Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2024i1.1426
*Biol. Clin. Sci. Res. J., Volume, **2024**: 1426*
Original research article

MYOCARDIAL FLOW RESERVE MEASUREMENT USING CADMIUM ZINC-TELLURIDE SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY MYOCARDIAL PERFUSION IMAGING AND RELATION TO ANGIOGRAPHIC CORONARY ARTERY DISEASE

ASLAM S[1*], ASLAM U[1], AHMED K[2], ASLAM S[3], KALEEM M[3], ASLAM S[4]

[1]*Armed Forces Institute of Cardiology & National Institute of Heart Diseases, Rawalpindi, Pakistan*
[2]*Children Hospital Lahore, Pakistan*
[3]*Azad Jammu Kashmir Medical College, AJK, Pakistan*
[4]*Combined Milltary Hospital Abbottabad, Pakistan*
**Correspondence author email address:* Soibaaslam4@gmail.com

(Received, 27th August 2024, Revised 20th December 2024, Published 30th December 2024)

Abstract: *The addition of Myocardial flow reserve (MFR) to Single Photon Emission Computed Tomography (SPECT) Myocardial Perfusion Imaging (MPI) by using Cadmium Zinc Telluride (CZT) camera for screening of CAD may improve high-risk patient identification and diagnostic performance.* ***Objective:*** *This study aimed to assess the severity of coronary artery disease using MFR by SPECT MPI and comparing it with angiography finding.* ***Methods:*** *It was a cross-sectional study which was carried out in Armed Forces institute of cardiology and National Institute of Heart Diseases, Rawalpindi from June to Oct 2024. The myocardial flow reserve was calculated using Cadmium Zinc Telluride with 99mTc-sestamibi as radiotracer using SPECT MPI. Disease severity was also assessed using coronary angiography. Chi-square and Fischer exact test was applied for cross-tabulation. Kappa statistics was used to determine the level of agreement between the procedures. P-value less than 0.05 was taken as statistically significant.* ***Results:*** *The 100 patients with mean age of 64.90 + 3.60 years. The mean myocardial blood flow at rest is 1.06 + 0.18 mL/g/min, and at stress is 2.42 + 0.74 mL/g/min. The Myocardial flow reserve mean was 2.23 + 0.52 mL/g/min across sample of study. There is no association between CAD severity determined by SPECT MPI and demographic factors (p > 0.05). Coronary artery disease severity determined by Myocardial flow reserve (MFR) using SPECT MPI and angiography showed statistical significance with p-value of <0.001 and strong agreement with kappa value of 0.784, suggesting MPI SPECT a valuable tool for determining coronary artery disease severity.* ***Conclusion:*** *Cadmium Zinc Telluride gamma camera in SPECT MPI is a user-friendly, non-invasive and low-dose dynamic modality which provides a role of effective indicator of CAD. Myocardial reserve flow played significant role in determination of coronary artery disease severity, suggesting lower the mean myocardial reserve flow the higher the severity of the coronary artery disease. The association between them is also independent of the patient demographics, traditional risk factors and cardiovascular health of the patients, which make SPECT MPI as an independent alternative viable option for diagnosis of CAD.*

Keywords: Coronary artery disease, Cadmium Zinc-Telluride, SPECT MPI, Myocardial blood flow, Myocardial flow reserve.

Introduction

Coronary artery disease (CAD) is not only the leading cause of mortality and morbidity, but it is also significantly impacting health and economic systems worldwide (1). It is more prevalent in low- and middle-income countries (LIMCs) (2). The possible risk factors of CAD are growing age of population, dietary habits, smoking, obesity and the change in lifestyle (3). Therefore, there is need for early detection to manage it timely to reduce risk factors and optimize treatment strategies for better health outcomes.
Traditional diagnostic techniques e.g. invasive coronary angiography or myocardial perfusion imaging (MPI) despite being effective has demonstrated risks include radiation exposure and high costs (4). This shifts the focus to the alternative diagnostic non-invasive technique. Cadmium Zinc telluride (CZT) Single photon Emission Computed Tomography Myocardial Perfusion Imaging (SPECT MPI) is crucial and provide non-invasive tool to diagnose CAD (5). It revolutionized imaging by quantifying myocardial blood flow (MBF) and myocardial flow reserve (MFR) due to its more sensitive as well as specific assessment as compared to traditional MPI (6).

