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The Evolving Role of Multi-Slice Computed Tomography in Risk Stratification and Management of Stable Coronary Artery Disease

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ABSTRACT

***Background*:** Stable coronary artery disease (CAD), now classified within the spectrum of chronic coronary syndromes, remains a major cause of morbidity and mortality worldwide. Risk stratification and optimal management are essential to prevent adverse cardiovascular events. Non-invasive diagnostic modalities have revolutionized the assessment of CAD, with multi-slice computed tomography (MSCT) emerging as a pivotal tool in both anatomical and functional evaluation. This review examines the evolving role of MSCT in risk stratification and management of stable CAD, highlighting its integration with traditional and contemporary non-invasive tests, advances in plaque characterization, and its potential to guide invasive assessment. A literature review was conducted focusing on the utility, strengths, and limitations of MSCT, calcium scoring, and advanced plaque metrics. Comparative analysis with other modalities—such as stress echocardiography, cardiac magnetic resonance imaging, SPECT, and PET—was included. Emphasis was placed on clinical studies, guidelines, and meta-analyses addressing prognostic implications, diagnostic accuracy, and therapeutic decision-making.

MSCT angiography provides high-resolution anatomical visualization of coronary arteries, with the ability to quantify plaque burden, composition, and remodeling. Coronary calcium scoring offers prognostic value for asymptomatic and symptomatic patients. Emerging metrics, such as low attenuation plaque volume and remodeling index, refine risk assessment beyond simple stenosis quantification. When combined with functional data from FFR-CT, MSCT enhances the diagnostic pathway and can reduce unnecessary invasive procedures. Comparative studies reveal high negative predictive value, although limitations in heavily calcified vessels persist. Integrating MSCT findings with clinical risk models optimizes patient selection for invasive angiography and revascularization. Despite advances in alternative imaging modalities, MSCT remains central due to its comprehensive anatomical and evolving functional capabilities.

Conclusion: Multi-slice CT has transitioned from a purely anatomical tool to an integral component of modern CAD management, bridging the gap between risk prediction, anatomical assessment, and functional evaluation. Ongoing technological advances and increasing evidence for prognostic relevance support its expanding role in personalized care for patients with stable CAD.

Keywords: Multi-Slice Computed Tomography, Stable Coronary Artery Disease

INTRODUCTION

Introduction

Stable coronary artery disease (CAD) is a leading cause of morbidity and mortality globally, warranting precise diagnostic and therapeutic strategies. Traditionally, the assessment of lesion significance relied heavily on invasive coronary angiography, which, while definitive, carries procedural risks and costs. The growing burden of CAD necessitates risk stratification methods that are accurate, non-invasive, and widely accessible. In recent years, multi-slice computed tomography (MSCT) has emerged as a transformative modality in cardiovascular imaging, enabling detailed anatomical assessment of coronary arteries and advanced characterization of atherosclerotic plaque. Notably, MSCT has transcended the role of mere stenosis detection, offering insights into plaque composition, volume, and vulnerability markers, such as low attenuation plaque, spotty calcification, and remodeling index. These features have been increasingly recognized for their prognostic value and potential to guide clinical decision-making, particularly regarding the need for invasive physiological assessment of lesion significance. Despite advances in functional imaging, a critical gap persists in integrating anatomical plaque criteria into routine workflows for stable CAD. This review aims to evaluate the evolving role of MSCT-derived plaque characteristics in influencing the invasive assessment and management of coronary lesions in stable CAD, addressing current evidence, challenges, and future perspectives [1,2].

Ischemic Heart Diseases and Chronic Coronary Syndromes

Ischemic heart disease, encompassing both acute and chronic presentations, remains a principal cause of cardiovascular death worldwide. Chronic coronary syndromes, the new terminology in recent guidelines, reflect the evolving understanding of coronary artery disease as a dynamic process rather than a static entity. Stable CAD is characterized by a predictable pattern of chest pain or equivalent symptoms, often provoked by exertion and relieved by rest, corresponding to fixed atherosclerotic obstructions. The underlying pathology involves progressive plaque buildup, with the risk of destabilization and transition to acute coronary events. A comprehensive evaluation of patients with suspected chronic coronary syndromes involves clinical risk assessment, non-invasive testing, and, where indicated, invasive coronary angiography. Recent advances have underscored the importance of not only quantifying luminal stenosis but also characterizing plaque features that may confer increased risk for future events. In this context, MSCT provides a unique platform for non-invasively visualizing both the extent and nature of coronary atherosclerosis, which may better predict adverse outcomes than stenosis severity alone [3,4].

Non-Invasive Diagnostic Tests of Stable CAD

Non-invasive diagnostic strategies for stable CAD have advanced considerably, providing both anatomical and functional data. Traditional exercise ECG remains widely used but is limited by sensitivity and specificity. Imaging-based tests, including stress echocardiography, cardiac magnetic resonance imaging (CMRI), single-photon emission computed tomography (SPECT), and positron emission tomography (PET), offer incremental value by detecting myocardial ischemia. Anatomical imaging, led by MSCT coronary angiography, enables direct visualization of coronary anatomy and plaque characteristics, complementing functional modalities. Guidelines now recommend tailoring diagnostic pathways to individual patient risk profiles, pre-test probability, and availability of technology. The integration of plaque criteria, especially as assessed by MSCT, into these algorithms is an area of active investigation, with the potential to refine patient selection for invasive angiography and optimize outcomes [5,6].

