

Emergency Department Discharge of Pulmonary Embolus Patients

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ABSTRACT

Background: Hospitalization for low-risk pulmonary embolism (PE) is common, expensive, and of questionable benefit.

Objective: The objective was to determine if low-risk PE patients discharged from the emergency department (ED) on rivaroxaban require fewer hospital days compared to standard of care (SOC).

Methods: Multicenter, open-label randomized trial in low-risk PE defined by Hestia criteria. Adult subjects were randomized to early ED discharge on rivaroxaban or SOC. Primary outcome was total number of initial hospital hours, plus hours of hospitalization for bleeding or venous thromboembolism (VTE), 30 days after randomization. A 90-day composite safety endpoint was defined as major bleeding, clinically relevant nonmajor bleeding, and mortality.

Results: Of 114 randomized subjects, 51 were early discharge and 63 were SOC. Of 112 (98.2%) receiving at least one dose of study drug, 99 (86.8%) completed the study. Initial hospital LOS was 4.8 hours versus 33.6 hours, with a mean difference of -28.8 hours (95% confidence interval [CI] = -42.55 to -15.12 hours) for early discharge versus SOC, respectively. At 90 days, mean total hospital days (for any reason) were less for early discharge than SOC, 19.2 hours versus 43.2 hours, with a mean difference of 26.4 hours (95% CI = -46.97 to -3.34 hours). At 90 days, there were no bleeding events, recurrent VTE, or deaths. The composite safety endpoint

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was similar in both groups, with a difference in proportions of 0.005 (95% CI = -0.18 to 0.19). Total costs were \$1,496 for early discharge and \$4,234 for SOC, with a median difference of \$2,496 (95% CI = -\$2,999 to -\$2,151).

Conclusions: Low-risk ED PE patients receiving early discharge on rivaroxaban have similar outcomes to SOC, but fewer total hospital days and lower costs over 30 days.

Of the approximately 900,000 annual venous thromboembolism (VTE) events occurring in the United States,¹ it is estimated that more than 250,000 are diagnosed with pulmonary embolus in the emergency department (ED).² In a U.S. National Hospital Ambulatory Medical Care Survey analysis, during 2006 to 2010, >90% of ED patients diagnosed with pulmonary embolism (PE) were hospitalized.³ Since the average PE hospitalization costs approximately \$14,000,¹ this represents >\$2 billion in annual expenditures. The necessity of routine PE admission is unclear. Although mortality rates of PE with shock exceed 30%,⁴ the 30-day mortality rate of low-risk PE (LRPE) patients is less than 1%.⁵ One study of LRPE patients, defined by a simplified PE severity index score = 0, found an average patient cost saving of >\$6,000 for discharged versus hospitalized patients.⁵

Importance

Avoidance of hospitalization may not only reduce costs, it is associated with fewer adverse clinical outcomes. In LRPE patients, longer hospitalization is associated with as much as an 880% greater risk (1.5% vs 13.3%; 95% confidence interval [CI] = 3.77%–19.94%) of hospital-acquired conditions.^{6,7} Although few prospective U.S. studies have discharged LRPE patients, the American College of Chest Physicians supports early discharge of these patients with adequate home circumstances.⁸

In 2012, rivaroxaban (an oral factor Xa inhibitor) was approved for the treatment of PE. Because anticoagulation onset occurs within 2 hours of oral administration, rivaroxaban could obviate the historical requirement for bridging therapy with a parenteral anticoagulant agent. As this strategy questions the necessity for hospitalization to simply take an oral medication, we performed the first U.S. study randomizing ED LRPE patients to hospital discharge on an oral factor Xa inhibitor (rivaroxaban) versus standard-of-care (SOC) therapy.

Goals of This Investigation

The goal of this investigation was to determine if LRPE patients discharged from the ED on rivaroxaban

require less time in the hospital and lower costs compared to SOC.

