Outpatient therapy of pulmonary embolism (PE) has gained greater acceptance in the current era of risk stratification and direct oral anticoagulant (DOAC)-based treatment regimens. A growing experience in the medical literature has documented the safety and improved patient satisfaction with outpatient treatment of low-risk PE (1–4). Furthermore, the opportunity to decongest emergency departments and inpatient units, and reduce the overall cost burden of PE on healthcare systems, compels clinicians to select this strategy when feasible (5). The 2019 European Society of Cardiology guidelines for diagnosis and management of acute PE recommend risk stratification to identify low-risk patients who may be considered for home treatment if outpatient care can be arranged and adequate anticoagulation initiated (6). The 2016 American College of Chest Physicians guidelines suggest early discharge or home treatment of PE over hospitalization in low-risk patients whose home circumstances are adequate (7). However, despite tools for identification of appropriate patients, options for safe and effective outpatient treatment, and endorsement by guidelines, patients with low-risk PE are still frequently hospitalized (4).

Current risk stratification strategies for acute PE rely on synthesis of clinical decision rules; cardiac biomarkers, such as troponin and BNP (brain-type natriuretic peptide); and imaging of right ventricular (RV) function (8). Although these tools have been most widely endorsed for prognostication of adverse outcomes, they are also used for identification of low-risk patients who may avoid hospitalization for acute PE. Specific criteria for eligibility for home therapy were assessed by the Hestia investigators in a prospective cohort study of 297 patients with PE (9). The Hestia criteria identified a cohort of patients with acute PE who completed outpatient therapy with a low risk of adverse events, including recurrent venous thromboembolism (2%), all-cause mortality (1%), and major bleeding (0.7%).

Further contributing to a low adverse event rate with outpatient therapy for acute PE is the widespread integration of DOACs into treatment algorithms. Compared with vitamin K antagonists, DOACs provide similar efficacy but enhanced safety with a 40% reduction in major bleeding and 60% reduction in intracranial hemorrhage (10). The relative ease with which the DOACs are initiated and the promise of consistent, safe, and effective anticoagulation without the need for dose adjustment make them preferred for PE treatment and a major advance in the movement toward outpatient therapy (6, 7).

In this issue of the Journal, Hendriks and colleagues (pp. 138–141) provide an important perspective on risk stratification in patients with PE who are eligible for outpatient therapy (11). The investigators report a post hoc analysis of combined data from the prospective Hestia and Vesta studies to assess the incremental prognostic value of increased computed tomographic–measured right ventricular–to-left ventricular (RV-to-LV) diameter ratio on recurrent venous thromboembolism and mortality. In the analysis of 752 patients with PE treated at home, 30% had RV enlargement (RV-to-LV diameter ratio > 1). Adverse events were infrequent in these otherwise low-risk patients with RV enlargement compared with those without (2.7% vs. 2.3%; odds ratio, 1.2; 95% confidence interval, 0.44–3.2). The investigators concluded that RV enlargement would have excluded a large proportion of their cohort from outpatient therapy without impacting prognosis.

Despite the main limitation of its post hoc design, the study findings support previous observations demonstrating that routine assessment of RV function and cardiac biomarkers in low-risk patients identified using clinical criteria provides little prognostic value and may come at the cost of hospitalizing patients who could otherwise be treated at home (Table 1). A previous analysis from the study investigators demonstrated that 35% of patients who were treated at home according to the Hestia criteria had RV dysfunction and were classified as intermediate risk according to the European Society of Cardiology criteria (12). Similarly, other studies from the investigators have shown that increased high-sensitivity cardiac troponin T (13) and N-terminal pro-BNP (14) were associated with a low rate of adverse events in patients with PE determined to be low-risk by the Hestia criteria. One potential explanation for infrequent adverse events in clinically
Table 1. The Incremental Prognostic Value of Risk Stratification Tools in Patients with Pulmonary Embolism Determined to Be Low-Risk by the Hestia Criteria

| Tool       | Adverse Event Rate | Odds Ratio (95% Confidence Interval) |
|------------|--------------------|--------------------------------------|
| hsTnT      | Elevated hsTnT, 0.9% vs. normal hsTnT, 0.7% | 2.5 (0.22–28)                      |
| NTproBNP   | Elevated NTproBNP and hospitalized, 0% vs. elevated NTproBNP and discharged, 0% | —                                  |
| RV-to-LV   | RV-to-LV > 1, 2.7% vs. RV-to-LV ≤ 1, 2.3% | 1.2 (0.44–3.2)                     |

Definition of abbreviations: hsTnT = high-sensitivity cardiac troponin T; LV = left ventricular; NTproBNP = N-terminal pro-brain natriuretic peptide; RV = right ventricular.

determined low-risk patients with PE with RV dysfunction may rest with the ability of DOACs to provide consistent and safe antithrombotic therapy in patients discharged from the emergency department (15).

