Subsegmental Pulmonary Embolism

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Abstract

Subsegmental pulmonary embolism (SSPE) is increasingly diagnosed with the growing use and technological advancements of multidetector computed tomography pulmonary angiography. Its diagnosis is challenging, and some presumed SSPE may actually represent imaging artifacts. Indirect evidence and results from small observational studies suggest that SSPE may be more benign than more proximal pulmonary embolism, and may thus not always require treatment. Therefore, guidelines suggest to consider a management strategy without anticoagulation in selected patients with SSPE at low risk of recurrent venous thromboembolism (VTE), in whom proximal deep vein thrombosis is excluded. Recently, a large prospective study among low-risk patients with SSPE who were left untreated showed a higher VTE recurrence risk than initially deemed acceptable by the investigators, and thus was prematurely interrupted after recruitment of 97% of the target population. However, the risk–benefit ratio of anticoagulation for low-risk patients with SSPE remains unclear, and results from randomized trials are needed to answer the question about their optimal management.

Keywords

- pulmonary embolism
- subsegmental pulmonary embolism
- overdiagnosis
- overtreatment
- anticoagulation

Zusammenfassung

Aufgrund der zunehmenden Anwendung und technischen Weiterentwicklung von CT-Angiographien steigt die Inzidenz der subsegmentalen Lungenembolien (SSLE). Ihre Diagnose kann herausfordernd sein, denn die Unterscheidung zwischen wirklichen Perfusionsdefiziten und Artefakten ist nicht immer klar. Indirekte Evidenz und Resultate von kleinen Beobachtungsstudien sind hinweisend auf einen gutartigeren Verlauf von SSLE im Vergleich zu proximaleren LE und werfen die Frage auf, ob SSLE immer einer Therapie bedürfen. Richtlinien empfehlen die Evaluation einer Behandlungsstrategie ohne Antikoagulation bei ausgewählten Patienten mit SSLE und einem tiefen Risiko für Thromboemboliezidive nach Ausschluss einer tiefen Beinvenenthrombose. Kürzlich wurden die Resultate der bisher grössten prospektiven Studie zu Tiefrisikopatienten mit SSLE ohne Antikoagulationstherapie publiziert: das Risiko für Thromboemboliezidive war höher als initial von den Autoren als akzeptabel definiert, weshalb die Studie nach Einschluss von 97% der geplanten Studienpopulation vorzeitig abgebrochen wurde. Das Nutzen-Risiko-Verhältnis einer Antikoagulationstherapie bei Tiefrisikopatienten mit SSLE bleibt jedoch weiterhin unklar, und es braucht Resultate von randomisierten Studien, um die optimale Behandlung dieser Patienten zu definieren.

Schlüsselwörter

- Lungenembolie
- Subsegmentale Lungenembolie
- Überdiagnose
- Übertherapie
- Antikoagulation

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Introduction

Pulmonary embolism (PE) affects up to 121 in 100,000 individuals each year,[1,2] and is responsible for 5 to 8 per 1,000 deaths.[3] The clinical spectrum of PE is highly variable, ranging from asymptomatic incidental findings to life-threatening massive PE with severe hemodynamic compromise and sudden death.[4] Clinical presentation and outcomes depend on patient factors,[5] as well as on clot burden and location of PE.[6] While the importance of timely diagnosis and anticoagulation treatment of proximal PE is undisputed, controversy exists about the clinical significance of emboli confined to the subsegmental pulmonary arteries,[7] the so-called subsegmental pulmonary embolism (SSPE), calling into question the longstanding paradigm that all PEs require anticoagulation treatment.

