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Prognostic Performance of Hestia Criteria in Acute Pulmonary Embolism: A Systematic Review and Meta-Analysis

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Abstract

Previous studies have suggested that Hestia criteria could effectively identifying patients with acute pulmonary embolism (PE) who were at low risk of mortality for outpatient treatment or early discharge. But the performance of Hestia criteria in stratifying patients at different risk class is still unknown. We sought to comprehensively evaluate the prognostic impact of Hestia criteria for PE. The literatures search was conducted in PubMed, Web of Science and EMBASE from 1 August 2011 to 31 October 2021. Finally, Eight studies with 4110 patients were included in our meta-analysis. Overall, the pool percentage of patients classified as low-risk group and high-risk group were 41.4%% and 58.6% respectively, and the all-course mortality rates of each group were 2.3% and 10.6%, respectively. The pooled rate of PE-related composite adverse outcomes in high-risk group was increasingly higher than in low-risk group (15.7% *vs* 4.4%). High risk group was also markedly associated with overall mortality (OR: 7.21, 95%CI: 4.96-10.46, $p < 0.00001$), and PE-related adverse outcomes (OR:5.38, 95% CI:3.95-7.32, $p < 0.00001$). The pooled sensitivity, specificity, PLR, NLR of Hestia criteria for overall mortality were 0.90 (95% CI:0.83-0.94), 0.43 (95% CI:0.31-0.55), 1.6 (95% CI:1.3-1.9), 0.23 (95% CI: 0.15-0.35), respectively. The area under SROC curve (AUC) was 0.81 (95% CI: 0.77-0.84). The result of our meta-analysis indicate that Hestia criteria can effectively identify PE patients at low risk of poor prognosis with high sensitivity and NPV, but its prognostic role in patients with higher risk class still need to be verified.

Keywords

pulmonary embolism, Hestia criteria, prognosis, meta-analysis

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Introduction

Acute pulmonary embolism (PE) is a life-threatening cardiovascular disease with a wide spectrum of prognosis. In patients presented with hemodynamic instability, the all-cause mortality for 30 days rises above 14%,[1] hence treatment guidelines recommend aggressive early thrombolytic therapy.[2] For normotensive patients with acute PE, identification of low-risk patients who may be candidates for outpatient treatment or early discharge can ease their financial burden of hospitalization and reduce the unnecessary waste of medical resources. Randomized trails suggest that treating selected patients at home using appropriate triaging tools can achieve a very low mortality rate from 0.27% to 0.28%.[3] Therefore, risk stratification of acute PE is crucial to not only therapy strategy but prognostic assessment.

Multiple clinical prediction rules have been developed for risk assessment of PE in recent years. The 2019 ESC guideline

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suggests using Pulmonary Embolism Severity Index (PESI) or the simplified PESI (sPESI) for further risk stratification if hemodynamic instability is not at presentation.[2] The Bova score[4] and the FAST score[5] have both been proved to achieved good prognostic performance in normotensive PE patients. However, to date, there is still no consensus for the best classification tool, and most of these novel risk models need to be extensively validated.

Derived from a large prospective cohort study in the Netherlands, the Hestia criteria was firstly designed as a triaging tool for home treatment.[6] This rule is a checklist containing medical and social items that might require hospitalization. Although the Hestia criteria was not developed for risk assessment, several studies have revealed that this simple rule had an excellent performance for identifying low-risk PE patients,[7–9] and 30-day mortality rate also increased as an increased number of Hestia criteria item.[10]

Although Hestia criteria was a widely used tool for decision-making of outpatient treatment, its prognostic performance in PE patients has not been comprehensively evaluated. Therefore, we conduct this meta-analysis aiming to explore the impact of Hestia criteria for predicting adverse outcomes in PE patients.

Methods

This systematic review and meta-analysis was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.[11] We also registered our review at PROSPERO (registration ID: CRD42021260407).

Literature Selection

We conducted a comprehensive study selection in PubMed, Web of Science and EMBASE, with only English literature included. The publication date was filtered from 1 August 2011 to 31 October 2021, since the Hestia criteria was first developed in 2011. The search terms included: "pulmonary embolism", "venous thromboembolism", "pulmonary thromboembolism", "venous thromboembolism", "Hestia", "Hestia criteria", "risk model" and "prognosis".

Inclusion and Exclusion Criteria

Eligible studies must meet following criteria: (1) patients were objectively diagnosed with PE; (2) risk assessment information of PE patients according to Hestia criteria should be presented; (3) enough data to assess the relationship between risk group and poor outcomes.

Studies are excluded if: (1) there was not available data; (2) studies were reviews, editorials, commentaries, abstracts, case reports, letters or meta-analysis.

Quality Assessment

Two reviewers (YBW, YHF) independently evaluated the quality of included literatures according to the Newcastle–Ottawa Scale (NOS).[12] The NOS contains eight items, which classified into three criteria: selection, comparability and outcomes assessment. Studies with the NOS scores≥7 were defined as high quality.

Data Extraction

Two reviewers (YBW, YHF) independently extracted the following data in each included study: first author, publication year, country of origin, study design, enroll year, patients' number, age and gender of patients, proportion of patients in each risk group, follow-up time, accurate data for adverse outcome in each risk class, and the NOS score. Adverse outcomes are defined as recurrent VTE, major bleeding and all-cause mortality. Extracted data were compared and checked for accuracy. Disagreements will be solved by a third reviewer.

