Comparison of YEARS and Adjust-Unlikely D-dimer Testing for Pulmonary Embolism in the Emergency Department

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Study objective: We prospectively assessed the diagnostic accuracy of YEARS and a modified age-adjusted clinical decision rule ("Adjust-Unlikely") for pulmonary embolism (PE) testing in the emergency department.

Methods: This study was conducted in tertiary care Canadian emergency departments. When the D-dimer was <500 ng/ml, PE was excluded. Pulmonary imaging for PE was performed when the D-dimer was ≥500 ng/ml. Patients were followed for 30 days, and PE outcomes were independently adjudicated. Physicians systematically recorded the presence or absence of YEARS items (PE most likely, hemoptysis, signs of deep venous thrombosis) prior to D-dimer testing and imaging. We analyzed the diagnostic accuracy of YEARS and the "Adjust-Unlikely" rule. Age adjustment (age x 10 in those >50 years old) was applied in patients where PE was not the most likely diagnosis and 500 ng/ml threshold when PE was most likely.

Results: One thousand seven hundred three patients were included, median age 62 (50, 74), 58% female, PE prevalence 8.0%. YEARS sensitivity for PE diagnosis was 92.6% (87.0, 96.0%) and specificity 45.0% (42.5, 47.5%). Adjust-Unlikely sensitivity was 100.0% (97.2, 100.0%) and specificity 32.4% (30.1, 34.8%). Posttest probability of PE in the group of patients with PE excluded by D-dimer between 500 ng/ml and the adjusted limit was 2.8% (1.6, 5.1%) for YEARS and 0.0% (0.0, 2.6%) for the "Adjust-Unlikely" rule.

Conclusion: The "Adjust-Unlikely" rule would modestly reduce imaging and identify all cases of PE. YEARS would substantially reduce imaging but miss 1 in 14 cases of PE. [Ann Emerg Med. 2022;■:1-8.]

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INTRODUCTION

Background

In North America, pulmonary embolism (PE) is diagnosed in only 8% of emergency patients who are tested.[1] Choosing Wisely advises limiting computed tomography (CT) and ventilation-perfusion (VQ) scan imaging to those with increased D-dimer or high clinical probability. Limiting diagnostic imaging is beneficial to avoid false positive PE diagnoses, avoid nonsignificant incidental findings, reduce radiation exposure, and ensure imaging availability for patients who most need it.[2,3]

Importance

Several new and sometimes conflicting approaches to excluding PE without imaging have been published.[4-6] In particular, a patient with a D-dimer between 500 ng/ml and 1,000 ng/ml may or may not be referred for diagnostic PE imaging, depending on which decision rule the emergency physician chooses to use. At the same time, research also shows that decision rules incorporating lengthy prediction rules (such as the Wells rule) are seldom used by emergency physicians because of rule complexity, rule credibility, and local culture.[7,8] Additionally, implicit estimation of clinical probability may allow emergency physicians to bypass using D-dimer in preference for imaging by stating the patient has a high clinical probability of PE.[7] An important barrier to widespread use of these newer decision rules is that none have been independently prospectively externally validated in North America. North American validation is important because the patients tested for PE in North American emergency departments differ from those in Europe, with lower PE prevalence and lower diagnostic imaging yield, even when the same evidence-based testing protocols are followed.[1]

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Editor's Capsule Summary

What is already known on this topic

Assessing the probability of pulmonary embolism before diagnostic testing is a key step in care.

What question this study addressed

What could be the diagnostic accuracy for pulmonary embolism in patients undergoing D-dimer testing that is integrated after adjusting for clinician estimation of whether pulmonary embolism is the "most likely diagnosis"?

What this study adds to our knowledge

In 1,703 consecutive prospectively identified patients, the adjusted rule was more sensitive than the YEARS rule, but only modestly reduced pulmonary imaging.

How this is relevant to clinical practice

Decision rules for pulmonary embolism diagnostic testing are of moderate utility at best and should be formally compared to physician unstructured gestalt.

