QT Interval and QT Dispersion Before and After Diet Therapy in Patients with Simple Obesity (44355)

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Abstract. **To evaluate whether a disordered QT interval and its dispersion in obese patients, if any, may be improved by therapeutic weight reduction, 36 obese patients admitted to our university hospital were examined over a 5-year period from April 1, 1992 to March 31, 1997. Participants included 18 males and 18 females whose mean age ± SD was 28 ± 9 and 33 ± 14 years, respectively, and whose mean body mass index ± SD was 35 ± 5 and 38 ± 6 kg/m^2, respectively. Thirty-six control patients were matched in age and gender with the obese patients. All the obese patients were treated with behavioral therapy together with very-low-calorie conventional Japanese diet (VLCD: 370 kcal/day). A standard 12-lead electrocardiogram (ECG) revealed longer maximum (445 ± 32 msec, mean ± SD) and minimum (388 ± 29 msec) heart rate corrected QT intervals (QTc intervals) in the obese group than in the control group ($P < 0.0001$ for each). QTc dispersion, defined as the difference between maximum and minimum QTc intervals derived from 12-lead ECG, was greater in the obese group (57 ± 19 msec) than in the control group (32 ± 13 msec) ($P < 0.0001$). Both the maximum and minimum QTc intervals in the obese patients were shortened, respectively, to 434 ± 28 msec and 377 ± 29 msec ($P < 0.05$ for each) with no significant change in either QTc dispersion, QRS voltage, or QRS duration following weight reduction. The coefficient value from the linear regression line between QT interval and RR interval in the obese group was less than in the control group. Together, the results show that obesity *per se* causes both a prolongation of QTc interval and an increase in QTc dispersion, and that weight reduction improves the prolonged QTc interval observed in obese patients.** [P.S.E.B.M. 1999, Vol 220]

Obesity has been demonstrated as an essential risk factor for development of ischaemic heart diseases together with hyperinsulinemia, diabetes mellitus including glucose intolerance, hypertension, dyslipidemia, hyperuricemia, smoking, and so on. Weight reduction is an efficient treatment of choice for obese patients. Obese patients have been reported to have not only an increased risk of arrhythmias (1) but also a prolonged QT interval (2–5). However, some controversies remain regarding the effect of weight loss on the QT interval. The effectiveness of weight reduction depended differently on the reporters (4–7), partly because the QT interval was measured by 24-hr Holter recording (7). The interval calculated from the Holter record was completely different from that in the 12-lead electrocardiogram (ECG) (8).

A prolonged QT interval reflects delayed cardiac repolarization and refractory period, and is a known precursor of cardiac arrhythmias (9). The QT interval, indeed, has been predictable for sudden death not only in patients with coronary artery disease but even in an apparently healthy large population (10, 11). QT dispersion represents a functional substrate of arrhythmias, because the parameter implies inhomogeneous ventricular repolarization and refractory period. In addition, an increase in QT dispersion is accompanied by unexpected sudden death in patients with chronic

Supported partly by Grants-in-Aid 02454129 (T.S.) and 06454342 (T.S.) from the Japanese Ministry of Education, Science and Culture, and by Research Grants for Intractable Diseases from the Japanese Ministry of Health and Welfare, 1992–97.
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Received August 10, 1998. [P.S.E.B.M. 1999, Vol 220]
Accepted October 22, 1998.

0037-9727/99/2203-0133$10.50/0

heart failure and hypertrophic cardiomyopathy (12, 13). For this reason, QT dispersion has frequently been utilized as well for the prognostic analyses of various cardiac diseases.

Despite evidence that QT dispersion is thus a crucial parameter indicating prognosis and severity of cardiovascular diseases, the parameter has not been studied in obese patients. The present study is aimed to answer a question as to whether a QT interval and its dispersion may abnormally be affected in obese patients compared with age- and gender-matched controls and may be improved by a therapeutic approach to weight reduction.

Materials and Methods

Subjects. Obese patients were admitted to our university hospital for weight reduction for 5 years ranging from April 1, 1992 to March 31, 1997. Excluding patients who had heart disease, diabetes mellitus, and who were taking medication known to affect the QT interval, 36 obese patients were enrolled as the experimental obese group (obese group). Nonobese control patients (control group, $n = 36$) were admitted to our university hospital for other ailments. The nonobese patients had no clinical history of obesity, heart disease, diabetes mellitus, or medication that affects QT interval, and they were age- and gender-matched with the obese group. In the present study, subjects who smoked more than 10 cigarettes per day over a year were defined as smokers.

