Computed Tomography Coronary Angiogram; updates regarding evidence, clinical applications, and emerging technologies : A literature of review

Abstract:

Assessing of the coronary artery disease (CAD) especially coronary stenosis by coronary computed tomography angiography (CCTA) has shown a classic shift in the last decades. Recent advancements in cardiac CT have improved the quality of image and decreased exposure of patients to radiation. CCTA is a noninvasive technique for visualizing the anatomy of CAD. CCTA, in combination with newer techniques like plaque characterization, physiologic and functional evaluation, leads to accurate diagnostic and prognostic evaluation of any low to intermediate subjects for prevention.

Evidence strongly recommends the use of CCTA all over the stages of CAD, early from detecting of minute subclinical diseases up to the estimation of acute chest pain. Furthermore, CCTA can be used to noninvasively quantify plaque burden and identify high-risk plaque, which can help with diagnosis, prognosis, and treatment. This is especially important in the evaluation of CAD in immune-driven conditions with a higher prevalence of cardiovascular disease.

Furthermore, key findings from large cohort trials have contributed to a better understanding of cardiovascular disease risk as a function of overall coronary plaque burden and the morphological appearance of individual plaques. With the introduction of CT-derived fractional flow reserve, an anatomical and functional test will be established within a single modality. Recent research has been published that looks at the short-term impact of CT-derived fractional flow reserve on downstream care and clinical outcomes. Furthermore, machine learning is a concept that is increasingly being applied to diagnostic medicine. Emerging CCTA applications based on hemodynamic indices and plaque characterization may provide personalized risk assessment, influence disease detection, and guide therapy further.

This review provides an update on the evidence, clinical applications, and emerging technologies related to CCTA. We also discuss how CCTA could be used to characterize coronary atherosclerosis, stratify asymptomatic subjects' prognosis, and guide medical therapy.

Keywords: coronary computed tomography, coronary atherosclerotic plaque, Computed tomography, Acute chest pain, Acute coronary syndrome, Myocardial infarction, Diagnostic triage, Review

Introduction:

CCTA is a useful noninvasive imaging modality that is becoming more widely regarded as the most important and the first test for diagnosing (CAD) and has prognostic consequences for patient management. CCTA can also be used to imaging anatomic different stages of atherosclerosis, early from formation of the plaque along through its progression and rupture especially in epicardial coronary arteries (1, 2). Also, it allows the least exposure to radiation(3, 4). CCTA has shown to have a highest diagnostic accuracy when compared with invasive coronary angiography (ICA), which has been the gold standard for evaluating coronary artery disease until now(5, 6).

CCTA-derived tools aid in risk stratification and medical decision-making for patients with CAD by allowing researchers to better comprehend the progression of atherosclerotic plaque. Minimal radiation exposure, effective coronary characterization, and thorough imaging of atherosclerosis over time have all been made possible thanks to advancements in CCTA. As a result, CCTA provides a central platform for a multidisciplinary approach that includes immunology, pathology, radiology, and cardiology to improve patient care and further our understanding of CAD.

Although many factors such as (e.g., arrhythmia, increase heart rate, and a high coronary calcium burden) may restrict overall evaluability, significant technological advancements in recent decades have opened new perspectives in cardiac imaging, allowing acquisition in a matter of seconds and with higher spatial resolution(7-10). On a per patient basis, a sensitivity and specificity of 98 percent and 90 percent, respectively, have been reported using at least a 64-slice multidetector row. To rule out obstructive coronary artery disease, the increased sensitivity translates into a negative predictive value (NPV) ranging from 95 to 100 percent (CAD)(11).