Goals of This Investigation

Previously, evidence-based exclusion of PE in the emergency department combined an unlikely clinical pretest probability (eg, unlikely Wells score) and negative D-dimer, or a high probability/positive D-dimer and negative imaging.[9] The YEARS rule[5] uses a simplified version of the Wells score, which has the potential to avoid diagnostic PE imaging in a larger proportion of patients. Age-adjusted D-dimer combines an age-adjusted D-dimer threshold with an unlikely Wells score or nonhigh simplified Geneva score[10] to exclude PE without imaging in more patients than conventional testing algorithms. Using findings from our prior research,[7,8] we developed a modified age-adjusted PE testing strategy (the Adjust-Unlikely rule) which requires D-dimer testing for all patients and uses the treating physician's judgment regarding "PE being the most likely diagnosis" to determine whether age adjustment is applied to the D-dimer threshold or not. We aimed to assess the diagnostic accuracy of the YEARS and the Adjust-Unlikely rules.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective diagnostic accuracy study involving a consecutive series of eligible patients tested for PE in 2 emergency departments in Hamilton, Ontario, Canada. The study was approved by the local research ethics board. We followed the Standards for Reporting of Diagnostic Accuracy Studies guidelines for reporting diagnostic accuracy studies[11] (Appendix E1, available at http://www.annemergmed.com).

Selection of Participants

Patients were eligible for inclusion if they were tested for PE by an emergency physician using the departmental PE order set. We excluded return patient visits, and we excluded patients if their physician did not record the presence or absence of YEARS items on the order set. No other exclusion criteria were applied. The study did not require patient consent as all data were extracted from the electronic medical record, and the study did not alter patient care.

PE Reference Standard

Both emergency departments introduced the same standardized PE testing order set at the study's outset (the order set can be reviewed in Appendix E2, available at http://www.annemergmed.com).[12] Physicians were trained on and expected to use this order set for all PE testing. The order set started with D-dimer (STA Liatest assay), renal function, and blood count testing. If D-dimer was $\geq$500 ng/ml, the patient underwent diagnostic imaging (CT pulmonary angiogram or VQ scan). PE was considered excluded by a D-dimer less than 500 ng/ml or a negative CT or VQ scan. We chose to use the manufacturer-recommended D-dimer cutoff as a single test to exclude PE because (1) 2 recent PE management studies reported no missed cases of PE among patients with a D-dimer $<$500 ng/ml,[4,6] and; (2) we preferred the reference standard to be independent of clinical probability because we were evaluating the diagnostic performance of the YEARS clinical items. When diagnostic imaging was required, it was performed during the same emergency department visit as the D-dimer test. All patients were followed forward in time for 30 days by medical record review in every hospital in the city (3 hospitals in total). PE was diagnosed by any CT or VQ scan reporting acute PE within 30 days of the index emergency department visit. The diagnosis of acute PE was independently adjudicated by thrombosis medicine physicians who had no other role in the study, blinded to the time point of PE diagnosis (initial presentation versus follow-up), the YEARS items, and D-dimer result. The adjudicators reviewed the imaging reports, thrombosis physician consult records and subsequent management.

YEARS

We evaluated the diagnostic accuracy of the YEARS rule, which excludes PE using a D-dimer threshold of 500

