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Assessing two D-dimer age-adjustment strategies to optimize CT utilization in ED evaluation of pulmonary embolism

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Abstract

Study Objective—Validate the sensitivity and specificity of two age adjustment strategies for D-dimer values in identifying patients at risk for pulmonary embolism (PE) compared to traditional D-dimer cutoff value (500ng/mL) to decrease inappropriate computed tomography pulmonary angiography (CTPA) utilization.

Methods—This institutional review board-approved, HIPAA-compliant retrospective study included all adult emergency department (ED) patients evaluated for PE over a 32-month period (1/1/11–8/30/13). Only patients undergoing CTPA and D-dimer testing were included. We used a validated natural language processing algorithm to parse CTPA radiology reports and determine presence of acute PE. Outcome measures were sensitivity and specificity of two age-adjusted D-dimer cutoffs compared to the traditional cutoff. We used chi-square tests with proportional analyses to assess differences in traditional and age-adjusted (age \times 10 ng/mL) D-dimer cutoffs, adjusting both by decade and by year.

Results—A total 3,063 patients with suspected PE were evaluated by CTPA during the study period and 1,055 (34%) also received D-dimer testing. The specificity of age-adjusted D-dimer values was similar or higher for each age group studied compared to traditional cutoff, without significantly compromising sensitivity. Overall, had decade age-adjusted cutoffs been used, 37

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Conflicts of Interest: None

CTPAs could have been avoided (19.6% of 189 patients aged >60 with Wells score 4); had yearly age-adjusted cutoffs been used, 52 CTPAs (18.2% of 286 patients aged >50 with Wells score 4) could have been avoided.

Conclusion—Each age-adjusted D-dimer cutoff strategy for the evaluation of PE was associated with increased specificity and statistically insignificant decreased sensitivity when compared to the traditional D-dimer cutoff value.

MeSH Keywords

Diagnostic Test; Pulmonary Embolism; D-dimer; Evidence-Based Practice

Introduction

Background

Validated evidence-based guidelines based on clinical criteria and D-dimer values have been established to guide clinicians to risk-stratify emergency department (ED) patients suspected to have pulmonary embolism (PE).^(1,2) Patients with high clinical pretest probabilities of PE warrant advanced imaging tests regardless of D-dimer levels, and most decision guidelines forego D-dimer testing in these patients. Conversely, the high sensitivity and negative predictive value of D-dimer allow its utilization to rule out PE in low to moderate risk patients. Therefore, only patients with an elevated D-dimer level undergo further advanced imaging.

Unfortunately, D-dimer testing has low specificity, resulting in increasing false positive results as the prevalence of disease decreases. However, recent studies have indicated that D-dimer levels tend to increase with age, and that the traditional cutoff value (500 ng/mL) may be associated with even lower specificity in older patients with low clinical probabilities on risk stratification.^(3–8) This decrease in specificity with advancing age may lead to an increased volume of unnecessary and expensive advanced imaging tests.

Some earlier studies examined the impact of age-adjustment of D-dimer cutoffs by decade (e.g., 600 ng/mL for patients aged 61–70, 700 ng/mL for patients aged 71–80) in order to improve specificity and decrease false positive results.⁽³⁾ A recent European prospective study⁽⁸⁾ has gone a step further, recommending stratifying patients over 50 years old with a yearly age-adjusted D-dimer cutoff value (specific age in years \times 10 ng/mL, e.g., a 560 ng/mL cutoff for a patient aged 56 years). While this study demonstrated that this strategy improves the specificity of D-dimer testing in aging populations, it may be associated with lower sensitivity and increased false negatives, and has not yet been validated in a U.S. population.

