Clinical Utility of Cardiac CTA

The current role and cost effectiveness of this modality.

BY SUNIL MIRCHANDANI, MD, AND JAMES K. MIN, MD

Cardiac CT angiography (CTA) has emerged as a highly accurate tool in the noninvasive diagnosis and risk assessment of patients with a broad spectrum of cardiac pathology. Although the primary application of CTA is coronary artery imaging, it is rapidly developing additional roles for the assessment of stent and bypass graft patency, for facilitation of interventional and electrophysiologic procedures, and for defining cardiac structure and function. Ultimately, the utility of CTA will lie not in the picture that it takes but in the clinical relevance the images confer. In this article, we define the current role of CTA in clinical cardiology, highlighting its safety and efficacy compared to invasive angiography (ICA) as well as its cost effectiveness compared to today's noninvasive alternatives.

DIAGNOSIS

Advances in multidetector CT technology have occurred rapidly, and current-generation 64-detector row CT scanners now permit routine clinical imaging of the coronary arteries noninvasively. Although initial correlation studies[1-10] in the 64-slice era were limited by small numbers, selection bias, and single-center data collection (Table 1), these former results have been uniformly consistent in defining a remarkably high negative predictive value (95%–100%) for the exclusion of significant coronary artery stenoses. Such a high negative predictive value suggests that the greatest use for CTA will be for exclusion of significant stenosis in patients at low-to-intermediate pretest likelihood for significant coronary artery disease. Recently, two prospective multicenter studies examining the diagnostic performance of 64-slice CTA have been presented. The Coronary Evaluation Using Multidetector Spiral Computed Tomography Angiography using 64 Detectors (CORE 64) study,[11] was a multicenter international study of nine sites, which elevated the level of evidence for CTA, with a per-patient sensitivity of 93%. Similarly, the Assessment by Coronary Computed Tomographic Angiography of Individuals

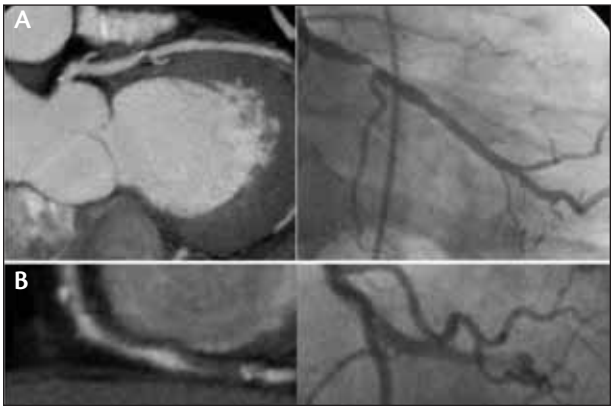

Figure 1. Example of a severe stenosis of the proximal left anterior descending artery diagnosed on CTA and confirmed by an invasive angiogram (A). Example of a complete occlusion of the distal right coronary artery (B). Collimation: 64 X 0.6 mm; gantry rotation: 350 ms.

Undergoing Invasive Coronary Angiography (ACCURACY) trial[12] enrolled 232 symptomatic patients at 16 US sites and demonstrated a high sensitivity (91%) and specificity (84%) and negative predictive value (99%) for the exclusion of a >70% (rather than the standard 50%) coronary artery stenosis. Because the prevalence of obstructive coronary artery stenosis was only 14% in the ACCURACY trial, it underscored the fact that despite studying a high-risk symptomatic patient population, a majority of such patients had nonobstructive disease and could have safely avoided ICA. In this manner, if CTA is used as the initial diagnostic test or a follow-up to an inconclusive stress test, there is promise that unnecessary invasive angiograms may be avoided.

MORE THAN JUST STENOSIS DETECTION

The detection of significant stenoses by CTA may be only a component of the important information gleaned by CTA (Figure 1). Whereas ICA may remain superior in its ability to evaluate the coronary artery lumen, CTA can

