ORIGINAL ARTICLE OPEN ACCESS

Prognostic Impact of Body Mass Index on Coronary Artery Disease Using Gated Myocardial Perfusion Imaging-Single Photon Computed Tomography

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ABSTRACT

Background: Gated Myocardial Perfusion Imaging Single-Photon Emission Computed Tomography (GMPI-SPECT) is a nuclear stress test; performed to observe perfusion of cardiac tissue and its related defects; to diagnose / stratifying risk in individuals either suspected or known cases of coronary artery disease (CAD) whereas body mass index (BMI) is used for screening of obesity. The objective of this study was to investigate the impact of BMI on the prognosis of intermediate-risk CAD patients, stratified by GMPI-SPECT results in both genders.

Methods: Ziauddin University Hospital was the setting of this prospective cross-sectional descriptive study, from March 2017 to December 2019 using non-probability purposive sampling. Non-obese and obese GMPI-SPECT patients (n=115) were divided into two major groups (male and female). Patients were interviewed after 18 months regarding cardiac events with/without interventional procedures. SPSS v.23 was used with $p<0.05$ considered significant.

Results: In the study, 56.5% were male, 57.4% were obese, and higher BMI males with an intermediate risk prognosis on GMPI-SPECT have a 7.5% risk of minor cardiac events. In post hoc analysis it was observed that samples with intermediate risk have significantly higher BMI as compared to high-risk samples $p=0.028$). Pearson Chi-Square test gives a significant association between GMPI-SPECT outcomes and 18-month intervals with a $p<0.01$. One-way ANOVA gives a significant mean difference in BMI concerning GMPI-SPECT outcomes ($p<0.05$).

Conclusion: The study findings suggest that men with higher BMI, multiple risk factors, and intermediate risk prognosis on GMPI-SPECT do have a risk of experiencing a minor cardiac incident within 18 months.

Keywords: Gated-Myocardial Perfusion Imaging-SPECT, Body Mass Index, Coronary Artery Disease.

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Doi: https://doi.org/10.36283/PJMD13-3/017

How to cite: Jalil A, Sattar S, Khurshaidi IUH, Rameez A. Prognostic Impact of Body Mass Index on Coronary Artery Disease Using Gated Myocardial Perfusion Imaging-Single Photon Computed Tomography. Pak J Med Dent. 2024;13(3): 123-131. Doi: 10.36283/PJMD13-3/017

Received: Tue, Aug 01, 2023 **Accepted:** Fri, Apr 19, 2024 **Published:** Wed, 24 July 2024

INTRODUCTION

Obesity is a chronic, multifactorial, neurobehavioral disease, that takes time to appear, resulting in deteriorating not only psychosocial health conditions but also metabolic and biochemical consequences in an individual. Risk factors that contribute to developing obesity are also considered involved in compromising cardiac health (i.e., unhealthy eating habits, lack of physical activity, inappropriate sleeping habits, mental stress, etc.). So, if obesity arises from unhealthy habits and has an impact on an individual's health metabolically and biochemically, then people who have disturbed body mass index may be more prone to develop cardiac illnesses. Central obesity if accompanied by dyslipidemia (lower high-density lipoprotein and raised triglycerides levels), hypertension, and raised fasting plasma glucose level, represents metabolic syndrome, that can deteriorate the cardiovascular system[1]. This is the reason why people who are obese are often advised to screen for cardiac diseases. Other than basic screening tests, nuclear cardiology is also receiving attention among physicians and cardiologists for patients who have risk factors and co-morbidities.

