Scanning the Literature

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Spiral CTs Are Cost-Effective

Paterson DI, Schwartzman K. Strategies incorporating spiral CT for the diagnosis of acute pulmonary embolism: a cost-effectiveness analysis. Chest 2001; 119:1791-1800.

Objective: To assess the cost-effectiveness of spiral CT for the diagnosis of acute pulmonary embolism. **Design**: Computer-based cost-effectiveness analysis. **Patients**: Simulated cohort of 1,000 patients with suspected acute pulmonary embolism (PE), with a prevalence of 28.4%, as in the Prospective Investigation of Pulmonary Embolism Diagnosis study. **Interventions**: Using a decision-analysis model, seven diagnostic strategies were compared, which incorporated combinations of ventilation-perfusion (V/Q) scans, duplex ultrasound of the legs, spiral CT, and conventional pulmonary angiography. **Measurements and Results**: Expected survival and cost (in Canadian dollars) at 3 months were estimated. Four of the strategies yielded poorer survival at higher cost. The three remaining strategies were as follows: (1) V/Q +/- leg ultrasound +/- spiral CT, with an expected survival of 953.4 per 1,000 patients and a cost of $1,391 per patient; (2) V/Q +/- leg ultrasound +/- pulmonary angiography (the "traditional" algorithm), with an expected survival of 953.7 per 1,000 patients and a cost of $1,416 per patient; and (3) spiral CT +/- leg ultrasound, with an expected survival of 958.2 per 1,000 patients and a cost of $1,751 per patient. The traditional algorithm was then excluded by extended dominance. The cost per additional life saved was $70,833 for spiral CT +/- leg ultrasound relative to V/Q +/- leg ultrasound +/- spiral CT. **Conclusions**: Spiral CT can replace pulmonary angiography in patients with nondiagnostic V/Q scan and negative leg ultrasound findings. This approach is likely as effective as—and possibly less expensive than—the current algorithm for diagnosis of acute PE. When spiral CT is the initial diagnostic test, followed by leg ultrasound, expected survival improves but costs are also considerably higher. These findings were robust to variations in the assumed sensitivity and specificity of spiral CT.

Comments: This Canadian cost-effectiveness study is based on incidence rates and diagnostic accuracies from the literature and local costs in Canada. These were fed into TreeAge's DATA 3.0 decision analysis software, and the article is a good review of this technique in developing cost-effective diagnostic algorithms.

The authors do an excellent job of listing their assumptions. The clinical assumptions for incidence rates and diagnostic sensitivity and specificity come from the worldwide literature, so it should be independent of Canada. An issue in evaluating foreign decision analysis studies for use in the United States is whether their local costs (base cost and ranges of cost used in sensitivity analysis) are similar enough to third party payers in the US such as Medicare and the average US health plan. The authors did obtain US Medicare costs in the Midwest to assist in establishing upper limits in their cost ranges. However, this does not resolve the issue.

In Canada, a spiral CT was more expensive than a V/Q scan by a factor of 2 ($203 vs. $102 in Canadian dollars) whereas their US Medicare data had spiral CTs being cheaper ($339 vs. $450 in US dollars). Hence, one of the conclusions in this useful study is in question for us: that when spiral CT is the initial diagnostic test, initial survival improves but costs are considerably higher ($70,833 per additional life saved). I suspect first doing a spiral CT is likely to be more cost effective given US costs. Even given their numbers, the cost per life saved may be acceptable in the US.

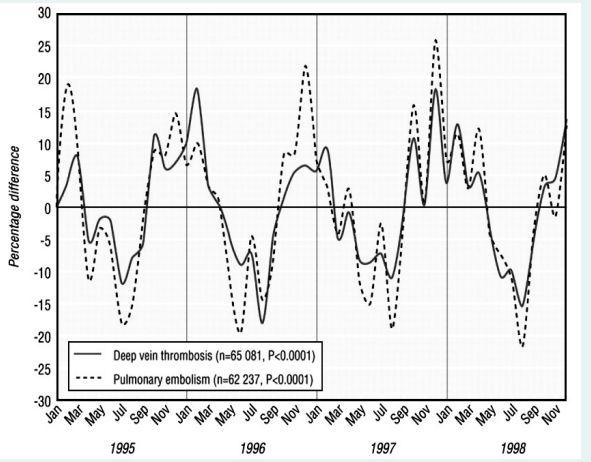
Lots More DVTs and PEs in the Winter!

