

Obesity, Cardiac Autonomic Dysfunction and QTc Prolongation in Patients with Myocardial Infarction: A Cross-Sectional Comparison with Healthy Controls



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Abstract

Background: Low vagal tone and a long QTc interval both raise the risk of arrhythmia and death after myocardial infarction (MI). Obesity may worsen both. This study compared heart rate variability (HRV), lipid profile, HbA1c and QTc among obese MI patients, non-obese MI patients and healthy controls, and tested whether BMI independently predicts low vagal HRV.

Methods: This cross-sectional study at Index Medical College, Malwanchal University, Indore included 100 obese MI patients (BMI ≥ 25 kg/m²), 100 non-obese MI patients (BMI 18.5–22.9 kg/m²) and 100 healthy controls, aged 35–65 years. HRV (SDNN, RMSSD, LF/HF ratio), fasting lipids, HbA1c, Troponin T, CK-MB and QTc were measured. ANOVA with Tukey's test, chi-square test, Pearson's correlation and multiple linear regression were used.

Results: RMSSD was 17.5 ± 4.9 ms in obese MI patients, 51.0 ± 11.1 ms in non-obese MI patients and 37.6 ± 7.6 ms in controls ($p < 0.001$). RMSSD was below 19 ms in 52% of obese MI patients and in none of the others. Low HDL was present in 96% of obese vs 28% of non-obese MI patients, and QTc prolongation in 13% vs 1% ($p = 0.001$). Among MI patients, RMSSD correlated negatively with BMI ($r = -0.81$), triglycerides ($r = -0.83$) and QTc ($r = -0.59$). On regression, BMI ($\beta = -0.30$), triglycerides ($\beta = -0.46$) and LDL ($\beta = -0.28$) independently predicted lower RMSSD (all $p < 0.001$; adjusted $R^2 = 0.76$).

Conclusion: Obese MI patients have a marked loss of vagal tone, a poor lipid profile and more frequent QTc prolongation. BMI and triglycerides independently predict low RMSSD. Obese MI patients should be screened with simple HRV and ECG measures.

Keywords: Obesity; Myocardial infarction; Heart rate variability; RMSSD; QTc interval; Dyslipidaemia; Autonomic dysfunction.

INTRODUCTION

Cardiovascular disease causes about one-third of all deaths worldwide, and MI is its most important form [1]. In India, heart disease occurs about ten years earlier than in the West [2]. Obesity is rising fast in Indian adults, and a BMI of 25 kg/m² or more is taken as obesity in Asian Indians [3,4].

After MI, sympathetic activity rises and vagal tone falls, which raises the risk of dangerous arrhythmias [5]. HRV is a simple, non-invasive measure of this balance [6]. RMSSD mainly reflects vagal activity, and SDNN reflects overall autonomic control [6,7]. Low HRV after MI predicts cardiac death [8,9]. Obesity also lowers HRV [10,11] through insulin resistance, leptin and higher sympathetic drive [12], and it is linked with a longer QTc interval [13]. However, some studies report better survival in overweight heart patients, the so-called obesity

paradox [14]. Few Indian studies have measured HRV, lipids and QTc together in obese and non-obese MI patients against healthy controls. This study aimed to (i) compare HRV, lipid profile, HbA1c, cardiac markers and QTc among the three groups; (ii) find how often abnormalities occur in each group; and (iii) identify independent predictors of low RMSSD and QTc in MI patients.

Materials and Methods

Study design. This hospital-based cross-sectional study was done at Index Medical College, Malwanchal University, Indore, India. The protocol was approved by the Institutional Ethics Committee, and written informed consent was taken from all participants.

Participants. Adults aged 35–65 years of either sex were enrolled in three groups of 100 each: obese MI patients (BMI ≥ 25 kg/m²), non-obese MI patients (BMI 18.5–22.9 kg/m²) and healthy controls of similar age and sex with normal BMI. MI was confirmed by the Fourth Universal Definition [15], and BMI was classified by Asian-Indian cut-offs [3]. Patients with unstable condition, serious arrhythmia, severe other illness, pregnancy or prior regular yoga practice were excluded.

