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Full Length Article

Isolated subsegmental pulmonary embolism identification based on international classification of diseases (ICD)-10 codes and imaging reports

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ABSTRACT

Background: Isolated subsegmental pulmonary embolism (issPE) is a commonly encountered diagnosis. Although the International Classification of Diseases (ICD)-10 codes are used for research, their validity for identifying

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Diagnosis
Sensitivity
Specificity

issPE is unknown. Moreover, issPE diagnosis is challenging, and the findings from radiology reports may conflict with those from expert radiologists.

Methods: Based on prespecified criteria, 1734 medical records of adult patients hospitalized within the Mass General Brigham health system (2016–2021) were selected in three equal groups: (1) patients with principal discharge diagnosis codes for PE, (2) patients with secondary discharge diagnosis codes for PE, and (3) patients with no PE codes. The accuracy of ICD-10 codes for issPE was verified by two independent physicians and weighted by total hospitalizations. In a randomly selected sample of 70 patients, the accuracy of initial radiology reports was determined through a blinded re-evaluation by two expert radiologists.

Results: In weighted estimates, ICD-10 codes in primary or secondary discharge positions, compared with chart reviews, showed a low sensitivity (7.0 %) and positive predictive value (25.2 %). Evaluation by two expert radiologists noted that initial radiology reports were sensitive (97.1 %) for issPE but had a low specificity (40.0 %). Two (3.6 %) out of 55 patients with initial issPE reports did not have PE, while 19 (34.5 %) had more proximal PE.

Conclusions: ICD-10 codes for issPE have poor sensitivity and positive predictive value and should not be used for research or quality improvement. Radiology reports for issPE may be inaccurate regarding the location or, less often, the presence of PE.

1. Introduction

Isolated subsegmental pulmonary embolism (issPE), pulmonary embolism (PE) that is restricted to small subsegmental vessels [1], has been more commonly diagnosed in the past two decades [2–4]. This is due to the widespread use of computed tomography (CT) for cancer surveillance as well as extensive utilization of multidetector CT pulmonary angiography (CTPA) [5], which has enhanced visualization of the peripheral pulmonary vasculature, particularly subsegmental pulmonary arteries [6]. Increased issPE diagnosis is thought, at least in part, to account for the rise in the number of PEs identified in recent years compared with the 1990s and early 2000s [7]. Accurate issPE detection is crucial as it can impact the clinical management of patients and provide prognostic insights [8,9]. Distinguishing patients with issPE properly from those without any PE can aid in appropriate management (e.g., anticoagulation therapy) and follow-up of these patients [10], as it has been demonstrated that patients with issPE are at risk of PE recurrence [11,12]. Moreover, differentiating issPE from more proximal PE may have critical consequences in terms of management and prognosis. Most data indicate that issPE, in the majority of instances, does not result in acute fatal events, which is different from more proximal PE [11].

For research purposes, efficient ways are needed to accurately identify patients with PE. Enrollment of patients with PE in large prospective registries is resource-intensive and costly [13]. In this regard, the International Classification of Diseases 10th revision (ICD-10) codes have been used to identify patients within electronic health record (EHR) data or administrative claims databases to conduct epidemiological studies and analyze disease incidence or outcome trends [14,15]. However, the validity of ICD-10 codes for identifying patients with issPE has not been comprehensively studied [13].

Furthermore, the diagnosis of issPE is contentious, with much uncertainty regarding its identification in imaging [8,16,17]. Although widespread use of multidetector CTPA as well as CT scans for cancer surveillance has contributed to the increasing identification of issPE [8], initial diagnoses may be negated upon re-examination of the images since breathing motion artifacts and endobronchial mucus plugs may be mistaken for thromboembolic material in subsegmental pulmonary arteries [18–20].

We sought to assess the accuracy of issPE ICD-10 codes in the primary or secondary discharge diagnosis positions for hospitalized patients using a manual review of records by two independent physicians who used pre-specified criteria and reviewed the medical notes and radiology reports. Two independent expert radiologists also reviewed a selected sample of CT images to validate the initial diagnoses.

2. Methods

2.1. Design

The PE-EHR+ study, funded by the American Heart Association (AHA) and Vascular InterVentional Advances (VIVA) Physicians, aimed to validate efficient tools for identifying patients with PE from EHR data [13]. Details about the study design have been described previously [13]. We used data from the Mass General Brigham (MGB) health system, the largest health system in Massachusetts, from January 2016 to December 2021. The MGB health system comprises two large academic medical centers, Massachusetts General Hospital and Brigham and Women's Hospital. In addition, it includes several community hospitals and medical centers (such as Newton-Wellesley Hospital, Brigham and Women's Faulkner Hospital, Salem Hospital, and others) [21]. Overall, in the PE-EHR+ study, records from 1734 hospitalized adult patients aged ≥ 18 years were randomly selected from the pool of patients based on ICD-10 codes for PE (Table S1): (1) 578 with principal discharge diagnosis codes for PE, (2) 578 with secondary discharge diagnosis codes for PE and without principal discharge diagnosis codes for PE, and (3) 578 without any codes for PE, either in principal or secondary position. The sample size calculation considerations for the PE-EHR+ study have been outlined previously [13]. The current study, although a pre-specified investigation from PE-EHR+, did not have a formal sample size estimation but included all patients from the MGB health system within the PE-EHR+ study. Up to 12 ICD-10 diagnosis codes (one principal and up to 11 secondary codes) could be recorded per hospitalization [22].