Statistical Analysis

The Hestia criteria was classified as low risk (none of items was presented) and high risk (at least one of items was presented). The pooled estimates for all outcomes were calculated as odds ratio (OR) and 95% confidence intervals (95% CI) by using Mantel and Haenszel method. The prognostic accuracy of Hestia criteria was evaluated by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), negative likelihood ratio (NLR) in each study. Summary receiver operating characteristic curve (SROC) and the area under the curve (AUC) value were applied to test the overall performance of Hestia criteria. We used the Cochran Q and I^2 test to explore the heterogeneity of studies. If $P < 0.10$ or I^2 value $> 50\%$, it suggests a significant heterogeneity existed across studies, thus, a random-effects model was performed. In absence of heterogeneity, a fixed-effects model was applied. A publication bias was explored by using funnel plots, Egger's regression test, and Begg's test. A value of $P < 0.05$ showed there was statistical significance. All the statistical analyses were assessed by using Review Manager (RevMan) 5.4.1 analysis software (The Cochrane Collaboration) and Stata software, version 14 (Stata Corp).

Results

Literature Selection

A total of 178 articles were identified through database search (43 from Pubmed, 84 from EMBASE and 51 from Web of Science), of these, 90 articles remained after eliminating 88 duplicate records, 78 articles were excluded because they were relevant studies, reviews, editorials or letters. After carefully reviewing full texts of remaining literatures, 4 articles were removed due to overlapping data. Finally, 8 eligible articles[3,8,9,13–17] with 4110 participants were enrolled in this meta-analysis. The detailed flow chart of literature selection is shown in Figure 1.

Study Characteristics and Quality Assessment

The summary characteristics of the 8 included articles were presented in Table 1. Among these studies, five[3,8,9,13,15] conducted in Europe, two[14,17] conducted in USA, and China[16] carried out one record. Published between 2013 and 2021, the enrolled eight studies consisted of four prospective studies and other four studies were retrospective. The median age of patients was from 58.1 to 76 years, the prevalence of cancer in included PE patients ranged from 13.1% to 100%. Six studies provided 30-day adverse outcomes, while three studies offered 3-month adverse outcomes. The quality assessment of included studies was presented in Supplement table 1, all studies gained NOS score from 7 to 8, indicating all articles achieved high quality.

Risk Class Assessment

According to evaluation of Hestia criteria in all included studies, the pool percentage of patients classified as low-risk group and high-risk group were 41.4% and 58.6%, respectively. Overall, 296 patients died in whole enrolled population, the all-course mortality was 2.3% in low-risk class compared with 10.6% in high-risk class. Similarly, five studies reported that 303 patients experienced PE-related composite adverse outcomes, and the pooled incidence in high-risk group was increasingly higher than in low-risk group (15.7% *vs* 4.4%). The detail incidence of adverse outcomes in each study according to Hestia criteria was presented in Table 2.

Main Meta-Analysis

Pooled results from 8 cohorts with 4110 patients revealed that high-risk group was markedly associated overall mortality in patients with PE compared with low-risk group (OR: 7.21, 95%CI: 4.96-10.46, $p < 0.00001$). The significant heterogeneity across studies was not observed ($P = 0.37$, $I^2 = 8\%$) (Figure 2A).

The incidence of composite poor outcomes across five included studies ranged from 7.5% to 20.2%. The pool analysis showed that adverse outcomes in patients with high-risk group were significantly higher than in those with low-risk group (OR:5.38, 95% CI:3.95-7.32, $p < 0.00001$). No heterogeneity was detected ($P = 0.46$, $I^2 = 0\%$) (Figure 2B).

Subgroup analysis was also performed according to the follow-up time. Six studies compared 30-day mortality in the low-risk group with the high-risk group. The result revealed a significant increase in 30-day mortality in high-risk group compared that in the low-risk group (OR: 6.43, 95%CI: 4.25-9.74, $p < 0.00001$) with mild heterogeneity ($P = 0.32$, $I^2 = 15\%$) (Figure 3). Similarly, high-risk group was markedly associated with 3-month mortality in PE patients (OR:11.13, 95%CI: 4.96-10.46, $p < 0.00001$). When assessing the 30-day and 3-month composite adverse outcome, patients in the high-risk group both had pooled ORs of 6.33 (95%CI: 4.21-9.52, $p < 0.00001$), 4.30 (95%CI: 2.82-6.58, $p < 0.00001$), respectively (Figure 4).

We further conducted another subgroup analysis based on two studies which only contained cancer patients with PE (Figure 5), 83 of 260 patients (31.92%) at high-risk group died compared with 25 of 324 (7.72%) patients at low-risk group, the pooled OR was 6.14 (95%CI: 3.70-10.22, $p < 0.00001$) with significant heterogeneity ($P = 0.04$, $I^2 = 75\%$).

Prognostic Performance

The prognostic performance of Hestia criteria for all-course mortality was summarized in Table 3. The Hestia criteria gained high sensitivity (73.5%-100%) with moderate specificity (20.2%-74.0%). The pooled sensitivity, specificity, PLR, NLR of Hestia criteria for overall mortality were 0.90 (95% CI:0.83-0.94), 0.43 (95% CI:0.31-0.55), 1.6 (95% CI:1.3-1.9), 0.23 (95% CI: 0.15-0.35), respectively. The SROC was displayed in Figure 6, the area under the curve (AUC) value was 0.81(95% CI: 0.77-0.84), demonstrating good predictive performance of Hestia criteria.

Publication Bias and Sensitivity Analysis

According to the funnel plots, there is no significant asymmetry for meta-analysis, indicating no obvious publication bias. And Egger's test also suggested no publication bias (Figure 7).

Sensitivity analysis was performed to test the one study's influence on the pooled data. It is shown that any single study was omitted, the pooled OR were not obvious changed, demonstrating that our results were relatively stable.

