-to-face	More proximal	Yes; heart rate >100 bpm, systolic BP 90-100 mmHg	≥4/NR	4.2	No	NR	29	7.5	3.4	247	68
Readm. 4	Bleeding	Male, 56	1	No	Genito-urinary	Distant metastases	Inc.	Telephone	More proximal	NR	NR/NR	1.5	No	NR	43	3.0	6.9	280	80
Readm. 5	Bleeding	Female,75	0	No	Genito-urinary	Locoregional metastases	Inc.	Face-to-face	More proximal	No	1/105	NR	No	NR	66	5.9	3.3	34	76

Abbreviations: ALAT, alanine aminotransferase; CVD, cardiovascular disease; ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate based on the MDRD equation; Inc., incidental; NR, not reported; PE, pulmonary embolism; (s)PESI, (simplified) Pulmonary Embolism Severity Index; Readm., readmission; RV, right ventricular; Symp., symptomatic.

*All patients were diagnosed in academic centers. N-terminal pro b-type natriuretic peptide measurements were missing.

Early discharge versus longer hospitalization

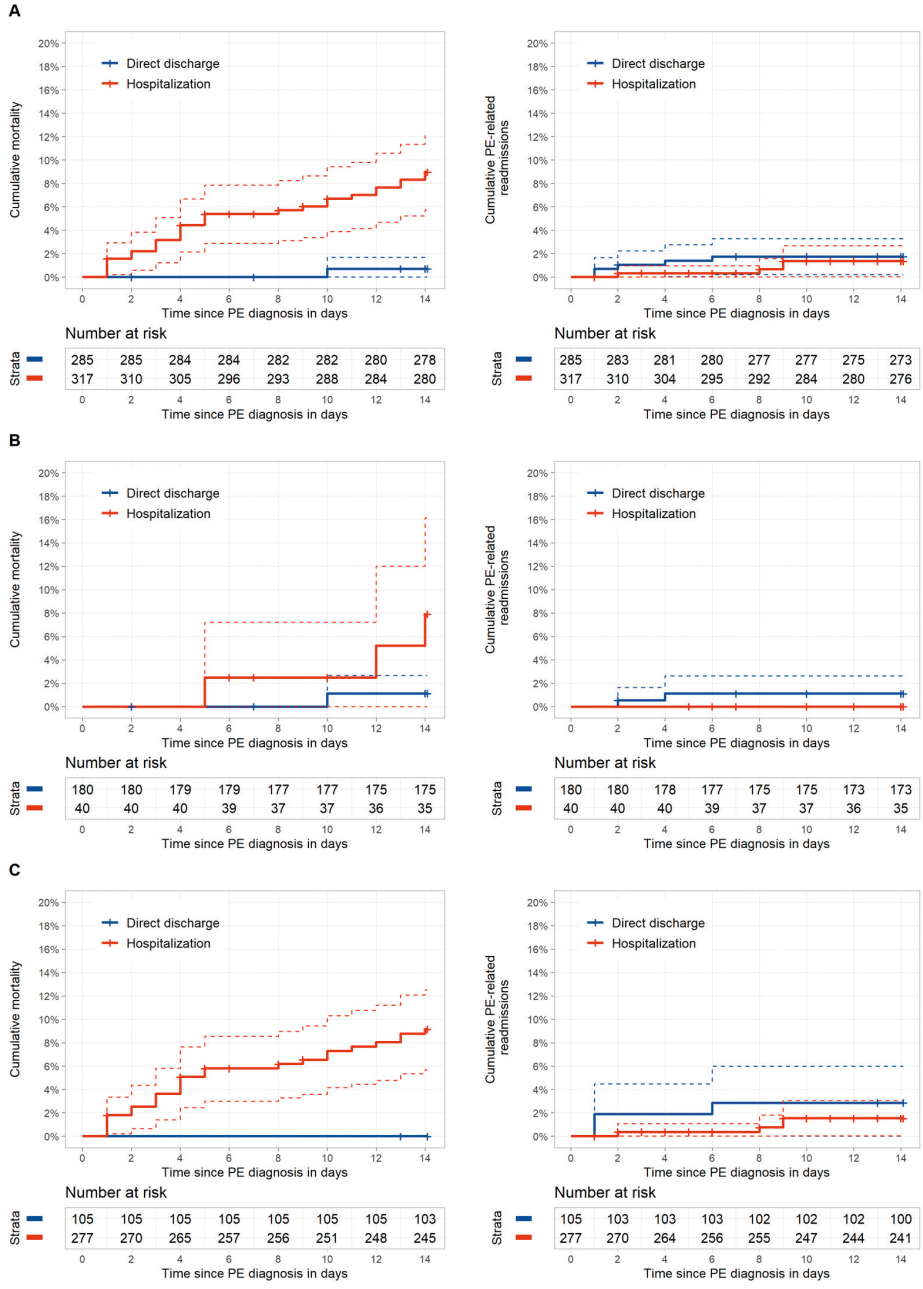
Of the patients who were initially hospitalized, 67 (21.1%) were discharged within 2 days, of whom 7 died within 14 days (10.4%); one death was judged to be caused by PE. The cumulative 14-day mortality incidence was 2.6% (95% CI, 0.9-4.2%) in the early discharged patients (n=352, 58.5%) and 8.9% (95% CI, 5.0-11.9%) in those hospitalized longer (n=250, 41.5%). The cumulative 14-day PE-related readmission incidence was 1.4% (95% CI, 0.5-3.1%) in early discharged and 1.7% (95% CI, 0.6-4.0%) in longer hospitalized patients.

