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ORIGINAL RESEARCH & CONTRIBUTIONS

Improving Appropriate Use of Pulmonary Computed Tomography Angiography by Increasing the Serum D-Dimer Threshold and Assessing Clinical Probability

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Abstract

Objective: To determine whether the implementation of an increased D-dimer threshold value and clinical probability assessment increases the prevalence of pulmonary embolism (PE) in patients undergoing pulmonary computed tomography angiography (PCTA) in an Emergency Department setting.

Methods: A retrospective review of all patients undergoing PCTA during 2 separate 12-month intervals, 1 before the implementation of an increased D-dimer threshold and recommendation for formal clinical probability assessment and the other after regional implementation. The primary outcome measure was the prevalence of acute PE in each of the samples.

Results: After the implementation of the increased D-dimer threshold and recommendation for formal clinical probability assessment, the prevalence of PE detected by PCTA increased from 4.7% to 11.7% ($p < 0.001$). Among all PCTAs performed after the new guidelines were promulgated, 8.6% were still performed on patients who had serum D-dimer values lower than the threshold of 1.0 µg/mL. Despite the recommendation for formal clinical probability assessment before ordering a PCTA, only 4% of patients had a formal clinical probability assessment recorded in their electronic medical record.

Conclusion: The implementation of an increased D-dimer threshold value increased the prevalence of PE in patients undergoing PCTA in an Emergency Department setting, but more consistent application of clinical probability assessment remains an elusive target.

Introduction

Three multicenter Prospective Investigations of Pulmonary Embolism Detection (PIOPED) studies have evaluated radionuclide ventilation perfusion, computed tomography, and magnetic resonance imaging to detect pulmonary embolism (PE; PIOPED I, II, and III, respectively).[1-3] The overall prevalence of PE exceeded 20% for each study: 33% for PIOPED I, 23% for PIOPED II, and 28% for PIOPED III. Yet in several single-center studies evaluating the efficacy of pulmonary computed tomography angiography (PCTA), the prevalence is less than 10%, suggesting that PCTA is overutilized.[4-6]

Recent studies have suggested that limiting use of PCTA to patients with an intermediate or high clinical risk of PE and an increased serum D-dimer could reduce the use of PCTA without significantly increasing the risk of missed PE.[7-9]

Objective

In this study, we sought to determine whether the implementation of an increased D-dimer threshold value and formal clinical probability assessment increases the prevalence of PE in patients undergoing PCTA in an Emergency Department (ED) setting.

Materials and Methods

Our institutional laboratory uses the STA D-DI latex agglutination assay (Diagnostica Stago, Parsippany, NY) to measure patient serum D-dimers. The manufacturer's threshold for a positive serum D-dimer value is 0.4 µg/mL. In August 2012, our health maintenance organization's (HMO) Medical Group attempted to decrease use of PCTA by engaging with the ED to increase the D-dimer threshold value for a positive result within our institution from 0.4 µg/mL to 1.0 µg/mL. The increase in the D-dimer threshold value was designed to increase specificity without reducing sensitivity to detect PE by PCTA on the basis of results from both a review of patients in our own electronic medical record (EMR)[10,11] and from the published literature.[12,13] ED physicians were requested to use a clinical algorithm (preferably, but not limited to, the Wells criteria) to determine pretest probability for PE. The Wells criteria includes 7 symptoms or characteristics of medical history and physical examination. A patient receives a score depending on which criteria they possess, as determined by Wells et al.[7] The score indicates the likeliness of a PE diagnosis. Using the Wells criteria or other validated clinical algorithms was a recommendation rather than a requirement for ordering a PCTA.

We obtained institutional review board approval with a waiver of consent to retrospectively review a common EMR to determine the age, sex, D-dimer result, if any, and PCTA result of all patients seen in the ED of the HMO with a possible diagnosis of acute PE who underwent PCTA.