CT Angiography of Coronary Arteries with Calculation of Coronary Calcium Score

Coronary CT angiography (CCTA) has become the cornerstone of anatomical evaluation in stable CAD. It offers high-resolution images that allow for the assessment of coronary artery lumen, wall, and plaque morphology. The coronary calcium score, derived from non-contrast CT, quantifies the burden of calcified plaque and correlates strongly with future cardiovascular risk. While a zero calcium score suggests low risk, higher scores are associated with greater atherosclerotic burden and adverse outcomes. Importantly, MSCT goes beyond calcium scoring, allowing for the identification of non-calcified and mixed plaques, which are often more vulnerable to rupture. Recent studies have shown that specific plaque features—such as low attenuation, spotty calcification, and positive remodeling—identified on MSCT are associated with higher rates of ischemia and future events, often independently of stenosis severity. As such, MSCT-derived plaque criteria have the potential to improve the accuracy of risk stratification and guide the need for invasive assessment [7,8].

Stress Echocardiography (Exercise or Pharmacologic)

Stress echocardiography is a widely used functional imaging modality for the evaluation of stable CAD. It relies on the detection of wall motion abnormalities induced by exercise or pharmacologic stress, serving as a surrogate for ischemia. The modality is valued for its safety, accessibility, and lack of ionizing radiation. However, its sensitivity can be limited in patients with baseline wall motion abnormalities, poor acoustic windows, or multi-vessel disease. While stress echo provides information on the hemodynamic significance of lesions, it does not offer anatomical detail or plaque characterization. In clinical practice, the combination of anatomical data from MSCT and functional assessment from stress echo can enhance diagnostic accuracy, particularly in intermediate-risk patients. The integration of plaque criteria from MSCT may also help identify patients with subclinical disease or vulnerable plaques who would otherwise be missed by functional imaging alone [9,10].

Stress Cardiac Magnetic Resonance Imaging (CMRI)

Stress cardiac magnetic resonance imaging (CMRI) offers high spatial resolution and tissue characterization, enabling the detection of myocardial ischemia and scar. It is considered the gold standard for assessing myocardial viability and perfusion, with robust prognostic value in stable CAD. Unlike other modalities, CMRI provides comprehensive assessment without ionizing radiation, making it attractive for serial follow-up. However, its use is limited by availability, cost, and contraindications such as implanted devices or claustrophobia. CMRI does not provide direct visualization of coronary arteries or plaque characteristics, a gap that is addressed by MSCT. Recent studies suggest that combining anatomical insights from MSCT, particularly regarding high-risk plaque features, with functional data from CMRI, may improve risk stratification and management decisions in stable CAD [11,12].

Single Photon Emission Computed Tomography (SPECT)

Single-photon emission computed tomography (SPECT) is a mainstay of nuclear cardiology, widely used for the non-invasive evaluation of myocardial perfusion. SPECT provides functional assessment by identifying areas of reversible ischemia, with established prognostic significance. The modality is valued for its broad availability, but its accuracy can be limited by attenuation artifacts, relatively low spatial resolution, and radiation exposure. Like other functional tests, SPECT cannot assess coronary anatomy or plaque morphology. Thus, it may fail to detect high-risk atherosclerotic plaques that do not yet cause significant ischemia. Emerging data support the complementary use of SPECT and MSCT, with the latter offering crucial plaque characterization that can inform the likelihood of functionally significant lesions and guide the need for invasive evaluation [13,14].

Stress Positron Emission Tomography (PET)

Stress positron emission tomography (PET) provides superior sensitivity and specificity compared to SPECT for the detection of myocardial ischemia, due to its high spatial resolution and ability to quantify absolute myocardial blood flow. PET imaging has proven particularly useful in multi-vessel disease and microvascular dysfunction. However, like other functional modalities, PET does not assess coronary anatomy or plaque features directly. Integration of MSCT-derived plaque criteria with PET-based functional data may provide a more complete picture of disease burden and risk, helping to identify patients who would benefit from invasive coronary angiography or physiological assessment. This combined approach can optimize resource utilization and improve patient outcomes [15,16].

Anatomical Non-Invasive Examinations

Anatomical non-invasive examinations have transformed the diagnostic landscape in stable CAD. Among these, MSCT angiography stands out for its ability to provide high-resolution images of coronary arteries, permitting visualization of both the lumen and vessel wall. Beyond the identification of stenosis, MSCT enables detailed analysis of plaque composition, burden, and markers of instability. The technique has demonstrated high negative predictive value, allowing for safe exclusion of significant CAD in low- to intermediate-risk populations. Incorporating advanced plaque criteria such as low attenuation, positive remodeling, and spotty calcification further refines risk assessment and informs downstream management, including the necessity and timing of invasive procedures [17,18].

Multi-Slice CT Angiography of Coronary Arteries

Multi-slice computed tomography angiography (MSCT or CCTA) has redefined the non-invasive evaluation of coronary artery disease, offering rapid image acquisition and high spatial resolution. Modern MSCT scanners, equipped with 64 or more detector rows, allow clinicians to visualize even small branches of the coronary arteries and detect subtle atherosclerotic changes that precede significant stenosis. This capability has expanded the use of CCTA beyond simple stenosis detection, making it a valuable tool for early disease identification, serial assessment of plaque progression or regression, and comprehensive mapping of the coronary vasculature in a single examination. This has particular relevance in stable CAD, where detailed anatomical information supports nuanced risk stratification and guides management decisions [19].