2.2. ICD-10 codes for issPE

ICD-10 codes for issPE are I26.93 (single subsegmental PE without acute cor pulmonale) and I26.94 (multiple subsegmental PE without acute cor pulmonale) [13]. These codes imply a single filling defect in the subsegmental vessels and multiple subsegmental defects, respectively, without involvement in more proximal vessels, such as segmental arteries. The accuracy of these codes for issPE detection was assessed by two independent physicians who reviewed discharge summaries, daily notes, and radiology reports (A.B. and C.D.K.). All the discrepancies were resolved by discussion with the senior investigator (B.B.). For the chart reviews, issPE was defined as reports of subsegmental filling defects consistent with the diagnosis of PE in radiology reports without the involvement of segmental, lobar, or central pulmonary arteries identified in other imaging studies during that index hospitalization [13]. We determined the sensitivity, specificity, positive predictive value, and negative predictive value of issPE ICD-10 discharge diagnosis codes in principal, secondary, and principal-or-secondary discharge positions to identify patients with issPE within EHR data compared with the chart reviews.

To assess the positive and negative predictive values, which are dependent on the condition's prevalence [23], weighted estimates were determined by considering the total number of hospitalizations at MGB hospitals in each of the three groups. From January 1st, 2016, to December 31st, 2021, there were 4878 patients with principal discharge diagnosis codes for PE, 3224 patients with secondary discharge diagnosis codes for PE, and 373,540 patients with no codes for PE at the MGB health system [13].

Codes for issPE (I26.93 and I26.94) were added to the ICD-10 list of codes in October 2019. As such, we conducted a sensitivity analysis to determine the accuracy of the issPE ICD-10 codes in the subset of patients hospitalized after October 1st, 2019. It should be noted that ICD-10 discharge diagnosis codes replaced ICD-9 codes on October 1st, 2015 [24]. As a result, most recent investigations from claims databases use ICD-10 discharge diagnosis codes from 2016 and after to identify their patient population of interest (e.g., patients with PE) [25–27]. Even though the dedicated codes for issPE were introduced on October 1st, 2019, some investigations based on ICD-10 discharge diagnosis codes for issPE had patient recruitment dates that preceded October 2019 [28]. As such, we evaluated the validity of issPE identification from January 1st, 2016, to December 31st, 2021, and conducted a sensitivity analysis to determine the accuracy of the issPE ICD-10 codes in the subset of patients hospitalized after October 1st, 2019.

2.3. Imaging review by two expert radiologists

Given the challenges in the diagnosis of issPE, we decided to pursue independent validation of the diagnosis in a subgroup of patients. We evaluated the accuracy of initial radiology reports compared with the reference reports of two expert radiologists for issPE detection. Previously, we had pre-specified that the radiological ascertainment phase of the study would include 50 to 100 patients [13]. In this regard, 70 patients were randomly selected from the cohort of patients with multi-detector CT angiographic examinations according to the following

criteria: 55 patients with chart reviews indicating issPE, 8 patients with chart reviews indicating PE but without issPE, and 7 patients with CTPA during hospitalization but without PE according to the manual review of the records. Two expert radiologists (A.A. and A.H.) with over ten years of experience in assessing CT angiograms independently reviewed the imaging of these 70 cases, blinded to the initial reports. Any discrepancies between the two radiologists were resolved by internal discussion. The accuracy of the initial radiology reports was ascertained with reference to the consensus findings of the two expert radiologists.

