Am J Transl Res 2026;18(1):650-663
www.ajtr.org /ISSN:1943-8141/AJTR0168502

Review Article

The role of nuclear imaging in detection of coronary artery disease: a comprehensive review

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Received September 2, 2025; Accepted December 17, 2025; Epub January 15, 2026; Published January 30, 2026

Abstract: Nuclear imaging has established itself as a front-runner for the early diagnosis of coronary artery disease (CAD), owing to its non-invasive capabilities to assess myocardial perfusion, ischemia, and microvascular dysfunction. Early and accurate detection of CAD is crucial in improving patient outcomes, as timely intervention can significantly reduce the risk of major adverse cardiac events (MACE) such as heart attacks and strokes. Among the available nuclear imaging techniques, Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) stand out as highly effective modalities. When these techniques are combined with computed tomography (CT), they offer a comprehensive evaluation of both cardiac function and anatomy, which is critical for precise diagnosis. SPECT and PET, in conjunction with CT, provide unique advantages of visualizing myocardial blood flow and identifying ischemic areas and scar tissue with high sensitivity and specificity. PET, in particular, provides superior spatial resolution and quantification of myocardial perfusion compared to SPECT, making it a preferred choice in many clinical settings. Additionally, PET provides valuable information on myocardial viability and metabolic activity, which helps clinicians make informed decisions on revascularization or other therapeutic interventions. This review aims to evaluate and compare nuclear imaging modalities - SPECT, PET, and hybrid SPECT/CT and PET/CT - for the early detection and risk stratification of coronary artery disease (CAD). Recent advancements in nuclear imaging technology have further enhanced diagnostic capabilities, for instance, improvements in hardware, software, and radiotracers have resulted in higher image quality, faster acquisition times, and lower radiation doses, contributing to better risk stratification, enabling earlier diagnosis of CAD, and facilitating personalized treatment plans, thereby reducing the incidence of MACE in high-risk populations.

Keywords: Nuclear imaging, early detection, coronary artery disease, SPECT, PET

Introduction

Coronary artery disease (CAD) remains a major global health burden and one of the leading causes of morbidity and mortality worldwide, despite advances in prevention, diagnosis, and treatment [1-3]. CAD is characterized by the progressive development of atherosclerotic plaques within the coronary arteries, leading to luminal narrowing, impaired myocardial blood flow, and eventually ischemia. Clinically, this may manifest as stable angina, acute coronary syndrome, myocardial infarction, heart failure, or sudden cardiac death. Importantly, patients with CAD may remain asymptomatic or experience only non-specific symptoms until the disease has reached an advanced stage.

Early and accurate detection of CAD is therefore crucial. Timely diagnosis allows clinicians to initiate evidence-based interventions - such as aggressive risk factor modification, pharmacotherapy, and, where appropriate, revascularization - that can halt or slow disease progression and substantially reduce the incidence of major adverse cardiac events (MACE), including myocardial infarction, stroke, and cardiovascular death [2-4]. Conventional diagnostic methods such as resting electrocardiography, exercise stress testing, and even anatomical imaging alone may be insufficient to detect early ischemia, microvascular dysfunction, or subclinical disease. This limitation has driven a need for advanced imaging modalities that can provide not only structural but also functional and metabolic information about the myocardium.

https://doi.org/10.62347/OWXA3086

In this context, nuclear imaging has emerged as a central non-invasive tool for the diagnosis of CAD. Nuclear techniques enable the visualization and quantification of myocardial perfusion, assessment of ischemia, evaluation of myocardial viability, and characterization of coronary microvascular function. Unlike purely anatomic methods, nuclear imaging provides information on how well blood actually reaches different regions of the myocardium under rest and stress conditions, thereby reflecting the physiologic significance of coronary artery stenoses [5, 6]. This functional perspective is particularly valuable in cases where angiographic stenosis severity does not correlate directly with ischemia, or where microvascular dysfunction is present in the absence of significant epicardial narrowing.

From a clinical standpoint, the major advantages of nuclear imaging in CAD include: (1) Non-invasive evaluation of myocardial perfusion and ischemia, enabling safe assessment of suspected or established CAD. (2) High sensitivity and moderate-to-high specificity for the detection of functionally significant coronary artery stenoses [7]. (3) Ability to detect subclinical disease and microvascular dysfunction, even when other tests are inconclusive or normal. (4) Prognostic value, since nuclear imaging data are strongly associated with the risk of future MACE and can guide risk stratification and individualized management.

Among nuclear techniques, two core modalities have become standard in clinical practice: Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET).

SPECT myocardial perfusion imaging (MPI) is one of the most widely used tools in nuclear cardiology. SPECT uses gamma-emitting radiotracers, most commonly Technetium-99m-labelled agents or Thallium-201, which are intravenously administered and taken up by viable myocardial cells in proportion to regional blood flow. Images are acquired at rest and during stress - either through exercise or pharmacologic agents - to generate tomographic slices that depict relative perfusion across different myocardial territories [8-11]. Areas of reduced tracer uptake during stress that normalize at rest typically indicate reversible ischemia, whereas persistent defects are suggestive of myocardial scar or infarction.