METHODS

Study Design and Setting

MERCURY PE (MultiCenter trial of Rivaroxaban for early discharge of pulmonary embolism from the Emergency Department, NCT02584660) was a randomized, open-label, parallel-group, multicenter study, initially planned to be conducted at 57 U.S. sites. All sites had institutional review board approval. This study is reported consistent with CONSORT standards and its methodology has been previously published.⁹

Selection of Participants

Adult patients presenting to the ED with objectively confirmed, LRPE were eligible for enrollment. LRPE was defined by the absence of any Hestia criteria, adapted for emergency medicine by removing 24-hour requirements^{10,11} (see Table 1). Patients were excluded for a troponin level above the institutional upper reference level, contraindications to anticoagulation, or by investigator determination of barriers to treatment or follow-up. Although the Hestia criteria exclude hemodynamically unstable patients, instability is not defined and was determined per the physician's judgment. Study logs were maintained to provide description of excluded patients.

Interventions

After obtaining written informed consent, patients were randomly assigned in a 1:1 ratio to ED discharge on open-label rivaroxaban or standard care (as determined by the attending physician) by an interactive Web system within 12 hours of diagnosis. Patients randomized to early discharge on rivaroxaban were discharged within 24 hours of ED triage and were instructed to take rivaroxaban with food, 15 mg twice daily for 21 days and then 20 mg once daily to study completion. SOC patients were treated per local protocol, which could include hospitalization and any Food and Drug

Administration (FDA)-approved anticoagulant strategy, including rivaroxaban. If receiving warfarin, the target international normalized ratio (INR) was 2.0 to 3.0, with testing per local protocol.

Measurements

Patients, nursing staff, physicians, and local investigators were aware of group assignment. Principal investigators and outcome adjudicators were masked to group assignment. Data collection was by trained research staff using standardized e-forms.

Outcomes

The primary efficacy outcome was the total amount of time spent in the hospital, expressed in hours for venous thromboembolic or bleeding events, in the 30 days after randomization. The primary safety outcome was major bleeding within 90 days. Patient safety was monitored by an independent data safety monitoring board. As participants could not be blinded to their own hospitalization, to reduce observer bias clinical and safety endpoints were adjudicated by a panel blinded to treatment allocation. The study protocol was approved by all participating institutional review boards.

For outcome definitions, hospital time included all the time a patient was admitted to an inpatient service or hospital observation unit. Readmissions were identified based on record review and patient self-report by telephone contact at 30 and 90 days. Readmissions for reasons unrelated to VTE were excluded. Adverse

events were reviewed by trained adjudicators blinded to study assignment.

Patient satisfaction with inpatient and outpatient care was rated using 5- and 3-point Likert scales, respectively, with higher scores indicating greater satisfaction. Satisfaction was further evaluated with the Anti-Clot Treatment Score, which uses two subscales of burdens (12 items) and benefits (three items), both measured on a 5-point Likert scale, with higher scores indicating greater satisfaction.

Prespecified secondary efficacy endpoints included 90-day rates of new/recurrent VTE, VTE-related death, unplanned hospital or physician office visits for VTE or bleeding, total length of initial and subsequent hospitalizations for any reason, and patient-reported satisfaction with the site of care assessed on Day 7; satisfaction with anticlot treatment assessed on Days 14, 30, and 90; and the total costs of care. A prespecified secondary safety endpoint was clinically relevant nonmajor bleeding, based on the International Society on Thrombosis and Haemostasis (ISTH) definitions.¹²

Standard U.S. FDA outcome definitions¹³ were utilized and included the following: 1) adverse event (AE), any untoward medical occurrence associated with the use of a drug in humans whether or not considered drug related, or 2) serious adverse event (SAE), any experience or reaction of any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, or results in persistent or significant disability/incapacity or a congenital anomaly/birth defect. Treatment-emergent adverse events are defined as adverse events with onset or worsening on or after date of first dose of study treatment up to and including 2 days after the last dose date

We evaluated total treatment costs for early discharge on rivaroxaban and SOC cohorts during 30 days following randomization for all patients in the intention to treat analysis. This consisted of direct medical care costs (2016 U.S. dollars), including the qualifying index PE encounter, all subsequent encounters related to any ISTH major or clinically relevant nonmajor bleeding, adjudicated recurrent PE or new/recurrent DVT, and the costs of anticoagulation and related monitoring. Since PE treatment costs are higher on the first 1 to 2 days of an inpatient or ED visit, we valued the cost of the initial encounter on an hourly basis using unit costs derived from a previous economic analysis of PE.¹⁴ The ED and outpatient

