Embolia polmonare subsegmentaria e anticoagulazione

Dr. Nathan Artom
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S.C. Medicina Interna 1 - Ospedale San Paolo

Il sottoscritto Nathan Artom
ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

dichiara

che negli ultimi due anni NON ha avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

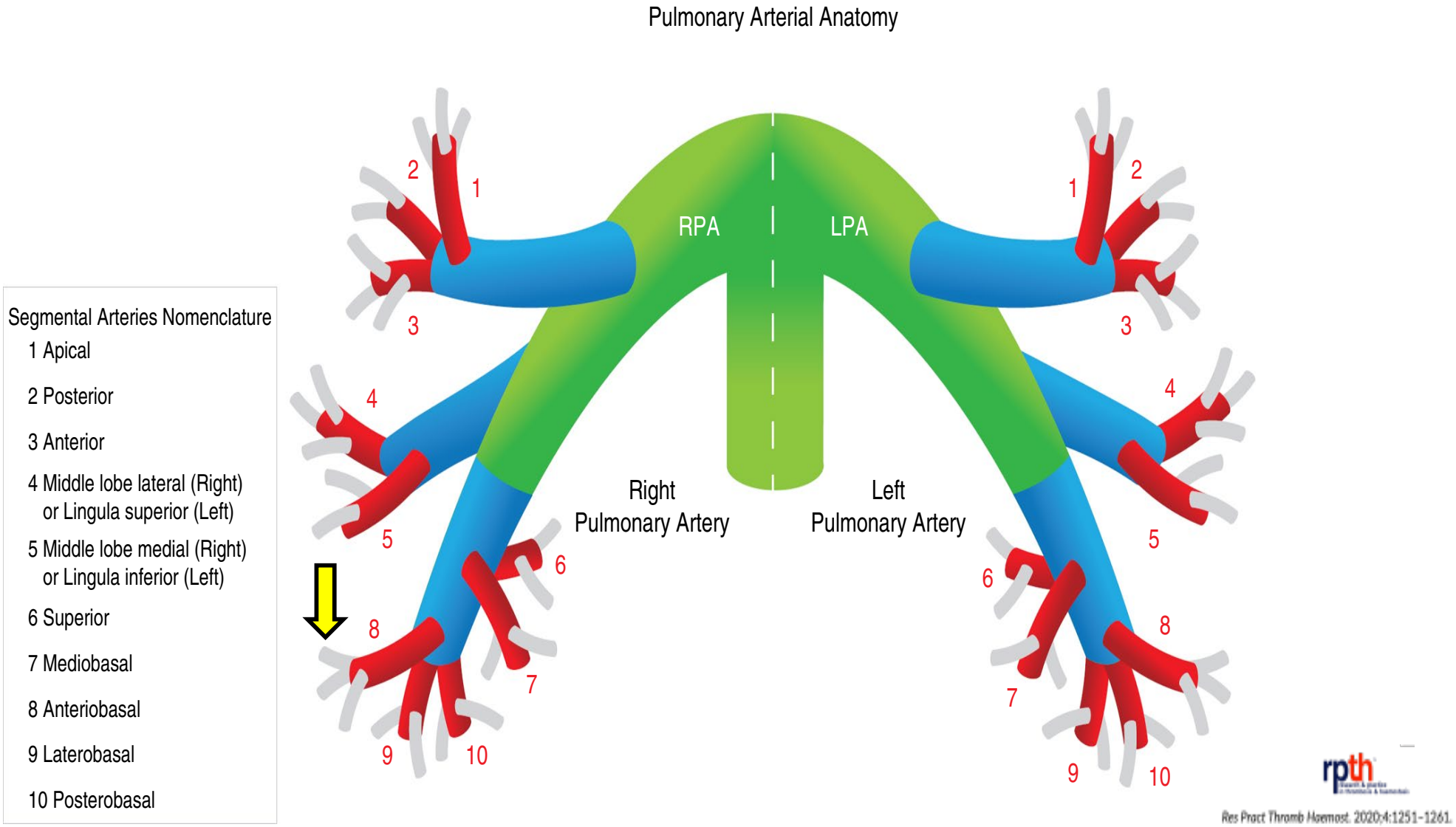
Embolia polmonare subsegmentaria

”A contrast defect in a subsegmental artery, i.e. the first arterial branch division of any segmental artery independent of artery diameter, visible in at least two subsequent axial mslices, using a Computed Tomography scanner with a desired maximum collimator width of ≤1 mm”

Establishing diagnostic criteria and treatment of subsegmental pulmonary embolism: A Delphi analysis of experts

Paul L. den Exter MD, PhD[1] | Lucia J. M. Kroft MD, PhD[2] | Carol Gonsalves MD, FRCPC, MMEd[3] | Gregoire Le Gal MD, PhD[3] | Cornelia M. Schaefer-Prokop MD, PhD[4,5] | Marc Carrier MD, MSc, FRCPC[3] | Menno V. Huisman MD, PhD[1] | Frederikus A. Klok MD, PhD[1]

Embolia polmonare subsegmentaria



AGENDA

- E’ un falso positivo o è un vero positivo ?
- Asintomatica o sintomatica ?
- Trattarla o non trattarla ?
- Dosaggio anticoagulante ?
- Durata terapia ?