Discussion

The main purpose of our work is to show the prognostic power of Hestia criteria in predicting poor outcomes of acute PE patients. In this meta-analysis, 1703 patients (41.4%) were classified as the low-risk group, while 2407 patients (58.6%) were categorized in the high-risk group. Rates of overall death, as well as composite poor outcomes were markedly low (2.3% and 4.4%) in PE patients stratified as low-risk group, indicating that Hestia rule effectively triaged normotensive PE patients for home treatment with a low rate of complications. Compared with low-risk group, PE patients in high-risk group had remarkably much higher risk for overall mortality (over sevenfold), as well as for adverse outcomes (over fivefold). For predicting all-course mortality, the Hestia criteria showed high sensitivity (73.5%-100%) and excellent NPV value (86.9%-100%). When using a predictive test to make decision to discharge early from hospital or revive treatment at home, high sensitivity and NPV are preferable to high specificity.

It is still challenging to determine which patients with acute PE can be stratified for home treatment. Because acute PE has a potential life-threatening course with high mortality and morbidity, it is extremely important to develop a risk stratification tool in clinical practice. In the 2019 ESC guideline, the definition of low-risk patients is based on PESI or sPESI or Hestia rule combined with no sign of RV dysfunction on CTPA or

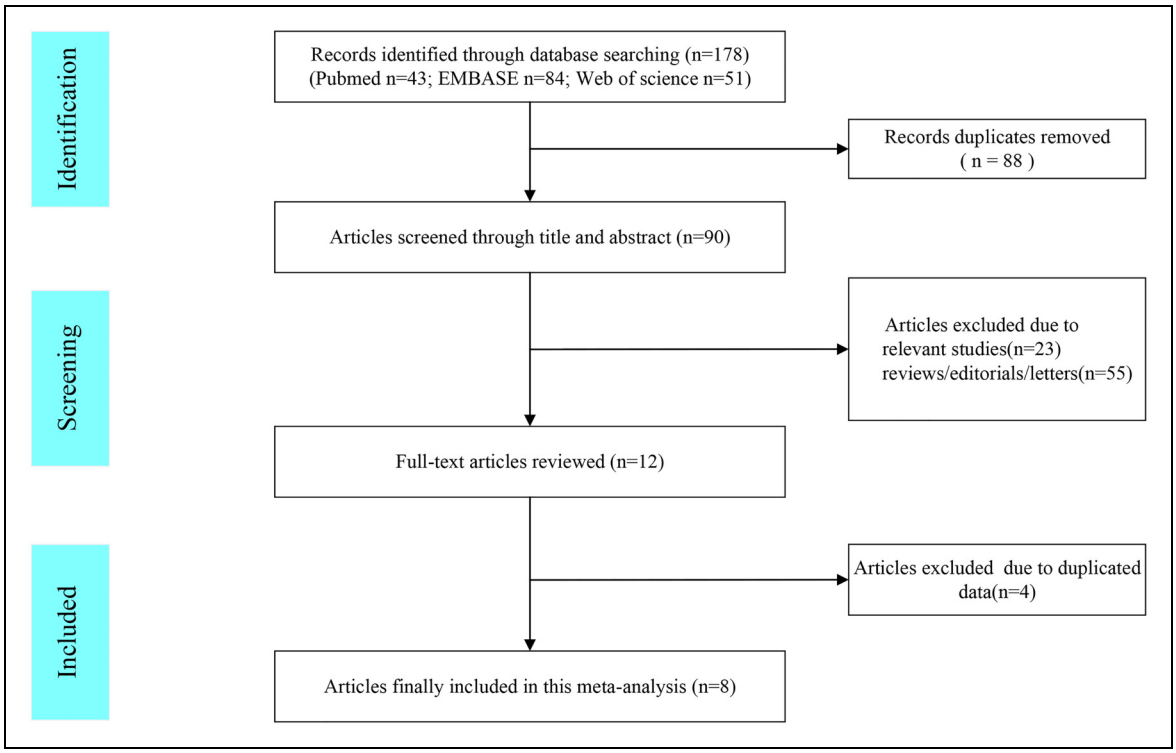

Figure 1. Flow chart of literature selection.

transthoracic echocardiography and elevated cardiac troponin.[2] If patients present no other reason for hospitalization such as family or social support, they are qualified for early discharge or outpatient therapy. However, the ESC's recommendation is characterized by complexity caused by multiple measurement tools and is mainly used to assess further aggressive treatment (eg systemic thrombolysis) for patients with intermediate or high risk PE. Moreover, the incremental value of adding laboratory testing or imaging procedures to clinical scores for selecting PE for outpatient treatment is still uncertain.[18,19] As for PESI rule, physicians have to check more items before the patient can be selected for outpatient treatment. This score may be too complicated and time consuming for use in busy emergency department. The checklist of Hestia rule is cheap, pragmatic, quick to perform and easy to accessible and bedside. Compared with sPESI, the Hestia rule selected fewer patients as eligible for outpatient treatment but its applicability was higher,[3] as one study had demonstrated that some items of Hestia criteria, including requirement of oxygen, medical or social reason for inpatient treatment, are required to add to the sPESI for deciding home treatment.[7] Another important clinical advantage is that unlike sPESI, Hestia rule do not exclude patients with cancer, sPESI defines all patients with cancer as high risk, which may limit its discriminatory power. Our subgroup analysis showed that mortality of cancer patients with PE was significantly higher at both risk classes compared unselective PE patients, despite heterogeneity existed. Although oncology patients with PE are at high risk of mortality, most of this mortality may not be related to PE, but to the progression of the underlying malignancy, what is more, a growing number of research suggested that nearly 45% of PE patients with malignancy can be safely and effectively treated at home,[20,21] longer duration of hospitalization may markedly damage the quality of life in active cancer patients.[22]