The obese group was treated with conventional Japanese diet consisting of a very-low-calorie diet (VLCD) of 370 kcal/day, a low-calorie diet (LCD) of 700 kcal/day, or a diet of 1000 kcal/day (14, 15). They were also treated with behavioral therapy and gradually introduced to the conventional Japanese diet therapy for a 2-week period until they attained the minimum intake of 370 kcal/day of VLCD. They were maintained by the VLCD for 2 weeks, followed by LCD and a 1000 kcal/day diet for 3 days.

Procedures of Measurement. Blood chemistry was assessed following an overnight fast (> 10 hr) every 2 days and specifically on the day of ECG recording. Lipid profile, plasma glucose, and immunoreactive insulin (IRI) after overnight fast were examined on a weekly basis. Blood pressure was measured with a standard sphygmomanometer while the patient was seated. Phase one and phase five Korotkoff sounds were used to measure systolic and diastolic blood pressure, respectively. Body height and body weight were measured to the nearest millimeter and 100 g, respectively, on the day of ECG recording, and they were used to calculate the body mass index (BMI).

Echocardiogram (UCG). UCG was recorded with the obese patients in a partial left decubitus position using an ultrasonograph equipped with 2.5 MHz and 3.75 MHz adjustable transducer (Toshiba, Tokyo, Japan). A two-dimensionally guided M-mode UCG tracing of the left ventricle (LV) was obtained in a standard manner and printed on a strip-chart paper at a speed of 50 mm/sec. LV measurements were carried out according to the recommendation of the American Society of Echocardiography (16). LV mass was calculated in patients who showed a good quality UCG according to the criteria of Devereux (17), as follows: LV mass = 1.04 ([LVID + IVST + PWT^3]– [$LVID^3$]) – 14 g, where LVID = left ventricular internal dimension; IVST = intraventricular septal thickness; PWT = posterior wall thickness. LV mass was divided by $height^{2.7}$ to calculate the LV mass index. Left ventricular hypertrophy (LVH) was defined as LV mass/$height^{2.7}$ > 50 g/$m^{2.7}$ in males and > 47 g/$m^{2.7}$ in females (18).

ECG. Within 2 days of enrollment, all of the patients underwent a standard resting 12-lead ECG. For the obese group, the ECG recording was also repeated at the end of therapy. The ECGs were recorded at a paper speed of 25 mm/sec in the morning from 10:00–11:30 AM. The ECG parameters were measured manually by vernier calipers with a resolution of 0.02 mm. The QT interval defined by Lepeschkin's method (19) was measured together with the preceding RR interval at all of the 12 leads in three consecutive cardiac cycles and averaged. Correlation between the QT and RR intervals was assessed at lead V2. QT dispersion was expressed as a difference between maximum and minimum QT intervals. Heart rate (HR), PR interval, QRS duration, and QRS voltage were also measured. Voltage was defined as the maximum amplitudes of the R and Q or S waves at leads I, II, and III. QT intervals were adjusted for heart rate according to Bazett's formula (20), to obtain QTc intervals.

Holter ECG. Over a 24-hr period, the Holter ECG was monitored in 22 subjects to determine the frequency of arrhythmias following diet therapy by use of a Marquette 8000 recorder and analyzed by use of a Marquette series 8000T scanner (Marquette Electronics, Inc., Milwaukee, WI).

All measurements were carried out by two cardiologists who were unaware of the physical conditions and grouping of the patients. The study was authorized by the ethics committee of Oita Medical University. All patients gave written informed consent to participate in the study.

Statistical Analysis. The measurements were expressed as mean ± SD. Statistical analysis of the physical and laboratory parameters between the obese and the control groups was carried out using the Student's t-test and in the obese group before and after weight reduction therapy was compared by the paired t-test. Correlation between QT and RR intervals was analyzed by the simple linear regression analysis method.

