Noninvasive Diagnosis of Coronary Artery Disease:
A Literature Review and Case Study

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Abstract

Coronary artery disease is a narrowing of the small blood vessels that supply the heart. It is caused by plaque buildup in the vessel walls and can result in serious complications such as angina, damaged heart muscle, and death. Because of its prevalence, timely and accurate diagnosis of coronary artery disease is crucial. Different noninvasive imaging modalities are compared with factors such as cost effectiveness, timeliness, accessibility and accuracy for patients. Invasive treatment options as well as prevention planning are considerations.
Introduction

For years, Coronary Artery Disease (CAD) has been a global health concern and is the leading cause of death in Americans. The National Heart Lung and Blood Institute (NHLBI) reports that one in four deaths annually are directly caused by coronary artery disease (Rosamond W, et al. 2008 as cited in Levine, 2011). CAD starts with fatty material and other substances forming plaque build-up on the walls of coronary arteries. Without proper blood flow to bring oxygen, cardiac muscle dies suffers and the heart will eventually stop contracting. Thus early screening for heart disease is crucial.

Literature Review

Symptoms

CAD can cause an array of heart problems mostly including angina or chest pain, myocardial infarction (MI), arrhythmias, and heart failure. An MI, commonly known as a heart attack, can cause ischemia to cardiac muscle (Whitaker et al., 2012). This is usually due to a rupture of atherosclerotic plaque or an unstable collection of lipids (cholesterol and fatty acids) and white blood cells in the walls of an artery. Whitaker then explains that typical symptoms of MI include sudden chest pain, shortness of breath, pain and numbness radiating to left side of body, nausea, vomiting, palpitations, sweating, and anxiety. Alspach (2012) notes that women may experience fewer typical symptoms than men, and many MI’s are silent, or without chest pain. According to patient data from the National Registry of Myocardial Infarction, of the total 1.14 million patients in the study with acute MI, “about 35% of patients with acute MI may not have chest pain upon their arrival [to the emergency department (ED)]” (Alspach, 2012, p. 10).

Noninvasive Imaging Diagnosis of Coronary Artery Disease
Coronary artery disease is rapidly placing an enormous strain on health care economics. For patients with obvious symptoms of CAD, an early invasive strategy with cardiac catheterization is generally recommended. Many researchers agree that it is not helpful to perform noninvasive imaging prior to catheterization on high risk emergency patients because these tests could delay treatment. As an alternative to invasive and expensive percutaneous coronary intervention (PCI), non-invasive imaging techniques are used to detect asymptomatic CAD patients at an early stage and guide optimal patient management thereafter. Current research focuses on two types of studies: anatomical and functional imaging. For anatomical imaging, Multi-slice computed tomography (MSCT), electron beam computed tomography (EBCT) and magnetic resonance imaging (MRI) are used: whereas, for functional imaging, nuclear cardiology and/or stress echocardiography are used (Weustink et al., 2010).

**Computed Tomography**

CT Chest Angiography (CTA) has a large role in imaging anatomical strictures using iodinated contrast. Both MSCT and EBCT use a rotating source of radiation to capture images with different slice thicknesses. The difference between the two is EBCT uses electronic manipulation of the x-ray and has a shorter exposure time and the more commonly used MSCT uses traditional mechanical manipulation (Shah and Coulter, 2012). CTA uses a calcium scoring system to determine heart attack risk of a patient. Coronary artery calcium (CAC) is defined as “a hyper attenuating lesion [above] 130 Hounsfield units with an area of greater than or equal to 3 pixels” and the risk associated is analyzed using “percentiles of calcification in a reference population that is stratified by [patient] age and sex” (Shah and Coulter, 2012, p. 240-241). A CAC score greater than one hundred is in the top 75th percentile for high risk of that set population. Many CT configurations also allow Positron Emission Tomography (PET) images to
be laid on top of cardiac landmarks in a CT to compare it to the physiology of PET scans. Another feature is that CTA has more reconstruction data to acquire useful three dimensional (3D) and four dimensional (4D) images. Radiologists, cardiologists, and surgeons can graphically manipulate and pinpoint coronary strictures on 3D and 4D images for accurate diagnosis and treatment.