As the most validated clinical rules for risk stratification in PE patients, PESI (or sPESI) and Hestia criteria were used for decision-making of home treatment. Several studies have previously evaluated the prognostic value of these three triaging tools in selecting low-risk PE patients, however, the results seemed not consistent.[8,14,23] One meta-analysis had demonstrated that the PESI and sPESI appeared to be more reliable for identifying low-risk patients suitable for outpatient treatment than Hestia rule, given their higher sensitivities.[24] On the contrary, recently, in the HOME-PE randomized trial, Roy et al revealed that the Hestia strategy was equal to the sPESI for selecting low-risk PE patients for home treatment, the rates of 30-day composite adverse outcomes were nearly the same (1.33%vs1.11%).[3] As a growing number of prospective studies aiming home-treatment decision are published, a new and comprehensive meta-analysis is strongly needed to address this issue.

In all enrolled studies, the rate of incidental PE (IPE) is not clarified. IPE is defined as an unsuspected filling defect in the pulmonary arteries seen on CT imaging, the patient is often asymptomatic.[25] IPE is a challenging clinical issue, and there is few data on how to manage these patients. Current validated risk scores (PESI or sPESI) are mainly based on symptomatic PE, thus these rules may not be suit for IPE. Although IPE

Table 1. Characteristics of Included Studies in this Meta-Analysis

Author/ year	Country or region	Research year	Study design	Patient number	Age	Male	Cancer	Risk class proportion		Follow-up time	Composite adverse outcomes	NOS
								low-risk	high-risk			
Zondag 2013	Netherlands	2008-2010	Prospective	530	58.1	54.3%	14.3%	54.2%	45.8%	3 months	RecurrentVTE,major bleeding,all-cause mortality	8
Weeda 2016	USA	2010-2015	Retrospective	573	64.1 ± 16.4	64.9%	44.3%	28.0%	72.0%	30 days	All-cause mortality	7
Vanni 2018	Italy	2014-2017	Prospective	547	76(65-83)	46.1%	39.5%	41.7%	58.3%	30 days	RecurrentVTE,major bleeding,all-cause mortality	8
Quezada 2019	Spain	2015-2017	Prospective	488	69.0 ± 17.1	50.6%	11.3%	27.0%	73.0%	30 days	All-cause mortality	7
Weeda 2019	USA	2010-2014	Retrospective	124	66.2 ± 12.8	50.0%	100.0%	18.5%	81.5%	30 days	All-cause mortality	7
Hendriks 2020	Netherlands	2013-2015	Retrospective	404	59 ± 16	48.3%	13.1%	46.0%	54.0%	3 months	RecurrentVTE,major bleeding,all-cause mortality	8
Li 2021	China	2014-2019	Retrospective	460	63(52-71)	57.1%	100.0%	65.4%	34.6%	30 days	RecurrentVTE,major bleeding,all-cause mortality	8
Roy 2021	Europe	2017-2019	Prospective	984	63.5 ± 17.7	51.7%	37.1%	38.4%	61.6%	3 months	RecurrentVTE,major bleeding,all-cause mortality	8

Data are shown as numbers (%), mean ± standard deviation or median (first quartile–third quartile).

Table 2. Incidence of PE Related Adverse Outcomes Regarding Different Risk Classes.

	All-course mortality			PE-related adverse outcomes		
Author/year	**incidence**	**low-risk class**	**high-risk class**	**incidence**	**low-risk class**	**high-risk class**
Zondag 2013	4.8%	1.0%	9.4%	10.0%	3.7%	18.0%
Weeda 2016	3.7%	0.0%	5.1%	NR	NR	NR
Vanni 2018	8.0%	2.2%	12.2%	9.9%	2.6%	15.4%
Quezada 2019	6.3%	2.3%	7.9%	NR	NR	NR
Weeda 2019	20.2%	13.0%	21.8%	NR	NR	NR
Hendriks 2020	3.9%	1.1%	6.4%	6.9%	3.2%	10.0%
Li 2021	18.0%	7.3%	38.4%	20.2%	8.9%	41.5%
Roy 2021	5.2%	0.5%	8.1%	7.5%	2.9%	10.4%

NR, not reported; PE, pulmonary embolism.