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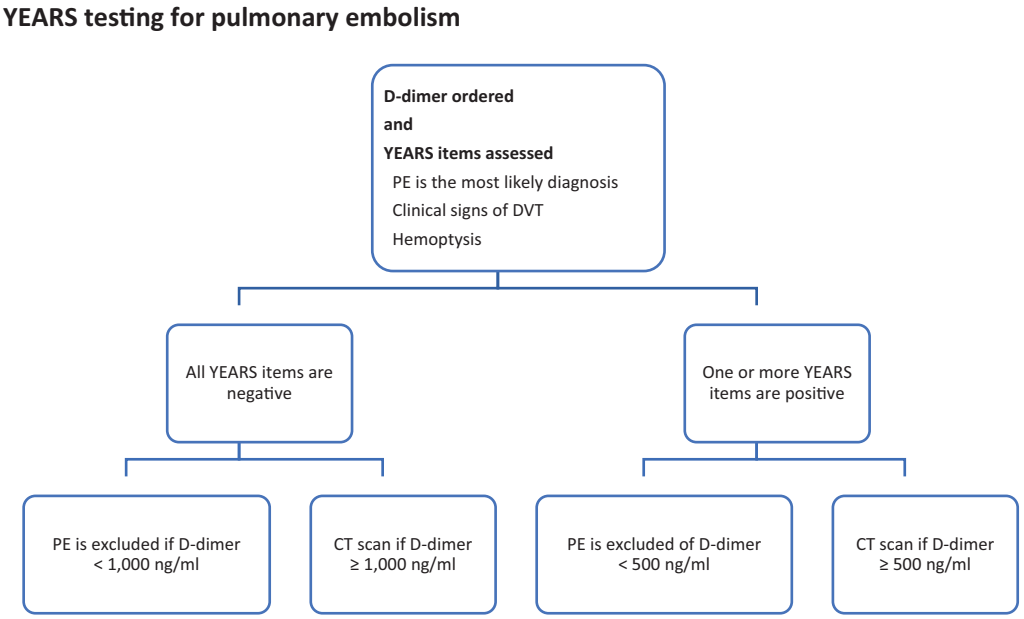
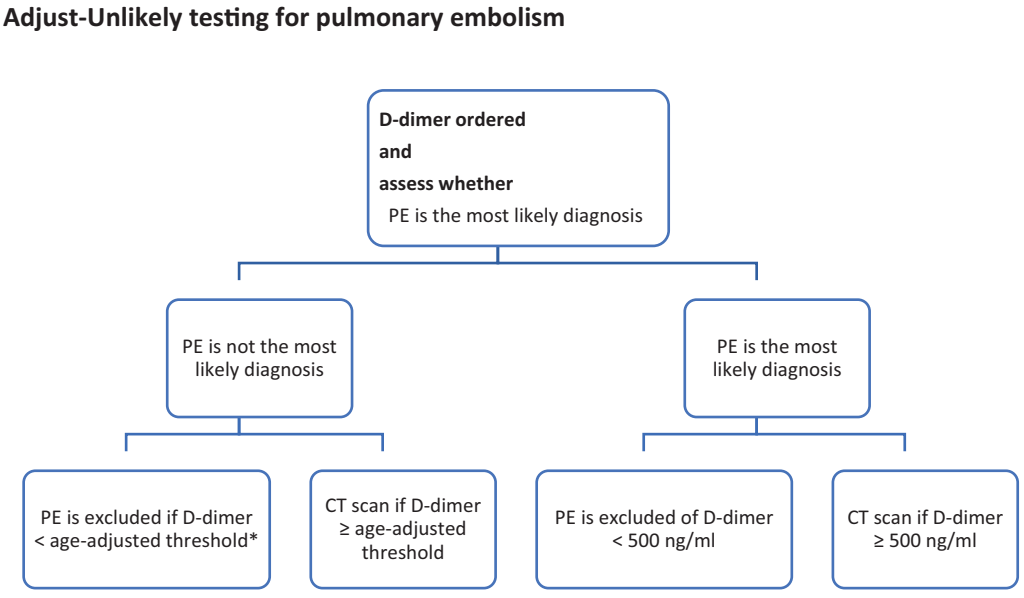
ng/ml in patients with one or more YEARS items, and excludes PE using a D-dimer threshold of 1,000 ng/ml in patients with no YEARS items (Figure 1). Physicians were asked to record the presence or absence of YEARS clinical probability items (by checking off at least one of: "PE most likely" (based on implicit estimation), "clinical signs of deep vein thrombosis," "hemoptysis" or "no YEARS items" after taking the patient history and performing an examination. The YEARS items were recorded in a table that appeared on the front page of the PE testing order set (Appendix E3, available at http://www.annemergmed.com). D-dimer testing had not been drawn at the point of completing the PE order set. This process ensured the physician was blinded to the D-dimer and imaging test





* Age-adjusted threshold is [age x 10] in patients > age 50. For patients ≤ age 50, use 500 ng/ml.
PE pulmonary embolism, CT computed tomography

Figure 1. YEARS and "Adjust-Unlikely" pulmonary embolism testing algorithms. *CT,* computed tomography; *DVT,* deep vein thrombosis. *Age-adjusted threshold is [age x 10] in patients > age 50. For patients ≤ age 50, use 500 ng/ml.