Table 1
Adapted HESTIA Criteria (Any Present Exclude Early Discharge Option)

Hemodynamically unstable by clinician judgment
Thrombolysis or embolectomy needed
Active bleeding or high risk for bleeding, GI bleeding or surgery ≤ 2 weeks ago, stroke ≤ 1 month ago, bleeding disorder or platelet count $< 75 \times 10^9/L$, uncontrolled HTN (sBP > 180 or dBP > 110)
Oxygen needed to maintain SaO ₂ $> 90\%$
PE diagnosed while on anticoagulation
Requiring IV pain medication
Medical or social reason for admission (e.g., concurrent infection, poor/no support system)
Creatinine clearance < 30 mL/min by Cockcroft-Gault
Severe liver impairment
Pregnant
Known history of heparin-induced thrombocytopenia

GI = gastrointestinal; HTN = hypertension; PE = pulmonary embolism.

physician office visits, procedures, and tests (including INR testing) were assigned costs based on current procedural terminology coding and the Medicare fee schedule.¹⁵ All anticoagulants were assigned costs based upon mean *Red Book* wholesale prices. When necessary, costs were inflated to 2016 U.S. dollars using the Consumer Price Index for Medical Care.¹⁶

Data Analysis

Analyses were conducted by intention-to-treat basis, regardless of anticoagulant used. Baseline characteristics (demographic and clinical data) are summarized with appropriate statistics. The primary clinical endpoint was calculated for each cohort and is presented as a two-sided 95% CI for the mean difference of length of hospital stay, dichotomized by treatment. Descriptive statistics are provided for other endpoints. Cost data are reported as medians and interquartile ranges (IQRs). The nonparametric Hodges-Lehman independent-samples test was used to estimate the difference in median cost between early discharge on rivaroxaban and SOC and is reported with 95% CIs

Sample Size and Power Calculation

A large-sample CI approach was used to determine the sample size required for estimating the difference in mean length of stay for VTE or bleeding related events during the first 30 days after randomization between groups. Using a standard deviation of 24 and 74.4 hours, for outpatient and inpatient groups, respectively,¹⁷ an average number of hours of hospitalization after discharge of <48, and the percentage of patients with VTE-related rehospitalization as <5%, we projected a total of 150 subjects per group would provide a two-sided 95% CI with about a 12-hour margin of error. Margin of error was defined as the quantity from the observed difference in means to the endpoint of the CI. This provided an 82% power to detect a 24-hour difference, or 99% power to detect a 48-hour difference, in total hospital hours. Because recurrent VTE rates are very low in LRPE patients,¹⁷ we did not power for this parameter.

RESULTS

Characteristics of Study Subjects

The flow of screened and randomized patients is presented in Figure 1. Because of an unanticipated funding decrease, only 35 hospitals participated, each enrolling a median (IQR) of 3 (1–5) patients. A total

of 114 subjects were randomized and 99 (86.8%) completed the study. Of 15 (13.2%) discontinuations, seven (13.7%) were on rivaroxaban, and eight (12.7%) received SOC. The most frequent reasons for early discontinuation were lost to follow-up (see Figure 1) and adverse events ($n = 4$, 7.8%), all on rivaroxaban (see Table 2). Demographic characteristics were similar between treatment groups (see Table 3). The median (range) duration of treatment was 90 (2–109) days; early discharge on rivaroxaban, 91 (3–109) days; and SOC, 89 (2–105) days. Overall, 60 patients (53.6%) received treatment for ≥ 90 days: early discharge on rivaroxaban, 33 (67.3%); and SOC, 27 (42.9%).

As the SOC arm was required to be per local practice patterns, our results reflect standard U.S. practice. We found > 75% of LRPE patients ultimately received some type of direct-acting oral anticoagulant (DOAC; see Table 4). However, nearly 75% of SOC patients were initially treated with some type of parenteral heparin (49.2% low molecular weight, 25.4% unfractionated).

Main Results

Primary Endpoint. The mean (\pm SD) duration of initial and subsequent hospitalizations for bleeding and/or VTE events within 30 days of randomization was shorter with early discharge on rivaroxaban than SOC: 4.8 (± 16.8) hours versus 33.6 (± 48.0) hours ($p < 0.0001$), respectively. The mean difference (95% CI) of LOS between treatment groups was 28.8 hours (-41.5 to -16.2).