Results

The basic characteristics of all the subjects who participated in the study are shown in Table I. The mean body weight of the obese patients at admission was significantly greater than that of the control patients ($P < 0.0001$). The BMI of the obese patients was also larger than that of the control patients ($P < 0.0001$) since heights of the two groups showed no significant difference. Comparison of smoking

TABLE I. Basic Characteristics of the Study Population

Variable	Obese $n = 36$	Controls $n = 36$
Sex (M/F)	18/18	18/18
Age (yrs)	31 ± 12	31 ± 12
Body weight (kg)	99 ± 18[a]	58 ± 8
Smoking (Y/N)	8/28	6/30
Height (m)	1.64 ± 0.1	1.64 ± 0.08
BMI (kg/m^2)	37 ± 5[a]	22 ± 2
HR (bpm)	72 ± 12	69 ± 11

Note. Values represent mean ± SD. BMI, body mass index; Control, the normal control group; HR, heart rate; F, female; M, male; *n*, number of patients; Obese, the obese patient group; Y, smoker; N, nonsmoker; [a], $P < 0.0001$ vs. corresponding controls.

history between the obese and control groups did not reach a significant level. The baseline plasma glucose and IRI levels were 90.0 ± 22.1 mg/dl and 8.1 ± 7.0 IU/l, respectively, in obese patients. No significant correlation between plasma glucose or IRI and QT or QTc interval was observed. As shown in Table II, after treatment the body weight and BMI of the obese group were reduced compared with the initial values ($P < 0.0001$). The mean percentage weight loss was 8%. Together with the reduction in body weight and BMI, the systolic blood pressure of the obese group also decreased significantly ($P < 0.0001$), but the diastolic blood pressure did not decrease significantly (Table II). Consistent with these changes, plasma lipids were concomitantly reduced ($P < 0.0001$). Among measured plasma lipids (Table III), only baseline triglyceride (TGL) showed significant correlation with QTc dispersion ($P < 0.05$). There was no correlation between blood pressure and QT or QTc interval ($r = 0.23$; $P = 0.24$ or $r = 0.43$; $P = 0.67$), respectively. There was no significant difference in HR between the obese and control groups, or before and after weight reduction in the obese group. Inorganic ion concentrations did not appear to be affected by the weight reduction.

TABLE II. Effect of Weight Loss on Physical and Laboratory Parameters in Obese Patients

Variables	Before ($n = 36$)	After ($n = 36$)
Body weight (kg)	99 ± 18	91 ± 16[b]
BMI (kg/m^2)	37 ± 5	34 ± 5[b]
HR (bpm)	72 ± 12	68 ± 11
SBP (mmHg)	135 ± 19	120 ± 16[b]
DBP (mmHg)	77 ± 13	74 ± 13
Potassium (mg/dl)	4 ± 0.2	4 ± 0.3
Calcium (mg/dl)	9.4 ± 0.5	9.4 ± 0.4
TC (mg/dl)	204 ± 46	159 ± 40[b]
TGL (mg/dl)	171 ± 100	98 ± 28[b]
HDL-C (mg/dl)	41 ± 12	31 ± 6[b]

Note. Values represent mean values ± SD. Before and After, before and after the weight reduction; BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; T.C, total cholesterol; TGL, triglyceride.; HDL-C, high density lipoprotein-cholesterol, [b], $P < 0.0001$ vs. corresponding value before weight reduction.

Holter ECG. In the present study, premature ventricular contractions (PVC) classified as rare (0–72 PVC/day) and sporadic (72–720 PVC/day) were observed in 86% and 14% of the 22 patients, respectively. Neither serious arrhythmias nor repetitive responses were noted after weight reduction therapy.

Changes in QT Interval and QT dispersion. The maximum QT interval was longer in the obese group (409 ± 36 msec) than in the control group (377 ± 26 msec; $P < 0.001$). The QT dispersion in the obese group (43 ± 22 msec) was greater than that in the control group (29 ± 14 msec; $P < 0.001$). The maximum and minimum QTc intervals and QTc dispersion were longer and larger in the obese group than in the control group, respectively (Table III). The prolonged maximum and minimum QTc intervals in the obese group improved following weight reduction ($P < 0.05$ for each), but not to the levels of the control group. As shown in Table III, QTc dispersion was not improved by weight loss, unlike the QTc interval. No significant correlation between body weight or BMI and QTc interval was found in either the obese or control groups.

As shown in Figure 1, in both the obese and control groups, the QT and RR intervals were positively correlated ($P < 0.0001$ for each). However, the coefficient of correlation in the obese group ($y_o = 0.101x + 300$, $r = 0.434$) was less than that in the control group ($y_c = 0.143x + 239$, $r = 0.735$) ($P < 0.01$). As shown in Figure 2, the coefficient (r) of the obese group was improved to 0.668 ($P < 0.0001$) after weight reduction therapy, with the regression represented by the equation: $y_a = 0.179x + 239$, $r = 0.668$. There were no significant differences in QRS voltage or PR interval between the obese and the control groups (Table III). Of the 20 obese patients who showed good quality UCG, 17 patients (85%) had LVH according to the definition in the Methods. The left ventricular mass index was positively correlated with the QTc interval ($r = 0.53$, $P < 0.01$).