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results when documenting the YEARS items. Of note, no D-dimer was drawn without the order of the treating physician who had assessed the patient. The hard copy order set forms were scanned into the electronic medical record after the patient was discharged from the hospital. The presence or absence of the YEARS items had no effect on PE testing because PE testing was standardized, and the decision to order a CT scan was guided by D-dimer, independent of PE clinical probability.

Adjust-unlikely

We also evaluated the diagnostic accuracy of "Adjust-Unlikely", which was prespecified to exclude PE by a D-dimer <500 ng/ml when PE is the most likely diagnosis (as per physician implicit estimation) and by age-adjusted D-dimer (age x 10 in patients older than 50 years of age) when PE is not the most likely diagnosis (Figure 1). This modification simplified the testing algorithm by avoiding Wells score calculation in response to our prior findings that emergency physicians dislike using the Wells score.[7]

Data Collection

We obtained hospital electronic medical record data on all patients who underwent D-dimer and/or CT pulmonary angiography or VQ scanning. Trained research assistants identified potentially eligible patients by the presence of the scanned PE testing order set in the electronic medical record. Research assistants extracted data on the YEARS items from the scanned PE testing order set. Patient age at presentation, patient sex, date of index presentation, D-dimer results, and disposition were extracted electronically from the electronic medical record. We did not extract data on comorbidities or anticoagulation use because these data were unavailable electronically. The reports for all CT pulmonary angiograms and VQ scans performed at index presentation and during 30-day follow-up in all 3 Hamilton hospitals were manually reviewed by the research assistants. Scans reporting acute or chronic PE were then adjudicated, blind to D-dimer and YEARS items. Research assistants were blinded to the analysis plan.

Analysis

We analyzed the sensitivity, specificity, negative predictive value, and positive predictive value for the YEARS and "Adjust-Unlikely" rules for diagnosing acute PE. Secondary outcomes included the posttest probability of PE among patients with PE excluded with a D-dimer between 500 ng/ml and 1,000 ng/ml for YEARS and between 500 ng/ml, the age-adjusted cutoff for the "Adjust-Unlikely" rule. We reported the proportional reduction in diagnostic imaging for each rule compared to using a D-dimer with a cutoff of 500 ng/ml (as per the reference standard). We used the Wilson score test to calculate 95% confidence intervals (CIs). The 95% CIs for the differences in proportions were estimated using the McNemar test. Analysis was conducted using SAS version 9.4 (SAS Institute, Inc, Cary, NC). Imaging studies reported as indeterminate or adjudicated as chronic PE was considered negative for acute PE. Our primary outcome of interest was sensitivity, given that emergency physicians consider missed PE to be more serious than ordering a potentially unnecessary CT PE scan.[7] We estimated PE prevalence to be 8%, according to a prior PE management study conducted in the same emergency departments.[6] A sample size of 1,700 patients would therefore demonstrate 99.0% sensitivity with 95% CI 98.5 to 99.5%.

RESULTS

Characteristics of Study Subjects

Between November 4th 2019 and June 7th 2021, 1,961 emergency department patients were tested for PE with the standardized order set, of whom 1,761 (89.8%) had the YEARS items recorded. We excluded 58 repeat patient visits leaving 1,703 patients included in the analysis. Compared to included patients, excluded patients had similar age and sex distribution (median age 62, 53.5% female) but a higher prevalence of PE (13.6%). Table displays the patient characteristics. In total, 136 patients (8.0%) were diagnosed with PE during their index emergency department visit. Figure 2 summarizes the reference standard testing results. None of the 1,567 patients who had PE excluded during their index emergency department visit were diagnosed with PE during the 30-day follow-up period.

Main Results

Figures 3 and 4 show the diagnostic performance of YEARS and "Adjust-Unlikely". One hundred and nineteen patients (7.0% of the cohort) with a positive YEARS rule and 151 patients (8.9% of the cohort) with a positive "Adjust-Unlikely" rule did not undergo diagnostic imaging. None of these patients were diagnosed with PE within the following 30 days.

The YEARS score would have missed the diagnosis of 10 PE cases: YEARS sensitivity for PE diagnosis was 92.6% (87.0, 96.0%), specificity 45.0% (42.5, 47.5%), negative predictive value 98.6% (97.4, 99.2%), positive predictive value 12.8% (10.7, 14.9%). Two out of 10 PE cases missed by the YEARS rule were limited to the subsegmental

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Table. Characteristics of the YEARS population.