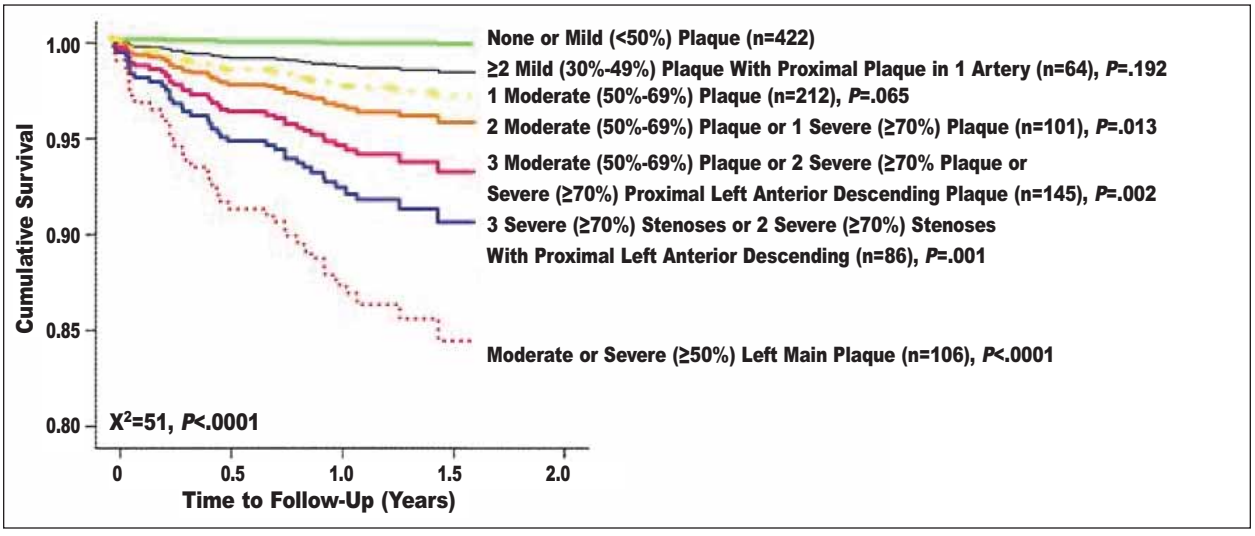

Figure 2. Unadjusted Cox Survival by Duke Prognostic CAD index. The modified Duke coronary artery score is important in stratifying high-risk and low-risk subgroups presenting with chest pain. (Adapted from Min et al. J Am Coll Cardiol. 2007;50:1161-1170.[22])

assess both luminal and extraluminal plaque. Furthermore, characterization of plaque components, as well as quantification of overall plaque burden and volume, may add incremental information beyond a single lesion's stenosis severity.

Historically, quantification of coronary artery atherosclerotic plaque by CT has been limited to coronary artery calcium scoring. Calcium score quantification, originally developed with electron-beam CT and subsequently validated on multidetector CT, has been used to assess future cardiovascular risk. In intermediate-risk patients, calcium scoring defines risk above and beyond traditional clinical risk factors.[13] Because arterial calcification is an integral active part of vascular plaque, a high correlation exists between atherosclerotic plaque burden and coronary artery calcification. However, the absence of calcium does not rule out atherosclerotic plaque,[14] and furthermore, two patients with equivalent calcium scores may possess different amounts of overall plaque. Accordingly, CTA may provide a new direction toward enhanced plaque analysis. Several studies have demonstrated CTA to be capable of defining plaque composition into at least noncalcified, mixed, and calcified groups.[15,16] CTA and intravascular ultrasound (IVUS) may be complementary tools in differentiating noncalcified and calcified plaques,[17,18] although at present, in the realm of plaque area/volume definition, CTA has compared poorly with IVUS.[19,20] Nevertheless, future advances in CT technology may permit highly accurate indexing of plaque character, plaque burden, and plaque remodeling, which may take the field one step closer to defining the anatomic characteristics associated with plaque vulnerability.[21]

TABLE 1. NEGATIVE PREDICTIVE VALUE OF *64*-SLICE CTA COMPARED TO ICA ON A PER-SEGMENT BASIS

Investigator	N	Collimation (mm)	Gantry Rotation (ms)	Negative Predictive Value (%)
Leschka et al[1]	53	64 X 0.6	370	99
Raff et al[2]	70	64 X 0.6	330	98
Leber et al[3]	59	64 X 0.6	330	99
Mollet et al[4]	52	64 X 0.6	330	99
Ropers et al[5]	82	64 X 0.6	330	99
Fine et al[6]	66	64 X 0.6	330	95
Pugliese et al[7]	34	64 X 0.6	330	99
Schuijf et al[8]	61	64 X 0.5	400	99
Ehara et al[9]	69	64 X 0.6	330	95
Nikolaou et al[10]	72	64 X 0.4	330	97

(Courtesy of James Earls, MD.)