Secondary Endpoints. There was no recurrence of VTE, or VTE-related death, within 7, 14, 30, or 90 days from randomization in any group, and there were no differences in the bleeding-related hospitalizations or physician visits within 90 days from randomization, 2 (3.9%) versus SOC, 4 (6.3%); 95% CI = -0.024 (-0.206 to 0.160). The mean (\pm SD) length of initial and subsequent hospitalizations for any reason within 90 days from randomization was shorter for early discharge on rivaroxaban than SOC, 19.2 (52.8) hours vs. SOC, 43.2 (64.8) hours ($p = 0.024$), respectively. The difference (95% CI) of LOS in the ED and hospital between groups was -26.4 (-47.0 to -3.3) hours.

Table 2 demonstrates safety outcomes. No ISTH major bleeding events occurred, although two (1.8%) subjects reported ISTH clinically relevant nonmajor bleeding, one from each randomization group. One SOC subject had a minimal bleeding event. There

were no deaths. The most frequent treatment-emergent (TE)-SAE was dyspnea, three (4.8%) in SOC; one was considered related to study drug. No TE-SAE was considered related to rivaroxaban. There were three TE-SAEs leading to study agent discontinuation: one (2.0%) on rivaroxaban (arthralgia) and two (3.2%) on SOC (one embolic pneumonia and one dyspnea). There were more TE-AEs on rivaroxaban, of which most were mild or moderate in severity (see Table 2).

As to patient reported satisfaction, most, 66 of 107 (61.7%), were “very satisfied” with their care, regardless of assignment to early discharge on rivaroxaban (60.4%) or SOC (62.7%; $p = 0.619$) or its location as outpatient (rivaroxaban cohort, 62.5%) or inpatient (SOC cohort, 59.3%; $p = 0.728$). However, a greater percentage of early discharge on rivaroxaban patients preferred outpatient care, 24 of 48 (50.0%), compared to SOC, 28 of 59 (47.5%; $p = 0.003$).

When patient perspective of early discharge on rivaroxaban versus SOC treatment was evaluated using the Anti-Clot Treatment Scale, more early discharge

on rivaroxaban subjects reported it as “not at all” (64.4% vs. 54.4%) or “a little” (28.9% vs. 18.2%) burdensome versus SOC patients who reported it as “moderately” (14.5% vs. 4.4%), “quite a bit” (7.3% vs. 2.2%), and “extremely” (5.5% vs. 0%) burdensome, although no comparisons were significantly different ($p = 0.099$). Similarly, a higher proportion reported early discharge on rivaroxaban as “extremely beneficial” versus SOC (37.8% vs. 23.6%), but without differences between groups ($p = 0.265$).

Overall, early discharge on rivaroxaban was markedly less expensive than the SOC. Index visits and total costs were \$2,638 ($p < 0.001$) and \$2,496 ($p < 0.001$) less with rivaroxaban (see Table 5).

DISCUSSION

This is the first prospective randomized trial to evaluate ED discharge in LRPE patients in the United States. Our primary endpoint demonstrates that the prospective identification of LRPE patients in the ED

Adapted HESTIA Criteria (any present exclude early discharge option)
Hemodynamically unstable by clinician judgment
Thrombolysis or embolectomy needed
Active bleeding or high risk for bleeding, GI bleeding or surgery ≤ 2 weeks ago, stroke ≤ 1 month ago, bleeding disorder or platelet count $< 75 \times 10^9/L$, uncontrolled HTN (sBP > 180 or dBP > 110)
Oxygen needed to maintain SaO ₂ $> 90\%$
PE diagnosed while on anticoagulation
Requiring IV pain medication
Medical or social reason for admission (e.g., concurrent infection, poor/no support system)
Creatinine clearance < 30 mL/min by Cockcroft-Gault
Severe liver impairment
Pregnant
Known history of heparin-induced thrombocytopenia (HIT)

Figure 1. CONSORT diagram.

