An Age-Adjusted D-dimer Threshold for Emergency Department Patients With Suspected Pulmonary Embolus: Accuracy and Clinical Implications

Adam L. Sharp, MD, MS*; David R. Vinson, MD; Fred Alamshaw, DO, MPH; Joel Handler, MD; Michael K. Gould, MD, MS

*Corresponding Author. E-mail: adam.l.sharp@kp.org, Twitter: @adamlsharp.

Study objective: We determine the accuracy of an age-adjusted D-dimer threshold to detect pulmonary embolism in emergency department (ED) patients older than 50 years and describe current ED practices when evaluating possible pulmonary embolism.

Methods: This was a retrospective study of ED encounters for suspected pulmonary embolism from 2008 to 2013. We used structured data to calculate the sensitivity, specificity, negative predictive value, and positive predictive value of different D-dimer thresholds. We describe the incidence of pulmonary embolism, the proportion of patients receiving imaging concordant with D-dimer levels, and the number of “missed” pulmonary embolisms. These findings were used to estimate patient outcomes based on different D-dimer thresholds.

Results: Among 31,094 encounters for suspected pulmonary embolism, there were 507 pulmonary embolism diagnoses. The age-adjusted D-dimer threshold was more specific (64% versus 54%) but less sensitive (93% versus 98%) than the standard threshold of 500 ng/dL; 11,999 imaging studies identified 507 pulmonary embolisms (4.2%); of these, 1,323 (10.6%) were performed with a D-dimer result below the standard threshold. Among patient encounters without imaging, 17.6% had D-dimer values above the threshold, including 5 missed pulmonary embolisms. Among patients who received imaging, 10.6% had a negative D-dimer result. Applying an age-adjusted D-dimer threshold to our sample would avert 2,924 low-value imaging tests while resulting in 26 additional cases of missed pulmonary embolism.

Conclusion: An age-adjusted D-dimer limit has the potential to reduce chest imaging among older ED patients and is more accurate than a standard threshold of 500 ng/dL. Our findings support the adoption of an age-adjusted D-dimer cutoff in community EDs. [Ann Emerg Med. 2016;67:249-257.]

Please see page 250 for the Editor's Capsule Summary of this article.

INTRODUCTION

Background

Pulmonary embolism can be a difficult condition to diagnose because the symptoms vary widely, and the risks and costs of diagnostic testing with computed tomography (CT) pulmonary angiography should ideally be avoided in patients with a low likelihood of pulmonary embolism. To limit the number of patients receiving advanced imaging, current recommendations suggest initial D-dimer testing for those who are at low to moderate risk.1,2 The conventional threshold for a positive test result is 500 ng/dL, with recommendations to order imaging for results above that level. This cutoff has excellent sensitivity but low specificity. Among patients who have a D-dimer test result above 500 ng/dL, only a small proportion actually have a pulmonary embolism, and the specificity worsens with age because of age-related increases in normal D-dimer concentrations.3-8 Low specificity results in more false-positive D-dimer values, leading to more imaging, which increases costs and potential harms from exposure to ionizing radiation and iodinated contrast agents. The latter is particularly important because although specificity decreases with age, the susceptibility to contrast-induced complications increases.9-11

Importance

The importance of appropriately evaluating emergency department (ED) patients with suspected pulmonary embolism was elevated recently when the American College of Emergency Physicians included the issue in its most
Editor’s Capsule Summary

What is already known on this topic
D-dimer normally increases with age, and adjusting for age can alter test specificity when pulmonary embolism is considered.

What question this study addressed
What is the false-negative rate for pulmonary embolism with age-adjusted D-dimer in a large sample?

What this study adds to our knowledge
This retrospective analysis of 31,094 patients with suspected pulmonary embolism and D-dimer showed that the false-negative rate at the standard cutoff was 0.06% (95% confidence interval [CI] 0.03% to 0.11%), and the false-negative rate for the age-adjusted cutoff was 0.18% (95% CI 0.1% to 0.25%), both independent of the pretest probability.

How this is relevant to clinical practice
These data support the use of D-dimer and age adjustment to further aid ability to exclude acute pulmonary embolism.