In this context, the severity of coronary stenosis is regarded as a powerful, albeit contentious, prognostic marker of CAD prognosis. Invasive and noninvasive angiographic studies have shown a link between stenosis severity and clinical outcomes Min et al. analyzed a large consecutive cohort of patients without a history of CAD and found a similar incidence of all-cause death in nonobstructive and 1-vessel obstructive CAD as measured by CCTA in a recent study (HR: 1.62 vs. 1.75)(12). Furthermore, non-obstructing lesions are thought to be responsible for more than two-thirds of acute myocardial infarction (MI)(13). Other factors, in addition to the degree of stenosis, have an important role in the course of events. Several clinical biomarkers and imaging modalities have been studied over the last few decades in the hopes of being able to predict events in individuals with plaques at high risk of rupturing (vulnerable plaque). While ICA focuses solely on determining the degree of coronary stenosis (lumino-graphy), CCTA consistently evaluates overall plaque burden, classifies plaque subtypes, and identifies unfavorable characteristics of coronary high-risk plaques by examining both the wall and the lumen of the coronary artery(11, 14).

Indeed, because a variety of drugs, mostly those that affect the lipid profile and inflammation, can slow or even reverse plaque progression, the hunt for simple procedures that can detect these changes could provide physicians with a useful tool for patient management(4). World experts in CCTA gathered in November 2019 at the National Heart, Lung, and Blood Institute for a summit to discuss the newest discoveries in the area,

consolidate the current research, and debate the evolving clinical applications of CCTA. In 2013, the European Society of Cardiology recommended CCTA as a treatment option for individuals with suspected stable CAD and a low-to-intermediate pre-test CAD risk. The NICE-UK guidelines for the therapy of patients with new onset chest pain were recently updated, and CCTA was recommended as a first-line diagnostic test for those with stable angina who couldn't be ruled out by clinical examination alone. Moving beyond coronary stenosis, the current review will discuss the characteristics of coronary susceptible plaques as well as the capacity of CCTA to perform noninvasive plaque characterization with practical prognostic implications in patient risk assessment. In addition, existing and future therapeutic views are discussed.

Literature of review:

1- Vulnerable plaque and its Characteristics by CCTA:

According to histological investigations it was found that plaque component appears to play an important role in the development and clinical consequences of epicardial lesions. Experts agree that the form, content, and degree of inflammation of coronary atherosclerotic plaques matter more than the degree of luminal stenosis(11).

If advancements in acute coronary syndromes (ACS) are to be made, it is crucial to understand the precursor lesions of ACS15, 16). An abrupt luminal "thrombosis" produced by one of three diseases is assumed to be the etiology of the majority of ACS. The most prevalent cause of thrombosis is plaque rupture. Less common dense calcified nodules can pierce the fibrous cap and induce thrombosis. In both males and females, plaque rupture is the most common cause of coronary thrombosis, accounting for roughly 76 percent of all fatal coronary thrombi. As a result, while the phrase "vulnerable plaque" should be used to describe plaques that mimic all three types of luminal thrombosis, it is commonly used to describe a plaque that is prone to rupture(15, 16).

Intimal thickening is seen early in the illness process. Smooth muscle cells make up the early lesion, which is influenced by an increase in macrophage and lipid influx. The following stage is the establishment of a necrotic core and the development of a fibrous cap atheroma. The necrotic core contains a little quantity of lipid and apoptotic macrophages. Intraplaque hemorrhages are also common in this condition, and they contribute to the expansion of the lipid core. A stable fibrous covering may prevent the lesion from rupturing. If the fibrous cap loses matrix proteins and smooth muscle cells, a thin cap atheroma can form. CTCA (cardiac computed tomography angiography) has emerged as a potential method for viewing the arterial lumen directly(17).