2.4. Statistical analysis

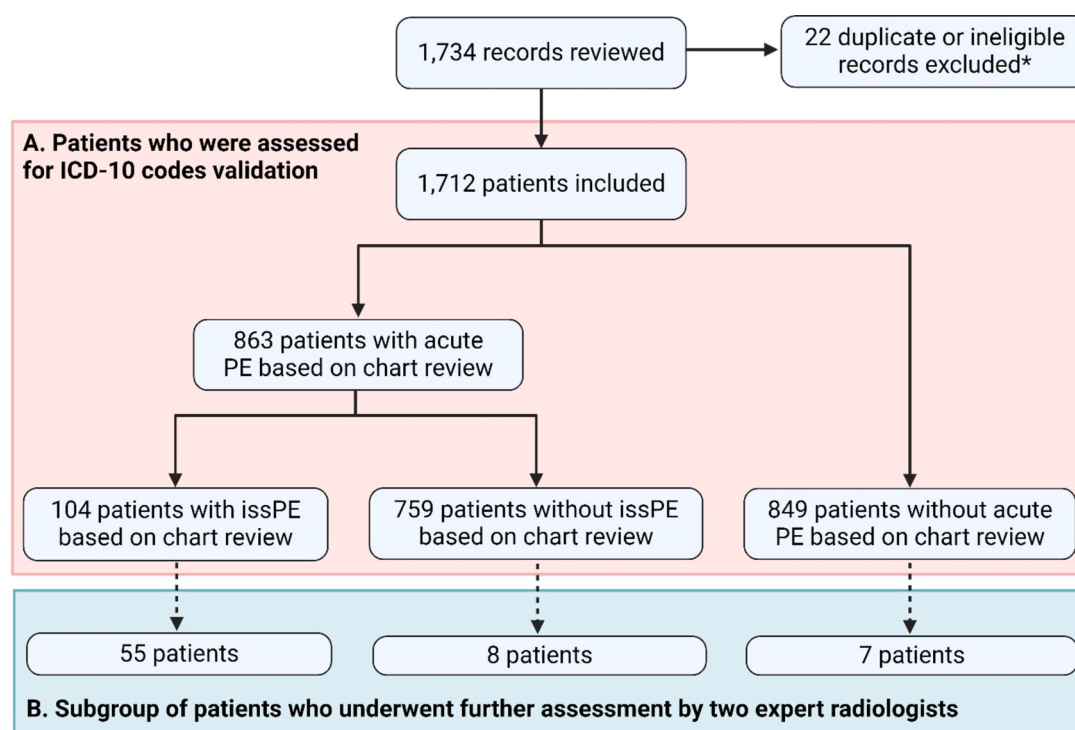
Continuous and categorical variables were reported as mean $\pm$ standard deviation and counts (percentages), respectively. Accuracy metrics (i.e., sensitivity, specificity, positive predictive value, and negative predictive value) with their corresponding 95 % confidence intervals (CIs) were calculated according to their standard epidemiological definitions using MedCalc [23,29].

3. Results

Of 1734 records reviewed, 22 duplicate or ineligible records were excluded, and 1712 patients were included in the main analyses (age: 60.6 ± 17.8 years, 52.3 % female, Fig. 1A, Table S2). Based on chart review, 863 (50.4 %) patients were diagnosed with acute PE during the index hospitalization, of whom 104 (6.1 %) had issPE.

3.1. Accuracy of ICD-10 codes for issPE according to chart review

Among 104 patients with issPE based on chart review, only 15 (14.4 %) had ICD-10 discharge diagnosis codes for issPE: 4 with principal codes and 11 with secondary codes for issPE (Fig. 2A). Of the remaining 89 patients who had issPE per manual review of the records but no specific issPE ICD-10 codes, 88 patients had other ICD-10 codes for PE

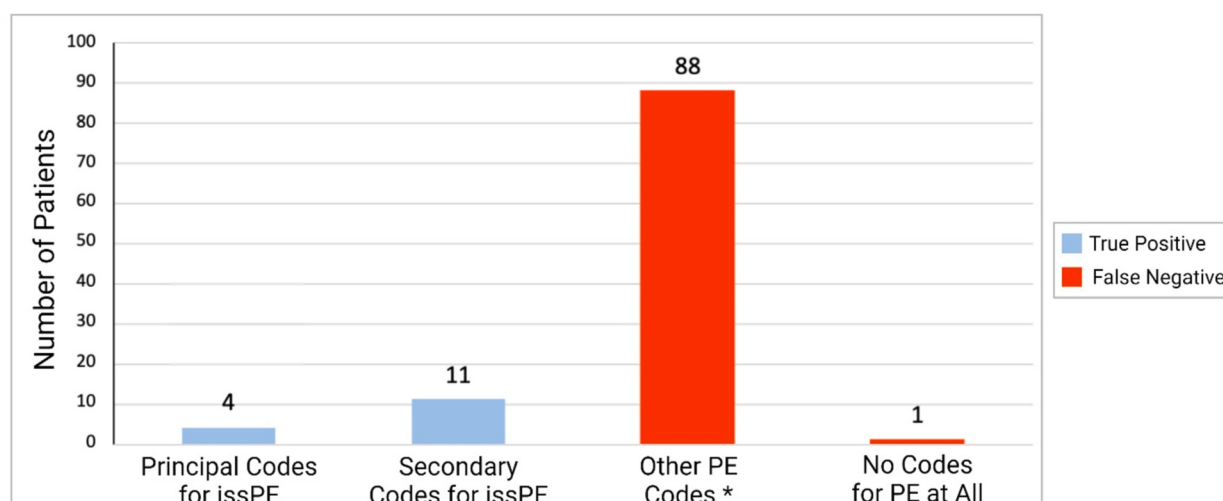


issPE, isolated subsegmental PE; PE, pulmonary embolism.

