Accuracy of the Diagnosis of Subsegmental Pulmonary Embolism Among General Radiologists

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ABSTRACT

Diagnosis and treatment of subsegmental pulmonary embolism (SSPE) are challenging. Contrary to segmental pulmonary emboli (PE), little is known about the accuracy of the diagnosis of SSPE. We aimed to assess the accuracy of SSPE in our retrospective cohort study. Patients with isolated SSPE were included. Concurrent segmental PE or deep venous thrombosis (DVT) were considered an exclusion criteria. Another radiologist reviewed each CTA. A total of 43 patients with SSPE were identified. Forty patients (93%) received therapeutic anticoagulation. The average duration of anticoagulation therapy was four months. Another radiologist's review of the CTA on admission revealed a discordant diagnosis: 13 out of 43 (30%) cases were reported negative for SSPE. One case was reported for segmental PE. As a conclusion, the accuracy of the diagnosis of SSPE is low as the discordance rate by different radiologists is high. More studies are needed to establish the diagnosis and guide treatment of SSPE.

KEYWORDS: Subsegmental Pulmonary Emboli (SSPE); Over diagnosis; Pulmonary Emboli (PE)

INTRODUCTION

SSPE affects the distal divisions of pulmonary arterial branches.[1,2] SSPE can be isolated or concurrent with segmental (lobar) PE, symptomatic or incidental, and may or may not be associated with thrombosis in other sites.[3-6]

Introduction of modern computed tomography (CT) scanners with very high sensitivity has led to detecting peripheral filling defects,[1] termed as SSPE; their clinical significance is, however, highly debatable and under discussion. While CT angiography (CTA) has been shown to be highly sensitive and specific when pretest clinical diagnostic tools are used, as high as 83% and 96% respectively,[2,7] it is less accurate in patients with low pretest probability, with false positive rates as high as 42%.[8] In the era of new CT scanners with more detector rows, rates of SSPE diagnosis have almost doubled to 9% in comparison to older studies.[7] The clinical significance of these findings is subject to debate.

Whether these peripheral filling defects truly represent a true blood clot or not is questionable. That is perhaps one of reasons behind the European Society of Cardiology (ESC) 2019 guidelines for SSPE, which suggest further imaging to confirm PE when isolated subsegmental filling defects are seen on CTA.[9]

The current chest guidelines suggest clinical surveillance over anticoagulation for patients with isolated SSPE and have low risk of recurrent venous thromboembolism (VTE), while anticoagulation is suggested over clinical surveillance for patients with high risk of recurrent VTE.[10] Many clinicians still initiate anticoagulation therapy on the basis of a positive result,[11] regardless of pretest probability,[12] and even in isolated SSPE,[13] which could lead to unnecessary treatment and potentially avoidable adverse events.[14]

As of now, the management of SSPE remain highly dependent upon clinicians' judgement and assessment of the disease severity and clinical presentation. In our study, we aim to assess the accuracy of SSPE diagnosis, present our institutional practice of treating isolated SSPE and discuss the deviation from the available guidelines.

MATERIALS & METHODS

This study is a retrospective matched cohort, conducted at a 300+ bed community hospital in Rhode Island between August 2018 to August 2021. The IRB committee approved the protocol.

We identified patients who were diagnosed with isolated SSPE by thoracic CTA through our radiology department. SSPE were detected as an incidental finding (unsuspected) or as a part of diagnostic evaluation for patients with clinical symptoms concerning for pulmonary embolism, including any of the following: shortness of breath, hypoxia (oxygen saturation <92% at room air), pleuritic chest pain, dizziness, elevated d-dimer, unexplained tachycardia, hemoptysis, or hypotension (<90/60).

An electronic medical record query was performed to identify all the patients meeting inclusion criteria. The patients were included if they are > 18 years old, had a chest imaging that confirmed isolated SSPE (either as incidental finding or symptomatic). Patients with segmental PE or thrombosis at other sites were excluded from the study.

