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Triple Rule-Out CT Angiography: 3 For the Price of 1?

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Chest Pain in the Emergency Department (ED)

Chest pain is a very common presenting complaint to EDs across the United States, accounting for up to 20% of all visits. Recent studies have reported suspected coronary artery disease and chest pain as the most common reasons for direct hospital admission from the ED. Many factors account for such high admission rates, including the lack of a quick, accurate exam to diagnose a myocardial infarction (heart attack), as well as the potential morbidity and fatality danger of missing this diagnosis. As a result, patients are often admitted for an array of diagnostic testing to rule out acute coronary syndrome (ACS), including serial ECG, cardiac enzymes, nuclear stress testing, and cardiac catheterisation. The cost of negative inpatient cardiac evaluations is high, estimated at \$6 billion annually in the U.S. Despite this extensive workup, 2-5% of patients who actually have ACS are still unfortunately misdiagnosed and discharged home; typically these are younger patients with atypical symptoms. Missed ACS is a major source of medicolegal burden for ED physicians, comprising about 20-39% of all malpractice liability.

Triple Rule-Out CT Angiography (TRO-CTA)

To complicate the problem further, the differential diagnosis for a patient presenting with acute chest pain is not simply limited to heart disease, but includes other serious, life-threatening diagnoses such as pulmonary embolism (PE) and aortic dissection (AD). Triple rule-out CT Angiography (TRO-CTA) was developed as a potential method to aid the ED physician and radiologist in tackling the complex diagnostic uncertainty of chest pain. TRO-CTA is a specialised computed tomography (CT) imaging exam tailored to evaluate for pathology within the coronary arteries, pulmonary arteries, and the aorta in a *single* CT study, hence the name 'triple-rule out'.

All sounds dandy, but what exactly is the role of TRO-CTA in the workup of chest pain in the ED? A study by Takakuwa et al. (2008) demonstrated that TRO-CTA has a high negative predictive value of >99% for ACS at 30 days in patients with mild or absent coronary artery disease, and provides additional diagnosis of non-coronary causes of chest pain in up to 11% of patients. Additionally, TRO-CTA precluded the need for additional diagnostic testing in over 75% of patients with low to intermediate risk of ACS. These advantages translate into decreases in patient anxiety, time spent in the ED, and overall radiation exposure accumulated during a hospital stay. Most importantly, it may save both the patient and hospital from a costly inpatient admission and workup.

Like any imaging study, proper patient selection is the key to correct utilisation and cost-effective application. Selection criteria for TRO-CTA include patients with low to moderate risk for ACS based on the Thrombolysis in Myocardial Infarction (TIMI) score, non-coronary pathologies among the diagnostic considerations, negative cardiac biomarkers (i.e. troponins), and normal or nonspecific ECG changes. In other words, patients who qualify for TRO-CTA do not have risk factors or laboratory/ECG evidence to suggest a clear cardiac source as a cause of their symptoms. The rationale is that if these patients are unlikely to have ACS, why admit and subject them to further testing and hospitalisation? On the contrary, patients who are at high risk for ACS or have elevated cardiac biomarkers or abnormal ECG changes should be appropriately triaged from the ED and admitted for further workup and possible cardiac catheterisation and intervention.

No Walk in the Park

While TRO-CTA is conceptually and intuitively appealing, there are notable pitfalls and problems with its use and implementation. First, substantial resources and training are necessary to carry out TRO-CTA on a routine basis. Since a 'triple rule-out' is designed for diagnosing the aforementioned three most serious aetiologies of chest pain, adequate and simultaneous contrast opacification of the coronary, pulmonary, and systemic vasculature is critical to accurate image interpretation. Obtaining optimal contrast opacification is challenging and requires specific injection protocols to be carried out by highly-trained CT technologists and nurses. Additionally, CT scanners need to be equipped with ECG gating and have at least 64 detector rows in order to scan the chest in a single 15 second breath hold. Without appropriate contrast injection

timing and CT technology, the study will be suboptimal for the evaluation of one, if not all three, of those diseases, limiting its usefulness and diagnostic accuracy.