Goals of This Investigation
The primary aim of this study is to evaluate the sensitivity and specificity of an age-adjusted D-dimer threshold in detecting pulmonary embolism among patients older than 50 years. The secondary aims are to (1) compare an age-adjusted limit to the current standard threshold (500 ng/dL), as well as a higher fixed limit (1,000 ng/dL) and (2) describe the frequency of pulmonary embolism among patients receiving advanced imaging, the proportion of patients receiving low-value imaging with a negative D-dimer test result, the percentage of those who did not receive imaging after a positive D-dimer test result, and the number of “missed” pulmonary embolisms identified within 30 days of initial ED visit. Last, we use our data and past reports of the frequency of contrast nephropathy to estimate outcomes based on different D-dimer thresholds.

MATERIALS AND METHODS
Study Design and Setting
We performed a retrospective study of ED encounters for suspected pulmonary embolism within Kaiser Permanente Southern California, a large integrated health care system that serves more than 4 million members, representative of the diversity of Southern California. The 14 EDs operated by Kaiser Permanente Southern California range in annual volume from 25,000 to 90,000 and collectively treat approximately 900,000 patients per year. During the study, no emergency medicine residency existed; therefore, all tests were ordered by fully trained physicians.

We used structured data from electronic health and administrative records collected during routine clinical care and operations. To ensure we captured every pulmonary embolism diagnosis, we also included claims for care received outside the health system within the given period. The sample was limited to patients with continuous membership for 30 days after the encounter. Data were extracted by trained research staff experienced in the collection and analysis of Kaiser Permanente’s structured data and verified by the research team to ensure accuracy. Human subjects approval was obtained through the Kaiser Permanente Southern California Institutional Review Board.

Selection of Participants
We included all ED visits for Kaiser Permanente Southern California members older than 50 years, from 2008 to 2013, who received a D-dimer test (Current Procedural Terminology code 85379). There are several D-dimer assays, but a rapid, highly sensitive, immunoturbidimetric assay is used at all Kaiser Permanente Southern California facilities. This study aimed to identify patients with a possible
pulmonary embolism, not deep venous thrombosis; therefore, we included only patients presenting with a chief complaint we considered related to a possible pulmonary embolism, such as chest pain or dyspnea (for a complete list see Figure 1), and excluded those who underwent ultrasonographic imaging evaluation for deep venous thrombosis. We also sought to capture the initial evaluation of a possible new pulmonary embolism and therefore excluded patients with a pulmonary embolism diagnosis in the previous 90 days (Figure 2).

Methods of Measurement
The unit of analysis was the patient visit. We gathered the following individual patient characteristics: age, sex, race, Elixhauser comorbidities, pulse rate (tachycardia >100 beats/min), and hypoxia (oxygen saturation <95%) (Table 1). The Elixhauser index is a validated measure of comorbidity burden and was calculated with International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes.28 Additionally, we identified patients with a history of thrombophilia (ICD-9 code 289.81). Because of the known increased risk in pulmonary embolism attributed to cancer, we used Elixhauser codes (ICD-9 codes 140 to 203) to specifically identify patients with a cancer diagnosis in the past year. We also identified 30-day mortality for patients in each group through Kaiser Permanente Southern California’s clinical and administrative data and the California death registry.

The primary outcome of our analysis was an encounter diagnosis of acute pulmonary embolism (ICD-9 codes 415.11, 415.13, and 415.19). A random sample of 30 chart reviews was performed, showing this diagnosis was 95% accurate because 5% of charts did not include an acute pulmonary embolism, but included a diagnosis based on a history of pulmonary embolism. We created individualized D-dimer cutoff by multiplying the patient’s age in years by 10.14 These dichotomous D-dimer limits were aggregated to calculate sensitivity, specificity, positive predictive value, and negative predictive value for the age-adjusted threshold. Similarly, the current D-dimer limit (500 ng/dL) and a higher fixed cutoff (1,000 ng/dL) were used to calculate and compare sensitivities, specificities, positive predictive values, and negative predictive values.

