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Management and Outcomes of Adults Diagnosed with Acute Pulmonary Embolism in Primary Care: Community-Based Retrospective Cohort Study

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BACKGROUND: The management and outcomes of patients diagnosed with acute pulmonary embolism in primary care have not been characterized.

OBJECTIVE: To describe 30-day outcomes stratified by initial site-of-care decisions

DESIGN: Multicenter retrospective cohort study

PARTICIPANTS: Adults diagnosed with acute pulmonary embolism in primary care in a large, diverse community-based US health system (2013–2019)

MAIN MEASURES: The primary outcome was a composite of 30-day serious adverse events (recurrent venous thromboembolism, major bleeding, and all-cause mortality). The secondary outcome was 7-day pulmonary embolism–related hospitalization, either initial or delayed.

KEY RESULTS: Among 652 patient encounters (from 646 patients), median age was 64 years; 51.5% were male and 70.7% identified as non-Hispanic white. Overall, 134 cases (20.6%) were sent home from primary care and 518 cases (79.4%) were initially referred to the emergency department (ED) or hospital. Among the referred, 196 (37.8%) were discharged home from the ED without events. Eight patients (1.2%; 95% CI 0.5–2.4%) experienced a 30-day serious adverse event: 4 venous thromboemboli (0.6%), 1 major bleed (0.2%), and 3 deaths (0.5%). Seven of these patients were initially hospitalized, and 1 had been sent home from primary care. All 3 deaths occurred in patients with known metastatic cancer initially referred to the ED, hospitalized, then enrolled in hospice following discharge. Overall, 328 patients (50.3%) were hospitalized within 7 days: 322 at the time of the index diagnosis and 6 following initial outpatient management (4 clinic-only and 2 clinic-plus-ED patients).

CONCLUSIONS: Patients diagnosed with acute pulmonary embolism in this primary care setting uncommonly experienced 30-day adverse events, regardless of initial site-of-care decisions. Over 20% were managed comprehensively by primary care. Delayed 7-day pulmonary embolism-related hospitalization was rare among the 51% treated as outpatients. Primary care management of acute pulmonary embolism appears to be safe and could have implications for cost-effectiveness and patient care experience.

KEY WORDS: pulmonary embolism; venous thromboembolism; general practice/family medicine; ambulatory care; outpatients.

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INTRODUCTION

Select ambulatory adult patients with acute pulmonary embolism can be safely managed without hospitalization.[1, 2] Society guidelines encourage risk-based identification of outpatient-eligible adults and discharge to home with education, anticoagulation, and close follow-up.[3–9] Studies supporting outpatient management were undertaken in specialty clinics (e.g., Canadian thrombosis units) and emergency departments (EDs), the latter often supplemented by observation or inpatient care prior to discharge to home.[10, 11]

We know little about the management of acute pulmonary embolism in primary care, including how short-term outcomes are affected by initial site-of-care decisions, such as referring patients to the ED or sending them directly home. In fact, *comprehensive* primary care–based PE management without referral is understood only through case reports.[12–14] This primary care–centered approach may be more convenient for

low-risk patients than the customary ED transfer or short hospital stay. It may also better steward healthcare resources, optimize continuity of care, and maximize home time, an important patient-centered outcome.[15, 16] The prevalence of comprehensive outpatient management for acute PE by primary care clinicians is unknown, however, as are the characteristics of these patients and their clinical outcomes.

We sought to identify adults diagnosed with acute PE in primary care and to describe their short-term outcomes, stratified by their clinicians' initial site-of-care decisions. We hypothesized that the incidence of 30-day serious adverse outcomes would be low among patients diagnosed with acute PE in primary care and lower still among the cohort selected for outpatient care without hospitalization, either by the primary care or the emergency clinician. This study will help us understand the management of acute pulmonary embolism in primary care and may expand the treatment options currently available.

METHODS

Study Design and Setting

This retrospective cohort study (PEPC, Pulmonary Embolism in Primary Care) was undertaken in Kaiser Permanente (KP) Northern California, a large US integrated health care system that serves over 4.5 million patients across 21 medical centers. Health plan members comprise one-third of the population in areas served and are representative of the racial, ethnic, and socioeconomic diversity of the surrounding population.[17] Primary care clinicians are residency-trained family or internal medicine physicians; few are independent nurse practitioners (< 2%). Care received outside the system, which is uncommon, is captured through claims data, significantly reducing missed outcomes and cases lost to follow-up. The study was approved by the KP Northern California Institutional Review Board with waiver of informed consent.

The diagnosis and management of acute pulmonary embolism were at the discretion of primary care clinicians. No system-wide training was conducted nor were management pathways in place prior to or during the study period. Primary care clinicians had ready access to laboratory testing as well as chest radiography, computed tomography pulmonary angiography (CTPA), and ventilation perfusion (VQ) scintigraphy. Radiologists, pulmonologists, and hematologists were available for phone consultation around the clock. We explain in the Supplement the system's anticoagulation recommendations and formulary changes during the study period, along with a concurrent study of ED decision support unavailable to primary care.