2. prognosis after localizing and detecting degree of stenosis

CAD stenosis severity was classified as 0 (0 percent), 1 (1 percent to 24 percent), 2 (25 percent to 49 percent), 3 (50 percent to 69 percent), 4A (70 percent to 99 percent in 1 to 2 vessels), 4B (70 percent to 99 percent in 3 vessels or 50 percent left main), or 5 (50 percent left main) using the novel coronary artery disease-Reporting and Data System (CAD-RADS) scores used to standardize CCTA reporting (100 percent). It should come as no

surprise that the CAD-RADS system is good in identifying patients who are at risk for adverse outcomes. The cumulative 5-year event-free survival rate for CAD-RADS 0 to 5 varies from 95.2 percent to 69.3 percent (p 0.0001). Increased event risk is linked to higher scores (hazard ratio: 2.46 to 6.09; p 0.0001). Its inclusion in coronary CTA reports is considered a good opportunity to indorse evidence-based care(18).

High-risk plaque (HRP) characteristics have also been linked to a higher incidence of events in those with nonobstructive CAD. Beyond the standard clinical (Diamond & Forrester) and coronary (based on presence and degree of stenosis) scores used in clinical practice, a recent study found that using an integrated score easily obtained with CCTA (based on the presence of mixed and remodeled atherosclerotic plaques) may improve MACE prediction in symptomatic patients without prior cardiovascular history but with intermediate pretest likelihood of CAD. Despite the low prevalence of specific high-risk plaque features, our findings highlight the importance of a complete coronary evaluation. (19).

It's impossible to know which plaques with high-risk characteristics may rupture and create problems. However, the prognostic efficacy of risk assessment based solely on plaque anatomy has been partially disappointing due to a low positive predictive value.(20).

3. Therapeutic Viewpoint

Non-obstructive CAD patients who seeking CCTA are offered aspirin or statins as a preventive therapy. This was noticed to lower the risk of revascularization, mortality, and incident myocardial infarction (17, 21, 22). We mainly focus on low-density lipoprotein (LDL) level, if it is equal or near normal, we give statin therapy which lessens the progression of the plaque and progression of atherosclerosis(23, 24).

The Coronary Artery Calcification Score (CAC), which is significantly linked to an elevated risk of cardiovascular disease, has traditionally been used in risk stratification with cardiac CT. New CAC scoring methods that separate calcium density from volume may be able to provide a more accurate assessment of treatment changes.(25)

Inoue et al. in a study on 32 suspected patients with CAD who performed CCTA, proved that statin reduces plaque progression and core volume of necrosis. This was noticed mainly in the morphology of plaque specifically when there is change in lipid profile(25).

Although serial scans are not currently indicated for monitoring the therapeutic efficacy of medical therapies, plaque modulation as part of risk reduction is an option. Direct visualisation of atherosclerosis' natural course, as well as the identification of clinical determinants of plaque progression or regression, has the potential to shift the paradigm of CAD monitoring in low- to moderate-risk patients with suspected CAD, with the goal of providing earlier therapeutic strategies. It is reasonable to anticipate that therapeutic intervention that reduces plaque vulnerability will lead to plaque stability and, as a result, decrease cardiovascular event rates. More research is needed to fully understand this issue.

4-CCTA in Clinical Practice

In the United States, CCTA is used in a variety of settings, including the evaluation of suspected ACS in the emergency room, planning before cardiac surgery, monitoring ischemic functional tests, and preceding lower-

probability catheterization cases. CCTA can also be used as part of the cardiac evaluation process prior to liver transplantation(26, 27).

CCTA may be a better predictor of obstructive CAD compared to traditional functional testing. Clinical utility is driven by its ability to effectively rule out CAD. A CCTA-first strategy significantly reduced the occurrence of myocardial infarction (MI) and coronary heart disease death without increasing invasive testing(28, 29).

CCTA is critical in the emergency setting, where approximately 7 million emergency department visits for chest pain occur each year, accounting for 5.4 percent of all visits and $10 billion in annual spending. Despite the fact that the majority of these presentations are noncardiac in nature, missed diagnosis of acute MI accounts for significant mortality and a significant proportion (20%) of emergency medicine litigation costs(30). Several multicenter clinical studies in the emergency setting have shown that CCTA is a safe, quick, and effective tool for ruling out CAD in patients at low to intermediate risk who present with acute chest pain, and it is associated with a shorter time to diagnosis and a shorter length of stay(31).

