

Journal Club Block 1

How can a better understanding of probability lead to more informed use of CT angiogram (ie CT-PE)?

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Scenario:

You're working a typical ED shift in a typical hospital. Your next patient is a 34 y/o female with CC "SOB". When you go in and speak with her you find that her complaint is somewhat vague. What she really seems to be complaining of is an occasional right sided chest pain that she's felt for the last several days. She told the nurse she had some shortness of breath climbing the stairs to her apartment earlier but she seems ok now. The pain isn't reproducible and there's no recent h/o trauma or msk injury to explain it. She denies any recent URI symptoms. She's otherwise healthy. Smokes cigarettes occasionally and takes an estrogen containing oral birth control pill. She drove several hours in a car to visit friends several four days ago. She's afebrile but mildly tachycardic with a HR 103. Physical exam is unremarkable. No signs of leg swelling or calf tenderness. You get an ECG- sinus tach. You get a CXR- clear. Now what? PERC? Wells? D-dimer? US? V/Q? CTA? The attending you're working with keeps looking over in your direction- probably a not to subtle hint that the charts are stacking up and the waiting room is starting to experience the late afternoon surge. You give him/her your quick presentation and they say "just scan her- it's the only way to be sure it's not a PE..." Do you agree?

Articles for Background Review of Discussion Article #1

1. The Diagnosis and Management of Pulmonary Embolism. Barritt DW. Postgrad Med J. 1964 Jul;40(465):414-22. PubMed PMID: 21313696; PubMed Central PMCID:PMC2482780.
2. Natural History of Pulmonary Embolism. James E. Dalen and Joseph S. Alpert. Cardiovascular Diseases, Vol. XVII, No. 4 (January/February), 1975.

Articles for Background Review of Discussion Article #4

1. When a test is too good: how CT pulmonary angiograms find pulmonary emboli that do not need to be found. Wiener RS, Schwartz LM, Woloshin S. BMJ. 2013 Jul 2;347:f3368. doi: 10.1136/bmj.f3368. PubMed PMID: 23820021.

Articles for Discussion:

1. The mortality of untreated pulmonary embolism in emergency department patients. Calder KK, Herbert M, Henderson SO. Ann Emerg Med. 2005 Mar;45(3):302-10. Review. PubMed PMID: 15726055.
2. Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. Kline JA, Courtney DM, Kabrhel C, Moore CL, Smithline HA, Plewa MC, Richman PB, O'Neil BJ, Nordenholz K. J Thromb Haemost. 2008 May;6(5):772-80. doi: 10.1111/j.1538-7836.2008.02944.x. Epub 2008 Mar 3. PubMed PMID: 18318689.
3. 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. . Wells PS, Anderson DR, Rodger M, Stiell I,

Dreyer JF, Barnes D, Forgie M, Kovacs G, Ward J, Kovacs MJ. Ann Intern Med. 2001 Jul 17;135(2):98-107. PubMed PMID: 11453709.

4. Multidetector computed tomography for acute pulmonary embolism. Stein PD, Fowler SE, Goodman LR, Gottschalk A, Hales CA, Hull RD, LEEPER KV Jr, Popovich J Jr, Quinn DA, Sos TA, Sostman HD, Tapson VF, Wakefield TW, Weg JG, Woodard PK; PIOPED II Investigators. N Engl J Med. 2006 Jun 1;354(22):2317-27. PubMed PMID: 16738268.

Introduction:

Pulmonary embolism has taken on a certain mythos in emergency medicine. This so called "silent killer" stalks the waiting rooms and inpatient wards of our local hospitals cloaked in a camouflage of vague complaints and mildly abnormal vital signs; ignore these subtle clues at your own peril, for if missed, experts and plaintiffs' attorneys can and will quote a 26% to 30% mortality rate. A favorite general consensus claim is that 400,000 PEs go undiagnosed annually in the US, and that 100,000-120,000 of these patients will go on to die. That's 180 Boeing-747s fully loaded with tachycardic hypoxic patients auguring into mountain sides every year. With numbers like those the stakes are high in terms of patient outcomes and rife with medical legal ramifications. Fear not, for we do not combat this beast unarmed. To battle we bring the dagger of physical exam, the charm of experience, the shield of d-dimer and the ultimate talisman- the CT angiogram.

What match is PE against the modern marvel of computerized axial tomography? The year is 1859 Dr. Rudolph Virchow, of triad fame, wrote of "embolia"- the small fragments of clot which he found so commonly lodged in vessels both large and small among the corpses of Berlin's morgue. The same year, less than 200 miles to the southeast, Professor Wilhelm Conrad Roentgen noticed a curious green fluorescence emanating from a cathode-ray tube in his laboratory. When a hand, the left hand of his wife Bertha's to be exact, was bathed in this light a ghoulish image was scattered onto a piece of film. Bertha described the striking "rotenogram" as if she were "seeing her own death"; today we would recognize this as the first x-ray image. 1859- the stage set, the two contenders stand opposite- venous thromboembolism vs the field of radiology. Fast forward through the next 100 years- past questionable epidemiologic conjectures of embolic prevalence, past arcane gelatinous-heparin based treatments, past frustratingly indeterminate V/Q scans, past aortogram gold-standards to the close of the 20th century. The year is now 1998, CT-angiogram is introduced into widespread use in hospitals across the United States. This digital geometry processing, three-dimensional imaging, multi-axial detecting rotenogram-on-steroids quickly became the imaging work-up of choice for acute PE. The donut-of-truth, the new gold-standard. The silent killer, no longer silent in the harsh beam of x-ray radiation would be forever banished from the differential of the non-specific chest pain work-up.