Study Population

The PEPC study cohort consisted of adult health plan members (≥ 18 years) with acute objectively confirmed pulmonary embolism diagnosed in primary care between January 1, 2013, and December 31, 2019. Cases were identified for manual chart review if they had undergone CTPA or VQ scintigraphy that was likely positive for pulmonary embolism (based on natural language-processing algorithms, explained in the Supplement) and received 1 of the following interventions within 72 h post-imaging: admission to the ED or hospital, or an anticoagulant prescription. We excluded those with negative CTPA or chronic pulmonary embolism, patients already taking anticoagulants at the time of imaging, residents of skilled nursing facilities, those receiving only comfort-focused care, those who left the ED against medical advice, those who were initially transferred to an outside facility, and those who were known to be pregnant (Fig. 1 and Supplement). The number of cases during the study period determined the sample size.

Data Collection, Definitions, and Outcomes

We combined electronic extraction from administrative and clinical databases with structured manual review of the electronic health record (EHR) by physician abstractors, using established training, monitoring, and adjudication methods, as in prior research.[2, 18] Starting with the time of the index image, we examined prior encounters to identify the date and mode (i.e., in-person or telemedicine) of the index primary care encounter for evaluation of specific pulmonary embolism–related symptoms.

The primary outcome was a composite of 30-day serious adverse events: major hemorrhage, as defined by the International Society on Thrombosis and Haemostasis[19]; radiologically confirmed recurrent venous thromboembolism, either an extension of the index clot(s) or a new clot; and all-cause mortality. To identify death, we used a health system mortality database that links to the Social Security death master file and the California State Department of Vital Statistics, which include deaths outside the system. We stratified outcomes by initial site-of-care management.

The secondary outcome was 7-day pulmonary embolism–related hospitalization (measured from the time of the index diagnostic image), either initial or delayed. We designated pulmonary embolism–related signs, symptoms, or interventions a priori, as with earlier studies (see Supplement).[2, 18]

We identified all out-of-system hospitalizations in the claims database and reviewed them for study outcomes. All 7-day and 30-day outcomes were adjudicated by 2 independent physician abstractors, who consulted a third if needed for consensus. Ten percent of cases were randomly selected for independent review by a second abstractor to assess inter-rater reliability for the following: Pulmonary Embolism Severity Index variables, the initial site-of-care decision, delayed 7-day pulmonary embolism–related hospitalization for outpatients, and 30-day serious adverse outcomes. We report the interrater reliability with a weighted kappa statistic and percent agreement.