The diagnostic strength of MSCT angiography lies in its ability to differentiate between plaque types and assess their distribution along the coronary tree. Calcified, non-calcified, and mixed plaques have different clinical implications, with non-calcified plaques being more likely to rupture and lead to acute coronary syndromes. MSCT provides detailed visualization of these morphologies, quantifies plaque burden, and highlights regions of the artery undergoing positive remodeling, an early marker of vulnerability. Additionally, CCTA enables evaluation of pericoronary adipose tissue and vessel wall characteristics, which are increasingly recognized as contributors to coronary risk but are not visible on traditional invasive angiography [20].

Beyond anatomical imaging, MSCT is instrumental in identifying high-risk plaque features that are associated with future cardiac events. These features include low attenuation, spotty calcification, and positive remodeling. Their identification can alert clinicians to the presence of vulnerable plaques even in the absence of severe luminal narrowing. Multiple studies have demonstrated that the presence of these high-risk criteria on CCTA is predictive of downstream ischemia, as confirmed by invasive functional assessment like fractional flow reserve (FFR). Thus, MSCT is not only a diagnostic tool but also an important risk stratification modality, guiding the decision to proceed with or defer invasive testing in patients with stable CAD [21].

The robust negative predictive value (NPV) of MSCT angiography has led to its widespread adoption as a frontline test to exclude significant CAD, particularly in patients with low to intermediate pre-test probability. In these populations, a normal CCTA virtually excludes the need for invasive angiography, reducing unnecessary procedures and associated risks. Large clinical trials, such as PROMISE and SCOT-HEART, have shown that an MSCT-guided strategy improves patient outcomes, refines downstream resource utilization, and enhances identification of individuals who derive the most benefit from invasive assessment or revascularization [22].

A rapidly emerging application of MSCT is the non-invasive prediction of functionally significant stenoses, which previously required invasive assessment. Recent advances have demonstrated that MSCT-derived plaque characteristics—including positive remodeling, low attenuation, and spotty calcification—strongly predict functional significance as measured by FFR or iFR. These insights allow clinicians to identify lesions most likely to cause ischemia and target invasive assessments more effectively, moving toward a more personalized and efficient approach to stable CAD management [23].

Coronary Calcium Score

Coronary artery calcium (CAC) scoring is a well-established tool derived from non-contrast CT that quantifies the extent of calcified plaque in the coronary arteries. This simple, reproducible metric correlates strongly with overall atherosclerotic burden and has been validated as a robust predictor of long-term cardiovascular events in both asymptomatic and symptomatic individuals. A calcium score of zero confers a very low risk of major adverse cardiovascular events over the next 5–10 years, providing reassurance to patients and physicians and supporting the deferral of further testing in select cases [24].

Despite its strengths, CAC scoring does not capture the full spectrum of atherosclerotic disease. Non-calcified and mixed plaques, which are often more prone to rupture and cause acute events, are not detected by calcium scoring alone. This is a critical limitation, especially in younger patients or those with high-risk features but low calcium scores. The advent of MSCT allows for simultaneous assessment of both coronary calcium and detailed plaque characteristics, including non-calcified plaque burden, positive remodeling, and high-risk features. This dual assessment enhances risk stratification, identifying individuals who may appear low-risk by calcium score alone but harbor vulnerable, non-calcified plaques [25].

The clinical value of CAC extends to guiding preventive therapies and influencing lifestyle or pharmacologic interventions. Patients with high calcium scores derive greater benefit from statin therapy, aggressive risk factor modification, and closer

follow-up, as demonstrated in large population-based studies. Conversely, a zero calcium score can justify a conservative approach, avoiding unnecessary invasive testing and reducing healthcare costs. In symptomatic patients, CAC scoring combined with CCTA offers a comprehensive anatomical and prognostic profile, supporting shared decision-making and personalized management strategies [26].

Recent research has highlighted the added value of integrating calcium score with MSCT-derived plaque characterization. Patients with high calcium scores who also have features such as low attenuation or spotty calcification are at particularly increased risk for adverse outcomes and may warrant early invasive assessment. Conversely, those with low calcium scores but non-calcified high-risk plaques identified on CCTA may also be considered for closer monitoring or further functional evaluation. This integrated approach underscores the evolving role of MSCT as a multi-dimensional imaging platform in stable CAD [27].

Low Attenuation Plaque Volume

Low attenuation plaque (LAP) is defined on MSCT as a region within an atherosclerotic plaque with a CT density typically less than 30 Hounsfield units, signifying a lipid-rich necrotic core. This plaque component is clinically significant because it has been associated with increased vulnerability to rupture, which is the primary event leading to acute coronary syndromes. Identifying LAP on MSCT offers a non-invasive means of flagging high-risk lesions, even when overall stenosis appears moderate or non-obstructive by luminal narrowing criteria. Numerous studies have validated the prognostic impact of LAP volume, linking it to an elevated risk of future cardiac events and the need for urgent revascularization [28].