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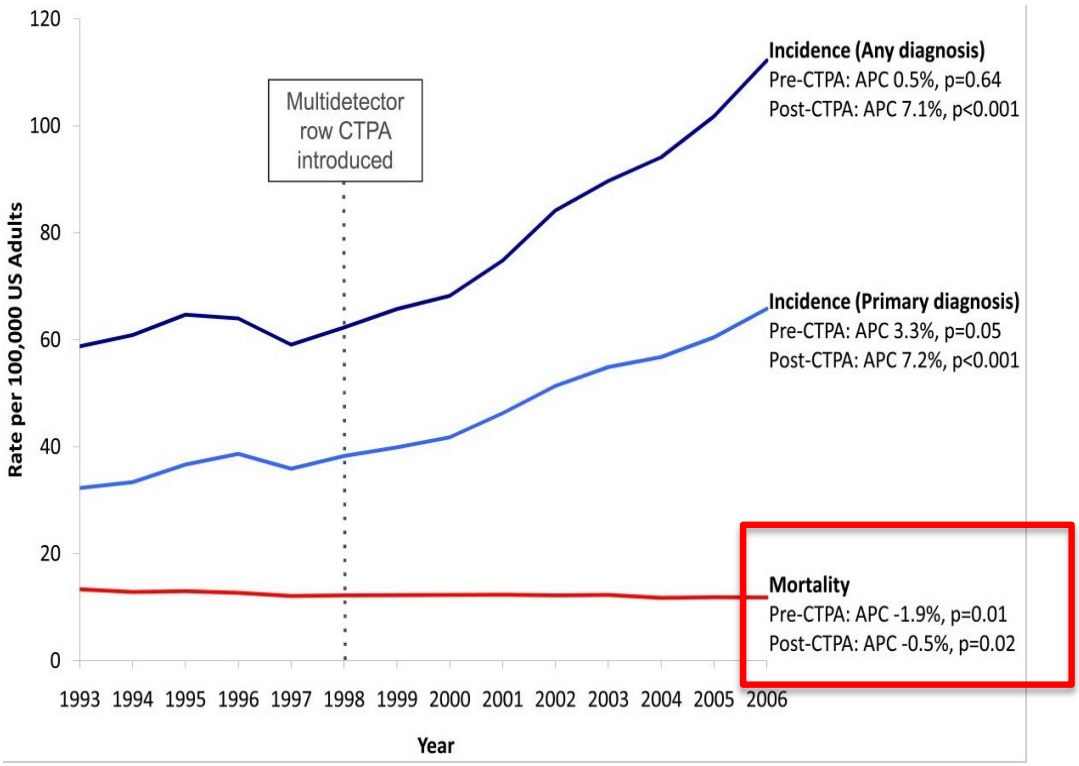
Vecchi e nuovi tomografi: tasso di recidive

	Single detector CTPA	Multiple detector CTPA
N	1123	1534
Proporzione di EPSSI (%; 95% CI)	4.7 (2.5-7.6)	9.4 (5.5-14.22)
Incidenza di recidive tromboemboliche in pazienti congedati senza terapia	**0.9 (0.4-1.4)**	**1.1 (0.7-1.4)**

Carrier M et al, J Thromb Haemost 2020:8:1716-22.

Vecchi e nuovi tomografi: mortalità



Wiener RS et al. Arch Int Med 2011;171:831-837.

Affidabilità della diagnosi?

- Bassa riproducibilità della diagnosi tra radiologi diversi
  - Kappa = 0.38 (95% CI: 0.0 to 0.89)

- Fino al 59% di diagnosi di EPSS si sono rivelate ‘falsi positivi’ in seguito a reinterpretazione da parte di radiologi toracici e/o dotati di maggiore esperienza

Ghanima W et al. *Acta Radiol* 2007;48:165-70; Hutchinson BD et al. *AJR* 2015;205:271-7; Pena E et al. *J Thromb Haemost* 2012;10:496-8; Miller WT et al. *Ann Am Thorac Soc* 2015;12:1022-9;
Pesavento R et al. *Thromb Res* 2018;175:6-7

Guidelines ESC

If the CTPA report suggests single subsegmental PE, consider the possibility of a false-positive finding. Discuss the findings again with the radiologist and/or seek a second opinion to avoid misdiagnosis, and unnecessary, potentially harmful anticoagulation treatment.

Further imaging tests to confirm PE may be considered in cases of isolated subsegmental filling defects.[115]	IIb	C
In patients with cancer, management of incidental PE in the same manner as symptomatic PE should be considered, if it involves segmental or more proximal branches, multiple subsegmental vessels, or a single subsegmental vessel in association with proven DVT.[376,377]	IIa	B

ESC European Society of Cardiology
European Heart Journal (2020) **41**, 543–603
doi:10.1093/eurheartj/ehz405

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Journal of *Clinical Medicine*

MDPI

Article

Clinical Significance and Outcome in Patients with Asymptomatic Versus Symptomatic Subsegmental Pulmonary Embolism

The major outcome was the occurrence of symptomatic, objectively confirmed pulmonary embolism (PE) recurrences appearing during anticoagulation or after its discontinuation in patients with asymptomatic SSPE vs. those with symptomatic SSPE.

2135 pazienti

Our findings, obtained from a large cohort of patients with SSPE, reveal that the incidence rate of symptomatic PE recurrences was similar in patients initially presenting with asymptomatic or symptomatic PE, both during anticoagulation (1.98 vs. 0.81 per 100 patient years) or after its discontinuation (4.38 vs. 3.45 per 100 patient years).

J. Clin. Med. **2023**, *12*, 1640. https://doi.org/10.3390/jcm12041640

Executive Summary

Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report

Scott M. Stevens, MD; Scott C. Woller, MD; Lisa Baumann Kreuziger, MD; Henri Bounameaux, MD; Kevin Doerschug, MD; Geert-Jan Geersing, MD, PhD; Menno V. Huisman, MD; Clive Kearon, MD, PhD; Christopher S. King, MD; Andrew J. Knighton, PhD; Erica Lake, MLS; Susan Murin, MD; Janine R. E. Vintch, MD; Philip S. Wells, MD; and Lisa K. Moores, MD

Whether to Treat an Incidentally Diagnosed Asymptomatic Acute PE

PICO Question: Should anticoagulant therapy vs no anticoagulant therapy be given to patients with incidentally diagnosed asymptomatic acute pulmonary embolism?:

Guidance statement:

4. In patients who are incidentally found to have asymptomatic PE, we suggest the same initial and long-term anticoagulation as for comparable patients with symptomatic PE (weak recommendation, moderate-certainty evidence).