Myocardial flow reserve (MFR) is a significant diagnostic tool due to its risk assessment value in CAD patients (7). Positron emission tomography (PET) is the gold standard for MFR measurement, but its restricted availability necessitates other methods (8). Stress MBF divided by rest MBF yields myocardial flow reserve (MFR), a valid indicator of coronary artery disease function (9). Diabetes, dyslipidemia, hypertension, renal dysfunction, obesity, and smoking are known to affect MFR, as in epicardial artery stenosis (10).
The "gold standard" for assessing coronary artery stenosis severity is coronary arteriography (11). Zampella et al (2021) initially tested the feasibility of quantifying regional and global MFR in humans using a CZT camera D-SPECT (12). Zhang et al (2023) found that the non-invasive MBF and MFR assessments in CAD patients are inversely and nonlinearly associated to angiography stenosis severity. Percentage area stenosis measures angiographic stenosis severity. Stable CAD patients are categorized by magnitude of luminal stenosis: <50%, 50% to 70%, 70% to 90%, and >90%. Interestingly, coronary lesions with 50%-70% area stenosis showed a considerably greater myocardial flow reserve with P < 0.05 (13). Myocardial flow reserve was

[Citation: Aslam, S., Aslam, U., Ahmed, K., Aslam, S., Kaleem, M., Aslam, S., (2024). Myocardial flow reserve measurement using cadmium zinc-telluride single photon emission computed tomography myocardial perfusion imaging and relation to angiographic coronary artery disease. *Biol. Clin. Sci. Res. J.*, **2024**: *1426*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1426]

significantly decreased in vessels with >90% area stenosis compared to vessels with <50% (13). De Souza et al. found that high-risk CAD patients had a lower global MFR than those without CAD (1.99 vs. 2.89) (14).
MFR using SPECT MPI CZT is possible and measures angiographic disease severity. (6) Adding MFR to SPECT MPI for CZT camera CAD screening may improve high-risk patient identification and diagnostic performance. MFR may help doctors decide on invasive coronary angiography. Accurate measurement of coronary stenosis' physiological severity may help objectively determine medical versus mechanical treatment and evaluate treatment effects. These assessments may also be beneficial in silent coronary artery disease patients as the only foundation for choosing medicinal or mechanical intervention to avert sudden death and myocardial infarction and for monitoring disease progression or regression. This study uses SPECT MPI by CZT camera to calculate the mean MFR to determine CAD severity.

Methodology

It was a cross-sectional study which was carried out in Armed Forces institute of cardiology and National Institute of Heart Diseases, Rawalpindi from June to Oct 2024. Consecutive non-probability sampling technique was used. World Health organisation (WHO) sample size calculator was used to calculate sample size. Sample size of 100 with confidence level 95% was estimated taking anticipated mean l.4+0.4, absolute precision 0.08 (15).
Adults with stable coronary artery disease (CAD) with age above 50 years were included. Patients of both gender with stable CAD were considered. However, Patients having BMI > 35 Kg / m2, heart failure (NYHA III/IV), acute coronary syndrome within 30 days prior to inclusion in the study, pregnant or active breastfeeding females, 2nd or 3rd degree AV Block, allergy to angiographic contrast media were excluded.
All patients meeting inclusion criteria undergoing coronary angiography and MFR calculation using SPECT MPI were included. Permission from the institutional ethical committee was also taken before the commencement of study. History of diabetes, hypertension, dyslipidaemia, smoking, BMI were taken from patients record. Patients underwent l-day protocol SPECT MPI Scan, with rest phase followed by pharmacological stress using adenosine. They were instructed to abstain from caffeine, methylxanthines-containing substances and smoking 24 hours before the scan. Scans were performed in a gamma camera with solid-state pixelated detectors made of cadmium-zinc-telluride with 99mTc-sestamibi as the radiotracer. Dynamic Imaging data and corresponding perfusion information was analyzed by using commercially available software corridor 4M. MBF was computed using the Leppo Renkin-Crone flow model. MFR was calculated as the ratio of the stress to rest MBF. The myocardial flow reserve (MBF stress / MBF rest) values were used to categorise CAD severity as mild (MFR 2.5-2.2), moderate (2.2-2) and severe (<2) stenosis. Patients were undergone coronary angiography using clinical standard techniques. Two experienced interventional cardiologists classified stenotic lesions visually as percentage of luminal area stenosis. A significant obstructive lesion was classified as 70% in a major epicardial artery or 50% in the left main artery. Patients were divided into 4 groups depending on degree of luminal stenosis (<50%, 50% to 70% and 7-% to 90%, >90%). Information was entered on annexed proforma.
All the collected data were entered and analyzed by using SPSS (version 28). The following variables were entered: age, sex, body mass index (BMI), hypertension, diabetes mellitus, smoking, dyslipidaemia, family history of CAD, known CAD. Continuous variables such as age, height, weight BMI, mean MFR were reported as mean + deviation. Categorical variables such as gender, diabetes, hypertension, dyslipidaemia, smoking, CAD stenosis was reported as frequency and percentages. A two-sided p-value < 0.05 was considered statistically significant. Cross-tabulation was done between demographic factors and severity of coronary artery disease determined by SPECT MPI. Chi-square test was applied to determine association and significance. The angiography was taken as gold standard and SPECT MPI scan was compared to determine and compare CAD severity through MFR values kappa statistics. The high kappa statistics indicated high agreement or vice versa.
The data were de-identified to ensure anonymity and confidentiality of patients. The patients were included after taking informed consent with briefing of the purpose and benefits of the study. They were also assured their data will only be used for the benefit of the patients.

