CRITICAL REVIEW FORM FOR A CLINICAL PREDICTION RULE

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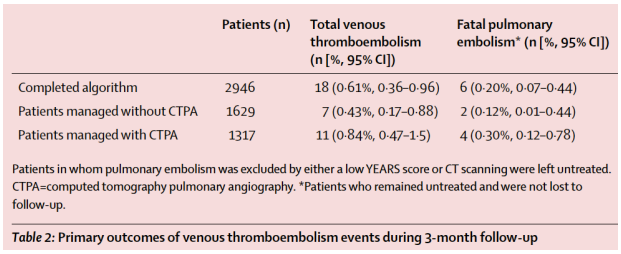
Study Objective: The **primary outcome** was the number of independently adjudicated events of venous thromboembolism during 3 months of follow-up after pulmonary embolism was excluded by YEARS. The **secondary outcome** was the number of required CTPA's performed compared with the Wells' diagnostic algorithm.

Study Methodology: Prospective multicentered cohort study in 12 hospitals in the Netherlands that evaluate the YEARS clinical decision rule. A simplified diagnostic algorithm that evaluaties the safety and efficiency of the YEARS algorithm in patients with suspected acute pulmonary embolism

Citation: van der Hulle et al. (2017**). Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study.** Lancet, 2017; 390: 289-97

GUIDE	COMMENTS
1. Is this a newly derived prediction rule? (Level IV)	
1a. Was validation restricted to the retrospective use of statistical techniques on the original database? (If so, this is a Level IV rule & is not ready for clinical application).	No. This was a prospective validation of a previously derived "simplified" wells score that included 3 components (hemoptysis, clinical signs of DVT and PE most likely diagnosis) and adjusted D-dimer thresholds. (YEARS)
2. Has the rule been validated? (Level II or III)	Yes. Authors previously published a derivation study (n=807) and a separate validation study (n=3306)
2a. Were all-important predictors included in the derivation process?	Based upon prior derivation study using logistical regression, authors identified 3 components of the Wells score with a ROC for the three components of AUC of 0.83 (95% CI, 0.80–0.87). Pregnancy was not an exclusion in the derivation study but it was in this validation study.
2b. Were all important predictors present in significant proportion of the study population?	Yes. All patients had "clinically suspected acute pulmonary embolism" and 1722 had at least one additional YEARS item.

2c. Does the rule make clinical sense?	Yes. Clinical suspicion clearly does and was the highest category reported. Hemoptysis and clinical suspicion of DVT seem less intuitive despite their previously reported derivation.
3. Did validation include prospective studies on several different populations from that used to derive it (II) or was it restricted to a single population (III)?	Uncertain. It appears the population cohort for the derivation and validation studies were from a similar if not the same patient populations in the Netherlands and France.
4. How well did the validation study meet the following criteria	
4a. Did the patients represent a wide spectrum of severity of disease?	Unlikely. Authors state "The study patients were relatively young. We have described a cohort of only hemodynamically stable patients." Pregnant patients were excluded. Majority 62% were women. Only 10% had a history of malignancy.
4b. Was there a blinded assessment of the gold standard?	True "gold standard" such as autopsy findings or CTA in all patients did not occur. Authors used 3-month follow-up outcome data as a surrogate "gold standard" in all patients. Clinicians were not blinded to D-dimer results.
4c. Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?	Two of three predictor variables are quite subjective (clinical suspicion for PE and DVT).
4d. Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?	Probably. D-dimer results were not blinded and may have been available prior to clinician assessment creating attribution or selection bias.
4e. How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)? 	**Primary Outcome**: Of the 2946 patients in whom PE was ruled out at baseline and were untreated, 18 patients were diagnosed with symptomatic VTE during the 3-month follow up – incidence of 0.61% (95% CI 0.36-0.96). No significant difference when accounting for those lost to f/u. Using YEARS criteria, CTA was excluded in 48% of patients compared to Wells and D-dimer <500ng/ml of 34% Absolute difference 14%. (95% CI 12-16) in favor of YEARS. Using age-adjusted Wells, 48% vs. 39% Absolute difference 9% (CI 6.4-11)

	Patients (n)	Total venous thromboembolism (n [%, 95% CI])	Fatal pulmonary embolism* (n [%, 95% CI])
Completed algorithm	2946	18 (0·61%, 0·36–0·96)	6 (0·20%, 0·07–0·44)
Patients managed without CTPA	1629	7 (0·43%, 0·17–0·88)	2 (0·12%, 0·01–0·44)
Patients managed with CTPA	1317	11 (0·84%, 0·47–1·5)	4 (0·30%, 0·12–0·78)

Patients in whom pulmonary embolism was excluded by either a low YEARS score or CT scanning were left untreated. CTPA=computed tomography pulmonary angiography. *Patients who remained untreated and were not lost to follow-up.

Table 2: Primary outcomes of venous thromboembolism events during 3-month follow-up

	A 14% absolute reduction in number of CTA's using YEARS with failure rates of: 0·11% (1 of 894, 95% CI 0·02–0·63) and 0·81% (6 of 740, 0·37–1·8) 3-month incidence of venous thromboembolism in patients who did not have CTPA according to the YEARS algorithm was 0·43% (seven of 1629, 95% CI 0·17–0·88) and of fatal pulmonary embolism: 0·12% (two of 1629, 0·01–0·44
5. Has an impact analysis demonstrated change in clinical behavior as a result of using the rule? (Level I). If so consider the following:	
1. How well did the study guard against bias in terms of differences at the start (concealed randomization, adjustment in analysis) or as the study proceeded (blinding, co-intervention, loss to follow-up)?	Entry criteria was purely subjective and likely vulnerable to bias. D-dimer results not blinded. No major loss to follow-up and no difference in outcome when worst-case-scenario of those lost to f/u was calculated.
2. What was the impact on clinician behavior and patient-important outcomes?	Decrease in rate of CT's appears to have

Limitations: Absence of a control group, autopsy was not done in 6 patients that died during follow up period, 43 violations of the protocol (d-dimer not done in 3 patients and 40 CTPA's were not indicated), not a large percentage of cancer patients (9.7%) (may not be applicable to cancer patients), pregnant patients were excluded

Bottom Line: Useful tool to help reduce the use of CTPA, especially in younger patients.