DISCUSSION

In this observational multicenter cohort study, 28% and 82% of ambulatory cancer patients diagnosed with symptomatic or incidental acute PE, respectively, were discharged directly. The cumulative 14-day mortality and PE-related readmission incidences in these patients were low, indicating that clinicians successfully identify a substantial proportion of outpatients with cancer-associated PE in whom direct discharge is safe. Potential determinants for direct discharge identified in the present analysis were incidental PE, normal vital parameters, and absence of cardiac damage and aggravating or comorbid conditions. The proportion of patients discharged varied considerably across academic and non-academic hospitals (57% vs. 34%), which likely reflects differences in case mix. For example, patients from academic hospitals more often had incidental PE or subsegmental PE only. Potentially, a higher inpatient bed capacity for non-critical care in non-academic hospitals, may have also contributed. Another 11% of the patients were discharged within 2 days after being hospitalized. The 14-day mortality incidence in the early discharged patients, including those directly discharged, was 2.6%. About 90% (8 out of 9) of these deaths were not PE-related; it cannot be said whether these deaths would have been prevented by (prolonged) hospitalization.

Discharging patients with acute PE directly may prevent hospital-related complications, including infection, improve quality of life, and reduce healthcare costs and utilization.[12,15] Therefore, the ESC 2019 and the American College of Chest Physicians 2021 guidelines recommend home treatment over hospitalization in patients at low risk of early adverse events (i.e. recurrent VTE, bleeding, and death).[6,16] In the HOME-PE[13] trial, 1,975 patients with acute symptomatic PE were randomized to triaging with sPESI or Hestia criteria. The trial demonstrated that both tools safely select about 37-38% acute PE patients to be discharged within 24h, with a 14-day all-cause mortality incidence of 0.1%, upon which these were endorsed by the current guidelines. Although the guidelines do not exclude cancer patients, sPESI cannot be used to guide direct discharge in this setting, as it classifies all cancer patients as high-risk, and Hestia lacks validation in cancer patients. Notably, 57% of the patients from the hospital that endorsed sPESI were discharged directly, suggesting that the conventional sPESI was often overruled.

Figure 2. Cumulative mortality and PE-related readmission incidences



Abbreviation: PE, pulmonary embolism.
A) All patients; B) Incidental PE; C) Symptomatic PE.

Although current guidelines recommend a similar management strategy for incidental and symptomatic PE, our data suggest that incidental PE patients are managed differently and less strictly. For example, in about 30% of incidental PE cases, only a telephone visit followed by at home start of anticoagulation was performed.

The higher overall discharge rate in our cohort of cancer patients, compared to the HOME-PE trial, is likely explained by the substantial number of patients with incidental PE; in symptomatic PE patients the direct discharge rate was somewhat lower (28% vs. 37-38%). Siragusa and colleagues reported a discharge rate from the ED of 53% in an Italian prospective cohort study of 68 cancer patients with PE.[17] Hendriks and colleagues reported discharge within 24 hours in 51% and 72% of outpatients diagnosed with cancer-associated symptomatic and incidental PE, respectively, between December 2015 and July 2018 in the LUMC.[18] Data on safety outcomes within 14 days in discharged patients are scarce and incidences for longer observation periods are often reported instead. However, deaths beyond 14 days are foremost caused by the ongoing cancer and less likely to be related to PE, and thus may not be preventable by initial hospitalization.

