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Bilateral Emboli and Highest Heart Rate Predict Hospitalization of Emergency Department Patients With Acute, Low-Risk Pulmonary Embolism

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Abstract

Objective: Some patients with acute pulmonary embolism (PE) will suffer adverse clinical outcomes despite being low risk by clinical decision rules. Emergency department (ED) physician decision making processes regarding which low risk patients require hospitalization is unclear. Higher heart rate (HR) or embolic burden may increase short-term mortality risk and we hypothesized that these variables would be associated with an increased likelihood of hospitalization for patients designated as low risk by the PE Severity Index.

Methods: This was a retrospective cohort study of 461 adult ED patients with a PE Severity Index score <86 points. Primary exposures were highest observed ED HR, most proximal embolus location (proximal vs. distal) and embolism laterality (bilateral vs. unilateral PE). The primary outcome was hospitalization.

Results: Of 461 patients meeting inclusion criteria, most (57.5%) were hospitalized, 2 patients (0.4%) died within 30 days and 142 (30.8%) patients were at elevated risk by other criteria (Hestia criteria or biochemical/radiographic right ventricular dysfunction). Variables associated with the increased likelihood of admission were highest observed ED HR ≥110 beats per minute (vs HR<90 beats per minute) (odds ratio [OR] 3.11; 95% CI 1.07–9.57), highest ED HR 90–109 (OR 2.03; 95% CI 1.18–3.50) and bilateral PE (OR 1.92; 95% CI 1.13–3.27). Proximal embolus location was not associated with likelihood of hospitalization (OR 1.19; 95% CI 0.71–2.00).

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Conclusions: Most patients were hospitalized, often with recognizable high-risk characteristics not accounted for by the PE Severity Index. Highest ED HR≥90 and bilateral PE were associated with a physician's decision for hospitalization.

Introduction

Background

Clinical decision rules are commonly used to risk-stratify patients with acute pulmonary embolism when deciding upon site of care.[1] However, some patients with acute pulmonary embolism will suffer adverse clinical outcomes despite being designated as low risk by common PE clinical decision rules.[2–5] Factors that physicians use to decide which low-risk patients will nonetheless require hospitalization are unclear, although recent studies have identified several key predictors of adverse outcomes.[5–7]

The European Society of Cardiology (ESC) recommends an assessment for PE severity, comorbidities and contraindications to home treatment for patients being considered for outpatient management.[1] The PE Severity Index is a validated decision rule that stratifies patients according to risk and can be used to identify patients at low risk of 30-day mortality (PE Severity Index Classes I and II).[8] The Hestia criteria assess suitability for outpatient management based upon PE severity, medical comorbidities, and social factors.[1,9] The presence of any Hestia criteria indicates a contraindication to outpatient management and hospitalization is recommended. Although both are validated approaches to identify low-risk patients, both the PE Severity Index and Hestia criteria contain failure rates inherent to clinical decision rules (i.e., the PE Severity Index considers a 30-day mortality risk of 3.5% to be low risk). In addition, meta-analysis data suggests that right ventricular (RV) dysfunction demonstrated on echocardiography or biochemically through laboratory assessment is associated with higher all-cause and PE-related short-term mortality.[5,7] The prognostic role of RV dilatation on computed tomography (CT) angiography is much less clear, however, and several studies show no association between RV dilatation on CT angiography and adverse events or mortality.[5,10,11] The PE Severity Index does not include a RV dysfunction/dilatation variable and physicians may be more likely to hospitalize patients with these findings regardless of nuance in prognosis.

Site-of-care medical decision making for patients with acute PE is incompletely understood but is influenced by facility-, physician- and patient-level factors.[4] Patients in this study setting have access to prompt primary care follow up, anticoagulation pharmacotherapy and specialty consult which addresses several key facility-level barriers. Physician-level barriers have been previously addressed in the study setting through implementation of a clinical decision support system (CDSS) providing risk-based recommendations for site-of-care disposition decision making for ED patients with acute PE.[12,13] Lastly, patient-level factors prompting hospitalization of low-risk patients are incompletely understood although the literature has identified several characteristics that may portend worse clinical outcomes in this subset of patients.[5–7,9,14–17]

Heart rate (HR) is an important prognostic vital sign for patients with acute PE and an important component of several clinical decision rules predicting PE-likelihood, PE-related

mortality and PE-related clinical deterioration.[8,15,16,18] The PE Severity Index incorporates HR directly into its risk assessment employing an explicit criterion of ≥110 beats per minute while the Hestia criteria combines HR and blood pressure into its assessment of hemodynamic instability. A recent study demonstrated an association between increased HR on hospitalization of ED patients with acute PE and 30-day mortality over a large continuum of HRs (30–200 beats per minute).[6] HR is an important reflection of hemodynamic stability and may prompt more hospital admissions when abnormal, even in patients deemed to be low risk by clinical decision rules.

On the other hand, the prognostic value of radiographic embolic burden on mortality in acute PE is conflicting.[14,17,19–25] Embolic distribution (unilateral embolism versus bilateral emboli), most proximal embolism location, and degree of arterial obstruction all contribute to embolic burden. The CT Obstruction Index (CTOI) quantifies embolic burden by considering the number of segments affected (1–20) and their degree of obstruction (partial or complete).[24] Embolic burden information does not appear in any clinical PE risk stratification tool and it is unclear to what extent physicians incorporate this readily-available radiographic information into their site-of-care decision making.

Importance

A more thorough understanding of predictors of hospitalization and patient-level contributors to this decision may guide quality improvement initiatives for outpatient PE management, provide insight into site-of-care decision making in a real-world setting, and inform new inquiries into the prognostic significance of key patient-level variables.

Goals of this investigation

Our goal was to understand the characteristics of patients with acute, low-risk PE who were selected for outpatient management vs. hospitalization and the prognostic value of highest observed ED heart rate, most proximal embolism location and embolism distribution on the likelihood of a physician's decision to hospitalize a low-risk patient.