Table 2
Summary of AEs

	Rivaroxaban (n = 49)	SOC (n = 63)	Total (n = 112)	Chi-square p-value
AE	29 (59.2)	25 (39.7)	54 (48.2)	0.0405
TE-AE	28 (57.1)	24 (38.1)	52 (46.4)	0.0450
Chest pain	6 (12.2)	3 (4.8)	9 (8)	0.1484
Dyspnea	1 (2)	7 (11)	8 (7.1)	0.0645
Headache	2 (4.1)	3 (4.8)	5 (4.5)	0.8627
SAE	5 (10.2)	7 (11.1)	12 (10.7)	0.8776
TE-SAE	5 (10.2)	7 (11.1)	12 (10.7)	0.8776
AE leading to study drug discontinuation	2 (4.1)	4 (6.3)	6 (5.4)	0.5970
Drug-related TE-AE leading to drug discontinuation	1 (2)	2 (3.2)	3 (2.7)	0.7124
SAE leading to hospitalization	5 (10.2)	7 (11.1)	12 (10.7)	0.8776
Deaths	0	0	0	

Data are reported as *n* (%). Percentages are calculated with the number of subjects in each treatment group as the denominators. Drug-related adverse event is defined as a relationship to the study drug is possible, probable, or very likely. AE = adverse event; SAE = serious adverse event; TE = treatment emergent.

Table 3
Demographics, Past Medical History, and Treatment

	Total (N = 114)	Rivaroxaban (n = 51)	SOC (n = 63)	Rivaroxaban vs. SOC (95% CI)
Characteristics				
Female	59 (51.8)	27 (52.9)	32 (50.8)	-0.1629 to 0.2059
White	77 (67.5)	29 (56.9)	48 (76.2)	-0.3651 to -0.0214
African American	34 (29.8)	20 (39.2)	14 (22.2)	0.0011 to 0.3387
Age (years)	48.26 (±15.5)	49.14 (±13.3)	47.56 (±17.2)	-4.2323 to 7.3957
18 to 65	100 (±87.7)	48 (±94.1)	52 (±82.5)	0.0019 to 0.2296
66 to <76	9 (±7.9)	3 (±5.9)	6 (±9.5)	-0.1335 to 0.0607
>76	5 (±4.4)	0	5 (±7.9)	-4.2323 to 7.3957
BMI	31.12 (±8.2)	31.41 (±8.7)	30.87 (±7.9)	-2.5557 to 3.6441
Past medical history				
PE	16 (14)	8 (15.7)	8 (12.7)	-0.0994 to 0.1592
DVT	6 (5.3)	2 (3.9)	4 (6.3)	-0.1047 to 0.0561
MI	0	0	0	
AF	4 (3.5)	4 (7.8)	0	0.0046 to 0.1522
CHF	1 (0.9)	1 (2)	0	-0.0184 to 0.0577
Cancer	7 (6.1)	3 (5.9)	4 (6.3)	-0.0930 to 0.0836
Diabetes	9 (7.9)	6 (11.8)	3 (4.8)	-0.0329 to 0.1729
ED medication				
Aspirin	3 (2.7)	1 (2)	2 (3.2)	-0.0700 to 0.0473
Heparin	29 (25.9)	12 (24.5)	17 (27)	-0.1878 to 0.1379
Low-molecular-weight heparin	6 (5.4)	3 (6.1)	3 (4.8)	-0.0717 to 0.0989

Data are reported as *n* (%) or mean (±SD).

AF = atrial fibrillation; BMI = body mass index; CHF = congestive heart failure; DVT = deep vein thrombosis; MI = myocardial infarction; PE = pulmonary embolism; SOC = standard of care.

is feasible, can result in much shorter hospitalization exposure, and markedly decreases costs without a negative impact on patient satisfaction and with no increase in VTE or bleeding events. While our small sample size limits safety statements, very large studies

(*n* > 3,500) have previously and definitively established that there are very low rates of bleeding and recurrent VTE events,^{18,19} such that a redundant repetition would contribute little to the safety literature (except to be extremely costly). Ultimately, the results

Table 4
Anticoagulant Medications in Use for the Longest Duration After Randomization in the SOC Group, Safety Analysis ($n = 63$)

Apixaban	16 (25.4)
Dabigatran	1 (1.6)
Unfractionated heparin	2 (3.2)
Low-molecular-weight heparin	2 (3.2)
Rivaroxaban	32 (50.8)
Warfarin	10 (15.9)

Data are reported as n (%).
SOC = standard of care.

of MERCURY-PE suggest a strategy of early discharge is feasible and demonstrates that the practice of admission for all PE patients should be questioned.

