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Original Article

Diagnostic Accuracy of Cadmium Zinc Tellurite (CZT) Detector-Based Dynamic Single Photon Emission Computed Tomography (D-SPECT) Myocardial Perfusion Imaging (MPI) in the Evaluation of Coronary Artery Disease (CAD)

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ABSTRACT

Objective: To assess the diagnostic accuracy of CZT detector-based dynamic SPECT MPI for detecting coronary artery disease (CAD), using coronary angiography as the reference standard.
Study Design: Cross-sectional Observational Study.
Place & Duration of Study: Department of Nuclear Cardiology, AFIC/NIHD, Rawalpindi, Pakistan, from Jan to Jun 2024.
Methodology: A total of 198 patients who underwent coronary angiography within three months of a D-SPECT MPI were included. Dynamic SPECT MPI was performed using a CZT detector-based camera following 99mTc-Sestamibi injection during rest and stress phases. Stress imaging incorporated Adenosine infusion. Myocardial blood flow (MBF) and myocardial flow reserve (MFR) values were calculated. An MFR value <2 indicated CAD. Coronary angiography, interpreted by two cardiologists.
Results: Of 198 patients, 167 (84.3%) were males and 31 (15.7%) were females, with a mean age of 56.03 ±11.83 years. D-SPECT MPI diagnosed CAD in 70 (35.4%) patients, while the actual number of patients having CAD as diagnosed by coronary angiography was 74 (37.4%). The calculated sensitivity, specificity, PPV, NPV, and diagnostic accuracy of D-SPECT MPI, keeping coronary angiography as the gold standard, were 87.8%, 95.9%, 92.8%, 92.9%, and 92.9%, respectively.
Conclusion: This single-center study demonstrates that CZT-based dynamic SPECT MPI offers shorter imaging time, less radiation exposure, and cost-effectiveness, making it a valuable non-invasive diagnostic modality. The system's enhanced resolution and faster imaging acquisition contribute to its clinical utility.

Keywords: Coronary artery disease, dynamic SPECT MPI, myocardial flow reserve, coronary angiography, diagnostic accuracy.

How to Cite This Article: *Saleem H, Nouman MI, Dar ZS, Raza MAM, Atif M. Diagnostic Accuracy of Cadmium Zinc Tellurite (CZT) Detector-Based Dynamic Single Photon Emission Computed Tomography (D-SPECT) Myocardial Perfusion Imaging (MPI) in the Evaluation of Coronary Artery Disease (CAD). Pak Armed Forces Med J 2026; 76(Suppl-8): S1250-S1255. DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-8.13354*

INTRODUCTION

Radionuclide Single Photon Emission Computed Tomography (SPECT) Myocardial Perfusion Imaging (MPI) is a widely used imaging technique used to visualize the distribution of radiopharmaceuticals in the myocardium. The uptake of these radiopharmaceuticals corresponds to myocardial blood flow (MBF), allowing for an assessment of blood flow patterns across different regions of the heart. As a non-invasive imaging method, SPECT MPI is an essential imaging tool in detecting ischemia and assessing risk factors in individuals with suspected or confirmed coronary artery disease (CAD)[1]

Although widely utilized, assessing regional perfusion defects in MPI, whether visually or semi-quantitatively, can sometimes lead to underestimation or misdiagnosis of "balanced" ischemia. This challenge is particularly evident in patients with balanced multi-vessel coronary artery disease (CAD) or microcirculatory dysfunction, where perfusion abnormalities may not be easily detected.[2]

Measuring myocardial blood flow (MBF) and myocardial flow reserve (MFR) through tracer kinetic methods in Positron Emission Tomography (PET) can help address these limitations.[3] Stress and rest flow measurements offer a comprehensive evaluation of ischemic burden caused by both microvascular and macrovascular disease.[4] Compared to relative perfusion imaging alone, these measurements provide superior accuracy in detecting early-stage coronary atherosclerosis, assessing cardiac risk, and predicting patient prognosis—regardless of conventional risk factors.[5] However, the widespread adoption of PET imaging is hindered by the high costs associated with establishing a PET tracer production system, making it less accessible in many regions.