MATERIALS AND METHODS

This study was approved by the Kaiser Permanente Northern California (KPNC) Institutional Review Board with a waiver of informed consent. This manuscript adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.[26]

Study Design and Setting

We conducted a retrospective cohort study from January 2019 to February 2020 of all 21 community-based EDs of Kaiser Permanente Northern California, an integrated health system that serves over 4.5 million members representing the surrounding racial, ethnic, and socioeconomic diversity of California.[27] The 21 EDs are staffed by board-certified (or board-eligible) emergency physicians. Patients with acute PE usually receive their diagnosis in the ED while those diagnosed in the clinic setting are commonly referred to the ED for definitive care.[28] The system recommended direct oral anticoagulants (DOACs) for the

treatment of most patients with acute PE. Patients receive timely follow-up [29] and have access to oral anticoagulants with long-term monitoring by a pharmacy-led telephone-based Anticoagulation Management Service, which contacts patients for education shortly after ED discharge.[30–32]

All ED sites had access throughout the study period to a web-based, electronic health record (EHR)-embedded CDSS (named RISTRA-PE for "risk stratification of PE") following diagnostic confirmation. CDSS use is physician-driven and entirely voluntary. The CDSS provides an auto-populating version of the PE Severity Index with risk-based recommendations to inform site-of-care decision-making.[12] Outpatient exclusion criteria derived from the early Canadian criteria and the validated Hestia clinical decision rule are also provided.[9,33] The CDSS recommended consideration of hospitalization for patients with right ventricular (RV) dysfunction (RV strain on echocardiography or RV dilatation on CT angiography), however, troponin, B-type natriuretic peptide (BNP) and echocardiography were not mandated.[5] We implemented RISTRA-PE as a pragmatic trial called eSPEED over an 8-month period in 2015 as previously described.[13] Four years following the aforementioned interventions, a subsequent retrospective cohort study (SUS EFX) demonstrated the sustainability of the original eSPEED interventions in the outpatient management of low-risk PE: former intervention EDs continued to discharge home more patients with acute low-risk (PE Severity Index class I-II) PE compared to former control EDs.[34] However, approximately 60% of low-risk patients were still hospitalized. Our current study examines the subset of patients with acute low-risk PE (PE Severity Index classes I-II) in the SUS EFX cohort. We were unable to capture CDSS use in our study population. However, it was used for the minority of eligible patients (11.3% at former intervention EDs and 7.4% at former control EDs) as previously reported.[34]

Study Participants

This study included patients 18 years of age or older who had at least one eligible ED visit from 01/2019 through 02/2020 with an ED diagnosis of non-gravid PE (*International Classification of Disease, Tenth Edition* [ICD-10], codes: I26.02, I26.09, I26.92, I26.93, I26.94, I26.99, O88.23). Included patients also had an accompanying CT angiography or scintigraphy imaging study that was positive for PE either in the ED or within the prior 12 hours.[35] Patients with one of the following were excluded: a diagnosis of acute venous thromboembolism in the previous 90 days, taking anticoagulants at diagnosis (or an elevated ED international normalized ratio >2.0), lack of adequate health plan membership in the prior 12 months (as this affects completeness of medical history), leaving the ED against medical advice, absence of any documented ED vital signs (precluding calculation of the PE Severity Index) except for temperature, non-PE diagnosis requiring hospitalization and known pregnancy (Figure 1). Variables of the PE Severity Index were extracted from the EHR as previously described.[12]

Data Collection and Study Outcomes

We obtained hospital site, clinical and demographic variables directly from the health system's EHR using automated electronic data extraction. Two emergency physicians performed structured chart review for manually abstracted data. Abstractors were not

blinded to the study hypothesis and abstracted data using a standardized, piloted form. Five percent of charts were dually extracted for ascertainment of accuracy and interrater reliability was assessed for patient disposition, highest observed ED HR, presence of ≥1 Hestia criteria, and embolic burden. Missing data were excluded from the analysis.

We used the validated PE Severity Index to estimate 30-day all-cause mortality and identify low-risk patients (PE Severity Index score <86 points) as previously described.[12] Altered mental status was the only component of the PE Severity index that was not reliably available. For our analysis, we assumed it was negative, as other studies have done, including the original validation studies.[36,37] Missing patient temperature data was also presumed to be normal for the PE Severity Index calculation.

Measurements

We developed a data collection tool using pre-defined variable definitions to guide manual abstraction of patient data (Appendix 1). We collected other variables potentially associated with hospitalization including: age (in years), patient-reported sex, body mass index (BMI), race/ethnicity, hospital site (former intervention or former control site in our pragmatic trial), chronic lung disease, heart failure (systolic or diastolic), cancer, history of prior venous thromboembolism, dementia, active substance abuse, acute psychiatric crisis, hospitalization within 30 days, major surgery within 30 days, major hemorrhage within 30 days, ischemic or hemorrhagic stroke within 30 days, non-PE related diagnosis requiring admission, thrombophilia, hemiplegia, presence of an in-dwelling vascular catheter, arrival by ambulance, PE symptoms (shortness of breath, chest pain, cough, palpitations, deep vein thrombosis (DVT) symptoms, syncope or pre-syncope, hemoptysis, ED vital signs (lowest systolic blood pressure, highest observed heart rate, highest respiratory rate, lowest oxygen saturation, lowest temperature, diagnosis by CT angiography, diagnosis by scintigraphy imaging, diagnosis made in ED (versus <12h prior in the outpatient setting), presence of pulmonary infarct, RV strain on echocardiography, RV dilatation on CT angiography, most proximal embolism location, embolic distribution (bilateral vs. unilateral PE), presence of ≥1 Hestia criteria, troponin, B-type natriuretic peptide, hemoglobin, platelet count, glomerular filtration rate (GFR) and lack of fixed residence.

Outcomes

Our primary study outcome was hospitalization which was defined as admission to inpatient status from the ED. Thirteen EDs had a short-term (<24-hour) outpatient observation unit based in the ED that was managed by emergency physicians or adult medicine hospitalists. We considered admission to an outpatient observation unit as a hospitalization.

Analysis

We used multi-variate logistic regression analysis to examine the association between our predictor variables selected *a priori* (highest observed HR, most proximal embolism location and bilateral PE) and likelihood of hospitalization. Variables included in our model were previously demonstrated to be of prognostic significance in the literature and included: age, sex, comorbidities (chronic lung disease history, hospitalization within 30 days), clinical data (PE Severity Index Class II, arrival by ambulance), assignment as an intervention or

control site in our previous pragmatic trial, troponin elevation, radiographic data (proximal embolism location, bilateral PE, RV dilatation) and ED vital signs (highest ED respiratory rate, lowest ED oxygen saturation, highest observed ED HR). The number of cases during the study period determined the sample size. Statistical analyses were conducted using the software environment R (4.2.1) and the Epitools package (v0.5–10.1; Aragon, 2020).[38]

Results

After excluding 807 patients, we identified 461 eligible candidates from the SUS EFX study who met inclusion criteria (Figure 1). Manual chart review interrater reliability for key study variables (final disposition, presence of Hestia criteria, highest observed ED heart rate, embolus laterality and most proximal embolus location) was excellent with a Cohen's Kappa of 1.0.

Characteristics of study subjects

Characteristics of included patients (n=461) are shown in Table 1. Most patients in our study (n=265, 57.5%) were hospitalized and the remainder (n=196, 42.5%) managed as outpatients with a median ED length of stay of 5.8 hours (IQR=3.9–7.7). Of those who met low-risk criteria based on the PE Severity Index alone, 142 patients (30.8%) met ≥1 Hestia criteria or had biochemical/radiographic RV dysfunction (Figure 2). There were 2 deaths (0.4%) observed in the study which were both among admitted patients belonging to a PE Severity Index class II (Appendix 2). Both patients were admitted for their acute PE with 1 patient expiring during catheter-directed thrombolysis and another expiring from unknown causes nearly one month following hospital discharge.