Importance

The use of D-dimer testing to risk stratify patients suspected of PE often leads to further diagnostic testing, including computed tomography pulmonary angiography (CTPA) imaging, ventilation/perfusion lung scan (V/Q), and pulmonary angiography. The use of an age-adjusted D-dimer cutoff may improve specificity while maintaining sensitivity, thereby

decreasing low utility CTPA utilization with resulting decreases in costs, patient radiation exposure, and risk of contrast nephropathy.(3–8)

Goals of this Investigation

We aimed to validate the sensitivity of higher, decade and yearly age-adjusted, D-dimer value cutoffs for the identification of patients at low risk for PE. We hypothesized that using either age-adjusted cutoff for D-dimer values in comparison to the traditional cutoff would allow for less CTPA imaging while not lowering the test's sensitivity for diagnosing PE. We further hypothesized that the yearly age-adjusted cutoff would lead to a higher specificity than the decade age-adjusted cutoff.

Materials and Methods

Study Setting

This retrospective study was performed in our adult ED, located in a 793-bed, urban, academic, quaternary, Level-1 trauma center. The requirement to obtain informed consent was waived by the institutional review board for this HIPAA-compliant study. The hospital's laboratory utilizes the STA-Liatest quantitative D-dimer latex-based automated assays with immunoturbidimetric readings, providing a traditional dichotomous cutoff value of 500 ng/mL.

Selection of Participants

From January 1, 2011 to August 30, 2013, consecutive adult patients presenting to our ED undergoing evaluation for potential PE with recorded D-dimer laboratory values and CTPA results were identified in our electronic health record (EHR). Patients in whom CTPA was not part of the workup (i.e., who were evaluated via V/Q scan) were not included, as the frequency of CTPA-alternative testing is low at our institution.

Study Design

We first stratified all patients over 60 years old with an age-adjusted D-dimer cutoff value (age in years \times 10 ng/mL) using decade cohorts (e.g., 600 ng/mL cutoff for 61–70 years old, 700 ng/mL cutoff for 71–80 years old, etc.).(3) We then stratified patients over 50 years old with a yearly age-adjusted D-dimer cutoff value (specific age in years \times 10 ng/mL, e.g., 560 ng/mL cutoff for a patient aged 56 years).(8) We applied both age-adjusted D-dimer strategies to all patients who received CTPA in our retrospective cohort to maximize generalizability.

Outcome Measures

The primary outcome measure was sensitivity of age-adjusted D-dimer laboratory testing in risk stratifying patients with suspected PE in comparison to the traditional cutoff. Our secondary outcome was specificity of age-adjusted D-dimer testing in comparison to the traditional cutoff.

Methods of Measurement

We used natural language processing (NLP) algorithms based on the GATE (General Architecture for Text Engineering) framework to parse all the CTPA radiology reports to determine presence of acute PE. The NLP model has been previously validated with accuracy of 97.8% compared to manual review.(9) All positive findings identified by NLP were further verified manually by an attending emergency physician (AG) by reviewing the radiology reports.

A board-certified emergency physician (AG) reviewed the EHR and data from a mandatory clinical decision support (CDS) tool(9,10) to determine Wells scores. All imaging orders in our ED are placed via computerized physician order entry (CPOE) system (Percipio, Medicalis Co, San Francisco, CA) with implementation described previously.(11) Our CPOE has an integrated CDS tool to prospectively capture granular data in the form of D-dimer and individual Wells score criteria entered by the ordering clinician to provide evidence-based decision support as to the appropriateness of CTPA for evaluation of PE; implementation has been described previously.(9) The validity of data input into the CPOE and CDS systems for PE has also been previously reported.(12)

Data Analysis

All data were entered into Microsoft Excel 2008 (Microsoft, Richmond, WA), and all statistical analyses were performed with JMP Pro 10 (SAS Institute, Cary, NC). The sample size was powered to detect a 2% effect size (power=0.8, alpha=0.05) with an estimated baseline sensitivity of 99%. This resulted in a desired sample size of 223 records for the primary outcome. Chi-square tests with proportional analyses were used to assess differences in traditional and age-adjusted D-dimer laboratory cutoffs. We used the Newcombe score method with continuity correction for 95% confidence intervals around estimated proportions.(13) A two-tailed p-value of <0.05 was defined as statistically significant.