Results

The cross-sectional study included 100 patients with mean age of 64.90 + 2.60 years. The gender distribution in this study is almost equally distributed with 53(53%) were males. The mean of body mass index (BMI) was 28.21 + 2.15 Kg/m2, indicating all of the patients were overweight and obese. Moreover, the mean blood flow at rest is 1.06 + 0.18 mL/g/min and mean blood flow at stress 2.42 + 0.74 mL/g/min, and myocardial flow reserve mean was 2.23 + 0.52 demonstrating some of the value fall under two (02), suggesting coronary artery disease (Table 1).

Table 1: Descriptive statistics and Cardiovascular health characteristics of patients (n = 100).

Descriptive variables	Mean	Standard Deviation
Age (years)	64.90	2.60
BMI (Kg/m^2)	28.21	2.15
Stress MBF (mL/g/min)	2.42	0.74
rest MBF (mL/g/min)	1.06	0.18
MFR	2.23	0.52

The study included 53(53%) men presented with cardiovascular risk factors e.g. diabetic history in 31(31%), hypertension in 83(83%), dyslipidaemia in 72(72%), and 21(21%) were currently smoking and the positive family history was reported in 40(40%) and the previous cardiovascular intervention was reported among few of

[Citation: Aslam, S., Aslam, U., Ahmed, K., Aslam, S., Kaleem, M., Aslam, S., (2024). Myocardial flow reserve measurement using cadmium zinc-telluride single photon emission computed tomography myocardial perfusion imaging and relation to angiographic coronary artery disease. *Biol. Clin. Sci. Res. J.*, **2024***: 1426*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1426]

patients e.g. 08(8%) underwent PCI, and only 03(3%) underwent CABG (Table 2).

Table 2: Cross-tabulation to determine association between CAD severity determined by myocardial flow reserve using SPECT MPI and demographic factors.

Effect modifiers			CAD severity Mild stenosis	Moderate stenosis	Severe stenosis	Total	(p- value)
Age	Middle age	Count	2	0	3	5	2.411* (0.299)
		% within	40.0%	0.0%	60.0%	100.0%	
	Older age	Count	23	31	41	95	
		% within	24.2%	32.6%	43.2%	100.0%	
Total		Count	25	31	44	100	
		% within	25.0%	31.0%	44.0%	100%	
Gender	Male	Count	17	14	22	53	3.182** (0.204)
		% within Gender	32.1%	26.4%	41.5%	100.0%	
	Female	Count	8	17	22	47	
		% within Gender	17.0%	36.2%	46.8%	100.0%	
Total		Count	25	31	44	100	
		% within Gender	25.0%	31.0%	44.0%	100.0%	
BMI category	Normal weight	Count	1	0	1	2	4.038* (0.671)
		% within	50.0%	0.0%	50.0%	100.0%	
	Overweight	Count	16	21	29	66	
		% within	24.2%	31.8%	43.9%	100.0%	
	Class I obese	Count	7	8	14	29	
		% within	24.1%	27.6%	48.3%	100.0%	
	Class II obese	Count	1	2	0	3	
		% within	33.3%	66.7%	0.0%	100.0%	
Total		Count	25	31	44	100	
		% within	25.0%	31.0%	44.0%	100.0%	
Type of CAD	Obstructive CAD	Count	16	17	31	64	1.925** (0.382)
		% within	25.0%	26.6%	48.4%	100.0%	
	Non-Obstructive CAD	Count	9	14	13	36	
		% within	25.0%	38.9%	36.1%	100.0%	
Total		Count	25	31	44	100	
		% within	25.0%	31.0%	44.0%	100.0%	
Previous CABG	Yes	Count	2	0	1	3	3.187* (0.203)
		% within	66.7%	0.0%	33.3%	100.0%	
	No	Count	23	31	43	97	
		% within	23.7%	32.0%	44.3%	100.0%	
Total		Count	25	31	44	100	
		% within	25.0%	31.0%	44.0%	100.0%	
Previous PCI	Yes	Count	4	1	3	8	3.127* (0.200)
		% within	50.0%	12.5%	37.5%	100.0%	
	No	Count	21	30	41	92	
		% within	22.8%	32.6%	44.6%	100.0%	
Total		Count	25	31	44	100	
		% within	25.0%	31.0%	44.0%	100.0%	
Previous family history	Positive	Count	14	12	14	40	3.195** (0.141)
		% within	35.0%	30.0%	35.0%	100.0%	
	Negative	Count	11	19	30	60	
		% within	18.3%	31.7%	50.0%	100.0%	
Total		Count	25	31	44	100	
		% within	25.0%	31.0%	44.0%	100.0%	
Dyslipidemia	Yes	Count	8	8	5	21	4.178** (0.095)
		% within	38.1%	38.1%	23.8%	100.0%	
	No	Count	17	23	39	79	
		% within	21.5%	29.1%	49.4%	100.0%	