To describe the proportion of ED patients receiving advanced imaging in the evaluation of possible pulmonary embolism, we identified from our cohort patients receiving CT pulmonary angiography, ventilation-perfusion scan, pulmonary angiography, or chest magnetic resonance angiography (Current Procedural Terminology codes 71260, 71270, 71275, 71555, 78579, 78580, 78582, 78584, 78585, 78586, 78587, 78588, 78591, 78593, 78594, 78596, 78597, 78598, 93451, and 93568). We included only imaging performed within 24 hours after ED arrival. We also stratified the overall sample by patients receiving imaging who had a D-dimer result below the standard cutoff during this study (500 ng/dL) and those who did not receive imaging despite a D-dimer result above the cutoff. We performed chart review on a random sample of 30 encounters for each of these groups to understand why the use or avoidance of imaging was discordant with current recommendations.

To identify any missed pulmonary embolism diagnoses, we report patients who neither received a pulmonary embolism diagnosis nor underwent imaging to identify pulmonary embolism at the initial ED encounter, but subsequently received a pulmonary embolism diagnosis within 30 days of the index ED encounter. Chart review was performed on each of these encounters to determine whether it was likely these patients had a pulmonary embolism that was missed at the initial ED visit or developed a pulmonary embolism within 30 days. Each

Abnormal Chest Radiograph Result
Acute asthma exacerbation Nausea
Angina pectoris Nausea and vomiting
Asthma Near fainting
Asthma w/o status asthmaticus Orthopnea
Call CTR chest pain—chest injury Painful respiration
Palpitations
Chest cold Pleurisy
Chest congestion Pleuritic chest pain
Chest discomfort Pneumonia
Chest mass Pulmonary edema
Chest pain Pulmonary embolus
Chest pressure Respiratory abnormal
Chest tightness Respiratory arrest
CHF exacerbation Respiratory complaint
Difficulty breathing Respiratory disease
Dyspnea on exertion Respiratory failure
Emphysema Respiratory therapy
Epigastric pain Shortness of breath
Hypotension Tachycardia-bradycardia
Interstitial lung disease Tachypnea
Lightheadedness Upper respiratory infection
Lung cancer URI symptoms
Lung mass Wheezing

Figure 1. Complete list of chief complaints related to a possible pulmonary embolism. CTR, Center; CHF, congestive heart failure; URI, upper respiratory infection.
case was discussed among our research team to reach a consensus. Patients identified as likely having a pulmonary embolism at the initial ED visit were reclassified into the pulmonary embolism outcome group for sensitivity and specificity calculations of the different D-dimer limits. Similarly, chart review of the patients who received a pulmonary embolism diagnosis but had no imaging (n=27) found that 7 patients did not have an acute pulmonary embolism but had a history of pulmonary embolism. These 7 patients’ data were placed in the no pulmonary embolism group for analyses.

Last, we used published estimates to predict the number of cases of contrast-induced nephropathy, episodes of severe renal failure, and deaths related to contrast-induced nephropathy according to the sensitivity and specificity of the different D-dimer thresholds. We relied on previously published prospective findings, which reported that the risks of contrast-induced nephropathy, renal failure, and death related to contrast-induced nephropathy were 11%, 0.9%, and 0.6%, respectively. To compare our results with these estimates, we identified patients with an acute kidney injury (ICD-9 code 584.x) or unspecified kidney failure diagnosis (ICD-9 code 586) within 30 days of the ED encounter and then stratified results by those who received imaging and those who did not. We tabulated the number of these adverse outcomes expected, along with diagnoses of pulmonary embolism that were identified or missed, according to different D-dimer thresholds. We used the results to estimate the number of patients who would receive imaging according to the different D-dimer thresholds and then normalized these numbers to events per 10,000.

RESULTS

Characteristics of Study Subjects

We identified 31,094 ED patients older than 50 years who were evaluated for pulmonary embolism from 2008 to 2013 (Figure 2). The mean age was 65 years and 61% were women. The mean Elixhauser score was 4.1, 10.3% had received a cancer diagnosis in the past year, and 0.4% had thrombophilia. The sample had the following distribution by race: 46.7% white, 27.9% Hispanic, 15.1% black, 9.0% Asian or Pacific Islander, and 1.3% other. Overall, 19.3% of patients were tachycardic on ED presentation, 17.7% were hypoxic, and 1.3% died within 30 days of the encounter. Statistically significant differences (P<.001) existed for each of these variables when patients who received a diagnosis of a pulmonary embolism were compared with those without pulmonary embolism, with the exception of thrombophilia (Table 1).