GMPI-SPECT (Gated-Myocardial Perfusion Imaging Single-Photon Emission Computed Tomography) is a nuclear stress test; performed to observe the perfusion of cardiac tissue and its related defects. It is a modern way to diagnose and stratify risk in individuals suspected with or known cases of coronary artery disease (CAD), accurately[2]. Relation of body mass index (BMI) with CAD is an important issue among individuals suffering from risk factors i.e., Diabetes Mellitus (DM), Hypertension (HTN), Positive Family History of Ischemic Heart Disease (IHD), Smoker/Tobacco addict, Dyslipidemia, etc. of IHD. Obesity has always been linked with cardiac diseases and many of the investigations for evaluation of ischemic heart diseases (including GMPI-SPECT) are advised in patients who are obese and have relevant symptoms i.e., dyspnea on mild to moderate exertion, chest pain or discomfort, palpitations, etc. However, as the GMPI-SPECT study is software dependent, differences in the size of myocardial perfusion defect and the function of the left ventricle (LV) are observed when different software is used for the study[3]. Although 3-dimensional myocardial perfusion cardiovascular magnetic resonance is considered an alternate for GMPI-SPECT, due to its lack of availability and patient-related issues, GMPI-SPECT remains in practice for the purpose[4].

BMI is an easy way to measure excess adipose tissue/-fat in the human body and is measured by dividing the weight of the body in kilograms by the height in meters squared. It is used for screening obesity and its related health risks. High BMI may predict future morbidity and mortality, including hypertension, diabetes mellitus, dyslipidemia, stroke, CAD, degenerative joint disease, psychosocial disability, and early death [5]. Among the South Asian population, Pakistani people have a higher margin of body fat as compared to that of white people of the same age/gender, thus our BMI range is different as compared to that of white people along with cardiac and vascular diseases [6,7]. Unfortunately currently in practice interventions and policies have not been able to put a pause in the rise in BMI in most countries [8,9].

The relationship between cardiac disease and future cardiac events with its risk factors has always been a topic of discussion [10]. Studies have been done in the past to evaluate the relationship between obesity and the risk of cardiac diseases[9]. Other than the conventional risk factors, the age and sex of the patients also contribute to the diagnostic accuracy of nuclear test [10]. Thus, the presence of non-modifiable factors (age, gender, family history, etc.) and modifiable factors (sedentary lifestyle, smoking, alcohol, nicotine-containing chewable items and co-morbidities like diabetes, hypertension, chronic renal disease, dyslipidemia) may be the reason for raising queries over the accuracy of cardiac nuclear imaging. Assessment of cardiac events in patients with normal BMI or normal GMPI-SPECT has also been done in the past[11].

GMPI-SPECT result has a great influence on the future handling of patients with coronary artery disease / ischemic heart disease. This is understood that patients with a "High-risk Prognosis" have more chances of developing future cardiac events as compared to those with an Intermediate and Low-risk patient group. "Intermediate Risk Prognosis" patients lie in between low and high-risk groups and thus should be assessed and followed up periodically by their cardiologists. This is one of the reasons for focusing on this group and correlating it with BMI among gender. The relationship of different groups of BMI (obese and non-obese) with intermediate-risk prognosis patients (based on GMPI-SPECT results), in both genders has not been assessed in Pakistan yet. The objective of this study was to investigate the impact of BMI on the prognosis of intermediate-risk CAD patients, stratified by GMPI-SPECT results in both genders.

METHODS

It was a prospective cross-sectional descriptive study, conducted in the Nuclear Medicine department, Dr. Ziauddin University Hospital North Campus, Karachi from March 2017 to December 2019, after the informed and written consent of the patients, approved by the ethical research committee Ziauddin University ERC Reference Code: 7871023AJNM. Our sample size was calculated using an open epi sample size calculator for proportion version 3.01, by inserting 34.9% of prevalence of CAD among underweight {European Heart Journal – Cardiovascular Imaging (2013) 14, 456–463}, at 10% error margin and confidence interval of 95% we need (n=115) patients for our research[12]. Our sampling technique is

non-probability purposive sampling.

Patients regardless of age and risk factors restrictions, who came for GMPI-SPECT advised by their respective cardiologists were included in the study, while the exclusion criteria were patients with acute chest pain / unstable angina (<48 hours), acute myocardial infarction (2-4 days of scan) uncontrolled arrhythmias, CCF, or hemodynamically unstable patients. The study population was split into two main groups regarding gender (male and female patients). These main groups are subdivided into two regarding BMI (obese and non-obese). The research was conducted by collecting data on all patients undergoing GMPI-SPECT in the local department, after informed and written consent. Firstly, BMI calculation was made by measuring height in meters square and weight in Kg before the start of the procedure in the Stress Lab. Secondly; all data including a complete history, relevant examination findings, and GMPI-SPECT result was collected.