Results

Characteristics of Study Subjects

A total of 3,063 patient-visits with suspected PE were evaluated by CTPA during the study period with an overall yield of 9.4% (289 positive studies). In 1,055 (34%) patients, D-dimer values were also obtained and these patients were included in the study cohort. Of the 1,055 patients, 729 (69.1%) were women, the mean age was 52.8 years (min 18, max 96, 95% CI 51.7–53.9), and the median documented Wells score was 4.5 (min 0, max 12.5, 95% CI 3.9–4.2). The prevalence of PE ranged from 5.8% in patients aged less than 50 years, to 10.1% in patients aged 61–70 (Table 4).

Main Results

The overall population sensitivity and specificity for PE using the traditional D-dimer cutoff value of 500 ng/mL were 100% (95% CI: 94.2–100%) and 7.4% (95% CI: 5.8–9.2%) (Table 1). The population sensitivity and specificity for PE using the decade age-adjusted D-dimer cutoff values were 98.7% (95% CI: 92.1–99.9%) and 13.5% (95% CI: 12.2–16.8%) (Table

2). The population sensitivity and specificity for PE using the yearly age-adjusted D-dimer cutoff values were 97.4% (95% CI: 90.2–99.6%) and 16.7% (95% CI: 14.4–19.2%) (Table 3).

The specificity of D-dimer testing with a traditional cutoff decreased with increasing age, from 10.5% in patients aged 51–60 years to 2.9% in patients aged more than 80 years (Table 4). The sensitivities remained constant for all decades at 100%.

The use of the decade age-adjusted cutoff value significantly increased specificity of D-dimer testing in all age groups, from 17.4% in patients aged 61–70 to 24.3% in patients aged more than 80 years (Table 4). The sensitivities also remained at 100% except for a single patient case in the >80 years group that reduced sensitivity to 85.7%.

The use of the yearly age-adjusted D-dimer cutoff value significantly increased specificity of D-dimer testing in all age groups, from 18.9% in patients aged 51–60 to 32.3% in patients aged more than 71–80 years (Table 4). The sensitivities also remained at 100% except for one 56 year-old patient in 51–60 year group who reduced sensitivity to 93.3% and one 87 year-old patient in the >80 years group who reduced sensitivity to 85.7%. However, these sensitivity changes were not statistically different from the traditional cutoff strategy.

Overall, had decade age-adjusted cutoffs been used, 37 CTPAs (19.6% of 189 patients >60 years old with Wells score ≥ 4) could have been avoided, as each of these patients had a D-dimer value between 500 ng/mL and the respective decade cutoff. Had yearly age-adjusted cutoffs been used, 52 patients with Wells score ≥ 4 could have avoided CTPA, as their D-dimer values were between 500 ng/mL and the respective yearly age-adjusted cutoff (18.2% of 286 patients >50 years old with Wells score ≥ 4).

Limitations

These data must be interpreted in the context of the study design. Our study was performed in a single academic setting utilizing the STA-Liatest immunoturbidimetric D-dimer assay. While this assay has been shown to have excellent sensitivity and specificity(14,15), the generalizability of our results is limited to institutions employing the same D-dimer assay. Nonetheless, the concept of age-adjusted D-dimers in evaluating PE should remain consistent across assays and has been shown previously.(15)

Our institution has CDS embedded within the CPOE system to provide evidence-based decision support to the ordering clinician as to the appropriateness of CTPA for evaluation of PE. Our implementation of CDS has previously shown decreases in utilization of CTPA, using traditional D-dimer cutoffs along with Wells score assessment.(9) While the setting of CDS may lower the generalizability of this study, its presence would likely underestimate the impact of the age-adjusted D-dimer cutoff strategies in further avoiding low utility CTPAs. Finally, in our cohort, 66% of patients with CTPA did not receive D-dimer testing. This likely reflects the current best practice of not obtaining D-dimer testing on patients in the “PE likely” subset of patients with Wells scores >4 , which may have been larger at our site than in others due to our large oncology patient population. Further prospective studies

for high-risk patients may provide additional insight into the application of age-adjusted D-dimer strategies in this patient population.

