



## Coronary CT Angiography in the Evaluation of Acute and Stable Chest Pain: An Executive Summary of the Data Supporting Widespread Coverage and Utilization

The rising cost of healthcare is prompting numerous policy and advocacy discussions regarding strategies for constraining growth and creating a more efficient and effective healthcare system. Coronary CTA (CCTA) is well-validated, with nearly 20 large clinical trials, as an equally effective, if not superior, strategy to functional testing with regards to patient outcomes and, in some trials greater improvement in symptoms, without added costs.<sup>1</sup> Despite this evidence, the utilization and growth of CCTA remains suboptimal relative to the evidence for clinical efficiency compared to other imaging modalities.

### Diagnostic Accuracy

The superior diagnostic accuracy of CCTA compared with invasive coronary angiography (ICA) and stress imaging modalities has been demonstrated in prospective trials, such as the ACCURACY Trial, Meijboom Trial, and CORE 64 trials demonstrated a diagnostic sensitivity of 85-99% and a specificity of 64-90% utilizing 64-slice multidetector CT (MDCT) platforms.<sup>2, 3, 4</sup> More contemporary trials including the EVINCI Trial and the PICTURE Trial showed higher sensitivities and specificities of CCTA compared with functional stress testing modalities.<sup>5, 6</sup>

### Clinical Outcomes – Stable Chest Pain

Multiple prospective, randomized trials have demonstrated net improvement in diagnostic certainty, initiation of preventive medications, and subsequent reduction in hard cardiovascular endpoints when utilizing CCTA compared with standard of care. The **CAPP trial** demonstrated that patients randomized to CCTA had an improvement in angina stability and overall quality of life as compared to exercise testing.<sup>7</sup> The **PROMISE trial** demonstrated that at three years, a composite of major cardiovascular events was similar for CCTA with similar three-year healthcare costs.<sup>8, 9</sup> The **SCOT-HEART Trial** demonstrated that at three years patients allocated to CCTA had numerically lower rates of coronary heart disease death, myocardial infarction (MI) with subsequent follow-up data demonstrating a 50% reduction in fatal and non-fatal MI.<sup>10, 11</sup> A subsequent **meta-analysis of the stable chest pain trials** demonstrated that CCTA was associated with a 31% reduction in annual MI rate compared to standard of care.<sup>12</sup> In addition, **CONFIRM Registry** with over 30 peer reviewed manuscripts has demonstrated that coronary CTA has effective risk stratification among a broad patient population encompassing racially and ethnically diverse patients with different risk factors.<sup>13, 14, 15, 16, 17, 18</sup> Finally, the **Dewey Trial** demonstrated that at three years, major cardiovascular outcomes were similar between direct ICA compared to CCTA.<sup>19</sup>

## **Clinical Outcomes – Acute Chest Pain**

The safety and efficiency of CCTA in the emergency department (ED) in the evaluation of low-intermediate risk patients with acute onset chest pain has been validated in three large prospective studies. The **ACRIN-PA Trial** demonstrated that coronary CTA was associated with a higher rate of discharge from the ED, had a higher rate of detection of CAD, and following a negative CCTA no patient died or had an acute MI.<sup>20</sup> The **ROMICAT II Trial** demonstrated that in patients allocated to CCTA, without signs of an acute coronary syndrome, the length of stay was reduced by 7.6 hours with no significant differences in major adverse cardiovascular events.<sup>21</sup> The **CT-STAT Trial** demonstrated that, compared to myocardial perfusion imaging, the time to diagnosis was shorter for coronary CTA with no differences in major adverse cardiovascular events following a negative study.<sup>22, 23</sup> A subsequent meta-analysis of **Clinical Outcomes after CCTA in the ED** demonstrated that CCTA was associated with decreased costs and length of stay but increased ICA and revascularization.<sup>24</sup>

## **CCTA in Societal Guidelines**

The 2012 ACC/AHA Stable Ischemic Heart Disease guidelines assign a class IIA recommendation for CCTA in low-intermediate risk patients who are unable to exercise or have an uninterpretable ECG.<sup>25</sup> Furthermore, CCTA is considered class IIA in patients with prior inconclusive functional testing or ongoing symptoms.<sup>25</sup> The 2011 ACC/AHA Unstable Angina/NSTEMI guideline gives CCTA a class IIA recommendation in low-intermediate risk patients with suspected ACS and a normal or nondiagnostic cardiac biomarker and ECG.<sup>26</sup> Both of these statements were published prior to the vast majority of large, prospective stable and acute chest pain trials previously discussed, thus the level of recommendation may increase in future iterations.