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Received: 27 Apr 2025; revision received: 27 Jun 2025; accepted: 30 Jun 2025

Quantifying MBF using standard SPECT cameras presents additional challenges due to the complexity of dynamic acquisitions in perfusion imaging. However, advancements in highly efficient cardiac cameras equipped with Cadmium Zinc Telluride (CZT) detectors have significantly enhanced imaging sensitivity.[5] These specialized detectors enable tomographic dynamic acquisition without requiring camera rotation around the patient, thereby facilitating in vivo radiotracer kinetic analysis.[6] Notably, MFR assessment using dynamic SPECT MPI has demonstrated a sensitivity of 83.3% and a specificity of 100%, with an area under the curve (AUC) of 0.94 for coronary artery disease (CAD) screening.[7]

CAD accounts for approximately 7 million deaths each year and is ranked as the third leading cause of mortality globally, with an estimated prevalence of 26.9% in Pakistan.[8] Early diagnosis and prompt management provide mortality benefits to these patients. Despite advancements in cardiac imaging, there is a lack of comprehensive data addressing the clinical utility of CZT detector-based dynamic SPECT MPI in detecting CAD. This highlights the potential need for focused research to evaluate the potential technical advancements offered by this specific imaging technique. This study aims to assess whether Cadmium Zinc Telluride (CZT) detector-based dynamic SPECT MPI can reliably and more efficiently detect coronary artery disease and help in high-risk patients' stratification, thereby improving diagnostic accuracy, patient care and clinical outcomes.

METHODOLOGY

The study was a clinical diagnostic accuracy study conducted in the Department of Nuclear Cardiology, AFIC/NIHD, Rawalpindi, Pakistan, from Jan to Jun 2024.

Inclusion Criteria: Successive patients of both genders, aged between 18 and 79 years, clinically diagnosed with or suspected of coronary artery disease (CAD), who were referred for myocardial perfusion imaging (MPI) and had undergone coronary angiography within three months before or after the MPI were included in the study.

Exclusion Criteria: Patients with a history of prior Coronary Artery Bypass Grafting (CABG) / Percutaneous Transluminal Coronary Angioplasty (PTCA), unstable angina pectoris, old myocardial infarction, cardiac disease other than CAD (Nonischemic cardiomyopathy, myocarditis, cardiac amyloidosis, valvular heart disease, congenital vascular anomalies, arteritis), and contraindications to pharmacological stress with adenosine were excluded from the study.

Sample size of 205 was calculated by using the sample size calculator for sensitivity and specificity studies, keeping confidence level at 95%, absolute precision of 10%, sensitivity at 83.3%[7], Specificity at 100% (95%), and Prevalence of CAD in the population at 26.9%.[9] Patients who were referred to Nuclear Cardiology Department for MPI, fulfilling the inclusion criteria, were selected using non-probability consecutive sampling. Informed consent was obtained from each patient, which included a detailed explanation of the procedure, utility of the study for their further management, and an explanation of the radiation hazards. Data privacy and ethical issues were considered and maintained throughout the study (IERB letter 9/2/R&D/2024/298 dated 10 Jan 2024). For patient acquisition, List-mode acquisitions were conducted on D-SPECT Cardiac CZT camera (Spectrum Dynamics). Initially 1mCi of 99mTc-Sestamibi was injected to position the patient's heart within the camera's field of view. A rest dynamic scan in List mode was then acquired immediately after an injection of 0.1mCi/Kg Body weight of 99mTc-Sestamibi for 10 minutes with the patient lying in supine position, followed by acquisition of gated rest images for 5 minutes with parameters of sixteen frames/cardiac cycle and energy window centered on photopeak of 140keV + 10%. At the peak of hyperemia (starting at the 3rd minute of adenosine infusion), a bolus injection of 99mTc-Sestamibi (0.1–0.3 mCi/kg body weight, three times the rest dose) was administered, followed by a 100 mL saline flush to ensure constant delivery. List mode stress dynamic acquisition was then acquired for 10 minutes with the patient in supine position, followed by acquisition of gated stress images for 5 minutes with parameters of sixteen frames/cardiac cycle and energy window centered on photopeak of 140kev + 10%. A flow chart of the events is shown in Figure-1. Coronary angiography data were evaluated by two interventional cardiologists, each with over three years of practical experience. The data, collected from procedures conducted within three months before or after D-SPECT MPI, were recorded using a pre-designed proforma. Stenosis of ≥2 mm of coronary artery diameter (visual assessment), or stenosis involving ≥50% for Left Main Stem (LMS) or ≥75% of regional coronary arteries, respectively, was labelled significant CAD.10 Statistical analyses were performed using SPSS 23. Descriptive statistics, including Mean±SD, were calculated for quantitative variables such as age, Body Mass Index (BMI), EF, MBF, and MFR. For qualitative variables (gender, presence or absence of diabetes, smoking, family history of CAD, hypertension, dyslipidemias, and presence or absence of CAD on coronary angiography and Dynamic SPECT MPI), frequencies and percentages were calculated. Additionally, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated for D-SPECT MPI, keeping invasive coronary angiography as the gold standard. CA patient flow diagram is shown in Figure-2.