All patients underwent a single-day, GMPI-SPECT Tc-99m SESTAMIBI study. Patients were asked to avoid tea, and coffee for 12 hours, hold rate limiting drugs (beta blockers/calcium channel blockers) for at least 12-24 hours, and have a light breakfast 2-4 hours before study. Physical stress was performed by exercising on a treadmill following "Bruce protocol" with injecting radiotracer at peak stress if tolerated. Pharmacological stress was performed using adenosine or persantin/dipyridamole infusion at 140 ug/Kg/min for 4-6 minutes with injection of radiotracer in adenosine in mid of infusion and in persantin/dipyridamole after 6 minutes of infusion. Antidote aminophylline was given as an antidote to patients who developed adverse effects from a pharmacological stress-inducing agent. The total effective radiation dose was around 10mSv[13]. Both stress and rest SPECT acquisition was performed using a single-headed E-CAM signature series Siemens Gamma Camera.

Patients were divided into two major groups on gender (>40 patients each). Then further two subgroups were made based on their BMI (non-obese and obese), then all patients/guardians were interviewed on the telephone/internet at around 18 monthly time intervals about any cardiac event with or without interventional procedure (i.e., Angina, NSTEMI, STEMI or Fatal MI, LHC, PCI, CABG). Study groups are divided into two subgroups obese and non-obese for both genders as per the international classification of BMI[6]. Obese if B.M.I ≥ 25 Kg/m2 & non-obese if B.M.I < 24.9 Kg/m^2. The following criteria for categorization of risk on GMPI-SPECT have been followed:

Low-Risk Prognosis: <1% chance of a cardiac event in the future. Normal or small myocardial perfusion defect at rest or with stress. Intermediate Risk Prognosis: 1-3% chance of a cardiac event in the future. Stress-induced moderate perfusion defect without LV dilation. High-Risk Prognosis: >3% chance of cardiac events in the future. Stress-induced large perfusion defect (particularly if anterior). Stress-induced multiple perfusion defects of moderate size. Large fixed perfusion defect with LV dilation. Image Reconstruction and Left Ventricular Functional Parameter: EF ≥55%, ESV <70ml & WM score of zero are being accepted as normal. GMPI with SSS and SDS <2 is considered as normal.

Data were stored and analyzed using IBM-SPSS version 23.0, and counts with percentages were reported for qualitative characteristics (Gender, obesity, MPI) of studied samples. Descriptive analysis included mean, standard deviation (SD), and minimum and maximum values reported for quantitative parameters (Age, BMI, Height, Weight, etc.). One way Analysis of variance using the F-test was used to compare the mean of BMI with MPI outcomes, Tukey's HSD test was used in post hoc analysis as a multiple comparison test, and Pearson Chi-square test was used to check the association of studied parameters and MPI outcomes. P-values <0.05 were considered statistically significant.

RESULTS

In the present study, there were 115 samples. The baseline characteristics of studied samples include a mean age of 56.0 ±11.0 years, mean height was 161.8 ±10.2 cm, mean weight was 72.1 + 13.4 kg, mean BMI was 27.5 + 4.6 kg/m2, mean waist circumference was 98.2 ± 18.8 cm, and mean hip circumference was 107.3 +21.8 cm. Minimum and maximum values of data were showing data were found within suitable ranges as per studied parameters. While qualitative characteristics of studied samples demonstrate that there was 56.5% male gender, 57.4% were obese, 68.7% of samples with Pharmacological MPI, 29.6% with Exercise MPI, 58.3% of samples were found with intermediate risk of MPI, samples with 18-month follow-up were 16.5% of minor and 1.7% with Major cardiac event, here major cardiac event is defined as the composite of total death, myocardial infarction, coronary revascularization, stroke, and hospitalization because of heart failure; while the minor cardiac event is any cardiac event other than major one, i.e., angina or limited hospitalization including non-ST elevation myocardial infarction. Table 1 represents the qualitative characteristics of the studied samples.