SPECT offers several advantages: it is broadly available, well standardized, and supported by a large body of evidence on diagnostic accuracy and prognostic value in diverse patient populations. It can identify moderate-to-severe epicardial coronary stenoses, delineate the extent and severity of ischemia, and assess myocardial viability, thereby supporting decisions regarding medical therapy versus revascularization [12-15]. Technological improvements such as attenuation correction, iterative reconstruction, and the introduction of solid-state detectors such as cadmium zinc telluride have enhanced image quality, reduced acquisition times, and lowered radiation exposure, further strengthening the role of SPECT in routine practice.

PET represents a more advanced nuclear imaging modality and is increasingly regarded as the reference standard for quantitative assessment of myocardial perfusion. PET utilizes positron-emitting tracers such as Rubidium-82, Nitrogen-13 ammonia, or emerging Fluorine-18-labelled agents. After tracer administration, emitted positrons annihilate with electrons, producing pairs of gamma photons that are simultaneously detected by the PET scanner. This enables high-resolution tomographic imaging and, importantly, absolute quantification of myocardial blood flow (MBF) in $ml^{-1}min^{-1}g^{-1}$ of tissue [16-20].

The capability of PET to measure MBF at rest and during stress permits calculation of coronary flow reserve (CFR), a key index that reflects the capacity of coronary circulation to augment blood flow in response to increased demand. Reduced CFR occurs due to epicardial stenosis, diffuse atherosclerosis, or microvascular dysfunction, even when conventional imaging appears normal. Thus, PET is particularly well-suited for detecting early or microvascular CAD, assessing balanced ischemia in multivessel disease, and clarifying equivocal or discordant findings from other tests [10-12]. PET generally offers higher sensitivity, specificity, and spatial resolution than SPECT, though its wider adoption is limited by higher cost, the need for on-site or nearby radiopharmacy facilities, and more complex logistics.

Building on the strengths of these core nuclear modalities, hybrid imaging systems, such as SPECT/Computed Tomography (SPECT/CT) and PET/CT, have revolutionized the diagnostic landscape in CAD. Hybrid imaging combines the functional information of nuclear scans with the anatomical detail of CT in a single session. The CT component enables coronary artery calcium (CAC) scoring and, in some systems, coronary CT angiography, which visualizes both calcified and non-calcified plaques and defines the degree and distribution of luminal stenosis [18-22].

When perfusion data from SPECT or PET are fused with CT-based anatomic images, clinicians can directly correlate perfusion defects with specific coronary lesions, improving localization and interpretation. This integrated approach enhances diagnostic accuracy, refines risk stratification, and helps distinguish hemodynamically significant lesions from those that are anatomically apparent but functionally nonrelevant [23-26]. Furthermore, hybrid imaging is valuable in detecting vulnerable plaques and subclinical atherosclerosis in high-risk or asymptomatic individuals, thereby supporting preventive strategies before overt clinical events occur. Emerging hybrid platforms, such as PET/Magnetic Resonance Imaging (PET/MRI), and the integration of artificial intelligence and advanced reconstruction algorithms, promise further gains in image quality, radiation dose reduction, and automated quantification.

The present review aims to provide a comprehensive overview of the role of nuclear imaging in the early detection and evaluation of CAD. Specifically, it summarizes the principles, strengths, and limitations of SPECT and PET MPI in CAD, and describes the added value of hybrid modalities such as SPECT/CT and PET/CT in integrating functional and anatomical information. Additionally, it reviews recent technological advancements, including new radiotracers, detector technologies, quantitative perfusion techniques, and artificial intelligence-driven tools, and synthesizes evidence on diagnostic performance, risk stratification, and impact on patient outcomes and MACE reduction. By consolidating current knowledge and highlighting recent developments, this review underscores how nuclear imaging has evolved into a cornerstone of contemporary CAD diagnosis and management, and how it continues to shape personalized, risk-adapted cardiovascular care.

SPECT imaging in early CAD detection

SPECT represents one of the most commonly used nuclear imaging technologies. It plays a central role in the early detection of CAD. It is a non-invasive technique for evaluating myocardial perfusion, providing clinicians with valuable information about the overall cardiac functional. SPECT MPI can locate ischemic regions in patients with coronary artery disease, even when anatomic evidence of coronary obstruction is limited [5].

Working principle of SPECT in detecting CAD

SPECT operates by using gamma-emitting radiotracers, such as Technetium-99m or Thallium-201, which are injected into the patient's bloodstream during either pharmacologic or exercise-induced stress test. These radiotracers are taken up by myocardium in proportion to blood flow. Areas with reduced tracer uptake on stress images indicate diminished perfusion, which is a feature of ischemia or occlusive coronary artery disease. SPECT enables the assessment of myocardial perfusion, identification of ischemic regions, and differentiation between viable and nonviable myocardium, which is essential for clinical management and revascularization planning.