Unadjusted analysis of our main variables of interest demonstrated that HR≥110 beats per minute as well as HR 90–109 beats per minute were associated with likelihood of admission (unadjusted OR 2.12; [95% CI 1.21–3.87] and OR 2.06; [95% CI 1.42–3.02]), compared to HR<90 beats per minute. The presence of bilateral PE (versus unilateral PE) was also associated with likelihood for hospitalization (unadjusted OR 2.64; [95% CI 1.79–3.89]). Proximal embolism location (versus distal) was associated with an unadjusted likelihood of hospitalization (unadjusted OR 1.86; 95% CI, 1.27–2.72). Comparing unadjusted data, 72% and 67% of patients with HR≥110 beats per minute and HR 90–109, respectively, were hospitalized compared to 41% of patients with HR<90. Also, 67% of patients with bilateral PE were hospitalized compared with 43% of patients with unilateral PE.

Main results

Multivariate analysis (Table 2) demonstrated that HR≥110 beats per minute as well as HR 90–109 beats per minute were independently associated with likelihood of admission (OR 3.11; [95% CI 1.07–9.57] and OR 2.03; [95% CI 1.18–3.50]), respectively] compared to HR<90 beats per minute. The presence of bilateral PE (versus unilateral PE) was independently associated with likelihood for hospitalization (OR 1.92; [95% CI 1.13–3.27]). Proximal embolism location (versus distal) was not independently associated with likelihood of hospitalization (OR 1.19; 95% CI, 0.71–2.00).

Limitations

We described the clinical context available for ED physicians when deciding to hospitalize a patient with an acute, low-risk PE within one healthcare setting. Our study setting included a population that had access to prompt primary care follow up, anticoagulation pharmacotherapy and specialty consultation and our results may not be generalizable to other settings. While we used strategies to minimize bias, our study is subject to limitations inherent in retrospective studies.[39] Given our observational study design, we cannot infer a causal relationship between variables and our outcome of interest and there may have been potential confounders not accounted for in our multivariate analysis. Our abstractors were unblinded to the study's hypothesis. Additionally, we did not use a standardized definition for RV dilatation on CT interpretations. RV dilatation was interpreted to be present if it was reported on by the interpreting radiologist but specific RV:LV ratios were rarely reported. The study period also occurred before the SARS-CoV-2 pandemic. Given the high rate of thromboembolic complications in patients with COVID-19, it is unclear if concurrent COVID-19 disease affects site-of-care decision making in patients with acute, low-risk PE.[40,41]

Discussion

Most patients in our study were hospitalized despite being classified as low risk by a validated risk-stratification tool and members of a health system well-resourced to accomplish outpatient management. We found that a substantial fraction of patients who were low risk by the PE Severity Index (class I or II; <86 points) had clinical, laboratory or radiographic findings that might place them at increased risk of adverse clinical events. Additionally, we found that tachycardia and bilateral PE was independently associated with likelihood of hospital admission.

Approximately 30% of patients in our low-risk cohort met ≥1 Hestia criteria or had biochemical/radiographic indicators of RV dysfunction (elevated BNP/troponin, RV dilatation or strain). Patients who met ≥1 Hestia criteria in our study had at least one contraindication to outpatient management and it is not surprising that the majority were hospitalized, in accordance with expert consensus statements.[7,42] A recent study demonstrated that over half of patients who were hospitalized for low-risk PE met ≥1 Hestia criteria.[43]

The hospitalization of low-risk patients who had biochemical and/or radiographic RV dysfunction observed in our study represents a more conservative approach to acute PE management than using PE Severity Index alone.[5,44–46] Prosperi-Porta and colleagues' recent meta-analysis of over 17,000 patients with acute PE found echocardiographic RV dysfunction to be associated with increased risk of mortality (PE-related and all-cause) and adverse events.[7] An individual patient-level meta-analysis by Becattini found an increased risk of short-term mortality for patients with biochemical/echocardiographic RV dysfunction or elevated troponin.[5,47,48] Interestingly, however, RV dilatation on CT angiography was not associated with all-cause or PE-related mortality in this study and the prognostic value of this finding is unclear.[1,5,49] Our results suggest that physicians perceive patients with RV dilatation on CT angiography to be at higher risk.

The percentage of patients in our study population chosen for outpatient management was higher than similar studies of outpatient low-risk PE management likely reflecting sustained effects of our pragmatic trial of CDSS implementation.[13,34,50,51] Notably, while most studies of outpatient PE management allowed for extended periods of observation prior to final disposition decision, physicians in our study achieved a median time to final disposition of <6 hours using an unstructured triage strategy for site-of-care decision making.[9,51–58]

Tachycardia at any time during the ED stay was independently associated with likelihood of admission. Tachycardia has been established as an independent risk factor for adverse clinical outcome for patients with acute PE and is included in many rules for PE prediction (Geneva score, Wells' criteria), PE exclusion (pulmonary embolism rule-out criteria), PE risk stratification (PE Severity Index, Bova score, PE short-term clinical outcomes risk estimation) and suitability for outpatient management (Hestia).[6,16,59–61] Our results suggest that physicians may assign incrementally increasing amounts of risk with increasing HRs rather than adhering to a strict binary cut-off such as the ≥110 beats per minute criterion used in the PE Severity Index calculation. A recent study of patients included in the Registro Informatizado de la Enfermedad TromboEmbólica (RIETE) registry may support this practice. In this study, Jaureguízar demonstrated increased PE-related and all-cause mortality with increasing HRs over a wide spectrum of HRs for patients with acute PE.[6] Abnormal respiratory rate and oxygen saturation, both which are components of the PE Severity Index, were also associated with increased likelihood of hospital admission although the thresholds used in our study (respiratory rate >24 breaths per minute, oxygen saturation <95%) were more conservative than those used in the PE Severity Index score (respiratory rate ≥30 breaths per minute, oxygen saturation <90%). Our results suggest that suggest that physicians perceive patients with these vital sign abnormalities to be higher risk although they may not meet PE Severity Index score thresholds.

After adjustment for patient demographic and clinical characteristics, the presence of bilateral PEs was statistically significantly associated with hospitalization and proximal embolism location was not. Numerous reports in the radiology literature have identified an increased CT Obstruction Index (CTOI) to be a predictor of PE-related mortality and adverse clinical outcomes.[17,19–24] The CTOI is calculated based upon the number of lung segments affected by PE as well as their degree of obstruction. Although radiologists in our health system do not report CTOI, it is plausible that physicians perceive bilateral emboli to be higher risk than a unilateral embolism. The actual risk of bilateral PE, however, is unclear although one small study found an unadjusted higher prevalence of echocardiographic RV dysfunction in patients with acute bilateral PE compared to patients with unilateral PE (64% vs. 16%).[62] It is unclear why proximal embolism location did not predict hospital admission in our study given that this variable would also contribute to the CTOI. Embolism location's prognostic significance is unclear in the literature as most studies of outpatient PE management do not report embolism location. Our finding that proximal embolic location does not predict hospitalization conflicts with a recent study which found the opposite; however, this study included all PE Severity Index risk classes.[63]

Our results raise the possibility that highest observed ED HR and bilateral PE are being used by physicians to guide site-of-care decision making. With increasing literature support

for outpatient management of suitable patients, our work provides insight into clinician decision-making in low-risk patients including factors outside of traditional PE severity risk scores that may be driving site-of-care decision making. Thus, initiatives aimed at increasing outpatient management of patients with low-risk PE should be aware that physicians may attribute increased perceived risk to patients with higher HRs and bilateral PE.