Characteristic	Median (Interquartile Range) or number (%)
Total # of patients	1,703
Age, (y)	62 (50, 74)
Female	982 (57.7)
ED presentation time	
8 AM to 5 PM	742 (43.6)
5 PM to 8 AM	961 (56.4)
Patients discharged home from ED	1,040 (61.1)
D-dimer	950 (540, 2,020)
PE is the most likely diagnosis	393 (23.1)
Hemoptysis	83 (4.9)
Clinical signs of DVT	168 (9.9)
Total number of YEARS items	
1	538 (31.6)
2	47 (2.8)
3	4 (0.2)
Underwent CT pulmonary angiogram	1,174 (68.9)
Underwent VQ scan*	2 (0.1)
Diagnosed with PE at index presentation	136 (8.0)
Diagnosed with PE during follow-up	0 (0.0)
PE in the subsegmental arteries only	8 (0.5)

DVT, deep venous thrombosis; *ED*, emergency department; *VQ*, ventilation-perfusion.
*One patient had both CT and VQ scan.

pulmonary arterial level. Among those patients with no YEARS items, 287 had a D-dimer <500 ng/ml, and 352 had a D-dimer result between 500 and 1,000 ng/ml. The incidence of PE among this latter group (no YEARS items and a D-dimer between 500 and 1,000 ng/ml) was 2.8% (1.6, 5.1%). Compared to using a stand-alone D-dimer threshold of 500 ng/ml, the YEARS rule increased the proportion of the total cohort who had PE excluded by D-dimer by 20.7% (18.7, 22.7%).

The "Adjust-Unlikely" rule would have missed no case of PE: "Adjust-Unlikely" sensitivity was 100.0% (97.2, 100.0%), specificity 32.4% (30.1, 34.8%), negative predictive value 100.0% (99.2, 100.0%), positive predictive value 11.4% (9.7, 13.3%). Among those where PE was not the most likely diagnosis, 322 patients had a D-dimer <500 ng/ml, and 145 had a D-dimer between 500 ng/ml and their age-adjusted threshold. The incidence of PE among those where PE was not the most likely diagnosis with a D-dimer between 500 and their age-adjusted threshold was 0.0% (0.0, 2.6%). Compared to using a stand-alone D-dimer threshold of 500 ng/ml, the "Adjust-Unlikely" rule increased the proportion who could have PE excluded by D-dimer by 8.5% (7.1, 9.9%).

LIMITATIONS

A small proportion of patients did not undergo PE diagnostic imaging as per the reference standard. PE may have dropped off the differential diagnosis list during workup, a phenomenon unlikely to be affected by choice of PE testing decision rule. The fact that there were no cases of missed PE in this group also supports the hypothesis that another more obvious diagnosis was found. Including these