Main Results

The age-adjusted D-dimer threshold was 92.9% sensitive and 63.9% specific, with a positive predictive value of 4.1% and a negative predictive value of 99.8% for detecting pulmonary embolism. The limit of 500 ng/dL yielded a sensitivity of 98.0% and specificity of 54.4%, with a positive predictive value of 3.4% and a negative predictive value of 99.9% for detecting pulmonary embolism. A cutoff of 1,000 ng/dL was 84.2% sensitive and 75.4% specific, with a positive predictive value of 5.4% and a negative predictive value of 99.7% for detecting pulmonary embolism. During the 6-year study period, the expected number of missed or delayed pulmonary embolism diagnoses because of false-negative D-dimer test results would have been 36 with the age-adjusted threshold, 10 with the threshold of 500 ng/dL, and 80 with the threshold of 1,000 ng/dL (Figure 3). In our sample, only 1 patient died within 30 days of the ED encounter. This individual died in hospice of severe heart failure, with a known pulmonary embolism and a D-dimer value below 500 ng/dL.

Overall, 12,486 patients (40.2%) received an imaging study to evaluate for pulmonary embolism, of which

Figure 2. Cohort of Kaiser Permanente ED patients (≥50 years) receiving D-dimer tests for PE from 2008 to 2013. PE, Pulmonary embolism.
87% were CT pulmonary angiography, 10.5% were pulmonary perfusion scans, and 2.5% were chest CTs with contrast. Of the patients who received imaging, 1,323 (10.6%) had a D-dimer result below the threshold of 500 ng/dL. Random chart review of 30 of these encounters showed that one third of providers documented that the purpose of imaging was to rule out other possible causes beyond pulmonary embolism, such as aortic dissection. Among 18,608 patients who did not receive imaging, 17.6% had a D-dimer value above the cutoff of 500 ng/dL (Table 2). Random chart review of 30 of these encounters showed that 60% had clinical explanations about their decision to omit further pulmonary embolism evaluation in the setting of a positive D-dimer result. We identified 5 patients with missed pulmonary embolisms (2.3%) at the initial encounter that were subsequently detected within 30 days, all of whom had a D-dimer concentration that was greater than the age-adjusted

### Table 1. Individual characteristics for our sample of patients evaluated for pulmonary embolism at one of 14 community EDs in Southern California from 2008 to 2013.

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Total (n = 31,094)</th>
<th>No PE (n = 30,580)</th>
<th>PE (n = 514)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>65.0 (10.9)</td>
<td>65.0 (10.9)</td>
<td>69.6 (11.1)</td>
</tr>
<tr>
<td>Female, %</td>
<td>61.0</td>
<td>61.2</td>
<td>48.5</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>46.7</td>
<td>46.5</td>
<td>59.3</td>
</tr>
<tr>
<td>Black</td>
<td>15.1</td>
<td>15.1</td>
<td>18.0</td>
</tr>
<tr>
<td>Hispanic</td>
<td>27.9</td>
<td>28.0</td>
<td>19.5</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>9.0</td>
<td>9.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Other</td>
<td>1.3</td>
<td>1.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Elixhauser index, mean (SD)</td>
<td>4.1 (3.1)</td>
<td>4.1 (3.1)</td>
<td>5.9 (3.2)</td>
</tr>
<tr>
<td>Cancer in past year, %</td>
<td>10.3</td>
<td>10.2</td>
<td>20.1</td>
</tr>
<tr>
<td>Thrombophilia, %</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Tachycardia (&gt;100 beats/min), %</td>
<td>19.3</td>
<td>19.1</td>
<td>30.7</td>
</tr>
<tr>
<td>Hypoxia (&lt;95% oxygen saturation), %</td>
<td>17.7</td>
<td>17.3</td>
<td>38.8</td>
</tr>
<tr>
<td>30-Day mortality</td>
<td>1.3</td>
<td>1.2</td>
<td>3.2</td>
</tr>
</tbody>
</table>

SD, Standard deviation.