In summary, more than half of patients with acute, low-risk PE were admitted during the study period in a health system well-resourced to facilitate outpatient management. A substantial fraction of these patients had clinical, laboratory or radiographic findings associated with adverse clinical outcomes and hospitalization was likely justified. Physicians may perceive patients with higher HRs and bilateral PE to be at elevated risk during disposition decision making.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. Jan 21 2020;41(4):543–603. doi:10.1093/eurheartj/ehz405 [PubMed: 31504429]
2. Singer AJ, Thode HC Jr., Peacock WFt. Admission rates for emergency department patients with venous thromboembolism and estimation of the proportion of low risk pulmonary embolism patients: a US perspective. Clin Exp Emerg Med. Sep 2016;3(3):126–131. doi:10.15441/ceem.15.096 [PubMed: 27752630]
3. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest. Feb 2016;149(2):315–52. doi:10.1016/j.chest.2015.11.026 [PubMed: 26867832]
4. Westafer LM, Shieh MS, Pekow PS, Stefan MS, Lindenauer PK. Outpatient Management of Patients Following Diagnosis of Acute Pulmonary Embolism. Acad Emerg Med. Mar 2021;28(3):336–345. doi:10.1111/acem.14181
5. Becattini C, Maraziti G, Vinson DR, et al. Right ventricle assessment in patients with pulmonary embolism at low risk for death based on clinical models: an individual patient data meta-analysis. Eur Heart J. Aug 31 2021;42(33):3190–3199. doi:10.1093/eurheartj/ehab329 [PubMed: 34179965]
6. Jaureguízar A, Jiménez D, Bikdeli B, et al. Heart Rate and Mortality in Patients With Acute Symptomatic Pulmonary Embolism. Chest. Feb 2022;161(2):524–534. doi:10.1016/j.chest.2021.08.059 [PubMed: 34478718]
7. Prosperi-Porta G, Ronksley P, Kiamanesh O, Solverson K, Motazedian P, Weatherald J. Prognostic value of echocardiography-derived right ventricular dysfunction in haemodynamically stable pulmonary embolism: a systematic review and meta-analysis. Eur Respir Rev. Dec 31 2022;31(166)doi:10.1183/16000617.0120-2022

8. Aujesky D, Obrosky DS, Stone RA, et al. Derivation and validation of a prognostic model for pulmonary embolism. Am J Respir Crit Care Med. Oct 15 2005;172(8):1041–6. doi:10.1164/rccm.200506-862OC [PubMed: 16020800]
9. Zondag W, Mos IC, Creemers-Schild D, et al. Outpatient treatment in patients with acute pulmonary embolism: the Hestia Study. J Thromb Haemost. Aug 2011;9(8):1500–7. doi:10.1111/j.1538-7836.2011.04388.x [PubMed: 21645235]
10. Hendriks SV, Klok FA, den Exter PL, et al. Right Ventricle-to-Left Ventricle Diameter Ratio Measurement Seems to Have No Role in Low-Risk Patients with Pulmonary Embolism Treated at Home Triaged by Hestia Criteria. Am J Respir Crit Care Med. Jul 1 2020;202(1):138–141. doi:10.1164/rccm.202002-0267LE [PubMed: 32203673]
11. Côté B, Jiménez D, Planquette B, et al. Prognostic value of right ventricular dilatation in patients with low-risk pulmonary embolism. European Respiratory Journal. 2017;50(6)
12. Vinson DR, Morley JE, Huang J, et al. The accuracy of an electronic Pulmonary Embolism Severity Index auto-populated from the electronic health record: setting the stage for computerized clinical decision support. Appl Clin Inform. 2015;66(2):318–333.
13. Vinson DR, Mark DG, Chettipally UK, et al. Increasing safe outpatient management of emergency department patients with pulmonary embolism: a controlled pragmatic trial. Ann Intern Med. Dec 18 2018;169(12):855–865. doi:10.7326/M18-1206 [PubMed: 30422263]
14. Gouin B, Blondon M, Jimenez D, et al. Clinical Prognosis of Nonmassive Central and Noncentral Pulmonary Embolism: A Registry-Based Cohort Study. Chest. Apr 2017;151(4):829–837. doi:10.1016/j.chest.2016.10.056 [PubMed: 27876590]
15. Jiménez D, Aujesky D, Moores L, et al. Simplification of the Pulmonary Embolism Severity Index for Prognostication in Patients With Acute Symptomatic Pulmonary Embolism. Archives of Internal Medicine. 2010;170(15):1383–1389. doi:10.1001/archinternmed.2010.199 [PubMed: 20696966]
16. Bova C, Sanchez O, Prandoni P, et al. Identification of intermediate-risk patients with acute symptomatic pulmonary embolism. Eur Respir J. Sep 2014;44(3):694–703. doi:10.1183/09031936.00006114 [PubMed: 24696111]
17. Meinel FG, Nance JW Jr., Schoepf UJ, et al. Predictive Value of Computed Tomography in Acute Pulmonary Embolism: Systematic Review and Meta-analysis. Am J Med. Jul 2015;128(7):747–59.e2. doi:10.1016/j.amjmed.2015.01.023 [PubMed: 25680885]
18. Keller K, Beule J, Coldewey M, Dippold W, Balzer JO. Heart rate in pulmonary embolism. Intern Emerg Med. Sep 2015;10(6):663–9. doi:10.1007/s11739-015-1198-4
19. Wu AS, Pezzullo JA, Cronan JJ, Hou DD, Mayo-Smith WW. CT Pulmonary Angiography: Quantification of Pulmonary Embolus as a Predictor of Patient Outcome—Initial Experience. Radiology. 2004;230(3):831–835. doi:10.1148/radiol.2303030083 [PubMed: 14739314]
20. van der Meer RW, Pattynama PMT, van Strijen MJL, et al. Right Ventricular Dysfunction and Pulmonary Obstruction Index at Helical CT: Prediction of Clinical Outcome during 3-month Follow-up in Patients with Acute Pulmonary Embolism. Radiology. 2005;235(3):798–803. doi:10.1148/radiol.2353040593 [PubMed: 15845793]
21. Zantonelli G, Cozzi D, Bindi A, et al. Acute Pulmonary Embolism: Prognostic Role of Computed Tomography Pulmonary Angiography (CTPA). Tomography. Feb 14 2022;8(1):529–539. doi:10.3390/tomography8010042 [PubMed: 35202207]
22. Praveen Kumar BS, Rajasekhar D, Vanajakshamma V. Study of clinical, radiological and echocardiographic features and correlation of Qanadli CT index with RV dysfunction and outcomes in pulmonary embolism. Indian Heart J. Nov-Dec 2014;66(6):629–34. doi:10.1016/j.ihj.2014.10.405 [PubMed: 25634397]
23. Chaosuwannakit N, Makarawate P. Prognostic value of right ventricular dysfunction and pulmonary obstruction index by computed tomographic pulmonary angiography in patients with acute pulmonary embolism. Journal of the Medical Association of Thailand. 2012;95(11):1457. [PubMed: 23252213]
24. Qanadli SD, El Hajjam M, Vieillard-Baron A, et al. New CT index to quantify arterial obstruction in pulmonary embolism: comparison with angiographic index and echocardiography. AJR Am J Roentgenol. Jun 2001;176(6):1415–20. doi:10.2214/ajr.176.6.1761415 [PubMed: 11373204]