Comments: Asymptomatic PE is diagnosed in about 1% of outpatients and about 4% of inpatients who have contrast-enhanced chest CT scans (notably performed during a diagnostic workup in patients with cancer) and may represent false-positive imaging findings; therefore it is important to ensure a false-positive result is not likely. Observational data suggest that asymptomatic PE carries a similar prognosis to symptomatic PE (data predominantly from patients with cancer), implying a similar approach to treatment is needed.[8]

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Cochrane Library

Cochrane Database of Systematic Reviews

Anticoagulant treatment for subsegmental pulmonary embolism (Review)

Yoo HHB, Nunes-Nogueira VS, Fortes Villas Boas PJ

Cochrane Database of Systematic Reviews 2020, Issue 2. Art. No.: CD010222.
DOI: 10.1002/14651858.CD010222.pub4.

Main results

We did not identify any studies that met the inclusion criteria.

Authors' conclusions

There is no evidence from randomised controlled trials to assess the effectiveness and safety of anticoagulation therapy versus control in patients with isolated subsegmental pulmonary embolism (SSPE) or incidental SSPE. Well-conducted research is required before informed practice decisions can be made.

Cochrane Database of Systematic Reviews 2020, Issue 2. Art. No.: CD010222.
DOI: 10.1002/14651858.CD010222.pub4.

Establishing diagnostic criteria and treatment of subsegmental pulmonary embolism: A Delphi analysis of experts

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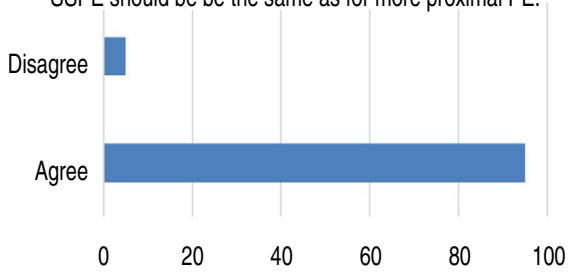
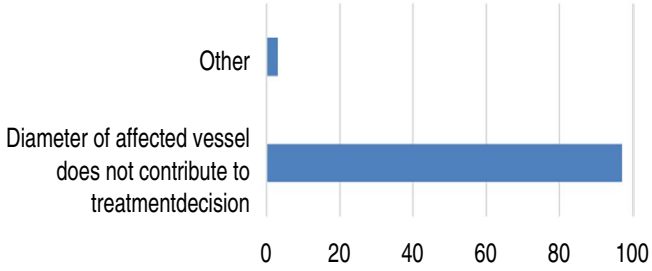
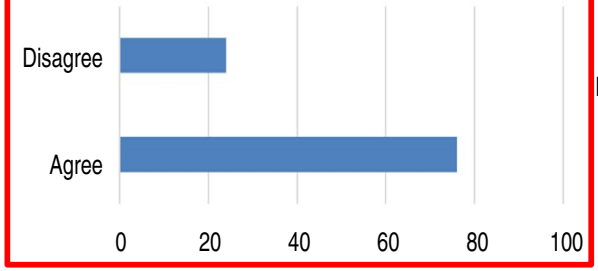
The type of anticoagulant (e.g. DOAC, VKA, LMWH) for SSPE should be be the same as for more proximal PE.



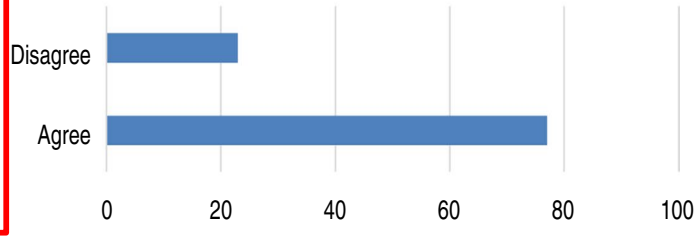
What is the maximum diameter size a ssPE may be left untreated?



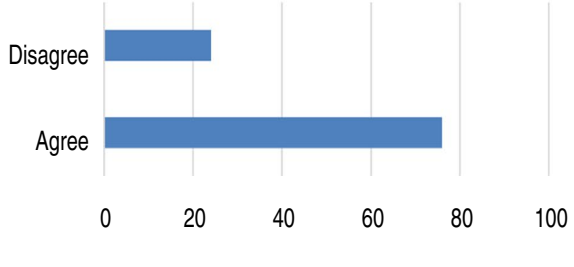
Patients with previous VTE and a new diagnosis of ssPE should be treated with anicoagulant therapy.



The treatment duration of ssPE should be the same as for more proximal PE in the setting of a comparable thromboembolic/bleeding risk profile.



Incidental ssPE should be left untreated.



Recommend anticoagulation for patients with multiple subsegmental pulmonary embolism

rpth
Res Pract Thromb Haemost. 2020;4:1251–1261.

PICO Question: Should anticoagulant therapy vs no anticoagulant therapy be given to patients with isolated subsegmental pulmonary embolism?:

3. In patients with subsegmental pulmonary embolism (PE) (no involvement of more proximal pulmonary arteries) and no proximal DVT in the legs who have a (i) low risk for recurrent VTE (see text), we suggest clinical surveillance over anticoagulation (weak recommendation, low-certainty evidence) or (ii) high risk for recurrent VTE (see text), we suggest anticoagulation over clinical surveillance (weak recommendation, low-certainty evidence).

Stevens SC et al. CHEST 2021; 160(6):2247-2259

Risk factors 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

Stevens SC et al. CHEST 2021; 160(6):2247-2259

Tasso di recidiva dopo primo episodio TEV (tutte non solo EPSS)

- Fattore di rischio transitorio: 3.3% per anno-paziente
  - ✦0.7% se fattore di rischio chirurgico (95% CI 0-1.5%)
  - ✦4.2% se fattore di rischio non chirurgico (95% CI 2.8-5.6%)
- Non provocato: 7.4% per anno-paziente (95% CI 6.5-8.2%)
- Cancro attivo: 20.7% ad 1 anno (95% CI, 15.6%-25.8%)

RISCHIO RICORRENZA ELEVATO (> 8%)

ANTICOAGULARE

Iorio et al. Arch Intern Med 2010;170:1710-1716
Prandoni P et al. Blood 2002; 100:3484-3488

Stima del rischio di ricorrenza di TEV a lungo termine (terapia anticoagulante interrotta dopo 3 mesi in pazienti con TVP prossimale) in base alla presenza di fattori di rischio transitori, persistenti o ignoti (modificata da ref. 7, 12)