Total		Count	25	31	44	100	
		% within	25.0%	31.0%	44.0%	100%	
Current Smoker	Yes	Count	15	23	34	72	2.466 ** (0.291)
		% within	20.8%	31.9%	47.2%	100.0%	
	No	Count	10	8	10	28	
		% within	35.7%	28.6%	35.7%	100.0%	
Total		Count	25	31	44	100	
		% within	25.0%	31.0%	44.0%	100.0%	
Diabetic	Yes	Count	22	26	35	83	0.509* (0.775)
		% within	26.5%	31.3%	42.2%	100.0%	
	No	Count	3	5	8	16	
		% within	18.8%	31.2%	50.0%	100.0%	
Total		Count	25	31	43	99	
		% within	25.3%	31.3%	43.4%	100.0%	
Hypertension	Yes	Count	8	10	13	31	0.078** (0.962)
		% within	25.8%	32.3%	41.9%	100.0%	
	No	Count	17	21	31	69	
		% within	24.6%	30.4%	44.9%	100.0%	
Total		Count	25	31	44	100	
		% within	25.0%	31.0%	44.0%	100.0%	

*LMS (left main stem), LAD (left anterior descending artery), LCX (left circumflex artery), RCA (right circumflex artery), PCI (percutaneous coronary intervention), CABG (Coronary artery bypass graft). * Indicated Fischer exact value, ** indicated Chi-Square value.*

Coronary artery disease (CAD) severity determined by myocardial flow reserve (MFR) calculated using SPECT MPI scan is strongly aligned with the CAD severity determined using gold standard angiography. There is statistical significance difference between them with p-value of <0.001 and high kappa value of 0.784, suggesting SPECT MPI a valuable tool for determining CAD severity (Table 3).

Table 3: Comparison between SPECT MPI and Angiography for determination of CAD severity.

			Angiography severity			**Total**	**Fischer exact (P-value)**
			Mild	**Moderate**	**Severe**		
CAD severity using MFR	Mild stenosis	Count	25	0	3	28	132.268 (<0.001)
		% of Total	25.0%	0.0%	3.0%	28.0%	
	Moderate stenosis	Count	0	23	3	26	
		% of Total	0.0%	23.0%	3.0%	26.0%	
	Severe stenosis	Count	0	8	38	46	
		% of Total	0.0%	8.0%	38.0%	46.0%	
Total		Count	25	31	44	100	
		% of Total	25.0%	31.0%	44.0%	100.0%	

Symmetric Measures					
		Value	Asymptotic Standard Error [a]	Approximate T[b]	Approximate Significance
Measure of Agreement	Kappa	0.784	0.054	11.001	<0.001
N of Valid Cases		100			
a. Not assuming the null hypothesis.					
b. Using the asymptotic standard error assuming the null hypothesis.					

Discussion

The cross-sectional study included 100 patients with mean age of 64.90 + 2.60 years and 53(53%) males to calculate mean myocardial flow reserve using Cadmium Zinc Telluride (CZT) camera in SPECT MPI because it is non-invasive procedure and measures angiographic disease