25. Vedovati MC, Germini F, Agnelli G, Becattini C. Prognostic role of embolic burden assessed at computed tomography angiography in patients with acute pulmonary embolism: systematic review and meta-analysis. J Thromb Haemost. Dec 2013;11(12):2092–102. doi:10.1111/jth.12429 [PubMed: 24134450]

26. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. PLoS Med. Oct 16 2007;4(10):e297. doi:10.1371/journal.pmed.0040297 [PubMed: 17941715]

27. Gordon N, Lin T. The Kaiser Permanente Northern California Adult Member Health Survey. The Permanente journal. Fall 2016;20(4):34–42. doi:10.7812/tpp/15-225

28. Vinson DR, Hofmann ER, Johnson EJ, et al. Management and Outcomes of Adults Diagnosed with Acute Pulmonary Embolism in Primary Care: Community-Based Retrospective Cohort Study. Journal of general internal medicine. Jan 12 2022;doi:10.1007/s11606-021-07289-0

29. Vinson DR, Ballard DW, Huang J, et al. Timing of discharge follow-up for acute pulmonary embolism: retrospective cohort study. The western journal of emergency medicine. Jan 2015;16(1):55–61. doi:10.5811/westjem.2014.12.23310 [PubMed: 25671009]

30. An J, Niu F, Zheng C, et al. Warfarin Management and Outcomes in Patients with Nonvalvular Atrial Fibrillation Within an Integrated Health Care System. J Manag Care Spec Pharm. Jun 2017;23(6):700–712. doi:10.18553/jmcp.2017.23.6.700 [PubMed: 28530526]

31. Sylvester KW, Ting C, Lewin A, et al. Expanding anticoagulation management services to include direct oral anticoagulants. J Thromb Thrombolysis. Feb 2018;45(2):274–280. doi:10.1007/s11239-017-1602-1 [PubMed: 29274044]

32. Clark NP. Role of the anticoagulant monitoring service in 2018: beyond warfarin. Hematology American Society of Hematology Education Program. Nov 30 2018;2018(1):348–352. doi:10.1182/asheducation-2018.1.348 [PubMed: 30504331]

33. Erkens PMG, Gandara E, P. W, et al. Safety of outpatient treatment in acute pulmonary embolism. Journal of Thrombosis and Haemostasis. 2010;8(11):2412–2417. doi:10.1111/j.1538-7836.2010.04041.x [PubMed: 20735722]

34. Vinson DR, Casey SD, Vuong PL, Huang J, Ballard DW, Reed ME. Sustainability of a Clinical Decision Support Intervention for Outpatient Care for Emergency Department Patients With Acute Pulmonary Embolism. JAMA Netw Open. May 2 2022;5(5):e2212340. doi:10.1001/jamanetworkopen.2022.12340

35. Vinson DR, Ballard DW, Mark DG, et al. Risk stratifying emergency department patients with acute pulmonary embolism: Does the simplified Pulmonary Embolism Severity Index perform as well as the original? Thromb Res. Sep 24 2016;148:1–8. doi:10.1016/j.thromres.2016.09.023

36. Aujesky D, Roy PM, Le Manach CP, et al. Validation of a model to predict adverse outcomes in patients with pulmonary embolism. European heart journal. Feb 2006;27(4):476–81. doi:10.1093/eurheartj/ehi588 [PubMed: 16207738]

37. Aujesky D, Perrier A, Roy PM, et al. Validation of a clinical prognostic model to identify low-risk patients with pulmonary embolism. Journal of internal medicine. Jun 2007;261(6):597–604. doi:10.1111/j.1365-2796.2007.01785.x [PubMed: 17547715]

38. R: A language and environment for statistical computing. R Foundation for Statistical Computing. Accessed 10/1/2022.

39. Kaji AH, Schriger D, Green S. Looking through the retrospectoscope: reducing bias in emergency medicine chart review studies. Ann Emerg Med. Sep 2014;64(3):292–8. doi:10.1016/j.annemergmed.2014.03.025 [PubMed: 24746846]

40. Shi L, Xu J, Duan G, Yang H, Wang Y. The pooled prevalence of pulmonary embolism in patients with COVID-19. Intensive Care Med. Nov 2020;46(11):2089–2091. doi:10.1007/s00134-020-06235-8 [PubMed: 32929580]

41. Kunutsor SK, Laukkanen JA. Incidence of venous and arterial thromboembolic complications in COVID-19: A systematic review and meta-analysis. Thromb Res. Dec 2020;196:27–30. doi:10.1016/j.thromres.2020.08.022 [PubMed: 32823173]

42. Kabrhel C, Vinson DR, Mitchell AM, et al. A clinical decision framework to guide the outpatient treatment of emergency department patients diagnosed with acute pulmonary embolism or deep

vein thrombosis: Results from a multidisciplinary consensus panel. J Am Coll Emerg Physicians Open. Dec 2021;2(6):e12588. doi:10.1002/emp2.12588 [PubMed: 34950930]

