

# EUROPEAN RESPIRATORY journal

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Early View

Correspondence

# Prevalence of pulmonary embolism in patients with COVID-19 at the time of hospital admission and role for pre-test probability scores and home treatment?

Mitja Jevnikar, Olivier Sanchez, Marc Humbert, Florence Parent

Please cite this article as: Jevnikar M, Sanchez O, Humbert M, *et al.* Prevalence of pulmonary embolism in patients with COVID-19 at the time of hospital admission and role for pre-test probability scores and home treatment?. *Eur Respir J* 2021; in press (https://doi.org/10.1183/13993003.01033-2021).

This manuscript has recently been accepted for publication in the *European Respiratory Journal*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJ online.

Copyright ©The authors 2021. This version is distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0. For commercial reproduction rights and permissions contact permissions@ersnet.org

**Title:** Prevalence of pulmonary embolism in patients with COVID-19 at the time of hospital admission and role for pre-test probability scores and home treatment?

Authors: Mitja Jevnikar<sup>1, 2, 3</sup>, Olivier Sanchez<sup>4, 5, 6</sup>, Marc Humbert<sup>1, 2, 3</sup> and Florence Parent<sup>1, 2, 3</sup>.

1. Université Paris-Saclay, Faculty of Medicine, Le Kremlin-Bicêtre, France

- 2. INSERM UMR\_S 999, Le Kremlin-Bicêtre, France
- 3. AP-HP, Service de Pneumologie et soins intensifs respiratoires, Hôpital Bicêtre, Le Kremlin-Bicêtre, France
- 4. AP-HP, Service de Pneumologie et Soins Intensifs, Hôpital Européen Georges Pompidou, Paris, France

5. INSERM UMR-S 1140; Paris, France and INNOVTE, St-Etienne, France.

6. Université Paris Descartes, Faculty of Medicine, Paris, France

#### **Correspondence:**

Florence Parent, MD

Service de pneumologie, Le Kremlin-Bicêtre, France

78 rue du général Leclerc, 94270 Le Kremlin Bicêtre, France.

Tél: +33 145 21 78 76

Fax: +33 145 21 79 71

### Email: <a href="mailto:florence.parent@aphp.fr">florence.parent@aphp.fr</a>

We thank Porfidia and colleagues for their interest in our study describing the prevalence of pulmonary embolism (PE) in patients with coronavirus disease (COVID-19) at the time of hospital admission (1). We fully agree on the need to consider a PE diagnostic algorithm in COVID-19 at the time of hospital admission, because indiscriminate execution of computed tomography pulmonary angiography (CTPA) cannot be a doable routine approach in such patients. In order to address Porfidia and colleagues' question, we have collected risk factors for venous thromboembolism (VTE) as well history of VTE, oestrogen treatment, prior history of cancer or active cancer and surgical intervention or immobilisation in the last month. Moreover, the YEARS clinical probability for PE was prospectively studied in the emergency department by the physician in charge of the patients before knowing the results of the D-dimer levels, with the application of the three items of the YEARS algorithm (clinical signs of deep vein thrombosis, haemoptysis, and PE as most likely diagnosis) (2). Of note, the YEARS clinical probability and D-dimer results were not used to guide whether or not to perform CTPA because all patients had CTPA at admission in our study. Nevertheless, we have been able to retrospectively evaluate the performance of the YEARS approach and the number of PEs that would have been missed, using the 1000 ng/mL D-dimer cut-off in patients without YEARS items or 500ng/mL in patients with one or more YEARS items to exclude PE at admission, and therefore the number of CTPA that would have been avoided with this approach. Due to the word limit allowed in a research letter, we could not present these results in our original publication and we thank our colleagues for giving us the opportunity to present them in response to their correspondence.

