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Review Article

Prognostic utility of coronary computed tomographic angiography

Yuka Otaki [a], Daniel S. Berman [a,b], James K. Min [a,b,*]

[a] Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA
[b] Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, CA, USA

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ABSTRACT

Coronary computed tomographic angiography (CCTA) employing CT scanners of 64-detector rows or greater represents a noninvasive method that enables accurate detection and exclusion of anatomically obstructive coronary artery disease (CAD), providing excellent diagnostic information when compared to invasive angiography. There are numerous potential advantages of CCTA beyond simply luminal stenosis assessment including quantification of atherosclerotic plaque volume as well as assessment of plaque composition, extent, location and distribution. In recent years, an array of studies has evaluated the prognostic utility of CCTA findings of CAD for the prediction of major adverse cardiac events, all-cause death and plaque instability. This prognostic information enhances risk stratification and, if properly acted upon, may improve medical therapy and/or behavioral changes that may enhance event-free survival. The goal of the present article is to summarize the current status of the prognostic utility of CCTA findings of CAD.

1. Introduction

Current professional societal guidelines endorse the use of noninvasive imaging tests for the diagnostic evaluation of symptomatic patients with at least intermediate pre-test likelihood of anatomically obstructive coronary artery disease (CAD). These tests have historically comprised physiologic stress testing by electrocardiography, echocardiography, cardiac magnetic resonance and myocardial perfusion imaging (MPI). More recently, coronary computed tomographic angiography (CCTA) has emerged as a noninvasive anatomic alternative that has gained increasing utilization and importance for the diagnosis of CAD, with generally high diagnostic performance compared to invasive coronary angiography (ICA).

In particular, CCTA demonstrates a very high negative predictive value for the exclusion of anatomically obstructive CAD, which may prove useful for preventing unnecessary ICA. Recent data from the National Cardiovascular Death Registry revealed that, amongst 398,978 patients who underwent elective ICA at 663 hospitals between January 2004 through April 2008, 39.2% of patients had no evidence of significant CAD, defined as <20% stenosis in any vessels.[1] Notably, noninvasive examinations, including stress testing, were performed in 83.9% of the patients in this study population prior to ICA. These findings suggest the need for improved noninvasive measures to curb unnecessary ICA, and proponents of CCTA have posited this anatomic test as a means to achieve this goal.

* *Corresponding author*. Department of Medicine, Imaging, and Biomedical Sciences, Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, 8700 Beverly Boulevard, S. Mark Taper Building, Room 1253, Los Angeles, CA 90048, USA. Tel.: +1 310 423 2707; fax: +1 310 423 0811.
E-mail addresses: Yuka.Otaki@cshs.org (Y. Otaki), james.min@cshs.org (J.K. Min).
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Over the last decade, significant technological advances have been introduced to improve multi-detector computed tomography (CT) technology, including the introduction of 64-detector row CT scanners in 2005, which enabled the reliable acquisition of generally motion-free images of the coronary arteries and allowing for assessment of coronary stenosis and atherosclerotic plaque. Since the introduction of 64-detector row scanners, an array of newer generation scanners have been introduced to improve upon the spatial and temporal resolution as well as the volume coverage. These have included high-definition scanners capable of 230 micron in-plane resolution; dual source and fast pitch helical scanners that achieve temporal resolution of 83 ms; and wide area detector CT which allow for 16 cm coverage within a single gantry revolution, therein allowing whole heart coverage during a single heart beat.

In a recent meta-analysis of 27 studies using 16 to 64-slice scanner, CCTA was reported to have a diagnostic sensitivity, specificity, negative predictive value (NPV), and positive predictive values (PPV) of 99%, 89%, 93% and 100%, respectively.[2] These meta-analytic findings mirror those of prospective multicenter trials. One such trial, the ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) study—represented the first prospective multicenter study evaluating 230 stable patients without known coronary artery disease undergoing CCTA before ICA[3]—demonstrated a diagnostic sensitivity, specificity, PPV, and NPV of 95%, 83%, 64%, and 99%, respectively, compared to a quantitative coronary angiographic reference standard. Subsequent to the ACCURACY study, two additional prospective multicenter studies also demonstrated high sensitivity, negative predictive value, and high diagnostic accuracy of 64-slice CCTA compared to invasive coronary angiogram—in particular for patients without known CAD—with study results similar to the ACCURACY trial.[4,5]