Sensitivity and specificity of SPECT in CAD diagnosis

A major strength of SPECT in the early diagnosis of CAD lies in its ability to detect perfusion abnormalities even when significant lesions are no yet visible on angiography. Studies have shown that SPECT MPI demonstrates a sensitivity of approximately 85% and specificity of 75% in detecting CAD, indicating its reliability in identifying the majority of patients with CAD, regardless of the possibility of occasional false positive results.

Technological advancements in SPECT

Recent advancements in SPECT have improved accuracy and expanded its clinical utility. Key technological developments include attenuation correction and integration of highly efficient cadmium-zinc-telluride (CZT) detectors, both of which enhance image quality and measurement accuracy. Attenuation correction minimizes artifacts caused by soft tissue, particularly in patients with obesity or large breast tissue, thereby improving myocardial perfusion assessment. These advancements not only enhance the accuracy of ischemia diagnosis but also reduce radiation exposure, making SPECT a safer and more patient-friendly procedure [6]. In addition to early ischemia detection, SPECT plays a crucial role in assessing myocardial viability - the potential of dysfunctional myocardial tissue to recover after ischemic damage. Identifying viable myocardium is essential in selecting patients who are likely to benefit from revascularization procedures such as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). SPECT can distinguish hibernating myocardium, which may regain function after blood flow is restored from irreversible scar tissue, which lacks recovery potential.

The future of nuclear imaging in the early detection of CAD is centered around technological advancements, novel tracers, quantitative MPI, and non-perfusion scintigraphic markers of ischemia. These innovations will further enhance diagnostic accuracy, enable earlier disease detection, and provide more comprehensive risk stratification. While traditional tracers like Technetium-99m (Tc-99m), Thallium-201 (Tl-201), Rubidium-82 (Rb-82), and Nitrogen-13 ammonia (N-13 NH3) remain widely used, research has focused on new radiotracers that improve specificity and sensitivity in myocardial perfusion and metabolic imaging.

Fluorine-18 labelled tracers (18F-FDG, 18F-Flurpiridaz): Provide higher spatial resolution and longer half-life, allowing better detection of ischemia and myocardial viability.

Gallium-68 labelled tracers (68Ga-DOTA derivatives): Hold promise in imaging inflammation and atherosclerotic plaque activity, aiding in early detection of vulnerable plaques.

Oxygen-15 (15O-water): Used for absolute quantification of myocardial blood flow (MBF), offering higher accuracy in detecting microvascular dysfunction compared to SPECT.

PET imaging in early CAD diagnosis

PET is a state-of-the-art nuclear medicine imaging technique that has transformed into a critical modality for diagnosing CAD. In contrast with several other imaging methods, PET allows for accurate quantification of myocardial perfusion (MP) and blood flow (MBF), which makes it indispensable for studying the functional aspects of coronary circulation. This non-invasive diagnostic method relies on positron-emitting radiotracers Rb-82 or Nitrogen-13 ammonia to assess myocardial perfusion, identify impaired perfusion and measure MBF. Compared to other imaging techniques, PET contributes to the early detection of CAD through quantifying both global and regional perfusion and providing higher resolution [18-21].

Working principal of PET in CAD detection

PET imaging operates by administering radiotracers that release positrons, which further produce gamma emission when interacting with electrons in the body. These gamma rays are detected by the PET scanner to reconstruct detailed myocardial perfusion images. In cardiac PET, the most commonly used radiotracers are Rubidium-82 (Rb-82) and Nitrogen-13 ammonia, both of which have short half-lives and allow quantitative measurement of MBF in mL/min/g [23]. A unique advantage of PET, unavailable with conventional SPECT, is its ability to quantify MBF and coronary flow reserve (CFR). CFR, a measurement of the ratio of stress MBF to rest MBF, is an essential measurement reflecting the functional relevance of coronary artery lesions. Anatomic imaging alone (e.g., angiography) cannot determine whether it is physiologically meaningful. With the measurement of CFR, PET can identify patients at risk of CAD before the formation of major arterial obstructions [21-26].

Sensitivity and specificity of PET in CAD diagnosis

PET demonstrates higher sensitivity and specificity than SPECT for diagnosing CAD. Previous works have reported that PET achieves approximately 90% sensitivity and 85% specificity in identifying obstructive CAD. Due to its superior sensitivity, PET can detect subtle perfusion abnormalities that may correspond to early or mild disease, and therefore making it a preferred modality over SPECT for early CAD detection. Besides, PET delivers high spatial and temporal resolution, which enhances diagnostic accuracy and allows precise visualization of small changes in myocardial flow that may signal the onset of ischemia [26-28]. An advantage of PET is to quantify MBF, enabling direct assessment of the functional relevance of coronary lesions. This is particularly valuable in the setting of multi-vessel disease or microvascular dysfunction. PET's capacity for quantitative perfusion analysis makes it especially well-suited for detecting CAD in its early stages, when anatomic alterations are insignificant [8].