Evidence for Overdiagnosis of Pulmonary Embolism

In the era of the first randomized trial demonstrating a survival benefit of anticoagulation for the treatment of PE in 1960, diagnosis of PE was based on findings from physical examination, conventional radiography, and electrocardiography.[8] Over time, diagnostic strategies have substantially evolved, and the diagnosis of PE has been revolutionized with the introduction of multidetector computed tomography pulmonary angiography (CTPA) in 1998, which largely replaced other imaging modalities for PE diagnosis.[9] Compared with ventilation-perfusion (V/Q) scanning or single-detector CTPA, multidetector CTPA offers a higher resolution and enables visualization of even the small peripheral subsegmental pulmonary vessels, thus increasing the sensitivity for diagnosing PE.[9,10] The widespread dissemination and increasing use of CTPA was paralleled with an increase in the incidence of PE.[11,12] For instance, a study using nationwide data from the United States showed an 80% increase in the incidence of PE diagnoses in the 8 years following the introduction of multidetector CTPA.[12] Despite the near doubling in PE diagnoses between the years 1998 and 2006, age-adjusted death from PE remained stable.[12] Although these findings may suggest an improvement in early diagnosis and treatment of PE, the efficacy of PE treatment has not substantially changed in this era.[9,11] Furthermore, the increasing incidence of PE occurred despite several initiatives to improve compliance with appropriate thromboprophylactic measures in patients at risk of PE,[13,14] and was not associated with an increase in known venous thromboembolism (VTE) risk factors.[11] These observations suggest that advanced imaging techniques have been a major driver of the observed increase in incidence of PE. Given that mortality did not substantially change during this time period, the rising PE incidence may suggest the possibility of overdiagnosis of clinically nonsignificant PE, including SSPE, using more sensitive diagnostic modalities such as CTPA. This observation is worrisome because presumed anticoagulation-related complications, such as gastrointestinal and intracranial hemorrhage or secondary thrombocytopenia, have simultaneously increased after the introduction of CTPA.[12]

Additional indirect evidence for potential overdiagnosis of clinically irrelevant PE arises from a randomized clinical trial that compared diagnostic strategies using multidetector CTPA or V/Q scanning for ruling out acute PE.[15] Compared with patients randomized to V/Q scanning, the incidence of PE was higher in the CTPA group (14.2 vs. 19.2%; absolute difference of 5%, 95% confidence interval: 1.1–8.9%). Despite the higher proportion of patients who were left untreated after initial exclusion of PE in the group of patients undergoing V/Q scanning, the risk of symptomatic VTE during the 3-month follow-up period did not significantly differ between the two groups.[15] These findings suggest that the additional cases of PE diagnosed on CTPA were on average more benign or potentially false-positive results.

The Challenge of Diagnosing Subsegmental Pulmonary Embolism: True Findings or Artifacts?

The increase in PE incidence related to the exploding use of CTPA coincided with an increase in the incidence of SSPE.[16] Advancements in multidetector CTPA technology with optimization of image resolution further contribute to increasing rates of SSPE diagnoses.[17,18] Based on a systematic review of 22 prospective studies and randomized trials of patients who underwent CTPA for suspected PE, the proportion of SSPE among all PE diagnoses was 7.1% with 4-detector CTPA, while the proportion increased to 15% with 64-detector CTPA.[18]

However, the actual incidence of SSPE is unknown, because diagnosis of SSPE is challenging, and some minor intraluminal filling defects in the subsegmental pulmonary arteries may represent imaging artifacts rather than true thrombotic material (e.g., due to poor contrast opacification, motion artifacts from cardiac pulsation or breathing, or attenuation artifacts).[19,20] For example, the positive predictive value of CTPA to diagnose SSPE was only 25% when compared with a composite reference standard in the PIOPED II study.[21] The diagnostic difficulty is further reflected by studies showing poor agreement between radiologists for diagnosing SSPE. While interobserver agreement was very good for the detection of proximal PE (mean kappa = 0.83), it was much lower for SSPE (mean kappa = 0.38) in a study examining the interobserver variability of radiologists in the interpretation of CTPA images.[22] Of CTPAs with an initial diagnosis of SSPE, 10 to 50% are reinterpreted as negative for any evidence of PE by experienced thoracic radiologists,[23–25] with particularly high false-positive rates for single isolated SSPE.[19,24] On the other hand, there is a risk of misdiagnosing more proximal PE: in a retrospective study, up to 37% of SSPE diagnoses were reinterpreted as segmental PE after review by expert thoracic radiologists.[25] Given that there are 26 proximal pulmonary vessels (1 pulmonary trunk, 2 main pulmonary arteries, 5 lobar, and 18 segmental arteries) but hundreds of subsegmental arteries, it is not surprising that accuracy of radiological SSPE diagnosis is suboptimal.[23]

