Methodology for a Rapid Protocol to Rule Out Pulmonary Embolism in the Emergency Department

We propose an emergency department (ED) pulmonary embolism rule-out protocol based on pretest probability assessment coupled with either a negative D-dimer assay result or a negative D-dimer assay result plus a normal alveolar dead-space measurement. We examine the safety, efficiency, and feasibility of such a protocol, paying special attention to implicit and explicit strategies of pretest probability assessment among patients with suspected pulmonary embolism. Finally, we assess the potential effect of the proposed pulmonary embolism rule-out protocol on use of imaging resources and ED throughput.

INTRODUCTION

Emergency physicians are frequently faced with the challenge of excluding or diagnosing pulmonary embolism. Studies at academic emergency departments (EDs) in Charlotte, NC, Detroit and Royal Oak, MI, Phoenix, AZ, Toledo, OH, and St. Louis, MO, have shown that emergency physicians order a pulmonary vascular imaging study (either a scintillation ventilation-perfusion lung scan or a contrast-enhanced computed tomographic [CT] angiogram of the chest) on approximately 0.6% to 2.0% of all patients visiting the ED at these hospitals. If these data are generalized to the US population, between 500,000 and 2 million ED patients undergo a pulmonary vascular imaging study annually. The cost (in US dollars) to the hospital to perform a ventilation-perfusion or CT scan is $100 to $200 in Canada and $200 to $500 in the United States, and the charge to the patient is more than $1,000 for either test in the United States.4-6 Both tests expose the patient to ionizing radiation. A further limitation is that these tests might be available only at certain times and can require several hours to complete.

Accordingly, multiple investigators interested in pulmonary embolism have focused on the utility of sensitive, inexpensive, less invasive, and more rapid methods to rule out pulmonary embolism. This report examines the published data evaluating D-dimer measurement in conjunction with other criteria to exclude the diagnosis of pulmonary embolism. We suggest the adoption of 3 guiding principles for the pulmonary embolism rule-out strategy: safety, efficiency, and feasibility.

SAFETY OF THE PROPOSED PROTOCOL

The safety of a pulmonary embolism rule-out protocol is primarily determined by the probability of false-negative results. This can be expressed as the posttest probability of pulmonary embolism after the pulmonary embolism rule-out protocol returns a negative result. Because it is unlikely that any protocol will yield a 0% posttest probability of pulmonary embolism, we suggest a maximum acceptable upper limit of 1.0% on the basis of 2 lines of evidence. First, reports of the rate of subsequent diagnosis of thromboembolism (deep venous thrombosis or pulmonary embolism) after a negative pulmonary angiogram range from 1.6% to 4.2%.7-10 Second, when contrast-enhanced CT chest scanning was performed in patients without recognized signs or symptoms of pulmonary embolism, the rate of pulmonary embolism diagnosis was approximately 1%.11

The selection of patients with a sufficiently low pretest probability comprises the single most important step in the derivation of a safe protocol. Two issues relevant to this remain focal points of ongoing investigation: (1) the methods used to decide which patients with suspected pulmonary embolism have a sufficiently low pretest probability to exclude pulmonary embolism in the presence of a negative D-dimer assay result (summarized in Table 1) and (2) the accuracy of the D-dimer assay used with or without the alveolar dead-space measurement.

Implicit and Explicit Methods of Estimating Pretest Probability of Pulmonary Embolism

Of these 2 broad categories, the most commonly used method is probably the empiric (implicit) method by which clinicians combine knowledge and experience to estimate the likelihood of pulmonary embolism. The intellectual procedure used by each clinician to estimate pretest probability cannot be directly measured but must be inferred.12 The problems with empiric assessment are the following: (1) clinicians often disagree substantially on the pretest probability of pulmonary embolism13,14; (2) the clinician’s experience level appears to influence the accuracy of pretest assessment15; (3) empiric probability estimates tend toward the middle so that few patients are categorized in the more useful low- and high-probability groups; and (4) empiric assessment of low risk might be inaccurate.14 In a multicenter study in Europe, Sanson et al16 found that clinicians using empiric estimates of pretest probability categorized only 14% of patients as low risk for pulmonary embolism. However, the posttest probability of pulmonary embolism in this
D-Dimer Assays