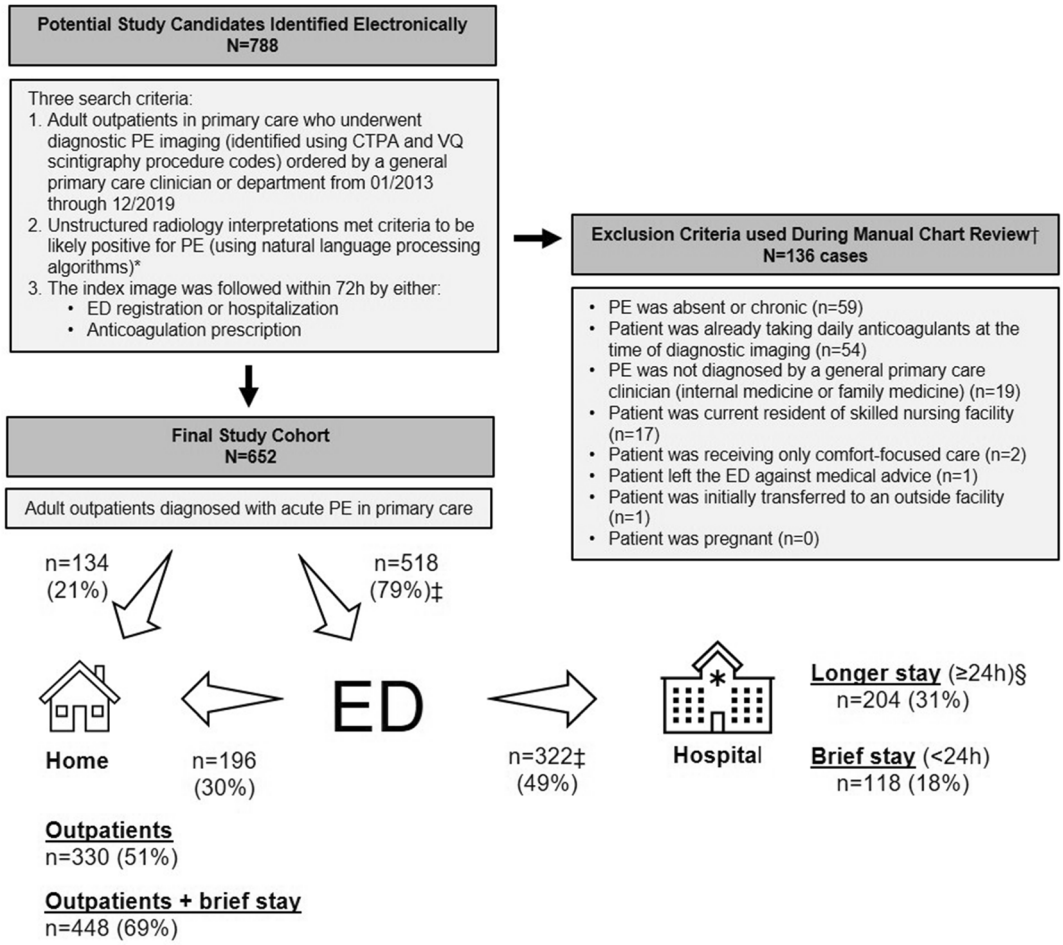

Figure 1 Cohort assembly and sites of care of adults diagnosed with acute pulmonary embolism in primary care. ***CTPA = computed tomography pulmonary angiography; ED = emergency department; ICU = intensive care unit; VQ = ventilation-perfusion. All percentages are from the total cohort. *The algorithms were designed to identify cases in which the CTPA was likely positive or the VQ scan was likely high or intermediate probability (see Supplement for more detail). † Patients may have had more than 1 exclusion criterion recorded. ‡ Includes 7 patients who were directly admitted to the hospital from the primary care clinic without an intermediary evaluation in the ED.***

We selected the validated Pulmonary Embolism Severity Index to estimate risk of 30-day all-cause mortality.[20–22] We explain our handling of vital signs in the Supplement. A study radiologist blinded to patient-level data used the diagnostic radiologists' interpretations to identify the most proximal clot location on CTPA as well as note documentation of right ventricular strain and cardiomegaly. We designated presyncope as a syncopal equivalent.[23–25] We defined an incidental pulmonary embolism[26] as 1 identified on imaging not intended to diagnose pulmonary embolism.

Primary Data Analysis

We characterized patients according to their clinician's initial site-of-care decision following diagnosis, comparing clinic-only versus ED/hospital referred patients. We also compared patients with and without 7-day pulmonary embolism–related hospitalization. We used multivariable regression analysis to identify variables independently associated with 7-day hospitalization. We included in the model demographics and variables associated with hospitalization (p value less than 0.10) in the bivariate analysis. We presented continuous variables as medians with IQRs and categorical data as frequencies and proportions. We used non-parametric (Wilcoxon) tests for continuous variables and chi-squared tests for categorical variables. We report key point estimates with 95% CIs. We considered a 2-tailed p value < 0.05 to be significant. All analyses were conducted with SAS (version 9.4; SAS Institute, Inc., Cary, NC).

Role of the Funding Source

KP Northern California Community Health and The Permanente Medical Group Delivery Science and Physician Researcher Programs funded the PEPC study. They were not involved in the design, conduct, interpretation, or reporting of the study.

Table 1 Demographic and Historical Characteristics of Adults Diagnosed with Acute Pulmonary Embolism in Primary Care, Stratified by Initial Site-of-Care Decision: Clinic Only Versus Referral to a Higher Level of Care

