PREDICTIVE VALUE OF BODY MASS INDEX (BMI) AND WAIST CIRCUMFERENCE (WC) FOR CORONARY ARTERY DISEASE (CAD) AND CLINICAL OUTCOMES USING GATED MYOCARDIAL PERFUSION IMAGING

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ABSTRACT

OBJECTIVE: Obesity is generally considered as a risk factor for coronary artery disease (CAD) and cardiac deaths but some reports suggest better survival in obese with CAD. The objective of this study was to find out predictive value of body mass index (BMI) and waist circumference (WC) for CAD and its outcome using gated myocardial perfusion imaging (GMPI). **MATERIAL AND METHODS:** This was a prospective study conducted at Nuclear Cardiology Department of Karachi Institute of Heart Diseases (KIHD), Karachi, Pakistan from August 2011 till May 2013. 400 patients who qualified study criteria were included and were divided in (a) to Obese (BMI ≥ 30 Kg/m^2) and Non-obese (BMI < 30 Kg/m^2) and (b) Low-WC group (male < 90 cm and female < 80 cm) and High-WC group (male ≥ 90 cm and female ≥ 80 cm). Rest and stress GMPI using Tc-99m MIBI was performed in all patients and abnormal GMPI was followed by coronary angiogram. These patients were followed for 12-18 months regarding fatal and non-fatal events. **RESULTS:** Non-Obese group included 281 patients (Male: Female = 131:150) with a mean age of 58 ±12 years and mean WC 100 ±15 cm. Obese group included 119 patients (Male: Female = 36:83) with a mean age of 55 ±11 years and mean WC 101±13 cm. Normal GMPI was found in 172 non-obese and 85 obese patients (p<0.05). GMPI was abnormal in 109 non-obese and 34 obese patients (p<0.05). WC was not found independent predictor of abnormal GMPI but high WC was found to a significant predictor of CAD in non-obese females (Odd ratio 8.04; 1.041 – 62.127). At 18 months event-free survival in normal GMPI group for non-fatal MI was 99.4% in non-obese group and 94.1% for obese (significant P value). For fatal MI, event-free survival was 99.4% in non-obese and 100% for obese (non-significant P value). In patients with abnormal GMPI event-free survival for non-fatal events was 95.4% in non-obese group and 82.3% in obese group (significant P value). While event-free survival for fatal MI was 96.3% in non-obese group and 98.1% for obese (significant P value). **CONCLUSION:** We conclude that CAD was found less prevalent in obese group and High-WC predicted CAD in non-obese females only and was not found an independent predictor. A normal GMPI predicted very high event free survival for fatal events in obese and non-obese but significantly lower for non-fatal events in obese group. Obese group with abnormal GMPI had lower risk for cardiac deaths but higher risk for non-fatal events than non-obese patients with abnormal scans.

Key words: Obesity; Waist circumference, GMPI; event free survival; fatal events

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Introduction

Obesity is now being reported as the new world epidemic afflicting more than 1 billion adults globally and developing nations are not to be spared.[1] There is a general consensus based upon large body of data that obesity (body mass index, BMI ≥ 30 Kg/^{2}m) and being overweight (BMI 25-29.9 Kg/^{2}m) increases risk for cardiovascular disease and also increases risk of total, cardiovascular and cancer mortality.[2,3] However, various well-designed studies have reported that in patients with coronary artery disease (CAD), congestive heart failure (CHF), rheumatoid arthritis, and renal failure on dialysis, higher BMI has been found to improve survival.[4,5,6,7] Central obesity measured by higher waist circumference (WC) indicates larger fat store around waist giving an apple shaped appearance and poses greater risk than fat elsewhere in body.[8] Waist circumference is independently associated with metabolic syndrome components including insulin resistance which is a prerequisite risk factor for diagnosis of syndrome.[9] Gated myocardial perfusion imaging (GMPI) using single photon emission computerized tomography (SPECT) has enjoyed great success over the past several decades as a technique for accurately diagnosing[10] and risk stratifying[11] patients with suspected or known CAD.