The high risk of inaccurate SSPE diagnosis underlines the importance of optimal image quality and reading of CTPA images by experienced radiologists. As the clinical presentation of PE (including SSPE) is nonspecific,[4] integration of clinical information may only be of limited value to support the diagnosis of SSPE. A relevant proportion of patients with SSPE is asymptomatic,[26] although the exact estimate is unknown. When compared with those with more proximal PE, patients with SSPE do not seem to significantly differ in terms of risk factors as well as clinical signs and symptoms.[27,28] Concomitant proximal deep vein thrombosis (DVT) is detected in up to 7% of patients with SSPE,[29,30] and thus seems to be less frequent than in proximal PE, where the prevalence is ~40%.[4]

The difficulty of diagnosing SSPE has been acknowledged by current guidelines. The 2019 European Society of Cardiology (ESC) guidelines suggest consideration of further imaging tests to confirm PE in cases of subsegmental filling defects, and advert that SSPE diagnoses should be confirmed by an experienced thoracic radiologist.[31] The 2021 CHEST guidelines provide a list of imaging and clinical findings that suggest true-positive SSPE (►Table 1). A panel of thoracic radiologists and VTE specialists recently published specific recommendations on criteria for diagnosing SSPE based on a Delphi analysis.[32] The radiologic criteria to establish SSPE were defined as "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."[32] In addition, the experts emphasized the importance of evaluating the CTPA quality to determine the possibility for reliable diagnosis of SSPE.[32]

The Clinical Significance of Subsegmental Pulmonary Embolism Is Unclear…

Based on evidence suggesting that SSPE may be a more benign form of PE that is increasingly diagnosed by more sensitive diagnostic tests, or that at least some SSPE may represent false-positive findings, the clinical significance of SSPE—and therefore the need for treatment—has been disputed.[9,13,33] Further fueling this controversy, some experts have postulated that SSPE might be the result of a physiologic filter function of the lung aimed at preventing small clots from entering the systemic circulation rather a sign of disease, and that SSPE might therefore occur even in healthy people without significant clinical consequences.[34,35] An angiographic study in the 1960s investigating the natural history of acute pulmonary embolism in individuals without coexisting cardiopulmonary disease showed that even sizeable emboli can resolve spontaneously within a few weeks.[36] Furthermore, a study on perfusion lung scans showed that perfusion defects occurred in 16% of healthy volunteers.[37]

Table 1 Imaging and clinical findings suggesting true subsegmental pulmonary embolism[31]

Findings
CTPA of high certainty with good opacification of distal arteries
Multiple intraluminal defects
Defects involving larger/more proximal subsegmental arteries
Defects seen on >1 image and in >1 projection
Defects surrounded by contrast (i.e., nonadherent to vessel wall)
Presence of symptoms
High clinical pre-test probability for pulmonary embolism
Elevated D-dimer, especially in case of a marked increase and no alternative explanation

Abbreviation: CTPA, computed tomography pulmonary angiography.

… and Risks and Benefits of Anticoagulation Treatment Need to Be Carefully Weighted

The uncertainty about the clinical relevance of SSPE translates into the question whether SSPE should be treated. Anticoagulation for at least 3 months is the standard treatment of VTE[31,38]; it is highly effective, and reduces the risk of recurrent VTE by more than 80%.[39] This benefit comes at the cost of an increase in the risk of bleeding, with an annual risk of major bleeding ranging from 1% to >4% depending on anticoagulation type and patient factors.[40–42] Major bleeding is associated with a case-fatality of 8 to 10%,[41] which is two- to threefold higher than case fatality from recurrent VTE,[43] and can result in long-term disability if bleeding is intracranial or intraocular. Non-major bleeding events, which occur even more often, can lead to reduced quality of life, distress, need for additional health care visits and interventions, and substantial societal costs.[44–46]