Stima del rischio di ricorrenza a lungo termine	Fattori di rischio per EP/TEV e loro tipologia (presenti in occasione dell'episodio acuto)	Esempi di condizioni a rischio
Basso (<3%/anno)	Fattori importanti transitori associati a un aumento del rischio >10 volte per un evento di TEV (rispetto a paziente senza il fattore di rischio)	• Chirurgia maggiore (anestesia generale >30 minuti) • Immobilità a letto in ospedale per ≥3 giorni a causa di una malattia acuta o dell'esacerbazione di una malattia cronica • Trauma con fratture
Intermedio (3-8%/anno)	Presenza di fattori transitori associati ad un aumento del rischio ≤10 volte per un evento indice di TEV	• Chirurgia minore (anestesia generale <30 min) • Ricovero per malattia acuta in ospedale per <3 giorni • Contraccezione/TOS/fecondazione in vitro • Gravidanza o puerperio • Immobilità a letto a domicilio per ≥3 giorni per malattia acuta • Lesione alla gamba (senza frattura) associata a ridotta mobilità per ≥3 gioni • Viaggi di lunga durata
	Fattori di rischio persistenti non associati a malignità	• Malattie infiammatorie intestinali • Malattie autoimmuni attive
Alto (>8% /anno)	Fattori di rischio maggiori persistenti	• Cancro in fase attiva • Uno o più episodi di TEV in assenza di fattori maggiori transitori • Sindrome da anticorpi antifosfolipidi • Trombofilia ereditaria • Storia familiare di trombosi
	Primo episodio di TVP in assenza di fattori di rischio identificabili	Il rischio di ricorrenza aumenta con il progredire dell'età ed è più alto nei seguenti casi: sesso maschile, TVP prossimale, EP concomitante, rialzo di D-dimero all'interruzione del trattamento.

Tabella 3. *Principali fattori di rischio emorragico dei pazienti con TEV e score di quantificazione del rischio di emorragia maggiore secondo le linee guida ACCP (modificata da ref. 7, 12)*

Fattori di rischio (punti per definire lo score)	- Età > 65 anni (1) - Età > 75 anni (1) - Precedente sanguinamento (1) - Cancro (1) - Cancro metastatico (1) - Insufficienza renale (1) - Insufficienza epatica (1) - Trombocitopenia (1) se grave (<50.000/µl) (2) - Precedente stroke (1) - Diabete (1) - Anemia (1) - Terapia antiaggregante (1) - Scarso controllo della terapia anticoagulante in corso (1) - Comorbidità e ridotta capacità funzionale (1) - Chirurgia recente (1) - Cadute frequenti (1) - Abuso di alcool (1)
Stratificazione del rischio	- Basso: (0) → 0,8%/anno - Intermedio,doppio rispetto al rischio basso: (1) → 1,6%/anno - Alto, 8 volte più alto: (≥2) → >6,5%/anno

Rischio di ricorrenza TEV per EPSS non trattata?

Annals of Internal Medicine

ORIGINAL RESEARCH

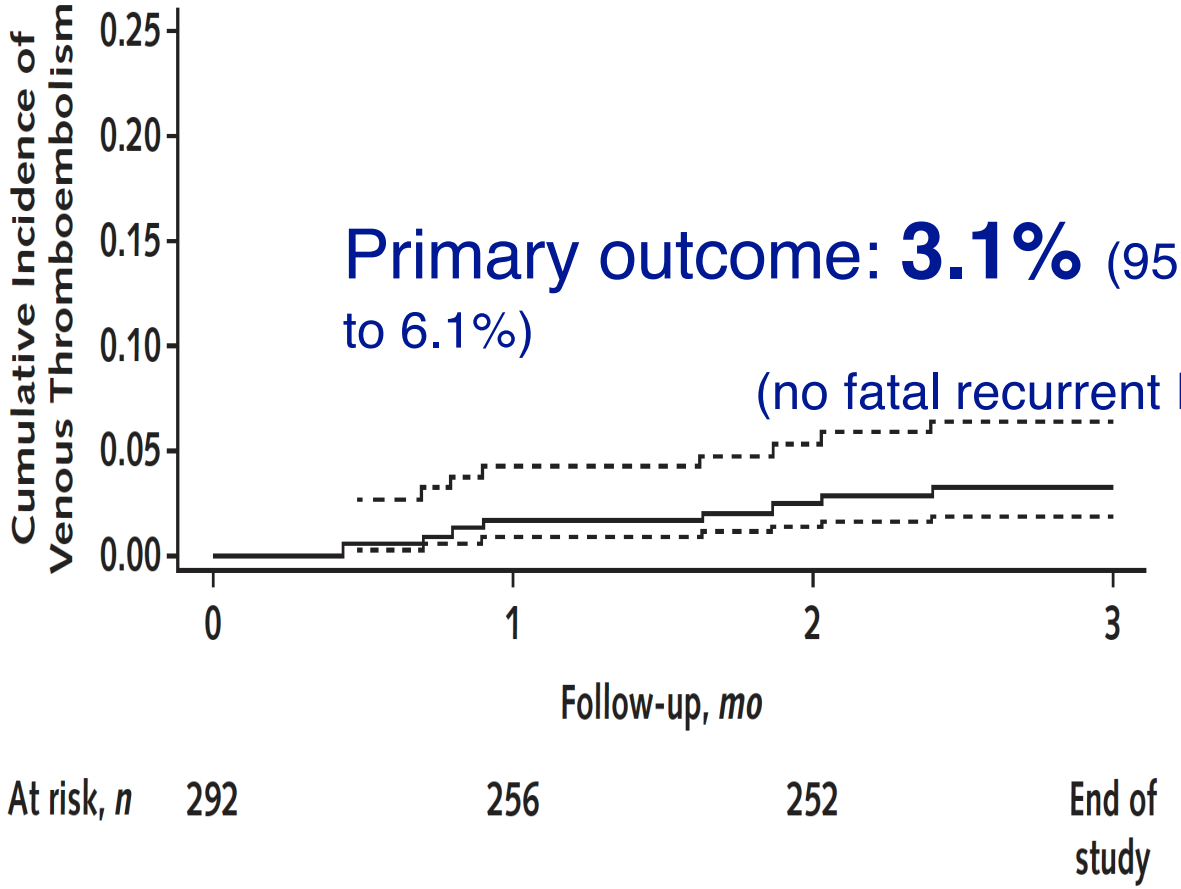
Risk for Recurrent Venous Thromboembolism in Patients With Subsegmental Pulmonary Embolism Managed Without Anticoagulation