Of the 106 included patients, 31% (95% CI 21.4-39.9) had risk factors of PE and only 16.0% of patients (95% CI 9.6-24.4) had  $\geq$  1 YEARS items, as compared to 49.7% of the patients included in the YEARS study (2). The YEARS algorithm was applied to the 98 patients with an available D-dimer assay. Among them, PE was diagnosed in 13 patients (13.3%). The application of the YEARS diagnostic algorithm would have avoided 39/98 CTPA (39.8%; 95% CI 30–50.2) at the cost of missing one patient with PE (2.6%). Briefly, this 81-year-old patient had a D-dimer level of 550 ng/ml and no YEARS items. CTPA on admission showed a distal, sub-segmental PE. Interestingly, the patient was treated with prophylactic anticoagulant treatment at home for a history of VTE, treated with oral apixaban 2.5 mg twice a day. There was no significant difference between the groups with or without acute PE at the time of hospital admission for COVID, in terms of VTE risk factors and YEARS items  $\geq$ 1 (Table 1). Last, we confirm that no patient received COVID-19 therapy such as corticosteroid of anticoagulation prior to hospitalisation (1, 3).

In conclusion, determining the probability of PE is challenging in COVID-19 and a validated and safe diagnostic algorithm would be useful for clinicians. Several diagnostic algorithms have been validated and recommended in outpatients with clinical suspicion of PE but none of these algorithms has been evaluated in patients with COVID-19. The YEARS algorithm was designed to be applied in a busy clinical practice, such as what hospitals have experienced during the COVID-19 pandemic period and for this

reason, we decided to test it rather than Pulmonary Embolism Rule Out Criteria (PERC) rules (4). Applying the YEARS algorithm in our study population, would have allowed to avoid almost 40% of CTPA at hospital admission at the cost of one false negative (2.6%). However, these data must be interpreted with caution because of the small number of patients studied. Larger prospective studies are needed to validate the value of PE diagnostic algorithms in that challenging clinical setting also due to the high PE prevalence despite a low level of clinical suspicion at hospital admission (1).

Table 1.

	All patients (n=106)	Patients with PE (n=15)	Patients without PE (n=91)	P- value
Patients with risk factors for VTE n (%):	32 (30)	8 (53)	26 (29)	0.1
<ul> <li>Malignancy / History of malignancy n (%)</li> <li>Immobilization/surgery in the past 4 weeks</li> </ul>	16 (15)	2 (13)	14 (15)	
n (%)	12 (11)	2 (13)	12 (13)	
- History of VTE n (%)	8 (7)	3 (20)	5 (5)	
- Oestrogen n (%)	2 (2)	1 (6)	1 (1)	
YEARS items ≥1 n (%)	17 (16)	5 (36)	12 (13)	0.08

VTE: venous thromboembolism. PE= pulmonary embolism

Data are expressed as number of occurrences, n (% of total)

## **REFERENCES:**

- Jevnikar M, Sanchez O, Chocron R, Andronikof M, Raphael M, Meyrignac O, Fournier L, Montani D, Planquette B, Soudani M, Boucly A, Pichon J, Preda M, Beurnier A, Bulifon S, Seferian A, Jaïs X, Sitbon O, Savale L, Humbert M, Parent F. Prevalence of pulmonary embolism in patients with COVID 19 at the time of hospital admission. Eur Respir J 2021; 57:2100116
- Van der Hulle T, Cheung WY, Kooij S, Beenen LFM. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. Lancet. 2017 Jul 15;390(10091):289-297. doi: 10.1016/S0140-6736(17)30885-1. Epub 2017 May 23.
- 3. Chalmers JD, Crichton ML, Goeminne PC, Cao B, Humbert M, Shteinberg M, Antoniou KM, Ulrik CS, Parks H, Wang C, Vandendriessche T, Qu J, Stolz D, Brightling C, Welte T, Aliberti S, Simonds AK, Tonia T, Roche N. Management of hospitalised

adults with coronavirus disease-19 (COVID-19): A European Respiratory Society living guideline. Eur Respir J 2021; 57:2100048.

4. Penaloza A, Soulié C, Moumneh T. Pulmonary embolism rule-out criteria (PERC) rule in European patients with low implicit clinical probability (PERCEPIC): a multicentre, prospective, observational study. Lancet Haematol. 2017 Dec; 4(12):e615-e621. doi: 10.1016/S2352-3026(17)30210-7. Epub 2017 Nov 14. PMID: 29150390.