Discussion

The present study has demonstrated that QT interval and its dispersion were greater in patients with simple obesity than in age- and gender-matched control patients. The linear regression between QT interval and RR interval for the obese group was significantly different from that of the control group ($P < 0.01$), with the line representing the relationship being flatter in the obese group than in the control group. Significant effects of weight loss on these parameters were also identified in the present study, as described below.

QT and QT Dispersion. To our knowledge, this is the first study to investigate the QT interval and its dispersion in both obese patients and age- and gender-matched controls. The results show that both QT and QTc dispersion are greater in obese patients than in normal weight controls.

In the present study, the QTc dispersion was not im-

TABLE III. A Comparison of Electrocardiographic Parameters Between Obese Patients and Nonobese Controls together with a Comparison of Values Before and After Treatment of Obesity

Variables	Controls (n = 36)	Obese (n = 36) (before treatment)	Obese (n = 36) (after treatment)
max QTc (msec)	402 ± 22	445 ± 32[a]	434 ± 28[b]
min QTc (msec)	371 ± 25	388 ± 29[a]	377 ± 29[b]
QTc dispersion (msec)	32 ± 13	57 ± 19[a]	57 ± 16
PR interval (msec)	180 ± 18	185 ± 15	186 ± 16
QRS Voltage (mV)	2.8 ± 0.8	3 ± 0.6	3 ± 0.7

Note. Values represent mean ± SD. Controls, the normal control group; Obese, the obese patient group; max, maximum; min, minimum; QTc, heart rate corrected QT interval; [a], $P < 0.0001$ vs. corresponding controls; [b], $P < 0.05$ vs. corresponding values before treatment.

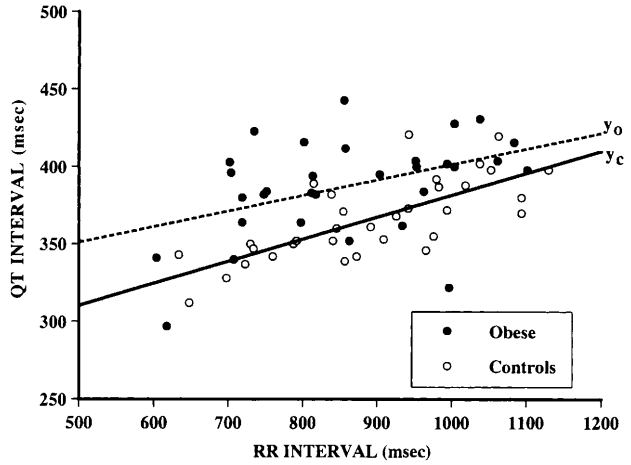

Figure 1. Correlations between QT and RR intervals for the obese and the nonobese control groups. y_o, linear regression for the obese group: $y_o = 0.101x + 300$, $r = 0.434$, $P < 0.0001$. y_c, linear regression for the control group: $y_c = 0.143x + 239$, $r = 0.735$, $P < 0.0001$.

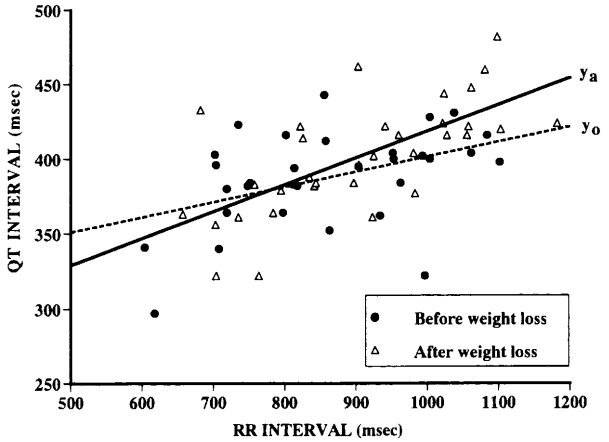

Figure 2. Change in the correlation between QT and RR intervals in the obese group before and after weight reduction. y_o, linear regression line before weight reduction (identical to the y_o in Figure 1). y_a, linear regression line after weight reduction: $y_a = 0.179x + 239$, $r = 0.668$, $P < 0.0001$.