43. Brikho S, Zughaib MT, Tsaloff G, Smythe K, Zughaib ME. Evaluating the Appropriateness of Pulmonary Embolism Admissions in a Community Hospital Emergency Department. Cureus. Apr 2022;14(4):e24292. doi:10.7759/cureus.24292 [PubMed: 35602808]
44. Furlan A, Aghayev A, Chang CC, et al. Short-term mortality in acute pulmonary embolism: clot burden and signs of right heart dysfunction at CT pulmonary angiography. Radiology. Oct 2012;265(1):283–93. doi:10.1148/radiol.12110802 [PubMed: 22993221]
45. Becattini C, Agnelli G, Vedovati MC, et al. Multidetector computed tomography for acute pulmonary embolism: diagnosis and risk stratification in a single test. Eur Heart J. Jul 2011;32(13):1657–63. doi:10.1093/eurheartj/ehr108 [PubMed: 21504936]
46. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. Jan 21 2020;41(4):543–603. doi:10.1093/eurheartj/ehz405 [PubMed: 31504429]
47. Barco S, Mahmoudpour SH, Planquette B, Sanchez O, Konstantinides SV, Meyer G. Prognostic value of right ventricular dysfunction or elevated cardiac biomarkers in patients with low-risk pulmonary embolism: a systematic review and meta-analysis. Eur Heart J. Mar 14 2019;40(11):902–910. doi:10.1093/eurheartj/ehy873 [PubMed: 30590531]
48. Becattini C, Agnelli G, Lankeit M, et al. Acute pulmonary embolism: mortality prediction by the 2014 European Society of Cardiology risk stratification model. Eur Respir J. Sep 2016;48(3):780–6. doi:10.1183/13993003.00024-2016 [PubMed: 27174887]
49. Hendriks SV, Klok FA, Exter PLd, et al. Right Ventricle–to–Left Ventricle Diameter Ratio Measurement Seems to Have No Role in Low-Risk Patients with Pulmonary Embolism Treated at Home Triaged by Hestia Criteria. American Journal of Respiratory and Critical Care Medicine. 2020;202(1):138–141. doi:10.1164/rccm.202002-0267LE [PubMed: 32203673]
50. Kabrhel C, Rosovsky R, Baugh C, et al. Multicenter Implementation of a Novel Management Protocol Increases the Outpatient Treatment of Pulmonary Embolism and Deep Vein Thrombosis. Acad Emerg Med. Jun 2019;26(6):657–669. doi:10.1111/acem.13640 [PubMed: 30341928]
51. Beer JH, Burger M, Gretener S, Bernard-Bagattini S, Bounameaux H. Outpatient treatment of pulmonary embolism is feasible and safe in a substantial proportion of patients. J Thromb Haemost. Jan 2003;1(1):186–7. doi:10.1046/j.1538-7836.2003.00005.x [PubMed: 12871557]
52. Vinson DR, Zehtabchi S, Yealy DM. Can selected patients with newly diagnosed pulmonary embolism be safely treated without hospitalization? A systematic review. Ann Emerg Med. Nov 2012;60(5):651–662 e4. doi:10.1016/j.annemergmed.2012.05.041 [PubMed: 22944455]
53. Kovacs M, Anderson D, Morrow B, Gray L, Touchie D, Wells P. Outpatient treatment of pulmonary embolism with dalteparin. Thrombosis and haemostasis. 2000;83(02):209–211. [PubMed: 10739374]
54. Wells PS, Anderson DR, Rodger MA, et al. A randomized trial comparing 2 low-molecular-weight heparins for the outpatient treatment of deep vein thrombosis and pulmonary embolism. Archives of internal medicine. 2005;165(7):733–738. [PubMed: 15824291]
55. Siragusa S, Arcara C, Malato A, et al. Home therapy for deep vein thrombosis and pulmonary embolism in cancer patients. Annals of Oncology. 2005;16:iv136–iv139. [PubMed: 15923414]
56. Rodríguez-Cerrillo M, Alvarez-Arcaya A, Fernández-Díaz E, Fernández-Cruz A. A prospective study of the management of non-massive pulmonary embolism in the home. European Journal of Internal Medicine. 2009;20(6):598–600. [PubMed: 19782920]
57. Agterof M, Schutgens RE, Snijder R, et al. Out of hospital treatment of acute pulmonary embolism in patients with a low NT-proBNP level. Journal of Thrombosis and Haemostasis. 2010;8(6):1235–1241. [PubMed: 20230418]
58. Aujesky D, Roy P-M, Verschuren F, et al. Outpatient versus inpatient treatment for patients with acute pulmonary embolism: an international, open-label, randomised, non-inferiority trial. The Lancet. 2011;378(9785):41–48.

59. Weekes AJ, Raper JD, Lupez K, et al. Development and validation of a prognostic tool: Pulmonary embolism short-term clinical outcomes risk estimation (PE-SCORE). PLoS One. 2021;16(11):e0260036. doi:10.1371/journal.pone.0260036 [PubMed: 34793539]

60. Gok G, Karadag M, Cinar T, Nurkalem Z, Duman D. In-hospital and short-term predictors of mortality in patients with intermediate-high risk pulmonary embolism. J Cardiovasc Thorac Res. 2020;12(4):321–327. doi:10.34172/jcvtr.2020.51 [PubMed: 33510882]

61. Gao Y, Ji C, Zhao H, Han J, Shen H, Jia D. Developing a scoring tool to estimate the risk of deterioration for normotensive patients with acute pulmonary embolism on admission. Respir Res. Jan 6 2021;22(1):9. doi:10.1186/s12931-020-01602-x [PubMed: 33407492]

62. Sukhija R, Aronow WS, Yalamanchili K, et al. Association of right ventricular dilatation with bilateral pulmonary embolism, pulmonary embolism in a main pulmonary artery and lobar, segmental and subsegmental pulmonary embolism in 190 patients with acute pulmonary embolism. Cardiology. 2005;103(3):156–157. [PubMed: 15785020]

63. Vinson DR, Ballard DW, Huang J, et al. Outpatient Management of Emergency Department Patients With Acute Pulmonary Embolism: Variation, Patient Characteristics, and Outcomes. Ann Emerg Med. Jul 2018;72(1):62–72.e3. doi:10.1016/j.annemergmed.2017.10.022 [PubMed: 29248335]