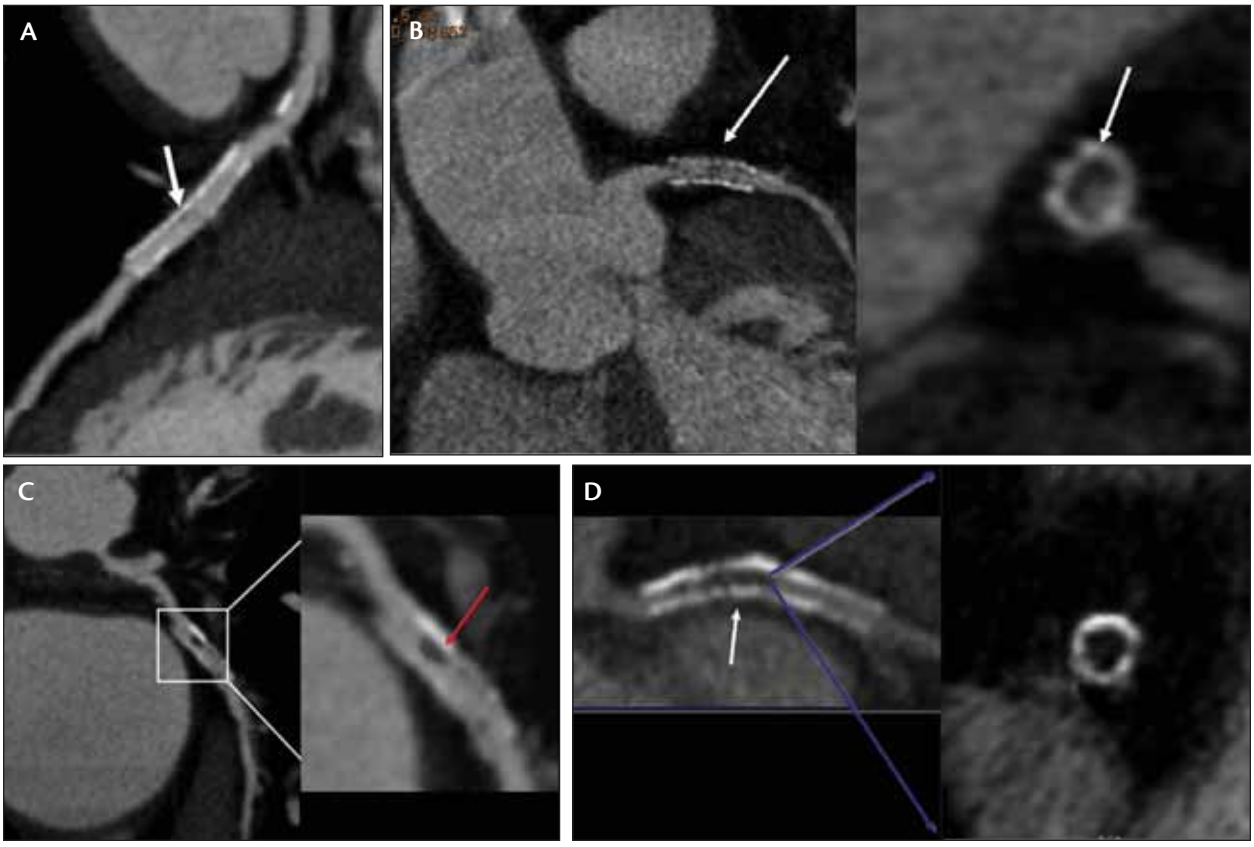

Figure 3. Stent patency is assessable in cases where stent diameter is ≥3 mm and heart rate, noise, and window/level are optimized. Mild neointimal hyperplasia in a 3.5-mm stent (A). In-stent restenosis (50%) (B). Severe (>70%) in-stent restenosis (C). Total occlusion within the stent lumen (D).

EMERGING PROGNOSTIC DATA

In addition to being diagnostically accurate, CTA must provide prognostic information in order to develop clinical traction. Although long-term prognostic data are currently limited, Min et al[22] recently delineated several CTA indices that predict intermediate-term all-cause mortality in patients presenting with chest pain. As might be expected, the risk of death increased with the severity of lesions detected, as well as the number of epicardial vessels involved. Proximal left anterior descending artery and left main disease in particular were the highest risk locations (Figure 2). Most importantly, a normal CTA predicted a very low incident mortality rate of only 0.3% at 15.3 months of follow-up, as compared with the overall mortality rate of 3.5%. This excellent short-term prognosis after a nonobstructive CTA has been shown in other studies,[23,24] including a small group of patients discharged directly from the emergency room after CTA.[24] Future investigation will answer whether plaque characteristics add additional prognostic information beyond current indices.