We identified a substantial number of patients with active cancer and acute PE from both academic and non-academic hospitals. Patients were identified using CTcue, which has been validated for identification of patients with metastatic renal cell carcinoma with a sensitivity of 99% and of patients with coronary artery disease with a sensitivity of 82%.[10,11] Since PE can only be confirmed by imaging, and since all imaging reports were searched for various forms of the term 'pulmonary embolism', we assumed that sensitivity would be similarly high for this condition. To prevent misclassification, all hits were manually reviewed for eligibility, thus the positive predictive value was 100%. Because of the retrospective design, we were unable to accurately identify the exact reason for hospitalization in many cases. Data on vital measurements and laboratory parameters were missing in a substantial proportion of patients (41-93%), in particular in directly discharged patients. Likely, missing data in these patients were within the normal range, which may have led to an overestimation of the proportions with abnormal values in this group. We were unable to evaluate the utility of the (s)PESI and Hestia criteria for triaging in cancer patients. Given the low number of deaths, in particular in patients discharged directly, predictors for mortality could not be evaluated. Only patients from Dutch hospitals were included, which limits the generalizability to other countries.

In conclusion, this multicenter, observational study suggests that many cancer patients with acute PE can be safely discharged from the ED or outpatient clinic, in particular those with incidental PE. Factors associated with direct discharge that were identified in this study may guide decisions about hospitalization during initial PE management in cancer patients.

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SUPPLEMENTARY MATERIAL

Table S1: Validated clinical predictions rules for pulmonary embolism severity

Clinical risk factors	PESI	sPESI	Hestia
Age	Age in years	-	-
>80 years	-	+1	-
Male sex	+10	-	-
Altered mental status	+60	-	-
Vitals	-	-	-
Temperature <36 °C	+20	-	-
Respiratory rate >30 breaths per min	+20	-	-
Pulse rate ≥110 bpm	+20	+1	-
Systolic BP <100 mmHg	+30	+1	-
Hemodynamically unstable to the discretion of the physician	-	-	Yes/No
Arterial oxyhemoglobin saturation <90%	+20	+1	-
More than 24 hours of oxygen supply required to maintain oxygen saturation >90%	-	-	Yes/No
Comorbidities and underlying conditions	-	-	-
Cancer	+30	+1	-
Chronic heart failure or pulmonary disease	+10	+1	-
Medical or social reason for treatment in the hospital for >24 hours (infection, malignancy, or no support system)	-	-	Yes/No
Pregnancy	-	-	Yes/No
Severe liver impairment to the discretion of the physician	-	-	Yes/No
Documented history of heparin-induced thrombocytopenia	-	-	Yes/No
Creatinine clearance <30 mL/min*	-	-	Yes/No
PE diagnosed while on anticoagulant treatment	-	-	Yes/No
Severe pain needing intravenous pain medication for >24 hours	-	-	Yes/No
Active bleeding or high risk for bleeding§		-	Yes/No
Thrombolysis or embolectomy necessary		-	Yes/No

Table S1: Continued

Clinical risk factors	PESI	sPESI	Hestia
PE-risk classification	≤85 points: low mortality risk (Class I and II). ≥86 points: moderate to very high mortality risk (Class III to V)	0 points: low mortality risk ≥ 1 point(s) high mortality risk	All answered with 'No': low mortality risk ≥ 1 answered with 'Yes': point(s) moderate to high mortality risk

Abbreviations: BP, blood pressure; bpm, beats per minute; PE, pulmonary embolism.
* Calculated CrCl according to the Cockcroft-Gault formula.
§ Gastro-intestinal bleeding or recent surgery <2 weeks ago, stroke <4 weeks ago, bleeding disorder or platelet count <75 x 10^9/L, or uncontrolled hypertension (systolic BP >180 mmHg or diastolic BP >110 mmHg)