Boulay F, Berthier F, Schoukroun G, et al. Seasonal variations in hospital admission for deep vein thrombosis and pulmonary embolism: analysis of discharge data. BMJ 2001; 323:601-602.

Comments: This French study used 1995-98 hospital discharge data to show significant seasonal variation in incidence rates of DVTs and PEs. Prior to this report, this type of seasonal variation had only been well documented in fatal PEs.

The authors suggest that thrombogenic factors are seasonal. This could involve cold and reduced activity leading to reduced blood flow in the lower limbs, or hypercoagulability induced by winter respiratory tract infections.

Perhaps we should encourage our patients to take up an exercise program they can continue on with in the Winter. Given the higher incidence rates, our index of suspicion should be higher in the late Fall and Winter seasons.



Monthly percentage variations in French hospital admissions for deep vein thrombosis and pulmonary embolism (0 represents the sum of monthly variations). Reprinted with the permission of BMJ Publishing Group.

Three Months of Warfarin for First, Low-Risk DVTs and PEs

Pinede L, Ninet J, Duhaut P, et al. Comparison of 3 and 6 months of oral anticoagulant therapy after a first episode of proximal deep vein thrombosis or pulmonary embolism and comparison of 6 and 12 weeks of therapy after isolated calf deep vein thrombosis. Circulation 2001; 103:2453-2460.

Background: The optimal duration of oral anticoagulant therapy after a first episode of venous thromboembolism remains controversial. **Methods and Results**: We performed an open-label, randomized trial comparing a short oral anticoagulant course (3 months for proximal deep vein thrombosis [P-DVT] and/or pulmonary embolism [PE]; 6 weeks for isolated calf DVT [C-DVT]) with a long course of therapy (6 months for P-DVT/PE; 12 weeks for C-DVT). The outcome events were recurrences and major, minor, or fatal bleeding complications. A total of 736 patients were enrolled. There were 23 recurrences of venous thromboembolism in the short treatment group (6.4%) and 26 in the long treatment group (7.4%); the 2 treatment regimens had an equivalent effect. For the hemorrhage end point, the difference between the short and the long treatment groups was not significant: 15.5% versus 18.4% for all events (p=0.302), 1.7% versus 2.8% (p=0.291) for major events, and 13.9% versus 15.3% for minor bleeding. Subgroup analysis demonstrated that the rate of recurrence was lower for C-DVT than for P-DVT or PE. **Conclusions**: After isolated C-DVT, 6 weeks of oral anticoagulation is sufficient. For P-DVT or PE, we demonstrated an equivalence between 3 and 6 months of anticoagulant therapy. For patients with temporary risk factors who have a low risk of recurrence, 3 months of treatment seems to be sufficient. For patients with idiopathic venous thromboembolism or permanent risk factors who have a high risk of recurrence, other trials are necessary to assess prolonged therapy beyond 6 months.

Comments: This article from a French group points out that the annual cumulative incidence of DVT/PE recurrence ranges from 4%-17% in prospective studies and 4%-8% in studies published since 1992.

They provide a solid evidence base for interpreting our usual rule of 3-6 months of oral anticoagulants after a first proximal DVT or PE. Since there was no difference in 3 and 6 months of therapy in this study, its better to do 3 months in low-risk cases and lessen the potential side effects, costs, and inconvenience of

doubling the time on oral anticoagulants. Low-risk, isolated calf DVTs can use a 6-week period.

High-risk cases must be individualized and may need longer periods. The authors review transient risk factors compatible with a short 3-month course: surgery, trauma, plaster for a broken leg, puerperium, and immobilization for medical conditions that will resolve soon. They contrast these with the permanent risk factors of obesity, varicosity, heart failure, bedridden status, malignancy, and thrombophilia. These and idiopathic cases should be treated for the longer 6-month period. There may be benefits to tailoring the length of anticoagulation to individual risk factors, but further studies will be needed to detail how to do this.