Discussion

We found that an age-adjusted D-dimer cutoff strategy in the evaluation of pulmonary embolus is associated with increased specificity while maintaining high sensitivity. This strategy increases the value of the D-dimer testing for the exclusion of PE in older patients.

Although D-dimers should only be applied to patients suspected of PE after assessment of pretest clinical probability (16,17), we applied the age-adjusted D-dimer strategies to all patients who received CTPA in our retrospective cohort to maximize generalizability.

We found that D-dimer specificity decreased with age when using the traditional D-dimer cutoff value, but that it significantly improved when using either the decade or yearly age-adjusted D-dimer cutoff values. Sensitivity remained high for both strategies. Overall, had decade age-adjusted cutoffs been used, 37 CTPAs (19.6% of 189 patients >60 years old with Wells score 4) could have been avoided; had yearly age-adjusted cutoffs been used, 52 patients (18.2% of 286 patients >50 years old with Wells score 4) could have avoided CTPA.

While a number of studies have evaluated the use of age-adjusting D-dimer cutoffs by patient decade, the strategy of using yearly age-adjusted cutoffs has not yet been extensively studied. Our results confirm those of the recent European study(8), which demonstrated that using yearly age-adjusted cutoffs would have resulted in 11.6% fewer CTPAs in their population. Their 3-month follow-up demonstrated only one missed PE in a patient with a D-dimer between 500 ng/mL and their age-adjusted cutoff.

Similarly, our cohort also included one patient who had a PE that was noted by the traditional D-dimer cutoff value, but missed by both the decade and yearly age-adjusted D-dimer cutoff values. This patient was 87 years old with a D-dimer value of 598 ng/mL and a low pretest clinical probability for PE with a documented Wells score of 3. On review of his EHR, this patient was found to have a subsegmental PE, was admitted to the hospital, was not treated with anti-coagulation as the risk of therapy was deemed to be greater than the benefits by his clinicians, and was discharged without apparent complications. It might be argued that this patient had an incidental finding with no clinical impact, intervention, or morbidity. The treatment of subsegmental PE is a topic of debate. Some studies have found considerable interobserver variability amongst radiologists in the diagnosis of subsegmental PE versus perfusion artifact and a recent meta-analysis suggested “that subsegmental PE may not be clinically relevant.”(18)

Our cohort included a second patient who had a PE that was missed by the yearly age-adjusted D-dimer cutoff only. This patient was 56 years old with a D-dimer value of 555 ng/mL. On review of her EHR, this patient had a high pretest clinical probability for PE with a documented Wells score of 7.5. Following validated guidelines for the evaluation of patients suspected for PE, this patient warranted CTPA evaluation regardless of her D-dimer value.

In summary, we found that implementation of yearly age-adjusted D-dimer cutoff for patients aged over 50 years suspected of PE would increase specificity with statistically insignificant reduction in sensitivity. This strategy may safely decrease the utilization of low utility CTPAs in patients >50 years old, resulting in increased patient protection from irradiation and the risk of contrast-induced nephropathy. Further, the yearly age-adjusted strategy may be simpler to calculate and may therefore be more likely to have widespread utilization in EDs compared to the decade strategy.