Table S2. CTcue searching strategy

Inclusion criteria	Sources	Content	Content for exclusion
Age ≥18 years	Demographics	Age ≥18 years	-
Malignancy			
Melanoma	ICD-10	'C43.5', 'C43.7', 'C43.9'	-
	DBC	'0313-842', '0303-350'	-
Breast	ICD-10	'C50.9'	-
	DBC	'0313-811', '0303-318', '0361-105'	-
Colorectal	ICD-10	'C18.9', 'C20'	-
	DBC	'0313-927' '0313-979', '0303-333', '0303-334', '0303-335', '0361-102'	-
Brain	ICD-10	'C79.3'	-
	DBC	'0330-0202', '0330-0203', '0330-0242'	-
Gynecological	ICD-10	'C54.1' 'C56'	-
	DBC	'0313-821', '0313-822', '0313-823', '0307-M11', '0307-M12', '0307-M13', '0307-M14', '0307-M15', '0307-M16', '0307-M17', '0307-M99', '0361-106'	-
Lung	ICD-10	'C34.9', 'C78.0'	-
	DBC	'0313-621','0313-622','0313-623','0313-624', '0313-629','0322 - 1303','0322 - 1304','0322 - 1305','0322 - 1306','0322 - 1307','0361-103'	-

Table S2. Continued

Inclusion criteria	Sources	Content	Content for exclusion
Hepatobiliary	ICD-10	'C78.7'	-
	DBC	'0313-955', '0303- 331', '0303-367'	-
Pancreatic	ICD-10	'C25.0', 'C25.9'	-
	DBC	'0313-964', '0303-332'	-
Hematological	ICD-10	'C77.9', 'C81.9', 'C82.9', 'C83.3', 'C85.9'	-
	DBC	'0313-751', '0313-752', '0313-753', '0313-754', '0313-756', '0313-757', '0313-761', '0313-771', '0313-773'	-
Esophageal or gastric	ICD-10	'C15.9', 'C16.9'	-
	DBC	'0313-904', '0313-914', '0313-979', '0303-319', '0303-346', '0361-102'	-
Genitourinary	ICD-10	'C61', 'C62.9', 'C64', 'C67.9'	-
	DBC	'0313-831', '0313-832', '0313-833', '0313-839', '0306-040', '0306-050', '0306-060', '0306-070', '0361-107'	-
Other	ICD-10	'C44.9', 'C73', 'C78.6', 'C79.5', 'C80.9'	-
	DBC	'0313-214', '0313-264', '0313-801, '0313-802', '0313-841', '0313-843', '0313-899', '0303-303', '0303-306' '0303-349', '0303-352', '0303-363', '0305-1140', '0305-1150', '0330-0222', '0330-0232', '0361-101', '0361-104', '0361-108', '0361-109'	-
Venous thromboembolism	Radiology reports from August 1st, 2017 to May 1st, 2021		
Pulmonary embolism	CT and PET-CT	Longembolie' + 16 synonyms	Geen longembolie' + 22 synonyms
Deep vein thrombosis	Ultrasound, CT, PET-CT, and MRI	DVT' + 13 synonyms	Geen DVT' + 25 synonyms
Splanchnic and portal vein thrombosis	CT, PET-CT and MRI	Porta trombose' + 6 synonyms, 'Niervene trombose' + 5 synonyms, 'V.hepatica trombose' + 4 synonyms	Geen aportatrombose', 'geen v. hepatica trombose', 'geen trombose', 'geen niervene trombose', 'geen niervenetrombose'

Table S2. Continued

Inclusion criteria	Sources	Content	Content for exclusion
Cerebral vein thrombosis	CT and MRI	Sinus trombose' + 6 synonyms	Geen sinustrombose' + 2 synonyms, 'geen trombose' + 2 synonyms

Abbreviations: CT, computed tomography; DBC, Diagnosis Treatment Combination; ICD-10, 10th International Classification of Diseases; MRI, magnetic resonance imaging; PET, positron emission tomography.

Table S3. STROBE Statement

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4,5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4,5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	6,9
Study size	10	Explain how the study size was arrived at	4,6

Table S3. Continued

	Item No	Recommendation	Page No
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how loss to follow-up was addressed	6
		(*e*) Describe any sensitivity analyses	6
Results			
Participants	13	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6,7
		(b) Give reasons for non-participation at each stage	6,7
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6,7, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	6,7
Outcome data	15	Report numbers of outcome events or summary measures over time	7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8; Table1; Figure 2
		(b) Report category boundaries when continuous variables were categorized	7-8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7-8; Figure 2
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			

Table S3. Continued

	Item No	Recommendation	Page No
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14--15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

Table S4. Reasons for hospitalization

Main reason, n (%)	**N=317**
Pulmonary embolism diagnosis	230 (72.6)
Cancer-related	39 (12.3)
Further diagnostical testing	18 (5.7)
Ileus treatment	5 (1.6)
Pleural effusion	3 (0.9)
Gastrointestinal perforation and/or fistula	3 (0.9)
Blood transfusion	3 (0.9)
Paracentesis	2 (0.6)
Intravenous pain medication	2 (0.6)
Concomitant infection	9 (2.8)
Social	7 (2.2)
Fracture	3 (0.9)
Other medical indication or unknown	31 (10.1)