Measurements. A 5-minute resting lead II ECG was recorded in the supine position. SDNN, RMSSD and the LF/HF ratio were calculated as per Task Force standards [6]. RMSSD below 19 ms was taken as reduced vagal tone [16]. Fasting total cholesterol (TC), triglycerides (TG) and HDL were measured, and LDL was calculated by the Friedewald formula [17]. HbA1c, Troponin T and CK-MB were also measured. QTc was calculated by Bazett's formula [18].

Definitions. QTc prolongation was > 450 ms in men and > 460 ms in women [19]. Low HDL was < 40 mg/dL in men and < 50 mg/dL in women; high TG was ≥ 150 , high LDL ≥ 130 and high TC ≥ 200 mg/dL

[20]. HbA1c $\geq 6.5\%$ was the diabetic range and 5.7–6.4% the prediabetic range [21].

Statistical analysis. Data are given as mean $\pm$ SD. The three groups were compared by one-way ANOVA with Tukey's test. Proportions were compared by the chi-square test and Fisher's exact test. Pearson's correlation and multiple linear regression (BMI, age, sex, LDL, HDL, TG and HbA1c entered together) were used among the 200 MI patients. A p value < 0.05 was significant.

Results

Group characteristics. The three groups differed significantly in HRV, lipids, HbA1c, cardiac markers and QTc (Table 1). The sex ratio was similar ($p = 0.99$), and obese MI patients were 3–4 years older. RMSSD differed between every pair of groups and was lowest in obese MI patients. SDNN was lower in obese than non-obese MI patients but not different from controls ($p = 0.097$). TC and QTc were similar in non-obese MI patients and controls but higher in obese MI patients. HbA1c was raised in both MI groups.

Table 1. Comparison of parameters among the three groups (mean $\pm$ SD, $n = 100$ each)

Parameter	Obese MI	Non-obese MI	Healthy controls	p (ANOVA)	Obese vs non-obese	Obese vs controls	Non-obese vs controls
Age (years)	49.7 $\pm$ 9.1	46.0 $\pm$ 7.0†	46.5 $\pm$ 6.9	0.001	0.002	0.011	0.866
BMI (kg/m ²)	27.5 $\pm$ 1.8	21.1 $\pm$ 1.8	21.6 $\pm$ 2.2	< 0.001	< 0.001	< 0.001	0.164
SDNN (ms)	69.9 $\pm$ 6.1	83.6 $\pm$ 17.9	74.1 $\pm$ 16.0	< 0.001	< 0.001	0.097	< 0.001
RMSSD (ms)	17.5 $\pm$ 4.9	51.0 $\pm$ 11.1	37.6 $\pm$ 7.6	< 0.001	< 0.001	< 0.001	< 0.001
LF/HF ratio	2.74 $\pm$ 0.47	3.45 $\pm$ 0.55	1.51 $\pm$ 0.30	< 0.001	< 0.001	< 0.001	< 0.001
LDL (mg/dL)	162.9 $\pm$ 14.2	95.0 $\pm$ 19.7	83.9 $\pm$ 22.7	< 0.001	< 0.001	< 0.001	< 0.001
HDL (mg/dL)	34.5 $\pm$ 3.3	50.2 $\pm$ 13.3	67.1 $\pm$ 14.3	< 0.001	< 0.001	< 0.001	< 0.001
Total cholesterol (mg/dL)	258.2 $\pm$ 11.8	173.9 $\pm$ 14.9	174.1 $\pm$ 16.1	< 0.001	< 0.001	< 0.001	0.995
Triglycerides (mg/dL)	303.9 $\pm$ 28.7	194.4 $\pm$ 16.9	115.6 $\pm$ 15.9	< 0.001	< 0.001	< 0.001	< 0.001
HbA1c (%)	6.29 $\pm$ 0.68	6.45 $\pm$ 0.86	5.07 $\pm$ 0.57	< 0.001	0.253	< 0.001	< 0.001
Troponin T (ng/mL)	1.77 $\pm$ 0.77	1.68 $\pm$ 0.87	1.46 $\pm$ 0.80	0.023	0.707	0.021	0.144
CK-MB (U/L)	79.8 $\pm$ 32.0	50.4 $\pm$ 18.5	2.6 $\pm$ 1.8	< 0.001	< 0.001	< 0.001	< 0.001
QTc (ms)	439.2 $\pm$ 12.6	399.1 $\pm$ 34.8	400.8 $\pm$ 38.5	< 0.001	< 0.001	< 0.001	0.925