Conclusions:

The ultimate purpose of events prediction is to monitor and guide the therapeutic strategy, and CCTA may be able to do so. Early detection of CAD, description of atherosclerotic process, assessment of ischemia-related plaque characteristics,, and assessment of "vulnerable plaque" are mandatory endpoints.

The ability of CCTA to quantify coronary plaque composition and identify coronary plaque morphology will aid in therapy monitoring and may one day become a cornerstone in treatment personalization. Emerging technologies that take advantage of lower radiation doses, advances in feature extraction, and computational fluid dynamics have increased CCTA's prognostic value.

References:

1. Moss AJ, Williams MC, Newby DE, Nicol ED. The Updated NICE Guidelines: Cardiac CT as the First-Line Test for Coronary Artery Disease. Current cardiovascular imaging reports. 2017;10(5):15.
2. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020;41(3):407-77.
3. Seitun S, De Lorenzi C, Cademartiri F, Buscaglia A, Travaglio N, Balbi M, et al. CT Myocardial Perfusion Imaging: A New Frontier in Cardiac Imaging. BioMed research international. 2018;2018:7295460-.
4. Andreini D, Martuscelli E, Guaricci AI, Carrabba N, Magnoni M, Tedeschi C, et al. Clinical recommendations on Cardiac-CT in 2015: a position paper of the Working Group on Cardiac-CT and Nuclear Cardiology of the Italian Society of Cardiology. Journal of cardiovascular medicine (Hagerstown, Md). 2016;17(2):73-84.
5. Abdulla J, Abildstrom SZ, Gotzsche O, Christensen E, Kober L, Torp-Pedersen C. 64-multislice detector computed tomography coronary angiography as potential alternative to conventional coronary angiography: a systematic review and meta-analysis. Eur Heart J. 2007;28(24):3042-50.
6. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, 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. J Am Coll Cardiol. 2008;52(21):1724-32.
7. Bittner DO, Mayrhofer T, Bamberg F, Hallett TR, Janjua S, Addison D, et al. Impact of Coronary Calcification on Clinical Management in Patients With Acute Chest Pain. Circ Cardiovasc Imaging. 2017;10(5):e005893.
8. Adile KK, Kapoor A, Jain SK, Gupta A, Kumar S, Tewari S, et al. Safety and efficacy of oral ivabradine as a heart rate-reducing agent in patients undergoing CT coronary angiography. Br J Radiol. 2012;85(1016):e424-e8.