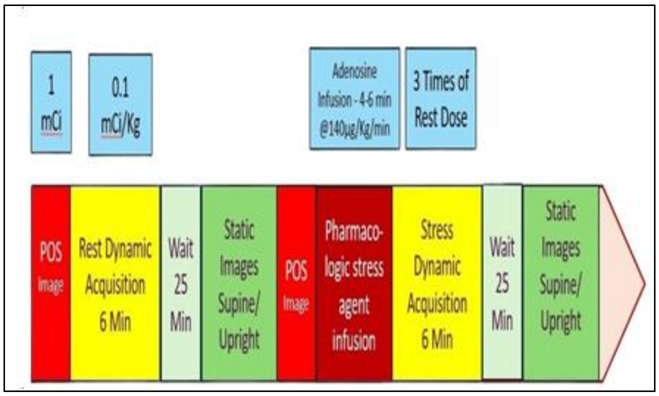

Figure-1: Flow Chart of events for a single-day stress rest protocol of dynamic SPECT MPI

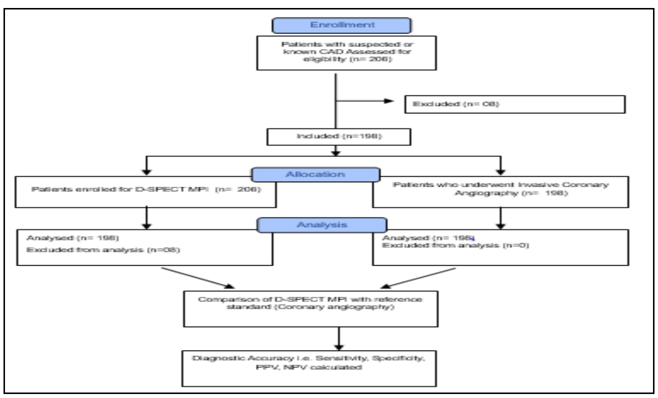

Figure-2:Patient Flow Diagram (n=198)

RESULTS

Of 198 patients, 167(84.3%) were males, and 31(15.7%) were females, with a mean age of 56.03 ±11.83 years (range: 20-86 years). The average BMI was 26.88 ± 4.22. In our study population, the primary cardiovascular disease risk factors included smoking in 48 patients (24.2%), diabetes mellitus in 70 patients (35.4%), hypertension in 103 patients (52.0%), dyslipidemia in 83 patients (41.9%), and a positive family history of CAD in 86 patients (43.4%), as shown in Table-I.

Table-I: Patients' Demographics and Risk Factors Distribution (n=198)

Variable	Values
Age (years)	56.12 ±11.79
Gender	
Male	167 (84.3%)
Female	31 (15.7%)
BMI (kg/m2)	26.88 ± 4.22
Risk Factors	
Smoking	48 (24.2%)
Diabetes mellitus	70 (35.4%)
Hypertension	103 (52.0%)
Dyslipidemia	83 (41.9%)
Family history	86 (43.4%)

Using a global MFR threshold of 2, D-SPECT MPI identified CAD in 70 patients (35.4%), whereas coronary angiography, considered the gold standard, confirmed CAD in 74 patients (37.4%). The sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and diagnostic accuracy of D-SPECT MPI, compared to coronary angiography, were 87.8%, 95.9%, 92.8%, 92.9%, and 92.9%, as shown in Table II.