A Multicenter Prospective Cohort Study

Grégoire Le Gal, MD, PhD; Michael J. Kovacs, MD; Laurent Bertoletti, MD, PhD; Francis Couturaud, MD, PhD; Carole Dennie, MD; Andrew M. Hirsch, MD; Menno V. Huisman, MD, PhD; Frederikus A. Klok, MD, PhD; Noémie Kraaijpoel, MD, PhD; Ranjeeta Mallick, PhD; Amanda Pecarskie, BSc; Elena Pena, MD; Penny Phillips, BSc; Isabelle Pichon, BSc; Tim Ramsay, PhD; Marc Righini, MD; Marc A. Rodger, MD; Pierre-Marie Roy, MD, PhD; Olivier Sanchez, MD, PhD; Jeannot Schmidt, MD, PhD; Sam Schulman, MD; Sudeep Shivakumar, MD; Albert Trinh-Duc, MD; Rachel Verdet, BSc; Ulric Vinsonneau, MD; Philip Wells, MD; Cynthia Wu, MD; Erik Yeo, MD; and Marc Carrier, MD; on behalf of the SSPE Investigators*

Risk for Recurrent Venous Thromboembolism in Patients With Subsegmental Pulmonary Embolism Managed Without Anticoagulation

Figure 2. Time-to-event analysis of recurrent venous thromboembolism.



Primary outcome: **3.1%** (95% CI, 1.6% to 6.1%)

(no fatal recurrent PE)

65 years or less: 1.8%

More than 65 years: 5.5%

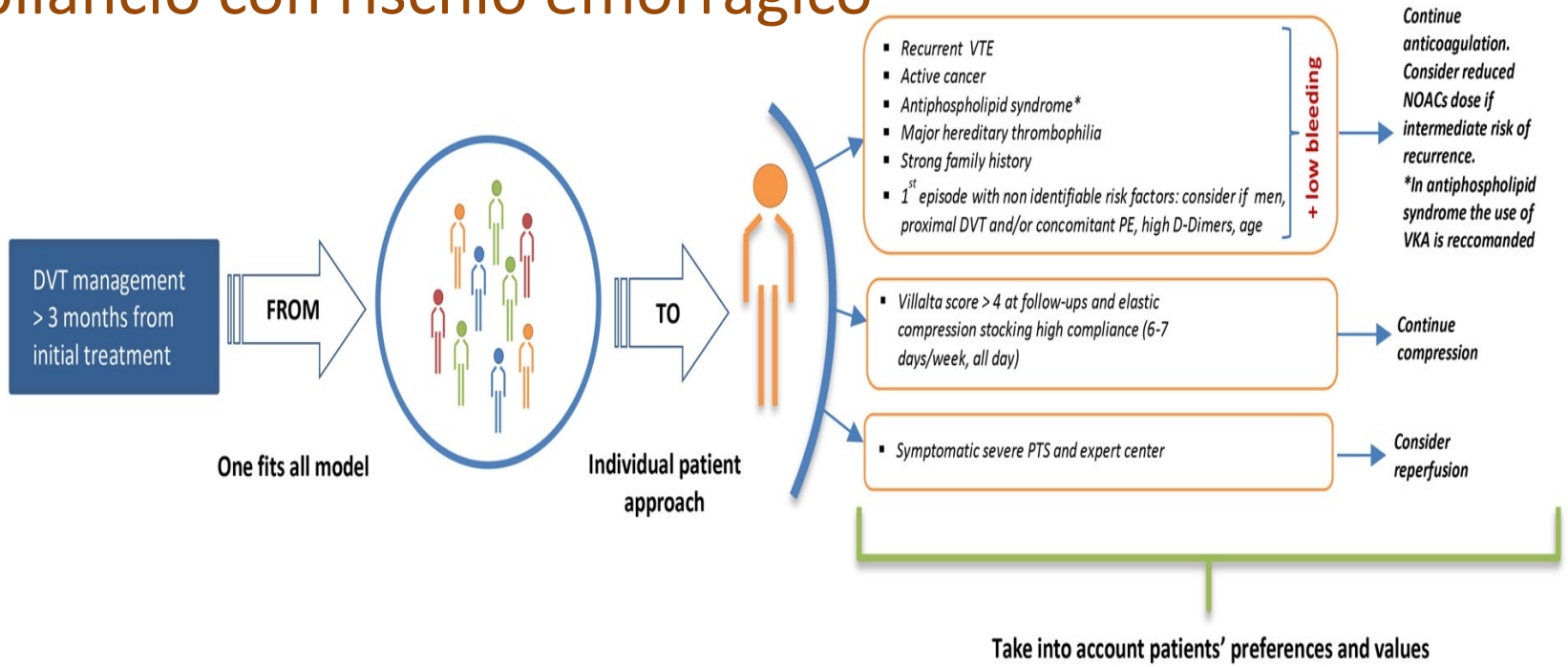
Single isolated subsegmental PE: **2.1%**

Multiple isolated subsegmental PE: **5.7%**

Le Gal G et al. Ann Intern Med . 2022;175:29-35

Pazienti con EPSS quando trattare ?

- Indifferente se sintomatici o asintomatici
- Se multipli trattare
- Rulling out TVP
- Se isolato e senza TVP fondamentale valutare rischio di ricorrenza individuale (considerando anche età)!!! e fare bilancio con rischio emorragico



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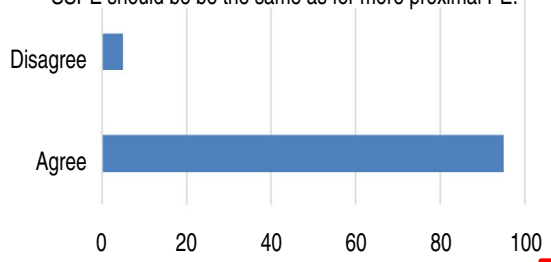
The type of anticoagulant (e.g. DOAC, VKA, LMWH) for SSPE should be be the same as for more proximal PE.