proved even after weight reduction by diet therapy. One possible explanation is that the 8% loss in body weight observed in the obese group might not be large enough to cause significant change in the QTc dispersion. The present study has confirmed and extended the previous findings that a prolonged QT interval is observed in obese subjects (2–5), by including age- and gender-matched control patients. Although some of the previous studies showed that weight loss was capable of correcting the prolonged QT interval (4, 5), other reports indicated that there was no change in the QT interval following weight reduction (6, 7). This discrepancy could be due to different methods of ECG recording and analysis. In one of the previous studies, Holter tapes were used to measure the QT interval (7), even though an earlier study had shown that the QT interval measured from Holter tapes was completely different from that measured from a 12-lead ECG (8). One of the previous studies concluded that the prolongation of QT interval was mainly due to the shorter RR interval (3). However, the present study has clearly demonstrated that both the QT and QTc intervals are longer in obese patients than in the matched control patients, although HR did not differ significantly between the obese and the control group. This finding suggests that factors other than HR are responsible for the prolongation of QT interval in obese patients.

QT and RR Interval. The relationship between the QT interval and the RR interval in obese patients has also been investigated in this study. No previous reports have focused on this relationship, which is critical to the correction of the QT interval since it determines the resulting QTc interval. Under normal circumstances, HR is the major determinant of the QT interval. However, in the present study, the QT interval showed less dependence to the RR interval in the obese group as compared to normal weight control subjects, shown by a difference in the coefficients (Fig. 1). Whereas the RR interval accounted for 54% of the total variation in the QT interval of the control group, it accounted for only 19% of the variation in the QT interval of the obese group. The dependence was increased to 45% following weight reduction therapy. This altered relationship may partly explain why the QT interval is prolonged in obese patients, and it raises a question as to whether Bazett's formula should be used to correct the QT interval of the obese patients. For this reason, both QT and QTc intervals were compared in the present study. The absence of a significant difference in HR between the control and obese groups and before and after diet therapy has made this comparison possible.

No significant correlation between weight or BMI and QT interval was found in the present study. The prolonged

QTc interval of the obese group might merely reflect the fact that the QTc interval depends upon regional fat distribution, particularly that of visceral fat, but not upon body weight, BMI, or other cardiovascular risk factors (3, 4, 21). It has previously been postulated that elevation of free fatty acids in the visceral obesity, which are known to have significant effects on cardiac rhythm and conduction (22), could cause prolongation of the QT interval. In support of this hypothesis, a positive correlation has been reported between levels of long-chain saturated fatty acids and the occurrence of ventricular arrhythmias in patients with myocardial infarction (23). Furthermore, the present study revealed significant correlation between baseline TGL and baseline QTc dispersion whereas others did not show significant correlation. After weight reduction, there was no correlation between TGL and QTc dispersion.

Although the present study has not revealed the mechanism underlying induction of the prolonged QTc interval in obese patients, it has shown that weight reduction is associated with significant shortening of the abnormally prolonged QTc interval. Previous postmortem and UCG studies have demonstrated that LVH occurs frequently in obese subjects, even in the absence of systemic hypertension (24). In the present study, UCG examination revealed that LVH was present in 85% of the obese patients who showed good quality UCG. LVH has previously been shown to induce suppression of the transient outward current that underlies the prolongation of the action potential duration (APD) and thus, the QT interval (25). The suppression of the ionic current was reversed by the regression of LVH. Weight reduction *per se* is also known to be associated with attenuation of LVH (26, 27). Similar mechanisms may underlie the changes in the QT intervals observed in the present study. To support this speculation, there was a positive correlation between left ventricular mass index and QTc interval.

Recent reports have demonstrated that changes in Na-K ATPase activity, ouabain binding capacity, and intracellular Na^+ and K^+ concentrations in the red blood cells occur in obese patients (28, 29). It seems possible that similar mechanisms may occur in the myocardium of obese patients, although there are no reports to date of such changes. The decrease in K^+ concentration adjacent to the sarcolemma due to increased Na-K ATPase activity can explain the prolongation of APD and prolongation of QT interval, *via* the decreased outward potassium currents. This is not likely in the present study because serum levels of Ca^{++}, K^+, Na^+, and Mg^{++} were kept within normal limits in both the obese and control groups, although we could not measure the K^+ concentration in the vicinity of sarcolemma.