The objective of this study was to find out predictive value of BMI and WC for CAD and its outcome using GMPI.

Material and Method

Study design, site and duration: This was a prospective study conducted at Nuclear Cardiology Department of Karachi Institute of Heart Diseases (KIHD), Karachi, Pakistan from August 2011 till May 2013. The study was duly approved by the ethical committee of the institute. Patients with an abnormal GMPI (with dynamic exercise or dipyridamole intervention) who has had a coronary angiogram (CA) done within 6-8 weeks were included. All patients/family were interviewed on telephone (12–18 months follow-up, mean 15 ± 3 months) regarding major cardiac events (MACE) like fatal or non-fatal cardiac events like hospitalization and/or revascularization. Patients with abnormal GMPI who did not have CA within 3 months or those who lost to follow up were excluded from the study.

Study population: From January 2010 till June 2011, 439 patients were accrued who fulfilled the inclusion criteria of the study. On the basis of cut off BMI 30 Kg/m^2 patients were grouped into High BMI ≥ 30 Kg/m^2 (Obese Group) and Low BMI < 30 Kg/m^2 (Non-Obese Group). Similarly depending upon central obesity criteria of International Diabetic Federation (IDF), patients were grouped into Low-WC group (male < 90 cm and female < 80 cm) and High-WC group (male ≥ 90 cm and female ≥ 80 cm).[9] Twenty one patients with abnormal GMPI refused to undergo CA and subsequently 18 more patients were lost to follow up. After excluding these 39 patients, the study cohort included 400 patients.

Acquisition protocol: All patients underwent same day (rest-stress or stress-rest)myocardial perfusion GSPECT using Tc-99m-labeled Methoxy Iso Butyll-sonitrile (MIBI). 10-15 mCi of Tc-99m MIBI was administered intravenously for first study (rest inrest-stress or stress in stress-rest protocol) and 25-30 mCi for second study (stress in rest-stress or rest in stress-rest protocol). Gated stress and non-gated rest SPECT acquisitions were performed using dedicated dual head cardiac (Cardio MD, Philips) gamma camera with low energy allpurpose (LEAP) collimator, 32 projections around a 180° arc, a 64 x 64 matrix and 16 frames per cardiac cycle. Image reconstruction and LV functional parameters [ejection fraction (EF); end diastolic volume (EDV); end systolic volume (ESV); and wall motion (WM)] were contemplated by using commercially available Astonish® and Autoquan® software packages respectively. An EF < 50%, ESV > 70 ml, and sum thickness score (STS) ≥ 2 were considered as abnormal.

Statistical analysis: Comparisons between patient groups were performed using Student's t test for continuous variables and the χ^2 test for categorical variables. Continuous variables were described by mean ± standard deviation (SD). Kaplan–Meier cumulative survival analysis for MACE like fatal and non-fatal events was performed, and survival curves were compared by the Logrank test. Statistical significance was defined as $p < 0.05$.

Results

Non-Obese group (BMI < 30 Kg/m^2) included 281 patients (Male: Female = 131:150) with a mean age of 58 ± 12 years. Risk factor assessment of non-obese

group revealed that 188/281 were hypertensive, 120/281 were diabetic, 110/281 were dyslipidemic, 35/281 were smoker and positive family history for CAD in 88/281 (with significant p value only for hypertension) (Tab.1). Obese group (BMI = 30 Kg/m^2) included 119 patients (Male: Female = 36:83) with a mean age of 55 ± 11 years. Risk factor assessment of obese group revealed that 100/119 were hypertensive, 56/119 were diabetic, 41/119 were dyslipidemic, 08/119 were smoker and positive family history for CAD in 45/119 (with significant p value only for hypertension) (Tab.1).