An increased D-dimer concentration (eg, >500 ng/mL) in the plasma indicates the presence of intravascular fibrin deposition. Because of the test’s generally high sensitivity and low specificity, a low D-dimer concentration can rule out the presence of a recently formed thrombosis, whereas a high D-dimer concentration does not necessarily indicate the presence of pulmonary embolism. Factors associated with false-negative D-dimer assay results include symptoms of pulmonary embolism for more than 3 days, small pulmonary embolism, and use of qualitative latex fixation tests. Factors associated with false-positive D-dimer assay results include malignancy, recent surgery, infection, pregnancy, and age older than 70 years. The type of assay also affects the accuracy of the D-dimer. All commercially available D-dimer assays incorporate the use of an antibody directed against the D-dimer peptide, which is a product of fibrin breakdown. However, not all assays use the same antibody epitope. As of August 2002, the US Food and Drug Administration (FDA) had approved 22 D-dimer assays for clinical use through the 510-K pathway and certified 34 D-dimer assays through the Clinical Laboratory Improvement Amendment. A current listing of FDA-approved D-dimer assays can be obtained from the FDA.

For practical purposes, D-dimer assays can be divided into 4 categories. In order of increasing sensitivity, they are as follows: (1) qualitative latex agglutination, (2) qualitative erythrocyte agglutination, (3) qualitative matrix screen immunoassays, and (4) quantitative D-dimer assays, which include the rapid enzyme-linked immunosorbent assay and turbidimetric techniques. We consider both the quantitative and qualitative D-dimer assays as objective tests, although we recognize that published studies have reported disparate results regarding the interobserver variability for the qualitative (SimpliRED) whole-blood D-dimer.22

In choosing the D-dimer assay to use in the pulmonary embolism rule-out protocol, the goal is to select a test that is simple to perform and will work well with the method selected for pretest probability estimation, as outlined in Table 4. At first glance, it might seem important to consider only the sensitivity of the D-dimer, given that patients can die if pulmonary embolism is erroneously ruled out. However, a useful pulmonary embolism rule-out protocol also depends on a reasonably high D-dimer specificity (approximately 50% or higher) for 2 reasons. The first is that a very sensitive test with a low specificity allows pulmonary embolism to be ruled out in only a small subset of patients. For example, a D-dimer assay with 98% sensitivity and 20% specificity (negative likelihood ratio [LR–]=0.1) would require that the pretest probability be less than 10% to provide a

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**Table 2.**

*Canadian score for assessment of pretest probability for pulmonary embolism.*

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected DVT</td>
<td>3.0</td>
</tr>
<tr>
<td>An alternative diagnosis is less likely than PE</td>
<td>3.0</td>
</tr>
<tr>
<td>Heart rate &gt;100 beats/min</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization or surgery in the previous 4 wk</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous DVT/PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Malignancy (on treatment, treated in the past 6 mo, or palliative)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**A. Creating the score.**

**B. Interpretation of the score.**

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Mean Probability of PE, %</th>
<th>Patients With This Score, %</th>
<th>Interpretation of Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–2 points</td>
<td>3.6</td>
<td>40</td>
<td>Low</td>
</tr>
<tr>
<td>3–6 points</td>
<td>20.5</td>
<td>53</td>
<td>Moderate</td>
</tr>
<tr>
<td>&gt;6 points</td>
<td>66.7</td>
<td>7</td>
<td>High</td>
</tr>
</tbody>
</table>

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**Table 3.**

*Geneva score for assessment of pretest probability for pulmonary embolism.*

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 60–79 y</td>
<td>1</td>
</tr>
<tr>
<td>Age &gt;79 y</td>
<td>2</td>
</tr>
<tr>
<td>Prior DVT/PE</td>
<td>2</td>
</tr>
<tr>
<td>Recent surgery</td>
<td>3</td>
</tr>
<tr>
<td>Heart rate &gt;100 beats/min</td>
<td>1</td>
</tr>
<tr>
<td>PaCO2, mm Hg</td>
<td>&lt;36 1</td>
</tr>
<tr>
<td>36–39</td>
<td>2</td>
</tr>
<tr>
<td>PaO2, mm Hg</td>
<td>&lt;49 4</td>
</tr>
<tr>
<td>49–60</td>
<td>1</td>
</tr>
<tr>
<td>&gt;60–71</td>
<td>2</td>
</tr>
<tr>
<td>&gt;71–82</td>
<td>1</td>
</tr>
<tr>
<td>Chest radiograph</td>
<td>1</td>
</tr>
<tr>
<td>Platelike atelectasis</td>
<td>1</td>
</tr>
<tr>
<td>Elevation of hemidiaphragm</td>
<td>1</td>
</tr>
</tbody>
</table>