Characteristics	Total cohort (n = 652)	Clinic only (n = 134)	Referral to ED or hospital (n = 518)	p value
Age, median (IQR)	64 (51–73)	65 (55–73)	64 (50–74)	0.46
Male, n (%)	336 (51.5)	74 (55.2)	262 (50.6)	0.34
Race/ethnicity, self-reported, n (%)				0.11
White	461 (70.7)	107 (79.9)	354 (68.3)	
African American	75 (11.5)	9 (6.2)	66 (12.7)	
Hispanic or Latinx	68 (10.4)	11 (8.2)	57 (11.2)	
Asian or Pacific Islander	44 (6.8)	6 (4.5)	38 (7.3)	
Other	4 (0.6)	1 (0.8)	3 (0.6)	
Comorbidities, n (%)				
Body mass index ≥ 30 kg/m^2*	312 (47.9)	61 (45.5)	251 (48.5)	0.75
Hypertension	252 (38.7)	55 (41.0)	197 (38.0)	0.52
History of venous thromboembolism	166 (25.5)	46 (34.3)	120 (23.2)	0.008
Chronic lung disease	147 (22.6)	31 (23.1)	116 (22.4)	0.85
Cancer (active or history of)	136 (20.9)	30 (22.4)	106 (20.5)	0.63
Active cancer†	52 (8.0)	10 (7.5)	42 (8.1)	0.81
Renal failure	58 (8.9)	9 (6.7)	49 (9.5)	0.32
Stage 4 or more severe	3 (0.5)	1 (0.8)	2 (0.4)	0.58
Heart failure (systolic or diastolic)	22 (3.4)	6 (4.5)	16 (3.1)	0.43
Thrombophilia	21 (3.2)	7 (5.2)	14 (2.7)	0.14
Diabetes	11 (1.7)	1 (0.8)	10 (1.9)	0.34
Elixhauser Comorbidity Score, median (IQR)	0 (− 2 to 3)	0 (0–3)	0 (− 2 to 3)	0.32
Venous thromboembolism risk factors, n (%)				
None documented	386 (59.2)	84 (62.7)	302 (58.3)	0.36
Travel, prolonged	113 (17.3)	22 (16.4)	91 (17.6)	0.75
Surgery < 90 d	62 (9.5)	13 (9.7)	49 (9.5)	0.93
Immobilization > 2 d within the prior 90 d	48 (7.4)	11 (8.2)	37 (7.1)	0.67
Hospitalization > 2 d within the prior 90 d	39 (6.0)	8 (6.0)	31 (6.0)	0.99
Estrogen, exogenous	36 (5.5)	6 (4.5)	30 (5.8)	0.55
Major trauma	5 (0.8)	1 (0.8)	4 (0.8)	0.98
Pulmonary embolism symptoms, n (%)				
Shortness of breath	509 (78.1)	91 (67.9)	418 (80.7)	0.001
Chest pain	295 (45.3)	59 (44.0)	236 (45.6)	0.75
Deep vein thrombosis symptoms	153 (23.5)	24 (17.9)	129 (24.9)	0.089
Cough	140 (21.5)	21 (15.7)	119 (23.0)	0.067
Hemoptysis	24 (3.7)	1 (0.8)	23 (4.4)	0.043
Syncope or presyncope	17 (2.6)	3 (2.2)	14 (2.7)	0.76
Duration of pulmonary embolism symptoms, n (%)				0.002
≤ 2 d	106 (16.3)	25 (18.7)	81 (15.6)	
> 2 d ≤ 7 d	199 (30.5)	33 (24.6)	166 (32.1)	
> 1 w ≤ 2 w	134 (20.6)	20 (14.9)	114 (22.0)	
>2 w ≤ 4 w	107 (16.4)	20 (14.9)	87 (16.8)	
>1 m	75 (11.5)	23 (17.2)	52 (10.0)	
Missing	31 (4.75)	13 (9.7)	18 (3.5)	

**Body mass index was missing for 7 patients*
†We defined active cancer as metastatic, undergoing treatment within the prior 12 months, or receiving palliative care

RESULTS

Patient, Diagnostic, and Clinician Characteristics

We identified 788 cases for manual chart review, 136 of which were excluded (Fig. 1). Our cohort included 646 patients with 652 encounters (6 patients had 2 study-eligible encounters). Median age was 64 years (IQR, 51–73); 336 (51.5%) were male and 461 (70.7%) identified as non-Hispanic white. The leading pulmonary embolism symptom was dyspnea (78.1%); 16.3% had ≤ 2 days and 67.3% had ≤ 2 weeks of symptoms at the index encounter. Incidental pulmonary embolism was uncommon (3.1%). Few patients had no pulmonary embolism–related symptoms (2.6%). Most (85.4 %) were low-to-intermediate risk on the Pulmonary Embolism Severity Index. We report patient characteristics in Tables 1 and 2. We describe the timing of diagnostic testing in the Supplement, along with characteristics of the diagnosing clinicians.

Site of Care, Anticoagulation, and Follow-Up

Among 652 cases of acute pulmonary embolism, 134 (20.6%) were sent directly home; these received *comprehensive* clinic-based care. Overall, 518 cases (79.4%) were initially referred: 511 to the ED and 7 directly to the hospital. Of the 511 ED referrals, 196 (38.4%; 30.0% of the entire cohort) were discharged home (Fig. 1). Those discharged home from the ED had a median stay (from the time of ED registration) of 3.0 h (IQR, 2.4–4.1) compared with a median length of stay (including ED evaluation) of 29.1 h (IQR, 21.8–49.7) among 322 initially hospitalized. Of those initially hospitalized, 118 (36.6% of the initially hospitalized; 18.1% of the total cohort) had a short observational stay (< 24 h). Four patients (0.6% of the study cohort) referred to the ED were initially admitted to the intensive care unit (ICU) (Supplementary Table 1).

