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Influence of BMI on inducible ventricular tachycardia and mortality in patients with myocardial infarction and left ventricular dysfunction: The obesity paradox

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ABSTRACT

Background: There is little known about the influence of obesity on ventricular electrical remodelling after myocardial infarction. The aim of our study was to assess the relationship between body mass index (BMI) and the primary outcome of inducible-VT and the secondary outcome of all-cause mortality in consecutive patients who presented with ST elevation myocardial infarction (STEMI) and LV-dysfunction (LVEF ≤ 40%).
Methods and results: Consecutive patients ($n = 380$) with STEMI and LV-dysfunction (LVEF ≤ 40%) underwent electrophysiological (EP) studies for risk-stratification. Inducible-VT ≥200 ms cycle-length (CL) with one to four extra-stimuli (ES) was considered abnormal. Patients were classified according their body mass index (BMI) to be normal (18.5–24.9), overweight (25–29.9) or obese (>30). The primary outcome of inducible-VT occurred in 42.7%, 21.5% and 21% of normal weight, overweight and obese patients respectively ($p < 0.001$). When adjusting for ejection-fraction, hypertension and triple-vessel-disease, normal BMI remained a significant predictor for inducible-VT. All-cause mortality was higher in patients with normal weight (12.8%) when compared to overweight (3.2%) and obese (3.8%) patients ($p = 0.002$) and was mainly driven by increased cardiac-death (6.8%, 1.9% and 1.9% in normal, overweight and obese patients respectively, $p = 0.05$). After adjusting for age, EF, and hypertension, normal BMI remained a significant predictor of mortality.
Conclusion: In patients presenting with STEMI and LV-dysfunction, BMI appears to be a significant predictor of inducible-VT and all-cause mortality, with worse outcomes for those with normal weight, when compared to overweight or obese individuals. These findings are consistent with the obesity-paradox.

1. Introduction

Ventricular arrhythmias are known to be associated with significant mortality and morbidity [1]. There is evidence that post-infarct ventricular tachycardia is caused by re-entry generated in the scar tissue often in the setting of impaired left ventricular ejection fraction after myocardial infarction [2]. Obesity has been associated with an increased risk of sudden cardiac death often attributed to ventricular tachycardia [3]. It is unclear however whether obesity plays a role in ventricular electrophysiological remodelling in patients with myocardial infarction. Inducible ventricular tachycardia (VT) in patients with coronary artery disease and left ventricular (LV) dysfunction has been found to be predictive of spontaneous ventricular arrhythmia and sudden cardiac death [4–6]. In this study, we aimed to assess whether body mass index (BMI) influenced the primary outcome of inducible VT and the secondary outcome of all-cause mortality in the subgroup of patients who presented with ST elevation myocardial infarction (STEMI) and left ventricular ejection fraction (LVEF) ≤40%.

2. Methods

2.1. Study population

Between 2004 and 2014, 380 consecutive patients who presented with STEMI and LVEF ≤40% and underwent electrophysiological study (EPS) for risk stratification [6–9] were recruited in a prospective fashion and after informed consent (Fig. 1, Panel A). Patients with positive EPS underwent ICD implantation. Underweight patients (BMI < 18.5) were excluded. Other exclusion criteria were prior insertion of ICD, death prior to EPS study, inability or refusal to give consent, patients who were deemed medically unfit by the treating physician (including severe COPD, end stage renal failure, dementia, high anaesthetic risk, etc.) and presence of LV apical thrombus. The patients recruited either presented directly to Westmead Hospital (Tertiary Centre) or were transferred after referral by four associated regional hospitals. The diagnosis of STEMI was confirmed on angiogram in all patients and all patients were transferred to the cardiac catheterisation laboratory with the purpose of undergoing PPCI. A total of 365