ACUTE CHEST PAIN IMAGING

Every year, 6,000,000 patients with acute chest pain[25] are seen in US emergency departments at a cost of $10 to $12 billion.[26,27] Despite our best efforts, 2% to 8% of acute coronary syndrome (ACS) patients are inappropriately discharged.[28-31] The use of CTA in the safe and early discharge of patients with acute chest pain may ultimately be one of its most important public health roles. History, physical, 12-lead ECG, and a single set of cardiac biomarkers are usually not sufficient for the firm exclusion of ACS. However, the addition of CTA has shown to be very effective for diagnosing ACS, as well as discharging low-risk patients. In a group of 103 patients (14 of whom ultimately had ACS), Hoffman et al[32] showed that the absence of significant coronary artery stenosis and nonsignificant coronary atherosclerotic plaque on the CT scan predicted the absence of ACS with a negative predictive value of 100%. Rubinshtein et al[24] added that patients sent home after a normal CTA had a very good short-term prognosis. Such emergency room protocols have also been shown to reduce overall diagnostic time

(Courtesy of James Earls, MD.)

Figure 4. Volume-rendered reconstruction and curved multiplanar reformat of bypass graft evaluation. Saphenous venous graft "jump" between OM2 and OM3 (A). Radial artery graft, both free and composite (B). Occluded stent within a saphenous venous graft to an obtuse marginal branch (C).

in the hospital at a lower cost.[33] Currently, a large multicenter trial, entitled CT-STAT (Systematic Triage of Acute Chest Pain Patients to Treatment), is enrolling emergency room patients with acute chest pain who will undergo either CTA or nuclear stress testing.

STENT/BYPASS GRAFT IMAGING

With current-generation, multidetector CT technology, stent imaging remains challenging. Metal alloys used in intracoronary stents can cause both beam hardening and partial volume averaging artifacts, which limits visualization of the lumen within the stent. Thus, sensitivity to detect in-stent restenosis, even in the 64-slice era, is more variable than that for the detection of native coronary artery stenosis (75%–95%).[34,35] Furthermore, the ability to assess stent patency depends on the type of stent,[36] as well as the diameter of the stent imaged,[37] and therefore a combination of prudent patient selection, as well as optimal postprocessing techniques, is required (Figure 3).

In contrast, coronary artery bypass grafts are generally large vessels and are primarily extracardiac in their course; thus, bypass graft imaging by CTA has been shown to be highly and reproducibly accurate. The negative predictive value of graft stenosis or occlusion in several 16-slice studies has been exceptional,[38-43] and the emerging 64-slice data[44] have improved spatial resolution to allow accurate visualization of complicated anatomy including jump grafts, radial arteries, and stents within grafts (Figure 4).

INTERVENTIONAL AND ELECTROPHYSIOLOGIC APPLICATIONS

CTA may provide a preprocedure road map, helping with the technical challenges of percutaneous revascularization. Often, three-dimensional rotation about the long axis of a vessel helps to define the anatomy of both ostial and bifurcation lesions. Procedural success rates in recanalizing chronic total occlusions (CTOs) are only approximately 70% and have not improved over time in the stent era.[45] Because 10% to 15% of all angioplasty procedures are CTO vessels, a large number of resources are invested toward procedures that may, in certain cases, be unsuccessful. Preimaging of the CTO may be used to screen patients in whom recanalization is unlikely. CTA parameters that are associated with lower rates of success of CTO interventions include transluminal calcification and overall plaque length (Figure 5).[46,47] In a small cohort, CTA guidance was shown to improve overall procedural success, reduce median fluoroscopy time, and minimize contrast load, as compared to traditional methods.[48] Similarly, in patients who have undergone unprotected left main stenting, CTA may be considered for follow-up. At present, conventional coronary angiography at 3 to 6 months is commonly practiced. Van Mieghem and colleagues[49] evaluated a small group of patients using CTA, as well as invasive angiography/IVUS for left main stenting follow-up, and in this cohort, CTA identified all patients with confirmed in-stent restenosis.

Electrophysiology procedures also benefit from CTA preprocedure imaging. Accurate visualization of the ablation catheter in relation to the complex left atrial anatomy is important for the success and safety of atrial fibrillation ablation. Hence, image integration and registration of volume-rendered models of the left atrium and pulmonary veins into electroanatomic mapping systems have been shown to improve procedural success in small, nonrandomized cohorts.[50,51] CTA is also currently used for evaluating the coronary sinus and venous anatomy before cardiac resynchronization therapy.[52] Such preprocedure anatomic definition may facilitate lead placement and also identify patients who may not have suitable vein anatomy to undergo cardiac resynchronization therapy.