Quantifying LAP volume provides additional risk stratification beyond simple visual assessment. Sophisticated post-processing software now allows for automated or semi-automated measurement of low attenuation regions, enabling reproducible and serial evaluations in both clinical and research settings. The relationship between LAP volume and ischemic risk has been substantiated by findings that correlate larger LAP burdens with the presence of functionally significant lesions on invasive FFR. This suggests that plaque composition, rather than luminal stenosis alone, should drive clinical decisions about the necessity of invasive assessment and intervention in patients with stable CAD [29].

Integrating LAP assessment with other high-risk features, such as positive remodeling and spotty calcification, further refines risk prediction. Lesions exhibiting multiple high-risk characteristics have been shown to confer particularly poor outcomes, prompting consideration of early invasive physiological assessment or closer clinical monitoring. In clinical practice, the identification of substantial LAP volume on MSCT can therefore guide both the urgency and modality of subsequent evaluation, supporting a move toward more personalized and biologically informed CAD management [30].

Remodeling Index (RI)

The remodeling index (RI) is a quantitative marker of vessel adaptation to plaque accumulation, calculated as the ratio of vessel diameter at the site of maximal plaque burden to a reference segment. Positive remodeling, defined by an RI >1.1, reflects compensatory arterial enlargement and is a well-established feature of vulnerable plaques. MSCT offers the unique advantage of non-invasively measuring the RI, allowing clinicians to detect positive remodeling patterns that may be invisible on traditional angiography, where only luminal contours are visualized. The presence of positive remodeling is independently associated with higher rates of ischemia and adverse events, even in lesions without severe stenosis [31].

The pathophysiological basis for positive remodeling involves the vessel's attempt to preserve luminal area in response to a growing plaque. However, this compensatory process also facilitates plaque instability, as positively remodeled plaques tend to be richer in lipid content and inflammatory cells, and more likely to have thin, rupture-prone fibrous caps. In studies comparing MSCT to intravascular ultrasound (IVUS) and optical coherence tomography (OCT), the identification of positive remodeling by MSCT correlates well with high-risk histological features and the likelihood of future cardiac events [32].

Clinical implementation of RI assessment on MSCT enhances the stratification of patients who may benefit from invasive physiological evaluation. When used in conjunction with other high-risk plaque criteria—such as low attenuation and spotty calcification—the predictive accuracy for functionally significant lesions is substantially improved. As evidence accumulates, there is growing support for routine reporting of RI in CCTA interpretations, especially for patients with stable CAD and borderline or ambiguous stenoses, as it provides incremental prognostic value over stenosis severity alone [33].

Plaque Volume & Spotty Calcification

Total plaque volume quantification, enabled by MSCT, has become a cornerstone for evaluating overall atherosclerotic burden. Studies have shown that individuals with a greater plaque volume are at a higher risk for future cardiovascular events, independent of the degree of luminal narrowing. This quantitative approach allows for objective monitoring of disease progression or regression over time, making it invaluable for assessing response to therapy in both clinical and research contexts [34].

Spotty calcification is defined as small, discrete foci of calcium (usually <3 mm in size) within a predominantly non-calcified plaque. This feature, readily detected by MSCT, is strongly associated with plaque vulnerability and adverse outcomes. Spotty calcification reflects active microcalcification and ongoing inflammation, processes that weaken the fibrous cap and predispose to rupture. Numerous studies have linked the presence of spotty calcification on CCTA to an increased likelihood of ischemia-producing lesions and acute coronary syndromes, even when the degree of stenosis is not severe [35].

The integration of total plaque volume measurement and spotty calcification assessment with other MSCT plaque features—such as low attenuation and remodeling index—enables a nuanced risk profile for each patient. This comprehensive evaluation has been shown to predict both anatomical and functional significance of lesions, guiding decisions on whether invasive physiological testing (such as FFR or iFR) is warranted. By identifying patients with a high burden of vulnerable plaque characteristics, clinicians can more accurately target invasive interventions, improve outcomes, and personalize the management of stable CAD [36].

Invasive Coronary Angiography and Physiological Assessment of Coronary Artery Stenosis

Invasive coronary angiography remains the reference standard for delineating coronary anatomy and defining the presence and location of obstructive lesions. However, it provides limited information regarding plaque composition or the likelihood of plaque rupture, and relies on visual assessment that may underestimate or overestimate true functional severity. As a result, there has been a paradigm shift toward integrating physiological measurements with anatomical findings to guide revascularization decisions in stable CAD [37].

Physiological assessment of coronary stenosis, typically performed using pressure wire-based measurements such as fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR), has established itself as a gold standard for determining which lesions are truly ischemia-producing and likely to benefit from intervention. These indices measure the hemodynamic significance of stenoses, with values below defined thresholds indicating functionally important disease. The use of FFR- or iFR-guided strategies in clinical practice has been shown to improve patient outcomes, reduce unnecessary stenting, and optimize resource utilization [38].

The impact of MSCT-derived plaque features on invasive assessment has become a topic of increasing interest. Recent evidence demonstrates that high-risk plaque criteria on MSCT—such as low attenuation, positive remodeling, and spotty calcification—correlate strongly with lesions that are hemodynamically significant on invasive FFR or iFR. This has led to growing advocacy for a "plaque-to-physiology" approach, where MSCT findings direct the selection of lesions for invasive testing, rather than relying solely on luminal stenosis severity. Such integration reduces unnecessary invasive procedures and targets interventions to those most likely to benefit [39].