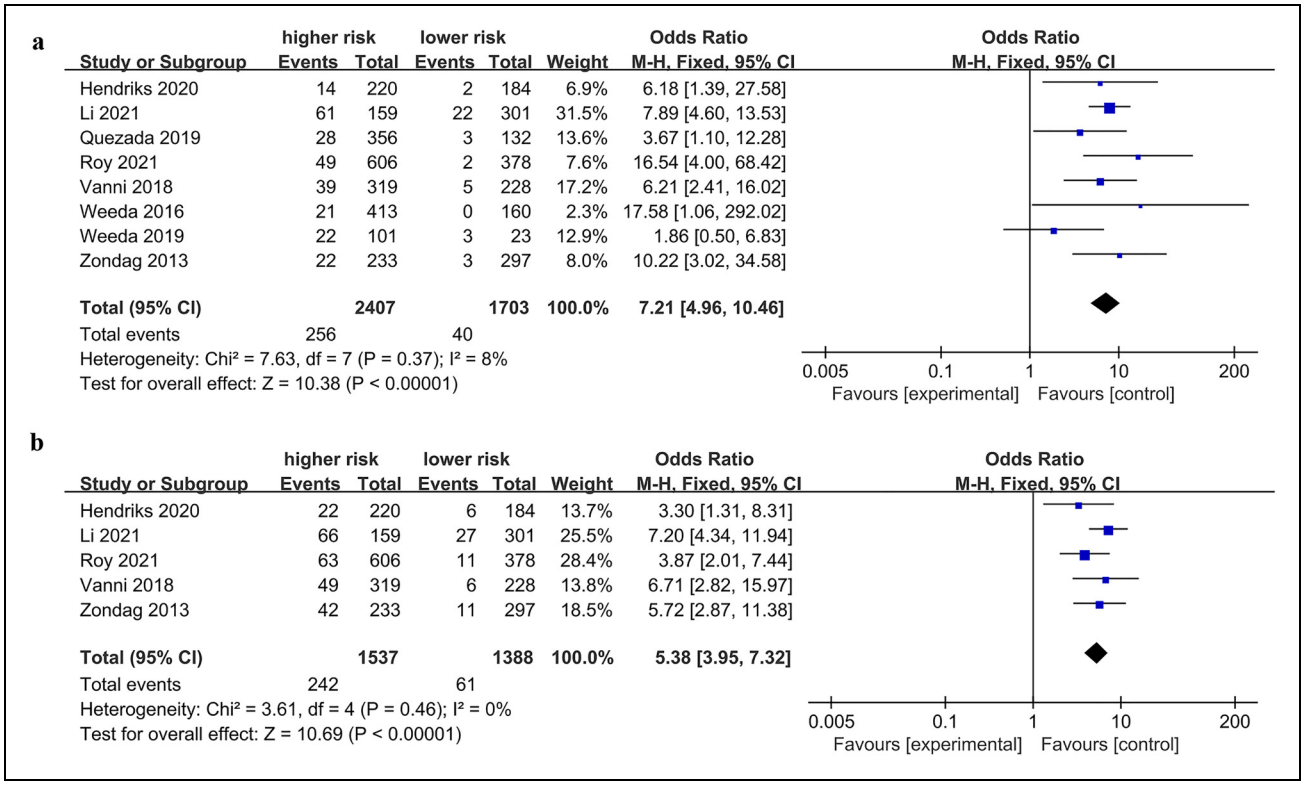

Figure 2. Forrest plots of overall mortality(a) and adverse outcomes(b) with regard to high risk and low risk.

refer to no symptoms, in a study with 70 patients with cancer and an IPE and 137 controls, shortness and fatigue were more common among IPE cases than controls,[26] however, it is difficult to know these symptoms were due to the IPE, or the cancer itself. Thus, specific symptoms may have important implications for risk assessment, and further studies should develop a new prognostic role focus on IPE.

Although Hestia rule exhibits high sensitivity and NPV value in selecting low-risk patients for outpatient treatment, its specificity and PPV does not seems to be satisfying. Generally, a prognostic scale rarely has both excellent sensitivity and specificity, considering the horrible consequences if a PE patient is selected to be at low-risk group for home treatment or discharged early, high sensitivity and NPV are preferable to high specificity. Thus, the clinical practice of the Hestia criteria should be emphasized on recognizing the suitable patients for outpatient therapy on its high sensitivity. Meanwhile, in recent years, some well validated models were specifically developed to identify intermediate-risk PE patients, such as the Bova score,[4] the modified FAST score.[27] One meta-analysis indicated that the Bova score had good prognostic performance in selecting PE patients at higher risk of adverse events.[28] Compared with the Bova score, the modified FAST score, which contained three easy obtained parameters: high-sensitivity troponin T (hsTnT), syncope and tachycardia, seems to provide more accurate performance in identifying normotensive PE patients at high-risk poor outcomes.[29] However, to date,