Figure 3. A comparison of the accuracy of different D-dimer thresholds to identify PEs in ED patients older than 50 years, using 3 different cutoff points.* CI, Confidence interval; PPV, positive predictive value; NPV, negative predictive value.

### Table 2. % (95% CI)

<table>
<thead>
<tr>
<th>Threshold</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>False Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 ng/dL</td>
<td>98.0 (96.4–98.2)</td>
<td>54.4 (53.9–55.0)</td>
<td>3.4 (3.2–3.8)</td>
<td>99.9 (99.9–100)</td>
<td>2.0 (1.0–3.6)</td>
</tr>
<tr>
<td>1,000 ng/dL</td>
<td>84.2 (80.8–87.3)</td>
<td>75.4 (74.9–75.9)</td>
<td>5.4 (4.9–5.9)</td>
<td>99.7 (99.6–99.9)</td>
<td>15.8 (12.7–19.3)</td>
</tr>
<tr>
<td>Age adjusted</td>
<td>92.9 (90.3–95.0)</td>
<td>63.9 (63.4–64.5)</td>
<td>4.1 (3.7–4.5)</td>
<td>99.8 (99.8–99.9)</td>
<td>7.1 (5.0–9.7)</td>
</tr>
</tbody>
</table>

*The age-adjusted limit was calculated by multiplying the patient’s age in years by 10.

†Among the patients with false-negative results for each threshold, 1 patient died, who was missed in all groups. Chart review showed the patient died in hospice, attributed to end-stage heart failure.

Figure 3. A comparison of the accuracy of different D-dimer thresholds to identify PEs in ED patients older than 50 years, using 3 different cutoff points.* CI, Confidence interval; PPV, positive predictive value; NPV, negative predictive value.
Threshold and greater than or equal to 1,000 ng/dL in absolute value.

In 2013, 89% of imaging tests for pulmonary embolism were CTs and the remaining 11% were perfusion studies or magnetic resonance imaging. We estimate that using an age-adjusted D-dimer value would have resulted in 1,266 cases of contrast-induced nephropathy (95% confidence interval [CI], 1,036 to 1,611 cases), 115 cases of severe renal failure (95% CI 38 to 228 cases), and 72 deaths related to contrast-induced nephropathy (95% CI 25 to 177 deaths). The threshold of 500 ng/dL would result in 1,588 cases of contrast-induced nephropathy (95% CI 25 to 177 deaths). These results were used to create estimates of clinical consequences associated with different D-dimer thresholds used to prompt imaging in the evaluation of low- to moderate-risk patients with suspected pulmonary embolus.

<table>
<thead>
<tr>
<th>D-dimer (ng/dL)</th>
<th>Scan</th>
<th>No Scan</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>11,163 (89.4)</td>
<td>3,271 (17.6)</td>
<td>14,434</td>
</tr>
<tr>
<td>Negative</td>
<td>1,323 (10.6)</td>
<td>15,337 (82.4)</td>
<td>16,660</td>
</tr>
</tbody>
</table>

*We show the number of patients receiving chest imaging (scan) or not (no scan), stratified by D-dimer concentrations above (positive) or below (negative) a 500 ng/dL limit.

**LIMITATIONS**

These results must be interpreted in the context of a retrospective observational study design. Specifically, we used ICD-9 codes derived from the ED diagnosis list as the primary outcome. The lack of prospective data collection may have affected our reported performance of various D-dimer cutoffs. The application of any threshold to different samples may have differing results because of evaluation and spectrum biases related to the population of interest. Also, variability may exist in the interpretation of imaging, and this may entail inaccuracies. However, we believe that this reference standard is most relevant to the real-world practice settings in which most patients receive care.

Review of missed pulmonary embolisms was conducted by the research team, the details of the encounters and the timing of subsequent pulmonary embolism were discussed, and through consensus the group determined whether the pulmonary embolism was likely to have been present at the initial encounter. This approach may have some unmeasured bias because the research team was not blinded to the eventual pulmonary embolism diagnosis.