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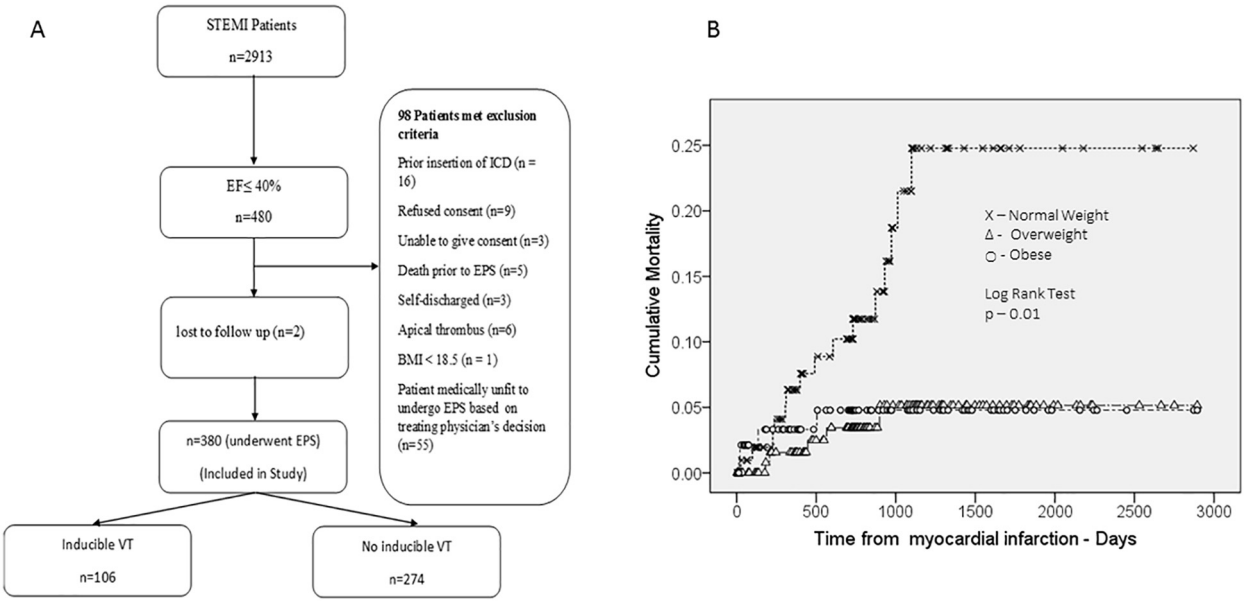

Fig. 1. A — Flowchart demonstrating patient recruitment. B — Kaplan Meier Survival Curve.

patients underwent PPCI, while 10 patients were referred for bypass surgery and 5 patients were managed with medical therapy with no patients receiving thrombolysis. 3–5 days post-myocardial infarction, patients underwent assessment of left ventricular (LV) function for the purpose of risk stratification by either gated heart pool scan (GHPS/360) or transthoracic echocardiogram, (TTE/20) when the former was not available. All the patients were commenced on guideline based optimal medical therapy. Ethics approval for the study was given by the Western Sydney Local Health District Human Research Ethics Committee.

2.2. Electrophysiology study

2.2.1. Use of EPS to identify patients with MI and LV dysfunction who have significant long term arrhythmic risk

In patients with myocardial infarction and LV dysfunction appropriate and early risk stratification is important while deciding which patients would benefit from ICD implantation. Although studies have shown that LVEF and low heart rate variability identify patients with increased risk of mortality, they lack the ability to differentiate between arrhythmic and non-arrhythmic causes of death [6]. Kumar et al. demonstrated that EPS performed early after MI identified patients who had significant long-term arrhythmic risk and in whom defibrillator implantation was protective [8]. Early ICD implantation in patients with impaired LVEF (≤40%) enabled low mortality after primary percutaneous coronary intervention for ST-elevation myocardial infarction [6]. In addition to this Zaman et al. showed that revascularized patients with ST-segment-elevation myocardial infarction with severely impaired left ventricular function but no inducible ventricular tachycardia had a favourable long-term prognosis without the protection of an implantable cardioverter–defibrillator [10]. Based on this patients with STEMI and EF ≤40% undergo EPS according to our institutional protocol.