One of the authors reviewed and assigned Wells scores for the patients on the basis of the EMR information associated

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with the ED encounter leading to the PCTA, unless the ED physician had already assigned a Wells score or used another clinical assessment algorithm for the patient. The reviewer was masked to the D-dimer value as well as the PCTA result for every patient. However, because the EMR including the ED physician note was reviewed to determine each patient's clinical probability, the emergency physician's clinical probability assessment was known if it was recorded in the physician's note. The Wells criteria have been validated as a method to stratify a patient's clinical probability of PE.[7] Points were assigned for each of the following clinical signs or symptoms: PE as likely or more likely than any alternative diagnosis, 3.0 points; signs or symptoms of deep venous thrombosis (leg swelling or painful palpation in the region of a deep vein), 3.0 points; heart rate higher than 100 beats/min, 1.5 points; immobilization (bed rest for 3 consecutive days) or surgery within past 4 weeks, 1.5 points; previous diagnosis of PE or deep venous thrombosis, 1.5 points; hemoptysis, 1.0 points; active malignancy (within past 6 months), 1.0 points. Most of these clinical signs and symptoms could be determined unambiguously from the EMR.

We used the following algorithm to determine whether PE was as likely or more likely than any alternative diagnosis: If the patient's chief complaint on record was shortness of breath or dyspnea, then we assumed PE was the most likely diagnosis unless 1) the patient had a history of congestive heart failure and chest x-ray was suggestive of edema, 2) the patient had signs and symptoms of a respiratory infection and an abnormal chest x-ray, or 3) the patient had a history of asthma/chronic obstructive pulmonary disease and clinical symptoms of an asthma/chronic obstructive pulmonary disease exacerbation. If the patient's chief complaint was chest pain, then we assumed PE was the most likely diagnosis unless the patient had a history of coronary artery disease, prior myocardial infarction, or cardiomyopathy. However, if the chest pain was further described as substernal, crushing, or radiating to the back or left arm, PE was not assumed to be the most likely diagnosis. For a chief complaint of unilateral leg pain or swelling, PE was assumed the most likely diagnosis unless there was a specific finding in the reported history to suggest a more likely alternative diagnosis.

The Wells criteria scores segregated patients into 3 clinical risk strata for PE: low (score < 2); intermediate (score 2-6); and high (score > 6).[7] The subjects were also segregated on the basis of their serum D-dimer levels into those with negative (<1.0 µg/mL) or positive (≥1.0 µg/mL) serum D-dimer using the latex agglutination technique.

Two data sets each covering 12 months were collected, 1 before and 1 after implementation of the higher D-dimer threshold and recommendation of using a clinical decision rule. The former spanned from June 1, 2008 through May 31, 2009, and the latter from September 1, 2012 through August 31, 2013. The 2 data sets were compared to see whether there was a significant change in the prevalence of PE and patient characteristics.

All statistical analysis was performed using STATA, version 7.0 (Stata, College Station, TX).

Results

The ED of this HMO, with about 227,000 members, sees approximately 36,000 patients annually. The number of members within this HMO has not appreciably changed from 2008 to 2013.

From June 1, 2008, through May 31, 2009, before implementation of the higher D-dimer threshold, the ED saw 510 consecutive patients who underwent PCTA for possible PE. This will be referred to as the 2008-2009 cohort in the rest of this article. There were 198 men and 312 women. The average (standard deviation [SD]) age among all patients was 59.2 (18.0) years (range, 16-96 years). For men, the average (SD) age was 59.2 (17.4) years (range, 19-90 years). For women, the average (SD) age was 59.2 (18.0) years (range, 16-96 years).

The overall prevalence of PE as determined by PCTA in the 2008-2009 cohort was 4.7% (24/510). Three hundred forty-seven patients (68.0%) had a D-dimer drawn at the time of their PCTA. Of these, 18 proved to have PE by PCTA (5.2%). Of the 161 patients who had a serum D-dimer level of at least 1.0 µg/mL, there were 15 cases of PE demonstrated by PCTA, a prevalence of 9.3%. Conversely, there were 186 subjects who had a D-dimer level less than 1.0 µg/mL, but only 1 (0.5%) proved to have PE. Among these 186 subjects, there were 160 who had a D-dimer level of at least 0.4 µg/mL, which included the patient who had a PE documented by PCTA. This 58-year-old man had a D-dimer level of 0.95 µg/mL. Of 163 patients without a D-dimer level drawn at the time of PCTA, there were 6 (3.7%) who proved to have PE. Excluding 3 patients in this group with known PE undergoing follow-up PCTA for persistent or progressive symptoms, only 3 (1.9%) of 160 proved to have PE by PCTA.

The clinical probability of PE was estimated for each of the patients in the 2008-2009 cohort using the Wells criteria.[7] Among 36 patients with high clinical probability for PE, there were 5 (13.9%) who had PE diagnosed by PCTA. Only 18 (5.5%) of the 328 moderate-risk patients had PE by PCTA. Finally, there was only 1 (0.7%) among 146 patients with low risk who had PE by PCTA.