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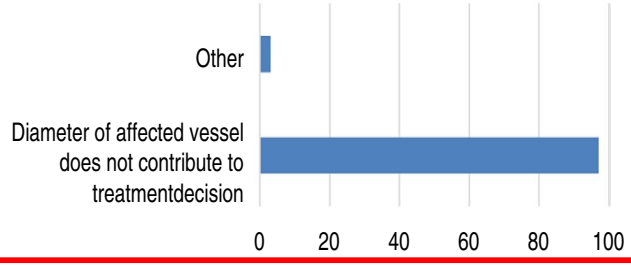
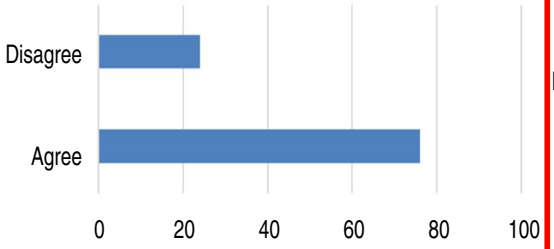
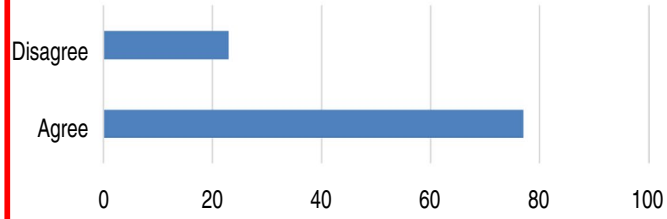


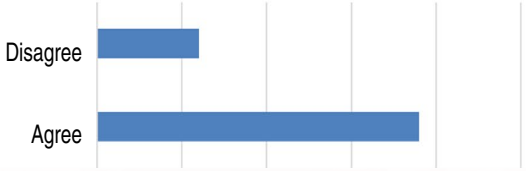
Patients with previous VTE and a new diagnosis of ssPE should be treated with anticoagulant therapy.



The treatment duration of ssPE should be the same as for more proximal PE in the setting of a comparable thromboembolic/bleeding risk profile.



Incidental ssPE should be left untreated.



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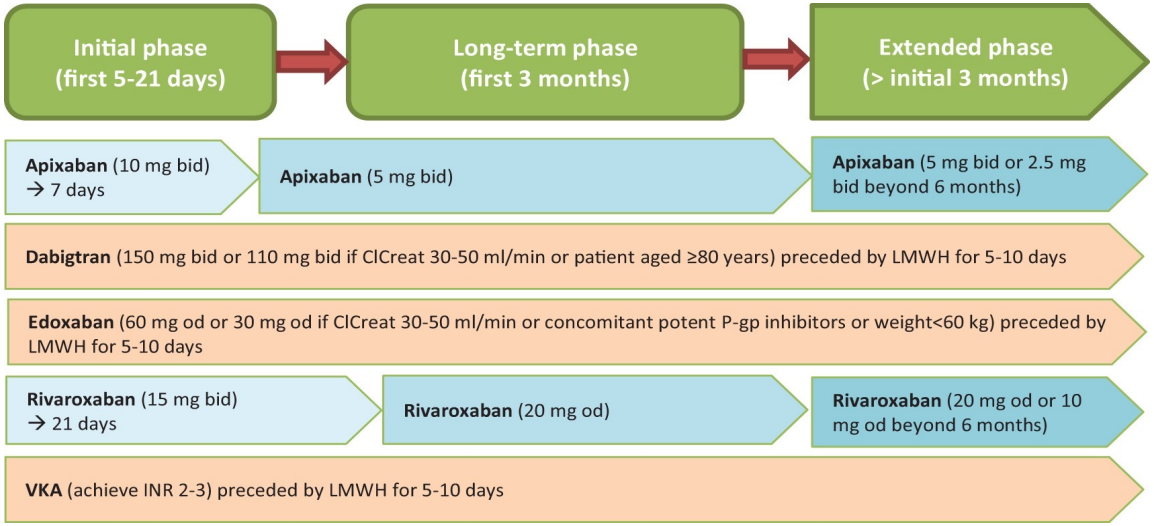
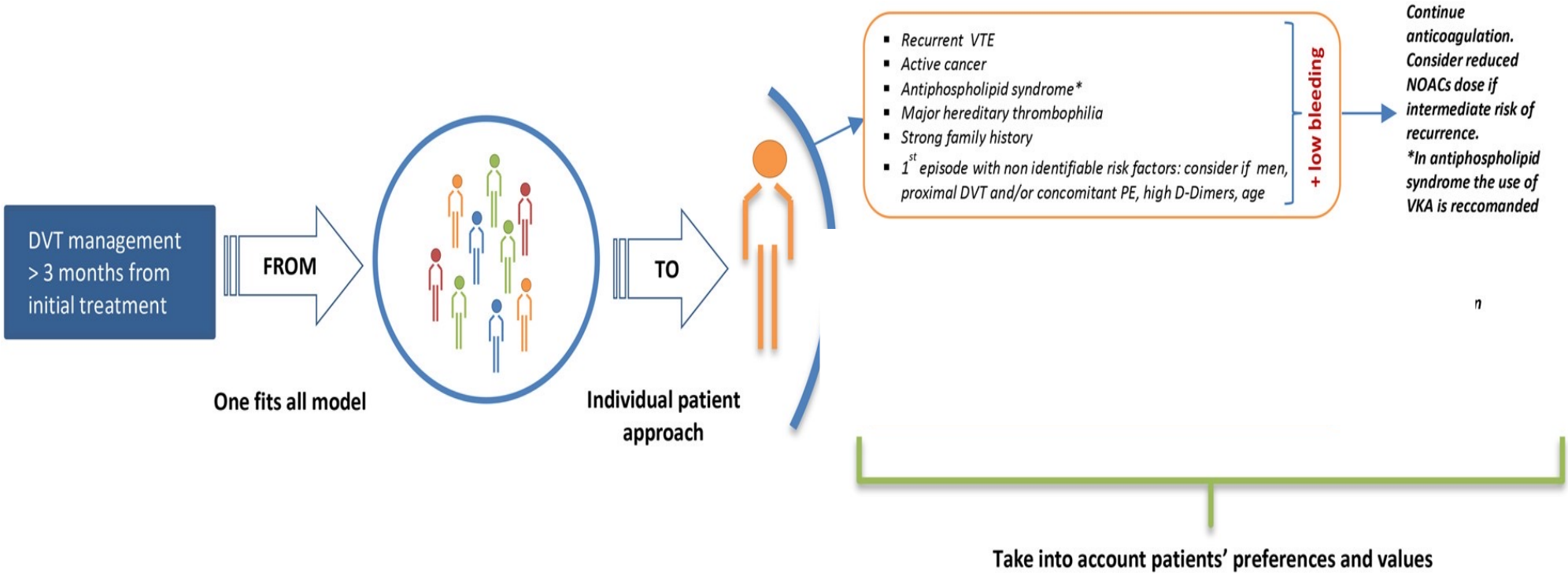
Res Pract Thromb Haemost. 2020;4:1251–1261.