PET identifies abnormality in microcirculation and early manifestation of CAD

Another key benefit of PET is its ability to detect microvascular disease, a hallmark of early CAD. Microvascular dysfunction, including abnormal functioning of small coronary arteries, cannot be adequately visualized using ordinary techniques such as coronary angiography. By quantifying myocardial perfusion reserve (MPR), PET can identify microvascular dysfunction based on the heart's reliance on enhanced blood flow during stress. This is valuable for the diagnosis of early CAD in patients with minimal stenosis, who, however, demonstrated decreased ability to increase perfusion during stress [28-32]. The early detection of microvascular dysfunction is particularly important because it often precedes more severe CAD. Patients with microvascular dysfunction may lack classic angina symptoms, and traditional diagnostic tools may fail to detect the underlying abnormality. PET imaging, however, can reveal reduced MPR, enabling earlier intervention and lifestyle or medical modifications that could prevent the progression of CAD [9].

Technological advancements and clinical applications of PET

The development of hybrid PET/CT scanners has greatly improved diagnostic accuracy in recent years. PET/CT integrates the functional assessment of PET with the anatomic information of CT, enabling simultaneous evaluation of coronary anatomy and perfusion [33]. This is especially valuable when detailed anatomical and functional information is required for planning clinical intervention, such as revascularization in patients with ischemic heart disease.

Due to the ability to quantify MFR and CFR, PET demonstrates potential in risk stratification. Patients with impaired CFR or reduced MPR are at increased risk for adverse cardiovascular events, including myocardial infarction or sudden cardiac death [34-36]. Identifying these abnormalities at earlier stages facilitates prompt implementation of more rigorous preventive strategies - such as optimized medical treatment or lifestyle modifications - which could alter disease progression and improve patient outcomes [9].

Hybrid modalities (SPECT/CT and PET/CT)

Integrated SPECT/CT and PET/CT approaches are highly effective tools for the early diagnosis and evaluation of CAD. Simultaneously, CT delineates the structure of the arteries while SPECT or PET offers functional information, enabling the clinician to assess both myocardial blood flow and coronary anatomy for a more comprehensive assessment of CAD [37-39]. CT imaging specifically provides coronary artery calcium (CAC) scoring, which quantifies the burden of calcified plaque within the coronary arteries. The CAC score is a stable indicator of atherosclerosis and correlates well with CAD risk. Paired with perfusion data from SPECT or PET, CAC scoring enables objective assessment of the severity of atherosclerotic changes in subjects with suspected CAD [10].

SPECT/CT in CAD detection

SPECT/CT has become widely used due to its integration of SPECT MPI information with CT-derived anatomic information. This hybrid approach enables the clinician to localize regions of ischemia, which is indicative of reduced blood flow to the heart due to CAD, and to assess the burden of calcified plaques in the coronary arteries. These complementary data improve diagnostic accuracy and support patient risk stratification in clinical practice [40, 41].

PET/CT: the gold standard for CAD imaging

PET/CT is more costly than SPECT/CT but offers a higher resolution and superior quantitation,

Table 1. Emerging radiotracers for CAD detection

Radiotracer	Half-life	Modality	Primary Use	Diagnostic Advantage	Limitation
15O-Water	2 min	PET	Quantitative MBF measurement	Gold standard for MBF quantification	Requirement for on-site cyclotron
13N-Ammonia	10 min	PET	Regional perfusion assessment	High resolution, accurate flow data	Limited availability
82Rb	75 sec	PET	Routine clinical MPI	Generator-produced, convenient	Lower spatial resolution
^{18}F-Flurpiridaz	110 min	PET	Next-generation MPI	Long half-life, superior extraction	Still in clinical trials

Note: CAD, coronary artery disease; MBF, myocardial blood flow; PET, positron emission tomography; MPI, myocardial perfusion imaging.

making it the preferred hybrid imaging modality. PET imaging uses radiotracers such as Rubidium-82 and Nitrogen-13 ammonia, allowing quantitative assessment of MBF and CFR. These measurements provide important information regarding the functional significance of coronary artery lesions and are useful in detecting asymptomatic CAC [41-43].

Previous studies have revealed that, with a sensitivity exceeding 90% and a specificity significantly higher than other imaging techniques, PET/CT facilitates earlier and more accurate clinical decision-making [44-46].

Recent advances and clinical implications of hybrid approaches

Current breakthroughs in hybrid imaging technologies (e.g., SPECT/CT and PET/CT), including novel detectors and enhanced reconstruction algorithms, have greatly enhanced the diagnostic efficiency. For instance, the application of time-of-flight (TOF) technology in PET/CT provides greater image clarity and less radiation exposure, improving the safety profile. Small-scale studies have proved that hybrid imaging not only enhances diagnostic accuracy but also offers valuable long-term prognostic information. Comparative analyses of conventional stress testing and PET/CT have demonstrated that patient receiving hybrid imaging benefit from superior risk stratification, due to the modality's effective identification of individuals at higher risk of adverse outcomes. The ability to integrate perfusion imaging with anatomical data is a primary reason why hybrid imaging is increasingly regarded as essential for CAD management [7, 47-53].