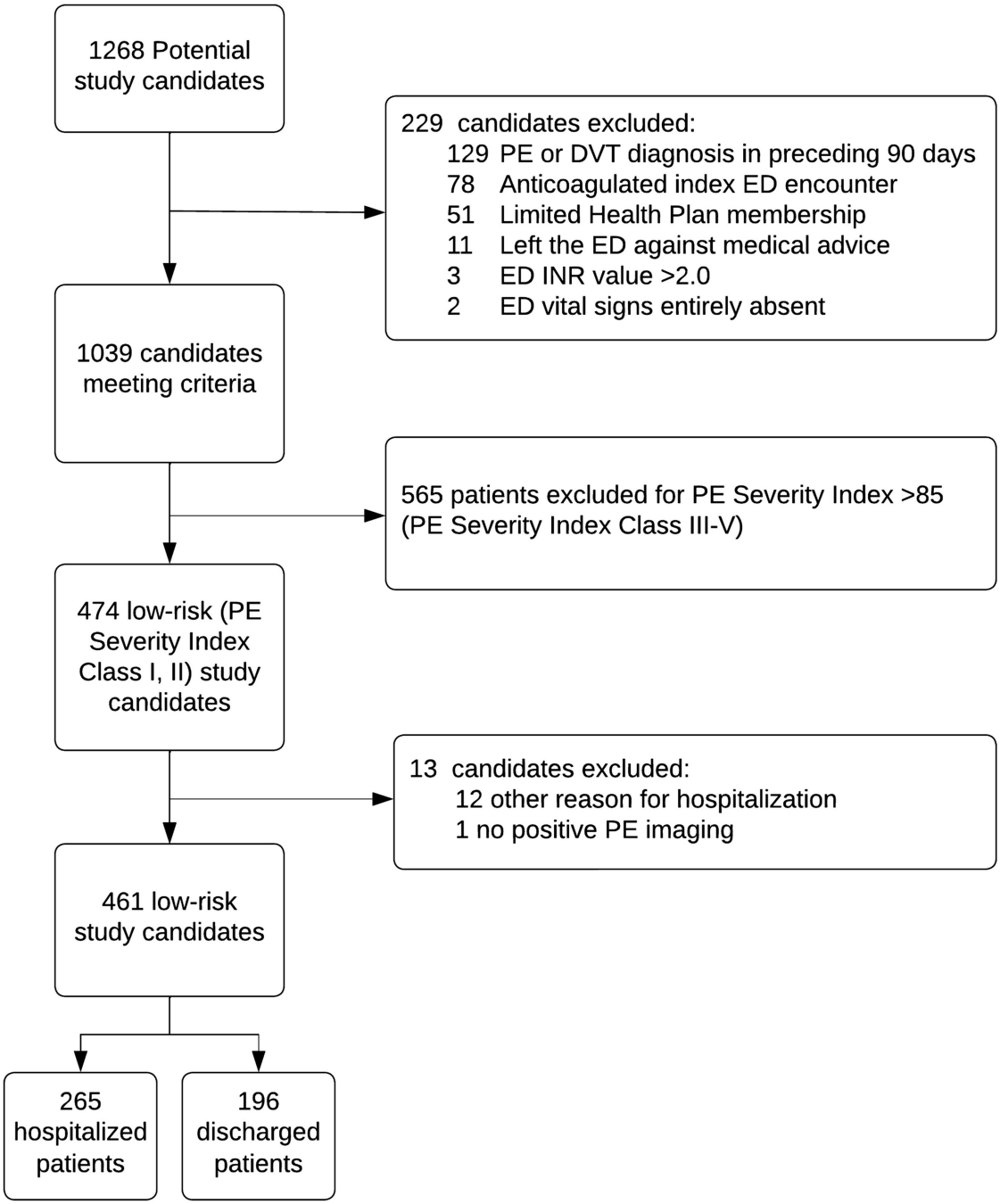

Figure 1.
Low-risk PE cohort assembly. DVT, deep venous thrombosis; INR, International normalized ratio.

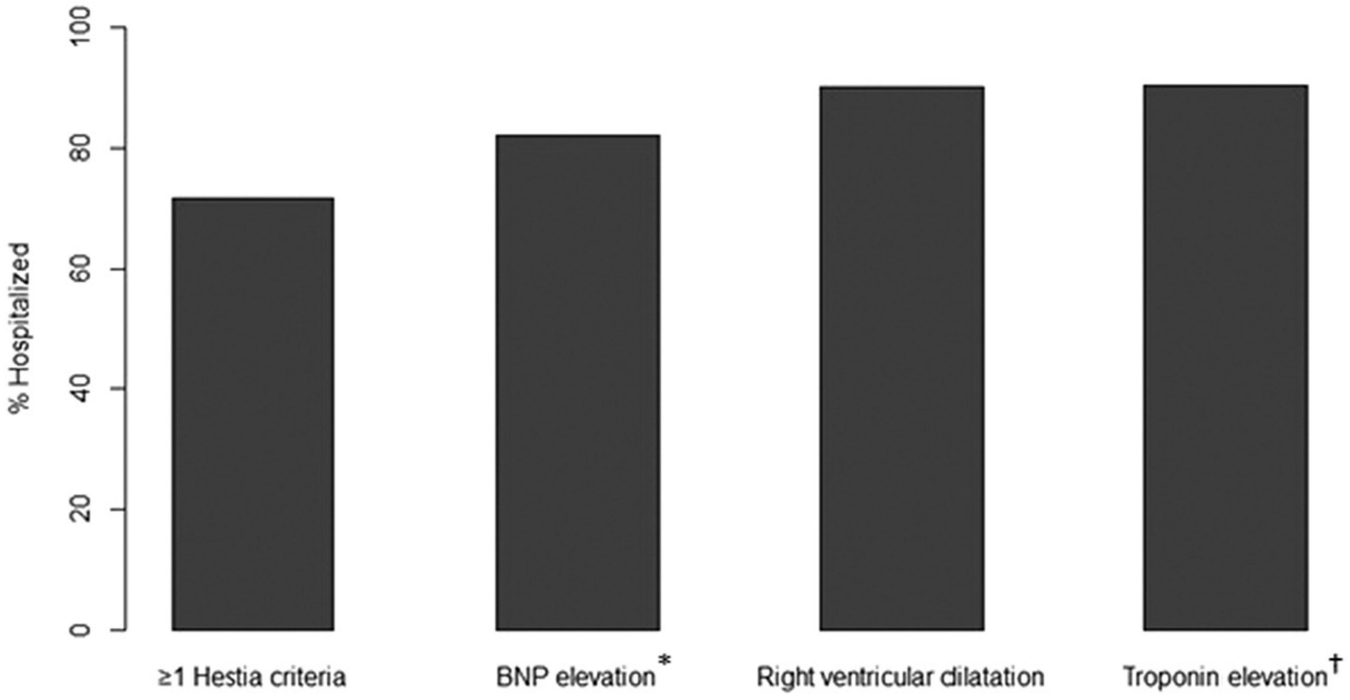

Figure 2.

Other high-risk criteria and the percentage of patients meeting these criteria who were hospitalized. Overall n=142. BNP, B-type natriuretic peptide. * 100 ng/L. † 0.04 ng/L.

Table 1.

Characteristics of Emergency Department Patients With Acute Low-Risk, Pulmonary Embolism, Stratified by Initial Site of Care.