In the last decade, Computed Tomography (CT) has improved the 64 slice multi-scanner to diagnose anatomical CAD with less invasive risk to the patient and a lower-cost alternative to cardiac catheterization. With traditional cardiac catheterization or PCI, iodine is injected into the main right and left coronary arteries. Coronary anatomy is outlined and areas of narrowing are identified. These are useful in diagnostic evaluation of selected patients with existing CAD. Delgado and Williams (2010) argue that asymptomatic patients subjected to PCI are put at risk for hemorrhage at the site of injection, occlusion of a vessels, and coronary dissection during the procedure. With cardiac CT imaging, patients can avoid a longer more expensive procedure with pre-screenings at $1400 compared to $3800 for a traditional cardiac catheterization (Delgado and Williams, 2010). On the other hand, Shah and Coulter (2012) disagree saying most insurance companies won’t cover CAD screening which can result in “an increased number of unnecessary tests and downstream procedures for individuals” (p. 242).

To analyze the accuracy of CT, Delgado and Williams (2010) used different slice thickness from 4 to 64 slices. The data showed increased sensitivity with an increase in slice thickness as well as a “high negative predictive value of 95% or better” (p.500). This shows that CT can somewhat accurately rule out the disease, although positive predictive value of all CT scanners remains lower at <90%. Garguilo et al. (2011) found CT’s role has recently reduced the need for conventional coronary angiography in patients with a low to intermediate probability of
CAD. However, in patients with high blood pressure, coronary calcifications “may cause blooming artifacts in CT angiography, leading to overestimation of lesion severity, which results in lower specificity and positive predictive value” (p. 2040). CT isn’t without risks which includes a small but measurable increase in the risk of cancer from radiation, possible renal failure, and anaphylaxis with the use of iodinated contrast. Kuller and Edmundowicz (2011) conclude that a single coronary CT angiography with a 10 millisievert dose increases the risk of cancer by 0.05%, when compared with a lifetime risk. Widespread use of coronary CT will require continued careful monitoring of radiation exposure and efforts to minimize dose.

Magnetic Resonance Imaging

Cardiac Magnetic Resonance (CMR) uses a powerful magnet and naturally occurring magnetic fields in the body to construct images of the scanned heart. A CMR study can include stress perfusion imaging for functional assessment of heart circulation and the presence of an MI. CMR is also a satisfactory modality for identifying “infarct location, infarct complications, the extent of edema or area at risk, [and] the amount of myocardial salvage….all in a single scan” (Budge and Salerno, 2011, p. 7). Kuller and Edmundowicz (2011) found CMR’s high spatial resolution and ability to show soft tissue structures with coronary arteries helps distinguish vulnerable plaques after an MI and especially right after percutaneous intervention.

CMR compares favorably to other noninvasive cardiac imaging modalities for diagnosing ischemia and stenosis related to CAD. In a study conducted by Nagel (1999), 208 patients with suspected CAD had both a dobutamine echo ultrasound and dobutamine stress CMR prior to cardiac catheterization. With CMR, sensitivity for detecting a 50% coronary stenosis was increased from “74.3% to 86.2% and from 69.8% to 85.7%, respectively, compared with echocardiography” (Nagel, 1999, as cited in Budge and Salerno, 2011, p.2). Attempting to cut
costs, an applied diagnostic protocol which included stress CMR was found to reduce inpatient admissions and produced a cost savings of over 20% in that facility (Budge and Salerno, 2011). CMR may be a future non-invasive standard to measure extent of CAD without exposing the patient to radiation and rule out unstable CAD in the ED.

**Echocardiography**

Echocardiography is a specialized subset of ultrasound that uses sound waves to create standard two-dimensional, 3D, and Doppler cardiac images. The most common echocardiography methods to evaluate CAD are transthoracic doppler echocardiogram (TTDE), stress echocardiograph, transesophageal echocardiograph (TEE), and intravascular ultrasound (IVUS). Like most doppler ultrasound, TTDE is used to measure the direction and speed of blood flow through the heart chambers, heart valves, and blood vessels to evaluate coronary artery physiology (Zang et al., 2010). Function can be measured by calculating the coronary flow velocity reserve (CFVR) in patients with CAD and comparing it with coronary artery stenosis. Stress echocardiograms are achieved by either stressing the patient’s heart by exercise or injecting a medicine, such as dobutamine, to make the heart beat faster (Chandrararatna et al. 2012). Running on a treadmill or having the patient squat in place before and after an echocardiogram can show a stenosis from changes in post and pre-stress images. Stress echo provides additional information regarding valve structures, chamber sizes, ejection fractions and regurgitated lesions (Levine, 2011). Yet Chandrararatna et al. (2012) found disadvantages of the procedure, including stress-induced MI, long scan times, and technologist variability in producing the same images.