One additional potential benefit of CCTA is its ability to characterize and quantify coronary atherosclerotic plaque and arterial wall features in addition to providing accurate evaluation of degree of coronary stenosis. Numerous prior studies have compared the ability of CCTA to characterize and quantify coronary plaque to a gold standard, typically employing gray scale intravascular ultrasound (IVUS).[6] In a recent meta-analysis of 33 studies that comprised 946 patients, CCTA was noted to demonstrate excellent correlation to IVUS for numerous additional atherosclerotic measures beyond stenosis severity, including cross sectional area, plaque area, area stenosis, plaque volume and arterial remodeling.[7]

In addition to its high diagnostic performance against invasive angiography and IVUS, CCTA findings of CAD have been evaluated for its ability to predict future adverse CAD events. We herein describe the most current findings from CCTA studies evaluating its prognostic utility for future adverse events.

2. Prognostic value of CCTA for all-cause death from initial studies

The first large single center prognostic study evaluated the association of all-cause mortality with CCTA defined extent and severity of CAD in 1127 patients with suspected disease.[8] In this study, the per-patient, per-vessel and per-segment stenosis severity by 16-detector raw CCTA was scored as minimal (<30%), mild (30%–49%), moderate (50%–69%), or severe (≥70%). Atherosclerotic plaque was assessed by 3 distinct methods: 1) presence or absence of moderate or severe plaque; 2) coronary artery plaque burden as categorized by a modified Duke CAD index; and 3) simple clinical scores grading plaque extent and distribution. During a 15 month follow-up period, CCTA predictors of death included proximal left anterior descending artery (LAD) stenosis and number of vessels with ≥50% and ≥70% stenosis (all $p < 0.0001$). Furthermore, survival worsened with higher-risk Duke scores, ranging from 96% survival for 1 stenosis ≥70% or 2 stenoses 50% ($p < 0.013$) to 85% survival for ≥50% left main (LM) artery stenosis ($p < 0.0001$). In addition, clinical scores measuring plaque burden and distribution predicted 5–6% higher absolute death rate (6.6% vs. 1.6% and 8.4% vs. 2.5%; $p < 0.05$ for both). Importantly, a negative CCTA was noted to provide an extremely low risk for death. Subsequent to this initial investigation, multiple studies to date examined the prognostic value of 64-detector row CCTA have done so, but were generally limited to single centers and/or relatively small sample sizes[9,10] (Table 1). One large-scale 2-center study examined 5330 consecutive patients without known CAD undergoing CCTA.[11] At 2.3 ± 0.6 year follow-up for an endpoint of all-cause mortality, obstructive CAD ≥ 70% correlated with higher incident death [hazards ratio (HR) 2.44, 95% confidence interval (CI) 1.61–3.72, $p < 0.001$]. Compared to those without obstructive CAD, individuals with increasing numbers of vessels with obstructive CAD experienced increased risk of death: 1-vessel (HR 2.23, 95% CI 1.34–3.72), 2-vessel (HR 3.29, 95% CI 1.62–6.71), or 3-vessel (HR 7.35, 95% CI 3.79–14.29) ($p < 0.001$ for all). Further, by measures of left ventricular ejection fraction (LVEF) made possible by retrospective electrocardiographic gating,

Table 1 – Prognostic CCTA studies for mortality.

No	Author	Year	Study type	No of patients	Time of follow-up	Population	Slice of CCTA
1	Min[8]	2007	Retrospective	1127	15 ± 4 mo	Patients ≥45 years old, chest symptoms	16
2	Ostrom[9]	2008	Retrospective	2538	78 ± 12 mo	Symptomatic	64
3	Min[11]	2010	Retrospective	5330	2 ± 1 years	Without known CAD	64
4	Lin[10]	2011	Prospective	2583	3 ± 1 years	non-obstructive CAD	64

CCTA = coronary CT angiography; mo = months; CAD = coronary artery disease.