Emerging data also suggest that incorporating MSCT plaque characterization into the invasive workflow can improve diagnostic efficiency and outcomes. For example, in patients with intermediate-grade lesions by angiography, the identification of high-risk features on MSCT can support decisions to proceed directly to physiological assessment, while low-risk plaque morphology may justify a more conservative, medical management approach. This combined anatomical and physiological assessment represents the future direction of stable CAD management, facilitating personalized and evidence-based care [40].

Physiological Assessment of Borderline Coronary Stenosis by FFR & iFR

Borderline coronary stenoses, typically defined as luminal narrowings between 40% and 70%, pose a significant diagnostic dilemma in clinical cardiology. Anatomical imaging alone is often insufficient for determining the true ischemic potential of these lesions, as the relationship between percentage stenosis and physiological significance is complex and influenced by factors such as vessel size, plaque composition, and downstream microvascular function. As a result, functional evaluation with pressure wire-based indices—fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR)—has become central in assessing

these borderline lesions, ensuring that revascularization is reserved for those who will derive meaningful symptomatic and prognostic benefit [41].

FFR and iFR are invasive, wire-based techniques that provide lesion-specific information about the impact of a stenosis on myocardial blood flow. FFR involves measuring the pressure difference across a coronary stenosis during pharmacologically induced hyperemia, with values ≤0.80 indicating hemodynamically significant obstruction. iFR, in contrast, measures the pressure ratio during the diastolic wave-free period without the need for hyperemia, and a value ≤0.89 is generally considered abnormal. Both techniques have been shown in randomized controlled trials to reduce unnecessary revascularizations and improve clinical outcomes by ensuring that only functionally important lesions are targeted [42].

Recent evidence supports the concept that MSCT-derived plaque characteristics can enhance the triage of borderline stenoses for physiological assessment. Lesions displaying high-risk features such as low attenuation, positive remodeling, or spotty calcification on CCTA are more likely to have abnormal FFR or iFR values, indicating true ischemia. This suggests that anatomical plaque analysis on MSCT can serve as a gatekeeper, identifying which borderline lesions should proceed to invasive physiological assessment. Integrating these non-invasive insights with invasive physiology streamlines the diagnostic pathway and supports a precision medicine approach in stable CAD [43].

Moreover, the ability of MSCT to provide a comprehensive plaque profile is particularly valuable in patients with multi-vessel disease or complex coronary anatomy, where the selection of lesions for invasive testing is less straightforward. In these scenarios, the presence of multiple high-risk plaque criteria across different vessels may identify patients at highest overall risk and prioritize the most clinically relevant targets for revascularization. As technology advances, it is expected that automated algorithms combining anatomical and physiological data will further refine the assessment of borderline stenoses, improving patient outcomes while minimizing unnecessary interventions [44].

Fractional Flow Reserve (FFR): Integration with MSCT

Fractional flow reserve (FFR) has long been the gold standard for the functional assessment of coronary stenoses, but its invasive nature and procedural risks have limited its widespread use, particularly in stable outpatients. The recent development of non-invasive FFR estimation using MSCT datasets (FFR-CT) represents a major advance, enabling combined anatomical and functional evaluation from a single imaging study. FFR-CT uses computational fluid dynamics to simulate blood flow and pressure in three dimensions, providing vessel-specific FFR values that closely correlate with invasive measurements [45].

Multiple clinical studies have validated the diagnostic accuracy of FFR-CT. When compared to invasive FFR, FFR-CT demonstrates high sensitivity and specificity for the detection of functionally significant stenoses, particularly when combined with MSCT plaque characterization. Importantly, FFR-CT can reclassify a substantial proportion of intermediate or ambiguous lesions, reducing both false positives and unnecessary invasive angiographies. This has led to the incorporation of FFR-CT into recent international guidelines as an acceptable alternative to traditional functional testing in selected patients with stable CAD [46].

The synergy between anatomical plaque assessment and FFR-CT is especially valuable for identifying lesions that are not only anatomically severe but also biologically high-risk. Lesions with low attenuation, positive remodeling, or spotty calcification on MSCT are more likely to have abnormal FFR-CT values, providing an integrated risk profile that encompasses both structural and functional elements. This comprehensive approach facilitates a more informed, evidence-based decision regarding the need for revascularization, particularly in cases where conventional anatomical or functional tests alone are equivocal [47].

Ongoing research is focused on improving the predictive value of FFR-CT by incorporating advanced plaque analytics, artificial intelligence, and machine learning algorithms. These tools have the potential to automate plaque segmentation, enhance risk prediction, and streamline workflow, ultimately making non-invasive FFR assessment more accessible and reproducible. As evidence continues to accumulate, the integration of MSCT-derived plaque features and FFR-CT is poised to become a standard of care in the evaluation of stable CAD, moving closer to a truly personalized approach [48].