For a more invasive approach, TEE involves sedation of the patient as a probe is moved down the esophagus to show clearer images of the heart. Because the probe is not obscured by
the lungs and bones of the thorax, these images are especially valuable for sensitive detection of CAD. Intravascular ultrasound (IVUS) is another successful invasive approach used to measure changes in atherosclerosis within the coronary arteries. In this procedure a specially designed catheter with a miniaturized ultrasound probe is used to see inside blood vessels to determine the extent of CAD within the vessel walls. This is especially used during PCI to pinpoint vessel blockage while the patient already has a catheter (Kuller and Edmundowicz, 2011).

Echocardiography has been proposed as an alternative to coronary calcium scoring in CT because of lower cost and no radiation exposure. This is crucial as evaluation for CAD is increasingly seen in middle-aged to younger individuals. However, echo is affected by respiratory pattern and overlying soft tissue. Additionally, Levine (2011) recognizes that interpretation of stress echoes can be quite challenging and “requires an advanced degree of expertise that is not universally available” (p.67) Kuller and Edmundowicz (2011) acknowledge the basic problem with the use of echocardiography is variability in vascular remodeling and being highly technician dependent for quality and reproducibility. Gibbons revealed in a Predictors of Response to Cardiac Resynchronization Therapy study that no single echocardiographic measure “predicted response to cardiac resynchronization therapy (CRT), in part due to high levels of variability in echocardiographic findings” (Jacobson, 2011 p. 25) Limiting the variability in measurements is a necessary step toward improving the predictive power of echocardiography.

**Nuclear Medicine Myocardial Perfusion Stress Testing**

The most common test in nuclear medicine (NM) for imaging heart function is a myocardial perfusion stress test. This test has been considered the gold standard for imaging studies prior to catheterization, before CT or MRI had developed cardiac imaging for CAD
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(Raman et al., 2010). During the procedure, the patient’s heart is stressed by exercise on a treadmill or medications such as adenosine, or dobutamine for vasodilation. The patient is injected with a radioisotope, thallium-201, and a gamma camera captures images of radiation circulating the body. The images focus on the heart during stress and the patient typically returns 2 hours later for rest shots. This camera, called a single-photon emission computed tomography (SPECT) compares stress and rest images with color shading, ejection fractions and polar-mapping of coronary arteries.

Lubbers (2009) argues that NM stress tests involve high radiation exposure and yields images with relatively low spatial resolution. Raman et al. (2010) adds that NM stress test are more time-consuming for patients compared to MRI stress tests. Large patients often have less accurate images by photon scatter; breast and stomach artifacts occasionally cover the upper and lower borders of the heart. In contrast, Levine (2011) concludes the stress technique is useful as a “deep-rooted” imaging tool in cardiology where many cardiologists are comfortable reading results. The test is also “extremely safe and able to detect ischemia with a great degree of sensitivity and specificity” (p. 67). Stress testing is also most valuable in patients with intermediate to high risk, where an abnormal result is most likely to reflect a true positive result.

Contraindications for exercise stress include patients with ECG abnormalities, heart murmurs, and those that cannot be without their hypertension medication for 24 hours. A study conducted by Gargiulo et al. (2011) indicated that stress NM is a very highly sensitive technique for detecting CAD in hypertensive patients, with only a modest loss of specificity compared to the general population. In contrast, stress echocardiography shows higher specificity but substantially reduced sensitivity compared to NM. Knowledge of sensitivity versus accuracy in comparison to other modalities may help to select the most appropriate test for diagnosing CAD.


**Treatment Options**

Patients with initial onset of angina are offered ACE, beta blockers, and statins as a primary treatment for angina caused by coronary artery disease (CAD). Early prevention of CAD is becoming very important with a heart healthy diet, exercise, and cholesterol management. Gibbons encouraged cardiologists to be strict about applying only evidence-based approaches to cardiac imaging (Jacobson, 2011). Additionally, Levine (2011) expands on this stating:

Strategies for risk reduction are well known and they include smoking cessation, blood pressure control, control of blood sugar and cholesterol lowering. "Routine" stress testing does not appear in the list of known effective strategies to reduce risk (nor does CT scanning, MRI and even percutaneous intervention). Prevention and counseling may be the clinician's single most important tool in long-term follow up (p. 68).