In view of the burden and potential consequences of bleeding complications, careful weighing of the risks and benefits of anticoagulation is required. This is particularly true for thromboembolic events of unclear clinical relevance. For example, distal DVTs may represent a more benign form of VTE, as they do not extend to the proximal veins in the majority of cases and are associated with a lower risk of recurrent VTE and death compared with their proximal counterparts.[47,48] As suggested by non-randomized and randomized studies, selected patients with distal DVT may not necessarily benefit from anticoagulation.[48,49] In patients with distal DVT at low risk of recurrence, the randomized CACTUS trial found no significant difference in the risk of VTE recurrence after 6 weeks, but a higher risk of clinically relevant bleeding in patients anticoagulated with nadroparin compared with those in the placebo group, although the study was terminated early due to recruitment difficulties.[49] Overall, an individualized approach is suggested for treatment of distal DVT, with anticoagulation treatment of patients at high risk of extension or severe symptoms, and clinical surveillance with serial imaging (or alternatively, shorter treatment, or treatment at lower anticoagulation dose)[50] in low-risk patients without severe symptoms.[38,50]

To Anticoagulate or Not to Anticoagulate?

Similar controversy exists about the risks and benefits of anticoagulation treatment in patients with SSPE. Several studies investigating outcomes of SSPE patients receiving anticoagulation treatment suggest that the risk for recurrent VTE and mortality is similar compared with patients with more proximal PE. In a prospective cohort study of 578 individuals aged ≥65 years with acute PE (11% SSPE), the cumulative incidence of recurrent VTE or death within 3 years did not significantly differ by location of PE, and SSPE was not associated with a lower risk of adverse clinical outcomes than more proximal PE in adjusted analyses.[28] Similarly, the 3-month risk of recurrent VTE and mortality was similar in patients with SSPE and those with more proximal PE in an analysis of data from two prospective cohort studies including 748 patients with acute PE (16% SSPE).[27] Adverse outcomes were similar for incidental and symptomatic SSPE,[51] and for single and multiple subsegmental emboli in observational studies.[52] A recent study using prospectively collected data from the RIETE registry on more than 15,000 patients newly anticoagulated for acute PE (5.2% SSPE) found an almost twofold higher risk of recurrent PE in patients with SSPE compared with those with more proximal PE, even after adjustment for potential confounders, exclusion of cancer patients, and accounting for concomitant DVT.[53] Although there is no clear biologic plausibility for this particular finding, the results of these studies suggest that SSPE may not per se represent a more benign disorder than more proximal PE. However, these findings can only be generalized to the population of SSPE patients in whom anticoagulation was deemed necessary by the treating physicians, and the studies cannot answer the question about the risk–benefit ratio of anticoagulation for SSPE. In addition, SSPE patients were not consistently examined for the presence of DVT, which is an important predictor of recurrent VTE and associated mortality.[54] Therefore, no clear conclusions can be drawn about outcomes of patients with isolated SSPE (i.e., SSPE without concomitant DVT).

Various small observational studies that investigated outcomes in patients with SSPE, both with and without anticoagulation treatment, have suggested that withholding anticoagulation may be a safe option.[55–57] A systematic review of 14 observational studies including 715 patients with SSPE found no significant difference in VTE recurrence or death between patients who received anticoagulants or those who did not.[58] However, given the high risk of confounding by indication and other limitations, such as inclusion of heterogeneous studies with mostly small sample sizes and lack of outcome adjudication, these results have to be interpreted with great caution. While the results of this meta-analysis question the benefit of anticoagulation for SSPE, the risk of treatment-related complications remains. For example, in a retrospective study including 71 patients with presumed isolated SSPE, 87% received anticoagulation treatment, and 21% had a decrease in hemoglobin of at least 2 g/dL or required transfusion within 3 months of diagnosis.[59]