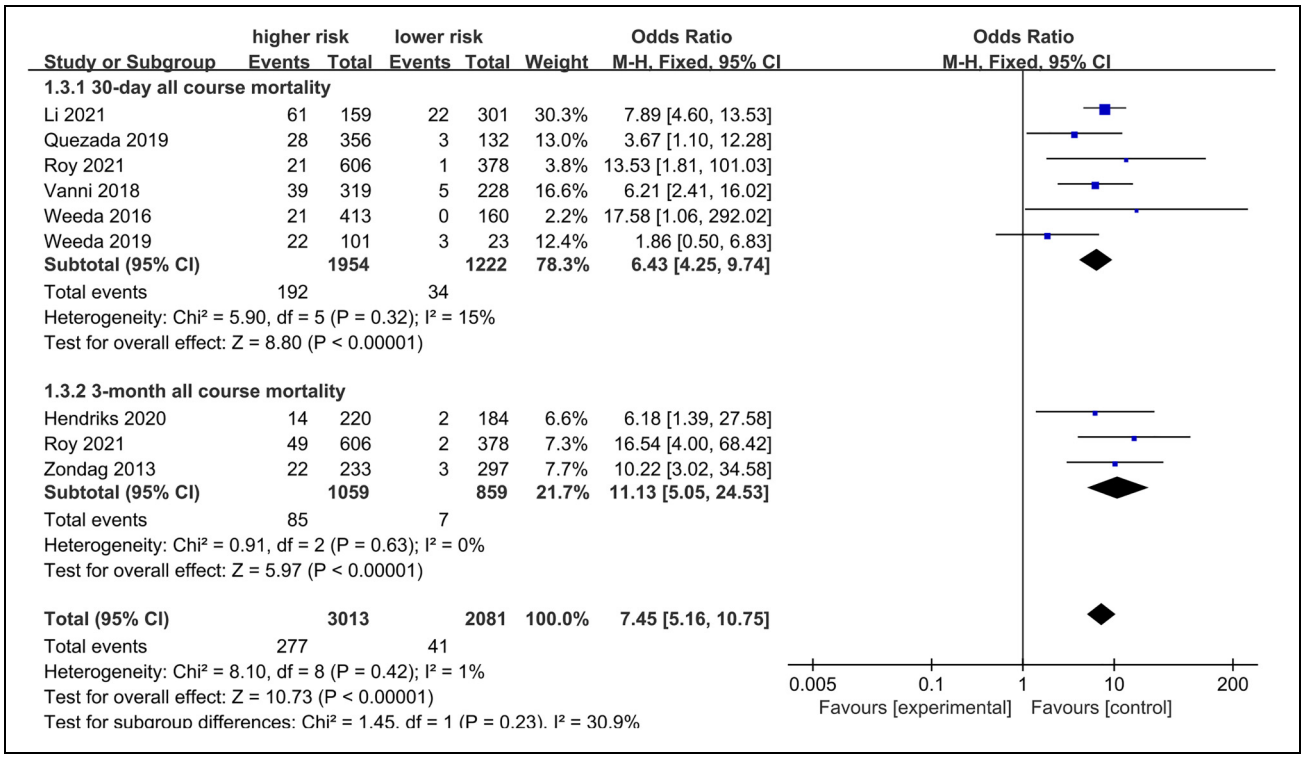

Figure 3. Subgroup analysis for overall mortality (high risk vs low risk) according to follow-up time.

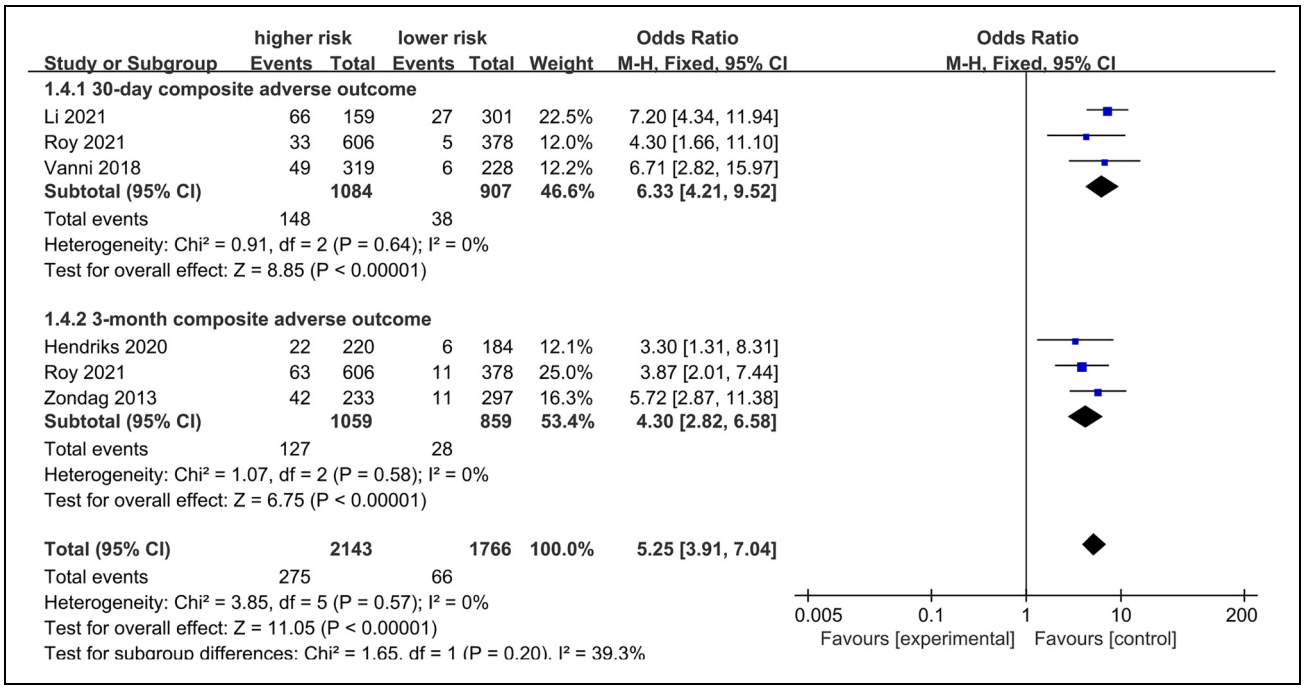

Figure 4. Subgroup analysis for adverse outcomes (high risk vs low risk) according to follow-up time.

both of two models have never been assessed in randomized trials to evaluate their clinical utility for acute PE management, thus it is unclear whether these novel scores can guide the treatment of potentially unstable PE patients.

As accumulating evidence recommend that adding biomarkers or radiological parameters to clinical scores may improve the risk stratification, several studies had been explored this issue to fulfill the Hestia criteria. A randomized trial by den

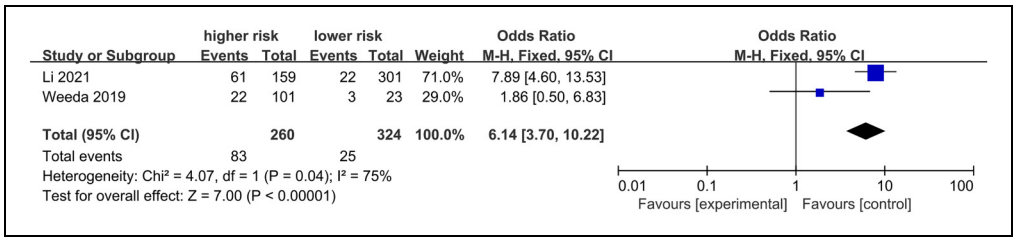

Figure 5. Subgroup analysis for overall mortality (high risk vs low risk) in PE patients with cancer.