[Citation: Aslam, S., Aslam, U., Ahmed, K., Aslam, S., Kaleem, M., Aslam, S., (2024). Myocardial flow reserve measurement using cadmium zinc-telluride single photon emission computed tomography myocardial perfusion imaging and relation to angiographic coronary artery disease. *Biol. Clin. Sci. Res. J.*, **2024***: 1426*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1426]

severity effectively. The sensitivity analysis showed that coronary artery disease (CAD) severity determined via myocardial flow reserve (MFR) estimation using MPI SPECT scan is strongly aligned with the CAD severity determined using gold standard angiography. There is statistical significance difference between SPECT MPI scan and angiography with p-value of <0.001 and high kappa value of 0.784, suggesting SPECT MPI a valuable tool for determining CAD severity. All the patients were presented with over-weight and obese with mean of body mass index (BMI) was 28.21 + 2.15 Kg/m2. The mean myocardial blood flow at rest is 1.06 + 0.18 mL/g/min, and at stress is 2.42 + 0.74 mL/g/min. The Myocardial flow reserve mean was 2.23 + 0.52 mL/g/min across sample of study ranging from 2.13 to 2.33 at 95% confidence interval. Moreover, there is statistically significant difference was found between mean MFR among patients of CAD with varying disease severity (p =0.019), demonstrating mean MFR decrease as the increase in severity of CAD. The least mean MFR was observed among severe CAD patients. After post-stratification of patient's demographics, patient cardiovascular risk factors and cardiovascular parameters, there is statistically not significant difference found (p > 0.05) suggesting no role of effect modifying of CAD by these factors.

This cross-sectional study found that myocardial flow reserve estimated using SPECT MPI is vital predictor for determination of coronary artery disease severity taking angiography as gold standard (P < 0.001; kappa = 0.784). Similarly, the finding is consistent with the study conducted by Joutsiniemi E et al. The authors found 81% sensitivity of predicting coronary artery stenosis using MFR optimal cut off value of 2.5 when took angiography as gold standard (16). Moreover, the predictive ability of MFR estimated using SPECT MPI scan is also aligned with the recent meta-analysis which also showed 82% sensitivity of myocardial flow reserve to predict CAD severity (17).

Myocardial reserve flow is comprehensive and critical indicator of myocardial microvascular function. It also increases the coronary circulation capacity when stress is imposed on it due to increase in oxygen demand. The reduced myocardial reserve flow indicated endothelial dysfunction and microvascular impairment. The mean myocardial blood flow at rest is 1.06 + 0.18 mL/g/min, and at stress is 2.42 + 0.74 mL/g/min. The myocardial blood flow is reduced after stress. Wang et al (2023) also found the stress MBF is reduced while quantifying MBF using stress cardiac magnetic resonance (CMR) imaging (18). Moreover, Gregg et al (2021) also explained that MBF quantification to determine CAD severity is credible to determine myocardial, endovascular, microvascular dysfunction (19). So, the findings and literature showed significance of accurate MBF quantification in both clinical as well as research setting, demonstrating comprehensive understanding of myocardial perfusion.

The lower mean myocardial reserve flow of 2.23 + 0.52 mL/g/min is found to be associated with increased coronary artery disease severity (p = 0.019). Similarly, Alahdab et al (2024) found in patients with aortic stenosis that MFR also correlated with worsening of coronary artery microvascular health and myocardial remodeling despite absence of ischemia, showing a association between decreased MFR and CAD severity (20). In another study, Maltseva et al (2023) also reported that impaired MFR is also linked with CAD severity among patients with non-obstructive coronary artery disease. Moreover, Maltseva et al (2023) also showed that lower MFR also linked with the known risk factors of cardiovascular disease e.g. higher levels of cholesterol and low-density lipoprotein (21). However, lowered MFR is not associated with the dyslipidemia among CAD patients of this study, which poised contrasting findings as compared to existing literature.

Mean myocardial flow reserve of 2.23 + 0.52 mL/g/min was measured using Cadmium Zinc Telluride SPECT MPI. When comparing the mean MFR value measured using 99mTc-sestamibi CZT SPECT MPI with other modality Positron Emission Tomography (PET) scan, there is consistency found in measuring MFR by two methodology (22). Similarly, Yamamoto et al (2022) compared SPECT using 99mTc-sestamibi and NH3-PET scan to measure MFR. The authors found strong and significant correlation (r = 0.6) between two modalities to estimate mean MFR (23). Furthermore, the findings are more validated and their credibility is ensured by Agostini et al (2018), who also found consistent MFR value measured by CZT in SPECT MPI while comparing it with 150-Water PET. It ensured the credibility and reliability of the MFR value measured by two methods (24). Therefore, the use of CZT in SPECT MPI is considered as credible and viable alternative tool to evaluate myocardial reserve flow in clinical setting.