Table S5. Characteristics at time of pulmonary embolism diagnosis, stratified by non-academic and academic hospitals

	Non-academic hospitals N=259	**Academic hospitals N=343**	**P-value**

Table S5. Continued

	Non-academic hospitals N=259	Academic hospitals N=343	P-value
Age in years, median [IQR]	69 [61, 75]	67 [56, 73]	0.001
Female sex, n (%)	114 (44.0)	190 (55.4)	0.01
ECOG performance status ≥2, n/N (%)	73/258 (28.3)	90/330 (27.3)	0.86
Cardiovascular disease, n (%)	42 (16.2)	57 (16.6)	0.98
COPD requiring medication, n (%)	31 (12.0)	19 (5.5)	0.01
Hospitalization >3 days in the preceding 4 weeks, n (%)	34 (13.1)	39 (11.4)	0.60
Ongoing anticoagulant treatment, n (%)	9 (3.5)	17 (5.0)	0.49
Cancer type, n (%)	-	-	<0.001
Gastrointestinal	66 (25.5)	126 (36.7)	0.004
Lung	62 (23.9)	34 (9.9)	<0.001
Genitourinary	31 (12.0)	53 (15.5)	0.27
Gynecological	26 (10.0)	40 (11.7)	0.62
Hematological	24 (9.3)	29 (8.5)	0.84
Breast	36 (13.9)	12 (3.5)	<0.001
Other or multiple primary tumors	14 (5.4)	49 (14.3)	0.01
Distant metastases, n/N (%)	151/234 (64.5)	193/314 (61.5)	0.52
Incidental PE, n (%)	69 (26.6)	151 (44.0)	<0.001
Subsegmental PE only, n/N (%)	15/203 (7.4)	124/329 (37.7)	<0.001
Symptoms*, n/N (%)	182/258 (70.5)	197/333 (59.2)	0.01
Abnormal vitals‡, n/N (%)	131/213 (61.5)	121/194 (62.4)	0.94
Modified sPESI score ≥2, n/N (%)	153/227 (67.4)	149/235 (63.4)	0.26
Modified PESI score ≥86, n/N (%)	194/201 (96.5)	148/162 (91.4)	0.13
Hemoglobin level in mmol/L, median [IQR]	7.6 [6.6, 8.4]	7.4 [6.5, 8.2]	0.07
Missing, n (%)	5 (1.9)	27 (7.8)	-
Leukocyte count x10^9/L, median [IQR]	8.9 [6.4, 11.7]	8.2 [5.8, 11.3]	0.03
Missing, n (%)	8 (3.1)	34 (9.9)	-
Platelet count x10^9/L, median [IQR]	232 [177, 307]	237 [177, 331]	0.34
Missing, n (%)	12 (4.6)	34 (9.9)	-
eGFR, n/N (%)	-	-	0.01
≥60 ml/min	168/252 (66.7)	213/270 (78.9)	-
45-59 ml/min	60/252 (23.8)	35/270 (13.0)	-
30-44 ml/min	15/252 (6.0)	17/270 (6.3)	-
<30 ml/min	9/252 (3.6)	5/270 (1.9)	-
Alanine aminotransferase in U/L, median [IQR]	21 [14, 35]	28 [18, 46]	<0.001
Missing, n (%)	21 (8.1)	120 (35.0)	-

Table S5. Continued

	Non-academic hospitals N=259	Academic hospitals N=343	P-value
Elevated cardiac troponins, n/N (%)	30/50 (60.0)	31/49 (63.3)	0.90
NT-proBNP in pg/mL, median [IQR]	43 (38.1)	15 (45.5)	0.57
Missing, n (%)	146 (56.4)	310 (90.4)	-
D-dimer in µg/mL, median [IQR]	6.2 [3.0, 8.1]	5.0 [2.7, 9.0]	0.51
Missing, n (%)	128 (49.4)	198 (57.7)	-
Signs of RV dysfunction, n/N (%)	45/226 (19.9)	41/222 (18.5)	0.79
Year of PE diagnosis, n (%)	-	-	0.63
2017	17 (6.6)	33 (9.6)	-
2018	72 (27.8)	93 (27.1)	-
2019	66 (25.5)	75 (21.9)	-
2020	75 (29.0)	101 (29.4)	-
2021	29 (11.2)	41 (12.0)	-