Table 2 Physician Examination and Testing Characteristics of Patients Diagnosed with Acute Pulmonary Embolism in Primary Care, Stratified by Initial Site-of-Care Decision: Clinic Only Versus Referral to a Higher Level of Care

Characteristics	Total cohort (n = 652)	Clinic only (n = 134)	Referred to the ED or hospital (n = 518)	p value
Index encounter, mode, n (%)				0.55
In-person	586 (89.9)	120 (89.6)	466 (90.0)	
Telemedicine (secure message or telephone)	61 (9.4)	12 (9.0)	49 (9.5)	
None*	5 (0.8)	2 (1.5)	3 (0.6)	
Index physical examination findings, n (%)				
N†	586 (89.9)	120 (89.6)	466 (90.0)	
Systolic blood pressure < 100 mmHg	19 (3.2)	7 (5.8)	12 (2.6)	0.072
Systolic blood pressure ≥ 160 mmHg	4 (0.7)	0 (0)	4 (0.8)	0.31
Heart rate ≥ 110 beats/min	43 (7.3)	4 (3.3)	39 (8.4)	0.059
Temperature < 36 °C	5 (0.8)	0 (0)	5 (1.1)	0.26
Temperature ≥ 38 °C	0 (0)	0 (0)	0 (0)	
Pulse oximetry < 90%‡	4 (0.7)	0 (0)	4 (0.9)	0.31
Respiratory rate documented	24 (4.1)	5 (4.2)	19 (4.1)	0.96
Rate ≥ 30 breaths/min	1 (4.2)	0 (0)	1 (5.3)	0.60
Altered mental status§	2 (0.3)	0 (0)	2 (0.4)	0.47
D-Dimer, n (%)				0.21
Elevated	320 (49.1)	60 (44.8)	260 (50.2)	
Negative	4 (0.6)	2 (1.5)	2 (0.4)	
Missing	328 (50.3)	72 (53.7)	256 (49.4)	
Troponin, n (%)‖				0.30
Elevated	0 (0)	0 (0)	0 (0)	
Negative	42 (6.4)	6 (4.5)	36 (7.0)	
Missing	610 (93.6)	128 (95.5)	482 (93.1)	
B-type natriuretic peptide, n (%)				0.22
≥ 500 pg/mL	3 (0.5)	1 (0.8)	2 (0.4)	
≥ 100 < 500 pg/mL	42 (6.4)	5 (3.7)	37 (7.1)	
< 100 pg/mL	112 (17.2)	18 (13.4)	94 (18.2)	
Missing	495 (75.9)	110 (82.1)	385 (74.3)	
Index 12-lead electrocardiogram, n (%)				0.44
No change from prior	15 (2.3)	5 (3.7)	10 (1.9)	
Normal	58 (8.9)	15 (11.2)	43 (8.3)	
Tachycardia	12 (1.8)	1 (0.8)	11 (2.1)	
Other finding	24 (3.7)	5 (3.7)	19 (3.7)	
Not obtained	543 (83.3)	108 (80.6)	435 (84.0)	
Compression ultrasonography, n (%)				0.19
Yes, negative for deep vein thrombosis	28 (4.3)	9 (6.7)	19 (3.7)	
Yes, positive for deep vein thrombosis	42 (6.4)	6 (4.5)	36 (7.0)	
Not obtained	582 (89.3)	119 (88.8)	463 (89.4)	
Diagnostic imaging, n (%)				0.44
CTPA	617 (94.6)	125 (93.3)	492 (95)	
Ventilation/perfusion scan	35 (5.4)	9 (6.7)	26 (5.0)	
Clinician ordering diagnostic imaging, n (%)				0.059
Primary care clinician	500 (76.7)	111 (82.8)	389 (75.1)	
Colleague	152 (23.3)	23 (17.2)	129 (24.9)	
Day of imaging, n (%)				0.098
Monday–Friday	626 (96.0)	132 (98.5)	494 (95.4)	
Saturday–Sunday	26 (4.0)	2 (1.5)	24 (4.6)	
Time of imaging, n (%)				0.009
0800 < 1600	418 (64.1)	105 (78.4)	313 (60.4)	
1600 < 0800	234 (35.9)	29 (21.6)	205 (39.6)	
CTPA clot location¶, n (%)				< 0.001
Proximal	256 (39.3)	25 (18.7)	231 (44.6)	
Distal	355 (54.5)	98 (73.1)	257 (49.6)	
Subsegmental only	65 (10.0)	30 (22.4)	35 (6.8)	
Unclear or missing	41 (6.3)	11 (8.2)	30 (5.8)	
Radiologist comment on heart from CTPA, n (%)				0.002
Heart normal or right ventricular strain absent	338 (51.8)	62 (46.3)	276 (53.3)	
Right ventricular strain present	24 (3.7)	2 (1.5)	22 (4.3)	
Heart enlarged	38 (5.8)	2 (1.5)	36 (6.9)	
Equivocal, not reported, blank, or other	252 (38.7)	68 (50.8)	184 (35.5)	
Pulmonary Embolism Severity Index Class, n (%)				0.79
I–II (lower risk)	378 (58.0)	74 (55.2)	304 (58.7)	
III–IV (intermediate risk)	179 (27.5)	41 (30.6)	138 (26.6)	
V (higher risk)	29 (4.4)	5 (3.7)	24 (4.6)	
Missing	66 (10.1)	14 (10.4)	52 (10.0)	

(continued on next page)

Table 2. (continued)