Table 3. Prognostic Performance of Hestia Criteria for Predicting All-Course Mortality.

Author/Year	Sensitivity %(95% CI)	Specificity %(95% CI)	PPV %(95% CI)	NPV %(95% CI)	PLR(95% CI)	NLR(95% CI)
Zondag 2013	88.0(75.2-100)	58.2(53.9-62.5)	9.4(5.7-13.2)	98.9(97.8-100)	2.11(1.76-2.51)	0.21(0.07-0.59)
Weeda 2016	100(87.0-100)	29.6(25.8-33.7)	8.0(5.6-11.1)	100(97.1-100)	1.41(1.33-1.48)	NA
Vanni 2018	88.6(79.2-98.0)	44.3(39.9-48.6)	12.2(8.6-15.8)	97.8(95.9-99.7)	1.59(1.39-1.81)	0.25(0.11-0.58)
Quezada 2019	90.3(79.9-100)	28.2(24.1-32.3)	7.8(5.1-10.7)	97.7(95.2-100)	1.26(1.11-1.43)	0.34(0.11-1.01)
Weeda 2019	88.0(75.3-100)	20.2(12.3-28.1)	21.8(13.7-29.8)	86.9(73.2-100)	1.10(0.92-1.31)	0.59(0.19-1.84)
Hendriks 2020	87.5(71.3-100)	46.9(41.9-51.9)	6.3(3.1-9.6)	98.9(97.4-100)	1.64(1.33-2.02)	0.26(0.07-0.98)
Li 2021	73.5(63.9-82.9)	74.0(69.5-78.4)	38.3(30.8-45.9)	92.7(89.7-95.6)	2.82(2.28-3.50)	0.36(0.25-0.51)
Roy 2021	96.1(90.7-100)	40.3(37.1-43.4)	8.1(5.9-10.2)	99.5(98.7-100)	1.61(1.49-1.73)	0.09(0.02-0.38)

PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio; NA, not available.

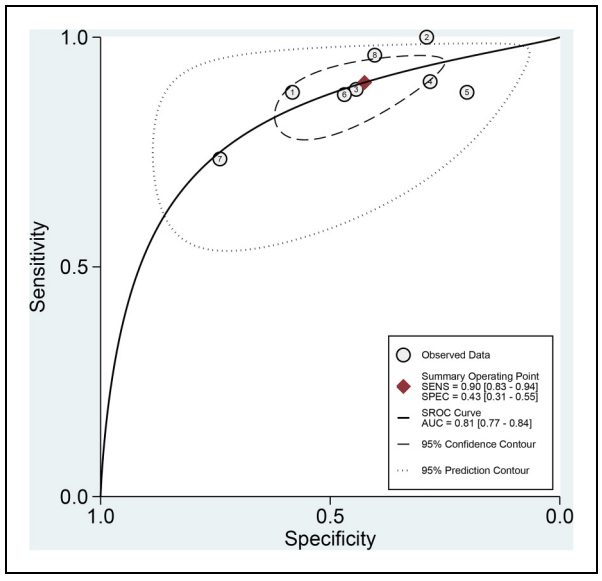

Figure 6. Summary receiver operator characteristic curve (SROC) of the prognostic performance of Hestia criteria for overall mortality. Each circle indicates a study. The red diamond shows the summary operating points.

Exter et al compared the safety of selecting PE patients for outpatient treatment of the Hestia criteria alone with the Hestia criteria combined with N-terminal pro-brain natriuretic peptide (NT-proBNP) testing, however, it showed that the Hestia criteria alone is feasible and related to a low risk of adverse outcomes, and the incremental value of NT-proBNP testing to improve the prognostic power of the Hestia rule is unconclusive due to the low number of patients with elevated NT-proBNP values in low-risk group.[30] What is more, two pos-hoc studies based on one cohort also failed to draw the conclusion that adding whether the right ventricle to left ventricle (RV/LV) diameter ratio >1.0 (sign of RV dysfunction) or the high-sensitive troponin (hsTnT) to the original Hestia model could establish an incremental value for guiding management in low-risk PE patients.[18,19] Current guideline demonstrated that further assessment of cardiac biomarker and RV function could certainly improve risk classification in patients with a sPESI of 0 points,[2] but these studies did not seem to support the same result for the Hestia criteria. Although low proportion of patients with elevated NT-proBNP, TnT or RV/LV ratio may lead to limited statistical power for the performed analyses in these studies, it also reinforced the strong preselection of low-risk group in PE patients by using Hestia criteria.

As Hestia criteria is a checklist designed for identifying PE patients at low risk of mortality, its impact on decision-making for intermediate or high-risk patients still remains unclear, this partly because lacking further stepwise stratification in patients at high-risk group by using Hestia rule. In one study, each Hestia variable was assigned for 1 point, the rate of 30-day mortality rosed as an increasing points of Hestia score were met (0 point 0%, 1point 3.2%, 2 points 9.5%, 3 points 17.0%, >3 points 21.1%).[10]

However, this retrospective observational study was conducted in a single center with limited generalizability and sample size, which may lead to bias of misclassification. Enough designed randomize controlled trials are still needed for assessing prognostic role of Hestia criteria in patients at high-risk group.

