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Editor's Spotlight/Take 5

Editor's Spotlight/Take 5: CT Pulmonary Angiography After Total Joint Arthroplasty: Overdiagnosis and Iatrogenic Harm?

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CT pulmonary angiography (CTPA) has become the accepted standard for the evaluation of a patient with suspected pulmonary embolism (PE) [3, 7]. The test is fast, relatively inexpensive, and believed to be even more sensitive (and better overall) than conventional pulmonary angiography with plain radiography — once considered the gold standard for evaluating suspected PE.

But in terms of sensitivity, it may be possible to have too much of a good thing. There is some evidence [4] to suggest that in an "all-comers" population of inpatients, the use of CTPA has resulted in overdiagnosis of PE, resulting in complications one would expect from the increased use of anticoagulation. D'Apuzzo and colleagues performed a similar study in total joint arthroplasty patients, and they present their results in *CORR*® this month.

Their results generalize well to the population of orthopaedic inpatients at large. How should physicians work up a patient presenting with nonspecific symptoms that suggest PE (moderate tachycardia or tachypnea, for example), when those same symptoms could just as easily be caused by numerous other postoperative diagnoses? This is not just a problem in arthroplasty or tumor surgery — the answer to this question, when we get it, will benefit all orthopaedic patients. Pulmonary emboli occur after ankle fractures and ACL reconstructions, too.

PE can cause sudden death, and deaths from PE are almost always are unexpected. For those reasons, PE is a dreadful and important diagnosis. CTPA identifies clots, but not all the clots it finds cause problems, and the treatment for those clots can cause harm. We still do not know when to order this test, or which CTPA findings deserve our worry (and our interventions). Preliminary work has been performed in orthopaedic populations [7] to try to obtain these answers, but we know much less than we need to know to do a good job for our patients when it comes to PE.

In the "Take 5" interview that follows, Dr. James Browne (Fig. 1), lead author on this important study, joins us to explore this critical topic in greater depth.

Take 5 Interview with Dr. James A. Browne

Senior author of CT Pulmonary Angiography After Total Joint Arthroplasty: Overdiagnosis and Iatrogenic Harm?

Note from the Editor-in-Chief:
In "Editor's Spotlight," *one of our editors provides brief commentary on a paper we believe is especially important and worthy of general interest. Following the explanation of our choice, we present* "Take Five," *in which the editor goes behind the discovery with a one-on-one interview with an author of the article featured in* "Editor's Spotlight."
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Fig. 1 James A. Browne MD said physicians should balance testing for PE with its treatment risks to ensure that patients are not subjected to unnecessary iatrogenic harm.

Seth S. Leopold MD: *Before we get into the specific questions you looked at in your study, let us talk about the database you used to get your answers. Not all our readers may know about the Nationwide Inpatient Sample. Please tell us a bit about it. What kinds of questions do you think it might help us best answer, and what are its major limitations for orthopaedic research?*

James A. Browne MD: The Nationwide Inpatient Sample is the largest publicly available all-payer hospital inpatient care database in the United States. The size of the Nationwide Inpatient Sample dataset makes it a valuable tool to identify, track, and analyze trends in health care utilization, access, charges, quality, and outcomes. The dataset includes more than 100 clinical and nonclinical data elements for each patient's hospital stay; however, many data elements that may be of interest to the orthopaedic researcher are not coded, such as surgical approach, estimated blood loss, anatomic deformity, severity or grade of orthopaedic condition, and type of implant.

Dr. Leopold: *It seems like almost overnight, CTPA became the standard test for PE; I have heard radiologists say that it is the "gold standard" test — more accurate than traditional pulmonary angiography — although I cannot imagine what kind of study could substantiate that assertion. In any case, it is in wide use. What could be wrong with a test that is sensitive, specific, and safe as CTPA appears to be? What caused you to do this study?*

Dr. Browne: CTPA is often considered to be the reference standard in diagnosing PE. However, the data on the sensitivity and specificity of this test are limited due to the lack of a gold standard. One recent study [3] used expert radiologists' interpretations as a gold standard to determine the accuracy of local radiologists in diagnosing PE using CTPA. These investigators found a 10% false-positive rate with CTPA, which is alarming considering potential harms of anticoagulant treatment to which these patients would have been needlessly exposed.

Furthermore, the value of a test or intervention does not just depend on the statistical measures of performance. A good test must also lead to demonstrated improvements in outcome when the disease being detected is treated. Recent studies have suggested that there may be a subset of PEs that does not require intervention, as they will not adversely affect the patient's health [4]. Additionally, the mortality benefit in treating PE with anticoagulation is unclear and has not truly been quantified. What is clear, however, is that anticoagulation for PE carries substantial risks to patients having just undergone total joint arthroplasty. We need to balance the testing and treatment risks to make sure that we are not subjecting patients to unnecessary iatrogenic harm.