## **Radiation Considerations**

The widespread implementation of prospective, ECG-triggered acquisition protocols has significantly reduced per-patient radiation exposure for CCTA. These recommendations were codified in a SCCT guideline statement on radiation dose optimization.<sup>27</sup> Essentially all prospective trials comparing CCTA to SPECT imaging have demonstrated a significant dose reduction when utilizing CCTA. Notably, this difference was seen when utilizing older, 64-slice MDCT platforms.<sup>8, 21, 23</sup> All vendors have subsequently released various solutions that even more dramatically reduce dose to the point where CCTA can be performed for ~1-2 mSv in select patients.<sup>28,29</sup>

## **Economic Impact of CCTA**

The concept of value-based imaging dictates that the optimal imaging guided strategy is one of the highest quality evidence demonstrating clinical effectiveness but at similar or reduced costs for a given strategy of care. Important considerations for any cardiovascular imaging modality would be how it will affect therapeutic decisions, downstream testing, and cost. Along with the comparative effectiveness evidence, abundant data are available with regards to the cost efficiency of CCTA.<sup>9, 30, 32</sup> Data from the PROMISE trial revealed no

differences in costs of care at three months through three years of follow-up and in the SCOT-HEART trial, cumulative six-month costs were slightly higher for coronary CTA but overall differences in costs were not statistically different from the standard of care arm of the trial.<sup>8, 11</sup>

## References

1. [Lubbers M, Dedic A, Coenen A et al. Calcium imaging and selective computed tomography angiography in comparison to functional testing for suspected coronary artery disease: the multicentre, randomized CRESCENT trial. European heart journal 2016;37:1232-43.](#)
2. [Budoff MJ, Dowe D, Jollis JG et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY \(Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography\) trial. Journal of the American College of Cardiology 2008;52:1724-32.](#)
3. [Meijboom WB, Meijs MF, Schuijf JD et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. Journal of the American College of Cardiology 2008;52:2135-44.](#)
4. [Miller JM, Rochitte CE, Dewey M et al. Diagnostic performance of coronary angiography by 64-row CT. The New England journal of medicine 2008;359:2324-36.](#)
5. [Budoff MJ, Li D, Kazerooni EA, Thomas GS, Mieres JH, Shaw LJ. Diagnostic Accuracy of Noninvasive 64-row Computed Tomographic Coronary Angiography \(CCTA\) Compared with Myocardial Perfusion Imaging \(MPI\): The PICTURE Study, A Prospective Multicenter Trial. Academic radiology 2017;24:22-29.](#)
6. [Neglia D, Rovai D, Caselli C et al. Detection of significant coronary artery disease by noninvasive anatomical and functional imaging. Circulation Cardiovascular imaging 2015;8.](#)
7. [McKavanagh P, Lusk L, Ball PA et al. A comparison of cardiac computerized tomography and exercise stress electrocardiogram test for the investigation of stable chest pain: the clinical results of the CAPP randomized prospective trial. European heart journal cardiovascular Imaging 2015;16:441-8.](#)
8. [Douglas PS, Hoffmann U, Patel MR et al. Outcomes of anatomical versus functional testing for coronary artery disease. The New England journal of medicine 2015;372:1291-300.](#)
9. [Mark DB, Douglas PS, Daniels MR. Economic Outcomes With Anatomical Versus Functional Diagnostic Testing for Coronary Artery Disease. Annals of internal medicine 2016;165:891.](#)
10. [CT coronary angiography in patients with suspected angina due to coronary heart disease \(SCOT-HEART\): an open-label, parallel-group, multicentre trial. Lancet 2015;385:2383-91.](#)