Pairwise p values from Tukey's HSD test. † $n = 98$ (age missing for 2 patients).

Prevalence of abnormalities. RMSSD below 19 ms was found only in obese MI patients (52%). Almost all obese MI patients had low HDL, high LDL and high TC, compared with 28%, 7% and 5% of non-obese MI patients (Table 2). QTc prolongation was more frequent in obese than non-obese MI patients (13% vs 1%, $p = 0.001$).

Table 2. Prevalence of autonomic, lipid, glycaemic and QTc abnormalities, n (%)

Abnormality	Obese MI	Non-obese MI	Healthy controls	p (3 groups)	p (obese vs non-obese)
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RMSSD < 19 ms	52 (52%)	0 (0%)	0 (0%)	< 0.001	< 0.001
LF/HF ratio > 2	95 (95%)	100 (100%)	0 (0%)	< 0.001	0.059
Low HDL	96 (96%)	28 (28%)	7 (7%)	< 0.001	< 0.001
LDL $\geq$ 130 mg/dL	100 (100%)	7 (7%)	0 (0%)	< 0.001	< 0.001
Total cholesterol $\geq$ 200 mg/dL	100 (100%)	5 (5%)	0 (0%)	< 0.001	< 0.001
Triglycerides $\geq$ 150 mg/dL	100 (100%)	100 (100%)	0 (0%)	< 0.001	1.00
HbA1c $\geq$ 6.5%	44 (44%)	55 (55%)	0 (0%)	< 0.001	0.16
HbA1c 5.7–6.4%	31 (31%)	19 (19%)	17 (17%)	0.037	0.072
QTc prolongation	13 (13%)	1 (1%)	10 (10%)	0.005	0.001

Chi-square test across three groups; Fisher's exact test between MI groups. Low HDL: < 40 mg/dL (men), < 50 mg/dL (women). QTc prolongation: > 450 ms (men), > 460 ms (women).

Correlations. Among MI patients, RMSSD correlated strongly and negatively with BMI, TG and LDL, and moderately with QTc (Table 3). BMI correlated positively with TG, LDL, QTc and CK-MB.

Table 3. Pearson correlations among MI patients (n = 200)

Parameter pair	r	p	Parameter pair	r	p
RMSSD – Triglycerides	–0.83	< 0.001	SDNN – Triglycerides	–0.41	< 0.001
RMSSD – BMI	–0.81	< 0.001	SDNN – QTc	–0.15	0.037
RMSSD – LDL	–0.77	< 0.001	BMI – Triglycerides	0.81	< 0.001
RMSSD – QTc	–0.59	< 0.001	BMI – LDL	0.79	< 0.001
RMSSD – HDL	0.48	< 0.001	BMI – HDL	–0.55	< 0.001
RMSSD – HbA1c	0.12	0.100	BMI – QTc	0.48	< 0.001
SDNN – LDL	–0.44	< 0.001	BMI – CK-MB	0.42	< 0.001
SDNN – BMI	–0.42	< 0.001			

Independent predictors. After adjustment, BMI remained an independent predictor of lower RMSSD (Table 4). Each 1 kg/m² rise in BMI was linked with a 1.5 ms fall in RMSSD. TG was the strongest predictor, and the model explained 76% of the variation in RMSSD. For SDNN, only male sex was significant ($\beta = -0.23$, $p = 0.002$). For the LF/HF ratio, only TG was significant ($\beta = -0.40$, $p < 0.001$). QTc was independently related to TG ($\beta = 0.42$), LDL ($\beta = 0.34$) and female sex, but not to BMI ($p = 0.223$).

