TITLE: PROGNOSTIC IMPACT OF BODY MASS INDEX ON CORONARY ARTERY DISEASE USING GATED MYOCARDIAL PERFUSION IMAGING-SINGLE PHOTON COMPUTED TOMOGRAPHY.

AUTHORS LIST & AFFILIATION:

Asad Jalil[1], Sajid Sattar[2], Imtiaz Ul Haque Khurshaidi[3], Aitadal Rameez[3]

[1]Nuclear Medicine & Theranostics, Dow University of Health Sciences, Karachi. [2]Nuclear Medicine Department, Sindh Institute of Urology and Transplantation, Karachi. [3]Nuclear Medicine Department, Dr. Ziauddin Hospital, Karachi.

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: This is a prospective cross-sectional descriptive study, conducted 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 $p<0.05$).

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.

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 system1 . 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), accurately2 . 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 study3 . 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 purpose4 . 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 death5 . 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 diseases6,7. Unfortunately currently in practice interventions and policies have not been able to put a pause in the rise in BMI in most countries8,9. The relationship between cardiac disease and future cardiac events with its risk factors has always been a topic of discussion10. Studies have been done in the past to evaluate the relationship between obesity and the risk of cardiac diseases9 . Other than the conventional risk factors, the age and sex of the patients also contribute to the diagnostic accuracy of nuclear test10. 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 past11. 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.

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.

According to the research data, that we had collect- ed 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. 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 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, $p=0.028$.

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 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.

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

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

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	

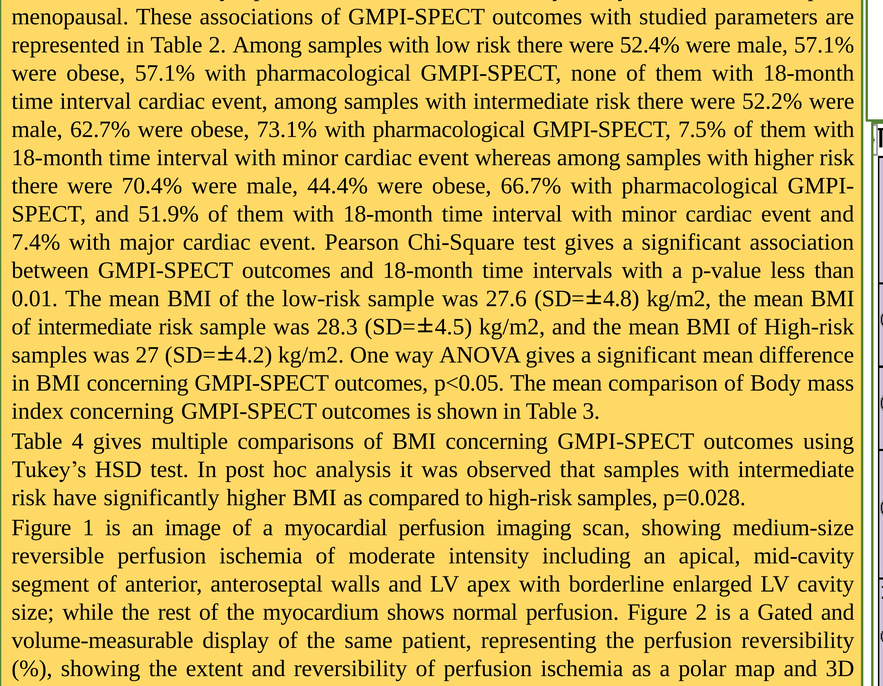

Figure 2: Gated and volume measurable display.

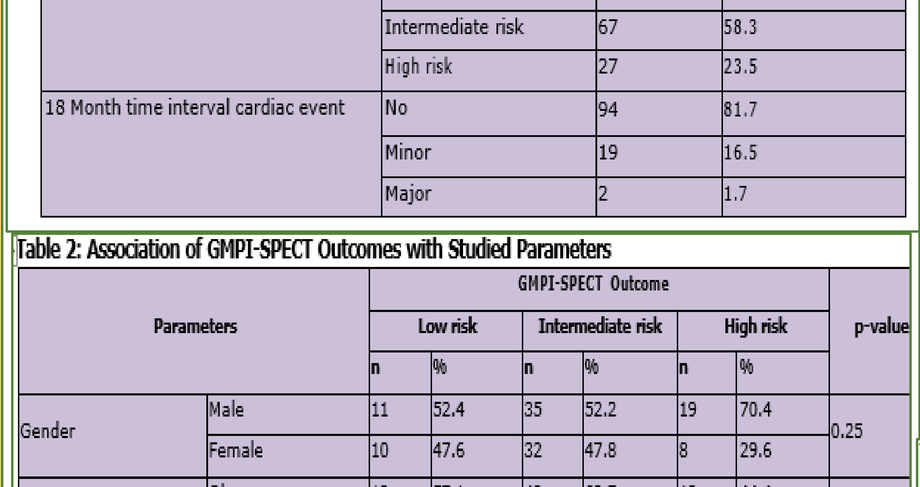

Figure 1: GMPI-SPECT Cardiac Stress image.

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 under- weight {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 research12. 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/K- g/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 10mSv13. 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 BMI6. Obese if B.M.I ≥ 25 Kg/m2 & non-obese if B.M.I <24.9 Kg/m2. 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.

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

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.

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