The advantage of potentially shorter inpatient hospitalization portends much greater benefits than simply cost reduction. The avoidance of hospitalization and shortening length of stay^{6,7} may be associated with a lower risk of hospital acquired conditions (e.g., hospital-acquired pneumonia, methicillin-resistant *Staphylococcus aureus* infection).

Our data are timely, as significant changes are occurring in the management of anticoagulation. When the MERCURY-PE protocol was first started, selected centers refused participation due to the perceived ethical, safety, and operational conflicts of discharging patients from the ED with a newly diagnosed pulmonary embolus. In fact, it was common at the participating study sites for enrollment to be met with initial trepidation. However, once implemented, the study protocol was rapidly adopted such that by the final enrollment period, SOC had frequently migrated to include early discharge on rivaroxaban in a number of the participating centers. This experience serves as a demonstration project on the feasibility of adoption of the MERCURY-PE model to improve patient care.

Reflective of the changing anticoagulant landscape, the majority of patients enrolled in MERCURY-PE received treatment with a DOAC, most commonly rivaroxaban (51%) or apixaban (25%). While both of

these agents have a rapid onset, 75% of all patients still were initially treated with unfractionated or low-molecular-weight heparin. The use of a heparinoid agent, despite no bridging therapy requirement with DOACs, may reflect historical patterns of early treatment in suspected PE or may represent concern for selecting a reversible agent (heparin can be reversed, factor Xa inhibitors do not currently have an available antidote) in the initial management period.

Finally, we noted a higher frequency of TE-AEs with rivaroxaban. This seem to be a composite of several subjective complaints, which in the final analysis did not result in study drug termination or an association with AEs. While the precise causality of these TE-AEs cannot be determined and are not reflected in very large investigations of rivaroxaban, it is possible that our finding represents a nociceptive bias (where subjects report a higher frequency of events in randomized controlled trials compared to observational registries, as they are specifically asked about these events randomized controlled trials).

LIMITATIONS

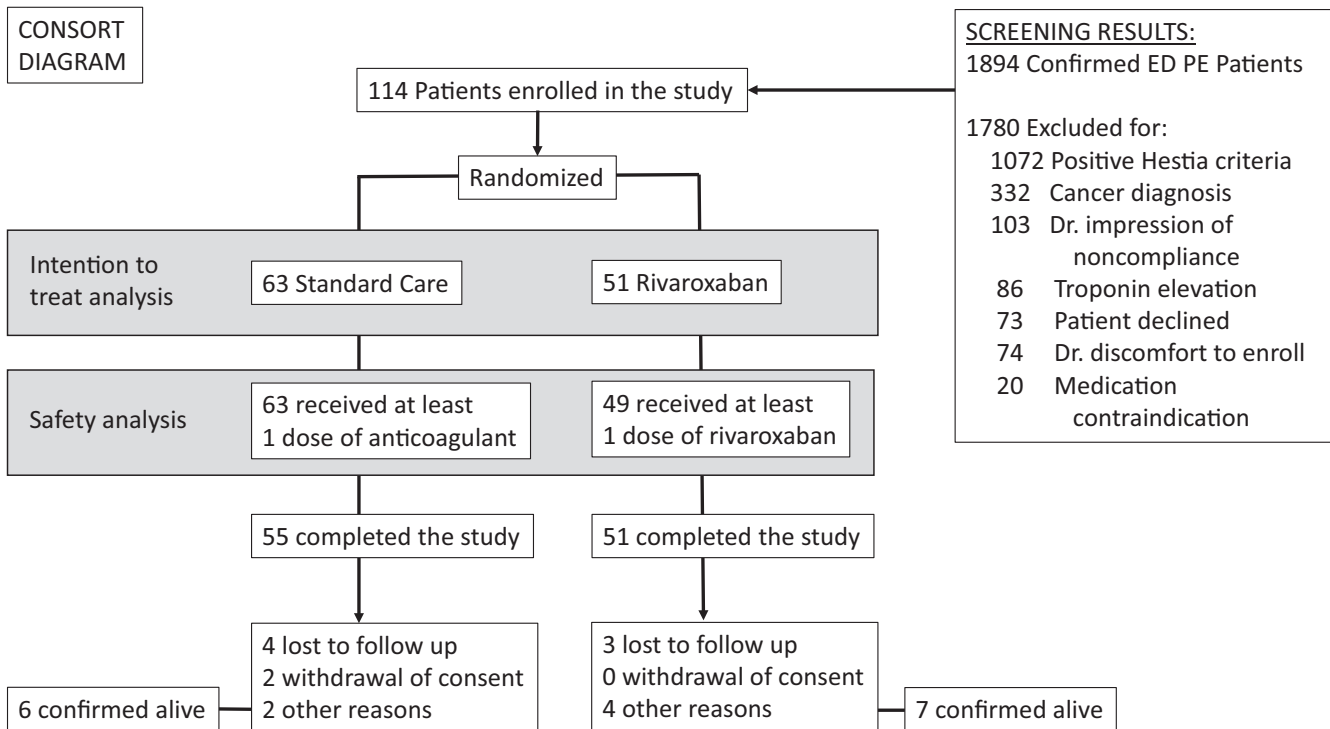
Our study has several limitations. First our sample size, originally powered to enroll 300 patients, was decreased due to slower than anticipated enrollment and unanticipated funding limitations. Nevertheless, it should be noted that our primary endpoint was met, which speaks to the large effect size attainable from immediate ED discharge. Our unexpectedly large effect size is most likely the result of practice differences in the rates of ED PE discharge in the United States compared to European studies used for its prediction.