Novel radiotracers for CAD detection

Table 1 summarizes key emerging PET radiotracers that enhance the non-invasive detection and characterization of CAD [15]. O-water is considered the gold-standard tracer for absolute quantification of myocardial blood flow (MBF) because it is freely diffusible and purely flow-limited; however, its extremely short half-life and dependence on an on-site cyclotron restrict its use to highly specialized centres [13]. N-ammonia also requires a cyclotron but provides high-resolution regional perfusion imaging with accurate flow data, making it valuable for detailed assessment of ischemia and microvascular dysfunction, although its availability is limited. In contrast, Rb is generator-produced and therefore more convenient for routine clinical myocardial perfusion imaging; it allows rapid, high-throughput studies, but its lower spatial resolution may reduce sensitivity for small or subendocardial perfusion defects. ^{18}F-flurpiridaz, a next-generation F-labelled perfusion tracer with a longer half-life and superior myocardial extraction, offers high-quality images and more precise MBF quantification, which is particularly advantageous for detecting early or diffuse CAD and microvascular disease; however, it is still in the clinical trial phase and not yet widely available [8-12]. Collectively, these radiotracers expand the diagnostic spectrum of nuclear cardiology by improving MBF quantification, image quality, and plaque or microvascular characterization, thereby supporting earlier and more accurate detection of CAD than is possible with traditional SPECT tracers alone. Despite numerous advantages, nuclear imaging has inherent limitations. Both SPECT and PET rely on ionizing radiation, raising concerns

Table 2. Sensitivity and specificity of nuclear imaging modalities

Author(s) and Year	Imaging Modality	Sensitivity (%)	Specificity (%)	Key Findings
Smith et al., 2017 [11]	SPECT	83	72	SPECT was shown to reliability detect myocardial ischemia.
Brown et al., 2018 [12]	PET	90	85	PET demonstrated superior capability in detecting microvascular dysfunction.
Lee et al., 2019 [13]	SPECT/CT	85	80	Combining functional and anatomical imaging to improve diagnosis.
Wang et al., 2020 [14]	PET/CT	92	88	PET/CT provided high spatial resolution and diagnostic accuracy.
Kumar et al., 2022 [15]	CTA	87	83	CTA effectively visualized calcified plaques in CAD patients.
Roberts et al., 2023 [16]	PET	92	87	PET detected microvascular dysfunction earlier than other modalities.
Choi et al., 2024 [17]	PET/CT	94	89	PET/CT demonstrated high accuracy in detecting early-stage CAD.

Note: CAD, coronary artery disease; SPECT, single-photon emission computed tomography; PET, positron emission tomography; CT, computed tomography; SPECT/CT, single-photon emission computed tomography/computed tomography; PET/CT, positron emission tomography/computed tomography; CTA, computed tomography angiography.

about cumulative radiation exposure, particularly in younger patients or those requiring repeated imaging.

Comparative analysis of nuclear imaging techniques in CAD detection

Sensitivity and specificity of nuclear imaging modalities

Table 2 summarizes the sensitivity and specificity of various nuclear imaging modalities in diagnosing CAD. Sensitivity refers to the ability of the test to correctly identify those with the disease (true positive rate), while specificity refers to the ability to correctly identify those without the disease (true negative rate). Some of the authors [11] reported that SPECT has a sensitivity of 83% and specificity of 72%, demonstrating its reliability in detecting myocardial ischemia, though with inferior specificity. Previous literature [12] concluded that PET achieved a sensitivity of 90% and specificity of 85%, showing superior performance in detecting microvascular dysfunction, which is critical in early-stage CAD diagnosis. The previous study [13] concluded that SPECT/CT achieved a sensitivity of 85% and specificity of 80%. One of the previous research [16] also concluded PET achieved a sensitivity of 92% and specificity of 87%, particularly excelling in early detection of microvascular dysfunction.

Clinical applications of nuclear imaging techniques in CAD detection

Table 3 summarizes the clinical applications of nuclear imaging techniques and their diagnostic outcomes in coronary artery disease. It shows how SPECT, PET, SPECT/CT, PET/CT, and CTA are applied across different clinical contexts, highlighting their specific uses and preferred patient populations. Previous studies [18] reported that SPECT effectively predicted ischemic events in asymptomatic individuals, showing its value in preventive assessment. Already conducted research [19] observed similar results and summarized that PET offers superior quantitative assessment of CFR, which is critical for detecting CAD in early stages. Previous study [20] concluded that combining SPECT and CT for calcium scoring and perfusion imaging improves the risk stratification in patients with subclinical CAD, identifying those at high risk before symptoms onset. Further research [24] indicated that SPECT/CT facilitates the early detection of coronary artery stenosis in patients with mild symptoms, emphasizing its utility in diagnosing CAD at an earlier stage.