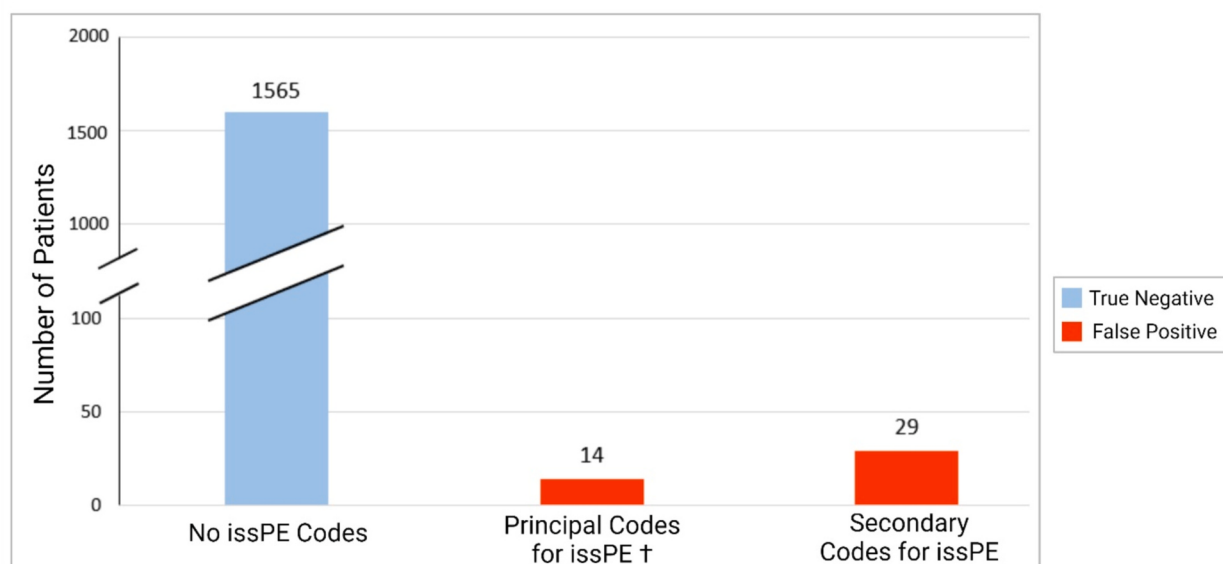
*Ineligible patients were those with septic emboli.

Fig. 1. Study flow diagram for (A) patients who were assessed for ICD-10 codes validation and (B) the subgroup of patients for whom two expert radiologists reviewed the imaging.

A. 104 patients with issPE based on chart review



B. 1,608 patients without issPE based on chart review



issPE, isolated subsegmental PE; PE, pulmonary embolism.

* Other PE codes excluding issPE codes (I26.93 and I26.94); 86 patients had I26.99 code which is for "other pulmonary embolism without acute cor pulmonale".

† 8 patients with codes for issPE with sub-segmental and more proximal PE, 4 with codes for issPE with segmental PE, and 2 with codes for issPE without any PE at all.

Fig. 2. Reasons for (A) false negative and (B) false positive findings of ICD-10 codes for issPE detection according to the reference manual chart review in the unweighted sample.

that were not specific to issPE, including 86 with I26.99 code, which is used to classify "other PE without acute cor pulmonale". One patient with issPE did not have any ICD-10 discharge codes for PE. Furthermore, among 1608 patients without issPE based on chart review, 43 had discharge diagnosis codes for issPE: 14 with principal codes and 29 with secondary codes for issPE (Fig. 2B).

In the unweighted analysis of 1712 patients, principal-or-secondary discharge diagnosis codes collectively reached a sensitivity of 14.4 % (95 % CI 8.3 %–22.7 %) and specificity of 97.3 % (95 % CI 96.4 %–98.1 %) (Fig. 3A). Restricting the analysis to the timeframe from October 1st, 2019, until the end of 2021 yielded 679 patients. For the principal-or-secondary discharge diagnosis codes, the unweighted estimates

revealed a slightly higher sensitivity of 33.3 % (95 % CI 20.0 %–49.0 %) and a similar specificity of 93.2 % (95 % CI 91.0 %–95.1 %).