When prevention is not enough, Singh (2012) discusses two invasive options for long-term treatment, both with associated risks and statistical benefits depending on the patient’s condition.

Physicians who treat with either percutaneous coronary intervention (PCI) or a coronary artery bypass graft (CABG) should consider patients age, health conditions, and recovery factors. In a CABG procedure, a vein from another part of the body is grafted onto the occluded atherosclerotic artery to maintain blood flow to the heart. Because of the more invasive nature of bypass surgery, it is preferred that people of very young or old age undergo PCI. In PCI a catheter is inserted peripherally in the groin and guided to the heart where a balloon inflates allowing blood flow. Placement of a stent in the repaired vessel is more easily repeated and involves less scarring and recovery time compared to a CABG. According to Singh (2010) however, patients who undergo PCI “were more likely than those undergoing CABG to require repeat revascularization (13.5% vs. 5.9%) but were less likely to have a stroke (0.6% vs. 2.2%)”
(p. 56). Other patients with multiple vessel disease and left main coronary artery occlusions and diabetes should seek surgical revascularization. Each invasive procedure has its advantages and disadvantages. While a CABG decreases the long term occurrence of angina, cardiac catheterization should be considered first as a less invasive procedure.

**Case Study**

A 53 year old Caucasian male who presented with recurring mild numbness in the extremities in 2004. The lifestyle of the patient did not include smoking or other known health conditions, although poor diet and hyperlipidemia was a known factor. The initial tests for heart abnormalities included a chest x-ray, EKG, and labs. All were within normal limits. The patient started to have mild chest discomfort and an echocardiogram was performed. The test concluded a false-positive result showing indications of reduced function where the left main coronary artery supplies blood flow to the heart. The cardiologist reading the results prompted further testing with angiography, although the echo result was a false-positive.

The patient consented and prepped for PCI. During the procedure, iodine was injected into main coronary arteries and no blockages were found. (See Figure 1) The cardiologist concluded a normal amount of plaque was present in his coronary arteries and no stents were needed to open occlusions. The patient was sent home many hours later and put on light duty for the next week at work. One of the cardiology staff suggested the patient be tested for diabetes. The patient went to his regular primary care provider and labs concluded the patient had type II diabetes. His primary doctor concluded that the neuropathy and pain in extremities was from the diabetes. He ordered the patient annual labs and suggested a SPECT stress test later on.

After seven years of normal labs, the patient went in 2011 for a nuclear medicine stress test. The EKG was normal and images from the SPECT camera indicated only a normal amount
of blockage considering his diabetes, high cholesterol, and age. There were only minimal changes in pre-stress and post-stress images according to the same cardiologist who read the images. (See Figure 2) The patient’s hospital costs of the echocardiogram were at least one fourth less the cost for PCI. The total cost for PCI was approximately $10,092 with insurance covering 80%. The patient was frustrated with the false-positive results and the avoidable PCI procedure. Advances in noninvasive imaging technology have given physicians more economical, accurate, and faster non-invasive procedures for ruling out CAD. This patient and similar non-emergent patients could be spared long expensive procedures with more accurate, noninvasive imaging options emerging and a conservative approach to ordering these tests.

**Discussion**

Informed physicians can weigh risks, costs, and the image accuracy of diagnosing CAD with noninvasive imaging modalities. With the amount of patients that present with CAD symptoms, diagnosis can be very difficult and costly in the practice of medicine. Conservative and evidence based approaches to ordering imaging studies should be utilized. There is no right or wrong answer: each modality has its advantages and disadvantages. CT and MRI can be useful for anatomical studies and echocardiography and NM are valuable for functional studies. New technologies should strive to improve sensitivity, decrease scan times, and give physicians the most accurate diagnosis possible. It’s up to an educated physician to weigh factors for each imaging tool and determine which is best for the patient’s demographics, presentation, and extent of coronary artery disease.
Figures

Figure 1. Image obtained during PCI on a 53 year old male showing no serious occlusions to the coronary arteries.

Figure 2. Normal stress test images of same patient using SPECT imaging. The heart is displayed in multiple views with brighter colors indicating more blood flow. Radiologists and cardiologists look for differences between rest and stress that would suggest problems with the coronary arteries.
References


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