Clinical Imaging 43 (2017) 97–105

Contents lists available at ScienceDirect

Clinical Imaging

journal homepage: http://www.clinicalimaging.org

Cost-effectiveness of diagnostic evaluation strategies for individuals with stable chest pain syndrome and suspected coronary artery disease

James K. Min [a,*], Amanda Gilmore [b], Erica C. Jones [a], Daniel S. Berman [d], Wijnand J. Stuijfzand [a], Leslee J. Shaw [c], Ken O'Day [b], Ibrahim Danad [a]

[a] The Department of Medicine and Radiology, Weill Medical College of Cornell University, Dalio Institute of Cardiovascular Imaging, The New York Presbyterian Hospital, New York, NY, United States
[b] Xcenda Corporation, Palm Harbor, FL, United States
[c] Cedars Sinai Medical Center, Los Angeles, CA, United States
[d] Emory University School of Medicine, Atlanta, GA, United States

ARTICLE INFO

Article history:
Received 23 March 2016
Received in revised form 17 January 2017
Accepted 25 January 2017
Available online xxxx

Keywords:
Cost effectiveness
Computed tomography
Stress testing
Echocardiography
Myocardial perfusion SPECT
Invasive angiography

ABSTRACT

Purpose: To determine lifetime cost-effectiveness of diagnostic evaluation strategies for individuals with stable chest pain and suspected coronary artery disease (CAD).
Methods: Exercise treadmill testing (ETT), stress echocardiography (SE), myocardial perfusion scintigraphy (MPS), coronary computed tomographic angiography (CCTA), and invasive coronary angiography (ICA) were assessed alone, or in succession to each other.
Results: Initial ETT followed by imaging wherein ETT was equivocal or unable to be performed appeared more cost-effective than any strategy employing initial testing by imaging.
Conclusion: As pre-test likelihood of CAD varies, different modalities including SE, CCTA, and MPS result in improved costs and enhanced effectiveness.

1. Introduction

Coronary artery disease (CAD) is the leading cause of morbidity and mortality [1]. Current clinical practice and appropriateness guidelines recommend either exercise treadmill testing (ETT) or non-invasive cardiac imaging tests—such as stress echocardiography (SE), myocardial perfusion scintigraphy (MPS) and coronary computed tomographic angiography (CCTA)—to diagnose, prognosticate risk and impact therapeutic decision making for patients with an intermediate pre-test likelihood of stable CAD [2–6]. Non-invasive cardiac testing with imaging has been favored by some as an initial test for symptomatic patients with at least intermediate pre-test likelihood of obstructive CAD, given its superior ability to diagnose CAD, reclassify CAD likelihood, predict CAD events, and guide subsequent treatment over testing without imaging [3,7–9]. Accordingly, rates of performance of non-invasive cardiac imaging tests have exploded, with growth in imaging outpacing that of other physicians services by more than a factor of two [10]. At present, >10 million CAD imaging tests are being performed annually in the United States [11]. Despite the high utilization and numerous options for non-invasive cardiac testing, uncertainty remains regarding the optimal testing strategies [12,13]. Multiple studies have investigated the value of ETT in comparison with non-invasive imaging modalities, however, a direct comparison of varying diagnostic strategies that employ non-invasive tests in isolation versus in succession to one another has to date not been assessed [9,13]. Further, the opportunity costs of testing strategies that begin with ETT as compared to that that begin with imaging have not been fully evaluated [13].

The aim of the present study was to determine the cost-effectiveness of the most widely available diagnostic evaluation strategies for individuals without known CAD presenting with stable chest pain syndrome.

2. Materials and methods

We assessed the cost effectiveness of 12 different diagnostic strategies for stable chest pain patients without known CAD: 1) ETT followed by invasive coronary angiography (ICA) for equivocal or positive ETT (ETT-ICA); 2) ETT followed by SE for equivocal ETT and ICA for positive ETT (ETT-SE-ICA); 3) ETT followed by MPS for equivocal ETT and ICA for positive MPS (ETT-MPS-ICA); 4) ETT followed by CCTA for equivocal ETT and ICA for positive ETT (ETT-CCTA-ICA); 5) SE followed by ICA for equivocal or positive SE; 6) SE followed by CCTA for equivocal SE and

Abbreviations: CAD, coronary artery disease; CCTA, coronary computed tomographic angiography; ECHO, echocardiogram; ETT, exercise treadmill testing; ICA, invasive coronary angiography; ICER, incremental cost-effectiveness ratio; MPS, myocardial perfusion scintigraphy; SE, stress echocardiography; QALY, quality adjusted life year.