Second, significant patient preparation is necessary to adequately image the coronary arteries. As with dedicated CT coronary angiography studies, an ideal heart rhythm is a sinus bradycardia at 50-60 beats per minute. To achieve sinus bradycardia, beta-blockers are often administered prior to the exam. It is important to make sure the patient has no contraindications to beta-blockers, such as high degree heart block or asthma. Additionally, sublingual nitrates can be given to dilate the coronary arteries for optimal imaging. The effects of these medications in a patient suffering an acute PE is unknown, but it certainly raises concern that these patients may become haemodynamically unstable with alterations in cardiac output and vascular tone.

Third, the extensive area of the body covered by a single TRO-CTA study has led to a substantial amount of incidental and arguable clinically irrelevant findings. A study by Lehman et al. (2009) demonstrated that incidental findings were detected in about 45% of patients, with pulmonary nodules and liver cysts comprising the majority of these findings. Yet only 1.3% of these findings actually affected inpatient clinical management and 20% led to further followup imaging tests. The more we look, the more we see – and what to do with these incidental findings will have important ramifications.

Radiation Dose

As a brief note, since the initial development of TRO-CTA, there have been numerous concerns over radiation exposure. As a result, newer techniques have evolved over time to decrease the radiation exposure to more acceptable levels. Technological advances such as prospective triggered high pitch ECG gating, tube current modulation in retrospective ECG gating, and 100 kV scanning are amongst the techniques available on most new CT scanners, and can significantly minimise radiation exposure to be in line with other imaging tests.

Controversy and Conclusion

Despite the potential benefits of an 'all-in-one' study to evaluate chest pain in the ED, widespread application of TRO-CTA in EDs across the U.S. remains controversial. In addition to the technical issues with implementation discussed above, there is, most importantly, a lack of rigorous scientific trials to justify the routine use of TRO-CTA. Opponents of TRO-CTA argue that a dedicated CT coronary angiogram should be performed when clinical suspicion is truly limited to ACS as opposed to subjecting patients to a 'triple study'. Dedicated CT coronary angiography provides superior detail and higher quality images of the coronary vasculature as compared to TRO-CTA. Just as important is the fact that dedicated studies are technically easier to perform and are rarely susceptible to artefacts. Oftentimes TRO-CTA is diagnostic in some vessels at the expense of other vessels, if the contrast bolus and motion factors are not absolutely timed right. In the only randomised controlled trial comparing TRO-CTA to a dedicated coronary CT angiogram for evaluation of PE, AD, or ACS, TRO-CTA was not shown to improve efficiency in managing patients in the ED and in hospital with respect to length of stay, rate of hospital discharge without additional imaging, cost of care, and number of repeat visits. Also, other studies have shown that the incidence of PE and AD is extremely low in patients with chest pain, comprising just <0.5% of diagnoses in these patients. So one must wonder – is TRO-CTA cost-effective or even necessary? At this point, the jury is still out, even amongst the experts. In 2010 a review of the appropriate use of cardiac CT, jointly issued by several medical societies, including the American College of Cardiology (ACC), American Heart Association (AHA) and the American College of Radiology (ACR), concluded that while dedicated coronary CTA had sufficient evidence for use in the ED, TRO-CTA did not, and was classified as an uncertain diagnostic method.

Overall, TRO-CTA has developed into a wonderful innovation, which has added to the ED physician's armamentarium of exams to work up chest pain. It has proven to be a safe and effective exam. However, given its high technical demand, as well as controversies regarding its utility relative to dedicated coronary CT angiography, further refinements will be necessary before this high-end exam can be adopted by the mass medical community. Further research will be necessary to ultimately determine the most effective application of TRO-CTA.

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