Table 1 shows the prevalence of positive PE by PCTA segregated by serum

Table 1. Prevalence of positive pulmonary computed tomography angiography segregated by Wells criteria score for clinical probability of pulmonary embolism and serum D-dimer level for patients in the 2008-2009 cohort

Wells/D-dimer	< 1 (%)	> 1 (%)	ND (%)[a]	Total (%)
< 2 (low)	0/52 (0)	1/41 (2.4)	0/53 (0)	1/146 (0.7)
2-6 (intermediate)	0/130 (0)	12/108 (11.1)	6/90 (6.7)	18/328 (5.5)
> 6 (high)	1/4 (25.0)	4/12 (33.3)	0/20 (0)	5/36 (13.9)
Total	1/186 (0.5)	17/161 (10.6)	6/163 (3.7)	24/510 (4.7)

[a] ND = serum D-dimer not drawn.

Table 2. Prevalence of positive pulmonary computed tomography angiography segregated by Wells criteria score for clinical probability of pulmonary embolism and serum D-dimer levels for patients in the 2012-2013 cohort

Wells/D-dimer	< 1 (%)	> 1 (%)	ND (%)[a]	Total (%)
< 2 (Low)	0/25 (0)	5/108 (4.6)	1/ 75 (1.3)	6/208 (2.9)
2-6 (Intermediate)	0/22 (0)	21/151 (13.9)	17/113 (15.0)	38/286 (13.3)
> 6 (High)	0/0 (0)	12/28 (42.9)	8/25 (32.0)	20/53 (37.7)
Total	0/47 (0)	38/287 (13.2)	26/213 (12.2)	64/547 (11.7)

[a] ND = serum D-dimer not drawn.

D-dimer and retrospective clinical probability using the Wells criteria for the 2008-2009 cohort. As expected, the prevalence of PE detected by PCTA is very low in all patients with a serum D-dimer level less than 1.0 µg/mL, irrespective of the patients' clinical probability assessment. In the 2008-2009 cohort, only when patients had a serum D-dimer of at least 1.0 µg/mL and an intermediate or high clinical probability of PE did the prevalence of PE exceed 10% in PCTA studies. Interestingly, none of the 20 patients with a high clinical probability of PE determined retrospectively from their EMR but who did not have a D-dimer level recorded at the time of the PCTA had detectable PE.

From September 1, 2012, through August 31, 2013, the ED saw 547 consecutive patients who underwent PCTA for suspected PE. This will be referred to as the 2012-2013 cohort in the rest of this article. There were 250 men and 297 women. The average (SD) age among all patients was 63.3 (18.0) years (range, 3-97 years). For men, the average (SD) age was 63.5 (17.7) years (range, 16-96 years). For women, the average (SD) age was 63.3 (18.0) years (range, 3-97 years).

The overall prevalence of PE as determined by PCTA in the 2012-2013 cohort was 11.7% (64/547). There were 334 patients (61.1%) who had a D-dimer drawn at the time of their PCTA. Of these, 38 (11.4%) proved to have PE by PCTA. Of the 287 patients with a serum D-dimer level of *at least* 1.0 µg/mL, there were 38 cases (13.2%) of PE demonstrated by PCTA. There were 47 patients who had a D-dimer level less than 1.0 µg/mL. None of these patients proved to have PE. Among these 47 patients, 28 had a D-dimer greater than 0.4 µg/mL. Of 213 patients without a D-dimer level drawn at the time of PCTA, 26 (12.2%) proved to have PE. Excluding 3 patients in this group with known PE undergoing follow-up PCTA for persistent or progressive symptoms, 23 (11.0%) of 210 proved to have PE by PCTA.

The clinical probability of PE was estimated for each of these patients in the 2012-2013 cohort using the Wells criteria. Among 53 patients with high clinical probability for PE, 20 (37.7%) had PE diagnosed by PCTA. Only 38 (13.3%) of the 286 moderate-risk patients had PE by PCTA. Finally, among 208 patients with low risk, there were 6 (2.9%) who had PE by PCTA.