Table-II: Diagnostic accuracy of D-SPECT MPI for detection of CAD with coronary angiography as the gold standard (n=198)

	Coronary Angiography		
D-SPECT MPI	Positive	Negative	Total
Positive	65 (92.9%)	5 (7.1%)	70 (100.0%)
Negative	9 (7.0%)	119 (93.0%)	128 (100.0%)
Total	74 (37.4%)	124 (62.6%)	198 (100.0%)

Sensitivity = 87.84%
Specificity = 95.97%
Positive predictive value = 92.86%
Negative predictive value = 92.97%
Diagnostic accuracy = 92.93%

**D-SPECT MPI - Dynamic Single Photon Emission Computed Tomography*

To assess the diagnostic accuracy of D-SPECT MPI in predicting coronary angiography results, a Receiver Operating Characteristic (ROC) curve analysis was performed. The resulting area under the ROC curve (AUC) was 0.919 (p-value <0.001), demonstrating excellent discrimination between patients with and without CAD, as depicted in Figure-3. An illustrative case is shown in Figure-4.

DISCUSSION

The findings of the present study suggest that the incorporation of myocardial flow reserve (MFR) assessment into conventional SPECT myocardial perfusion imaging (MPI) using a cadmium-zinc-telluride (CZT) detector-based dynamic SPECT system significantly enhances the diagnostic accuracy for detecting coronary artery disease. Beyond its favorable diagnostic performance, this approach offers practical advantages, including improved image quality, shorter acquisition time, lower radiation exposure, and greater cost-effectiveness compared with cardiac PET, making it a particularly valuable imaging modality in resource-limited healthcare settings.

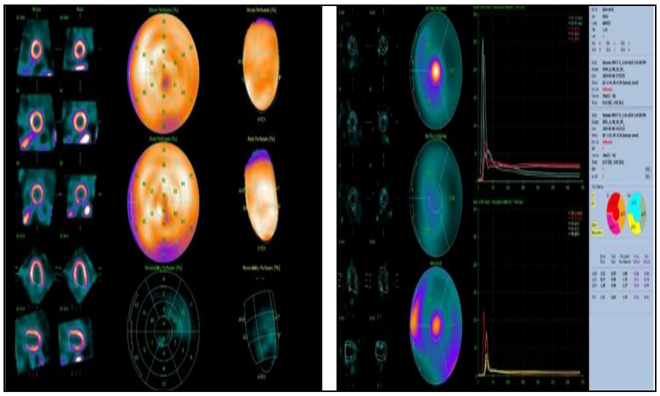

Figure-4: illustrative case with normal conventional spect mpi results and significantly deranged mfr values in territories of all 3 vessels. Later on, invasive coronary angiography confirmed triple-vessel coronary artery disease.

MFR assessment using dynamic SPECT MPI serves as a valuable tool in identifying individuals who are at high risk of adverse cardiovascular events, despite normal visual assessment of conventional SPECT MPI, i.e., patients with false-negative results. Bateman *et al.*, and Murthy *et al.*, have shown that balanced ischemia, vasodilator failure, and microvascular disease may add to these false-negative results and affect the sensitivity of conventional SPECT MPI.[10,11] Mach *et al.*, have demonstrated in their studies that targeted pharmacological interventions, addressing thrombotic and lipid-related risks, significantly reduce cardiovascular events.[12] This is especially important for people with a higher risk for atherothrombotic events, such as those with a history of stable or unstable angina, acute myocardial infarction, ischemic stroke, peripheral arterial disease, or atrial fibrillation. These patients can benefit from aspirin or other antiplatelet therapies to help reduce their risk.[13] Additionally, lipid-lowering medications like statins play a crucial role in preventing major cardiovascular events, with their effectiveness being more pronounced in higher-risk individuals. By helping to identify these high-risk patients, MFR can enhance preventive strategies and optimize treatment decisions.[14]

An MFR value above 2, as measured by PET, is considered normal and is linked to a very low risk of adverse cardiovascular events. Regarding significant CAD, Pang *et al.*, demonstrated a sensitivity of 89.2%, a NPV of 89.3%, and an accuracy of 80.6% with an AUC of 0.832 with coronary artery stenosis > 75%, as taken in our study.[15] Our results are also comparable with a recent meta-analysis published by Panjer *et al.*, which showed a pooled sensitivity of 79% and specificity of 85%.[16] As per the literature search, this is the first study of its kind conducted in Pakistan, as this technology is not widely available yet; therefore, no local comparison was done.