Variable	Non Obese (BMI <30) 281	Obese (High BMI>30) 119	Test values (χ^2/t-test)	P value
Age mean ±SD (years)	58 ± 12	55 ± 11	-2.342	0.019*
Male: Female	131 : 150 (47%:53%)	36 : 83 (30%:70%)	9.236	0.0024*
Weight mean ±SD (Kg)	65 ± 09	86 ± 12	19.232	<0.0001*
Height mean ±SD (cm)	161 ± 08	158 ± 9	-3.301	0.0010*
BMI mean ±SD (Kg/m^2)	25.105 ± 3.242	34.559 ± 3.726	25.478	<0.0001*
Waist circumference mean ±SD (cm)	100 ± 15	101 ± 13	0.633	0.526
Hypertension	188 (67%)	100 (84%)	11.170	0.0008*
Diabetes Mellitus	120 (43%)	56 (47%)	0.392	0.531
Dyslipidemics	110 (39%)	41 (34%)	0.691	0.405
Family history for CAD	88 (31%)	45 (38%)	1.548	0.213
Smoking	35 (12%)	08 (7%)	1.722	0.189
Abnormal MPI %STS mean ± SD %LVEF mean ± SD	109 (39%) 17 ± 8 %45 ± 15	34 (29%) 14 ± 6 %52 ± 12	3.939 -3.675 2.483	0.0472* 0.0003* 0.0142*
Normal MPI %LVEF mean ± SD	172 (61%) 65±12	85 (71%) 66±09%	3.939 0.667	0.0472* 0.505

*P<0.05
BMI-Body Mass Index
CAD=Coronary Artery Disease
MPI=Myocardial perfusion Imaging
STS=Sum Thickness Score
LVEF=Left Ventricular Ejection Fraction

Table 1: Patients' demographic; total population is 400

Gated MPI was normal in 257 patients (172 in non-obese group and 85 in obese group) with mean EF 65 ± 12 % in non-obese and 66 ± 09 % in obese group. GMPI was found abnormal in 109 patients with non-obese with a mean EF 45 ± 15% and STS 17 ± 8%. In obese group 34 patients had abnormal GMPI with a mean EF % 52 ± 12 and mean STS 14 ± 6% (p <0.05). Obese male had significantly higher abnormal GMPI than obese female (Tab. 2). Waist circumference was not found to be independent predictor of abnormal GMPI (non-significant p values). But high WC was found to a significant predictor of CAD in non-obese females than Low WC (Odd ratio 8.04; 1.041 - 62.127). While in rest, no significant association was found between BMI and WC (Tab. 2).

Variable	Abnormal MPI	Odd ratio (95% CI)	Z statistics	P value
Males with obesity (BMI=30) (36) Vs Females with obesity (BMI=30)	55% : 17% (20 : 14)	6.160 (2.573 to14.750)	4.082	<0.0001*
Low WC (136) Vs High WC (264)	26% : 21% (36:56)	1.287 (0.792 to 2.089)	1.021	0.307
Females with BMI=30 & high WC (31) Vs Females with BMI <30 & low WC (72)	6% : 9% (2:7)	1.562 (0.306 to 7.980)	0.535	0.592
Females with BMI<30 & High WC (129) Vs Females with BMI <30 & Low WC (21)	29% : 5% (37: 1)	8.043 (1.041 to 62.127)	1.999	0.0456*
Males with BMI =30 & Low WC (20) Vs Males with BMI =30 & High WC (16)	55%:31% (11 :5)	2.200 (0.540 to 8.957)	1.101	0.271
Males with BMI <30 & Low WC (84) Vs Males with BMI <30 & High WC (47)	30%:45% (25:21)	1.906 (0.908 to 4.000)	1.706	0.0881

BMI=Body mass index in Kg/m^2
WC=Waist Circumference in inches

Table 2: Gender Based correlation of Body Mass Index and Waist Circumference with abnormal myocardial perfusion findings.

On follow up, in patients with normal GMPI, non-fatal events was reported 01 in non-obese and 05 in obese group; however, 01 fatal event in non-obese and no fatal event was reported in obese group. Kaplan–Meier curve for event-free survival in normal GMPI group for non-fatal MI at 18 month follow-up was 99.4% in non-obese group and 94.1% for obese (significant P value) (Fig.1).

