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Surgery for Obesity and Related Diseases ▮ (2014) 00–00

SURGERY FOR OBESITY AND RELATED DISEASES

Original article

Improvement of heart rate variability after decreased insulin resistance after sleeve gastrectomy for morbidly obesity patients

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Received June 18, 2014; accepted September 13, 2014

Abstract

Background: Morbidly obese patients display both an autonomic nervous imbalance and impaired glucose metabolism, and both of these conditions can be partially reversed after bariatric surgery. The aim of the present study was to investigate changes in heart rate variability (HRV) and glucose metabolism in patients after laparoscopic sleeve gastrectomy (SG).

Methods: Eighteen morbidly obese patients who underwent SG were examined before surgery and at 7, 30, 90, and 180 days after surgery. Indices of HRV included time-domain, frequency-domain, and nonlinear parameters. Glucose metabolism was evaluated by the measuring levels of insulin resistance, glycated hemoglobin (HbA_{1c}), and gut hormones.

Results: The study included 9 men and 9 women with a mean age of 34 years. In the HRV study, the average R-R interval, median R-R interval, standard deviation of the R-R intervals, root mean squared successive difference of the R-R intervals (RMSSD), and the number of pairs of successive normal-to-normal beat intervals that differed by >50 ms significantly increased at 180 days after surgery. Regarding the frequency-domain indices, the low frequency (LF)/high frequency (HF) ratio was more balanced at 90 days after SG compared with baseline, and increases in the total power, LF band, and HF band were observed at 180 days. The assessments of insulin resistance, glucose metabolism, and gut hormones revealed not only improvements in the homeostasis model assessment of insulin resistance and HbA_{1c} levels but also increases in the levels of glucagon-like peptide-1 at 90 and 180 days after surgery compared with baseline. A multivariable regression model revealed significantly negative associations between the perioperative changes in HOMA-IR and changes in both the RMSSD and HF band.

Conclusions: SG leads to early improvements in insulin resistance and glucose metabolism that are followed by improvements in HRV indices. Improvements in insulin resistance were associated with increases in the RMSSD and HF band index, but the mechanism of these changes require further study. (Surg Obes Relat Dis 2014;▮:00–00.) © 2014 American Society for Metabolic and Bariatric Surgery. All rights reserved.

Keywords: Heart rate variability; Glucose metabolism; Sleeve gastrectomy

The prevalence of morbid obesity has progressively increased over recent decades in the United States and in Asian countries [1,2]. Previous studies [3–5] have shown the existence of critically important relationships between obesity and metabolic diseases, diabetes, hypertension, fatty

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http://dx.doi.org/10.1016/j.soard.2014.09.011

1550-7289/

liver, and heart failure. Long-term obesity can result in sympathetic nervous system overactivity and autonomic nervous system (ANS) dysfunction due to sympathovagal tone imbalances [6,7]. Heart rate variability (HRV) refers to the variations in heartbeat intervals. HRV is due to the autonomic neural regulation of the heart and circulatory system. The results of HRV analyses are recognized as reflective of the ANS activities of diverse patients, including patients undergoing intraaortic balloon counterpulsation [8], coronary disease patients exposed to procedural stress [9], the effects of different anesthetics on pneumoperitoneum cases [10], in obese children [11,12], and in obese hypertensive patients [13].

Bariatric surgery is considered to be the most effective method of managing morbid obesity, not only in terms of weight reduction but also in terms of its contribution to the resolution of metabolic syndrome [14,15]. Insulin resistance syndrome has long been considered to be the main factor responsible for obesity-induced cardiovascular morbidity [16]. The relationship between insulin resistance and HRV in morbidly obese patients remains inconclusive [17–19]. In a previous study, gastric bypass has been shown to potentially contribute to improvements in HRV that are inversely correlated with insulin resistance [19]. Sleeve gastrectomy (SG) is a relatively new "restrictive" type of bariatric surgery. SG includes the surgical removal of most of the stomach along the greater curvature and the detachment of the gastric fundus, which is the site of the greatest level of ghrelin production. Therefore, postSG weight loss is thought to be attributable to both changes in appetite and postprandial fullness [20,21]. Nonetheless, clinical data regarding the relationship between insulin resistance and HRV in morbidly obese patients undergoing laparoscopic SG are lacking. The aim of the present study was to investigate the effects of laparoscopic SG on HRV and glucose metabolism in morbidly obese patients.

Materials and methods

Eighteen morbidly obese patients who underwent SG were consecutively recruited and prospectively studied. The protocol was approved by the hospital's institutional review board. All patients provided written informed consent for inclusion in the study. All patients abstained from medications on the day before and day of an electrocardiogram (ECG), and the patients were asked to fast overnight for 12 hours before undergoing the ECG recording and blood sampling. The tests were performed in the hospital upon admission and at 7 days after surgery, as well as in the outpatient clinic of our hospital at 30, 90, and 180 days after surgery. All ECG recordings were obtained between 9 and 11 a.m.. Blood samples (5 cc) were collected to examine gut hormones, insulin, glucose, and glycated hemoglobin (HbA_{1c}). The blood samples were maintained on ice until the preparation of the plasma and then subsequently at –70°C until they were assayed in batches by radioimmunoassay. HbA_{1c} (%) was measured as an indicator of postoperative changes in glucose homeostasis.

Surgical technique

All patients underwent laparoscopic SG, as described previously [22].

Analysis of glucose, insulin, GIP, and GLP-1

Plasma GLP-1 levels were measured using the GLP-1 enzyme immunoassay kit (Millipore Corporation, St. Charles, MO), and plasma GIP levels were measured using the human GIP assay enzyme immunoassay kit (Immuno-Biological Laboratories Co., Ltd., Gunma, Japan). Plasma insulin levels were measured with a human insulin assay kit (DIAsource, Inc., Nivelles, Belgium).

Heart rate variability

HRV is the beat-to-beat variation of the heart rate and is calculated based on the oscillations of the R-R intervals. Electrodes were attached according to the modified lead II method (i.e., the right clavicle and left iliac crest), with a reference electrode on the left clavicle, and connected to a laboratory ECG that sampled at 1000 Hz (PowerLab 8/30: ADInstruments, Sydney, Australia). The patients were placed in a supine position after resting. All ECG measurements were performed in a quiet room and recorded for 30 minutes. The data were exported and analyzed using LabChart 8 software (ADInstruments, Dunedin, New Zealand). The heart rate and the following measures of HRV were determined: time-domain parameters (average R-R interval, median R-R interval, standard deviation of R-R intervals [SDRR], the standard deviation of averaged R-R intervals over a 5-minute period [SDARR], the square root of the mean of the sum of the squares of the successive differences between adjacent normal-to-normal beats [RMSSD], and the number of pairs of successive normal-to-normal beat intervals that differed by > 50 ms [pRR50]), frequency-domain parameters (total power, very low frequency [VLF] band [.0033–.04 Hz], low frequency [LF] band [.04–.15 Hz], high frequency [HF] band [.15–.4 Hz], and the LF/HF ratio), and nonlinear parameters (SD1 and SD2). Poincaré scatter plots were constructed and investigated as nonlinear tool, including the transverse axes (SD1, an indicator of parasympathetic activity) and the longitudinal axes (SD2, an inverse function of sympathetic activity) [23].

Statistical analyses

All values are expressed as the mean ± the standard deviation. All HRV indices were nonnormally distributed and were logarithmically transformed for statistical analysis.