Our study does not evaluate the use of common decision rules, such as Wells’s criteria, but all pulmonary embolism decision rules recommend further diagnostic testing for a positive D-dimer test result and omitting advanced imaging for a negative D-dimer result. We found, however, that a substantial number of patients received diagnostic testing contrary to current recommendations. We also acknowledge the controversy surrounding contrast-induced nephropathy and the potential for error in applying previously published results to our analysis of D-dimer thresholds. However, we were not able to compare cases of actual adverse events to the literature when we estimated cases of contrast-induced renal failure.

---

**Table 3.** Estimated clinical consequences associated with different D-dimer thresholds used to prompt imaging in the evaluation of low- to moderate-risk patients with suspected pulmonary embolus.

<table>
<thead>
<tr>
<th>Threshold (ng/dL)</th>
<th>Diagnosed PE</th>
<th>Missed PE</th>
<th>Potential CTPAs</th>
<th>CIN</th>
<th>Severe Renal Failure</th>
<th>Death Related to CIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>500</td>
<td>160 (144–174)</td>
<td>6 (0–16)</td>
<td>4,642 (4,582–4,702)</td>
<td>511 (418–650)</td>
<td>44 (15–92)</td>
<td>29 (7–73)</td>
</tr>
<tr>
<td>1,000</td>
<td>137 (115–159)</td>
<td>35 (28–40)</td>
<td>2,556 (2,473–2,639)</td>
<td>283 (230–359)</td>
<td>24 (8–51)</td>
<td>16 (4–40)</td>
</tr>
<tr>
<td>Age adjusted</td>
<td>151 (133–169)</td>
<td>19 (10–26)</td>
<td>3,702 (3,632–3,772)</td>
<td>409 (333–520)</td>
<td>35 (12–74)</td>
<td>23 (6–58)</td>
</tr>
</tbody>
</table>

CTPA, CT pulmonary angiography; CIN, contrast-induced nephropathy.

*Estimates are based on the use of the most common mode of diagnostic imaging for PE, CT pulmonary angiography. Our estimates are based on sensitivities and specificities calculated from our sample of 31,094 ED patients aged 50 years or older and evaluated for PE, and on previously reported risks of CIN, severe renal failure, and associated death from CT imaging with contrast. We report expected events per 10,000 suspected PE encounters.

The age-adjusted threshold is derived by multiplying the patient’s age by 10.
because comparisons between thresholds were hypothetical. We confirmed that patients receiving imaging in our sample had a higher percentage of acute kidney injury, similar to estimates we derived from literature review (0.7% versus 0.9%). Therefore, we used published data to estimate the potential numbers of adverse events to better understand the risks and benefits of different D-dimer thresholds.

DISCUSSION
In this large retrospective cohort study, we found that an age-adjusted D-dimer threshold was more specific but less sensitive than a conventional threshold of 500 ng/dL and resulted in approximately 20% fewer false-positive test results requiring follow-up imaging. These results confirm other recent reports and extend generalizability about the potential benefits of using this D-dimer cutoff for patients older than 50 years who are treated in a community ED setting.14,33

In addition, we found that approximately 40% of ED patients with suspected pulmonary embolism received advanced chest imaging, including 11% who had a D-dimer value below the conventional threshold recommended to prompt radiologic testing. Conversely, among patients who did not receive chest imaging, 17.6% had a D-dimer concentration above the threshold for a positive test result. Further review of these “low-value” encounters appeared to indicate that D-dimer testing is frequently incorporated into general laboratory ordering practices, without thoughtful consideration of how it may change further management regardless of a positive or negative test result. With our study design, we were not able to determine to what extent providers overused laboratory testing, imaging, or both, but clearly there is room for improvement in the application of evidence-based practices. In this study, missed pulmonary embolisms were rare (2.3%). Our results show the prevalence of pulmonary embolism to be lower than that previously reported.13,34

We hypothesize this was due to differences in the patient populations treated at academic medical centers and community hospitals, and possibly higher rates of imaging test use in community ED practice.