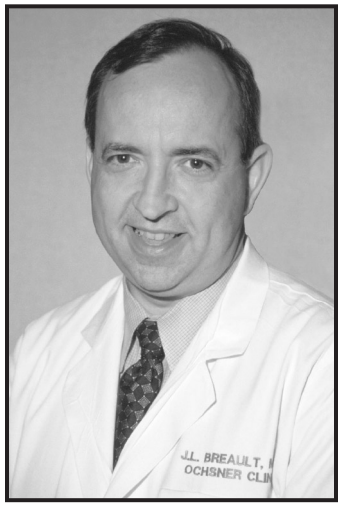
When We R/O PE, 1-year Mortality is 15%!

Poulsen SH, Noer I, Moller JE, et al. Clinical outcome of patients with suspected pulmonary embolism. A follow-up study of 588 consecutive patients. J Intern Med 2001; 250:137-143.

Objective: To investigate the clinical outcome in patients with clinically suspected pulmonary embolism (PE). **Design and Setting**: In a retrospective design we studied 588 consecutive patients with suspected PE and referred for lung scintigraphy from 1995 to 1998. The mean follow-up time was 653 +/- 424 days. **Results**: The diagnosis of PE was confirmed in 194 and excluded in 394 patients, respectively. The overall prevalence of PE was 33%. Amongst clinical and paraclinical variables, age, chronic obstructive pulmonary disease (COPD), heart rate, pleuretic pain, presence of deep venous thrombosis (DVT), electrocardiographic signs of right ventricular (RV) strain were identified as independent predictors of the diagnosis of PE. Amongst patients with PE anticoagulation was given in 96% for at least 3 months and 13% received thrombolytic therapy. Recurrent PE was seen in 6% of patients with PE whereas none of the patients with no diagnosis of PE suffered PE during follow-up. The 1 year mortality was 18% amongst patients with PE and 15% in patients with excluded PE (P = NS). The cause of death amongst patients with PE was cancer (49%) and PE (28%), whereas patients without PE had an excess mortality because of cancer, COPD, acute myocardial infarction and heart failure. **Conclusion**: Patients admitted to hospital on suspicion of PE have increased risk of adverse clinical outcome whether the diagnosis of PE is confirmed or not. This indicates that the patients where the diagnosis is excluded often suffer from other serious illness that warrants further investigations.

Comments: This Danish study gives us information on what happens to those patients we suspect may have a PE. Their outcomes tend to be poor even for those in the majority who have a PE ruled out. Pulmonary angiography was rarely used in this population even with intermediate probability lung scans so the diagnosis in borderline cases may be in question.

The take home message here is that excluding a PE should not end our work-up. If we are worried about a PE and then rule it out, we should look further for cancers, coronary artery disease, congestive heart failure, and chronic obstructive pulmonary disease. Spending time optimizing management of these conditions may lessen their high 1-year mortality.



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D-Dimer Verus V/Q — Not Yet

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 department by using a simple clinical model and D-dimer. Ann Intern Med 2001;135:98-107.