Finally, while generally considered safe, CTPA does carry risk in the form of renal failure from contrast, allergic reactions, cancer from exposure to radiation, and false-positives as noted above. We identified these concerns in our clinical practice, and decided we needed to analyze the data further to begin to understand the role of CTPA in the total joint population.

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Dr. Leopold: *It seems like part of the problem is the test may detect small or "physiological" pulmonary emboli, which should not cause symptoms or harm. Another part of the problem may be with how clinicians use it (ordering the test when we do not really have a moderate diagnostic suspicion of PE). How do you see CTPA fitting into the evaluation of the orthopaedic patient after surgery? What kinds of studies will help us refine our approaches to ordering CTPAs, and what kinds of studies will help us understand what kinds of pulmonary emboli we have to worry about?*

Dr. Browne: There are many examples in other areas of medicine where testing and treatment of certain patients can be very beneficial, but when applied indiscriminately, can be useless or even harmful. Algorithms have been developed to try to identify high-risk patients and reduce the harm of overtreatment. A group from the Rothman Institute in Philadelphia published an algorithm designed to identify patients clinically at high-risk for PE and increase the threshold at which a CTPA was ordered [7]. They reduced the number of patients worked up for hypoxia with CTPA, and increased the number of positive findings per PE workup, without increasing mortality rates. These types of evidence-based algorithms, coupled with studies examining the clinical relevance of subsegmental PEs, should help us figure out when to order the test and what to do with the results.

Dr. Leopold: *You found that the frequency of the diagnosis of PE went up, but the mortality associated with PE went down rather appreciably. This can be read in (at least) two ways: Early diagnosis and treatment of a life-threatening diagnosis saves lives (a good thing), or we are catching and treating clinically insignificant PE (a bad thing, as the treatment involves anticoagulants, which themselves cause complications). How do you see it, and how might we get the answer to this question more definitively?*

Dr. Browne: The first possibility you describe is that of an effective test, where CTPA improves our ability to detect PEs and patients benefit from treatment. The second scenario is that of overdiagnosis, where the additional PEs detected by CTPA are mild or clinically insignificant, and patients do not benefit from treatment.

My sense is that we are increasing the number of patients diagnosed with PE and that the case-fatality is decreasing as we pick up PEs that would not result in death, regardless of treatment. One randomized study [1] comparing CTPA with ventilation-perfusion (V/Q) scanning for suspected PE showed that a significantly higher number of PEs were diagnosed with CTPA, but the 3-month thromboembolic risk was the same for patients in both groups that were not diagnosed with a PE. This suggests that the small PEs that may have been missed by the V/Q scan were not clinically relevant and did not cause problems despite a lack of treatment. Another recent systematic review [2] came to a similar conclusion and suggested that the incremental increase in the diagnosis subsegmental PEs detected by more sensitive multi-detector CTPA scanners did not lower the 3-month risk of thromboembolism in patients with a negative scan who were left untreated. These studies question whether subsegmental PEs are clinically important and justify the risks of anticoagulation in postoperative arthroplasty patients. Similar prospective studies are needed in the total joint population to help get more definitive answers.

Dr. Leopold: *Your study suggested that patients diagnosed with PE will spend more time in the hospital, and have more complications. This is perhaps related to the anticoagulation we use for patients with PE, including hematomas, other bleeding complications, and postoperative infections. I believe most clinicians would accept those complications if they believed they were saving lives. What kinds of studies would help us figure out whether that is so?*

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Dr. Browne: PE is a serious and potentially life-threatening complication after total joint arthroplasty. Conventional wisdom is that all PEs require immediate and aggressive pharmacologic anticoagulation to reduce mortality. However, the studies that have supported the benefit of anticoagulation for PE are dated, used small sample sizes, and often diagnosed patients with PE on clinical grounds. These studies, therefore, did not include small subsegmental PEs detected using a highly sensitive CT scan. We do not know the true risks of an untreated PE, nor do we know the mortality benefit of treating certain types of PE with anticoagulation.

While prospective randomized trials would be of great value, these studies may not be feasible due to cost, power, and ethical considerations. We will likely rely on high quality prospective studies to help risk-stratify different types of PEs to guide treatment. At the same time, quantifying the risks of anticoagulation following total joint arthroplasty, as we have tried to do in this study, can help clinicians with one side of the risk/benefit equation.

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