To the best of our knowledge, this is the first meta-analysis to comprehensively evaluate the prognostic performance of Hestia criteria. However, there are still some limitations to be discussed. First, we only assessed the performance of the

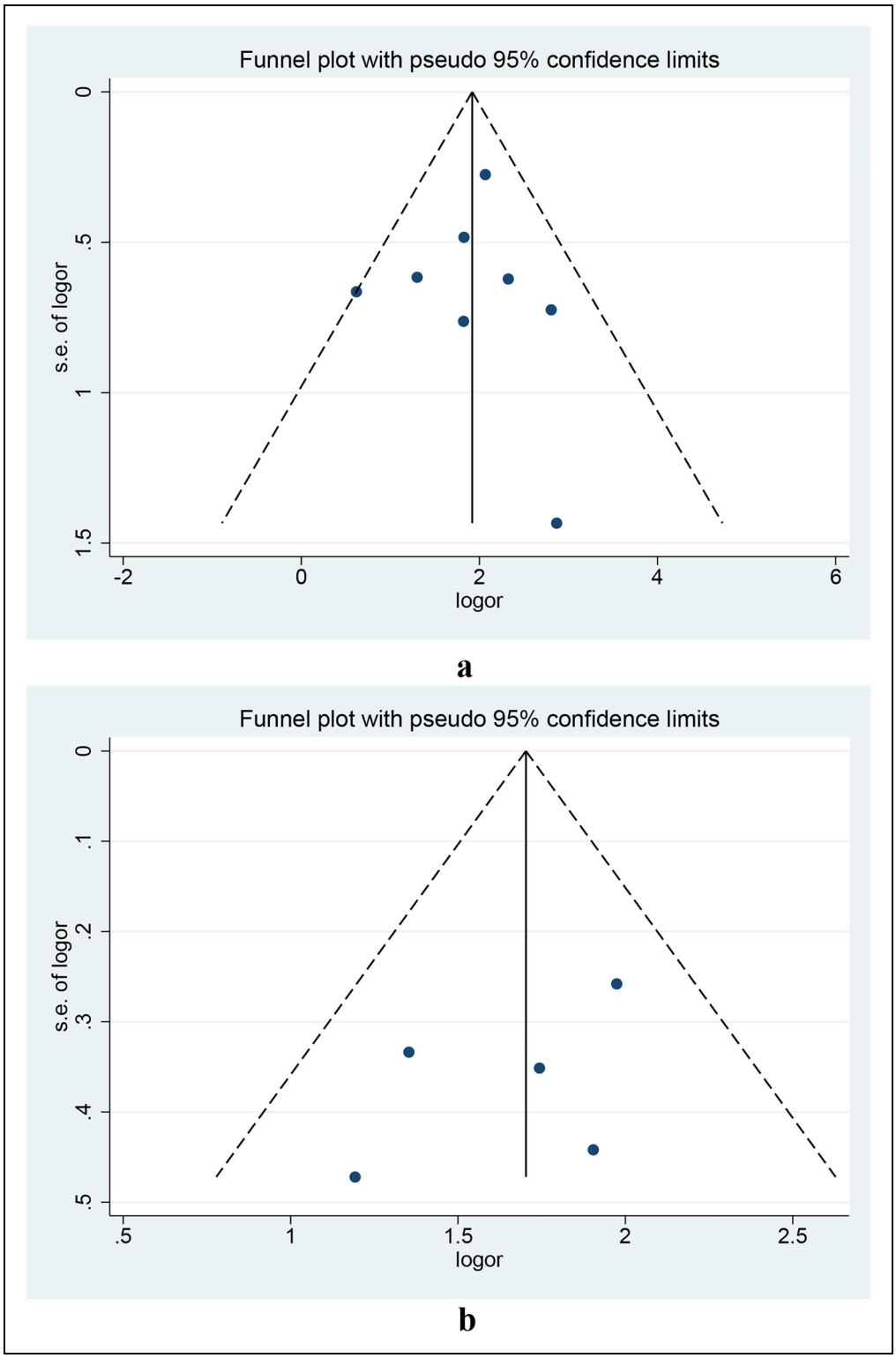

Figure 7. Funnel plots for publication bias: (a) for all-course mortality studies; (b) for adverse outcomes studies.

Hestia criteria, the comparison between the PESI (or sPESI) and the 2019 ESC tools was not conducted. Previous meta-analysis conducted in 2015 indicated that PESI, sPESI, and ESC algorithm appeared to be more reliable for selecting low-risk patients for outpatient treatment over the Hestia rule.[24] However, this meta-analysis only contained one retrospective study with low sample size (496 patients), as a growing number of RCTs based on the Hestia criteria have been published, further comparison study of these prediction rule is needed. Second, due to the original purpose of Hestia criteria,

its role to guide therapeutic decision in intermediate or high-risk patients is relatively limited, since the Hestia rule has been never examined in controlled trials to testify its value in selecting the sickest normotensive PE patients, this score should not be suitable for predicting prognosis of non-low-risk PE patients before further validation. Third, only eight articles were enrolled in the final analysis, two of the included studies were conducted by one author, which may have overlapped information of included patients and bring about bias, what's more, our research only included studies published in English language, which may decrease the lever of evidence and increase the publication bias.

Conclusion

Our meta-analysis demonstrates that the Hestia criteria can effectively identify PE patients at low risk of poor prognosis with high sensitivity and NPV, and it can be suited for use in routine clinical practice, eligible patients can be safely treated at home, with a low rate of complications. However, its value of guiding management of PE patients at intermediate or high-risk group and the prognostic performance compared with other models are still needed to be validated.

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Declaration of Conflicting Interests

All authors have submitted complete ICMJE uniform disclosure forms. The authors declare no conflicts of interest.

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Supplemental Material

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