Abbreviations: COPD, chronic obstructive pulmonary disease; DOAC, direct oral anticoagulant; ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate based on the MDRD equation; IQR, interquartile range; LMWH, low-molecular-weight heparin; NT-proBNP, N-terminal pro b-type natriuretic peptide; PE, pulmonary embolism; PESI, Pulmonary Embolism Severity Index; RV, right ventricular; sPESI, simplified Pulmonary Embolism Severity Index.
* Symptoms included chest pain, dyspnea or syncope.
‡ Abnormal vital measurements included heart rate >100 bpm, systolic blood pressure <90 mmHg, respiratory rate >20/min, peripheral oxygen saturation <90%, and temperature <36°C or >38°C.

Table S6. Characteristics at time of incidental pulmonary embolism diagnosis, stratified by type of evaluation

	Face-to-face evaluation N=149	Telephone evaluation N=69	P-value
Age in years, median [IQR]	69 [56, 74]	64 [56, 71]	0.32
Female sex, n (%)	75 (50.3)	35 (50.7)	1.00
ECOG performance status ≥2, n/N (%)	25/147 (17.0)	12/67 (17.9)	1.00
Cardiovascular disease, n (%)	16 (10.7)	5 (7.2)	0.57
COPD requiring medication, n (%)	7 (4.7)	3 (4.3)	1.00
Hospitalization >3 days in the preceding 4 weeks, n (%)	8 (5.4)	5 (7.2)	0.81
Ongoing anticoagulant treatment, n (%)	6 (4.1)	6 (8.7)	0.28
Cancer type, n (%)	-	-	0.68
Gastrointestinal	79 (53.0)	28 (40.6)	-
Lung	15 (10.1)	11 (15.9)	-
Genitourinary	19 (12.8)	13 (18.8)	-

Table S6. Continued

	Face-to-face evaluation N=149	Telephone evaluation N=69	P-value
Gynaecological	17 (11.4)	8 (11.6)	-
Hematological	3 (2.0)	2 (2.9)	-
Breast	4 (2.7)	2 (2.9)	-
Other or multiple primary tumors	12 (8.1)	5 (7.1)	-
Distant metastases, n/N (%)	98/145 (67.6)	48/67 (71.6)	0.66
Subsegmental PE only, n/N (%)	30/125 (24.0)	18/61 (29.5)	0.53
Symptoms*, n/N (%)	27/144 (18.8)	10/65 (15.4)	0.69
Abnormal vitals‡, n/N (%)	30/76 (41.1)	1/1 (100)	0.87
Modified sPESI score ≥2, n/N (%)	42/88 (47.7)	13/13 (100)	<0.001
Modified PESI score ≥86, n/N (%)	63/67 (94.0)	NA	NA
Hemoglobin level in mmol/L, median [IQR]	7.2 [6.4, 8.1]	7.2 [6.5, 8.4]	0.64
Missing, n (%)	16 (10.7)	10 (14.5)	-
Leukocyte count x10^9/L, median [IQR]	7.5 [5.7, 10.0]	6.7 [5.0, 8.6]	0.04
Missing, n (%)	19 (12.8)	13 (18.8)	-
Platelet count x10^9/L, median [IQR]	235 [177, 323]	239 [166, 334]	0.91
Missing, n (%)	17 (11.4)	12 (17.4)	-
eGFR, n/N (%)	-	-	0.99
≥60 ml/min	77/108 (71.3)	29/39 (74.4)	-
45-59 ml/min	18/108 (16.7)	6/39 (15.4)	-
30-44 ml/min	10/108 (9.3)	3/39 (7.7)	-
<30 ml/min	3/108 (2.8)	1/39 (2.6)	-
Alanine aminotransferase in U/L, median [IQR]	25 [17, 41]	23 [15, 41]	0.37
Missing, n (%)	56 (37.6)	36 (52.2)	-
Elevated cardiac troponins, n/N (%)	4/13 (30.8)	NA	NA
NT-proBNP in pg/mL, median [IQR]	238 [109, 377]	NA	NA
Missing, n (%)	126 (84.6)	69 (100)	-
D-dimer in µg/mL, median [IQR]	6.1 [3.5, 7.4]	1.2 [1.2-1.2]	0.38
Missing, n (%)	144 (96.6)	68 (98.6)	-
Signs of RV dysfunction, n/N (%)	13/83 (15.7)	1/33 (3.0)	0.12
Year of PE diagnosis, n (%)	-	-	0.002
2017	12 (8.1)	7 (10.1)	-
2018	42 (28.2)	22 (31.9)	-
2019	45 (30.2)	5 (7.2)	-