The average age of subjects was calculated. The clinical variables evaluated included age, gender, race, reason for chest CTA (incidental versus symptomatic), previous venous thromboembolic (VTE) events, previous anticoagulation, disposition (admitted versus discharged from the emergency department), offered anticoagulation versus observed, type of anticoagulation if offered, average duration of anticoagulation, repeat chest CTA within 3-6 months of diagnosis, outcomes/adverse events, and recurrent VTE. Risk of VTE recurrence at diagnosis was identified and categorized into low or high risk as per CHEST guidelines as below.[10]

As per CHEST guidelines, any of the following was considered a risk factor for recurrent or progressive VTE:

1. Are hospitalized or have reduced mobility for another reason
2. Have active cancer (particularly if metastatic or being treated with chemotherapy)
3. Have no reversible risk factor for VTE such as recent surgery
4. Are pregnant

Patients with confirmed SSPE were either admitted or discharged from the emergency department (ED), offered anticoagulation or observed. All chest CT reports were reviewed by a different senior general radiologist (Head of ED radiology department at a university hospital) later to identify discordance rate between different radiologists regarding the diagnosis of SSPE and assess the potential for overdiagnosis. An established diagnostic criteria for SSPE by a panel of expert thoracic radiologists was followed on the second review; a contrast defect in a subsegmental artery, that is, the first arterial branch division of any segmental artery independent of artery diameter, visible in at least two subsequent axial slices, using a computed tomography scanner with a desired maximum collimator width of ≤1 mm.[4]

Figure 1. Baseline characteristics for patients with SSPE.

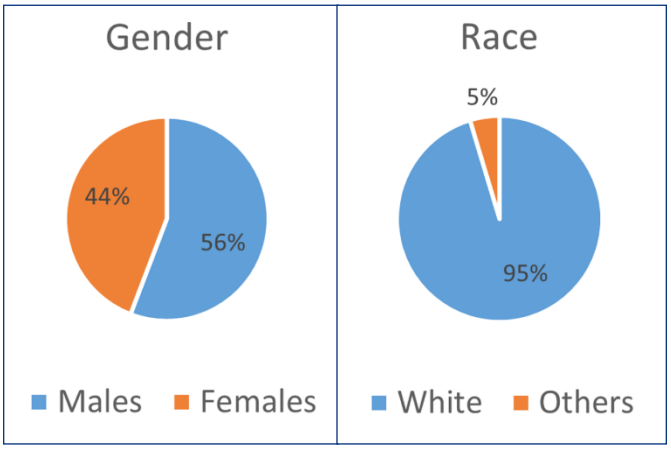
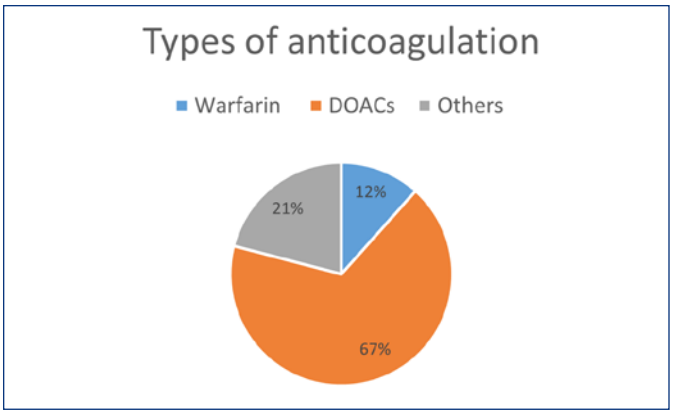


Figure 2. Represents types of anticoagulation that was offered. Majority of patients (67%) were treated with direct oral anticoagulation therapy (DOACs).



RESULTS

During the three-year period, a total of 120 patients were detected to have SSPE. After reviewing chest CT reports, 69 patients were excluded because of concurrent diagnosis of segmental PE, and another 8 patients for concurrent diagnosis of DVT. A total of 43 patients were ultimately identified to have isolated SSPE and were included in this study. Incidence rate of coinciding DVT with SSPE was 15% (8 out of 51).

The average age for patients with SSPE was 67.1 years, 24 out of 43 (56%) were males, 95% of patients included in the study were White, as represented in **Figure 1**.

Forty-two (42) out of 43 (97%) chest CTAs were performed for symptomatic patients. 2 out of 43 (5%) had previous thromboembolic events in the past. Four (4) out of 43 (9%) were already on anticoagulation before the diagnosis of SSPE. According to CHEST guidelines for risk of VTE recurrence at time of diagnosis, 35 (81%) patients were at low risk of VTE recurrence.