In the absence of data from randomized clinical trials,[60] guidelines have published recommendations concerning the management of SSPE based on the evidence from these observational studies and indirect data suggesting a benign course of some SSPE. The 2019 ESC guidelines suggest clinical surveillance in outpatients with single SSPE and no cancer or proximal DVT, while anticoagulation treatment is suggested for hospitalized patients, or those with cancer, concomitant DVT, or multiple SSPE.[31] Similarly, the most recent CHEST guidelines published in 2021 suggest that in SSPE patients who do not have concomitant DVT and are at low risk of recurrent VTE, clinical surveillance should be favored over anticoagulation.[38] Conversely, anticoagulation is suggested for patients at high risk of recurrent VTE, defined as hospitalized or pregnant patients or those who have a reduced mobility for another reason, active cancer, or no reversible risk factor.[38] In contrast to the ESC guidelines, management recommendations do not per se differ for single or multiple SSPE. The guidelines stress the importance of individualized treatment decisions with consideration of bleeding risk, cardiopulmonary reserve, and patient preferences. There are no data supporting an optimal clinical surveillance and follow-up strategy of patients with SSPE who are left untreated. Proximal DVT needs to be excluded if management without anticoagulation is an option, and in case of proximal compression ultrasonography only, serial examinations should be performed to exclude evolving proximal DVT.[38,61] Suggestions for the management of SSPE based on current guideline recommendations are summarized in ►Fig. 1. Despite guidelines suggesting the option of withholding treatment in low-risk patients, the majority of patients with SSPE seem to receive anticoagulants,[26,59] and average treatment duration does not substantially differ from patients with more proximal PE.[53] This fact could possibly reflect clinicians' uncertainty regarding these weak recommendations in guidelines, which are based on low-quality evidence.[38]

Prospective Management Study of Patients with Subsegmental Pulmonary Embolism Managed without Anticoagulation: Does It Move the Needle Towards Treatment?

The largest prospective management study of patients with SSPE who were managed without anticoagulation treatment has been published after the release of the latest guideline recommendations.[30] This study enrolled low-risk patients with SSPE, excluding those with hospital-acquired SSPE, active cancer, a history of VTE, need for supplemental oxygen, or pregnancy.[30] All patients underwent bilateral leg ultrasonography at the time of enrollment to exclude proximal DVT, and, if negative, did not receive anticoagulation. Ultrasonography was repeated after 5 to 7 days, and participants were continued to be managed without anticoagulation if the exam remained without evidence of proximal DVT. Patients with proximal DVT were started on anticoagulation, and the decision to start treatment in case of distal DVT was at the discretion of the treating physician. Recurrent VTE