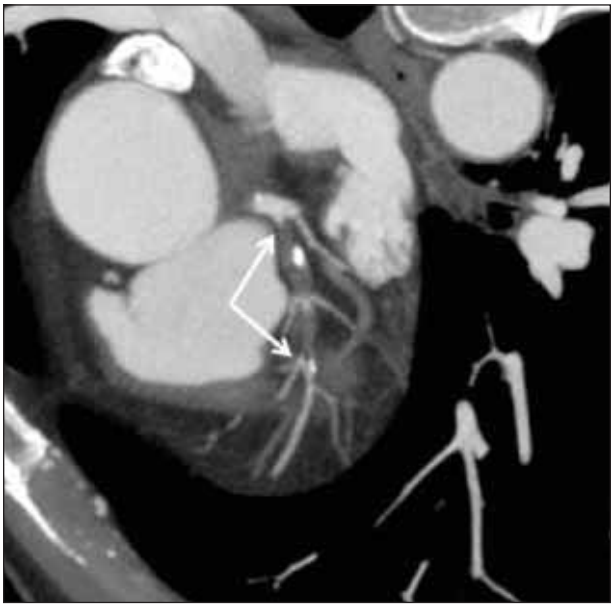

Figure 5. CTA of a CTO of the proximal left anterior descending artery spanning more than 10 cm with small amount of transluminal calcification. Collimation: 64 X 0.6 mm; gantry rotation: 350 ms.

COST EFFECTIVENESS

Results from the COURAGE trial[53] have provided compelling evidence for the role of optimal medical therapy as first line in patients with stable coronary artery disease. Such results have questioned the benefits of percutaneous revascularization in these patients. Therefore, the use of CTA in carefully selected patients may preclude the need for downstream invasive coronary angiography or percutaneous revascularization. In this regard, careful measure of the opportunity costs of CTA versus other methods of coronary artery evaluation should be considered. Recently, investigators at William Beaumont Hospital in Michigan conducted a study assessing the feasibility and cost effectiveness of acute chest pain imaging by CTA.[54] These investigators randomized 197 patients with acute chest pain to CTA or standard of care. Cardiac CT either excluded or identified coronary artery disease as the cause of acute chest pain in 75% of patients. The remaining 25% required further testing because of equivocal results. Workup time and overall cost were effectively reduced by nearly 12 hours and $300 per patient.

SAFETY CONCERNS

Recently, cancer-risk models[55] have raised concerns about the safety of CTA. According to the BEIRV VII risk model, the lifetime attributable risk of cancer after a CTA may approach 0.7% in the highest risk categories (ie, young women). In other groups, radiation risk may be present as well. Although there are many assumptions made in quantifying the risk, it is generally agreed that some sort of risk-benefit analysis should employed before performing CTA. Indeed, CT vendors are each taking an active role in minimizing the overall exposure to ionizing radiation. A prospectively triggered protocol exposes the patient to radiation for a small portion of the cardiac cycle and, in this way, has been demonstrated to reduce doses to as low as 1 to 3 mSv (lower than the annual background radiation exposure), without any effect on image quality.[56]

FUTURE DIRECTIONS AND CHALLENGES

As data accrue to support the use of CTA as an initial diagnostic strategy in patients requiring coronary artery evaluation, a major upcoming challenge for CTA will be to integrate it effectively into daily clinical practice. Will CTA be the initial diagnostic test, with SPECT (single-photon emission computed tomography) imaging only to determine physiologic significance? Or will CTA be used to clarify SPECT results? Currently, the best diagnostic algorithm is unclear, and therefore, we should individualize our approach. New data are emerging that CTA may be useful to quantify regional myocardial perfusion.[57] Thus, when CTA can offer a simultaneous combination of anatomy and perfusion, a further honing of the diagnostic pathway will be required.

Plaque imaging may also be a new facet of the diagnostic capability of CTA. Plaque characterization, volume, and remodeling are all CTA indices that may make up a new paradigm of coronary artery imaging. Whether any single one of these characteristics, or combination of these characteristics, can effectively engender CTA as a gatekeeper to reduce unnecessary ICAs is as yet unknown. However, rapid advances in CT technology will invariably assist in coronary artery assessment with higher safety and efficacy. Currently, several CT scanners offer methods of radiation reduction, including prospective-triggered scanning and tube current modulation. The 320-slice scanner is the first scanner to provide whole-heart coverage in a single heartbeat, which has the potential to reduce both radiation exposure and motion artifacts. Dual-source scanners have an additional x-ray source, improving temporal resolution to scan at higher heart rates, which will be particularly useful in the emergency department setting.

As this array of technology floods the clinical arena, we should continue to responsibly apply the modality to the appropriate patient. Patient selection will remain the key to the success of CTA, and by applying rigorous standards of appropriateness and evidenced-based use, this modality may likely improve health outcomes and limit downstream costs. ■

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