Background: The limitations of the current diagnostic standard, ventilation-perfusion lung scanning, complicate the management of patients with suspected pulmonary embolism. We previously demonstrated that determining the pretest probability can assist with management and that the high negative predictive value of certain D-dimer assays may simplify the diagnostic process. **Objective**: To determine the safety of using a simple clinical model combined with D-dimer assay to manage patients presenting to the emergency department with suspected pulmonary embolism. **Design**: Prospective cohort study. **Setting**: Emergency departments at four tertiary care hospitals in Canada. **Patients**: 930 consecutive patients with suspected pulmonary embolism. **Interventions**: Physicians first used a clinical model to determine patients' pretest probability of pulmonary embolism and then performed a D-dimer test. Patients with low pretest probability and a negative D-dimer result had no further tests and were considered to have a diagnosis of pulmonary embolism excluded. All other patients underwent ventilation-perfusion lung scanning. If the scan was nondiagnostic, bilateral deep venous ultrasonography was done. Whether further testing (by serial ultrasonography or angiography) was done depended on the patients' pretest probability and the lung scanning results. **Measurements**: Patients received a diagnosis of pulmonary embolism if they had a high-probability ventilation-perfusion scan, an abnormal result on ultrasonography or pulmonary angiography, or a venous thromboembolic event during follow-up. Patients for whom the diagnosis was considered excluded were followed up for 3 months for the development of thromboembolic events. **Results**: The pretest probability of pulmonary embolism was low, moderate, and high in 527, 339, and 64 patients (1.3%, 16.2%, and 37.5% had pulmonary embolism), respectively. Of 849 patients in whom a diagnosis of pulmonary-embolism had initially been excluded, 5 (0.6% [95% CI, 0.2% to 1.4%]) developed pulmonary embolism or deep venous thrombosis during follow-up. However, 4 of these patients had not undergone the proper diagnostic testing protocol. In 7 of the patients who received a diagnosis of pulmonary embolism, the physician had performed more diagnostic tests than were called for by the algorithm. In 759 of the 849 patients in whom pulmonary embolism was not found on initial evaluation, the diagnostic protocol was followed correctly. Only 1 (0.1% [CI, 0.0% to 0.7%]) of these 759 patients developed thromboembolic events during follow-up. Of the 437 patients with a negative D-dimer result and low clinical probability, only 1 developed pulmonary embolism during follow-up; thus, the negative predictive value for the combined strategy of using the clinical model with D-dimer testing in these patients was 99.5% (CI, 99.1% to 100%). **Conclusion**: Managing patients for suspected pulmonary embolism on the basis of pretest probability and D-dimer result is safe and decreases the need for diagnostic imaging.

Comments: The expectation that this study would possibly provide statistical justification to use the D-dimer assay at the bedside as a sensitive screening tool for the presence of a pulmonary embolism was not met. The study has two significant limitations: (1) it was performed in an area of Canada in which there is extremely low prevalence of pulmonary embolism, and (2) the specific D-dimer assay used had very low sensitivity but very high specificity as opposed to the other assay available, which has significantly higher sensitivity. When combining low prevalence rates with high specificity, the result is understandably going to be an investigative tool with very high negative predictive value, as occurred in this study.

The approach of the authors was to develop a clinical pretest tool that placed patients in either low, medium, or high pretest probabilities based upon the bedside evaluation. In addition, a D-dimer assay was performed. Patients with low pretest probabilities and a negative D-dimer were considered not to have pulmonary embolism, discharged, and followed-up for downstream occurrence of pulmonary embolism. Patients with moderate to high probability or a positive D-dimer went on to further diagnostic imaging, specifically, V/Q scan. Of those patients discharged from the study to follow-up because of low probability and negative D-dimer, only one eventually developed pulmonary embolism. The resultant negative predictive value was 97.3%. The negative predictive value drops to 88.5% in the high probability group.

Therefore, as the prevalence rates of pulmonary embolism go higher in any given community, the utility of the D-dimer as a screening tool in deciding whether to proceed on with additional diagnostic testing drops dramatically.

Pulmonary Embolism: The Most Under-diagnosed and Overdiagnosed Illness

Wolfe TR, Hartsell SC. Pulmonary embolism: making sense of the diagnostic evaluation. Ann Emerg Med 2001; 37:504-514.

Despite the publication of the Prospective Investigation of Pulmonary Embolism Diagnosis in 1990, the diagnostic evaluation of pulmonary embolism continues to be approached in an inconsistent fashion. The reasons for this are unclear but likely have to do with inadequate methods for predicting pretest probability of disease and the inconvenience and perceived risk of pulmonary angiography. Because pulmonary embolism and its treatment carry substantial risk of morbidity and mortality, a consistent approach to evaluation is desirable. This article reviews large, prospective studies that suggest that it may be unnecessary to diagnose pulmonary embolism with the certainty that pulmonary angiography allows. Finally, the article proposes an algorithm that may be acceptable to patients and clinicians alike if safety is confirmed in future prospective studies.

Comments: The authors of this article provide us once again with an outstanding review of the literature and current understanding of the diagnostic pearls and pitfalls of pulmonary embolism (PE) with an extremely critical eye. It makes no attempt to sidestep the evidence that emergency physicians and internists both predict PE probability poorly, to the point of suggesting that PE is not a clinical diagnosis. Amazingly, they present data to support that view but yet go on to caution the reader that it does not mean that we should stop the aggressive search for the diagnosis when clinically indicated.