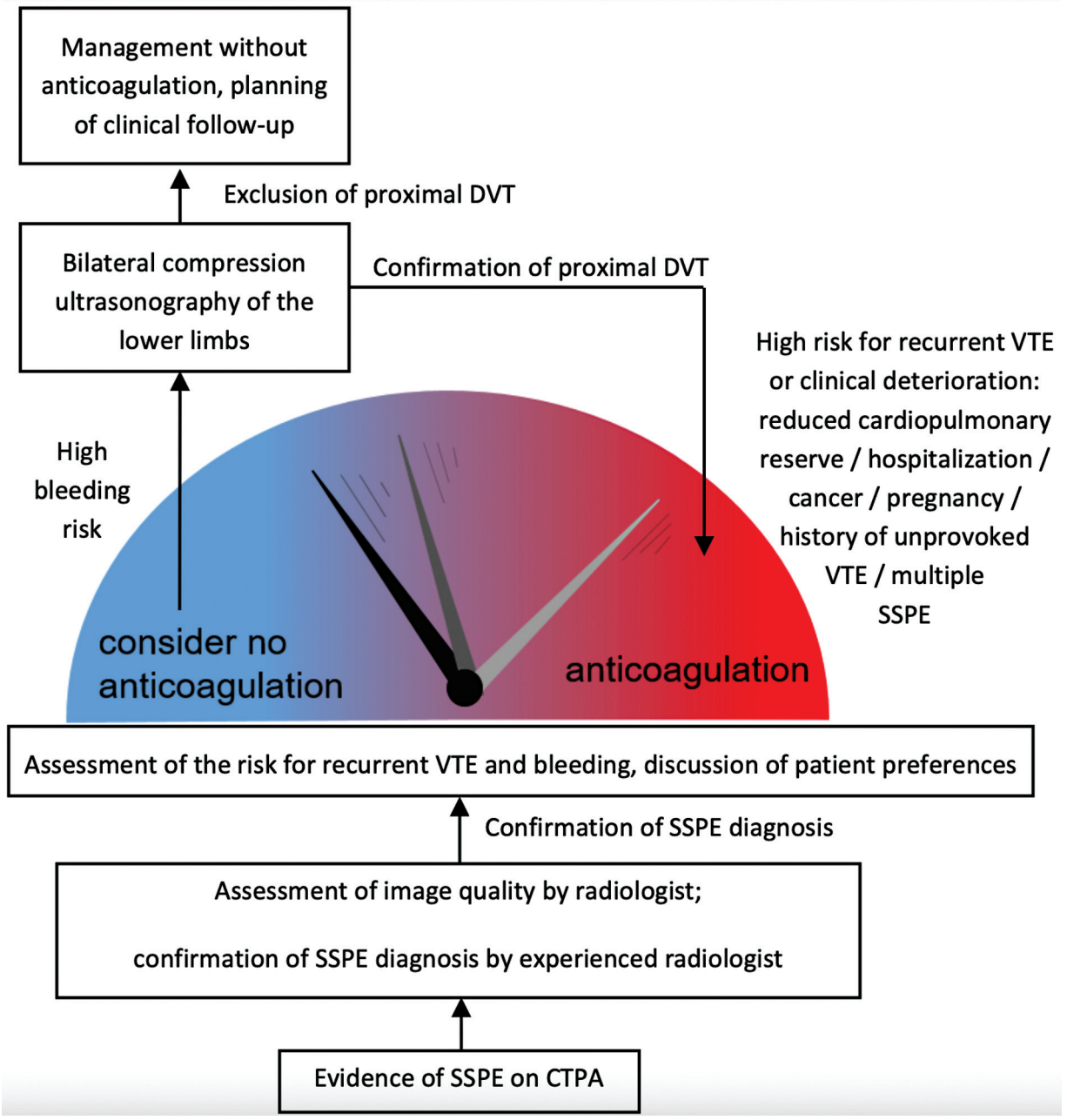

Fig. 1 Suggested management of subsegmental pulmonary embolism, based on current guideline recommendations.[31,38] A single bilateral whole leg compression ultrasonography with examination of the proximal and distal veins or serial proximal compression ultrasonography (with a second examination within 5–7 days in case of normal findings) can be used to diagnose deep vein thrombosis. CTPA, computed tomography pulmonary angiography; DVT, deep vein thrombosis; SSPE, subsegmental pulmonary embolism; VTE, venous thromboembolism.

outcomes were assessed during a follow-up period of 90 days. The trial was terminated early after inclusion of 292 of the targeted 300 patients (97%) because the a priori–defined stopping rule was met (i.e., if the upper bound of the 95% confidence interval of the VTE recurrence risk at 90 days exceeded 5.0%). Among the 292 participants enrolled in 18 Canadian and European centers during a 10-year period from 2011 to 2021, mean age was 56 years, 53% were female, and >95% had symptoms consistent with PE. Twenty patients were started on therapeutic anticoagulants due to presence of DVT (6 proximal, 22 distal), and an additional 6 patients initiated anticoagulation during follow-up because of an indication other than recurrent VTE, resulting in 266 SSPE patients who were managed without anticoagulation. Among those, eight had recurrent VTE during the 90-day follow-up (no fatal events), resulting in a cumulative incidence of 3.1% (95% confidence interval: 1.6–6.1%). In subgroup analyses, the risk of recurrence was higher in older patients (5.5% for those aged ≥65 years vs. 1.8% for aged <65 years), in those with multiple SSPE (5.7 vs. 2.1% with single SSPE), and those with concomitant distal DVT (12.5%). Overall, the risk of recurrent VTE was higher than initially expected by the authors, and higher than in patients who are left untreated after a negative CTPA.[15] There are several