Table S6. Continued

	Face-to-face evaluation N=149	Telephone evaluation N=69	P-value
2020	40 (26.8)	23 (33.3)	-
2021	10 (6.7)	12 (17.4)	-
Academic hospitals, n (%)	100 (67.6)	49 (70.0)	0.84

Abbreviations: COPD, chronic obstructive pulmonary disease; DOAC, direct oral anticoagulant; ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate based on the MDRD equation; IQR, interquartile range; LMWH, low-molecular-weight heparin; NA, not assessable; NT-proBNP, N-terminal pro b-type natriuretic peptide; PE, pulmonary embolism; PESI, Pulmonary Embolism Severity Index; RV, right ventricular; sPESI, simplified Pulmonary Embolism Severity Index.
* Symptoms included chest pain, dyspnea or syncope.
‡ Abnormal vital measurements included heart rate >100 bpm, systolic blood pressure <90 mmHg, respiratory rate >20/min, peripheral oxygen saturation <90%, and temperature <36°C or >38°C.

Table S7. Characteristics at time of pulmonary embolism diagnosis, stratified by type of pulmonary embolism

	Incidental			Symptomatic		
	Direct discharge N=180	Hospitalization N=40	P-value	Direct discharge N=105	Hospitalization N=277	P-value
Age in years, median [IQR]	66 [55, 73]	70 [61, 74]	0.08	66 [58, 72]	68 [60, 75]	0.02
Female sex, n (%)	89 (49.4)	20 (50.0)	1.00	50 (47.6)	139 (50.2)	0.74
ECOG performance status ≥2, n/N (%)	25/176 (14.2)	12/40 (30.0)	0.03	28/102 (27.5)	98/270 (36.3)	0.14
Cardiovascular disease, n (%)	15 (8.3)	6 (15.0)	0.32	15 (14.3)	63 (22.7)	0.09
COPD requiring medication, n (%)	6 (3.3)	4 (10.0)	0.16	3 (2.9)	37 (13.4)	0.01
Hospitalization >3 days in the preceding 4 weeks, n (%)	9 (5.0)	4 (10.0)	0.40	7 (6.7)	53 (19.1)	0.01
Ongoing anticoagulant treatment, n/N (%)	10/179 (5.6)	2/40 (5.0)	1.00	3 (2.9)	11 (4.0)	0.83
Cancer type, n (%)	-	-	0.92	-	-	0.42
Gastro-intestinal	89 (49.4)	18 (45.0)	0.74	24 (22.9)	61 (22.0)	0.97
Lung	20 (11.1)	6 (15.0)	0.68	14 (13.3)	56 (20.2)	0.16
Genitourinary	28 (15.6)	5 (12.5)	0.81	14 (13.3)	37 (13.4)	1.00
Gynecological	20 (11.1)	5 (12.5)	1.00	9 (8.6)	32 (11.6)	0.51
Hematological	3 (1.7)	2 (5.0)	0.49	19 (18.1)	29 (10.5)	0.07
Breast	5 (2.8)	1 (2.5)	1.00	12 (11.4)	30 (10.8)	1.00
Other or multiple primary tumors	15 (8.4)	3 (7.5)	1.00	13 (12.4)	32 (11.6)	0.90
Distant metastases, n/N (%)	124/177 (70.1)	24/37 (64.9)	0.67	42/86 (48.8)	154/248 (62.1)	0.04
Hemoglobin level in mmol/L, median [IQR]	7.3 [6.5, 8.2]	7.0 [6.4, 8.1]	0.30	7.7 [6.7, 8.3]	7.5 [6.6, 8.5]	0.83
Leukocyte count x10^9/L, median [IQR]	6.9 [5.2, 9.0]	9.0 [7.2, 11.6]	0.001	7.7 [5.8, 11.0]	9.8 [7.6, 13.3]	0.001
Platelet count x10^9/L, median [IQR]	232 [170, 310]	265[203, 351]	0.14	228 [181, 333]	234 [175, 307]	0.48
Creatinine clearance, n/N (%)	-	-	0.65	-	-	0.02