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References

1. Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost.* 2000 Mar; 83(3):416–20. [PubMed: 10744147]
2. Le Gal G, Righini M, Roy P-M, Sanchez O, Aujesky D, Bounameaux H, et al. Prediction of Pulmonary Embolism in the Emergency Department: The Revised Geneva Score. *Ann Intern Med.* 2006 Feb 7; 144(3):165–171. [PubMed: 16461960]
3. Schouten HJ, Geersing GJ, Koek HL, Zuithoff NPA, Janssen KJM, Douma RA, et al. Diagnostic accuracy of conventional or age-adjusted D-dimer cut-off values in older patients with suspected venous thromboembolism: systematic review and meta-analysis. *BMJ.* 2013 May 3; 346(may03 1):f2492–f2492. [PubMed: 23645857]
4. Crop MJ, Siemes C, Berendes P, van der Straaten F, Willemsen S, Levin MD. Influence of C-reactive protein levels and age on the value of D-dimer in diagnosing pulmonary embolism. *Eur J Haematol.* 2013 Oct 25.
5. Jaffrelot M, Le Ven F, Le Roux P-Y, Tissot V, Rame E, Salaun P-Y, et al. External validation of a D-dimer age-adjusted cut-off for the exclusion of pulmonary embolism. *Thromb Haemost.* 2012 May; 107(5):1005–7. [PubMed: 22399072]
6. Harper PL, Theakston E, Ahmed J, Ockelford P. D-dimer concentration increases with age reducing the clinical value of the D-dimer assay in the elderly. *Intern Med J.* 2007; 37(9):607–13. [PubMed: 17543005]
7. Haase C, Joergensen M, Ellervik C, Joergensen MK, Bathum L. Age- and sex-dependent reference intervals for D-dimer: Evidence for a marked increase by age. *Thromb Res.* 2013 Dec; 132(6):676–80. [PubMed: 24139507]
8. Righini M, Van Es J, Den Exter PL, Roy P-M, Verschuren F, Ghuysen A, et al. Age-Adjusted D-Dimer Cutoff Levels to Rule Out Pulmonary Embolism: The ADJUST-PE Study. *JAMA.* 2014 Mar 19; 311(11):1117. [PubMed: 24643601]
9. Raja AS, Ip IK, Prevedello LM, Sodickson AD, Farkas C, Zane RD, et al. Effect of Computerized Clinical Decision Support on the Use and Yield of CT Pulmonary Angiography in the Emergency Department. *Radiology.* 2012 Feb 1; 262(2):468–74. [PubMed: 22187633]
10. Raja AS, Gupta A, Ip IK, Mills AM, Khorasani R. The Use of Decision Support to Measure Documented Adherence to a National Imaging Quality Measure. *Acad Radiol.* 2014 Mar; 21(3): 378–83. [PubMed: 24507424]
11. Ip IK, Schneider LI, Hanson R, Marchello D, Hultman P, Viera M, et al. Adoption and Meaningful Use of Computerized Physician Order Entry With an Integrated Clinical Decision Support System for Radiology: Ten-Year Analysis in an Urban Teaching Hospital. *J Am Coll Radiol.* 2012 Feb; 9(2):129–36. [PubMed: 22305699]

12. Gupta A, Raja AS, Khorasani R. Examining clinical decision support integrity: is clinician self-reported data entry accurate? *J Am Med Inform Assoc JAMIA*. 2014 Jan 1; 21(1):23–6.
13. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. *Stat Med*. 1998 Apr 30; 17(8):857–72. [PubMed: 9595616]
14. Ghanima W, Abdelnoor M, Mowinckel M-C, Sandset PM. The performance of STA-Liatest D-dimer assay in out-patients with suspected pulmonary embolism. *Br J Haematol*. 2006 Jan; 132(2): 210–5. [PubMed: 16398655]
15. Mullier F, Vanpee D, Jamart J, Dubuc E, Bailly N, Douxfils J, et al. Comparison of five D-dimer reagents and application of an age-adjusted cut-off for the diagnosis of venous thromboembolism in emergency department. *Blood Coagul Fibrinolysis Int J Haemost Thromb*. 2013 Nov 15.
16. Warren DJ, Matthews S. Pulmonary embolism: investigation of the clinically assessed intermediate risk subgroup. *Br J Radiol*. 2011 Sep 21; 85(1009):37–43. [PubMed: 21937613]
17. Gupta RT, Kakarla RK, Kirshenbaum KJ, Tapson VF. D-Dimers and Efficacy of Clinical Risk Estimation Algorithms: Sensitivity in Evaluation of Acute Pulmonary Embolism. *Am J Roentgenol*. 2009 Aug 1; 193(2):425–30. [PubMed: 19620439]
18. Carrier M, Righini M, Wells PS, Perrier A, Anderson DR, Rodger MA, et al. Subsegmental pulmonary embolism diagnosed by computed tomography: incidence and clinical implications. A systematic review and meta-analysis of the management outcome studies. *J Thromb Haemost JTH*. 2010 Aug; 8(8):1716–22.