The post-stratification of patient demographics, cardiovascular risk factors and cardiovascular parameters showed that there is no significant difference between these factors and mean myocardial reserve flow (MFR) p > 0.05. This indicated that the mean MFR is correlated CAD severity independent of traditional cardiovascular factors. Tsao et al (2024) also found similar results that angiographic CAD burden is independent of the traditional risk factors, showing these factors did not account for CAD severity (25). However, Mangalesh et al (2022) found atherogenic index plasma as significant predictor of coronary artery disease severity despite absence of conventional risk factors (26). Therefore, there is comprehensive clinical assessment and examination is needed in clinical practice to evaluate and screen all patients. Future researchers must explore these diverse risk factors to give a clear clinical picture while evaluation of CAD patients.

Cadmium Zinc Telluride SPECT MPI is beneficial due to its non-invasive and low-dose dynamic imaging. It also helpful in quantification of myocardial blood flow and myocardial reserve flow which is vital in diagnosing coronary artery disease and endothelial dysfunction despite any need of invasive modalities such as coronary angiography (6). Gobbo et al (2022) also explained that SPECT MPI assessed different pathophysiological mechanism of microvascular dysfunction of myocardial tissue among patients with ischemia as well as non-constructive coronary arteries, which further validate and enhanced its diagnostic abilities (27). Moreover, the cadmium Zinc Telluride Gamma camera is an advanced technology which makes it more valuable tool in nuclear cardiology (28). Therefore, SPECT MPI is a user friendly and non-invasive technique to manage and diagnose coronary artery disease patients effectively.

The study design of cross-sectional study limits its ability to determine causal factors and only involve one-time findings without any follow-up. The study is observational and it does not directly compare CZT SPECT MPI with other modalities to give direct comparison. Therefore, it is recommended to conduct future randomized controlled trails to directly compare studies. The study is based on single center which limits its generalizability. Therefore, the multicentre study is needed to further validate the findings. The progression of disease cannot be determined due to cross-sectional study design, which suggested future researchers to conduct longitudinal studies. However, there are some strengths of the study such as the interpretation is drawn by the expert radiologist to infer the images findings to ensure validity of the findings as the findings are also discussed with the resident consultants to ensure authenticity. The finding also presented non-invasive credible and authentic modality to implicate its use in clinical set ups to ensure evidence-based practice. The findings are also applicable to easily diagnose also those patients which don't have any symptoms of coronary arteries disease but likely to be suffer myocardial tissue lack of perfusion.

Conclusion

The addition of Cadmium Zinc Telluride gamma camera in SPECT MPI make it valuable tool and user-friendly, non-invasive and low-dose dynamic modality which provides a role of effective indicator of coronary artery disease severity. Coronary artery disease (CAD) severity determined using myocardial flow reserve (MFR) using CZT camera in MPI SPECT scan is strongly aligned with the CAD severity determined using gold standard angiography. There is statistical significance difference between them with p-value of <0.001 and high kappa value of 0.784, suggesting MPI SPECT using CZT camera a valuable tool for determining coronary artery disease severity. The association between them is also independent of the patient demographics, traditional risk factors and cardiovascular health of the patients, which make CZT SPECT MPI as an independent alternative viable option for diagnosis of CAD. Furthermore, the comprehensive clinical evaluation of risk factors is needed to diagnose and indicate factors which may play role in the progression of CAD. This study is limited to answer it due to its study design. Therefore, there is need for longitudinal studies to assess these factors through follow ups and present the clear clinical picture of predictors and risk factors in modifying coronary artery disease.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate.
Approved by the department Concerned. (IRBEC-TCHMM-02996/23)
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

Authors Contribution

SOIBA ASLAM (Resident FCPS Cardiology)
Final Approval of version
USMAN ASLAM (Fellow Intervention Cardiology)
Revisiting Critically
KAMRAN AHMED (Resident Paeds)
Data Analysis
SIDRA ASLAM (Assistant Professor Of Hematology MBBS)
Drafting
MOHAMMAD KALEEM (Assistant Professor Pathology MBBS) & SANA ASLAM (FCPS Dermatologist)
Concept & Design of Study