11. [Williams MC, Hunter A, Shah AS et al. Use of Coronary Computed Tomographic Angiography to Guide Management of Patients With Coronary Disease. Journal of the American College of Cardiology 2016;67:1759-68.](#)
12. [Bittencourt MS, Hulten EA, Murthy VL et al. Clinical Outcomes After Evaluation of Stable Chest Pain by Coronary Computed Tomographic Angiography Versus Usual Care: A Meta-Analysis. Circulation Cardiovascular imaging 2016;9:e004419.](#)
13. [Min JK, Dunning A, Lin FY et al. Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiography findings results from the International Multicenter CONFIRM \(Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry\) of 23,854 patients without known coronary artery disease. Journal of the American College of Cardiology 2011;58:849-60.](#)
14. [Villines TC, Hulten EA, Shaw LJ et al. Prevalence and severity of coronary artery disease and adverse events among symptomatic patients with coronary artery calcification scores of zero undergoing coronary computed tomography angiography: results from the CONFIRM \(Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter\) registry. Journal of the American College of Cardiology 2011;58:2533-40.](#)
15. [Shaw LJ, Hausleiter J, Achenbach S et al. Coronary computed tomographic angiography as a gatekeeper to invasive diagnostic and surgical procedures: results from the multicenter CONFIRM \(Coronary CT Angiography Evaluation for Clinical Outcomes: an International Multicenter\) registry. Journal of the American College of Cardiology 2012;60:2103-14.](#)
16. [Rana JS, Dunning A, Achenbach S et al. Differences in prevalence, extent, severity, and prognosis of coronary artery disease among patients with and without diabetes undergoing coronary computed tomography angiography: results from 10,110 individuals from the CONFIRM \(CORONARY CT ANGIOGRAPHY EVALUATION FOR CLINICAL OUTCOMES\): AN INTERNATIONAL MULTICENTER REGISTRY. Diabetes care 2012;35:1787-94.](#)
17. [Leipsic J, Taylor CM, Grunau G et al. Cardiovascular risk among stable individuals suspected of having coronary artery disease with no modifiable risk factors: results from an international multicenter study of 5262 patients. Radiology 2013;267:718-26.](#)
18. [Leipsic J, Taylor CM, Gransar H et al. Sex-based prognostic implications of nonobstructive coronary artery disease: results from the international multicenter CONFIRM study. Radiology 2014;273:393-400.](#)
19. [Dewey M, Rief M, Martus P et al. Evaluation of computed tomography in patients with atypical angina or chest pain clinically referred for invasive coronary angiography: randomised controlled trial. BMJ \(Clinical research ed\) 2016;355:i5441.](#)
20. [Litt HI, Gatsonis C, Snyder B et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. The New England journal of medicine 2012;366:1393-403.](#)
21. [Hoffmann U, Truong QA, Schoenfeld DA et al. Coronary CT angiography versus standard evaluation in acute chest pain. The New England journal of medicine 2012;367:299-308.](#)

22. [Goldstein JA, Gallagher MJ, O'Neill WW, Ross MA, O'Neil BJ, Raff GL. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. Journal of the American College of Cardiology 2007;49:863-71.](#)
23. [Goldstein JA, Chinnaiyan KM, Abidov A et al. The CT-STAT \(Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment\) trial. Journal of the American College of Cardiology 2011;58:1414-22.](#)
24. [Hulten E, Pickett C, Bittencourt MS et al. Outcomes after coronary computed tomography angiography in the emergency department: a systematic review and meta-analysis of randomized, controlled trials. Journal of the American College of Cardiology 2013;61:880-92.](#)
25. [Fihn SD, Gardin JM, Abrams J et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation 2012;126:e354-471.](#)
26. [Anderson JL, Adams CD, Antman EM et al. 2011 ACCF/AHA Focused Update Incorporated Into the ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2011;123:e426-579.](#)
27. [Halliburton SS, Abbara S, Chen MY et al. SCCT guidelines on radiation dose and dose-optimization strategies in cardiovascular CT. Journal of cardiovascular computed tomography 2011;5:198-224.](#)
28. [Einstein AJ, Elliston CD, Arai AE et al. Radiation dose from single-heartbeat coronary CT angiography performed with a 320-detector row volume scanner. Radiology 2010;254:698-706.](#)
29. [Schuhbaeck A, Achenbach S, Layritz C et al. Image quality of ultra-low radiation exposure coronary CT angiography with an effective dose <0.1 mSv using high-pitch spiral acquisition and raw data-based iterative reconstruction. European radiology 2013;23:597-606.](#)
30. [Xie JX, Shaw LJ. Measuring Diagnostic Health Care Costs in Stable Coronary Artery Disease: Should We Follow the Money? Annals of internal medicine 2016;165:147-8.](#)
31. [Goodacre S, Thokala P, Carroll C et al. Systematic review, meta-analysis and economic modelling of diagnostic strategies for suspected acute coronary syndrome. Health technology assessment \(Winchester, England\) 2013;17:v-vi, 1-188.](#)