The Hestia investigators should be commended for their body of work establishing that systematic clinical assessment identifying low-risk patients should be the primary driver in decision-making regarding outpatient therapy for PE and not assessment of RV function or cardiac biomarkers, which in approximately one-third provides a discordant prognostic picture without adding additional precision to risk stratification. In this current era of overcrowding in emergency departments and inpatient wards, the opportunity to manage clinically determined low-risk patients with PE at home should not be dismissed hastily for fear of RV dysfunction or positive troponin. Hopefully, reports such as this one will prompt clinicians evaluating patients with PE in the emergency medicine and urgent care settings to listen to their hearts (and follow their clinical instincts with the aid of tools like the Hestia criteria), lest their eyes deceive them. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

Gregory Piazza, M.D., M.S.
Department of Medicine
Brigham and Women’s Hospital and Harvard Medical School
Boston, Massachusetts

References

1. Barco S, Schmidtmann I, Ageno W, Bauersachs RM, Becattini C, Bernardi E, et al.; HoT-PE Investigators. Early discharge and home treatment of patients with low-risk pulmonary embolism with the oral factor Xa inhibitor rivaroxaban: an international multicentre single-arm clinical trial. Eur Heart J 2020;41:509–518.

2. Khatib R, Ross S, Kennedy SA, Florez ID, Ortel TL, Nieuwlaat R, et al. Home vs hospital treatment of low-risk venous thromboembolism: a systematic review and meta-analysis. Blood Adv 2020;4:500–513.

3. Frank Peacock W, Coleman CI, Diercks DB, Francis S, Kabriel C, Keay C, et al. Emergency department discharge of pulmonary embolus patients. Acad Emerg Med 2018;25:995–1003.

4. Peacock WF, Singer AJ. Reducing the hospital burden associated with the treatment of pulmonary embolism. J Thromb Haemost 2019;17:720–736.

5. Fanikos J, Rao A, Seger AC, Carter D, Piazza G, Goldhaber SZ. Hospital costs of acute pulmonary embolism. Am J Med 2013;126:127–132.

6. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al.; ESC Scientific Document Group. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2020;41:543–603.

7. Kearon C, Akl EA, Ormelas J, Blaivas A, Jimenez D, Bounamaux H, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest 2016;149:315–352.

8. Giri J, Sista AK, Weinberg I, Kearon C, Kumbhani DJ, Desai ND, et al. Interventional therapies for acute pulmonary embolism: current status and principles for the development of novel evidence. A scientific statement from the American Heart Association. Circulation 2019;140:e774–e801.

9. Zondag W, Mos IC, Creemers-Schild D, Hoogerbrugge AD, Faber LM, 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 2020;202:138–141.

10. van der Hulle T, Kooiman J, den Exter PL, Dekkers OM, Klok FA, Huisman MV. Effectiveness and safety of novel oral anticoagulants as compared with vitamin K antagonists in the treatment of acute symptomatic venous thromboembolism: a systematic review and meta-analysis. J Thromb Haemost 2014;12:320–328.

11. Hendriks SV, Klok FA, den Exter PL, Eijsvogel M, Faber LM, Hofstee HMA, et al.; Hestia/Vesta Investigators. 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 2011;8:1500–1507.

12. Zondag W, Vingerhoets LM, Durian MF, Dolmsa A, Faber LM, Hiddinga BI, et al.; Hestia Study Investigators. Outpatient treatment in patients with acute pulmonary embolism: the Hestia Study. J Thromb Haemost 2013;11:686–692.

13. Hendriks SV, Lankeit M, den Exter PL, Zondag W, Brouwer R, Eijsvogel M, et al.; Vesta Investigators. Uncertain value of high-sensitive troponin T for selecting patients with acute pulmonary embolism for outpatient treatment by Hestia criteria. Am J Respir Crit Care Med 2016;194:998–1006.

14. den Exter PL, Zondag W, Klok FA, Brouwer RE, Dolmsa J, Eijsvogel M, et al.; Vesta Study Investigators. Efficacy and safety of outpatient treatment based on the Hestia clinical decision rule with or without N-terminal pro-brain natriuretic peptide testing in patients with acute pulmonary embolism: a randomized clinical trial. Am J Respir Crit Care Med 2016;194:998–1006.

15. Beam DM, Kahlert ZP, Kline JA. Immediate discharge and home treatment with rivaroxaban of low-risk venous thromboembolism diagnosed in two U.S. emergency departments: a one-year preplanned analysis. Acad Emerg Med 2015;22:788–795.

Copyright © 2020 by the American Thoracic Society