**A. Creating the score.**

**B. Interpretation of the score.**

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Mean Probability of PE, %</th>
<th>Patients With This Score, %</th>
<th>Interpretation of Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4 points</td>
<td>10</td>
<td>49</td>
<td>Low</td>
</tr>
<tr>
<td>5–8 points</td>
<td>38</td>
<td>44</td>
<td>Moderate</td>
</tr>
<tr>
<td>9–12 points</td>
<td>81</td>
<td>6</td>
<td>High</td>
</tr>
</tbody>
</table>
posttest probability of less than 1% in the pulmonary embolism rule-out group. This would return a negative result in less than one third of patients tested. Second, a \( D \)-dimer assay with a low specificity will lead to increased use of imaging in relatively low-risk patients with a false-positive test result who might not have been studied at all if an imaging study was the only option for testing.

In the Prospective Investigation of Pulmonary Embolism Diagnosis study, ventilation-perfusion scanning yielded a false-positive (high probability) result in approximately 3% of patients without pulmonary embolism, and meta-analyses suggest a false-positive rate of CT angiography of approximately 5% to 10%. Warfarin anticoagulation is associated with a 0.3% to 3% yearly risk of intracranial hemorrhage. Moreover, one must consider the effect of an erroneous diagnosis of pulmonary embolism on a patient's anxiety and personal expenditure on health and life insurance. The probability of this type of error will increase if a pulmonary embolism rule-out protocol increases imaging of low-risk patients. This possibility must be considered in light of reports that the specificity of the quantitative (enzyme-linked immunosorbent assay) \( D \)-dimer assay is less than 50% in hospitalized patients and unselected ED patients undergoing evaluation for pulmonary embolism.

### Alveolar Dead-Space Measurements

The diagnostic accuracy of a pulmonary embolism rule-out protocol might be increased by the addition of the alveolar dead-space measurement to the \( D \)-dimer assay. One reason is that the alveolar dead space might remain increased for a longer period than the \( D \)-dimer after pulmonary embolism. The pulmonary embolism rule-out protocol at Carolinas Medical Center uses the combination of the SimpliFY \( D \)-dimer (Agen, Inc., Brisbane, Queensland, Australia) and the alveolar dead-space measurement. Both measurements are performed by respiratory therapists in the ED. The alveolar dead-space measurement requires a measurement of the end-tidal CO\(_2\) and the arterial PCO\(_2\) in a patient breathing ambient air for 2 minutes. The therapist measures the average of 3 deep exhaled CO\(_2\) measurements immediately preceding arterial puncture of the radial artery, followed by 3 more deep exhaled CO\(_2\) measurements, each separated by 30 seconds. The average of all 6 deep exhaled CO\(_2\) measurements is used to calculate the dead space from a modification of the Enghoff equation:

\[
\text{Percentage alveolar dead space} = 100 \times \frac{(\text{PaCO}_2 - \text{PetCO}_2)}{\text{Paco}_2}
\]

Kline et al\(^1,29\) considered a normal dead space to be less than 20%, whereas Rodger et al\(^30\) used 15% as the upper limit of normal.

In summary, we propose that the benchmark for a safe pulmonary embolism rule-out protocol is an accurate posttest probability of less than 1%. This requires a suitable pretest probability assessment before the use of an objective test. It is desirable for the protocol to use a test that has a specificity of at least 50% to avoid a possible increase in unnecessary imaging.
EFFICIENCY OF PROPOSED PROTOCOL

D-Dimer Assays

The efficiency of a pulmonary embolism rule-out protocol can be defined by its effect on resource use. The process of pretest probability assessment has no measurable cost, and therefore, the bulk of the direct cost of the pulmonary embolism rule-out protocol can be calculated from the cost of the objective tests, the D-dimer assay (plus or minus the dead-space measurement), incurred as a result of the protocol plus the cost of additional imaging. In the United States, the bedside qualitative D-dimer tests, such as the SimpliRED and SimpliFY, cost approximately $20 for each use. Qualitative D-dimer assays can be completed within 10 minutes and can be done on capillary blood from a finger stick, as well as on citrate- or ethylenediamine tetraacetic acid–treated venous whole blood as a point-of-care test in the ED. In our experience, a nurse or respiratory therapist can be trained within 30 minutes to accurately perform the qualitative D-dimer assay. We recommend that training should include viewing a videotape supplied by the manufacturer, practicing the test on several volunteers, and then performing the test under supervision for the first 10 patients. Potential challenges of using the qualitative D-dimer assay in the ED include the fact that the reagents must be stored in a clinical refrigerator in the ED and warmed before use. A control test is incorporated into the assay. Also, to maintain standards set by the College of Analytical Pathologists for the use of the bedside d-dimer, it is recommended that the results of the qualitative test be compared with results of an FDA-approved quantitative D-dimer test on a semiannual basis.