Clinical Implication of Increased QT Interval and Its Dispersion. A prolonged QTc interval was shown to correlate with increased risk of arrhythmias (9–11), including torsades de pointes, which cause sudden death. In the present study, however, life threatening arrhythmias were not observed, even though the QTc interval was significantly prolonged in the obese patients. This may principally depend on the fact that neither maximum QT(409, ± 36 msec) nor maximum QTc(445, ± 32 msec) interval approaches the level at which spontaneous arrhythmias occur. According to another report (10), a QTc interval of more than 440 msec was accompanied by a high risk for sudden death due to cardiac arrest. Furthermore, a healthy population with prolongation of the QTc interval for more than 420 msec was reported to be predictable for all causes of mortality during the first 15-year follow-up period (11). Together with those findings and the present result that the mean maximum value of the QTc interval showed slight prolongation, but more than 440 msec in the obese group, we cannot rule out the possibility that our obese patients may develop life threatening arrhythmias during a long-term period.

The mean QTc dispersion(57 ± 23 msec) in the present study was smaller than that of patients with chronic heart failure who died suddenly (98 msec), or that of patients with hypertrophic cardiomyopathy (> 60 msec) who developed serious ventricular arrhythmias (12, 13). However, 14 (44%) of the obese patients in the current study had their QTc dispersion well above the 60 msec above which arrhythmias were reported. The obese patients may be at an increased risk of developing serious ventricular arrhythmias and sudden death due to cardiac arrest compared with normal weight control patients.

Study Limitations. In the present study, we examined UCG only before treatment of obesity and Holter ECG only after the diet therapy. The UCG findings were important in explaining some of the possible causes of QT interval prolongation, but the direct effect of weight loss on LV mass and hence QT interval remains to be elucidated. The Holter ECG findings were also important for the assessment of the QT interval based on arrhythmia risk; however, the paired study before and after dieting is necessary in future study.

In conclusion, the obese patients were found to have a longer QT or QTc interval and a greater QT or QTc dispersion than the nonobese control patients. Because these factors are known to predispose patients to cardiac arrhythmias, monitoring of the QT interval and its dispersion could provide a promising means for sorting obese patients who are at risk for developing life threatening arrhythmias or sudden death. Obese subjects should be treated irrespective of their QT intervals, but much care is necessary to avoid rapid and excessive weight loss, which could precipitate arrhythmias and cause sudden death during the treatment.

The authors thank Dr. D.S. Knight and Dr. K.A. Hamilton, Department of Anatomy, Louisiana State University, for their help in preparation of this manuscript.

1. Messerli FH, Nunez BD, Ventura HO, Synder DW. Overweight and sudden death: Increased ventricular ectopy in cardiopathy of obesity. Arch Intern Med **147:**1725–1728, 1987.