2.2.2. EPS protocol

The electrophysiological study was performed under conscious sedation in 380 patients with LVEF ≤40%. Antiarrhythmic medications were withheld prior to the procedure. Apart from Sotalol, beta-blockers were not withheld. A programmable stimulator was used to perform programmed ventricular stimulation from the right ventricular apex (single site). The drive train (S1S1) consisted of eight beats at 400 ms and was followed by up to 4 extra stimuli [4]. The stimuli consisted of rectangular pulses which were of 2 ms duration at twice the diastolic threshold. A 3-second delay was maintained between each drive train. The coupling interval of the initial extra stimulus was 300 ms following which 10 ms decrements were applied until ventricular refractoriness was noted. If the first extra stimulus did not result in induction of VT, that extra stimulus was delivered 10 ms outside the ventricular effective refractory period. An additional extra stimulus at a coupling interval of 300 ms was delivered. For the additional extra stimulus, 10 ms decrements were applied in the same manner until refractory. This process was continued until up to four extra stimuli. The end point was until the last extra stimulus was refractory or either VT or ventricular fibrillation was induced [4]. We did not set a lower limit for the shortest extra stimulus coupling interval and Isoprenaline was not used during the study.

We defined a positive EPS as sustained monomorphic VT with a cycle length (CL) ≥200 ms of ≥30 s duration if hemodynamically tolerated or ≥10 s duration if associated with hemodynamic instability [8,11]. If no arrhythmia was induced or only inducible ventricular fibrillation/ventricular flutter with CL <200 ms occurred, then that was considered as a negative EPS. Programmed ventricular stimulation was repeated if no arrhythmias or ventricular fibrillation/flutter was induced [7]. Patients with positive EPS underwent ICD implantation prior to discharge.

2.3. Follow-up

Patients were followed at 1, 6, and 12 months. Subsequent follow-up was carried out on a yearly basis, unless symptoms intervened. Telephone contact, clinics, and review of hospital medical records were methods used for follow-up.

2.4. BMI

The presence of obesity was assessed using BMI, which was defined as weight in kilograms divided by height in meters squared (kg/m^2). BMI was categorized according to the World Health Organisation Criteria as normal (18.5–24.9), overweight (25–29.99) and obese (>30) [12].

2.5. Primary and secondary outcomes

The primary endpoint was inducible ventricular tachycardia (≥200 ms cycle length) early after MI. The secondary endpoints were all cause mortality and cardiac and non-cardiac mortality. Three local investigators blinded to the EPS results or BMI category were responsible for adjudication of the cause of death (cardiac vs non-cardiac). Information collected from witnesses, relatives, inpatient records, ICD data, and death certificates from the Registry of Births, Deaths, and Marriages was used to make a decision regarding the cause of death.

2.6. Statistical analysis

We used the Statistical Package for the Social Sciences for Windows (SPSS release 15.0, SPSS, Inc., Chicago, IL, USA) for analysis. Chi-square test was used to test for association between categorical variables and One-way ANOVA for the association between categorical and continuous variables. Binary logistic regression analysis was used to derive independent predictors of the primary endpoint using the variables as demonstrated in Table 2. The cumulative risk mortality was estimated using the Kaplan–Meier procedure and log rank Chi-square tests. We used Cox regression multivariable analysis to derive independent predictors of the mortality using the variables listed in Table 3. $p < 0.05$ was considered significant. Receiver Operator Curve analysis was used to derive the sensitivity and specificity of the independent predictors of primary and secondary outcomes.

3. Results

A total of 2913 patients presented with STEMI and were treated with PPCI, CABG or medical therapy. 480 (18.1%) patients had LVEF ≤40%. 97 patients were excluded. Reasons for exclusion were prior insertion of