Characteristics	Total cohort (n = 652)	Clinic only (n = 134)	Referred to the ED or hospital (n = 518)	p value
Echocardiography, n (%)[#]	129 (19.8)	1 (0.07)	128 (24.7)	< 0.0001
Telephone consultation with pulmonologist or hematologist after diagnosis secured, n (%)	60 (9.2)	44 (32.8)	16 (3.1)	< 0.001

CTPA computed tomography pulmonary angiography, ED emergency department
[*]Several patients with an incidental diagnosis of acute pulmonary embolism had their imaging study ordered by primary care without an index encounter
[†]Physical examination findings reported only for patients who had an in-person initial encounter; excludes those who had a telemedicine encounter or had no index encounter at all
[‡]Includes post-exertional pulse oximetry measurements
[§]Disorientation, lethargy, stupor, or coma
[‖]Troponin and B-type natriuretic peptide were obtained prior to the diagnosis of pulmonary embolism. Serum troponin values were obtained using a fourth-generation troponin I assay. Values above the 99th percentile were considered elevated
[¶]We defined proximal as clearly lobar or more proximal. Pulmonary embolism described as lobar or segmental was categorized as distal. Those described as "either segmental or subsegmental" were not categorized as subsegmental. Location was missing in 41 patients: it was unclear on CTPA in 6 patients; it was unavailable in 35 patients who were diagnosed by ventilation-perfusion scintigraphy
[#]We identified echocardiograms obtained at the time of or shortly following the diagnosis of pulmonary embolism

The clinic-only patients and their referred counterparts differed in several ways. Patients selected for comprehensive clinic–based care more commonly had a history of prior venous thromboembolism and less commonly reported dyspnea or hemoptysis. They more commonly had received diagnostic imaging during the daytime and were found to have more distal clots and less evidence of right ventricular strain or cardiomegaly on CTPA. After diagnostic confirmation, the primary care clinicians less commonly ordered echocardiography and more commonly consulted specialists (Tables 1 and 2).

We describe characteristics of diagnosing clinicians and report timing of diagnostic testing in the Supplement. We report the frequency and annual incidence of comprehensive clinic–based care in Supplementary Figures 1 and 2. We identified no change in annual frequency of comprehensive care across the study period. We describe the anticoagulation treatment of those managed as outpatients in Supplementary Table 2. Outpatients were followed closely by the pharmacy-led, telephone-based Anticoagulation Management Service (88.5% were contacted within 7 days of the index encounter) and by primary care (67.9% had a follow-up appointment within 7 days).

Primary and Secondary Outcomes

Eight patients (1.2%; 95% CI: 0.5–2.4%) experienced a 30-day serious adverse event (Table 3 and Supplementary Table 3). Seven of these occurred among patients initially hospitalized. Only 1 event, a venous thromboembolism recurrence, occurred among those sent home directly from primary care (0.75%; 95% CI 0.02–4.09%; 0.3% among the larger cohort of 330 managed as outpatients; 95% CI 0.01–1.7%). The 3 deaths occurred in patients with known metastatic cancer initially referred to the ED, hospitalized, then enrolled in hospice following discharge. There were no 30-day serious adverse events among the 196 patients discharged home from the ED. The small number of primary outcomes prevented detailed multivariable adjustment.

Table 3 Outcomes of Adults Diagnosed with Acute Pulmonary Embolism in Primary Care, Stratified by Clinicians' Initial Site-of-Care Decisions: Clinic Only Versus Referral to a Higher Level of Care

	Total cohort (n = 652)	Clinic only (n = 134)	Referral (n = 518)	
			Discharged from ED to home (n = 196)	Initially hospitalized[*] (n = 322)
Outcomes, n (col. %; 95% CI)				
7-d pulmonary embolism-related hospitalization[†]	328 (50.3; 46.4–54.2)	4 (3.0; 0.8–7.5)	2 (1.0; 0.1–3.6)	322 (100)
30-d adverse outcomes				
Venous thromboembolism recurrence	4 (0.6; 0.2–1.6)	1 (0.7; 0–4.1)	0 (0; 0–1.9)	3 (0.9; 0.2–2.7)
Major bleed	1 (0.2; 0–0.9)	0 (0; 0–2.7)	0 (0; 0–1.9)	1 (0.3; 0–1.7)
All-cause mortality	3 (0.5; 0.1–1.3)	0 (0; 0–2.7)	0 (0; 0–1.9)	3 (0.9; 0.2–2.7)
Sum	8 (1.2; 0.5–2.4)	1 (0.7; 0–4.1)	0 (0; 0–1.9)	7 (2.2; 0.9–4.4)

ED emergency department
[*]Seven of these 322 were directly hospitalized from primary care without ED evaluation
[†]Note that 6 had a delayed hospitalization after initial outpatient management. We define "pulmonary embolism-related" in the Supplement and describe the 6 patients and their clinical courses in Supplement Table 4