CT angio was so good, in fact, that whole new subsets of PE victims were uncovered- the low risk toe pain subset, the elbow pain subset, the weak and dizzy subset and of course the "I just don't feel good subset". You see the donut-of-truth does not lie and if a mind-numbingly vague complaint could be fed into the CT scanner chances were you just might hit the radiology-read

jackpot and find that wily PE lurking in the far reaches of a subsegmental pulmonary backwater. Nurse kindly hang the heparin and call for report. Next patient please. Another life saved.

However, as time went on and the novelty of the CT angio began to fade some inconvenient numbers began to sprout up. More and more PE's were being diagnosed but people still seemed to be dying of the disease at a strikingly constant rate. How could this be? If more PEs were being found, then more patients should have received treatment and that obviously should have resulted in a decreased mortality rate- it's just plain common sense. Right? Well in 2013 a paper, out of the Boston University School of Medicine, titled "When a test is too good: how CT pulmonary angiograms find pulmonary emboli that do not need to be found" was published in BMJ- the title speaks for itself, the honeymoon for CTA had officially come to an end.

Maybe the so called silent killer wasn't a killer at all. Maybe the small "silent" clots that bedeviled Virchow's autopsies and pepper the radiology reads of CTAs were silent because they were physiologic- a logical result of the constant ebb and flow of the clot vs bleed balance within our vasculature. Maybe these clots were an entirely different beast than the massive PEs that strained the right ventricle and send already visibly sick patients into crash-and-burn ACLS death spirals. Maybe a day would come when all the pats-on-the-back for the "good catch" PE would come home to roost. In the 17 years since CTA's induction many people have gone in one end of the donut of truth to come out the other with a diagnosis of PE and a 3-6 month membership to their local Coumadin clinic. How many kidneys were shwaked, cells irradiated and units of blood thinned all in the pursuit of a phantom diagnosis?

So how did we get to this point? Fear of the missed PE is tangible in the ED. The mortality of untreated PE, if the numbers mentioned above are valid, is a sobering statistic that is hard to ignore. But have you ever wondered where these eye-popping stats come from? Are these numbers empirically derived or have they just become dogma? The folks from LAC-USC (the emrap/hippo crew) posed this same question in a fascinating paper and came up with some surprising answers. While you read through this first paper think about the concept of a literature "deep dive". In the future when you're reading piece of current literature take a close look at some of the references. If something is presented as fact, but your Spidey senses tell you otherwise, you may want to follow the references down the rabbit hole to the original source literature; you may be surprised how shaky some of these foundation/historical studies are.

Included in this bundle is the paper from Mel Herbert and friends as well as two of the most often cited source papers on the mortality and prevalence of PE. While reading these papers consider the following questions. Do you think that the data presented in the Barritt & Jordan and Dalen & Alpert papers can be extrapolated to a modern day Emergency Department cohort? Why or why not? Do you think the study design and mathematical models used in these papers would hold up to modern day peer review? Why or why not? What are some of the specific flaws?

How do you think these numbers impact our current ED attitude towards diagnosis of PE? A key concept in diagnostic medicine is how dependent post-test probability is on the underlying disease prevalence in the tested population.

The second bundle of papers focuses on the interplay between pre-test probability, disease incidence and diagnosis. As you read these papers, you'll recognize some familiar friends- notably the Wells score and PERC. Consider why these scoring systems were created. Understand the difference between implicit and explicit risk factors. Take a minute to learn what an Odds ratio is and what the numbers actually mean. Why is it that some of the risk factors we strongly associate with PE had such low Odds ratios? Is it that we've just been wrong, or does it have more to do with how we test for PE?

The final paper is one of the big dogs of recent Evidence Based Medicine- PLOED II. When published in 2006 it was the largest study to date to look at the diagnostic properties of CTA in the diagnosis of PE. This paper does have some infamous flaws- see if you can pick them up. I'll give you a hint- what was the gold-standard CTA was compared against? During our discussion we'll pick some numbers out of this paper to illustrate some key points using some basic EBM tenants like sensitivity and specificity as well as more advanced concepts like Bayesian analytics.

This journal club is not intended to be a clinical review of pulmonary embolism, nor is it intended to be a user's guide to PE diagnostics. While the topic is PE, this particular disease is more of a convenient catalyst to a discussion that is meant to focus more on the abstract notion of conditional probability and attempt to distill it into a palpable clinical tool. In the past we've spent far too much time reciting book reports, bogged down in the mundane details of relatively insignificant clinical topics. The point of this exercise, while called journal club, should not even be the journal articles themselves but instead on the process of critical appraisal that will foster innate critical thinking. In today's environment where undue corporate influence, basic statistical misunderstanding and unscrupulous manipulation of data undermine the very foundation of what we call EBM it is more important than ever to be able to critically appraise this overwhelming cascade of new data.

Discussion and topic revisited:

The statistical theory behind medical decision making can at times seem abstract. However with a better understanding the clinical utility of these calculations the clinical utility becomes obvious. I think the topic was well received and the walk through of some basic statistical exercises went well. Unfortunately the reality of our litigious society will likely continue to push providers to continue to order expensive and unnecessary testing. However as the medical risks of these tests become more obvious as well as the additional costs of testing become more scrutinized a cultural shift may occur. Regardless of the motivations- be it legal, financial or patient care centered- it is of paramount importance to understand that every test or imaging study that is ordered has associated risks and potential false results that need to be weighed against the actual clinical risk of disease.