After the diagnosis of SSPE was made, 40 out of 43 (93%) were offered anticoagulation for management of pulmonary embolism as represented in **Figure 2**. Only three out of 43 (7%) were discharged from the ED, the rest were admitted for inpatient management. Average duration of treatment with anticoagulation was four months. These clinical findings are shown in **Table 1**.

In 33% of the patients, chest CTA was repeated within 3–6 months to confirm resolution of SSPE before making the decision to stop anticoagulation. Five (5) out of 43 (11%) died during the same admission when SSPE diagnoses was made, but death was unrelated to pulmonary embolism. Recurrent VTE events were reported in 2 out of 43 (5%), both were treated with anticoagulation after diagnosis of SSPE but were non-adherent to anticoagulation at time of recurrence. **Figure 3** represents total number of outcomes/adverse events.

After a second review of CT scans by a different radiologist, 13 out of 43 (30%) were read as negative for SSPE, 1 out of 43 (2.5%) was read as segmental and subsegmental PE, the rest confirmed SSPE concordant with the first read. **Figure 4** represents thoracic CT read by a different radiologist.

Table 1. Clinical findings in the study

Clinical variable	No. (%)
Reason for chest CTA	*Symptomatic 42 (97%) Incidental 1 (3%)
Previous VTE	2 (5%)
Previous anticoagulation	4 (9%)
Risk of VTE recurrence according to CHEST Guidelines (low Vs high)	35 (81%) low risk 8 (19%) high risk
Disposition	Admitted 40 (93%) Discharged 3 (7%)
Management	Offered anticoagulation 40 (93%) Observed 3 (7%)
Average duration of anticoagulation	4 months
Repeat chest CTA within 3–6 months	14 (33%)

* Symptomatic: shortness of breath, hypoxia (oxygen saturation <92% at room air), pleuritic chest pain, dizziness, elevated d-dimer, unexplained tachycardia, hemoptysis, or hypotension (<90/60)
** PESI score: low risk I, II. High risk III-V.

Figure 3. Represents total number of outcomes/adverse events. As mentioned, deaths were not related to SSPE.

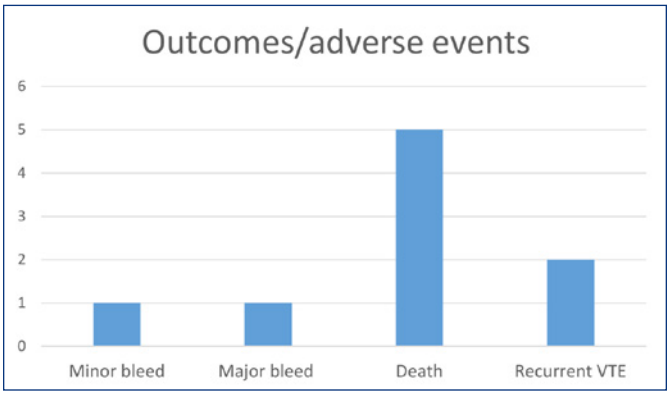
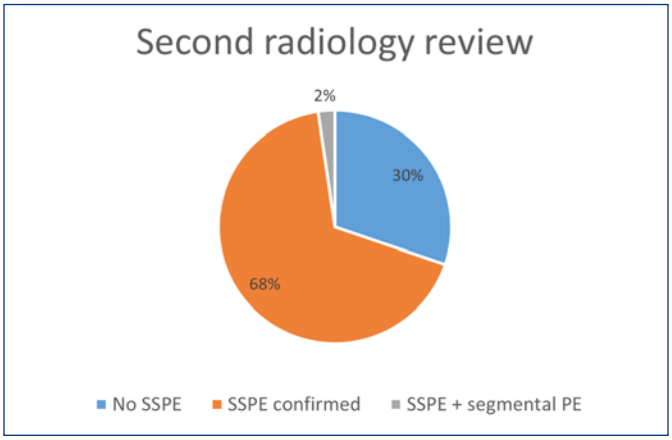


Figure 4. Represents chest CTA reports after a second review by a different radiologist.