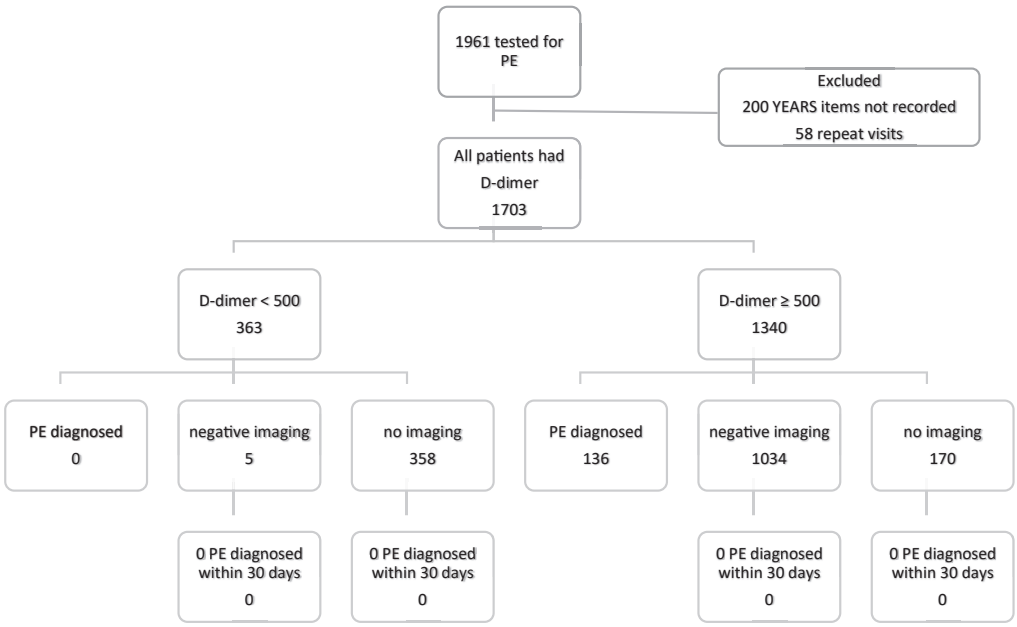

Figure 2. Reference standard testing.

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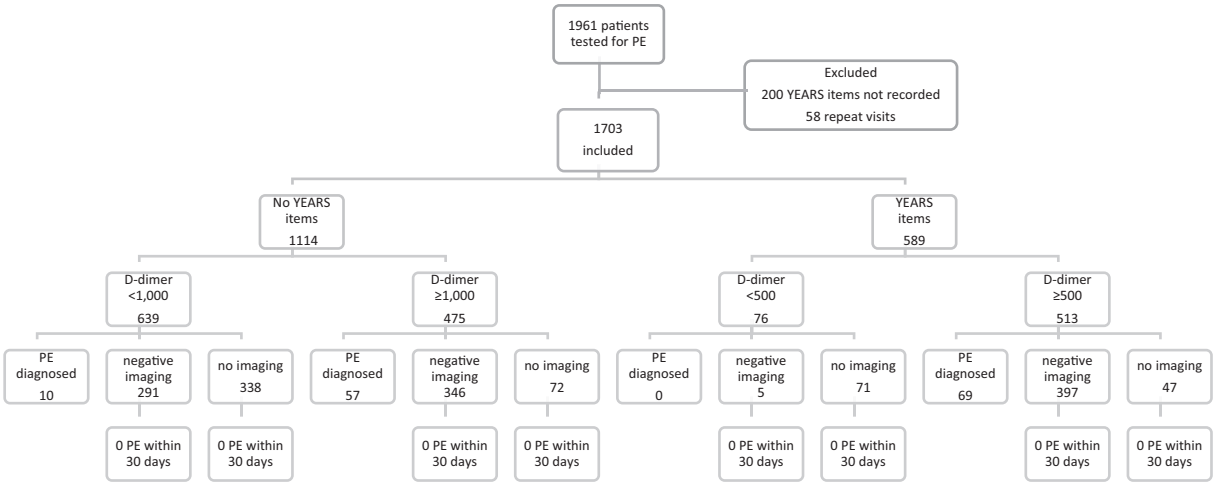

Figure 3. YEARS diagnostic testing.

cases reduces the reported decision rule specificities. We did not study the PE Rule-out Criteria[13] decision rule combined with either YEARS or "Adjust-Unlikely" decision rules. Excluded patients had a higher prevalence of PE, which could have introduced spectrum bias. There were some differences in our study, which could influence the comparison of our results to those of other diagnostic PE studies, as follows: (1) We did not consider deep venous thrombosis diagnosis as a surrogate marker for PE; (2) We followed each patient for 30 and not 90 days. Our follow-up time was determined by a survey of thrombosis medicine physicians who advised that PE diagnosis within 30 days was likely a missed event, whereas, after 30 days, it was more likely to represent de novo venous thrombosis, and; (3) We did not incorporate in-person participant follow-up which means we do not know whether all patients survived 30 days or whether they had been diagnosed with PE in another city. Although these points would reduce our reported follow-up venous thrombosis rate, there is no reason to suspect that if our follow-up had been in person and longer, the YEARS and "Adjust-Unlikely" algorithms would have been differentially affected. A greater rate of venous thrombosis reported during follow-up might minimally reduce the reported sensitivities for both rules.