In the weighted estimates, ICD-10 codes in primary or secondary discharge positions showed a low sensitivity (7.0 %, 95 % CI 5.7 %–8.5 %) and positive predictive value (25.2 %, 95 % CI 21.2 %–29.7 %) (Fig. 3B). Findings were largely similar when principal discharge diagnosis codes and secondary discharge diagnosis codes were analyzed separately (Table S3).

A. ICD-10 codes vs. manual chart review in the unweighted sample

	01/2016 - 12/2021 (n = 1,712)		10/2019 - 12/2021* (n = 679)	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Principal discharge diagnosis	3.8	99.1	8.9	97.8
Secondary discharge diagnosis	10.6	98.2	24.4	95.4
Principal or secondary discharge diagnosis	14.4	97.3	33.3	93.2

B. ICD-10 codes vs. manual chart review in the weighted estimates (n = 381,642)

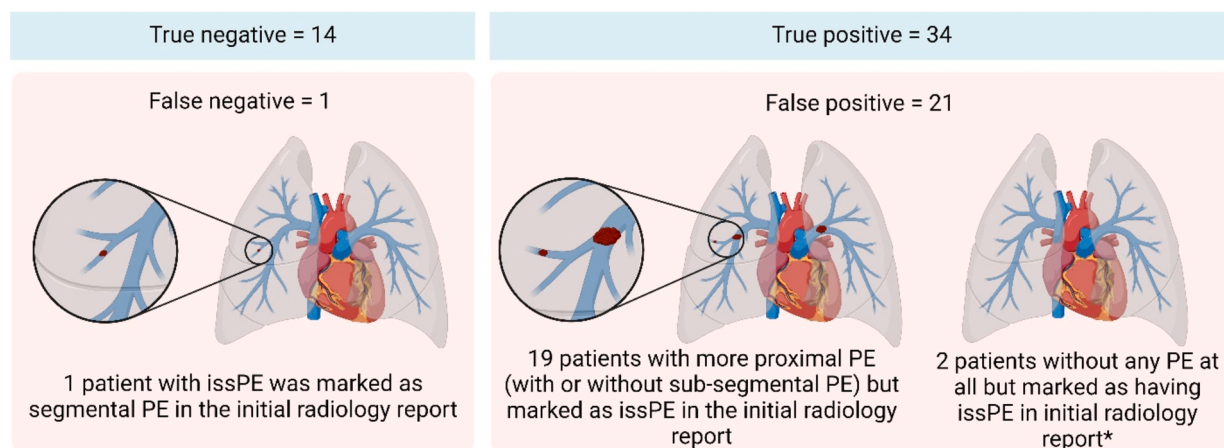
	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Principal discharge diagnosis	2.5	99.9	22.1	99.7
Secondary discharge diagnosis	4.5	99.9	27.3	99.7
Principal or secondary discharge diagnosis	7.0	99.9	25.2	99.7

0% 50% 100%

ICD, International Classification of Diseases; issPE, isolated subsegmental pulmonary embolism.

*Dedicated codes for issPE (I26.93 and I26.94) were introduced in October 2019.

Fig. 3. Accuracy of ICD-10 codes for issPE detection according to the reference manual chart review in the (A) unweighted sample and (B) weighted estimates.



issPE, isolated subsegmental PE; PE, pulmonary embolism.

*Due to the presence of an artifact.

Fig. 4. Accuracy of initial radiology reports compared with imaging review by two expert radiologists for issPE detection (n = 70).

3.2. Accuracy of initial radiology reports for issPE according to two expert radiologists

Among the 70 patients (mean age 61.8 ± 17.6 and 50 % female) randomly selected to be reviewed by two expert radiologists (Fig. 1B), 55 had initial issPE diagnosis per review of original records. Of these 55 patients, independent expert assessments agreed with the diagnosis in 34 (61.8 %) cases and identified more proximal PE in 19 (34.5 %) patients, while in 2 (3.6 %) patients there was no PE at all (Fig. 4). Both of these patients were prescribed anticoagulation following initial issPE reports. Among the 15 patients without initial issPE reports, 14 were confirmed to be negative for issPE. One patient with segmental PE in the initial report was shown to have issPE following expert review (Fig. 4). The initial imaging reports compared with the reference radiological ascertainment by two expert radiologists exhibited high sensitivity (97.1 %, 95 % CI 85.1 %–99.9 %) but low specificity (40.0 %, 95 % CI 23.9 %–57.9 %) for issPE detection.

4. Discussion

Our findings revealed that principal-or-secondary ICD-10 discharge diagnosis codes demonstrate low sensitivity (7.0 %) and positive predictive value (25.2 %) for detecting issPE, according to chart reviews. These results were consistent after restricting the analysis to the period ICD-10 codes for issPE were introduced (October 2019); sensitivity rose to 33.3 % but remained suboptimal. These results argue against future research studies relying on ICD-10 codes to identify issPE. Furthermore, initial radiology reports, compared with imaging review by expert radiologists, were sensitive (97.1 %) for issPE but had a high false positive rate and a low specificity (40.0 %). While in most cases, the expert radiologists agreed that there was a PE, in 2 out of 55 patients with initial issPE diagnosis, the expert read did not indicate PE, which may alter the management course. In fact, both cases in routine care had received anticoagulation for PE.