2. Frank S, Colliver JA, Frank A. The electrocardiogram in obesity: Statistical analysis of 1,029 patients. J Am Coll Cardiol **7:**295–299, 1986.
3. El-Gamal A, Gallagher D, Narwas A, Gandhi P, Gomez J, Allison DB, Steinberg JS, Shumacher D, Blank R, Heymsfield SB. Effects of obesity on QT, RR, and QTc intervals. Am J Cardiol **75:**956–959, 1995.
4. Carella MJ, Mantz SL, Rovner DR, Willis PW 3rd, Gossain VV, Bouknight RR, Ferenchick GS. Obesity, adiposity, and lengthening of the QT interval: Improvement after weight loss. Int J Obes Relat Metab Disord **20:**938–942, 1996.
5. Pietrobelli A, Rothacker D, Gallagher D, Heymsfield SB. Electrocardiographic QTc interval: Short-term weight loss effects. Int J Obes Relat Metab Disord **21:**110–114, 1997.
6. Seim HC, Mitchell JE, Pomeroy C, de Zwaan M. Electrocardiographic findings associated with very low calorie dieting. Int J Obes Relat Metab Disord **19:**817–819, 1995.
7. Zuckerman E, Yeshurun D, Goldhammer E, Shiran A. 24-hr electrocardiographic monitoring in morbidly obese patients during short-term zero calorie diet. Int J Obes Relat Metab Disord **17:**359–361, 1993.
8. Garson A Jr. How to measure QT interval: What is normal? Am J Cardiol **72:**14B–16B, 1993.
9. Day CP, McComb JM, Campbell RWF. QT dispersion: An indication of arrhythmia risk in patients with long QT intervals. Br Heart J **63:**342–344, 1990.
10. Algra A, Tijssen JGP, Roelandt JRTC, Pool J, Lubsen J. QTc prolongation measured by standard 12-lead electrocardiography is an independent risk factor for sudden death due to cardiac arrest. Circulation **83:**1888–1894, 1991.
11. Schouten EG, Dekker JM, Meppelink P, Kok FJ, Vandenbroucke JP, Pool J. QT interval prolongation predicts cardiovascular mortality in an apparently healthy population. Circulation **84:**1516–1523, 1991.
12. Barr CS, Naas A, Freeman M, Lang CC, Struthers AD. QT dispersion and sudden unexpected death in chronic heart failure. Lancet **343:**327–329, 1994.
13. Buja G, Miorelli M, Turrini P, Melacini P, Nava A. Comparison of QT dispersion in hypertrophic cardiomyopathy between patients with and without ventricular arrhythmias and sudden death. Am J Cardiol **72:**973–976, 1993.
14. Sakata T, Kurata K, Ito K, Fujimoto K, Terada K, Etou H, Matsuo H. A means of complementing and prolonging the benefits of a very-low-calorie diet and behavioral meal scheduling therapies for moderately obese patients. J Jpn Soc Nutr Food Sci **40:**271–277, 1987.
15. Sakata T. A very-low-calorie conventional Japanese diet: Its implications for prevention of obesity. Obes Res **3** (Suppl 2)**:**233s–239s, 1995.
16. Sahn DJ, Demaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: Results of a survey of echocardiographic measurements. Circulation **58:**1072–1077, 1978.
17. Devereux RB, Reicheck N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. Circulation **55:**613–618, 1977.
18. de Simone G, Daniels SR, Devereux RB, Meyer RA, Roman MA, de Divitiis O, Alderman MH. Left ventricular mass and body size in normotensive children and adults: Assessment of allometric relations and impact of overweight. J Am Coll Cardiol **20:**1251–1260, 1992.
19. Lepeschkin E, Surawicz B. The measurement of the QT interval of the electrocardiogram. Circulation **6:**378–388, 1952.
20. Bazett HC. An analysis of the time-relations of electrocardiograms. Heart **7:**353–370, 1920.
21. Peiris AN, Thakur RK, Sothmann MS, Gustafson AB, Hennes MI, Wilson CR, Kissebah AH. Relationship of regional fat distribution and obesity to electrocardiographic parameters in healthy premenopausal women. South Med J **84:**961–965, 1991.
22. Kurien VA, Oliver MF. Free fatty acids during acute myocardial infarction. Prog Cardiovasc Dis **13:**361–373, 1971.
23. Abraham R, Riemersma RA, Wood D, Elton R, Oliver MF. Adipose fatty acid composition and the risk of serious ventricular arrhythmias in acute myocardial infarction. Am J Cardiol **63:**269–272, 1989.
24. Chakko S, Mayor M, Allison MD, Kessler KM, Materson BJ, Myerburg RJ. Abnormal left ventricular diastolic filling in eccentric left ventricular hypertrophy of obesity. Am J Cardiol **68:**95–98, 1991.
25. Yokoshiki H, Kohya T, Tomita F, Tohse N, Nakaya H, Kanno M, Kitabatake A. Restoration of action potential duration and transient outward current by regression of left ventricular hypertrophy. J Mol Cell Cardiol **29:**1331–1339, 1997.
26. MacMahon SW, Wilchen DEL, McDonald GJ. The effect of weight reduction in left ventricular mass: A randomized controlled trial in young overweight hypertensive patients. N Engl J Med **314:**334–339, 1986.
27. Alpert MA, Lambert CR, Terry BE, Kelly DL, Panayiotou H, Mukerji V, Massey CV, Cohen MV. Effect of weight loss on left ventricular mass in nonhypertensive morbidly obese patients. Am J Cardiol **73:**918–921, 1994.
28. Landin K, Lindgèrde F, Saltin B, Wilhelmsen L. Increased skeletal muscle Na/K-ratio in obese men, but not in women, with glucose intolerance. J Intern Med **225:**89–94, 1989.
29. Simat BM, Mayrand RR, From AHL, Morley JE, Billington C, Fullerton DS, Ahmed K. Is the erythrocyte sodium pump altered in human obesity? J Clin Endocrinol Metab **56:**925–929, 1983.