Effect of Weight Loss on Ventricular Repolarization in Normotensive Severely Obese Patients With and Without Heart Failure

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Abstract: *Background:* Obesity has been reported to be associated with delayed ventricular repolarization. The purpose of this study was to assess ventricular repolarization in normotensive severely obese subjects with and without heart failure (HF) and to assess the effect of weight loss on ventricular repolarization in such patients. *Methods:* Twenty-eight patients with and 39 patients without HF (body mass index $\geq$ 40 kg/m^2) were studied before and after weight loss from bariatric surgery. Corrected QT interval (QTc) was measured on 12-lead electrocardiograms using Bazett's formula. QTc dispersion was calculated by subtracting the minimum from the maximum QTc on each 12-lead electrocardiogram. Electrocardiograms and transthoracic echocardiograms were performed preoperatively and at the nadir of postoperative weight loss. *Results:* Mean QTc and QTc dispersion were significantly longer/greater in subjects with HF than in those without HF ($P < 0.0001$). Weight loss produced significant reductions in mean QTc and QTc dispersion in both subgroups ($P < 0.0001$). Pre-weight loss left ventricular (LV) mass/height$^{2.7}$ and presence or absence of HF independently predicted pre-weight loss QTc and QTc dispersion ($P < 0.0001$). Weight loss-induced decrease in LV mass/height$^{2.7}$ independently predicted weight loss-induced decreases in QTc and QTc dispersion ($P < 0.0001$). *Conclusions:* HF independently predicts QTc and QTc dispersion in normotensive severely obese patients. Decrease in the LV mass resulting from weight loss independently predicts reduction in QTc and QTc dispersion in such patients.

Key Indexing Terms: Obesity; Heart failure; Weight loss; Corrected QT interval; Corrected QT interval dispersion; Ventricular repolarization. **[Am J Med Sci 2015;349(1):17–23.]**

Ventricular repolarization is commonly assessed electrocardiographically by measuring the corrected QT interval (QTc) and either QT or QTc dispersion.[1,2] Multiple studies of obese subjects have reported prolongation of QTc and/or increased QT or QTc dispersion, suggesting an association between obesity and delayed ventricular repolarization.[3–16] Some studies have reported improvement in ventricular repolarization after weight loss in obese subjects.[3,10–16] Patient populations in these studies were heterogeneous. They included subjects with different degrees of severity of obesity, patients with and without systemic hypertension and patients with and without heart failure.[3–16] Several studies have reported QTc prolongation and increased QTc dispersion in patients with left ventricular (LV) hypertrophy, particularly in association with hypertension.[1,7–20] LV hypertrophy occurs commonly in severely obese persons, even in those who are normotensive.[21,22] Recently, LV mass was identified as a key predictor of QTc and increased QTc dispersion in normotensive severely obese subjects.[3,23] Abnormal ventricular repolarization has been identified in studies of animals and humans with heart failure (HF).[24–33] Little information exists, however, concerning the interrelationship of obesity, ventricular repolarization and HF. This study compares QTc and QTc dispersion in normotensive severely obese patients with and without HF before and after substantial weight loss from bariatric surgery.

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PATIENTS AND METHODS

Patient Selection

This was a prospective cohort study. Patients whose body mass index (BMI) was $\geq$ 40 kg/m^2 and whose blood pressure was <140/90 mm Hg on 3 consecutive clinical encounters separated by at least 1 week were considered for entry into the study. All patients were initially referred to a bariatric surgery clinic by their primary care physician to determine their eligibility for bariatric surgery. Patients were subsequently referred to one of the investigators (M.A.A.) for cardiac evaluation. All patient evaluations were performed in the outpatient setting. HF was defined in accordance with the criteria of McKee et al[34] in the Framingham study. Patients with current, previous or treated hypertension were excluded from the study. Patients with clinical, electrocardiographic, radiographic or echocardiographic evidence of coronary heart disease, idiopathic or secondary cardiomyopathies, valvular stenosis or moderate to severe valvular regurgitation, pericardial disease or congenital heart disease were excluded from the study. Given the absence of underlying organic heart disease from causes other than obesity, we believe that all patients with HF had obesity cardiomyopathy. Also excluded from the study were patients with any cardiac arrhythmia on a 12-lead electrocardiogram (including premature beats and atrial fibrillation) and patients with primary pulmonary disease based on clinical and radiographic assessment and pulmonary function tests. Patients with disorders of potassium, magnesium and calcium, those with hyperthyroidism or hypothyroidism, patients with acute myocardial infarction, collagen vascular disease, mitral valve prolapse, intracranial disease, those on liquid protein or starvation diets and patient receiving drugs that might affect ventricular repolarization were also excluded. Consecutive eligible patients who underwent bariatric surgery (vertical banded gastroplasty) were entered into this study. A total of 67 patients were entered including 28 with HF and 39 without HF.

Clinical and Anthropometric Assessment

A complete medical history and physical examination were performed by a single investigator (M.A.A.) just before

bariatric surgery and at the nadir of postoperative weight loss (5.0 ± 0.6 months after surgery). Blood pressure was measured with a cuff sphygmomanometer in accordance with the recommendations of Russell et al.[35] Body weight was obtained after a 12-hour fast using wheelchair-accessible scales with a weight limit of 800 pounds (361 kg). Weight was measured in the upright position with the patient wearing a thin lightweight gown. BMI was calculated using this information. Duration of severe obesity was estimated from patient report. Anthropometric measurements were recorded just before bariatric surgery and at the nadir of postoperative weight loss.