Table 2 shows the prevalence of positive PE by PCTA segregated by serum D-dimer and retrospective clinical probability assessment for the 2012-2013 cohort. Again, the prevalence of PE detected by PCTA is very low in all patients with a serum D-dimer level less than 1.0 µg/mL, irrespective of the patients' clinical probability assessment. All patients in the second cohort with intermediate or high clinical probability of PE had a prevalence of PE exceeding 10% of their PCTA studies, irrespective of whether they had a serum D-dimer of at least 1.0 µg/mL or did not have one drawn.

There was a statistically significant difference between cohorts in their age and sex distributions. The 2012-2013 cohort was older than the 2008-2009 cohort (2012-2013 age: 63.4 [18.0]; 95% CI, 61.8-64.9 years; vs 2008-2009 age: 59.2 [18.0]; 95% CI, 57.6-60.7 years; $t = -3.776$, $p < 0.001$). Also, men constituted only 38.8% of the 510 patients in the 2008-2009 cohort, but they represented 45.7% of the 547 patients in the 2012-2013 cohort ($\chi^2 = 5.116$, $p = 0.024$).

There was a significantly higher prevalence of PE detected by PCTA in the 2012-2013 cohort (11.7%) than for the 2008-2009 cohort (4.7%) ($\chi^2 = 16.917$, $p < 0.001$).

Despite the recommendation that all patients undergoing PCTA have a D-dimer drawn without compromising patient care, there was a significantly higher proportion of patients who underwent PCTA without having a D-dimer level drawn in the 2012-2013 cohort (38.9%) than in the 2008-2009 cohort (32.0%) ($\chi^2 = 5.609$, $p = 0.018$).

Among patients who did have a serum D-dimer drawn before PCTA, there was a much higher proportion of patients who had a serum D-dimer level less than 1.0 µg/mL in the 2008-2009 cohort (53.6%) than in the 2012-2013 cohort

Table 3. The number of individuals for whom each of the Wells criteria were present for each cohort

Wells criteria	2008-2009 cohort, n = 510 (%)	2012-2013 cohort, n = 547 (%)	χ^2	p value
Pulmonary embolism considered the most likely diagnosis	335 (65.7)	234 (42.8)	55.726	<0.001
Signs or symptoms of deep venous thrombosis	64 (12.5)	103 (18.8)	7.752	0.005
Tachycardia (heart rate > 100)	153 (30.0)	196 (35.8)	4.056	0.044
Recent prolonged immobility or major surgery	65 (12.7)	92 (16.8)	3.510	0.061
Prior history of pulmonary embolism or deep venous thrombosis	37 (7.3)	59 (10.8)	3.986	0.046
Hemoptysis	11 (2.2)	20 (3.7)	2.084	0.149
Active or recent cancer	92 (18.0)	128 (23.4)	4.603	0.032

(14.1%) (χ^2 = 118.155, p < 0.001). In addition, among patients with a D-dimer level less than 1.0 µg/mL, there was a much higher proportion of patients who had a serum D-dimer level between 0.4 and 1.0 µg/mL in the 2008-2009 cohort (86%) than in the 2012-2013 cohort (60%) (χ^2 = 16.840, p < 0.001).

Though there was no significant difference between the 2 cohorts for prevalence of PE detected by PCTA among patients with a D-dimer value less than 1.0 µg/mL (2008-2009: 0.5% vs 2012-2013: 0%, Fisher exact = 1.000, p = 0.80) and at least 1.0 µg/mL (2008-2009: 10.6% vs 2012-2013: 13.2%, χ^2 = 0.689, p = 0.407), there was a significant difference among patients who did not have a D-dimer value drawn (2008-2009: 3.7% vs 2012-2013: 12.2%, χ^2 = 8.620, p = 0.003).

Table 3 lists the presence of the individual Wells criteria in each of the patient cohorts on the basis of their review of the EMR. We recorded a 23% higher prevalence of the first criterion (PE as the most likely diagnosis) for patients in the 2008-2009 cohorts than in the 2012-2013 cohorts. Since this criterion is worth 3 points in the Wells algorithm and its presence gives the patient at least an intermediate clinical risk, the fact that 101 more patients in the earlier cohort met this criterion likely explains the smaller proportion of low-risk patients in the 2008-2009 cohort (28.6%) compared with the 2012-2013 cohort (38.0%) (χ^2 = 10.465, p = 0.001).