The predominant use of the I26.99 code (86 out of 104), which indicates “other PE without acute cor pulmonale”, instead of specific codes for single- and multi-vessel issPE (i.e., I26.93 and I26.94) contributed to the low sensitivity of ICD-10 codes for the detection of issPE. Similar trends were observed for the period after the introduction of specific issPE codes (October 2019), as the I26.99 code was used for 30 out of 45 patients with issPE. Even in recent years and after the publication of standardized criteria, the diagnosis of issPE remains challenging, with poor interobserver agreement among radiologists. Consequently, the accuracy of specific ICD-10 codes for issPE is poor as well. It is possible that these difficulties have shifted clinicians and coders toward using the more convenient code of I26.99. While the I26.99 code may be convenient for clinicians and billers to use for a broad range of patients with PE, it fails to provide accurate information related to the anatomic location of PE or its severity.

Only a few studies have previously addressed the diagnostic accuracy of ICD codes for identifying issPE. In a recent study of 970 randomly selected healthcare encounters with a multidetector CTPA by Johnson et al., ICD-10 codes similarly resulted in a low sensitivity (8.3 %) for issPE detection compared with the reference standard manual chart reviews [28]. However, unlike our findings, the investigators reported a higher positive predictive value of 77.8 % for ICD-10 codes [28]. This discrepancy could be due to the high prevalence of issPE (8.7 %) in their study sample, which was comprised of patients with CTPA [28]. Unlike our study, the results were not adjusted for true issPE prevalence in a pool of hospitalized patients [28]. The issPE prevalence in our weighted estimate was 0.3 %. The prevalence of acute PE among hospitalized patients is nearly 1.0 % [30], and issPE comprises a subset of these patients [1]. Therefore, our study shows that low positive predictive values can be expected for ICD-10 codes to detect issPE among hospitalized patients.

The radiological assessment phase of our study underscored the

challenging nature of issPE diagnosis. Among 55 patients with initial issPE reports, 21 (38.2 %) were negative for issPE following imaging assessment by two expert radiologists, and 19 of these false positive cases were related to those with more proximal PE. There are 26 proximal pulmonary arteries (one pulmonary trunk, two main pulmonary arteries, five lobar arteries, and 18 segmental arteries), but hundreds of subsegmental arteries [1], which further contributes to the complexity of issPE diagnosis. Similar results were shown by Pena et al., who investigated the diagnostic accuracy of 70 patients with clinical suspicion of PE who underwent multidetector CTPA and were initially diagnosed with issPE [18]. Based on re-examination by expert thoracic radiologists, the investigators noted that 34 (48.6 %) were falsely designated as having issPE, among whom 26 had segmental PE [18]. Such errors in identifying issPE may impact how short- and long-term outcomes are attributed to issPE both in routine clinical care and in clinical research studies that include issPE among the outcome measures, such as studies of patients with cancer [8,12].

More importantly, imaging artifacts (due to cardiac pulsation or breathing, poor contrast opacification, or endobronchial mucus plugs) may be misinterpreted as minor intravascular filling defects in subsegmental vessels and resemble thromboembolic material [1,31]. Prior investigations indicated that 10 % to 60 % of CTPAs initially diagnosed with issPE might be ultimately interpreted as negative for PE following reevaluation by experienced thoracic radiologists [18–20,31] (Table 1). In the current study, 3.6 % (2 out of 55) of patients with initial issPE reports were verified to be negative for any PE after radiological ascertainment. While we cannot be certain about the reasons for this observation, it could be that experienced radiologists who work in large academic health systems are more experienced in detecting issPE. It should be noted that both of these patients received anticoagulation upon the initial issPE report. Considering these complexities in issPE diagnosis, the 2019 European Society of Cardiology guideline recommended that additional imaging confirmation may be considered in patients with isolated subsegmental filling defects [9]. Moreover, due to the possibility of false positive results in CTPA reports of issPE, the guideline suggested that CTPAs indicating issPE diagnosis should be corroborated by expert radiologists [9]. On the other hand, we noted that initial radiology reports have high sensitivity (97.1 %) for issPE, with only one false negative case labeled as segmental instead of issPE. Future studies can also determine if automated first or confirmatory reads by artificial intelligence tools can efficiently improve the accuracy of initial reads from radiologists related to issPE and be incorporated into clinical workflow [32].