DISCUSSION

We report the first North American prospective study with the primary aim to validate the YEARS rule and the first evaluation of the "Adjust-Unlikely" decision rule. We found YEARS to be less sensitive and more specific than the "Adjust-Unlikely" rule. We believe our findings are useful for North American emergency physicians because

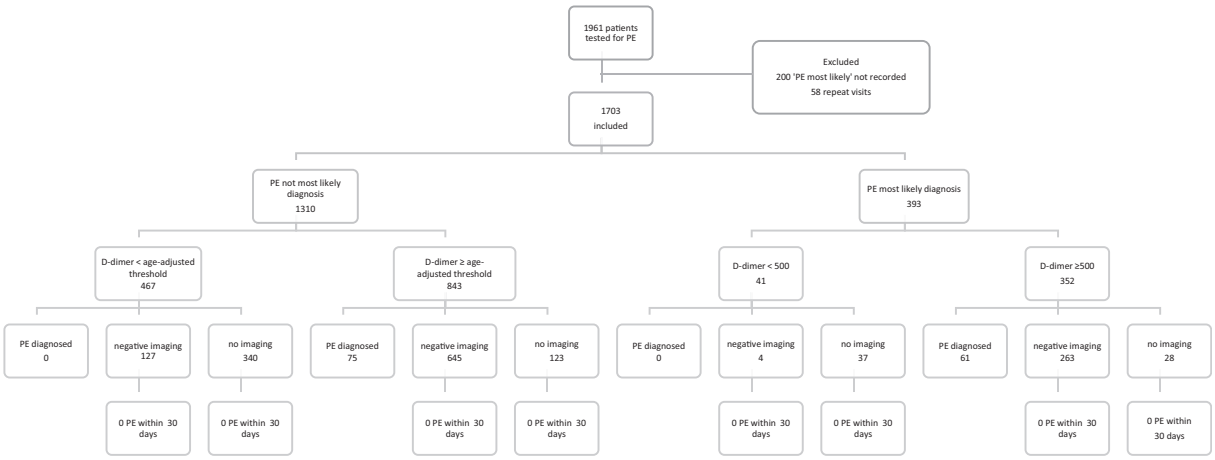

Figure 4. Adjust-Unlikely diagnostic testing.

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these PE testing decision rules are simple and do not require calculating the Wells or Geneva rules.

We found YEARS had a lower sensitivity than reported elsewhere. The YEARS rule was previously assessed in a 1,789-patient American study, finding that the YEARS rule sensitivity was 97.6% (91.7, 99.7).[14] However, patients with high pretest clinical probability were excluded from the study, and although we found a lower sensitivity, the 95% CIs of both studies overlap. YEARS was also assessed in a secondary analysis of 3,314 European patients tested for PE, with a reported sensitivity of 97.7% (96.3, 98.5),[15] which is also a higher sensitivity compared to our study, and our CIs do not overlap. The reason for our lower sensitivity is unclear. Between studies, differences include the passage of time and different study locations. A difference in disease spectrum (with European physicians diagnosing severe PE disease and Canadian physicians diagnosing less severe disease) could also explain our findings. We do not know whether the diagnostic accuracy of implicit classification that PE is the most likely diagnosis varies between studies. Finally, a recent individual patient meta-analysis that excluded American emergency department patients reported YEARS sensitivity to be 96.1% (95.0, 97.1).[16]

The "Adjust-Unlikely" rule is based on age-adjusted D-dimer. Age-adjusted D-dimer was prospectively validated in Europe with a posttest prevalence of venous thromboembolism after PE exclusion of 0.07% (0.01, 0.40), similar to our findings. We designed "Adjust-Unlikely" to avoid the need for Wells score calculation, using only the Wells score item 'PE is the most likely diagnosis' to determine whether PE is excluded using a D-dimer cutoff of 500 ng/ml or using an age-adjusted D-dimer. Our study cannot comment on the influence of this new design compared to the standard use of age-adjusted D-dimer, although both approaches appear safe.

Our study has several strengths. The study was conducted during the COVID-19 pandemic, so our results are valid during the pandemic period. We included consecutive eligible patients. The YEARS items were recorded in real-time by the treating emergency physician, blind to the patient's diagnosis, and all PE cases were independently adjudicated, blind to the YEARS items and D-dimer.