9. Pontone G, Andreini D, Guaricci AI, Baggiano A, Fazzari F, Guglielmo M, et al. Incremental Diagnostic Value of Stress Computed Tomography Myocardial Perfusion With Whole-Heart Coverage CT Scanner in Intermediate- to High-Risk Symptomatic Patients Suspected of Coronary Artery Disease. JACC Cardiovascular imaging. 2019;12(2):338-49.
10. Lee JH, Hartaigh BÓ, Han D, Rizvi A, Lin FY, Min JK. Fractional Flow Reserve Measurement by Computed Tomography: An Alternative to the Stress Test. Interv Cardiol. 2016;11(2):105-9.
11. Carità P, Guaricci AI, Muscogiuri G, Carrabba N, Pontone G. Prognostic Value and Therapeutic Perspectives of Coronary CT Angiography: A Literature Review. BioMed research international. 2018;2018:6528238-.
12. Min JK, Dunning A, Lin FY, Achenbach S, Al-Mallah M, Budoff MJ, 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. J Am Coll Cardiol. 2011;58(8):849-60.
13. Corcoran D, Hennigan B, Berry C. Fractional flow reserve: a clinical perspective. Int J Cardiovasc Imaging. 2017;33(7):961-74.
14. Lu G, Ye W, Ou J, Li X, Tan Z, Li T, et al. Coronary Computed Tomography Angiography Assessment of High-Risk Plaques in Predicting Acute Coronary Syndrome. Front Cardiovasc Med. 2021;8:743538-.
15. Naghavi M, Libby P, Falk E, Casscells SW, Litovsky S, Rumberger J, et al. From vulnerable plaque to vulnerable patient: a call for new definitions and risk assessment strategies: Part I. Circulation. 2003;108(14):1664-72.
16. Fleg JL, Stone GW, Fayad ZA, Granada JF, Hatsukami TS, Kolodgie FD, et al. Detection of high-risk atherosclerotic plaque: report of the NHLBI Working Group on current status and future directions. JACC Cardiovascular imaging. 2012;5(9):941-55.
17. Carità P, Guaricci AI, Muscogiuri G, Carrabba N, Pontone G. Prognostic Value and Therapeutic Perspectives of Coronary CT Angiography: A Literature Review. BioMed research international. 2018;2018:6528238.
18. Kumar P, Bhatia M. Coronary Artery Disease Reporting and Data System: A Comprehensive Review. J Cardiovasc Imaging. 2022;30(1):1-24.
19. Kanda A, Velangi PS, Kenny B, Duval S, Nijjar PS. Interplay of CT Coronary Plaque Characteristics and Ischemia to Predict Adverse Outcomes. Radiol Cardiothorac Imaging. 2021;3(6):e210189-e.
20. Arbab-Zadeh A, Nakano M, Virmani R, Fuster V. Acute coronary events. Circulation. 2012;125(9):1147-56.
21. Arrey-Mbi TB, Klusewitz SM, Villines TC. Long-Term Prognostic Value of Coronary Computed Tomography Angiography. Current treatment options in cardiovascular medicine. 2017;19(12):90-.
22. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, et al. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet (London, England). 2005;366(9493):1267-78.
23. Nissen SE, Tuzcu EM, Schoenhagen P, Brown BG, Ganz P, Vogel RA, et al. Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial. Jama. 2004;291(9):1071-80.
24. Lardizabal JA, Deedwania PC. Benefits of statin therapy and compliance in high risk cardiovascular patients. Vasc Health Risk Manag. 2010;6:843-53.
25. Kim HJ, Kim JH, Joo MC. Association of Exercise Capacity, Cardiac Function, and Coronary Artery Calcification with Components for Metabolic Syndrome. BioMed research international. 2018;2018:4619867.
26. An J, Shim JH, Kim SO, Lee D, Kim KM, Lim YS, et al. Prevalence and prediction of coronary artery disease in patients with liver cirrhosis: a registry-based matched case-control study. Circulation. 2014;130(16):1353-62.
27. Kim YJ, Yong HS, Kim SM, Kim JA, Yang DH, Hong YJ, et al. Korean guidelines for the appropriate use of cardiac CT. Korean J Radiol. 2015;16(2):251-85.
28. Dedic A, Lubbers MM, Schaap J, Lammers J, Lamfers EJ, Rensing BJ, et al. Coronary CT Angiography for Suspected ACS in the Era of High-Sensitivity Troponins: Randomized Multicenter Study. J Am Coll Cardiol. 2016;67(1):16-26.
29. Goldstein JA, Chinnaiyan KM, Abidov A, Achenbach S, Berman DS, Hayes SW, et al. The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. J Am Coll Cardiol. 2011;58(14):1414-22.
30. Linde JJ, Hove JD, Sørgaard M, Kelbæk H, Jensen GB, Kühl JT, et al. Long-Term Clinical Impact of Coronary CT Angiography in Patients With Recent Acute-Onset Chest Pain: The Randomized Controlled CATCH Trial. JACC Cardiovascular imaging. 2015;8(12):1404-13.

31. Nieman K, Hoffmann U. Cardiac computed tomography in patients with acute chest pain. Eur Heart J. 2015;36(15):906-14.