MFR is highly effective in identifying high-risk individuals. A normal global MFR, even in the presence of slightly or moderately abnormal conventional SPECT MPI perfusion results, has a high negative predictive value for excluding the possibility of high-risk CAD on coronary angiography.[17]

While MFR is a powerful predictor of cardiovascular mortality and surpasses stress MBF alone, it is influenced by both hyperemic and resting blood flows. Gupta *et al.*, confirmed in cases of hibernating myocardium, both stress and resting MBF may be low, leading to a seemingly normal MFR. Conversely, an abnormal MFR can be observed despite a normal stress MBF if resting MBF is elevated. Therefore, combining the assessment of stress MBF and MFR enhances diagnostic accuracy and provides a more comprehensive evaluation of myocardial perfusion.[18]

In our dynamic SPECT MPI protocol, we administered 350 MBq for stress acquisition and 750 MBq for rest acquisition. Unlike some studies, the authors used the same-day stress/rest protocol. While this approach was longer for patients, it allowed for multiple prone and/or supine static acquisitions, enhancing the overall quality of MPI images. This was particularly beneficial in reducing artifacts caused by parietal attenuation or digestive uptake, especially in the inferior wall.[19]

Our study found that patients with severe coronary artery stenosis had significantly lower overall SPECT MFR. Additionally, our results suggest that global SPECT MFR may serve as a reliable marker for identifying angiographically significant coronary artery lesions. These findings are consistent with earlier PET studies, further supporting the clinical value of SPECT MFR in assessing coronary artery disease.

Conversely, an MFR value of less than 1.5 is known to be strongly associated with poor prognosis, regardless of other risk factors. Our findings align with a recent dynamic SPECT MPI study by Bailly *et al.*, which demonstrated a correlation between MFR calculated using CZT SPECT MPI and obstructive coronary artery lesions confirmed by coronary angiography. Their study identified that global MFR is an independent predictor of CAD, with dynamic SPECT MPI achieving a sensitivity of 83.3% and a specificity of 100%, along with an AUC of 0.94.7. They have further demonstrated in their study that MFR results remain consistent irrespective of attenuation correction. In this study, the authors chose not to apply it in this research.[25]

LIMITATION OF STUDY

This study is limited by its relatively small sample size and lack of direct comparison with PET-derived MFR, the gold standard; however, prior studies report comparable MBF and MFR quantification using CZT-based dynamic SPECT MPI with 99mTc-sestamibi. Dynamic SPECT MPI is a functional test, whereas ICA is anatomical, and the weak correlation between stenosis severity and ischemia may have influenced diagnostic performance. Routine attenuation correction was impractical because most CZT-based SPECT cameras lack CT integration. Motion correction was not applied, although all data were reviewed for artifacts. Inter- and intra-observer variability and MBF/MFR reproducibility were not assessed.

In future large-scale multi-center studies with clinical follow-up, further validation of the prognostic value of MFR-guided risk stratification and evaluation of its impact on patient outcomes, healthcare resource utilization, and overall cost-effectiveness in diverse population groups are necessary.

CONCLUSION

This study demonstrated that adding MFR to conventional SPECT MPI using a CZT detector-based dynamic SPECT MPI provides high diagnostic accuracy for detecting coronary artery disease. In addition to superior image quality and high diagnostic performance, it offers shorter imaging time, lower radiation exposure, and cost-effectiveness compared with cardiac PET, which is particularly important in resource-intensive healthcare settings. Given the high burden of CAD and limitations of healthcare infrastructure, dynamic SPECT MPI offers a valuable and practical advancement in noninvasive cardiac imaging, with subsequent enhanced clinical outcomes. These findings support incorporating MFR assessment into routine SPECT MPI, particularly in high-risk clinical settings.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

HS & MIN: Data acquisition, data analysis, critical review, approval of the final version to be published.

ZS & MA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MR & MA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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