Table 4. Multiple linear regression for RMSSD among MI patients (n = 198)

Predictor	B (95% CI)	Standardised β	p
BMI (kg/m ²)	–1.53 (–2.19 to –0.86)	–0.30	< 0.001
Triglycerides (mg/dL)	–0.14 (–0.18 to –0.10)	–0.46	< 0.001
LDL (mg/dL)	–0.14 (–0.21 to –0.07)	–0.28	< 0.001
HDL (mg/dL)	–0.19 (–0.36 to –0.02)	–0.13	0.028
Age (years)	0.18 (0.02 to 0.34)	0.08	0.031
HbA1c (%)	1.85 (0.14 to 3.56)	0.08	0.035
Male sex	1.34 (–1.66 to 4.33)	0.04	0.380

Model $R^2 = 0.77$, adjusted $R^2 = 0.76$, $p < 0.001$. Two patients with missing age were excluded.

Discussion

This study shows that obese MI patients have a much greater loss of vagal tone than non-obese MI patients or healthy adults. RMSSD in obese MI patients was about one-third of that in non-obese MI patients, and half of them had RMSSD below the normal range. Similar results were found in studies by Karason et al. [10] and Yadav et al. [11]. BMI remained linked with low RMSSD even after adjusting for lipids, glucose, age and sex, which suggests that body fat itself reduces vagal control of the heart [12]. Because low HRV after MI predicts cardiac death [8,9], obese MI patients are a high-risk group.

TG was the strongest predictor of low RMSSD. High TG reflects insulin resistance and visceral fat, which increase sympathetic drive [12]. SDNN showed a smaller difference because it reflects both sympathetic and vagal activity [7]. The LF/HF ratio was higher in both MI groups than in controls, as expected after MI [5], but it was lower in obese than non-obese patients. This ratio is not a reliable measure of sympathovagal balance [22], so RMSSD is the more dependable marker.

Obese MI patients had a QTc about 40 ms longer than non-obese patients, and prolongation was 13 times more frequent. Omran et al. showed that obesity prolongs ventricular repolarisation and

weight loss shortens QTc [13]. In our study QTc was related to TG and LDL rather than BMI, and it also correlated with lower RMSSD ($r = -0.59$). All obese MI patients had high LDL and TC, while HbA1c was raised equally in both MI groups. CK-MB was higher in obese patients but Troponin T was not, so a larger infarct in obese patients cannot be concluded. RMSSD from a 5-minute ECG and QTc from a routine ECG are cheap bedside measures that can help identify obese MI patients at higher risk. The obesity paradox reported in some studies [14] should not lead to neglect of obesity after MI. Weight reduction, lipid control and cardiac rehabilitation are logical targets for this group.

Limitations. The cross-sectional design cannot prove that obesity causes autonomic dysfunction. Only short-term HRV was recorded. Waist circumference, blood pressure, smoking, drug therapy and time from MI to recording were not analysed. Non-obese MI patients had higher SDNN and RMSSD than healthy controls, which is unexpected and may reflect recording conditions. The study was done at a single centre.

Conclusion

Obese MI patients show a marked loss of vagal tone, with half having RMSSD below the normal range. They also have near-universal dyslipidaemia and more frequent QTc prolongation. BMI and triglycerides independently predict low RMSSD. Short-term HRV and QTc are simple tools to identify high-risk obese MI patients, who need weight reduction, lipid control and cardiac rehabilitation. Prospective studies are needed to confirm these findings.

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