Table 4 Independent Association of Candidate Predictor Variables with 7-Day Pulmonary Embolism-Related Hospitalization

Candidate predictor variable	Adjusted odds ratio	95% CI
Demographics		
Age, years		
50–64 (vs < 50)	1.16	0.70–1.94
65–74 (vs < 50)	0.82	0.47–1.42
75 or older (vs < 50)	1.46	0.80–2.65
Male sex (vs female)	0.85	0.59–1.22
White, non-Hispanic race/ethnicity (vs other)	0.79	0.54–1.18
Comorbidities		
Body mass index ≥ 30 kg/m^2 (vs < 30)	1.10	0.76–1.58
Hypertension (vs none)	1.04	0.69–1.55
Active cancer (vs none)	2.03	1.01–4.06
Renal failure (vs none)	1.98	1.01–3.89
Heart failure (vs none)	1.92	0.71–5.23
Surgery < 90 d (vs none)	2.24	1.19–4.20
Symptoms		
Shortness of breath (vs none)	1.86	1.16–2.98
Chest pain (vs none)	1.22	0.83–1.80
Deep vein thrombosis symptoms (vs none)	1.59	1.04–2.44
Duration		
3 d–2 w (vs ≤ 2 d)	1.48	0.90–2.44
> 2 w (vs ≤ 2 d)	0.91	0.52–1.60
Unknown (vs ≤ 2 d)	0.44	0.15–1.23
Physical examination		
In-person index encounter vs other	1.00	0.55–1.83
Heart rate ≥ 110 beats/min (vs < 110)	3.54	1.64–7.64
Diagnostic imaging		
Time of imaging 1600 < 0800 (vs 0800 < 1600)	2.33	1.61–3.37
CTPA clot location proximal (vs distal)	2.93	2.01–4.27
CTPA clot location undocumented (vs distal)	1.03	0.48–2.23
Heart abnormal or not described on CTPA (vs normal)	1.48	1.02–2.13
Primary care consultation of pulmonologist or hematologist after diagnosis secured		
No (vs yes)	2.27	1.14–4.53

We included demographics in this multivariable regression model, as well as variables from the bivariate analysis with a p value < 0.10 (Supplement Table 5). We did not include pulse oximetry < 90% because all hypoxemic patients were hospitalized. We did not include echocardiography because the results did not precede site-of-care decision-making. Missing body mass index was assumed to be < 30 kg/m^2; missing heart rate (in patients without an in-person index encounter) was assumed to be < 110 beats/min

Overall, 328 patients (50.3%; 95% CI, 46.4–54.2) were hospitalized within 7 days: 322 (49.4%) initially and 6 (0.9%) in a delayed fashion, after initial outpatient management. Four delayed hospitalizations occurred in the 134 patients (3.0%) sent home from the clinic and 2 in the 196 patients (1.0%) discharged home from the ED. The 6 delayed hospitalizations were uncomplicated and without sequelae or 30-day serious adverse events (Supplementary Table 4).

We compare those without and those with a 7-day hospitalization in Supplementary Table 5. Characteristics independently associated with 7-day hospitalization include comorbidities, venous thromboembolic symptoms, heart rate ≥ 110 beats/min, CTPA undertaken after hours, and proximal clot and cardiac dilatation on CTPA interpretation (Table 4). Consults from primary care were inversely associated with hospitalization. All patients with pulse oximetry < 90% also were hospitalized. Our interrater reliability results were excellent (see Supplement).

DISCUSSION

This multicenter retrospective cohort study is the first, to our knowledge, to describe the management and outcomes of adults diagnosed with acute pulmonary embolism in primary care. These results suggest that community-based primary care clinicians can manage patients with acute pulmonary embolism safely and effectively. We did not exclude patients thought to have a short life expectancy, as some ED-based outpatient pulmonary embolism studies have done.[27–29] The 30-day incidence of serious adverse events we observed is similar to those of adults with acute pulmonary embolism selected for outpatient management by ambulatory medical units and EDs, whose care is often supplemented with monitoring in observational or inpatient units prior to discharge.[2, 30–32]

The infrequency of adverse outcomes may be attributable to a relatively low-risk population, as their limited health care resource use suggests. Nearly 50% were managed without hospitalization, a rate reported only from some Canadian EDs and thrombosis units,[33, 34] but far higher than many US EDs, where the outpatient rate is less than 10%.[35] An additional 18% of patients diagnosed with PE in primary care had a short observational stay (< 24 h) before being discharged home, something considered by many researchers to fall under the umbrella of "outpatient management."[10, 11] Patients diagnosed with acute pulmonary embolism in primary care are lower risk than those diagnosed in the ED of the very same health system: initial hospitalization was lower (49% versus

81%), as was initial ICU admission (0.6% vs 6.6%) and 30-day all-cause mortality (0.5% versus 4.7%).[2, 18, 36]

Why might patients diagnosed with pulmonary embolism in primary care be a particularly low-risk population? We think passing through 2 "triage turnstiles" selects for low-risk patients.[36] First, these patients themselves chose initially not to go to the ED, but to present to primary care or to contact the system's advice call center, which may have then directed them to primary care.[37] Second, their primary care clinicians deemed them suitable for an outpatient diagnostic evaluation.