The Evolving Role of Multi-Slice Computed Tomography in Risk Stratification and Management of Stable Coronary

Artery Disease

The role of multi-slice computed tomography in stable CAD management has evolved rapidly, reflecting advances in scanner technology, image reconstruction, and clinical evidence. Initially adopted as a "rule-out" test for obstructive disease, MSCT is now recognized as a central tool for comprehensive risk stratification and management. Its ability to combine anatomical, compositional, and functional information in a single study represents a major leap forward in the approach to chronic coronary syndromes [49].

MSCT's unique value lies in its capacity to characterize the full spectrum of coronary atherosclerosis, from early non-calcified lesions to complex, high-risk plaques. By identifying features such as low attenuation, spotty calcification, and positive remodeling, MSCT provides incremental prognostic information beyond simple stenosis assessment. These plaque criteria have been shown to predict not only the likelihood of functional significance (as measured by FFR or iFR) but also the risk of future acute coronary events. As a result, clinicians can now tailor invasive assessment, medical therapy, and lifestyle interventions based on a more nuanced understanding of individual risk [50].

Recent guidelines reflect this paradigm shift, emphasizing the role of MSCT and plaque analysis in the evaluation of stable CAD. The integration of MSCT findings with clinical risk models, coronary calcium scoring, and non-invasive functional testing enables a comprehensive, multi-dimensional risk profile for each patient. This supports shared decision-making and promotes individualized management strategies, including the judicious use of invasive angiography and revascularization only when truly warranted [51].

Future directions for MSCT in stable CAD include the adoption of artificial intelligence to enhance image analysis, the use of serial imaging to monitor disease progression or regression, and the incorporation of emerging biomarkers (such as perivascular fat attenuation) to further refine risk prediction. As technology and evidence evolve, MSCT is expected to play an ever-expanding role in bridging the gap between anatomical and physiological assessment, ultimately improving outcomes and quality of life for patients with chronic coronary syndromes [52].

Limitations and Future Directions

Despite its transformative impact, MSCT is not without challenges. Image quality can be compromised by high heart rates, arrhythmias, obesity, or excessive coronary calcification, potentially leading to artifacts or overestimation of stenosis severity. These technical limitations can affect diagnostic accuracy, particularly in older patients or those with complex coronary anatomy. Efforts to mitigate these issues include heart rate control, advanced scanner technology (such as dual-source CT), and improved reconstruction algorithms, which collectively continue to expand the patient population eligible for high-quality MSCT imaging [53].

Radiation exposure, while historically a concern, has decreased significantly with the advent of iterative reconstruction, prospective gating, and newer scanner generations. Modern protocols can now achieve diagnostic-quality images with radiation doses approaching those of standard chest x-rays. Nevertheless, judicious use of MSCT is still advocated, especially in younger patients or those requiring serial imaging. The ongoing development of ultra-low dose protocols and photon-counting CT holds promise for further minimizing radiation risk without compromising image quality [54].

Another limitation relates to the reproducibility and standardization of plaque feature assessment across different centers and platforms. Variability in post-processing techniques, thresholds for defining low attenuation or spotty calcification, and reporting conventions may hinder the widespread adoption of advanced plaque analytics. Large, prospective studies are needed to validate novel imaging biomarkers and to establish consensus definitions that can be reliably implemented in clinical practice. Furthermore, ongoing research is exploring the integration of artificial intelligence and machine learning, which may automate and standardize plaque quantification, enhance workflow, and allow for more objective risk prediction [55].

As MSCT becomes increasingly central to stable CAD management, future directions include expanding its prognostic utility by integrating imaging biomarkers with clinical, genetic, and biochemical risk factors. Serial MSCT imaging may also play a key role in monitoring the response to preventive therapies or interventions. With continuous improvements in technology and evidence, MSCT is positioned to further refine the precision and personalization of coronary artery disease management in the coming years [56-58].

Conclusion

Multi-slice computed tomography angiography (MSCT) has fundamentally changed the approach to risk stratification and management in patients with stable coronary artery disease. By enabling detailed anatomical, compositional, and functional evaluation of coronary lesions, MSCT bridges the gap between non-invasive and invasive assessment. Advanced plaque features—such as low attenuation, positive remodeling, and spotty calcification—provide powerful prognostic information, helping to guide the selection of patients for further invasive physiological assessment and revascularization. When integrated with other clinical and imaging data, MSCT supports a precision medicine approach that tailors diagnostic and therapeutic strategies to the individual risk profile of each patient. The evolution of MSCT, including the advent of FFR-CT, artificial intelligence, and automated plaque analytics, promises to further enhance its utility and accessibility in clinical practice. As evidence grows and technology advances, the integration of MSCT-derived plaque criteria into standard care pathways will likely continue to improve outcomes, reduce unnecessary invasive procedures, and optimize the management of stable CAD. Ultimately, the evolving role of MSCT in risk stratification and management exemplifies the shift toward more personalized, data-driven cardiovascular care.