References

1. Vliegenthart R. Future Trends in CT for Coronary Artery Disease: From Diagnosis to Prevention. Radiology. 2023 May;307(3):e223285. doi: 10.1148/radiol.223285.
2. Zilla P, Bolman RM 3rd, Boateng P, Sliwa K. A glimpse of hope: cardiac surgery in low- and middle-income countries (LMICs). Cardiovasc Diagn Ther. 2020 Apr;10(2):336-349. doi: 10.21037/cdt.2019.11.03.
3. Shao C, Wang J, Tian J, Tang YD. Coronary Artery Disease: From Mechanism to Clinical Practice. Adv Exp Med Biol. 2020;1177:1-36. doi: 10.1007/978-981-15-2517-9_1.
4. Alam L, Omar AMS, Patel KK. Improved Performance of PET Myocardial Perfusion Imaging Compared to SPECT in the Evaluation of Suspected CAD. Curr Cardiol Rep. 2023 Apr;25(4):281-293. doi: 10.1007/s11886-023-01851-4.
5. D'Antonio A, Assante R, Zampella E, Mannarino T, Buongiorno P, Cuocolo A et al. Myocardial blood flow evaluation with dynamic cadmium-zinc-telluride single-photon emission computed tomography: Bright and dark sides. Diagn Interv Imaging. 2023 Jul-Aug;104(7-8):323-329. doi: 10.1016/j.diii.2023.02.001.
6. Pang ZK, Wang J, Chen Y, Chu HX, Zhang MY, Li JM. [Diagnostic efficiency and incremental value of myocardial blood flow quantification by CZT SPECT for patients with coronary artery disease]. Zhonghua Xin Xue Guan Bing Za Zhi. 2022 May 24;50(5):494-500. Chinese. doi: 10.3760/cma.j.cn112148-20211124-01018.
7. Aljizeeri A, Ahmed AI, Alfaris MA, Ahmed D, Farea J, Elneama A et al. Myocardial Flow Reserve and Coronary Calcification in Prognosis of Patients With Suspected Coronary Artery Disease. JACC Cardiovasc Imaging. 2021 Dec;14(12):2443-2452. doi: 10.1016/j.jcmg.2021.01.024.
8. Dahdal J, Jukema RA, Harms HJ, Cramer MJ, Raijmakers PG, Knaapen P et al. PET myocardial perfusion imaging: Trends, challenges, and opportunities. J Nucl Cardiol. 2024 Oct;40:102011. doi: 10.1016/j.nuclcard.2024.102011.
9. Miller RJH, Manabe O, Tamarappoo B, Hayes S, Friedman JD, Slomka PJ et al. Comparative Prognostic and Diagnostic Value of Myocardial Blood Flow and Myocardial Flow Reserve After Cardiac Transplantation. J Nucl Med. 2020 Feb;61(2):249-255. doi: 10.2967/jnumed.119.229625.
10. Mohammed AQ, Abdu FA, Liu L, Yin G, Mareai RM, Mohammed AA et al. Coronary microvascular dysfunction and myocardial infarction with non-obstructive coronary arteries: Where do we stand? Eur J