Additional limitations include the fact that ED physicians could exclude patients based on a subjective evaluation of hemodynamic stability and their impression of the patient's ability to adhere to the protocol. While some exclusion bias may have occurred, this does not detract from the pragmatic decision strategies required of contemporary ED practice, and the use of

Table 5
Total Costs of Rivaroxaban Versus SOC in LRPE Patients

	Rivaroxaban* ($n = 51$)	SOC* ($n = 63$)	Median Difference (95% CI)	p-value
Total costs	\$1,496 (\$1,410 to \$1,641)	\$4,234 (\$3,191 to \$5,827)	-\$2,496 (-\$2,999 to -\$2,151)	<0.001
Index stay costs	\$704 (\$618 to \$849)	\$3,461 (\$2,534 to \$5,553)	-\$2,638 (-\$3,288 to -\$2,287)	<0.001
Anticoagulation costs	\$792 (NA)	\$792 (\$575 to \$792)	NA	NA

*Data are reported as median (IQR).
LRPE = low-risk pulmonary embolism; SOC = standard of care.



the Hestia criteria provides relatively objective data supported guidance for candidate selection.

Further, because a patient would know their admission status, they could not be blinded to their assigned cohort. Thus the use of an endpoint committee, blinded to the intervention, mitigated but did not eliminate this potential bias.

Some may consider the fact that 75% of our control group were discharged on a NOAC as a limitation and that randomization alone may have contributed to our between group differences. We would point out that this reflects current ED practice patterns of hospitalization on an intravenous anticoagulant, then followed by discharge on a NOAC. It should be clear from this analysis that, in selected patients, ED admission for a limited period of intravenous anticoagulation provides little benefit over immediate ED discharge.

Finally, this was a pragmatic trial, and as such we did not dictate SOC, especially when intravenous therapy could result. This strategy was chosen because SOC is not well defined (as demonstrated by our control group), and our dictating therapy would have required a degree of arbitrary decision making (we would have to pick one of several reasonable pathways). Although allowing the physician to define SOC (thus rivaroxaban could be included in the standard care arm) may have contributed to bias to the null, we

feel that this actually strengthens our ultimately positive results.

CONCLUSIONS

Compared to standard of care, early ED discharge of low-risk pulmonary embolus patients on rivaroxaban results in markedly lower costs and shorter duration of initial and subsequent hospitalizations without an increase in serious adverse events or patient dissatisfaction.

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