When we compared the 2 cohorts for the prevalence of PE detected by PCTA among patients with low clinical risk as retrospectively assessed using the Wells criteria, there was no significant difference (2008-2009: 0.7% vs 2012-2013: 2.9%, Fisher exact = 0.247, p = 0.14). However, the one patient with acute PE in the 2008-2009 cohort and 5 of the 6 patients with acute PE in the 2012-2013 cohort all had a serum D-dimer level less than or equal to 1.0 µg/mL. One patient with acute PE had a low clinical probability of PE as assessed retrospectively and did not have a serum D-dimer. No patients with low clinical probability and serum D-dimer less than 1.0 µg/mL had acute PE detected by PCTA in either cohort.

Table 4. Number of pulmonary computed tomography angiographies performed per 1000 Emergency Department visits within each study period

Month	2008-2009	2012-2013
September	11.74	13.28
October	15.67	7.36
November	13.94	10.08
December	13.43	13.08
January	18.49	10.41
February	16.22	14.25
March	16.92	11.86
April	21.62	13.97
May	18.70	11.72
June	14.71	13.65
July	15.18	17.45
August	11.06	13.33
Average	15.64	12.54

For patients with either intermediate or high clinical risk, there was a significant difference in the prevalence of PE between cohorts (intermediate: 2008-2009: 5.5% vs 2012-2013: 13.3%, χ^2 = 11.211, p = 0.001; high: 2008-2009: 13.9% vs 2012-2013: 37.7%, χ^2 = 6.035, p = 0.014). This difference may be explained by the much higher proportion of patients with intermediate clinical risk in the 2012-2013 cohort who had a serum D-dimer greater than 1.0 µg/mL than in the 2008-2009 cohort (52.8% vs 32.9%, χ^2 = 24.734, p = 0.001). However, there is no statistically significant difference in the proportion of patients with serum D-dimer of at least 1.0 µg/mL in the patients at high clinical risk (χ^2 = 3.293, p = 0.07).

Table 4 lists the number of PCTAs performed per 1000 ED visits by month during each study period. There was a statistically significant decrease in the monthly PCTAs performed per 1000 ED visits during the later 2012-2013 study period (rank sum test, Z = -2.483, p = 0.01).

Although many of the ED physicians mentioned the possibility of PE within a list of other differential diagnoses, only 22 (4.0%) of 547 physician notes specifically mentioned a clinical probability of PE. In only 4 of the 22 notes was a specific Wells score given. In one other note, the Pulmonary Embolism Rule-out Criteria were mentioned. This is despite the Medical Group's recommendations that some type of pretest clinical probability assessment of PE be performed in addition to ordering the serum D-dimer before ordering a PCTA.

When we compared the ED physicians' clinical probability of PE against our study's retrospectively determined clinical probability, there was concordance in the assessed level of risk for 20 of 22 patients. However, a 40-year-old woman with tachycardia and active cancer was noted as "low risk" for PE whereas we recorded moderate risk (Wells score, 2.5), and a 59-year-old woman presenting with syncope and a remote history of PE was noted as "high risk," however we recorded moderate risk (Wells score, 4.5).

Discussion

In August 2012, the serum D-dimer threshold level for positive possible acute PE was increased in our institution from at least 0.4 µg/mL to at least 1.0 µg/mL, on the basis of both a literature review and our own experience, which suggested that an increased threshold would increase specificity without reducing sensitivity.[9-13]

We demonstrated a significant decrease in the number of PCTAs performed per 1000 ED visits as well as a significant increase in the prevalence of positive studies after the implementation of the recommendations (from 4.7% to 11.7%). We suggest that this increase in prevalence of positive PCTA studies represents more appropriate patient selection for PCTA because the prevalence of PE has increased in those patients who had a serum D-dimer drawn as well as those who did not. The same selection process results in an overall decrease in the number of PCTAs ordered per 1000 ED visits.

On the basis of the results, patients with high clinical risk as assessed using a clinical algorithm such as the Wells criteria may not require a serum D-dimer before proceeding to PCTA. Conversely, patients with low clinical risk may not require a serum D-dimer to be drawn to avoid a PCTA. This emphasizes the importance of documenting a high or low clinical probability in the medical record using some type of decision rule. Patients

with intermediate clinical risk benefit most from a serum D-dimer evaluation because only those patients with an elevated D-dimer need to proceed with PCTA.