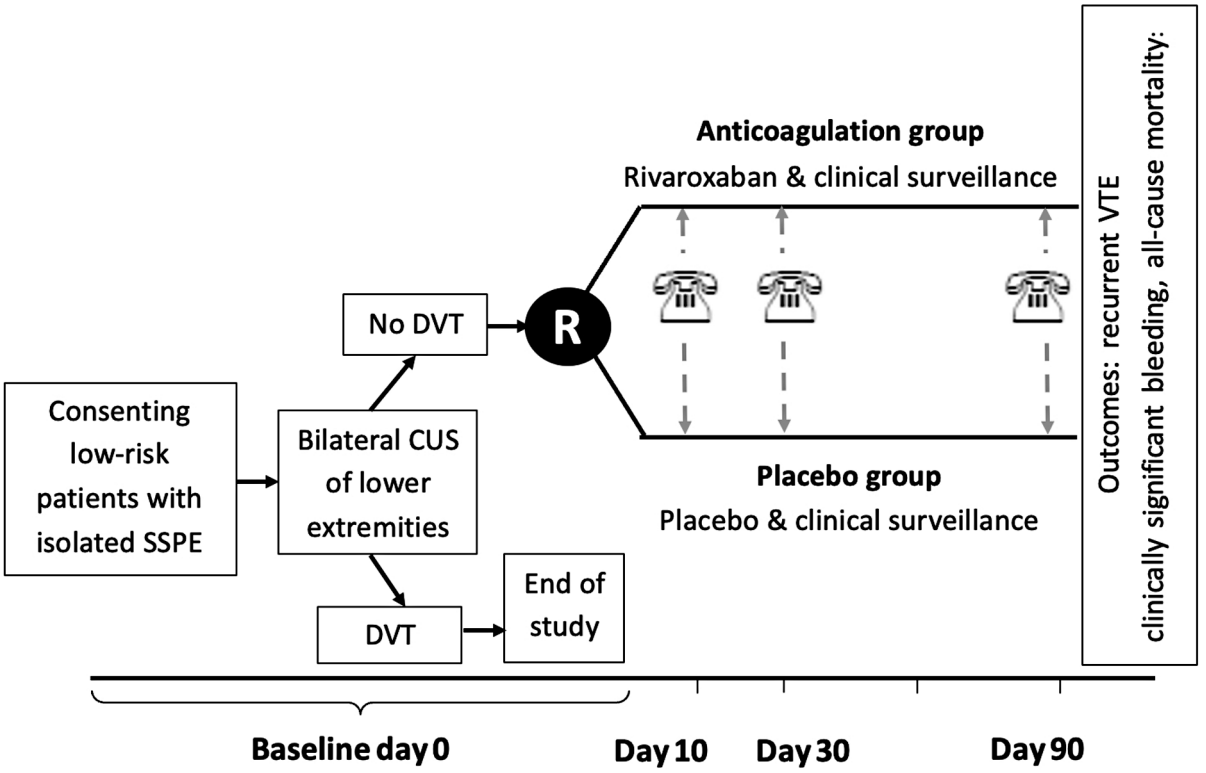

Fig. 2 Study flow of the randomized, placebo-controlled, non-inferiority SAFE-SSPE trial. Consenting low-risk patients with isolated SSPE undergo bilateral whole leg CUS. If concomitant DVT is excluded, participants are randomized in a 1:1 ratio to receive placebo ("clinical surveillance group") or anticoagulant treatment with rivaroxaban ("anticoagulation group"). Patients are followed up for 90 days after randomization, with follow-up phone calls at 10, 30, and 90 days. The primary outcome is symptomatic recurrent VTE and secondary outcomes include clinically significant bleeding and all-cause mortality within 90 days of randomization. CUS, compression ultrasonography; DVT, deep vein thrombosis; SSPE, subsegmental pulmonary embolism; VTE, venous thromboembolism.

ways to interpret these results.[62] One possible conclusion is that all patients with SSPE should be treated, given that recurrence risk was higher than expected in this low-risk population. Another possible conclusion is, however, that there may still be some patients who can be managed without treatment, such as younger patients or those with single SSPE, given that the risk of recurrent VTE in trials comparing direct oral anticoagulants to vitamin K antagonists was 1.5 to 3% even with treatment,[40,63,64] whereas treatment carries the risk of bleeding. Of note, no fatal events occurred in this study of patients who were managed without anticoagulation. Finally, the study does not answer the question about the risk–benefit ratio of anticoagulation in low-risk patients with SSPE.

… and What Now?

Results from randomized controlled trials are needed to answer the question about the optimal management of low-risk patients with SSPE. In this regard, the multicenter randomized placebo-controlled SAFE-SSPE trial (ClinicalTrials.gov NCT04263038) is currently ongoing in more than 25 centers in Switzerland, the Netherlands, and Canada.[65] Low-risk patients with SSPE are randomized to a treatment strategy without anticoagulation (placebo-group) or therapeutic-dose anticoagulation with rivaroxaban for 90 days after systematic exclusion of DVT using bilateral whole-leg ultrasound (►Fig. 2). The primary outcome is recurrent VTE within 90 days; safety outcomes include clinically relevant bleeding and all-cause mortality. The results of this non-inferiority trial have the potential to close an important gap of knowledge and clarify whether anticoagulation treatment and associated bleeding complications could be avoided in selected patients with SSPE.