Table 1: Qualitative Characteristics of Studied Samples (n=115)

Characteristics		n	%
Gender	Male	65	56.5
	Female	50	43.5
Obesity	Obese	66	57.4
	Non-Obese	49	42.6
GMPI SPECT	Pharmacological	79	68.7
	Exercise	34	29.6
	Viability	2	1.7
GMPI SPECT Outcome	Low risk	21	18.3
	Intermediate risk	67	58.3
	High risk	27	23.5
18 Month time interval cardiac event	No	94	81.7
	Minor	19	16.5
	Major	2	1.7

According to the research data, that we had collected from patients; regarding risk factors for CAD, there were 38.3% had ischemic heart disease, 22.6% had CABG/PCI, 50.4% were diabetes mellitus, 75.7% were Hypertensive, 22.6% were tobacco users/smokers, 7% were chronic kidney disease, 33.9% having a positive family history of ischemic heart disease, 47.8% were dyslipidemia, 37.4% with a sedentary lifestyle and 34.8% with post-menopausal.

These associations of GMPI-SPECT outcomes with studied parameters are represented in Table 2. Among samples with low risk there were 52.4% were male, 57.1% were obese, 57.1% with pharmacological GMPI-SPECT, none of them with 18-month time interval cardiac event, among samples with intermediate risk there were 52.2% were male, 62.7% were obese, 73.1% with pharmacological GMPI-SPECT, 7.5% of them with 18-month time interval with minor cardiac event whereas among samples with higher risk there were 70.4% were male, 44.4% were obese, 66.7% with pharmacological GMPI-SPECT, and 51.9% of them with 18-month time interval with minor cardiac event and 7.4% with major cardiac event. Pearson Chi-Square test gives a significant association between GMPI-SPECT outcomes and 18-month time intervals with a p-value less than 0.01.

Table 2: Association of GMPI-SPECT Outcomes with Studied Parameters

Parameters		GMPI-SPECT Outcome						p-value
		Low risk		Intermediate risk		High risk		
		n	%	n	%	n	%	
Gender	Male	11	52.4	35	52.2	19	70.4	0.25
	Female	10	47.6	32	47.8	8	29.6	
Obesity	Obese	12	57.1	42	62.7	12	44.4	0.27
	Non-Obese	9	42.9	25	37.3	15	55.6	
GMPI-SPECT	Pharmacological	12	57.1	49	73.1	18	66.7	0.51
	Exercise	9	42.9	17	25.4	8	29.6	
	Viability	0	0.0	1	1.5	1	3.7	
18 Month time interval cardiac Event	No	21	100.0	62	92.5	11	40.7	<0.01*
	Minor	-	-	5	7.5	14	51.9	
	Major	-	-	0	0.0	2	7.4	

**p-value was obtained using the Pearson-Chi Square test*

The mean BMI of the low-risk sample was 27.6 (SD=±4.8) kg/m2, the mean BMI of intermediate risk sample was 28.3 (SD=±4.5) kg/m2, and the mean BMI of High-risk samples was 27 (SD=±4.2) kg/m2. One-way ANOVA gives a significant mean difference in BMI concerning GMPI-SPECT outcomes, p<0.05. The mean comparison of Body mass index concerning GMPI-SPECT outcomes is shown in Table 3.

Table 3: Mean Comparison of Body Mass Index with GMPI-SPECT Outcomes

GMPI-SPECT Outcomes	n	Mean	SD	p-value
Low risk	21	27.6	4.8	0.037*
Intermediate risk	67	28.3	4.5	
High risk	27	25.6	4.2	

Table 4 gives multiple comparisons of BMI concerning GMPI-SPECT outcomes using Tukey's HSD test. In post hoc analysis it was observed that samples with intermediate risk have significantly higher BMI as compared to high-risk samples, p=0.028.