Only 4% of the notes … mention a clinical probability of PE. … only 5 of these … mention [use] of a clinical decision rule …

There are still a number of patients in the 2012-2013 cohorts with low serum D-dimer levels who underwent PCTA. The reason for this is unclear because the retrospective assessment of the clinical risk for PE was either low or moderate for all 47 of these patients. It is also unclear how older age and male sex in the 2012-2013 cohort compared with the 2008-2009 cohort influenced the higher prevalence of PEs.

The implementation of the higher D-dimer threshold set to at least 1.0 µg/mL did not reduce the sensitivity of PCTA for the detection of acute PE. Only 1 among all 233 patients in both cohorts with a D-dimer value less than 1.0 µg/mL was noted to have PE detected by PCTA. Given the published coincidental PE rate of approximately 2% among all patients undergoing chest computed tomography for reasons other than PE, this higher D-dimer threshold is acceptable.[14-16]

We did not achieve a reasonable level of compliance among ED physicians with respect to documenting their pretest clinical probability assessment within the medical record. Only 4% of the notes on the 547 patients in the 2012-2013 cohort made mention of a clinical probability of PE. In only 5 of these 22 notes was there a specific mention of a clinical decision rule such as the Wells criteria or the Pulmonary Embolism Rule-out Criteria. Although there is controversy as to the most appropriate decision rule to be used for patients being evaluated for PE, there is no controversy as to recording the clinical likelihood assessment.[17] Because this HMO has a fully integrated EMR for all emergency, ambulatory, and hospital-based services including radiology ordering, a higher rate of compliance will likely entail the use of some type of electronic decision support tool embedded within the radiology ordering mechanism that requires the input of a clinical pretest probability.

Study Limitations

A primary limitation of this study was the necessity to assign Wells scores retrospectively through EMR review. EMR review provides less information in comparison with direct patient examination because not every finding may be documented electronically. In our ED, physicians may mentally estimate their patient's pretest probability of PE using a standard algorithm such as the Wells criteria, but they rarely record that clinical probability in their written notes. To increase the documentation of clinical probability, it may be necessary to include a step in the computed tomography ordering process where the physician is required to input a clinical probability assessment. A pop-up screen could be included within the ordering process that requires the physician to input specific findings that could then generate a clinical probability assessment using a standard algorithm such as the Wells criteria.

A population analysis based on an HMO population may not be representative of other clinical settings. Our study results, although indicative of a general community hospital, may not be applicable for other institutions, such as tertiary institutions or academic institutions where more selective populations may be encountered.

Finally, this HMO uses only one method of serum D-dimer measurement (STA D-DI). It is unclear whether the use of the 1.0 µg/mL threshold value could be applied to other methods of D-dimer measurement, although other authors have suggested different threshold values with other methods of serum D-dimer measurement.[12,13] We recommend that those institutions that use a different D-dimer assay, review their own PCTA results to ensure that the higher threshold does not significantly reduce their sensitivity for the detection of PE.

Conclusion

The implementation of an increased D-dimer threshold value increased the prevalence of PE in patients undergoing PCTA in an ED setting, but more consistent application of clinical probability assessment remains an elusive target. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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References

1. PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA 1990 May 23-30;263(20):2753-9. DOI: http://dx.doi.org/10.1001/jama.1990.03440200057023.
2. Stein PD, Fowler SE, Goodman LR, et al; PIOPED II Investigators. Multidetector computed tomography for acute pulmonary embolism. N Engl J Med 2006 Jun 1;354(22):2317-27. DOI: http://dx.doi.org/10.1056/NEJMoa052367.
3. Stein PD1, Chenevert TL, Fowler SE, et al; PIOPED III (Prospective Investigation of Pulmonary Embolism Diagnosis III) Investigators. Gadolinium-enhanced magnetic resonance angiography for pulmonary embolism: a multicenter prospective study (PIOPED III). Ann Intern Med 2010 Apr 6;152(7):434-43, W142-3. DOI: http://dx.doi.org/10.7326/0003-4819-152-7-201004060-00008.
4. Prologo JD, Gilkeson RC, Diaz M, Asaad J. CT pulmonary angiography: a comparative analysis of the utilization patterns in emergency department and hospitalized patients between 1998 and 2003. AJR Am J Roentgenol 2004 Oct;183(4):1093-6. DOI: http://dx.doi.org/10.2214/ajr.183.4.1831093.
5. Abcarian PW, Sweet JD, Watabe JT, Yoo HC. Role of a quantitative D-dimer assay in determining the need for CT angiography of acute pulmonary embolism. AJR Am J Roentgenol 2004 Jun;182(6):1377-81. DOI: http://dx.doi.org/10.2214/ajr.182.6.1821377.
6. Donohoo JH, Mayo-Smith WW, Pezzullo JA, Egglin TK. Utilization patterns and diagnostic yield of 3421 consecutive multidetector row computed tomography pulmonary angiograms in a busy emergency department. J Comput Assist Tomogr 2008 May-Jun;32(3):421-5. DOI: http://dx.doi.org/10.1097/RCT.0b013e31812e6af3.
7. Wells PS, Anderson DR, Rodger M, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency departmet by using a simple clinical model and d-dimer. Ann Intern Med 2001 Jul 17;135(2):98-107. DOI: http://dx.doi.org/10.7326/0003-4819-135-2-200107170-00010.
8. van Belle A, Büller HR, Huisman MV, et al; Christopher Study Investigators. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. JAMA 2006 Jan 11;295(2):172-9. DOI: http://dx.doi.org/10.1001/jama.295.2.172.
9. Gimber LH, Leong J, Todoki L, Yoon HC. Avoiding unnecessary pulmonary CT angiography by using a combination of clinical criteria and D-dimer thresholds. Open Journal of Radiology 2013;3:78-84. DOI: http://dx.doi.org/10.4236/ojrad.2013.32012.