Table S7. Continued

	Incidental			Symptomatic		
	Direct discharge N=180	Hospitalization N=40	P-value	Direct discharge N=105	Hospitalization N=277	P-value
≥60 ml/min	83/114 (72.8)	24/35 (68.6)	0.79	85/101 (84.2)	189/272 (69.5)	0.01
45-59 ml/min	19/114 (16.7)	6/35 (17.1)	1.00	13/101 (12.9)	57/272 (21.0)	0.10
30-44 ml/min	10/114 (8.8)	3/35 (8.6)	1.00	3/101 (3.0)	16/272 (5.9)	0.38
<30 ml/min	2/114 (1.8)	2/35 (5.7)	0.50	0/101	10/272 (3.7)	0.11
Alanine aminotransferase in U/L, median [IQR]	24 [16, 41]	27 [17, 46]	0.58	21 [17, 32]	24 [16, 44]	0.25
PE location, n/N (%)	-	-	0.06	-	-	1.00
Segmental or more proximal	109/153 (71.2)	31/35 (88.6)	-	72/98 (73.5)	181/246 (73.6)	-
Subsegmental only	44/153 (28.8)	4/35 (11.4)	-	26/98 (26.5)	65/246 (26.4)	-
Confirmed concomitant DVT, n (%)	15 (8.3)	6 (15.0)	0.32	6 (5.7)	15 (5.4)	1.00
Signs of RV dysfunction, n/N (%)	7/89 (7.9)	7/28 (25.0)	0.04	5/86 (5.8)	67/245 (27.3)	<0.001
Elevated cardiac troponin levels, n/N (%)	0/4	4/9 (44.4)	0.34	3/16 (18.8)	54/70 (77.1)	<0.001
NT- proBNP in pg/mL, median [IQR]	165 [136, 263]	294 [109, 670]	0.30	204 [108, 599]	576 [166, 2609]	0.01
D-dimer levels in µg/mL, median [IQR]	1.6 [1.2, 2.5]	7.4 [6.7, 10.8]	0.05	3.6 [1.5, 7.5]	5.8 [3.6, 8.5]	0.001
Modified sPESI score ≥2, n/N (%)	34/64 (53.1)	16/38 (42.1)	0.79	41/87 (47.1)	205/273 (75.1)	<0.001
Modified PESI score ≥86, n/N (%)	31/35 (88.6)	32/32	0.15	56/65 (86.2)	223/231 (96.5)	0.004
Symptoms*, n/N (%)	28/171 (16.4)	10/40 (25.0)	0.29	91/104 (87.5)	250/276 (90.6)	0.49
Abnormal vital measurements, n/N (%)	11/40 (27.5)	20/34 (58.8)	0.01	36/78 (46.2)	181/251 (72.1)	<0.001
Therapeutic PE treatment, n (%)	-	-	0.25	-	-	0.13
DOAC	70 (38.9)	10 (25.0)	-	62 (59.0)	138 (49.8)	-

Table S7. Continued

	Incidental			Symptomatic		
	Direct discharge N=180	Hospitalization N=40	P-value	Direct discharge N=105	Hospitalization N=277	P-value
LMWH	99 (55.0)	26 (65.0)	-	37 (35.2)	127 (45.8)	-
Other	11 (6.1)	4 (10.0)	-	6 (4.8)	12 (4.4)	-
Year of PE diagnosis, n (%)	-	-	0.03			0.50
2017	14 (7.8)	5 (12.5)	-	9 (8.6)	22 (7.9)	-
2018	58 (32.2)	7 (17.5)	-	24 (22.9)	76 (27.4)	-
2019	34 (18.9)	16 (40.0)	-	31 (29.5)	60 (21.7)	-
2020	55 (30.6)	9 (22.5)	-	27 (25.7)	85 (30.7)	-
2021	19 (10.6)	3 (7.5)	-	14 (13.3)	34 (12.3)	-
Academic hospitals, n (%)	132 (73.3)	19 (47.5)	0.003	65 (61.9)	127 (45.8)	0.01
Non-academic hospitals, n (%)	48 (26.7)	21 (52.5)	0.003	40 (38.1)	150 (54.2)	0.01

Abbreviations: COPD, chronic obstructive pulmonary disease; DVT, deep vein thrombosis; DOAC, direct oral anticoagulant; ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate based on the MDRD equation; IQR, interquartile range; LMWH, low-molecular-weight heparin; NS, not significant; NT-proBNP, N-terminal pro b-type natriuretic peptide; PE, pulmonary embolism; PESI, Pulmonary Embolism Severity Index; RV, right ventricular; sPESI, simplified Pulmonary Embolism Severity Index.