Table 4: Multiple Comparison of BMI with GMPI-SPECT Outcomes

Comparison of	Comparison with	Mean Difference	p-value
Low risk	Intermediate risk	-0.65	0.834
Low risk	High risk	2.04	0.273
Intermediate risk	High risk	2.70	0.028*

**p<0.05 was considered significant using Tukey's HSD test*

Figure 1 is an image of a myocardial perfusion imaging scan, showing medium-size reversible perfusion ischemia of moderate intensity including an apical, mid-cavity segment of anterior, anteroseptal walls and LV apex with borderline enlarged LV cavity size; while the rest of the myocardium shows normal perfusion.

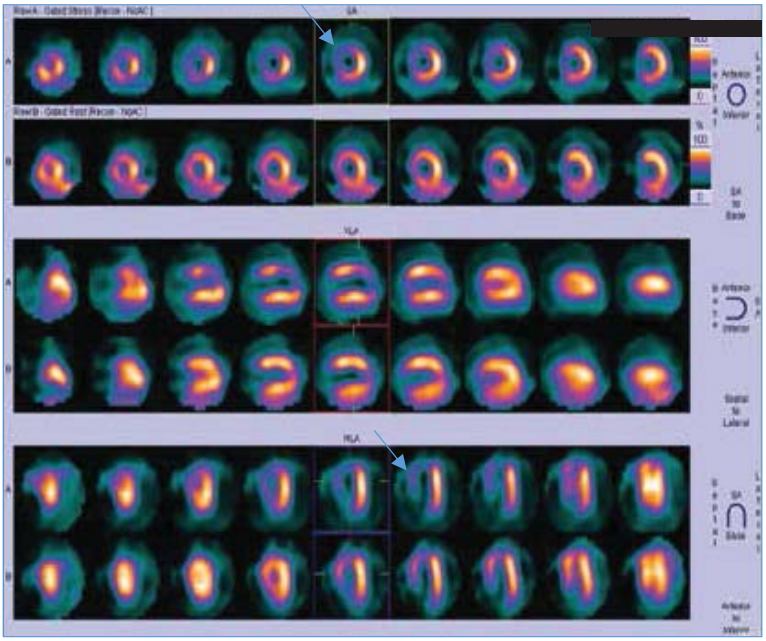

Figure 1: GMPI-SPECT Cardiac Stress image.

 DOI: https://doi.org/10.36283/PJMD13-3/017

Figure 2 is a Gated and volume-measurable display of the same patient, representing the perfusion reversibility (%), showing the extent and reversibility of perfusion ischemia as a polar map and 3D volume display. On the right; the stress extent (%) & reversibility are shown graphically.