Considering the above issues, the two key implications of this study are that (1) the specific codes for issPE are not reliable for clinical research or quality improvement related to issPE and “(2) even for research using EHR data and radiology reports, inaccuracies will likely occur unless the original reads are verified by expert radiologists using standardized criteria. Even if clinical trials focus on issPE, independent adjudication by expert radiologists brings more confidence in the results by distinguishing true issPE from more proximal PE missed in the original read or from false positive cases that do not have PE at all [33].

Some limitations of this study merit consideration. The data for the PE-EHR+ study were derived from several centers in the United States. Variations may exist in issPE code utilization in other health systems in other centers in the United States and worldwide. However, previous investigations from other centers in the United States similarly noted the extensive use of the I26.99 code rather than specific sub-categories of codes such as those for issPE [28]. Moreover, we did not employ natural language processing tools to detect patients with issPE from EHR data [34]. Although these tools may have the potential to improve issPE case selection from EHR data, many large databases in the US and internationally do not include radiology reports or discharge summaries required for natural language processing algorithms and instead rely on ICD codes.

In conclusion, ICD-10 discharge diagnosis codes for issPE in primary

Table 1
Studies investigating the accuracy of initial issPE diagnosis on multidetector CTPAs^a.

Study	Design	Patient population	Comparison	Main findings	Comments
Castañer et al., 2022 [20]	Single-center, prospective, observational study	3839 adult patients who underwent multidetector CTPA for evaluation of clinically suspected acute PE	- Accuracy of initial issPE diagnosis on multidetector CTPA vs. - Reevaluation by a team of experienced thoracic radiologists based on recommended criteria by the ACCP guideline ^b [35]	- Of 3839 patients, 1021 had an initial PE diagnosis, 98 had an initial single or multiple issPE diagnosis, and 59 had an initial single issPE diagnosis. - Among 59 patients with an initial diagnosis of single issPE, 38 (64.4 %) were true positive, and 21 (35.6 %) were false positive (negative for PE). - The most common reasons for false positive cases were (1) the effect of partial volume in vascular bifurcation zones (7 out of 21), (2) flow alteration by distal pathological conditions (5 out of 21), and artifacts due to respiratory motion (5 out of 21).	- The study did not evaluate the patients without an initial issPE diagnosis. Therefore, the sensitivity and specificity of initial issPE reports could not be determined.
Miller et al., 2015 [19]	Multicenter, retrospective, observational study	728 multidetector CTPAs performed for PE evaluation and deemed definite or probable for PE in the initial reports (177 with initial subsegmental vascular defects)	- Accuracy of subsegmental vascular defect diagnosis by community hospital radiologists vs. - Reevaluation by a team of academic thoracic radiologists	- Of 177 initial subsegmental vascular defects identified by community radiologists, 27 (15.3 %) were false positive, and 48 (27.1 %) were deemed indeterminate after review by subspecialty thoracic radiologists. - The most common reason for false positive findings in subsegmental arteries was motion artifacts (16 out of 27). - The probability of a false-positive diagnosis and indeterminate examinations progressively increased with the more peripheral locations of the lesion.	- The study did not evaluate the CTPAs without an initial PE diagnosis. Therefore, the sensitivity and specificity of initial subsegmental PE reports could not be determined.
Hutchinson et al., 2015 [31]	Single-center, retrospective, observational study	174 patients with multidetector CTPAs performed for PE evaluation and deemed positive for PE in the initial reports	- Accuracy of initial issPE diagnosis by radiologists vs. - Reevaluation by three expert chest radiologists	- Of 174 patients, 32 had issPE in the initial reports (including 24 with single issPE). - Among 32 patients with an initial diagnosis of issPE, 19 (59.4 %) were negative for PE after reviewing by expert radiologists. - Among 24 patients with an initial diagnosis of single issPE, 16 (66.7 %) were negative for PE after reviewing by expert radiologists. - The most common cause of diagnostic difficulty was breathing motion artifact.	- The study did not evaluate the patients without an initial issPE diagnosis. Therefore, the sensitivity and specificity of initial issPE reports could not be determined.
Pena et al., 2012 [18]	Multicenter, retrospective, observational study	70 patients with clinical suspicion of PE who underwent multidetector CTPA and were initially diagnosed with issPE (4 normal CTPAs and 2 CTPAs with index segmental filling defect were added for control.)	- Accuracy of index diagnosis of issPE by radiologists vs. - Reevaluation by expert thoracic radiologists	- Of 70 patients with index diagnosis of issPE, 36 (51.4 %) were true positive, and 34 (48.6 %) were false positive. - The expert radiologist agreed with the number of filling defects (i.e., single vs. multiple issPE) in 83 % (30/36; 95 % CI, 67–94 %) of the cases. - Of 34 false positive cases, 8 had no PE at all, and 26 were re-interpreted to have segmental PE after expert review. Therefore, 11.4 % (8/70) of patients with initial issPE reports did not have PE at all.	- Similar to our study, this study showed that most false-positive findings for issPE were related to those with more proximal PE.
Stein et al., 2006 [36] (PIOPED II)	Multicenter, prospective, observational study	824 adult patients who underwent multidetector CTPA for clinical suspicion of acute PE	- Accuracy of multidetector CTPA vs. - Composite reference standard of ventilation-perfusion lung scanning, pulmonary angiography, venous	- Out of 8 patients with a positive diagnosis for subsegmental PE based on multidetector CTPA, there were 2 true positive and 6 false positive cases according to the	- The study reported the accuracy of multidetector CTPA for subsegmental PE against a composite reference standard of multiple imaging modalities and clinical follow-up rather