10. Hirai LK, Takahashi JM, Yoon HC. A prospective evaluation of a quantitative D-dimer assay in the evaluation of acute pulmonary embolism. J Vasc Interv Radiol 2007 Aug;18(8):970-4. DOI: http://dx.doi.org/10.1016/j.jvir.2007.04.020.
11. Gimber LH, Travis RI, Takahashi JM, Goodman TL, Yoon HC. Computed tomography angiography in patients evaluated for acute pulmonary embolism with low serum D-dimer levels: a prospective study. Perm J 2009 Fall;13(4):4-10. DOI: http://dx.doi.org/10.7812/TPP/09-060.
12. Kline JA, Hogg MM, Courtney DM, Miller CD, Jones AE, Smithline HA. D-dimer threshold increase with pretest probability unlikely for pulmonary embolism to decrease unnecessary computerized tomographic pulmonary angiography. J Thromb Haemost 2012 Apr;10(4):572-81. DOI: http://dx.doi.org/10.1111/j.1538-7836.2012.04647.x.
13. Kabrhel C, Courtney D, Camargo CA Jr, et al. Potential impact of adjusting the threshold of the quantitative D-dimer based on pretest probability of acute pulmonary embolism. Acad Emerg Med 2009 Apr;16(4):325-32. DOI: http://dx.doi.org/10.1111/j.1553-2712.2009.00368.x.
14. Hui GC, Legasto A, Wittram C. The prevalence of symptomatic and coincidental pulmonary embolism on computed tomography. J Comput Assist Tomogr 2008 Sep-Oct;32(5):783-7. DOI: http://dx.doi.org/10.1097/RCT.0b013e31815a7aea.
15. Farrell C, Jones M, Girvin F, Ritchie G, Murchison JT. Unsuspected pulmonary embolism identified using multidetector computed tomography in hospital outpatients. Clin Radiol 2010 Jan;65(1):1-5. DOI: http://dx.doi.org/10.1016/j.crad.2009.09.003.
16. Dentali F, Ageno W, Becattini C, et al. Prevalence and clinical history of incidental, asymptomatic pulmonary embolism: a meta-analysis. Thromb Res 2010 Jun;125(6):518-22. DOI: http://dx.doi.org/10.1016/j.thromres.2010.03.016.
17. Lucassen W, Geersing GJ, Erkens PM, et al. Clinical decision rules for excluding pulmonary embolism: a meta-analysis. Ann Intern Med 2011 Oct 4;155(7):448-60. DOI: http://dx.doi.org/10.7326/0003-4819-155-7-201110040-00007.

Excessive Bed Rest

I had known that excessive bed rest gave rise to thromboembolic complications. … The death rate from thromboembolism was always much less at the County Hospital … When [the County Hospital patients] got up to go to the bathroom, [they] dislodged only tiny clots from their veins and these did not harm them when they got to the lungs and were dissolved, while the wealthier patients … [at a private hospital] who remained in bed and formed large clots in their legs and pelvises suffered the major consequences of large pulmonary emboli.

— William Dock, MD, 1898-1990, cardiologist, known for coining "Sutton's Law"