There are other differences between the primary care and ED settings. Pulmonary embolism diagnoses were less common in the primary care setting, which diagnosed only 1 adult with acute pulmonary embolism for every 12 or so ED pulmonary embolism diagnoses in this health system.[2, 18, 36] The diagnosis of acute pulmonary embolism also took longer in the clinic setting compared with the ED.[38, 39] Still, the diagnostic process in primary care was relatively short for most patients: 75% within 44 h, not long given the varying number of sequential steps that the process may require.[5, 6, 40]

Another novel finding of the PEPC study is that 1 in 5 patients diagnosed with acute pulmonary embolism were managed comprehensively in primary care. Adults managed without transfer to the ED or hospital had a very low incidence of 7-day pulmonary embolism–related hospitalization. Thirty-day serious adverse events were also low. These reassuring results suggest that patient selection for comprehensive care was appropriate. There are no studies of primary care–based comprehensive PE management similar to ours with which to compare our findings.[10] But the 30-day adverse outcomes we observed compare favorably with those of adults managed as outpatients in specialty clinics and EDs.[11]

Our physicians did not document reliance on established triage tools, like risk-stratification instruments or clinical decision rules to inform site-of-care decision-making—even when such tools would have supported their decision. Lack of documentation does not mean lack of use but suggests triage tool use is not prevalent. It seems likely that unstructured clinical judgment was the operative paradigm. This approach is commonly used by non-primary care physicians in the management of patients with acute pulmonary embolism.[41, 42] Clinical judgment is endorsed by the American College of Chest Physicians in site-of-care decision-making, strongly recommending outpatient management for patients who meet the following common-sense low-risk criteria: "clinically stable with good cardiopulmonary reserve; no contraindications such as recent bleeding, severe renal or liver disease, or severe thrombocytopenia (i.e., <50,000/mm^3); expected to be compliant with treatment; and the patient feels well enough to be treated at home. Additionally, a system to assure outpatient follow-up and access to prompt care… should be in place."[4, 5, 22] Clinical judgment along these lines may be guiding patient selection for comprehensive primary care–based management.

We identified several factors associated with comprehensive PE care. Patients with prior venous thromboembolism were more commonly managed comprehensively, likely because they were more experienced with anticoagulation and issues of home care. Clinic-only care was also more common in those without dyspnea or hemoptysis, and those with more distal clots (particularly isolated subsegmental emboli)[43], as these categories of patients may have appeared lower risk and hence more suitable for outpatient care. Patients with diagnostic pulmonary imaging occurring before 4:00 p.m. would also be better candidates for home care as the physician would have more time that day to provide patient education and initiate anticoagulation. Patients diagnosed after hours might be more commonly referred to the ED for timely care.

Our study has several limitations. Case ascertainment may have been subject to selection bias, as study inclusion required intervention, either referral or anticoagulation. Patients with isolated subsegmental PE managed without anticoagulation, for example, would have been missed.[43–45] We also did not include patients treated for presumed pulmonary embolism who lacked confirmatory pulmonary imaging. Lead time bias was also possible because patients had to survive long enough to receive both diagnostic imaging and intervention. The study's retrospective study design entailed incomplete or imprecise documentation of unstructured variables, like duration of symptoms and risk factors. Structured variables, however, such as comorbidities, vital signs, sites of care, and study outcomes, are reliably captured in the system's comprehensive, integrated EHR. Our access to claims data ensured identification of out-of-system outcomes. The absence of similar studies precludes a comparison with other primary care settings. Our results may not be generalizable to other practices and geographic locations. Study patients, for example, were all insured health plan members with established primary care clinicians and access to secure messaging, online appointment booking, and around-the-clock advice services.[37, 46] Our integrated model of patient care may have also facilitated comprehensive care (Supplementary Table 6), with ready access to diagnostic imaging and a pharmacy-led telephone-based Anticoagulation Management Service to educate and monitor patients taking vitamin-K antagonists and direct oral anticoagulants.

In summary, this multicenter community-based retrospective cohort study describes the safety and effectiveness of management of adults diagnosed with acute pulmonary embolism in primary care, regardless of initial site-of-care decision-making. Approximately half of this population was initially managed without hospitalization—20% received comprehensive clinic-based care and another 30% were referred to the ED for evaluation then discharged home—with infrequent delayed 7-day hospitalization and rare 30-day adverse outcomes. Research from other health care settings will

help us better understand primary care pulmonary embolism management and its public health implications, including its potential to reduce health care costs and improve patient care experience.

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Conflict of Interest: *The authors declare that they do not have a conflict of interest.*

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