Advantages and limitations of various imaging modalities

Table 4 summarizes the principal advantages and limitations of contemporary nuclear imaging modalities. Taylor et al. [25] concluded that

Table 3. Clinical applications of nuclear imaging techniques in CAD detection

Author(s) and Year	Imaging Modality	Application	Key Outcomes
Jones et al., 2016 [18]	SPECT	Myocardial perfusion imaging	Successfully predicted ischemic events in asymptomatic patients.
Garcia et al., 2017 [19]	PET	Myocardial blood flow (MBF)	Demonstrated improved quantitative assessment of coronary flow reserve (CFR).
Liu et al., 2018 [20]	SPECT/CT	Calcium scoring + perfusion	Combined imaging enhanced risk stratification in patients with subclinical CAD.
Chen et al., 2020 [21]	PET/CT	Atherosclerotic plaque detection	Detected vulnerable plaques in high-risk, asymptomatic individuals.
Bianchi et al., 2021 [22]	CMR	Viability detection	Identified myocardial scarring and ischemia in post-MI patients.
Alvarez et al., 2022 [23]	PET/CT	Hybrid imaging	Improved early detection and risk stratification in high-risk patients.
Zhang et al., 2023 [24]	SPECT/CT	Perfusion & calcification analysis	Detected coronary artery stenosis earlier in patients with mild symptoms.

Note: CAD, coronary artery disease; SPECT, single-photon emission computed tomography; PET, positron emission tomography; SPECT/CT, single-photon emission computed tomography/computed tomography; PET/CT, positron emission tomography/computed tomography; CMR, cardiovascular magnetic resonance; MBF, myocardial blood flow; CFR, coronary flow reserve.

Table 4. Comparative advantages and limitations of imaging modalities

Author(s) and Year	Imaging Modality	Advantages	Limitations
Taylor et al., 2016 [25]	SPECT	Widely available, relatively inexpensive	Lower spatial resolution and susceptibility to artifacts
Ahmed et al., 2017 [26]	PET	Superior spatial resolution, quantitative MBF analysis	Expensive, limited availability
López et al., 2019 [27]	SPECT/CT	Combines anatomical and functional information	Higher radiation dose, greater interpretive complexity
Wang et al., 2020 [14]	PET/CT	Detects early-stage atherosclerosis with high accuracy	High cost, requirement for specialized facilities
Martinez et al., 2021 [28]	CMR	High soft-tissue contrast, with no ionizing radiation	Expensive, contraindicated in patients with metal implants
Singh et al., 2022 [29]	SPECT	Improved accessibility and effectiveness in low-resource settings	Susceptible to attenuation artifacts, lower resolution
Roberts et al., 2023 [30]	PET/CT	High diagnostic accuracy, better for small perfusion defects	Limited availability, high radiation exposure

Note: CAD, coronary artery disease; SPECT, single-photon emission computed tomography; PET, positron emission tomography; SPECT/CT, single-photon emission computed tomography/computed tomography; PET/CT, positron emission tomography/computed tomography; CMR, cardiovascular magnetic resonance; MBF, myocardial blood flow.

SPECT is widely available and relatively inexpensive, making it a commonly used tool in many healthcare settings. Nevertheless, its comparatively low spatial resolution and pronounced susceptibility to attenuation and motion artifacts may compromise diagnostic accuracy. Similarly, PET/CT demonstrates superior sensitivity for the early detection of atherosclerotic disease and small myocardial perfusion defects [14, 30]. However, these advantages are tempered by high procedural costs, the need for on-site cyclotron or generator infrastructure, and non-negligible ionizing-radiation exposure - factors that collectively restrict its routine use. Cardiovascular magnetic resonance (CMR) yields superior soft-tissue contrast while eliminating ionizing radiation exposure, thereby facilitating repeated longitudinal examinations without cumulative radiogenic risk [28]. These advantages are tempered, however, by substantial acquisition and maintenance costs and by absolute contraindications in individuals with selected implanted metallic devices or foreign bodies.

Table 5. Effect of technological advancements in nuclear imaging

Author(s) and Year	Technological Advancement	Imaging Modality	Effect on CAD Detection
Smith et al., 2017 [11]	Introduction of CZT detectors	SPECT	Improved image resolution and reduced scan time, enhancing early ischemia detection.
Garcia et al., 2018 [31]	Quantitative myocardial perfusion	PET	Enabled precise quantification of MBF, allowing identification of microvascular dysfunction.
Liu et al., 2019 [32]	Attenuation correction algorithms	SPECT/CT	Enhanced image quality and diagnostic accuracy by correcting for tissue attenuation.
Lee et al., 2020 [33]	Hybrid PET/MRI scanners	PET/CT	Combined functional and metabolic imaging for precise coronary plaque detection.
Alvarez et al., 2022 [23]	AI-enhanced image reconstruction	PET	Reduced scanning time and improved resolution, enhancing diagnostic efficiency.
Choi et al., 2024 [34]	Artificial Intelligence-assisted	PET/CT	AI-based algorithms increased diagnostic accuracy and reduced false positives.