* Corresponding author at: Institute for Cardiovascular Imaging, Department of Radiology, Weill Cornell Medical College, 413 E 69th Street, Suite 108, United States.
E-mail address: jkm2001@med.cornell.edu (J.K. Min).

http://dx.doi.org/10.1016/j.clinimag.2017.01.015

ICA for positive SE (SE-CCTA-ICA); 7) MPS followed by ICA for equivocal or positive MPS (MPS-ICA); 8) MPS followed by CCTA for equivocal MPS or ICA for positive MPS (MPS-CCTA-ICA); 9) CCTA followed by ICA for equivocal or positive CCTA (CCTA-ICA); 10) CCTA followed by SE for equivocal CCTA or ICA for positive CCTA (CCTA-SE-ICA); 11) CCTA followed by MPS for equivocal CCTA or ICA for positive CCTA (CCTA-MPS-ICA); and 12) direct ICA.

2.1. Economic model and assumptions

We developed an economic model over a lifetime horizon in order to evaluate the costs and cost effectiveness of different diagnostic work-up strategies for stable chest pain patients without known CAD. Test sensitivity, specificity, rates of equivocal results, and disease prevalence were used to classify patients undergoing testing as true positive, false positive, true negative, false negative, or equivocal for obstructive CAD. All positive results were assumed to be referred to ICA, and ICA was assumed to have perfect sensitivity and specificity, notwithstanding that this may not be a flawless reflection of clinical practice. Depending on the strategy, patients with equivocal results were assumed to be referred to either additional downstream non-invasive testing or ICA.

For the post-diagnosis period, we employed a Markov model based on 1-year cycles to account for outcomes and costs of treatment for those correctly diagnosed with CAD, diagnosis of false negatives, and clinical events such as coronary revascularization, myocardial infarction and death. Costs were modeled from a payer perspective.

To compare degrees of abnormality of anatomic and functional measurements and their implications for subsequent treatment, we considered 4 categories relating to the extent and severity of abnormality by each method: none, mild, moderate and severe.

CAD was defined angiographically (for ICA and CCTA) as absent, mild, moderate or severe. Mild CAD was defined as non-obstructive coronary artery stenosis ranging from 1 to 69% in all affected vessels, not including the left main artery. Moderate CAD was defined as ≥70% stenosis in one or two major epicardial coronary artery vessels, not including the left main artery. Severe CAD was defined as ≥50% stenosis in the left main artery or ≥70% stenosis in three major epicardial coronary artery vessels. Following the diagnostic phase, patients experiencing post-test myocardial infarction were also considered to have severe CAD.

For functional cardiac imaging tests—including SE and MPS—the following classification schema was employed: for purposes of considering post-test management and costs, patients with no wall motion abnormalities or perfusion abnormalities were considered to have no CAD. Patients with mild, moderate, and severe SE and MPS test results were considered to have disease of equivalent severity to those defined angiographically.

For ETT, patients with no ST-segment changes were considered to have no CAD. Patients with ST-segment depression or elevation were considered to have obstructive CAD. Patients with positive ETT tests were considered to have moderate or severe CAD, which was confirmed at the time of ICA. For evaluation purposes, individuals were considered ineligible for ETT in the presence of baseline electrocardiogram (ECG) abnormalities, including pre-excitation; electronically paced ventricular rhythm; >1 mm of resting ST segment depression or complete left bundle branch block; <1 mm of basleine ST depression and taking digoxin; or ECG criteria for left ventricular hypertrophy with <1 mm baseline ST depression. For individuals who could not exercise, ETT was considered not able to be performed.