Initial phase (first 5-21 days)
Long-term phase (first 3 months)
Extended phase (> initial 3 months)
Apixaban (10 mg bid) → 7 days
Apixaban (5 mg bid)
Apixaban (5 mg bid or 2.5 mg bid beyond 6 months)
Dabigtran (150 mg bid or 110 mg bid if ClCreat 30-50 ml/min or patient aged ≥80 years) preceded by LMWH for 5-10 days
Edoxaban (60 mg od or 30 mg od if ClCreat 30-50 ml/min or concomitant potent P-gp inhibitors or weight<60 kg) preceded by LMWH for 5-10 days
Rivaroxaban (15 mg bid) → 21 days
Rivaroxaban (20 mg od)
Rivaroxaban (20 mg od or 10 mg od beyond 6 months)
VKA (achieve INR 2-3) preceded by LMWH for 5-10 days


DVT management > 3 months from initial treatment
FROM
One fits all model
TO
Individual patient approach
Recurrent VTE
Active cancer
Antiphospholipid syndrome*
Major hereditary thrombophilia
Strong family history
1st episode with non identifiable risk factors: consider if men, proximal DVT and/or concomitant PE, high D-Dimers, age
+ low bleeding
Continue anticoagulation. Consider reduced NOACs dose if intermediate risk of recurrence.
*In antiphospholipid syndrome the use of VKA is reccomanded
Take into account patients' preferences and values

CONCLUSIONI

subsegmental pulmonary embolism: to treat or not to treat?

Marc Carrier[1] *and Fredrikus A. Klok*[2]

[1]*Department of Medicine, Ottawa Hospital Research Institute, University of Ottawa, Ontario, Canada; and*
[2]*Department of Thrombosis and Hemostasis, Leiden University Medical Center, Leiden, The Netherlands*

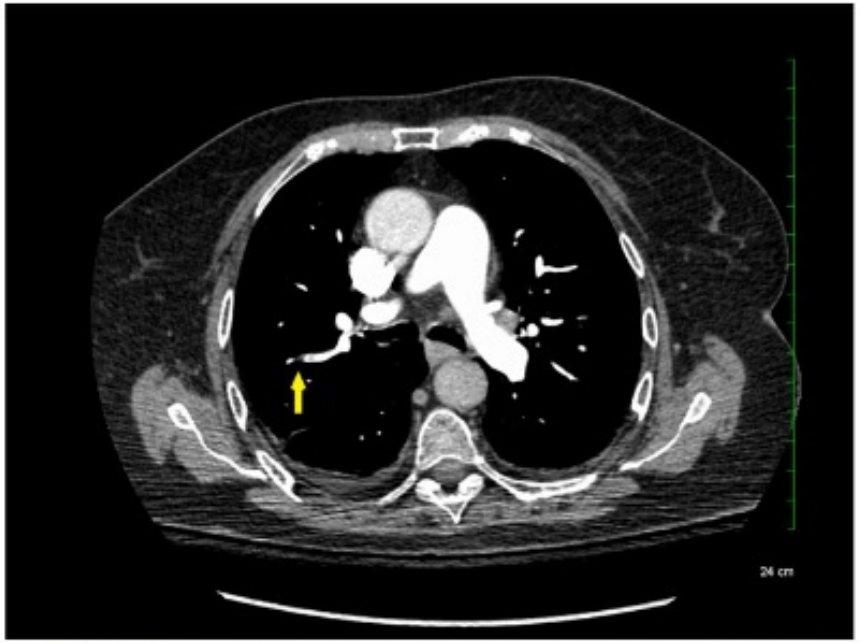


Figure 1. Subsegmental pulmonary embolism on computed tomographic pulmonary angiography.