However, as opposed to the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study, the authors of this review propose a diagnostic pathway that minimizes bad outcomes rather than maximizing diagnostic sensitivity. The authors use very good data from a number of significant studies in the last 2-3 years that show PE to be far more common than we have ever realized. But, based on the overall low morbidity and mortality associated with this disease, it just does not make sense to be overly aggressive in making a diagnosis and, furthermore, the use of pulmonary angiography should be limited.

Citing a number of recent studies looking at incorporating pretest clinical probability and D-dimer assays, the authors go on to propose a thoughtful diagnostic algorithm utilizing those two diagnostic tools and CT with the goal of detecting only clinically significant pulmonary emboli, thereby maximizing outcome and virtually eliminating any invasive diagnostic study.

In the end, the authors refute the rarely used PIOPED approach and instead incorporate pretest clinical probability and D-dimer analysis to determine which patients need V/Q or CT scanning, reserving pulmonary angiography for those patients in which the diagnosis remains allusive.

The authors make a great case for an outcomes approach to PE, choosing to underdiagnose clinically insignificant PE.

LMWH for DVT: Simple, Safe Outpatient Care

Vinson DR, Berman DA. Outpatient treatment of deep venous thrombosis: a clinical care pathway managed by the emergency department. Ann Emerg Med 2001;37:251-258.

Study Objective: We evaluate the effectiveness and safety of an outptient clinical care pathway for the initial treatment of acute proximal lower-extremity deep venous thrombosis (DVT) with low molecular weight heparin (LMWH) managed by the emergency department of 2 affiliated community hospitals. **Methods**: This observational, retrospectively defined, population-based study with 392 months of preintervention analysis and 322 months of postintervention analysis was conducted in 2 suburban EDs of a large group model health maintenance organization. Our outpatient DVT clinical care pathway used careful patient selection and multidisciplinary follow-up. Ninety-six patients before the intervention and 178 patients after the intervention met eligibility criteria for the pathway. Adverse events during the first 2 weeks of treatment included symptomatic pulmonary embolism (PE), progressive DVT, minor and major bleeding, and death. **Results**: Demographic and baseline clinical characteristics of the 2 groups were similar. Five (5.2%) of 96 preintervention subjects (95% confidence interval [CI] 2.4 to 8.1) developed adverse events compared with 5 (2.8%) of 178 postintervention subjects (95% CI 1.5 to 4.1; difference between groups 2.4%; P=.50). In each group, 1 (1.0% versus 0.6%) subject developed a PE, 2 (2.1% versus 1.1%) developed progressive symptoms of progressive DVT, and 2 (2.1% versus 1.1%) developed minor bleeding. Major bleeding occurred in 1 (1.0%) preintervention subject and no postintervention subjects. No patient in either cohort died. **Conclusion**: Managed by the ED, an outpatient DVT clinical care pathway using careful patient selection and an integrated multidisciplinary approach can provide a similar degree of effectiveness and safety as customary inpatient therapy.

Comments: The authors conducted a study of one of the largest reported cohorts of patients with deep vein thrombosis (DVT) treated outside of the hospital, though the absolute numbers are small. The study was simple yet elegant. The purpose was to determine whether low molecular weight heparin therapy managed by the emergency department for the initial treatment of acute lower extremity DVT was effective and safe. Though this was a retrospective study, the potential for disparity between the study group and the control group was minimized, if not eliminated, by drawing both study groups from the same socioeconomic population with identified, comparable demographic and clinical characteristics. A second potential liability of the study centered around the fairly narrow patient population which, in this case, were insured persons of a large health maintenance organization with very little, if any, significant penetration by the indigent population in the area.

The results were clear and the statistical analysis was as simple and straightforward as the study. In both the control group and the study group 5.2% and 2.8% of the patients, respectively, experienced adverse events. Additionally, 1% of patients in the control group developed pulmonary embolism compared to .6% of patients in the study group and 2.1% versus 1.1% developed progressive DVT, respectively.