Kaplan-Meier curve for event-free survival in normal GMPI group for fatal MI at 18 month follow-up was 99.4% in non-obese group and 100% for obese (non-significant P value) (Fig.2). In patients with abnormal GMPI, non-fatal events were 05 in non-obese and 06 in obese groups. Four fatal cardiac deaths were reported in non-obese and 01 in obese group with abnormal GMPI. Kaplan-Meier curve in patients with

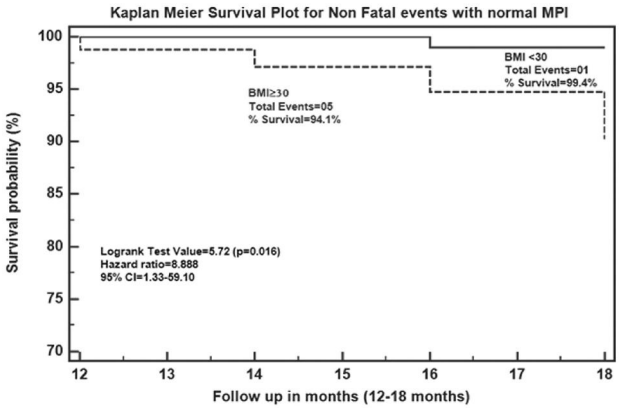

Figure 1: Kaplan Meier Survival Curves for non fatal myocardial events (hospitalization/ischemic attacks) among both groups of body mass index at cut off 30 Kg/m^2 with normal myocardial perfusion imaging results.

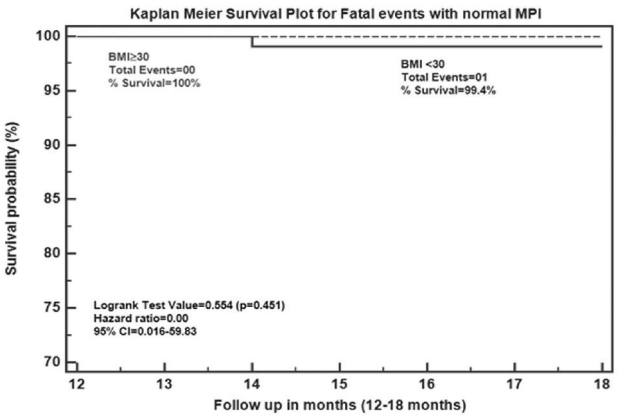

Figure 2: Kaplan Meier Survival Curves for fatal myocardial events among both groups of body mass index at cut off 30 Kg/m^2 with normal myocardial perfusion imaging results.

abnormal GMPI for event-free survival for non-fatal events at 18-month follow-up was 95.4% in non-obese group and 82.3% in obese group (significant P value) (Fig.3). Kaplan-Meier curve for event-free survival for

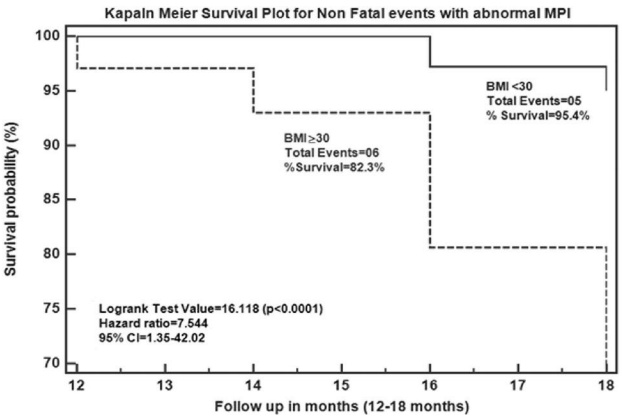

Figure 3: Kaplan Meier Survival Curves for non fatal myocardial events (hospitalization/ischemic attacks) among both groups of body mass index at cut off 30 Kg/m^2 with abnormal myocardial perfusion imaging results.

fatal MI at 18 month follow-up was 96.3% in non-obese group and 98.1% for obese (significant P value) (Fig. 4).