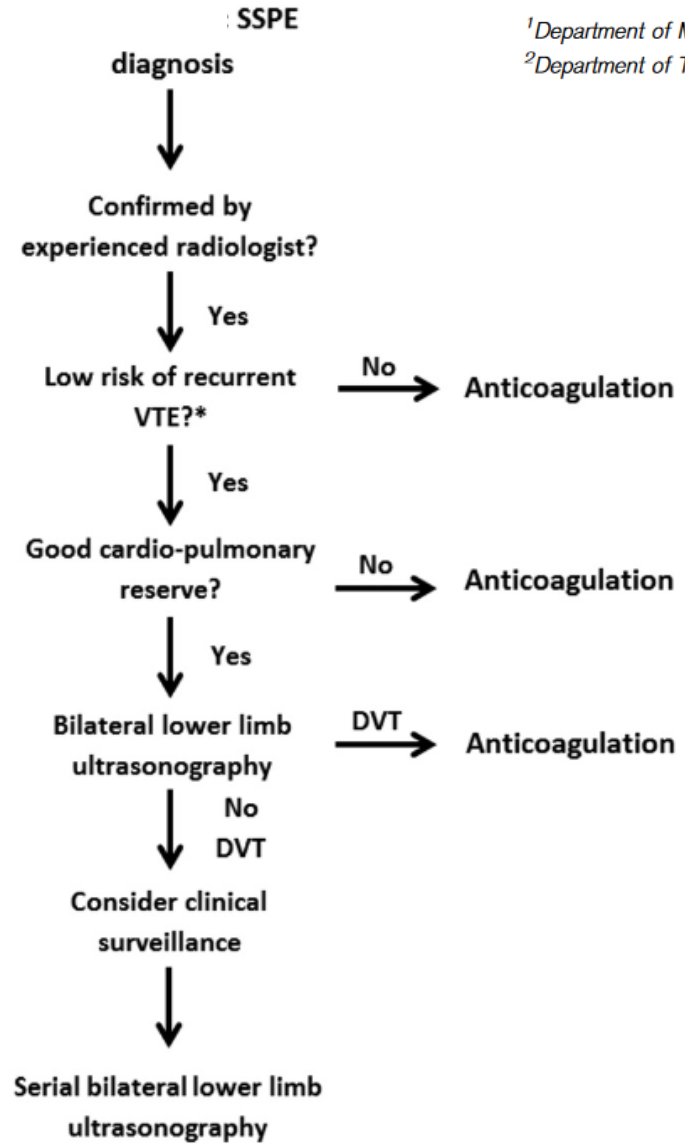


Figure 2. Management strategy for symptomatic subsegmental pulmonary embolism. DVT, deep vein thrombosis; SSPE, subsegmental pulmonary embolism; VTE, venous thromboembolism.

PICO Question: Should anticoagulant therapy vs no anticoagulant therapy be given to patients with isolated subsegmental pulmonary embolism?:

3. In patients with subsegmental pulmonary embolism (PE) (no involvement of more proximal pulmonary arteries) and no proximal DVT in the legs who have a (i) low risk for recurrent VTE (see text), we suggest clinical surveillance over anticoagulation (weak recommendation, low-certainty evidence) or (ii) high risk for recurrent VTE (see text), we suggest anticoagulation over clinical surveillance (weak recommendation, low-certainty evidence).

Stevens SC et al. CHEST 2021; 160(6):2247-2259

JAMA Network Open

Original Investigation | Pulmonary Medicine

Prevalence of and Eligibility for Surveillance Without Anticoagulation Among Adults With Lower-Risk Acute Subsegmental Pulmonary Embolism

Samuel G. Rouleau, MD; Mahesh J. Balasubramanian, MD; Jie Huang, PhD; Tad Antognini, MD; Mary E. Reed, DrPH; David R. Vinson, MD

Key Points

Question How prevalent is structured surveillance without anticoagulation for subsegmental pulmonary embolism in community practice, and what proportion of patients are surveillance eligible using modified American College of Chest Physicians (CHEST) criteria?

Findings In this cohort study of 666 outpatients examined over 5 years after publication of the 2016 CHEST guideline, only 1 patient (<1%) with subsegmental pulmonary embolism underwent surveillance without anticoagulation in a community setting with excellent follow-up access. Using modified CHEST criteria, 35 patients (5%) with subsegmental pulmonary embolism were surveillance eligible.

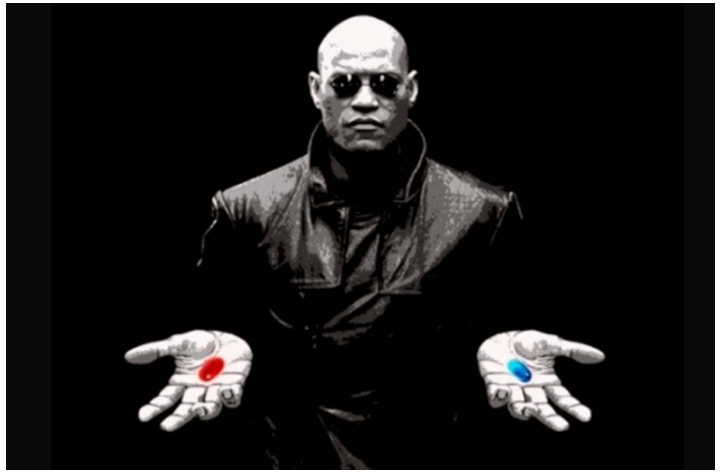
Meaning These findings suggest that only a small proportion of patients with subsegmental pulmonary embolism may be surveillance eligible, and structured surveillance is rarely used despite the CHEST guideline.

We estimated that few outpatients (35 [5.3%]) with acute subsegmental PE in this study would have been eligible for structural surveillance without anticoagulation

We identified only 1 patient (0.4% [95% CI, 0.01%-2.4%]) among our lower-risk cohort who underwent a guideline-recommended regimen of structured surveillance, receiving repeat compression ultrasonography of the lower extremities 9 days after the index diagnosis.

difficult for many primary care and emergency medicine clinicians to identify and apply structured surveillance in practice. Based on the current literature, we think it prudent to treat patients with subsegmental PE like those with a more proximal PE: anticoagulate unless contraindicated.

EPSS: a clinical dilemma



Grazie per l’attenzione

Rischio trombotico Rischio emorragico

- TVP prossimale (con o senza EP) a rischio di ricorrenza intermedio e rischio emorragico:

  basso → **considerare** l'estensione del trattamento

  alto → **si raccomanda** la sospensione del trattamento al 3° mese

- TVP prossimale (con o senza EP) a rischio di ricorrenza alto e rischio emorragico:

  basso → **si raccomanda** l'estensione del trattamento

  alto → **considerare** la sospensione del trattamento al 3° mese

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RESEARCH ARTICLE

Extended anticoagulation for the secondary prevention of venous thromboembolic events: An updated network meta-analysis

Vicky Mai, Laurent Bertoletti, Michel Cucherat, Sabine Jardel, Claire Grange, Steeve Provencher, Jean-Christophe Lega

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