We considered several possible diagnostic outcomes of non-invasive diagnostic test strategies. For ETT, we considered 3 possibilities, which included no exercise-induced ST-segment changes, exercise-induced ST-segment changes or equivocal ST-segment abnormalities, including up-sloping ST segment depression or rapid return to baseline of ST segment depression early during recovery. These findings were interpreted as no CAD, moderate or severe CAD, and equivocal results, respectively. For SE and MPS, we considered 5 possibilities, which included identification of 1) normal myocardial perfusion or wall motion, 2) mild perfusion or wall motion abnormalities, 3) moderate perfusion or wall motion abnormalities, 4) severe perfusion or wall motion abnormalities, and 5) equivocal testing due to inadequate images, low workload, or artifact. All perfusion or wall motion abnormalities that were non-equivocal were assumed to represent flow-limiting coronary artery stenosis.

For CCTA, we considered 6 possible diagnostic outcomes, which included identification of 1) absence of CAD, 2) mild CAD, 3) moderate CAD, 4) severe CAD; 5) equivocal testing due to artifact or due to presence of a 50–69% stenosis in any epicardial coronary artery vessel for which the functional significance was unclear.

For ICA, we considered 4 possibilities, which included identification of 1) no CAD, 2) mild CAD, 3) moderate CAD and 4) severe CAD. While gradations of CAD severity by ICA were identical to those defined for CCTA, ICA was considered the reference standard and thus, did not produce equivocal or indeterminate test results.

Given the substantial results of the COURAGE and SYNTAX trials, as well as changing practice patterns for treatment of stable CAD, we considered four post-testing treatment strategies: 1) No therapy for patients with absence of CAD; 2) Medical therapy for patients with mild CAD; 3) Percutaneous intervention (PCI) plus optimal medical therapy (OMT) for 50% and OMT alone for 50% of patients with moderate CAD, and 4) Coronary artery bypass surgery (CABG) plus OMT for 50% and PCI plus OMT for 50% patients with severe CAD [14,15].

2.2. Patient population

Base case values, sensitivity estimate ranges, costs and sources for our model variables are listed in Table 1. The base case model is a 55-year old man with stable chest pain syndrome and no prior history of CAD with a 20% likelihood of obstructive CAD. Obstructive CAD was defined as a luminal stenosis severity of ≥50% in the left main artery or ≥70% in any other major epicardial artery.

2.3. Test performance characteristics

Sensitivity and specificity of non-invasive diagnostic tests within our model were based upon a bivariate analysis of data from published multicenter trials [Table 1] [16]. This approach of using a bivariate random effects model was chosen to produce unbiased estimates and 95% confidence intervals that preserve the joint distribution or correlation between test sensitivity and specificity.

2.4. Risks of diagnostic testing

Invasive coronary angiography was associated with a 0.1% risk of mortality [17,18]. Thus, even though ICA was considered the gold standard diagnostic test, deaths due to ICA were not treated as a correct diagnosis in the diagnostic model.

Table 1
Costs, effectiveness and incremental cost effectiveness ratio for individuals with a 20% prevalence of obstructive CAD.

Strategy	Cost	Effect	Δ Cost	Δ Effect	ICER
ETT-SE-ICA	$10,995	16.106	–	–	–
SE-CCTA-ICA	$11,235	16.1102	$240	0.0042	ExtDominated
ETT-MPS-ICA	$11,269	16.1045	$34	-0.0057	Dominated
SE-ICA	$11,356	16.1097	$122	-0.0005	Dominated
ETT-CCTA-ICA	$11,564	16.1176	$569	0.0116	$49,021
MPS-CCTA-ICA	$11,677	16.1078	$113	-0.0098	Dominated
MPS-ICA	$11,798	16.1073	$122	-0.0005	Dominated
CCTA-SE-ICA	$12,087	16.1275	$524	0.0099	$52,899
CCTA-MPS-ICA	$12,119	16.1274	$32	-0.0001	Dominated
CCTA-ICA	$12,274	16.1283	$187	0.0008	$233,138
ETT-ICA	$12,635	16.1127	$361	-0.0156	Dominated
ICA	$14,003	16.1205	$1729	-0.0078	Dominated