Until the availability of more robust data on the optimal treatment of SSPE, efforts should be undertaken to prevent overdiagnosis and overtreatment of PE (►Table 2). First, unnecessary CTPA imaging should be avoided by using validated diagnostic algorithms based on assessment of pre-test probability and D-dimer testing.[31] Algorithms with higher cut-offs for high-sensitive D-dimer tests, such as age-adjusted thresholds or the YEARS algorithm (which uses a D-dimer threshold of 1,000 µg/L in patients with low pre-test probability based on three items) were shown to be safe and reduce the number of CTPA compared with algorithms using the standard cut-off of 500 µg/L.[66,67] In addition, algorithms with higher D-dimer thresholds can result in a lower prevalence of SSPE, as shown in a post hoc analysis from two prospective studies.[68] In the cohort managed with the YEARS algorithm, the prevalence of SSPE was significantly lower with 10% compared with 16% in the cohort managed with a conventional diagnostic strategy using the Wells score

Table 2 Strategies to prevent overdiagnosis and overtreatment of pulmonary embolism

Strategy	Measure
Prevention of unnecessary imaging	In case of suspected VTE, use a validated diagnostic algorithm based on clinical pre-test probability and D-dimer testing
	Consider using an algorithm with higher D-dimer cut-offs, such as age-adjusted thresholds or the YEARs algorithm
Prevention of false-positive findings of SSPE	Confirm the SSPE diagnosis by an experienced radiologist
	In case of suboptimal image quality, consider further imaging/repeating CTPA
Evaluation of a management strategy without anticoagulation in selected patients with SSPE and no concomitant DVT	Carefully assess the individual risk of recurrent VTE and bleeding for the decision whether or not to treat
	Take into account patient preferences, use shared-decision making
Generation of more robust evidence for diagnosis and treatment of SSPE	Establishment of better criteria to distinguish imaging artifacts from true SSPE
	Evidence from randomized trials investigating the net clinical benefit of a treatment strategy with and without anticoagulation in low-risk patients with SSPE (e.g., ClinicalTrial.gov NCT04263038)

Abbreviations: CTPA, computed tomography pulmonary angiography; DVT, deep vein thrombosis; SSPE, subsegmental pulmonary embolism; VTE, venous thromboembolism.

and a D-dimer cut-off of 500 µg/L.[68] Application of the Pulmonary Embolism Rule-Out Criteria (PERC) consisting of eight clinical items can further reduce the use of CTPA without affecting safety in patients with suspected PE who have a low clinical probability for PE as estimated by gestalt.[69] Second, false-positive findings of SSPE should be prevented by confirmation of the diagnosis by an experienced radiologist and consideration of further imaging in case of suboptimal CTPA quality.[31] In centers with expertise and availability, the American Society of Hematology recommends the use of V/Q scanning over CTPA as the first-line imaging test in patients with low or intermediate pre-test probability who are likely to have a diagnostic scan, not only to limit radiation exposure, but also to reduce findings of unclear clinical relevance, such as SSPE.[70] Third, a treatment strategy without anticoagulation can be considered in selected low-risk patients with SSPE after exclusion of concomitant DVT and careful assessment and integration of individual risk factors for VTE recurrence and bleeding as well as patient preferences.[38]

In conclusion, the clinical significance and optimal management of SSPE remain unclear. Although a recent prospective management cohort study, that showed a higher than expected risk of recurrent VTE in patients who were left untreated, may move the needle further towards anticoagulation treatment, its results do not allow to draw a firm conclusion about the risk–benefit ratio of anticoagulation in selected low-risk patients with SSPE. While awaiting more robust evidence on optimized diagnosis and management of these patients, efforts should focus on reducing overdiagnosis of PE.

Conflict of Interest

The authors declare that they have no conflict of interest.

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