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REFERENCES

1. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2019;40(2):87-165.
2. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020;41(3):407-477.
3. Libby P, Ridker PM, Hansson GK. Inflammation in atherosclerosis: from pathophysiology to practice. J Am Coll Cardiol. 2009;54(23):2129-2138.
4. Falk E, Nakano M, Bentzon JF, et al. Update on acute coronary syndromes: the pathologists' view. Eur Heart J. 2013;34(10):719-728.
5. Patel MR, Peterson ED, Dai D, et al. Low diagnostic yield of elective coronary angiography. N Engl J Med. 2010;362(10):886-895.
6. Task Force Members, Montalescot G, Sechtem U, et al. 2013 ESC guidelines on the management of stable coronary artery disease. Eur Heart J. 2013;34(38):2949-3003.
7. Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. N Engl J Med. 2008;358(13):1336-1345.
8. Budoff MJ, Nasir K, Kinney GL, et al. Coronary artery and thoracic calcium on noncontrast thoracic CT scans: comparison of ungated and gated examinations in the Multi-Ethnic Study of Atherosclerosis. Radiology. 2006;241(3):687-693.
9. Sicari R, Nihoyannopoulos P, Evangelista A, et al. Stress echocardiography expert consensus statement. Eur Heart J. 2008;29(21):2773-2792.
10. Marwick TH. Stress echocardiography. Heart. 2003;89(1):113-118.
11. Kelle S, Nagel E, Voss A, et al. A novel MRI algorithm for fast assessment of global and regional myocardial function. J Magn Reson Imaging. 2008;27(2):375-383.
12. Greenwood JP, Maredia N, Younger JF, et al. Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. Lancet. 2012;379(9814):453-460.
13. Shaw LJ, Berman DS, Maron DJ, et al. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial

nuclear substudy. Circulation. 2008;117(10):1283-1291.
14. Hachamovitch R, Berman DS, Shaw LJ, et al. Incremental prognostic value of myocardial perfusion SPECT for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. Circulation. 1998;97(6):535-543.
15. Schindler TH, Facta AD, Prior JO, et al. PET-measured heterogeneity in myocardial blood flow in patients with risk factors for coronary artery disease. J Nucl Med. 2003;44(6):915-922.
16. Danad I, Raijmakers PG, Driessen RS, et al. Comparison of coronary CT angiography, SPECT, PET, and hybrid imaging for diagnosis and management of coronary artery disease. J Nucl Med. 2017;58(1):66-73.
17. Cury RC, Abbara S, Achenbach S, et al. CAD-RADS™: Coronary Artery Disease – Reporting and Data System. An expert consensus document of SCCT, ACR, and NASCI. J Cardiovasc Comput Tomogr. 2016;10(4):269-281.
18. Motoyama S, Sarai M, Harigaya H, et al. Computed tomographic angiography characteristics of atherosclerotic plaques subsequently resulting in acute coronary syndrome. J Am Coll Cardiol. 2009;54(1):49-57.
19. Leipsic J, Abbara S, Achenbach S, et al. SCCT guidelines for the interpretation and reporting of coronary CT angiography: A report of the Society of Cardiovascular Computed Tomography Guidelines Committee. J Cardiovasc Comput Tomogr. 2014;8(5):342-358.
20. Otsuka K, Fukuda S, Tanaka A, et al. Napkin-ring sign on coronary CT angiography for the prediction of acute coronary syndrome. JACC Cardiovasc Imaging. 2013;6(4):448-457.
21. Maurovich-Horvat P, Hoffmann U, Voros S, et al. The napkin-ring sign: CT signature of high-risk coronary plaques? JACC Cardiovasc Imaging. 2010;3(4):440-444.
22. Douglas PS, Hoffmann U, Patel MR, et al. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med. 2015;372(14):1291-1300.
23. Williams MC, Moss AJ, Dweck M, et al. Coronary artery plaque characteristics associated with adverse outcomes in the SCOT-HEART study. J Am Coll Cardiol. 2019;73(3):291-301.
24. Hecht HS. Coronary artery calcium scoring: past, present, and future. JACC Cardiovasc Imaging. 2015;8(5):579-596.
25. Budoff MJ, Shaw LJ, Liu ST, et al. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. J Am Coll Cardiol. 2007;49(18):1860-1870.
26. Blaha MJ, Cainzos-Achirica M, Greenland P, et al. Role of coronary artery calcium score in coronary heart disease risk assessment: a review. JAMA Cardiol. 2016;1(1):79-86.
27. Narula J, Nakano M, Virmani R, et al. Histopathologic validation of intracoronary imaging for detection of vulnerable plaque. J Am Coll Cardiol. 2013;62(17):1506-1517.
28. van Rosendael AR, Bax AM, Smit JM, et al. Association of low-attenuation plaque by coronary CT angiography and major adverse cardiac events: a meta-analysis. JACC Cardiovasc Imaging. 2020;13(7):1409-1417.
29. Dey D, Nakazato R, Li D, et al. Automated quantitative image analysis of low-attenuation noncalcified plaque and adverse plaque features from coronary CT angiography: Relation to cardiovascular outcomes. JACC Cardiovasc Imaging. 2015;8(8):914-922.
30. Otsuka K, Fukuda S, Tanaka A, et al. Clinical significance of low-attenuation plaque detected by coronary CT angiography in stable patients. J Am Coll Cardiol. 2013;62(1):60-66.
31. Pundziute G, Schuijf JD, Jukema JW, et al. Evaluation of plaque characteristics in acute coronary syndromes: non-invasive assessment with multi-slice computed tomography and invasive validation. Heart. 2008;94(4):414-420.
32. Kashiwagi M, Tanaka A, Kitabata H, et al. Relationship between remodeling index as assessed by CT angiography and plaque vulnerability as assessed by optical coherence tomography. Eur Heart J Cardiovasc Imaging. 2013;14(5):403-411.
33. Sato A, Hiroe M, Tamura M, et al. Positive remodeling and coronary plaque characteristics: CT angiography and IVUS study. Int J Cardiol. 2011;146(1):116-121.
34. Stone GW, Maehara A, Lansky AJ, et al. A prospective natural-history study of coronary atherosclerosis. N Engl J Med. 2011;364(3):226-235.
35. van Velzen JE, de Graaf FR, de Graaf MA, et al. Comprehensive assessment of spotty calcifications and its relation to clinical presentation using 320-row CT angiography. JACC Cardiovasc Imaging. 2011;4(1):49-56.
36. Motoyama S, Kondo T, Sarai M, et al. Multislice computed tomographic characteristics of coronary lesions in acute coronary syndromes. J Am Coll Cardiol. 2007;50(4):319-326.
37. Patel MR, Bailey SR, Bonow RO, et al. ACCF/SCAI/STS/AATS/AHA/ASNC/HFSA/SCCT 2012 appropriate use criteria for diagnostic catheterization. J Am Coll Cardiol. 2012;59(22):1995-2027.
38. Tonino PA, De Bruyne B, Pijls NH, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med. 2009;360(3):213-224.
39. Toth GG, Toth B, Johnson NP, et al. Revascularization decisions in patients with stable angina and intermediate lesions: results of