Quantitative D-dimer testing requires a relatively large (>$10,000) capital expenditure for the equipment needed to perform the measurement and an acquisition cost of approximately $15 to $20 for each assay performed. In most settings, quantitative D-dimer assays must be run from the hospital laboratory on citrated (“blue top tube”) plasma. Quantitative rapid enzyme-linked immunosorbent assay and turbidimetric D-dimer assays can produce a test result within 15 minutes from the time the laboratory receives the sample. All of the maintenance, procedural, and administrative issues of the quantitative D-dimer assay are handled by the central laboratory. However, the requirement for venipuncture, together with the documentation and procedure to transfer the blood to the laboratory, add significantly to the time required to perform the test.

Alveolar Dead-Space Measurements

The equipment required to measure alveolar dead space includes a capnometer and an arterial blood gas machine. Deep exhaled CO₂ can be measured with any commercially available handheld time-based capnomet-

<table>
<thead>
<tr>
<th>D-Dimer Format</th>
<th>Safe Maximum Pretest Probability, %</th>
<th>Explicit Criteria That Will Produce the Required Pretest Probability Based on Calculation</th>
<th>Validated Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole blood (SimpliRED)</td>
<td>0.15–0.25</td>
<td>Canadian score &lt;2 or Geneva score &lt;4</td>
<td>Canadian score &lt;2</td>
</tr>
<tr>
<td>Whole blood (SimpliFY)</td>
<td>0.15–0.25</td>
<td>Canadian score &lt;2 or Geneva score &lt;4</td>
<td>None</td>
</tr>
<tr>
<td>Turbidimetric D-dimer (&lt;500 ng/mL)</td>
<td>0.05–0.15</td>
<td>Canadian score &lt;4 or Charlotte criteria or Geneva score &lt;5</td>
<td>None</td>
</tr>
<tr>
<td>Rapid ELISA D-dimer (&lt;500 ng/mL)</td>
<td>0.05–0.15</td>
<td>Canadian score &lt;4 or Charlotte criteria or Geneva score &lt;5</td>
<td>None</td>
</tr>
<tr>
<td>SimpliRED or SimpliFY + normal alveolar dead space</td>
<td>0.03–0.06</td>
<td>Canadian score &lt;4 or Charlotte criteria or Geneva score &lt;5</td>
<td>Charlotte criteria</td>
</tr>
</tbody>
</table>

ELISA, Enzyme-linked immunosorbent assay.
*Ranges are given for certain tests because of study heterogeneity.
†Calculated on the basis of the midpoint of the estimate for the LR– to produce a posttest probability of <1%.
‡Pooled estimate from summary receiver operating characteristic curve analysis of data in Oger et al.47
ter that can be taken into the patient’s room. Many manufacturers now make these devices, but we have the most experience with Novametrix Tidal Wave 710 (Novametrix Medical Systems, Inc., Wallingford, CT) and the Nellcor NPB75 (Nellcor Puritan Bennett, Pleasanton, CA). The acquisition cost for a handheld, standard, time-based capnometer is approximately $3,500, and the cost of an adapter required for standard CO₂ measurement is approximately $10 to $15. To reduce the requirement for a new adapter between patients, a microbial filter (cost of $1.50 each; Clear Guard Midi, 99.9% Efficient Filter, Intersurgical Inc., Liverpool, NY) is placed on the end of the adapter into which the patient breathes. The more costly adapter is replaced after 10 uses. After the respiratory therapist obtains the arterial blood, the therapist analyzes it in the ED, and a drop of arterial blood is placed on the SimpliFY D-dimer immunoassay test cartridge for 10 minutes. Thus, the PaCO₂ required for the alveolar dead-space measurement and the blood for the D-dimer both come from the same arterial sample.