	Hospitalized (n=265; 57.5%) n (%)	Outpatient (n=196; 42.5%) n (%)
Patient characteristics		
Age (years), median (IQR)	56 (44.5–67.5)	53 (41.5–64.5)
Female	140 (52.8%)	120 (61.2%)
Male	125 (47.2%)	76 (38.8%)
BMI (kg/m^2), median	31.5	31.1
Race/ethnicity, self-reported *		
African American	49 (18.5)	35 (17.9)
Asian	21 (7.9)	11 (5.6)
Hispanic or Latinx	39 (14.7)	24 (12.2)
White	152 (57.4)	125 (63.8)
Other	4 (1.5)	1 (0.5)
Hospital site †		
Former intervention site	115 (43.4)	113 (57.7)
Former control site	150 (56.6)	83 (42.3)
Comorbidities		
Chronic lung disease	34 (12.8)	37 (18.9)
Heart failure (systolic or diastolic)	3 (1.1)	3 (1.5)
Cancer (active only)	1 (0.4)	9 (4.6)
History of venous thromboembolism	46 (17.4)	57 (29.1)
Dementia	0	6 (3.1)
Active substance abuse‡	--	--
Acute psychiatric crisis‡	--	--
Hospitalization within 30 days	39 (14.7)	24 (12.2)
Major surgery within 30 days	28 (10.6)	17 (8.7)
Major hemorrhage within 30 days	5 (1.2)	1 (0.5)
Ischemic stroke within 30 days	1 (0.4)	2 (1.0)
Thrombophilia	14 (5.3)	12 (6.1)
Bed-bound or hemiplegia	3 (1.1)	2 (1.0)
In-dwelling vascular catheter	2 (0.7)	0
Arrival by ambulance	35 (13.2)	11 (5.6)
PE Symptoms		
Shortness of breath	213 (80.4)	127 (64.8)
Chest pain	158 (59.6)	126 (64.3)

	Hospitalized (n=265; 57.5%) n (%)	Outpatient (n=196; 42.5%) n (%)
Cough	57 (21.5)	26 (13.3)
Palpitations	17 (6.1)	7 (3.6)
Deep vein thrombosis symptoms	79 (29.8)	48 (24.5)
Syncope/presyncope	21 (7.9)	3 (1.5)
Hemoptysis	7 (2.6)	7 (3.6)
ED vital signs		
Systolic blood pressure (mmHg)		
≥110	196 (74.0)	166 (84.7)
<110	69 (26.0)	30 (15.3)
Heart rate (beats/minute)		
≥110	47 (17.7)	18 (9.2)
≥90 and <110	146 (55.1)	73 (37.2)
<90	72 (27.2)	105 (53.6)
Respiratory rate (breaths/min)		
≥24	101 (38.1)	25 (26.0)
≥20 and <24	106 (40.0)	77 (39.3)
<20	58 (21.9)	94 (48.0)
Pulse oximetry, % [§]		
≥95	122 (46.0)	156 (79.6)
<95	143 (54.0)	40 (24.5)
Temperature (°C)		
Temperature <36.5	43 (16.2)	31 (15.8)
Temperature ≥36.5	215 (81.1)	163 (83.2)
Temperature not recorded	7 (2.5)	2 (1.0)
Diagnostic imaging		
Diagnosed by scintigraphy	3 (1.5)	1 (0.5)
Diagnosed by CT in ED	244 (92.1)	162 (82.7)
Pre-arrival imaging study (<12h)	21 (7.9)	34 (17.3)
Embolism location on CT		
Proximal	176 (66.4)	101 (51.5)
Distal	89 (33.6)	95 (48.5)
Pulmonary infarct	48 (18.1)	20 (10.2)
Embolic distribution		
Unilateral PE	76 (28.7)	101 (51.5)
Bilateral PE	189 (71.3)	95 (48.5)
RV dilatation by CT	37 (14.0)	4 (2.1)
Echocardiographic RV dysfunction	1 (0.4)	0 (0)
PE Severity Index Class		
I (lowest risk)	96 (36.2)	101 (51.5)

	Hospitalized (n=265; 57.5%) n (%)	Outpatient (n=196; 42.5%) n (%)
II (low risk)	169 (63.4)	95 (48.5)
Hestia Criteria [/]		
≥1 Hestia criteria	35 (13.2)	13 (6.6)
No Hestia criteria	230 (86.8)	183 (93.4)
Laboratory values		
Troponin concentration (ng/L) [¶]		
Within reference range (<0.04)	174 (65.7)	143 (73.0)
Elevated (≥0.04)	56 (21.1)	6 (3.1)
Not performed[#]	35 (13.2)	47 (24.0)
BNP (ng/L)		
BNP<100	131 (49.4)	74 (37.8)
BNP≥100	37 (14.0)	7 (3.6)
Not performed[#]	97 (36.6)	115 (58.7)
Hemoglobin (g/dL)		
Hemoglobin ≥ 11	238 (89.8)	173 (88.3)
Hemoglobin < 11	27 (10.2)	20 (10.2)
Not performed[#]	1 (0.36)	3 (1.5)
Platelets (K/μL)		
Platelets ≥150	243 (91.7)	188 (95.9)
Platelets <150	22 (8.3)	5 (2.6)
Not performed[#]	0	2 (1.0)
GFR (mL/min/1.73m^2)		
GFR≥60	240 (90.6)	187 (95.4)
GFR<60	25 (9.4)	7 (3.6)
Not performed[#]	0 (0)	2 (1.0)
Psychosocial barriers to outpatient care		
Lack of fixed residence[‡]	--	--

Abbreviations: BMI, body mass index; BNP, B-type natriuretic peptide; GFR, glomerular filtration rate.

[*] Race and ethnicity were self-reported. “Other” includes Native American and Hawaii and Pacific Islander

[†] EDs were assigned to the intervention (10 EDs) or control (11 EDs) in the 2014/2015 pragmatic trial based on the presence of an on-site physician champion

[‡] Cells replaced with ‘--’ indicate cell counts of less than 10 patients or cell counts that could be used to derive cell counts with less than 10 patients; these cells were suppressed to protect patient identity.

[§] With or without oxygen supplementation

[/] The Hestia criteria comprise a bedside checklist of exclusions to outpatient PE management

[¶] Highest Troponin I concentration during the ED encounter

[#]Missing values were common with only 53.5% of patients having a BNP value obtained during their ED stay

Table 2.

Adjusted Odds Ratios from multivariable model for likelihood of hospitalization.

	Adjusted OR for Hospitalization	95% Confidence Interval
Highest heart rate ≥110 (vs <90 beats per minute)	3.11	1.07–9.57
Highest heart rate 90–109 (vs <90 beats per minute)	2.03	1.18–3.50
Bilateral PE *	1.92	1.13–3.27
Proximal embolism location †	1.19	0.71–2.00
Age (per 1-year increment)	0.99	0.97–1.02
Female sex ‡	0.82	0.48–1.41
Chronic lung disease history	0.77	0.39–1.51
Hospitalization within 30 Days	1.78	0.82–4.02
PE Severity Index class II §	1.85	0.90–3.84
Arrival by ambulance	2.48	1.04–6.32
Former intervention site /	0.39	0.23–0.65
Troponin elevation (≥0.04 ng/L)	2.79	1.09–8.20
RV dilatation by CT angiography	3.55	1.22–13.01
Lowest oxygen saturation <95%	2.76	1.61–4.78
Highest respiratory rate >24 breaths per minute	2.47	1.33–4.72

Variables of interest on grey background

* Compared to unilateral PE

† Compared to distal location. Proximal emboli are those that were clearly lobar in location or more proximal

‡ Patient-reported sex

§ Compared to PE Severity Index Class I

/ Compared to former control site in our 2015 pragmatic trial