Table 1

Pulmonary Embolism (PE) prevalence for all patients using traditional D-dimer cutoff values.

	PE +	PE -	Total
D-dimer +	78	905	983
D-dimer -	0	72	72
Total	78	977	1055

Sensitivity = 100% (95% CI: 94.2–100%)

Specificity = 7.4% (95% CI: 5.8–9.2%)

Positive Predictive Value (PPV) = 7.9% (95% CI: 6.3–9.8%)

Negative Predictive Value (NPV) = 100% (95% CI: 93.7–100%)

Table 2

PE prevalence for all patients using decade age-adjusted D-dimer cutoff values.

	PE +	PE -	Total
D-dimer +	77	790	922
D-dimer -	1	132	133
Total	78	977	1055

Sensitivity = 98.7% (95% CI: 92.1–99.9%)

Specificity = 13.5% (95% CI: 12.2–16.8%)

PPV = 8.4% (95% CI: 7.1–11.0%)

NPV = 99.2% (95% CI: 99.2–99.9%)

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Table 3

PE prevalence for all patients using yearly age-adjusted D-dimer cutoff values.

	PE +	PE -	Total
D-dimer +	76	814	890
D-dimer -	2	163	165
Total	78	977	1055

Sensitivity = 97.4% (95% CI: 90.2–99.6%)

Specificity = 16.7% (95% CI: 14.4–19.2%)

PPV = 8.5% (95% CI: 6.8–10.6%)

NPV = 98.8% (95% CI: 95.2–99.8%)

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Table 4

Comparing traditional, decade age-adjusted, and yearly age-adjusted D-dimer cutoff values in evaluation of patients suspected of PE by age cohort.

Age in years	Patient count	PE prevalence	Sensitivity			Specificity		
			Traditional cutoff (95% CI)	Decade cutoff (95% CI)	Yearly cutoff (95% CI)	Traditional cutoff (95% CI)	Decade cutoff (95% CI)	Yearly cutoff (95% CI)
50	485	5.80%	100% (85.0–100)	100% (85.0–100)	100% (85.0–100)	7.88% (5.7–10.8)	7.88% (5.7–10.8)	7.88% (5.7–10.8)
51–60	205	7.30%	100% (74.7–100)	100% (74.7–100)	93.3% (66.0–99.7)	10.53% (6.7–16.0)	10.53% (6.7–16.0)	18.95% (13.8–25.4)
61–70	179	10.10%	100% (78.1–100)	100% (78.1–100)	100% (78.1–100)	4.35% (1.9–9.1)	17.39% (12.1–24.3)	24.22% (18.0–31.7)
71–80	109	9.20%	100% (65.5–100)	100% (65.5–100)	100% (65.5–100)	7.07% (3.1–14.5)	31.31% (22.6–41.5)	32.32% (23.5–42.6)
>80	77	9.10%	100% (56.1–100)	85.71% (42.0–99.2)	85.71% (42.0–99.2)	2.86% (0.5–10.9)	24.29% (15.2–36.3)	28.57% (18.7–40.8)