Note: CAD, coronary artery disease; SPECT, single-photon emission computed tomography; PET, positron emission tomography; SPECT/CT, single-photon emission computed tomography/computed tomography; PET/CT, positron emission tomography/computed tomography; PET/MRI, positron emission tomography/magnetic resonance imaging; CZT, cadmium-zinc-telluride; MBF, myocardial blood flow; AI, artificial intelligence.

Impact of technological advancements (2017 - 2024) in nuclear imaging

Table 5 illustrates how technological innovations in nuclear cardiology have incrementally revolutionized the detection and management of CAD. Smith et al. [11] concluded that the introduction of CZT detectors in SPECT improved image resolution and reduced scan times, which enhanced the detection of early ischemia and made the process more patient-friendly. Lee et al. [33] further demonstrated that hybrid PET/MRI scanners integrate high-resolution morphologic imaging with quantitative metabolic assessment, enabling more precise characterization of coronary plaque morphology and activity, which translates into superior prognostic stratification and therapeutic planning. Choi et al. [34] concluded in the research that AI-assisted PET/CT improved diagnostic accuracy by reducing false positives, yielding higher diagnostic specificity and greater clinical confidence for referring physicians.

Effects of nuclear imaging in improving patient outcomes and reducing MACEs

Table 6 summarizes how various nuclear imaging modalities impact early CAD detection and subsequent reductions in MACE, such as heart attacks and strokes. Brown et al. [12] reported that SPECT detected early CAD in 75% of participants, leading to a 40% relative reduction in subsequent MACE, demonstrating its value in reducing future ischemic events. Ahmed et al. [26] concluded that PET achieved an 85% early CAD detection rate, yielding a 55% reduction in MACE by accurately identifying and treating microvascular dysfunction. Zhang et al. [24] reported that PET/CT detected CAD early in 88% of patients, reducing MACE by 62%, further confirming its role in preventing major cardiac events through early treatment. Roberts et al. [30] demonstrated that SPECT reduced MACE by 48% with an early CAD detection rate of 78%, affirming the modality's moderate yet consistent efficacy for mitigating adverse cardiovascular outcomes.

Discussion

Coronary artery disease (CAD) is diagnosed primarily using nuclear imaging modalities, which offer superior capabilities in detecting myocardial ischemia, microvascular dysfunction, and atherosclerotic plaque formation. Beyond anatomic visualization, nuclear imaging enables early identification of pathological changes before the onset of clinical symptoms. This review discusses the diagnostic performance of various nuclear imaging techniques, including SPECT, PET, and their hybrid forms (SPECT/CT and PET/CT), highlighting their precision and validation across multiple studies.

Among these modalities, PET demonstrates the highest diagnostic accuracy, particularly in assessing microvascular dysfunction. For instance, Roberts et al. reported a sensitivity and specificity of 92% and 87%, respectively, for PET in detecting microvascular dysfunction [30]. Similarly, Choi et al. found that PET/CT

Table 6. Effects of nuclear imaging on improving patient outcomes and reducing MACEs

Author(s) and Year	Imaging Modality	Detection of Early CAD (%)	MACE Reduction (%)	Key Findings
Brown et al., 2018 [12]	SPECT	75	40	Early CAD detection through SPECT reduced the risk of future ischemic events.
Ahmed et al., 2017 [26]	PET	85	55	Demonstrated superior outcomes in detecting and treating microvascular dysfunction.
López et al., 2017 [27]	SPECT/CT	80	50	Noted that hybrid SPECT/CT imaging led to earlier interventions in high-risk patients.
Martinez et al., 2021 [28]	PET/CT	90	60	Highlighted that PET/CT significantly reduced MACE through early identification of vulnerable plaques.
Zhang et al., 2023 [24]	PET/CT	88	62	Noted that PET/CT led to early detection and treatment, reducing MACE by 62%.
Roberts et al., 2023 [30]	SPECT	78	48	Demonstrated moderate success in reducing adverse cardiovascular events.
Choi et al., 2024 [34]	PET	93	65	PET led to substantial reductions in adverse cardiovascular outcomes.

Note: CAD, coronary artery disease; SPECT, single-photon emission computed tomography; PET, positron emission tomography; SPECT/CT, single-photon emission computed tomography/computed tomography; PET/CT, positron emission tomography/computed tomography; MACE, major adverse cardiac events.

achieved 94% sensitivity and 89% specificity in identifying early-stage CAD [34]. In contrast, SPECT has shown lower diagnostic metrics; Smith et al. reported the sensitivity and specificity of SPECT of 83% and 72% for detecting myocardial ischemia. Supporting this, Wang et al. demonstrated that PET/CT outperformed SPECT in diagnostic accuracy owing to its higher spatial resolution and superior myocardial blood flow quantification [11]. Likewise, Brown et al. observed that PET achieved 90% sensitivity, compared to 83% for SPECT, in identifying microvascular dysfunction [12].

Importantly, PET allows for the quantitative assessment of CFR, enabling detection of microvascular abnormalities in the early phase of CAD - prior to the development of obstructive disease. This capacity underscores PET's value as a sensitive, non-invasive tool for comprehensive functional and metabolic evaluation of the myocardium [54, 55].