DISCUSSION

The introduction of modern multi-detector CT scanners allow for better visualization of peripheral vessels, thereby increasing the rates of small filings defects detection.[1,15] The prevalence of SSPE diagnosis from available literature is 3–5%.[2,16] As opposed to segmental PE, the potential for overdiagnosis adds more complexity to the management of SSPE.[17-21] SSPE is commonly encountered as an in incidental finding in patients with cancer while undergoing routine chest CT imaging as part of staging, follow-up or surveillance imaging. [22]

Many pulmonologists and thoracic radiologists, however, suggest that majority of filling defects in the subsegmental arteries are not necessarily clinically significant and may not truly exist in the first place. That is concordant with the current CHEST guidelines,[10] which support and suggest clinical surveillance over anticoagulation for patients with isolated SSPE and have low risk of recurrent venous thromboembolism because the abnormalities are small and likely will resolve without anticoagulation therapy. In addition to the CHEST guidelines, the ESC 2019 guidelines suggest further imaging when isolated subsegmental filling defects are seen on CTA to check for concurrent thromboemboli which, if present, might be a strong indication and provide more reasoning behind anticoagulation decision.[9]

In our study, despite eligibility for clinical surveillance in 80% of patients at time of SSPE diagnosis per CHEST guidelines, 90% of patients were anticoagulated regardless of risk of VTE recurrence. This deviation from the current guidelines was seen in our institution, and in similar studies but to a lesser extent 50–60%.[23] In our study, almost every patient with a diagnosis of SSPE was treated with anticoagulation, perhaps due to concerns of cardiopulmonary compromise, emboli extension/progression, recurrent VTE, or fatal outcomes from untreated emboli. Furthermore, the CHEST guidelines are labeled as "weak", low-certainty evidence, which probably impacted the generalizability and applicability of these recommendations in clinical practice.

Discordance in SSPE diagnosis is not uncommon. Concordant to the literature, our institutional experience also revealed 30% risk of overdiagnosis, potentially leading to unnecessary treatment with blood thinners at the expense of financial and physical toxicity. Other studies reported false positive SSPE diagnosis with 9% discordance rate.[24] This might be in part explained by the high level of expertise necessary for diagnosis. Indeed, it has been demonstrated that the sensitivity of SSPE diagnosis is higher among thoracic radiologists than among non-thoracic radiologists.[25-27] In our study, after a second review of imaging, 30% discordance rate was mostly attributed to lack visibility of filling defect in at least two subsequent axial slices.

The magnitude of treatment in incidental, asymptomatic cases remain undefined. Mortality rate in untreated SSPE patients has been reported to be around 3% in some

studies in comparison to treated patients 2.1%.[28] This finding is contradictory to a recent large multicentric prospective cohort study (Le Gal et al)[19] and a large systematic review[28] showing no fatal recurrent VTE in untreated SSPE patients[19] that is concordant to our study, which showed no recurrence amongst untreated group, while 5% recurrence was reported in the treated group, which is attributed to non-adherence to anticoagulation or after discontinuation. In the same study (Le Gal et al), amongst untreated patients, the incidence of recurrent VTE was higher and more seen in multifocal versus unifocal SSPE, perhaps suggesting a rational approach to treat patients with multifocal SSPE. The likelihood of concurrent DVT with SSPE was low, 7.1%, in comparison to concurrent diagnosis of segmental PE, 41.8%. In our institution, the incidence of concurrent DVT with SSPE was 15%, which is slightly higher than what is reported in the literature. Concurrent diagnosis of DVT or segmental PE with SSPE, if present, can be a useful information to decide on anticoagulation; this is also supported in the ESC 2019 guidelines which suggest further imaging when isolated subsegmental filling defects are seen on CTA.

As a conclusion, in our study, we highlight the potential for SSPE overdiagnosis and deviation SSPE management from the available guidelines. We suggest reviewing the current CHEST and ESC 2019 guidelines when treating patients with SSPE to differentiate between low vs high risk SSPE.

Limitations to our study include retrospective analysis, unmeasured variables and control selection bias. Furthermore, our study is a single institutional observation with a small sample size. Large prospective studies are needed.

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Acknowledgment/Disclosures

We certify that all authors are listed. All authors have a) contributed substantively to the conception, design, or analysis and interpretation of the data, b) contributed substantively to the drafting of the manuscript or critical revision for important intellectual content, c) given final approval of the version to be published, and d) agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

We certify that all the authors have no conflict of interest to declare and have no affiliations with or involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript.

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