Electrocardiographic Measurements

A standard 12-lead electrocardiogram was obtained on all patients just before bariatric surgery and at the nadir of postoperative weight loss 5.0 ± 0.6 months after surgery in the supine position using a standard technique with a Hewlett-Packard 1D: electrocardiograph (Andover, Massachusetts) with a filter setting of 100 Hz at a paper speed of 25 mm/s. All electrocardiograms were obtained in the fasting state in a quiet room at room temperature of 20°C to 22°C. Ventricular repolarization was assessed by measuring QTc and QTc dispersion. QT intervals were measured manually in all 12 leads by a single investigator (M.A.A.) who was blinded to patient identity and to clinical radiographic and echocardiographic data. QTc was calculated using Bazett's formula. The R-R interval used to calculate QTc was derived from the cycle containing the QRST complex from which the QT interval was measured. After careful examination of the QT intervals in all leads, QTc dispersion was calculated by subtracting the minimum QTc interval from the maximum QTc interval on the standard 12-lead electrocardiogram used for QTc dispersion analysis. The number of leads per electrocardiogram with measurable QT intervals ranged from 9 to 12 (mean value 10.12 ± 1.10). The upper limits of normal are 440 milliseconds for QTc and 71 milliseconds for QTc dispersion.

Echocardiographic Measurements

M-mode and 2-dimensional transthoracic echocardiograms were obtained just before bariatric surgery and at the nadir of postoperative weight loss (5.0 ± 0.6 months after surgery). Echocardiograms were obtained in the left lateral and supine positions using a Hewlett-Packard Sonos 1000 echocardiography with a 2.25 MH_2 transducer (Palo Alto, CA). Echocardiographic images were obtained and echocardiographic measurements were performed in accordance with American Society of Echocardiography guidelines.[36] LV mass was calculated using the formula proposed by Devereux et al[37,38] and was indexed to height. LV hypertrophy was defined as LV mass/height$^{2.7}$ ≥ 51 g/m$^{2.7}$ (non–gender-specific criterion).[39] Echocardiograms were interpreted by a single investigator (M.A.A.) who was blinded to patient identity, and to clinical, radiographic and electrocardiographic data.

Other Studies

Serum potassium, magnesium and calcium levels were obtained in the fasting state on the same day as the electrocardiograms and echocardiograms. These levels were obtained just before bariatric surgery and at the nadir of postoperative weight loss. A posteroanterior and lateral chest x-ray was performed within 2 weeks of the preoperative clinical, electrocardiographic and echocardiographic assessment.

Statistical Analysis

SPSS 19 (IBM, Armonk, NY) was used for statistical analysis. The Student's *t* test for paired data was used to compare mean values of continuous variables before and after weight loss. The Student's *t* test for unpaired data was used to compare mean values of continuous variables in those with and without HF. Bivariate correlations were performed using Pearson correlation coefficients. Multiple stepwise linear regression analysis was conducted on the group as a whole and on subgroups with and without HF. Dependent (response) variables included pre-weight loss QTc and QTc dispersion, and weight loss-induced changes in QTc and QTc dispersion. For the group as a whole, independent (predictor) variables considered included BMI, duration of severe obesity, presence or absence of HF, LV mass/height$^{2.7}$, systolic blood pressure, LV fractional shortening and transmitral E-wave deceleration time before weight loss and weight loss-induced changes in BMI, LV mass/height$^{2.7}$, systolic blood pressure, LV fractional shortening and transmitral E-wave deceleration time. Pre-weight loss heart rate, LV internal dimension in diastole and LV end-systolic wall stress and weight loss-induced changes in these variables were excluded from the analysis to avoid multicollinearity. Analysis of subgroups with and without HF proceeded in a similar fashion except for exclusion of the presence or absence of HF as a predictor variable.

Ethical Considerations

Informed consent was obtained from all study patients. The research protocol was approved by the University of Missouri Institutional Review Board.

RESULTS

Patient Characteristics

A total of 105 patients were referred from the bariatric surgery clinic for consideration of entry into the study, including 40 patients with HF and 65 patients without HF. Reasons for exclusion in the HF group were failure to qualify for or agree to bariatric surgery in 4, current, previous or treated hypertension in 4, moderate to severe mitral regurgitation in 2 and atrial fibrillation in 2. Reasons for exclusion in the group without HF were failure to qualify for or agree to bariatric surgery in 11, current, previous or treated hypertension in 10, moderate to severe mitral regurgitation in 3 and atrial fibrillation in 2. Table 1 lists the baseline demographic, clinical, electrocardiographic and echocardiographic patient characteristics for the group as a whole and for the subgroups with and without HF. Pre-weight loss QTc ranged from 418 to 495 milliseconds in the HF group and from 397 to 469 milliseconds in the group without HF. Pre-weight loss QTc dispersion ranged from 47 to 83 milliseconds in the HF subgroup and from 24 to 70 milliseconds in the group without HF. Pharmacotherapy with drugs used commonly to treat HF in the subgroups with and without HF, respectively, were as follows: diuretics: 28 and 6, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers: 18 and 8, aldosterone receptor blockers: 2 and 0, beta-blockers: 2 and 0, and digoxin: 2 and 0. Diuretic use in patients without criteria for heart failure was for lower extremity edema. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in patients without criteria for heart failure were used exclusively in patients with diabetes mellitus for renal protection.

Effect of Weight Loss on Selected Clinical, Electrocardiographic and Echocardiographic Variables in Patients With and Without HF

Table 2 summarizes the effect of weight loss on selected clinical, electrocardiographic variables in severely obese