Finding balance between sensitivity and specificity is always an important and difficult consideration when laboratory thresholds are used to prompt further evaluation or treatment. An important consideration in setting a D-dimer cutoff is the current trend in the detection of minor, nonlife-threatening pulmonary embolisms.35,36 Because an increasing proportion of pulmonary embolisms are of uncertain significance, the risks of missed pulmonary embolism are inherently smaller than in previous years, and there is evidence to suggest that delayed diagnosis is not necessarily associated with a worse outcome.37,38 Our results support previous findings, with only 1 death at 30 days for our community ED patients with a pulmonary embolism. In comparison, the risks of pulmonary angiography are small but not trivial, especially among the elderly and patients with multiple chronic conditions.39-44 Our estimates show that using an age-adjusted D-dimer threshold would miss or delay diagnosis of 26 more pulmonary embolisms than the current standard, but it would prevent 322 cases of contrast-induced nephropathy, 29 cases of severe renal failure, and 19 deaths related to contrast-induced nephropathy in this sample. The cutoff of 1,000 ng/dL had the best specificity (75.4%) and is another threshold that has merit and warrants consideration, but we believe that the sensitivity is too low (84.2%) to justify use in current clinical practice. A more tailored increase in the age-adjusted method accounts for the physiologic changes between a 51-year-old and a 100-year-old, which is not accounted for in the threshold of 1,000 ng/dL.

Beyond the performance of an age-adjusted D-dimer limit, this study found that the use of follow-up imaging was not always consistent with recommendations from current guidelines. For example, 10.6% of patients receiving CT pulmonary angiography or a ventilation-perfusion scan had a D-dimer value less than 500 ng/dL, and 22.7% of patients with a D-dimer value above 500 ng/dL did not receive ultrasonography or chest imaging. Given current recommendations, it is unclear why physicians would order a D-dimer test and not pursue further testing among patients with a positive result. Fortunately, few patients in our sample had missed pulmonary embolisms, but all of them had a D-dimer value greater than 1,000 ng/dL and did not undergo subsequent imaging. Similarly, it is not clear whether the use of imaging among patients with a negative D-dimer test result reflects inappropriate use of the D-dimer test in patients with a high pretest probability of pulmonary embolism or unnecessary use of imaging after incorrect interpretation of the D-dimer test result. In either case, the finding suggests a need to implement recommendations such as the pulmonary embolism rule-out criteria, now supported through the American College of Emergency Physicians’ Choosing Wisely campaign.12

We conclude that an age-adjusted D-dimer limit has the potential to reduce unnecessary or low-value chest imaging among ED patients older than 50 years, but application of a Bayesian approach to alternative D-dimer thresholds remains important. Our research validates previous reports in a community setting and supports an age-adjusted D-dimer threshold in similar EDs. We believe this change
would improve outcomes for patients and affordability for health systems. However, our results also show that further efforts are needed to implement current recommendations in the ED management of patients with suspected pulmonary embolism.

Supervising editors: Jeffrey Kline, MD; Donald M. Yealy, MD

Author affiliations: From the Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA (Sharp, Gould); the Department of Emergency Medicine, Los Angeles Medical Center, Kaiser Permanente Southern California, Los Angeles, CA (Sharp); the Department of Emergency Medicine, Kaiser Permanente Sacramento Medical Center, Sacramento, CA, and the Kaiser Permanente Division of Research, Oakland, CA (Vinson); and the Department of Family Medicine (Alamshaw) and Department of Internal Medicine (Handler), Anaheim Medical Center, Kaiser Permanente Southern California, Anaheim, CA.

Author contributions: ALS and MKG conceived the study, designed the project, and drafted the article. All authors edited and approved the final article and analyzed and interpreted the data. ALS takes responsibility for the paper as a whole.

Funding and support: By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist and provided the following details: This study was funded by the Kaiser Permanente Southern California Care Improvement Research Team.

Publication dates: Received for publication February 23, 2015. Revisions received May 27, 2015; and June 24, 2015. Accepted for publication July 9, 2015. Available online August 29, 2015.

REFERENCES


36. Wiener RS, Schwartz LM, Woloshin S. When a test is too good: how CT pulmonary angiograms find pulmonary emboli that do not need to be found. BMJ. 2013;347:f3368.