Intern Med. 2023 Nov;117:8-20. doi: 10.1016/j.ejim.2023.07.016.
11. Thakur U, Nogic J, Comella A, Nerlekar N, Chan J, Abrahams T, et al. Computed tomography coronary angiography assessment of left main coronary artery stenosis severity. J Cardiovasc Comput Tomogr. 2024 Jul 17:S1934-5925(24)00393-9. doi: 10.1016/j.jcct.2024.07.005.
12. Zampella E, Assante R, Gaudieri V, Nappi C, Acampa W, Cuocolo A. Myocardial perfusion reserve by using CZT: It's a long way to the top if you wanna standardize. J Nucl Cardiol. 2021 Jun;28(3):885-887. doi: 10.1007/s12350-019-01817-6.
13. Zhang J, Xie J, Li M, Fang W, Hsu B. SPECT myocardial blood flow quantitation for the detection of angiographic stenoses with cardiac-dedicated CZT SPECT. J Nucl Cardiol. 2023 Dec;30(6):2618-2632. doi: 10.1007/s12350-023-03334-z.
14. de Souza ACDAH, Gonçalves BKD, Tedeschi AL, Lima RSL. Quantification of myocardial flow reserve using a gamma camera with solid-state cadmium-zinc-telluride detectors: Relation to angiographic coronary artery disease. J Nucl Cardiol. 2021 Jun;28(3):876-884. doi: 10.1007/s12350-019-01775-z.
15. Di Carli M, Czernin J, Hoh CK, Gerbaudo VH, Brunken RC, Huang SC et al. Relation among stenosis severity, myocardial blood flow, and flow reserve in patients with coronary artery disease. Circulation. 1995 Apr 1;91(7):1944-51. doi: 10.1161/01.cir.91.7.1944.
16. Joutsiniemi E, Saraste A, Pietilä M, Mäki M, Kajander S, Ukkonen H, Airaksinen J, Knuuti J. Absolute flow or myocardial flow reserve for the detection of significant coronary artery disease?. Eur Heart J Cardiovasc Imaging. 2014 Jun;15(6):659-65. doi: 10.1093/ehjci/jet274.
17. Ding A, Qiu G, Lin W, Hu L, Lu G, Long X, Hong X, Chen Y, Luo X, Tang Q, Deng D. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in ischemia-causing coronary stenosis: a meta-analysis. Jpn J Radiol. 2016 Dec;34(12):795-808. doi: 10.1007/s11604-016-0589-4.
18. Wang S, Kim P, Wang H, Ng MY, Arai AE, Singh A, et al. Myocardial Blood Flow Quantification Using Stress Cardiac Magnetic Resonance Improves Detection of Coronary Artery Disease. JACC Cardiovasc Imaging. 2024 Sep 6:S1936-878X(24)00313-9. doi: 10.1016/j.jcmg.2024.07.023.
19. Gregg S, Keramida G, Peters AM. Measuring myocardial blood flow with ^{82}rubidium using Gjedde-Patlak-Rutland graphical analysis. Ann Nucl Med. 2021 Jul;35(7):777-784. doi: 10.1007/s12149-021-01591-x.
20. Alahdab F, Ahmed AI, Nayfeh M, Han Y, Abdelkarim O, Alfawara MS et al. Myocardial Blood Flow Reserve, Microvascular Coronary Health, and Myocardial Remodeling in Patients With Aortic Stenosis. J Am Heart Assoc. 2024 Jun 4;13(11):e033447. doi: 10.1161/JAHA.123.033447.
21. Maltseva A, Kop'eva K, Mochula A, Gulya M, Dymbrylova O, Grakova E, et al. Association of impaired myocardial flow reserve with risk factors for cardiovascular diseases in patients with nonobstructive coronary artery disease. Russian Journal of Cardiology. 2023;28(2):5158. https://doi.org/10.15829/1560-4071-2023-5158.
22. Ko KY, Ko CL, Lee CM, Cheng JS, Wu YW, Hsu RB et al. Myocardial Flow Assessment After Heart Transplantation Using Dynamic Cadmium-Zinc-Telluride Single-Photon Emission Computed Tomography With ^{201}Tl and ^{99m}Tc Tracers and Validated by $^{13}N\text{-}NH_3$ Positron Emission Tomography. Circ Cardiovasc Imaging. 2023 Jun;16(6):e015034. doi: 10.1161/CIRCIMAGING.122.015034.
23. Yamamoto A, Nagao M, Ando K, Nakao R, Matsuo Y, Sakai A et al. First Validation of Myocardial Flow Reserve Derived from Dynamic ^{99m}Tc-Sestamibi CZT-SPECT Camera Compared with ^{13}N-Ammonia PET. Int Heart J. 2022;63(2):202-209. doi: 10.1536/ihj.21-487.
24. Agostini D, Roule V, Nganoa C, Roth N, Baavour R, Parienti JJ et al. First validation of myocardial flow reserve assessed by dynamic ^{99m}Tc-sestamibi CZT-SPECT camera: head to head comparison with ^{15}O-water PET and fractional flow reserve in patients with suspected coronary artery disease. The WATERDAY study. Eur J Nucl Med Mol Imaging. 2018 Jul;45(7):1079-1090. doi: 10.1007/s00259-018-3958-7.
25. Tsao NL, Abramowitz S, Shakt G, Judy R, Damrauer SM, Levin M. Angiographic Burden Of Coronary Atherosclerosis Contributes To Adverse ASCVD Outcomes Independent Of Traditional Risk Factors. Arteriosclerosis, Thrombosis, and Vascular Biology. 2024;44(Suppl_1):A3119-A.
26. Mangalesh S, Yadav P, Dudani S, Mahesh NK. Atherogenic index of plasma predicts coronary artery disease severity and major adverse cardiac events in absence of conventional risk factors. Coron Artery Dis. 2022 Nov 1;33(7):523-530. doi: 10.1097/MCA.0000000000001166.
27. Gobbo MY, Meretta AH, Sciancalepore M, Retamozo E, Beber E, Rosa D, et al. INOCA: Evaluación no invasiva de los mecanismos fisiopatológicos mediante CZT-SPECT. Revista argentina de cardiología. 2022;90(3):194-202. https://doi.org/10.7775/rac.es.v90.i3.20515.
28. Bereta M, Babečka J, Straka J, Valko P, Lacko A, editors. The Benefits of Nuclear Cardiology Examinations Using Cardiologic SPECT Gamma Camera. 2023 14th International Conference on Measurement; 2023: IEEE. 10.23919/measurement59122.2023.10164545.

[Citation: Aslam, S., Aslam, U., Ahmed, K., Aslam, S., Kaleem, M., Aslam, S., (2024). Myocardial flow reserve measurement using cadmium zinc-telluride single photon emission computed tomography myocardial perfusion imaging and relation to angiographic coronary artery disease. *Biol. Clin. Sci. Res. J.*, **2024***: 1426*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1426]