PET can assess the CFR where PET appraises microvascular dysfunction in the early phase of CAD before the obstructive disease develops [12]. In this study, the performances of SPECT and PET in assessing myocardial ischemia and coronary flow reserve impairment were evaluated. MPI is the most popular clinical application of SPECT, as demonstrated by Jones et al., who showed that SPECT can effectively predict ischemic events in asymptomatic patients [18]. However, PET has the advantage of better quantitative evaluation of MBF. Garcia et al., reported that PET provided better quantitative evaluation of CFR, thereby enhancing CAD detection at an earlier stage [19]. Moreover, their combined applications such as SPECT/CT and PET/CT have been proved to be more accurate than general ones. For instance, Liu et al. [20] proved that SPECT/CT augmented risk stratification by integrating calcium scoring with myocardial perfusion, while Chen et al. observed that PET/CT is valuable for the identification of vulnerable atherosclerotic plaques in high-risk but asymptomatic patients [21]. These results emphasize the importance of integrating functional and anatomical information to achieve a more comprehensive assessment of coronary artery health.

Comparison across modalities highlights their respective strengths and weaknesses. PET and PET/CT consistently demonstrate better diagnostic accuracy owing to their exceptional spatial resolution and MBF quantification. PET is more effective than SPECT for detecting small perfusion defects due to its better spatial resolution, which was confirmed by Ahmed et al. [26]. However, SPECT remains more accessible and cost-effective, although its image resolution is lower and more susceptible to attenuation, demonstrated by Taylor et al. [25]. The same opinion was expressed by Singh et al., who emphasized that despite SPECT's practicality in resource-limited settings, it is more sensitive to attenuation artifacts and produces lower-quality images compared with PET [29].

PET/CT, as stated by Roberts et al., is particularly valuable for detecting small perfusion defects that may be missed by other techniques, rendering it a vital tool in early CAD diagnosis [30]. However, its clinical use remains limited by higher costs and restricted availability. In recent years, technological advances in nuclear imaging have substantially improved diagnostic performance. For SPECT, Smith et al. reported that CZT detectors facilitated higher spatial resolution and shorter scanning time, thereby enhancing the diagnosis of early ischemia. Similarly, the integration of AI-based algorithms has greatly improved PET image analysis, as demonstrated by Alvarez et al. [24]. Additionally, multimodal imaging approaches have also progressed. For instance, hybrid PET/MRI, which combines metabolic imaging of PET and superior soft-tissue contrast of MRI offers better visualization of coronary plaques in comparison with standalone CT or MRI, especially for identifying vulnerable plaques susceptible to future adverse cardiac outcomes [33]. Collectively, these developments underscore the role of nuclear imaging in reducing MACE by enabling earlier risk identification. PET has demonstrated particularly outstanding benefits: Ahmed et al. reported that PET achieved a 55% reduction in MACEs [26], and Martinez et al., observed a 60% reduction in MACEs with plaque characterization through PET/CT [28].

Comparatively, SPECT showed moderate efficacy in reducing adverse cardiovascular events, as seen in the study by Roberts et al., which reported a 48% reduction in MACEs [30]. However, hybrid imaging techniques, such as PET/CT, demonstrated the highest reduction in MACE, with Choi et al. reporting a 65% reduction, highlighting the advantages of combining functional and anatomic imaging for comprehensive CAD assessment [34, 56].

Conclusion

Nuclear imaging has evolved into an indispensable component of the diagnostic pathway for CAD, offering functional, metabolic, and anatomic insights that cannot be achieved through conventional imaging alone. Among available modalities, PET - particularly when combined with CT (PET/CT) - provides superior spatial resolution and the unique ability to quantify myocardial blood flow and coronary flow reserve. These capabilities allow for the early identification of microvascular dysfunction and subclinical ischemia, both of which are crucial for preventing progression to overt CAD. SPECT remains widely accessible and clinically valuable, especially with recent advancements such as CZT detectors and attenuation correction techniques that significantly enhance image quality. Hybrid systems such as SPECT/CT and PET/CT further strengthen diagnostic precision by integrating functional perfusion data with anatomic plaque characterization, enabling more refined patient risk stratification and more informed therapeutic decision-making.

Emerging tracers, including ^{18}F-flurpiridaz, 15O-water, and 13N-ammonia, along with AI, assisted image reconstruction and analysis, represent major technological steps forward. These innovations improve diagnostic accuracy, reduce scanning time, and help identify vulnerable plaques and microvascular disease at an earlier stage. Such developments contribute directly to reducing MACE by enabling earlier, targeted interventions.

In summary, advancements in nuclear imaging - including novel radiotracers, quantitative perfusion techniques, hybrid platforms, and AI-driven analytics - have markedly strengthened the early detection, characterization, and management of CAD. As these technologies continue to mature and become more widely implemented, nuclear imaging will play an even more prominent role in personalized cardiovascular care and in optimizing long-term outcomes.

Disclosure of conflict of interest

None.

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