Effect on Imaging and ED Length of Stay
An important point about the efficiency of a pulmonary embolism rule-out protocol is that every patient who does not rule out undergoes an imaging study for pulmonary embolism. This adds to the patient’s charges and length of stay, regardless of whether pulmonary embolism is ultimately diagnosed. Conversely, every time the screening system result is negative, precluding formal imaging, there is a saving of money and time. The net effect on ED length of stay depends on 3 variables: the median time required for the standard imaging test, the fraction of all ED patients evaluated for pulmonary embolism who undergo the pulmonary embolism rule-out protocol, and the fraction of screening test results that are negative. The net change in the length of stay can be computed from an equation, as shown in the Appendix (available at www.mosby.com/AnnEmergMed). In general, at EDs in which ventilation-perfusion or CT scanning require more than 4 hours to complete, a pulmonary embolism rule-out protocol is highly likely to reduce the median length of stay for patients evaluated for pulmonary embolism. At centers in which imaging can be obtained in less than 3 hours, the pulmonary embolism rule-out protocol needs to be completed in less than 1 hour to significantly reduce the length of stay (see calculation in the Appendix).

Goldstein et al³⁴ implemented a D-dimer–based screening system for hospitalized patients and found a 40% increase in the rate of ventilation-perfusion scanning. At one of our centers, when a rapid pulmonary embolism rule-out protocol was implemented in October 2001, the rate of evaluation for pulmonary embolism more than doubled, increasing from 0.7% of all ED patients when CT angiography was the sole method to 1.5% of all ED patients after implementing a 30-minute pulmonary embolism rule-out protocol. If the pulmonary embolism rule-out protocol causes the rate of evaluation for pulmonary embolism to double, then the pulmonary embolism rule-out protocol result must be negative in approximately one half of patients screened to avoid increased use of imaging. This underscores the imperative for the pulmonary embolism rule-out protocol to be rapid (preferably <30 minutes) and to have a specificity of greater than 50%. However, even if a pulmonary embolism rule-out protocol does not yield a net savings in time, it can have other positive influences. In the study by Goldstein et al, although the D-dimer protocol led to an increase in the rate of ventilation-perfusion scanning of inpatients, the proportion of ventilation-perfusion scan results ultimately read as positive increased significantly, as did the total number of patients given a diagnosis of pulmonary embolism. The authors have had similar experiences at our institutions. We conservatively estimate that a pulmonary embolism rule-out protocol would facilitate the diagnosis of at least one case of pulmonary embolism per 5,000 to 10,000 ED patients that otherwise would have been missed if only ventilation-perfusion or computed tomographic scanning was available. The potential for increased rate of pulmonary embolism diagnosis offered by a pulmonary embolism rule-out protocol probably varies significantly.
among centers. At hospitals in which pulmonary vascular imaging is not available at night or on weekends, the results of a pulmonary embolism rule-out protocol might offer a rational method to decide which patients should receive temporary anticoagulation.35

Point-of-Care Testing

If appropriate pretest assessment is followed by point-of-care testing (either a qualitative D-dimer assay alone or a qualitative D-dimer assay combined with the dead-space measurement), the operational efficiency of the pulmonary embolism rule-out protocol might improve substantially. In our studies, the use of point-of-care testing in the ED allows the pulmonary embolism rule-out protocol to be completed in less than 30 minutes, and more than one half of patients with suspected pulmonary embolism can have pulmonary embolism ruled out.1,35 Despite the fact that a pulmonary embolism rule-out protocol might double the rate of evaluation for pulmonary embolism, the net rate of pulmonary vascular imaging might not increase. Implementation of the Canadian rule in conjunction with the SimpliRED D-dimer in 4 Canadian hospitals was associated with a significant decrease in imaging.35,36 Implementation of the Charlotte criteria together with a point-of-care D-dimer (SimpliFY) and dead-space measurement at one hospital did not increase the census-adjusted rate of pulmonary vascular imaging but did increase the proportion of imaging test results read as positive for pulmonary embolism and decreased ED length of stay for patients evaluated for pulmonary embolism.37