The clinical implications of our findings are that applying the YEARS rule to exclude PE in these emergency department patients would have missed a very small number of PE cases and substantially reduced pulmonary imaging. The "Adjust-Unlikely" rule would have identified all PE cases, but the reduction in pulmonary imaging would have been more modest compared to the YEARS rule. Physicians should follow guidelines to use D-dimer as a rule-out tool for PE,[17,18] and weigh these pros and cons when deciding on their approach to PE exclusion without diagnostic imaging.

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Author contributions: This study was designed by KdW and FG. The study was conducted by KdW, FG, FA, YH, JK, NC, NC, and RI. The analysis was performed by QI and KdW. The manuscript was drafted by KdW and FG. All authors contributed to and approved the final version of the manuscript. KdW takes responsibility for the paper as a whole.

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REFERENCES

1. Germini F, Zarabi S, Eventov M, et al. Pulmonary embolism prevalence among emergency department cohorts: A systematic review and meta-analysis by country of study. *J Thromb Haemost*. 2021;19:173-185.
2. Miller WT, Marinari LA, Barbosa E, et al. Small pulmonary artery defects are not reliable indicators of pulmonary embolism. *Ann Am Thorac Soc*. 2015;12:1022-1029.

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3. Anjum O, Bleeker H, Ohle R. Computed tomography for suspected pulmonary embolism results in a large number of non-significant incidental findings and follow-up investigations. *Emerg Radiol*. 2019;26:29-35.
4. Righini M, Van Es J, Den Exter PL, et al. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. *JAMA*. 2014;311:1117-1124.
5. van der Hulle T, Cheung WY, Kooij S, et al. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. *Lancet*. 2017;390:289-297.
6. Kearon C, de Wit K, Parpia S, et al. Diagnosis of pulmonary embolism with d-dimer adjusted to clinical probability. *N Engl J Med*. 2019;381:2125-2134.
7. Zarabi S, Chan TM, Mercuri M, et al. Physician choices in pulmonary embolism testing. *CMAJ*. 2021;193:E38-E46.
8. Abdulla S, Swarup V, Soomro A, de Wit K. Mapping emergency physician reasoning for adhering to evidence-based pulmonary embolism testing. *Acad Emerg Med*. 2022;29:658-661.
9. Pasha SM, Klok FA, Snoep JD, et al. Safety of excluding acute pulmonary embolism based on an unlikely clinical probability by the Wells rule and normal D-dimer concentration: A meta-analysis. *Thromb Res*. 2010;125:e123-e127.
10. Robert-Ebadi H, Robin P, Hugli O, et al. Impact of the age-adjusted D-dimer cutoff to exclude pulmonary embolism: A Multinational Prospective Real-Life Study (the RELAX-PE Study). *Circulation*. 2021;143:1828-1830.
11. Cohen JF, Korevaar DA, Altman DG, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. *BMJ Open*. 2016;6:e012799-e012799.
12. Germini F, Hu Y, Afzal S, et al. Feasibility of a quality improvement project to increase adherence to evidence-based pulmonary embolism diagnosis in the emergency department. *Pilot Feasibility Stud*. 2021;7:4-5.
13. Kline JA, Mitchell AM, Kabrhel C, et al. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. *J Thromb Haemost*. 2004;2:1247-1255.
14. Kabrhel C, Van Hylckama Vlieg A, Muzikanski A, et al. Multicenter evaluation of the YEARS criteria in emergency department patients evaluated for pulmonary embolism. *Acad Emerg Med*. 2018;25:987-994.
15. Eddy M, Robert-Ebadi H, Richardson L, et al. External validation of the YEARS diagnostic algorithm for suspected pulmonary embolism. *J Thromb Haemost*. 2020;18:3289-3295.
16. Geersing GJ, Takada T, Klok FA, et al. Ruling out pulmonary embolism across different healthcare settings: A systematic review and individual patient data meta-analysis. *PLOS Med*. 2022;19(1):e1003905-e1003906.
17. Lim W, Le Gal G, Bates SM, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. *Blood Adv*. 2018;2:3226-3256.
18. Wolf SJ, Hahn SA, Nentwich LM, et al. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with suspected acute venous thromboembolic disease. *Ann Emerg Med*. 2018;71:e59-e109.

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