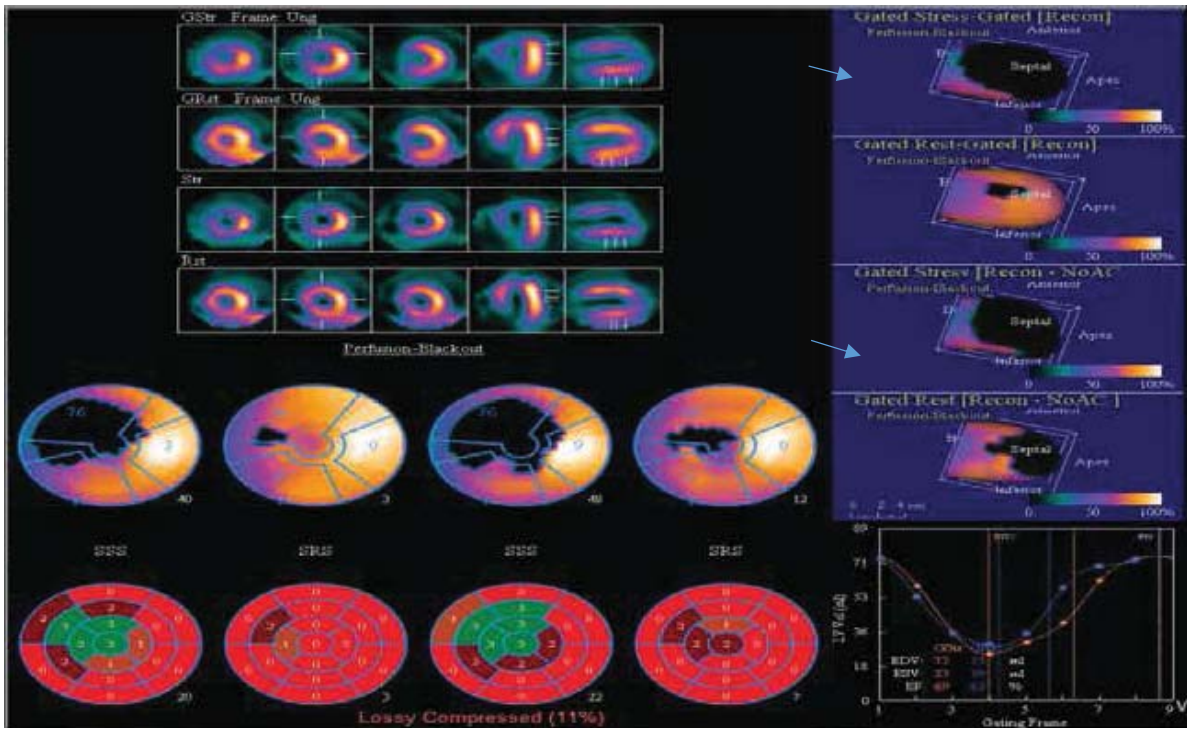

Figure 2: Gated and volume measurable display.

DISCUSSION

Studies have justified that the risk of developing cardiovascular illnesses begins in early life[14]. Lifestyle in early childhood and adolescence that includes unhealthy habits such as high fat and high-calorie diet, smoking or chewing tobacco, with lack of physical activities or from home / sedentary way of living, leads to the development of early onset of risk factors unfortunately these unhealthy habits in lifestyle is found in Pakistani children[15]. If remain uncontrolled for a long time, these risk factors develop cardiovascular disease, which in the South Asian population is an important cause of morbidity and is one of the leading contributors to mortality among the population[16]. For evaluation of suspected, high-risk, or known cases of CAD and its long-term prognosis there are several non-invasive tests like ECG, echocardiography, exercise tolerance test, etc. which assess myocardial function, viability, and coronary anatomy. Among these tests, GMPI-SPECT possesses an important place specifically for candidates with ECG anomalies, weak exercise capacity, or median pre-test possibility of ailment corresponding to the ECS guidelines[17].

GMPI-SPECT visualized the relative allocation of blood flow in coronary vessels that is usually unchanged in the absence of MI / CAD. GMPI-SPECT gamma camera receives the gamma rays emitted by a radiopharmaceutical from the patient's cardiac tissue and proselytizes the raw data into digital data representing the magnitude of tracer uptake and its site from the myocardium. By getting dynamic scintigraphic data, left ventricle functional information can be estimated in a cine pattern referred to as a gated study. Therefore, merging GMPI-SPECT to ECG monitor in physical or pharmacological stress tests provides information regarding regional ischemia resolution, regional wall motion abnormalities evaluation, and myocardial viability. By providing quantitative data regarding myocardial tissue blood flow (ESV, EDV) with cardiac vessels and cardiac tissue anatomy, hybrid imaging (SPECT/CT) offers room for a little descriptive non-invasive assessment of atherosclerosis in cardiac tissue and arteries (CAD) [18,19].

Obesity is measured as a threat for CAD and augmented death ratio from variable causes including cardiovascular disease. The incidence of an intermediate-risk GMPI-SPECT in a patient having

an excess of body fat was meaning fully advanced than patient that falls in the "non-obese" category. The reason might be because of somewhat aged patients and higher male predominance in the obese group. The frequency of well-perfused GMPI-SPECT in our obese group was less (12 out of 66 individuals / 18.1%) than published data (113 out of 267 individuals / 42.3%) with patients younger than our group with female dominance as well, however sample sizes differ[20]. Likewise, a negative predictive value of more than 99% in both male and female patients with normal GMPI-SPECT complies with different studies5. Somewhat more minor cardiac incidents (including angina or limited hospitalization) in the non-obese group conflict with a study on obese patients with a normal GMPI-SPECT[21].