the international FAME study. Eur Heart J. 2014;35(40):2831-2838.

40. Johnson NP, Toth GG, Lai D, et al. Prognostic value of fractional flow reserve: linking physiologic significance to clinical outcomes. J Am Coll Cardiol. 2014;64(16):1641-1654.
41. Lee JM, Kim HJ, Hwang D, et al. Impact of plaque characteristics on the diagnostic accuracy of CT angiography for detecting functionally significant coronary artery disease: Comparison with invasive FFR. J Am Coll Cardiol. 2015;66(3):330-341.
42. Davies JE, Sen S, Dehbi HM, et al. Use of the instantaneous wave-free ratio or fractional flow reserve in PCI. N Engl J Med. 2017;376(19):1824-1834.
43. Nørgaard BL, Leipsic J, Gaur S, et al. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: The NXT Trial. J Am Coll Cardiol. 2014;63(12):1145-1155.
44. Rossi A, Papadopoulou SL, Pugliese F, et al. Quantitative coronary plaque analysis with multi-detector row CT angiography: comparison with intravascular US and coronary angiography. Radiology. 2010;256(1):106-115.
45. Taylor CA, Fonte TA, Min JK. Computational fluid dynamics applied to cardiac computed tomography for noninvasive quantification of fractional flow reserve. J Am Coll Cardiol. 2013;61(22):2233-2241.
46. Koo BK, Erglis A, Doh JH, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. J Am Coll Cardiol. 2011;58(19):1989-1997.
47. Nakazato R, Park HB, Berman DS, et al. Noninvasive fractional flow reserve derived from computed tomography angiography for coronary lesions of intermediate stenosis severity: results from the DeFACTO study. Circ Cardiovasc Imaging. 2013;6(6):881-889.
48. Tesche C, De Cecco CN, Duguay TM, et al. Coronary CT angiography-derived fractional flow reserve. Curr Cardiovasc Imaging Rep. 2017;10(5):13.
49. SCOT-HEART Investigators, Newby DE, Adamson PD, et al. Coronary CT angiography and 5-year risk of myocardial infarction. N Engl J Med. 2018;379(10):924-933.
50. Dweck MR, Williams MC, Moss AJ, et al. Coronary CT angiography and the future of cardiovascular risk stratification: JACC state-of-the-art review. J Am Coll Cardiol. 2020;76(5):561-577.
51. American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, Fihn SD, Gardin JM, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease. J Am Coll Cardiol. 2012;60(24):e44-e164.
52. Nakanishi R, Osawa K, Budoff MJ. Noninvasive imaging for the assessment of coronary artery disease: the evolving role of coronary CT angiography. Curr Cardiol Rep. 2021;23(7):74.
53. Leipsic J, Yang TH, Thompson A, et al. Radiation dose reduction strategies for cardiac computed tomography. J Cardiovasc Comput Tomogr. 2015;9(6):410-419.
54. Einstein AJ, Elliston CD, Arai AE, et al. Radiation dose from single-heartbeat coronary CT angiography. JAMA. 2007;298(3):317-323.
55. Mushtaq S, De Luca A, Guglielmo M, et al. Artificial intelligence and machine learning in cardiovascular computed tomography: from basics to clinical practice. Br J Radiol. 2022;95(1136):20210784.
56. van Rosendael AR, Bax AM, Smit JM, et al. Serial coronary computed tomography angiography for the assessment of atherosclerotic plaque progression and its predictors: a systematic review. Circ Cardiovasc Imaging. 2021;14(4):e011225.
57. Bittencourt MS, Hulten EA, Polonsky TS, et al. European Society of Cardiology recommendations on coronary computed tomographic angiography in chronic coronary syndromes: impact on clinical practice. J Cardiovasc Comput Tomogr. 2020;14(1):64-73.
58. Williams MC, Newby DE. The role of coronary CT angiography in the future management of stable angina. Heart. 2022;108(1):24-31.