(continued on next page)

Table 1 (continued)

Study	Design	Patient population	Comparison	Main findings	Comments
			ultrasonography, and clinical follow-up for diagnosis of acute PE	reference standard (positive predictive value = 25 %).	than reevaluation by expert radiologists.

ACCP, American College of Chest Physicians; CI, confidence interval; CTPA, computed tomographic pulmonary angiography; issPE, isolated subsegmental pulmonary embolism; PE, pulmonary embolism.

^a In this table, we summarized the studies with at least five patients with initial issPE diagnosis.

^b The ACCP guidelines have suggested the following features favoring true positive results for issPE [35,37]: (1) CTPA with high certainty and good opacification for the distal pulmonary arteries, (2) multiple intraluminal defects, (3) more proximal and larger defects in subsegmental arteries, (4) defects seen on more than one image, (5) defects surrounded by contrast rather than appearing to be adherent to the pulmonary artery walls, (6) defects seen on more than one projection, (7) symptomatic PE rather than incidental PE, (8) high clinical pretest probability for PE, and (9) elevated D-dimer, particularly marked elevation without other explanation.

or secondary positions demonstrate poor sensitivity and positive predictive value. This is compounded by the fact that the diagnosis of issPE remains challenging in routine practice, which can impact the patients’ clinical management and their prognostic evaluation. There was a high rate of false-positive findings due to discrepancies between the initial radiology reports and independent imaging review by two expert radiologists, which, in many cases, suggested more proximal PE and, in two cases, refuted the presence of PE, including issPE. Based on our findings, implementing ICD-10 codes to identify patients with issPE in research studies is not recommended. The initial issPE radiology reports may be inaccurate regarding the location or, less often, the presence of PE.

CRedit authorship contribution statement

Sina Rashedi: Writing – review & editing, Writing – original draft, Investigation, Formal analysis. **Antoine Bejjani:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Andetta R. Hunsaker:** Writing – review & editing, Validation. **Ayaz Aghayev:** Writing – review & editing, Methodology, Investigation. **Candrika D. Khairani:** Writing – review & editing, Validation, Methodology, Investigation. **Bridget McGonagle:** Writing – review & editing. **Ying-Chih Lo:** Formal analysis. **Shiwani Mahajan:** Writing – review & editing, Methodology, Investigation. **César Caraballo:** Writing – review & editing, Methodology, Investigation. **Jose Victor Jimenez:** Writing – review & editing, Methodology, Investigation. **Darsiya Krishnathan:** Writing – review & editing. **Mehrdad Zarghami:** Writing – review & editing. **Manuel Monreal:** Writing – review & editing, Methodology, Investigation. **Stefano Barco:** Writing – review & editing, Methodology, Investigation. **Eric A. Secemsky:** Writing – review & editing, Methodology, Investigation. **Frederikus A. Klok:** Writing – review & editing, Methodology, Investigation. **Alfonso Muriel:** Writing – review & editing, Methodology. **Mohamad A. Hussain:** Writing – review & editing, Methodology, Investigation. **Abena Appah-Sampong:** Writing – review & editing, Methodology, Investigation. **Farbod N. Rahaghi:** Writing – review & editing, Validation, Methodology. **Parham Sadeghipour:** Writing – review & editing. **Zhenqiu Lin:** Writing – review & editing. **Hamid Mojibian:** Writing – review & editing. **Sanjay Aneja:** Writing – review & editing. **Stavros Konstantinides:** Writing – review & editing, Methodology. **Samuel Z. Goldhaber:** Writing – review & editing, Methodology, Investigation. **Liqin Wang:** Writing – review & editing, Methodology. **Li Zhou:** Writing – review & editing. **David Jimenez:** Writing – review & editing, Methodology. **Harlan M. Krumholz:** Writing – review & editing, Supervision, Methodology, Investigation. **Gregory Piazza:** Writing – review & editing, Supervision, Methodology. **Behnood Bikdeli:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization.

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Declaration of competing interest

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All figures are created with [BioRender.com](#).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.thromres.2025.109271>.

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