The study confirms the validity of the findings in larger prospective studies comparing the management of patients with DVT as outpatients with low molecular weight heparin versus those treated as inpatients with standard unfractionated heparin. Most importantly, the study confirmed that this program could be safely initiated and managed by a moderately sized community emergency department.

Spiral CTs — Not Ready For Prime Time?

Holbert JM, Costello P, Federle MP. Role of spiral computed tomography in the diagnosis of pulmonary embolism in the emergency department. Ann Emerg Med 1999;33:520-528.

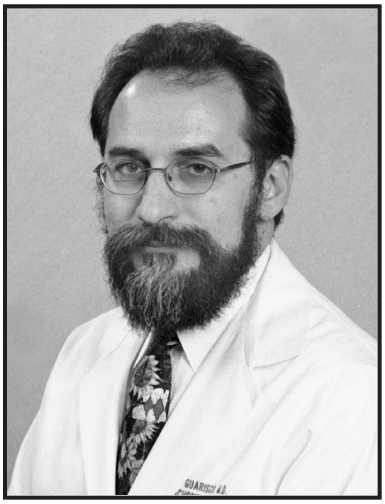
Recently a debate has developed in the medical community as radiologists in some centers suggest the selective substitution of spiral computed tomography (CT) for ventilation-perfusion (V/Q) nuclear medicine imaging as a screening test for the diagnosis of acute pulmonary embolism. Proponents of spiral CT argue that it is more accurate than the usual practice of combining the (V/Q) scan and the physician's best clinical judgment. V/Q scans classify patients into groups according to the probability of pulmonary emboli, whereas the thrombus is visible with spiral CT. Opponents point out that large-scale patient outcome studies using spiral CT have not been completed, but such information is available for (V/Q) scans. Most clinicians are familiar with the strengths and limitations of an assessment that relies primarily on the (V/Q) scan, because this examination has been available for many years. Although spiral CT does not perform as well as pulmonary arteriography in detecting subsegmental emboli, the importance of smaller peripheral emboli is controversial. This review explores the advantages and disadvantages of investigations currently available for the diagnosis of acute pulmonary embolism from the perspective of the emergency physician, presenting the view that spiral CT is likely to have an increasingly important place in patient evaluation.

Comments: The authors of this review article had a goal of providing the reader with a simple algorithmic approach to the evaluation and triage of patients presenting with clinical symptoms suggestive of pulmonary embolism. The article compares the advantages and disadvantages of the various modalities, specifically, V/Q, pulmonary arteriography, and spiral CT. The limitations of these specific studies are also discussed in relationship to their ability, or rather failure, to diagnose subsegmental emboli. The final recommendations in the suggested algorithm were somewhat surprising considering that the authors' comments in the body of the article would have led one to a different conclusion.

The authors were very critical of two issues with the PIOPED study, probably the most famous of the modern pulmonary embolism prospective studies. Specifically, they had a great deal of problems with interobserver variation of V/Q and the fact that the study provides clear guidelines for treatment in only 25% of the patients referred for V/Q scanning, leaving three-fourths of all patients with unclear guidelines for management and the need for further diagnostic work-up. In discussing spiral CT, the authors conclude that the European Multicenter Trial (ESTIPEP) will clearly define the role of spiral CT in much the same way as the PIOPED study determined the role of V/Q scan several years ago.

The authors concluded that all of the imaging modalities, V/Q, angiography, and CT, were poor at imaging the subsegmental emboli and that this limitation was not only a CT issue. This observation, when combined with the controversy as to whether subsegmental emboli are at all dangerous, led the authors to discount this issue until further studies clarify the controversy. The authors were impressed by the ability of spiral CT to provide an alternative diagnosis in those patients who do not have pulmonary embolism, a significant advantage over the other imaging modalities.

The authors make a surprising final recommendation considering that the content of the article was compelling in favor of CT as the procedure of choice in the evaluation of pulmonary embolism in the ED. It was the authors' recommendation that patients presenting to the ED with normal chest x-rays should receive V/Q scans and those patients presenting with abnormal chest x-rays CT scans. However, stopping short of a full endorsement of CT, the authors hint that, in those institutions in which spiral CT is available 24 hours a day with radiologists proficient in its interpretation, CT may be the diagnostic choice.



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