FEASIBILITY OF THE PROTOCOL

At many centers, methods to augment the administrative feasibility must be considered before implementation of a pulmonary embolism rule-out protocol. At some hospitals, the pulmonary embolism rule-out protocol might improve the efficiency of evaluation for pulmonary embolism, which can be used to help justify its use. If the protocol is to be implemented with a point-of-care test, we believe that the hospital should use the whole-blood agglutination assay (SimpliRED) or a newer-generation nylon screen assay (SimpliFY) because these tests have been better studied and appear to perform better than the qualitative latex D-dimer assay.19 Some laboratory directors might cite difficulties with Clinical Laboratory Improvement Amendment guidelines as a reason to have the central hospital laboratory perform any D-dimer assay. In that case, the hospital might need to purchase the equipment required to measure the quantitative D-dimer assay. Many hospital laboratory hematologic analyzing systems that measure coagulation times now offer the option of measuring an FDA-approved quantitative D-dimer assay for a relatively low acquisition cost. Many EDs do not have the resources to train respiratory therapists to perform the dead-space and D-dimer assay in the ED. If the dead-space measurement is used, specific protocol approval might be required from local respiratory and infectious disease committees.

In summary, we have presented the rationale for the development of a pulmonary embolism rule-out protocol and discussed its safety, efficiency, and feasibility. A well-designed protocol can preclude ventilation-perfusion or CT scanning of large numbers of ED patients with suspected pulmonary embolism and might improve detection of pulmonary embolism in the ED, without increasing the use of pulmonary vascular imaging or length of stay. Whether this proposal will indeed accomplish these goals must await empiric confirmation in clinical trials.

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REFERENCES


Method to calculate the net change per patient in the length of stay caused by the introduction of a pulmonary embolism rule-out protocol:

\[ T_{\text{new}} = (F_r + (T_s + t) + F_r - (t) + F_{rNS} (T_s)) \]

\[ \Delta T = T_s - T_{\text{new}}, \]

where \( T_{\text{new}} \) is defined as the median time required to work up pulmonary embolism with a pulmonary embolism protocol in place; \( T_s \) is defined as the median time required for standard imaging (time data are usually positively skewed, and therefore means are less useful); \( t \) is defined as the median time required for the screening test; \( F_r + \) is defined as the fraction of patients tested for pulmonary embolism with a positive screening test result; \( F_r - \) is defined as the fraction of patients tested for pulmonary embolism with a negative screening test result; \( F_{rNS} \) is defined as the fraction of patients tested for pulmonary embolism with standard imaging without a screening test; and \( \Delta T \) is defined as the net change in workup time for pulmonary embolism after implementing a pulmonary embolism rule-out protocol.

Example case: Suppose that an ED uses helical CT angiography to evaluate for pulmonary embolism, and the median time required to complete this test and get the result is 3.0 hours. We shall consider the results of the CT scan to be definitive. The ED implements a pulmonary embolism rule-out protocol that uses a decision rule that allows 75% of patients to be deemed at low enough risk for pulmonary embolism to permit the quantitative d-dimer assay (<500 ng/mL, normal) to be safely used as a screening test. The d-dimer requires 1 hour to complete, and the result is normal in 40% of patients. Patients with a normal d-dimer result are not tested further for pulmonary embolism, and patients with a positive d-dimer result all go on to receive CT scanning. The outcome variable of interest is the net effect of the screening system on the median time required to evaluate pulmonary embolism.

\[ T_s = 3 \text{ h} \]
\[ t = 1 \text{ h} \]
\[ F_r + = 0.6 \times 0.75 = 0.45 \]
\[ F_r - = 0.4 \times 0.75 = 0.30 \]
\[ F_{rNS} = 0.25 \]

First, we calculate \( T_{\text{new}} \), which is the time spent on the fraction of patients with a positive d-dimer (ie, 0.45(3 h + 1 h)) plus the time required for patients with a negative d-dimer (ie, 0.3(1 h)) plus the time spent on patients who went straight to the CT scanner (ie, 0.25(3 h)). This yields the following:

\[ T_{\text{new}} = (0.45(3+1)+0.3(1)+0.25(3)) = 2.85 \text{ h}. \]

To obtain the actual change in time from baseline \( \Delta T \), we subtract the \( T_{\text{new}} \) from the \( T_s \) as follows:

\[ \Delta T = 3.0 \text{ h} - 2.85 \text{ h} = 0.15 \text{ h}. \]

Thus, in this setting, the pulmonary embolism rule-out protocol would afford a median time savings of only about 9 minutes per person evaluated for pulmonary embolism. This calculation does not consider the overall change in length of stay required to evaluate all ED patients for suspected pulmonary embolism.43-47