Incidence of abnormal GMPI-SPECT was relatively high in the obese group (54 out of 66 individuals / 81.8%) and the reason for this could be the relatively older age and higher male dominance who are supposed to be at higher risk for CAD. Further significant information from our study was that higher body fat content was an important predictor of CAD in the male gender. This information opposes a decade-old published study that demonstrates that the incidence of CAD in female gender progresses with raised BMI[22]. Event-free survival for patients with intermediate-risk prognosis GMPI-SPECT was significantly lower in the non-obese group and this could be explained by the inclusion of hospital visits or admission, predominantly for illnesses not related to ischemia or cardiac pathology in the non-obese group. Few publications show less supportive results in obese patients despite having a normal GMPI-SPECT [21,22].

Raised non-fatal incidents in the non-obese group in comparison to the obese cohort can be justified by poor compliance to medicine, unwillingness to seek adequate medical help, or insufficient healthcare management proceeding to multiple symptomatic events and hospital visits. No fatal cardiac event was observed in the study; however, major non-fatal events were found in obese male patients but the percentage was not high. This result goes with a couple of studies that showed fewer in-hospital deaths of patients and major cardiac incidents in patients after cardiac tissue damage or interventions. The reason for the increase in the number of minor cardiac events in the non-obese subject could be uncontrolled risk factors of CAD or higher tolerance of ACE-inhibitor treatment in obese patients. Our study shows that individuals with intermediate risk have significantly higher BMI as compared to high-risk patients; but Simati S. with colleagues shows only BMI determination is not sufficient, however, other factors also play a role in the development/progression of cardiovascular disease (i.e., body compartment quantitative determination, duration of risk factors and obesity and use of cardioprotective medications in past[23].

We conclude that, with a follow-up of around 18 months, the risk of developing future cardiac events was higher in obese males as compared to that in non-obese and female patients that fall in the category of an intermediate-risk prognosis in GMPI-SPECT. Low-risk prognosis GMPI-SPECT shows an event-free follow-up in both genders, regardless of body fat content. Obese males that fall in the high-risk prognosis group of GMPI-SPECT showed major but non-fatal cardiac events; while no fatal or non-fatal major cardiac event was found in non-obese males, obese and non-obese female patients.

Our study is single-centered and has a limited sample size (due to participants' refusal to study participation, lower incidence of CAD and /or ignorance of its related symptoms among young patients (≤ 40 years), lack of seeking medical advice, and expenses/cost of the test). Larger multi-center studies are needed to enhance sample size and include young participants, individuals from all socioeconomic backgrounds, different comorbidities, and BMI variability (including underweight patients' category as well) in the research; duration follow-up might be more helpful for further evaluating cardiac event incidences in an intermediate risk prognosis group.

CONCLUSION

The study indicates that men with higher BMI, multiple risk factors, and intermediate risk prognosis on GMPI-SPECT do have a risk of experiencing a minor cardiac incident within 18 months. However, no major cardiac incidents were observed during this observation period. It is important to note that the risk of major cardiac events may persist if risk factors remain uncontrolled, underscoring the need for long-term monitoring and management. Long-term follow-up would be required to assess major cardiac events. The take-home message is to keep the modifiable risk factors under control, proper monitoring, and regular follow-ups; because it may decrease the chances of experiencing future cardiac events, especially among individuals whose prognosis isn't good.

ACKNOWLEDGEMENTS

I like to acknowledge the staff of the Nuclear Medicine Department, Dr. Ziauddin University Hospital North Campus for their contribution.

CONFLICT OF INTERESTS

No conflict of interest.

ETHICS APPROVAL

Ethical approval was obtained from the Ethics

Review Committee of Ziauddin University ERC Reference Code: 7871023AJNM.

PATIENT CONSENT

Informed consent was obtained from each participant of the study. Proforma and history having information on demographic profile and variables like age, gender, BMI, and risk factors of coronary heart disease were filled by the principal investigator.

AUTHORS CONTRIBUTION

All authors equally contributed to this research study.

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