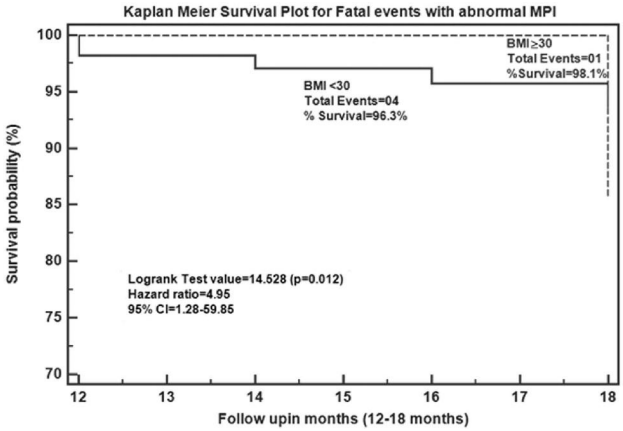

Figure 4: Kaplan Meier Survival Curves for fatal events among both groups of body mass index at cut off 30 Kg/m^2 with abnormal myocardial perfusion imaging results.

Discussion

Obesity is considered as a risk factor for CAD and increase mortality from cardiovascular and other causes.[2,3] However, the results of this study are very interesting and challenging as well.

The incidence of normal GMPI in obese group was significantly higher than non-obese group. This could be due to relatively younger patients and higher female dominance in obese group. Incidence of normal GPMI in our obese group was higher than published data with patients younger than our group with female preponderance as well,[12] although sample size was smaller in that study. Similarly the NPV of >99% in our patients with normal GMPI (except for non-fatal event in obese) is in concordance with other published studies[13] and marginally higher (about 1% hard event rate) in other published study with a longer follow up. Relatively high non-fatal event rate (brief hospitalization for vague) in obese group is in concordance with a study on morbidly obese subject with a normal GMPI.[14]

Incidence of abnormal GMPI was significantly lower in obese group and this could again be explained by the relatively younger and higher female preponderance who are supposed to be at lower risk for CAD. However, this incidence is significantly lower than published studies[12,13] which had relatively elder patient population (33% patients > 77 years).[13]

Another important finding of this study was that obesity was a strong predictor of CAD in male gender. This finding is in contradiction to recently published Million

Women Study which proved that incidence of CAD in women increases progressively with BMI.[15] But a High WC in female with Low BMI (< 30 Kg/m^2) exposes them significantly to CAD and this could be explained by a recent study which depicted that central obesity or "apple appearance" (High WC) was linked with a higher mortality risk even in individuals with normal BMI.[16] High WC was found to be strong predictor of CAD in non-obese patients. However in rest of group no significant correlation was found between BMI and WC.

Event free survival for non-fatal events in patient with normal GMPI was significantly lower in obese group and this could be explained by inclusion of hospitalization which were mostly due to non-cardiac / non-ischemic reasons in obese group. While for fatal events, no significant change was seen among two cohorts with normal GMPI. This is in accordance with a large published trial included more than 14000 patients.[13] However, there are also studies which show less favorable outcome in obese patients despite of having a normal GMPI.[12,14] Higher non-fatal events in obese group than non-obese cohort could be explained by inadequate medical management or poor com-pliance resulted in more episodes hospitalization. But despite of higher non-fatal events in obese group, fatal events were significantly lower than non-obese group. This is in accordance with many published data which have shown lower in-hospital mortality and major cardiac events in obese patients after infarction, angioplasties or by-pass surgeries.[6,17,18] This inverse correlation of obesity with cardiac mortality signifies that obesity appears to be risk factor for CAD but possibly not a risk marker.[19] This protective role of obesity in patients with CAD has fueled the concept of obesity paradox or reverse epidemiology.[13] Possible mechanisms of higher mortality in non-obese patients could be a malnutrition / inflammation complex syn-drome or a greater tolerance of angiotensin-converting enzyme inhibitor therapy in obese patients.[7]

We conclude that CAD was found less prevalent in obese group and High-WC predicted CAD in non-obese females only and not found an independent predictor. A normal GMPI predicted very high event free survival for fatal events in obese and non-obese but significantly lower for non-fatal events in obese group. Obese group with abnormal GMPI had lower risk for cardiac deaths but higher risk for non-fatal events than non-obese patients with abnormal scans.

Confilict of interest: None

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