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Early Weight Loss Independent Effects of Sleeve Gastrectomy on Diet-Induced Cardiac Dysfunction in Obese, Wistar Rats

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Abstract

Introduction—Several reports suggest that bariatric surgery significantly improves cardiac function in patients with obesity cardiomyopathy. The mechanism is unknown but may be due to weight-loss independent factors. We predict that the changes in gastrointestinal anatomy after a rodent model of sleeve gastrectomy (SG) will have weight-loss independent effects on cardiac dysfunction.

Methodology—Cardiac dysfunction was induced by feeding a 60% kcal from fat diet to male Wistar rats for 10 weeks. Rats underwent either a SG ($n = 12$) or pair-fed, PF ($n = 8$) sham surgery. Echocardiograms were performed pre- and post-operatively at 6 and 13 weeks. Blood samples were obtained at 10 weeks post-operatively for assessment of insulin sensitivity and heart failure.

Results—Forty-four percent of SG rats had a normal ejection fraction (EF) at 13 weeks (“responders”) compared to five SG rats who did not recover EF (“non-responders”). Zero percent of the PF rats normalized EF ($p = 0.03$). SG responders had a smaller left ventricular internal diameter in systole and end systolic volume with improved systolic function compared to SG non-responders (EF 90.7 ± 1.7 vs. $75.4 \pm 3.6\%$, $p = <0.001$). At 10 weeks post-operatively, plasma glucose and B-type natriuretic peptide levels were significantly lower in SG rats compared to PF rats.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All applicable institutional and/or national guidelines for the care and use of animals were followed.

Conclusions—A SG significantly improved systolic function in 44% of rats with diet-induced obesity and cardiac dysfunction. This improvement is related to weight-loss independent effects of the surgery on the entero-cardiac axis. These results offer a novel weight-loss independent, metabolic role for bariatric surgery as a potential treatment modality for obesity-associated cardiac dysfunction.

Keywords

Metabolic surgery; Obesity cardiomyopathy; Heart failure; Echocardiogram; Ejection fraction

Introduction

In patients with heart failure with reduced ejection fraction (EF), 30–50% are obese. There is an even higher prevalence of obesity in patients with heart failure with preserved EF [1, 2]. For every 1 kg/m² unit body mass index (BMI) increase, the risk of heart failure increases 5% for men and 7% for women [3]. Obesity cardiomyopathy is defined as heart failure originating from myocyte dysfunction due to the disease of obesity. The pathophysiology of obesity cardiomyopathy is complicated by other obesity-associated comorbidities which affect cardiac function including hypertension, hyperlipidemia, obstructive sleep apnea, and type 2 diabetes mellitus.

Morbidly obese patients with advanced heart failure are ineligible for cardiac transplantation due to organ-specific BMI limits. In advanced heart failure patients, bariatric surgery was initially used for weight loss as a bridge to cardiac transplantation [4, 5]. Surprisingly, bariatric surgery significantly improved both symptoms of heart failure and cardiac function in 50% of patients [5–7]. Post-surgical cardiac changes include significant improvements in cardiac geometry and function including decreased hypertrophy and dilation with increased EF and improved relaxation [8]. Bariatric surgery is also associated with a decline in the rate of heart failure exacerbations requiring emergency department evaluation or hospitalization in the first 12 months after surgery [9].

Clinical studies of patients with heart failure and bariatric surgery have focused on patient safety and functional outcomes and have not been able to explore any novel mechanisms generated by the surgery for cardiac recovery. There is a precedent for weight-loss independent mechanisms induced by a bariatric surgery on metabolic disease, such as type 2 diabetes mellitus and non-alcoholic fatty liver disease [10–12]. Supporting a weight-loss independent mechanism, weight reduction through dieting alone in symptomatic heart failure patients improves symptoms and quality of life but does not affect cardiac structure or function [13–15].

Although the inciting mechanisms are unknown, a sleeve gastrectomy (SG), which removes 75–80% of the stomach, induces positive changes in the bile acid profile, the microbiome, peripheral to central neural signaling, and gastrointestinal hormones. These post-operative changes are likely to impact energy expenditure, food intake, satiety, glucose, and lipid homeostasis in a weight-loss independent manner [16]. We predict in this exploratory study that performance of a SG has weight-loss independent effects on cardiac dysfunction induced by diet-induced obesity. To test this hypothesis, we performed SG in rats with diet-

induced obesity and cardiac dysfunction and assessed for weight-loss independent improvements in EF and left ventricular (LV) hypertrophy and dilation compared to pair-fed (PF) sham rats.

Methods

Study Design

We examined the effect of SG or dieting (PF to food intake of SG rats) on the progression or regression of cardiac dysfunction induced by a high-fat diet (HFD). This study and all procedures were approved by the Medical College of Wisconsin's Institutional Animal Care and Use Committee. Four-week-old male Wistar rats were fed either a HFD Open Source Research Diet D12492 ($n = 20$) or a control low-fat diet (LFD, $n = 6$) Open Source Research Diet D12450H (Research Diets, New Brunswick, NJ) for 10 weeks. D12452 is a 60% kcal HFD with lard as the primary fat source. D12450H is a 10% kcal LFD matched for sucrose content per kcal (7% sucrose) with D12492. The LFD served as a control to demonstrate the normal cardiac functional analysis of lean, Wistar rats compared to those on a HFD. At 13 weeks of age, all rats underwent a trans-thoracic echocardiogram (TTE). HFD fed rats were pair-matched by cardiac function and then randomized to undergo either a SG ($n = 12$) or PF ($n = 8$) sham surgery. SG or PF sham rats underwent two additional echocardiograms at 6 and 13 weeks post-operatively. Fasting plasma samples were obtained at 10 weeks post-operatively for the measurement of fasting glucose and insulin; the calculation of quantitative insulin-sensitivity check index (QUICKI) was used as a measurement of insulin resistance, as well as B-type natriuretic peptide (BNP).

Animals and Pair-Feeding

Animals were kept in pairs until they underwent the first TTE. HFD animals were then individually caged for the duration of the study with environmental enrichment to include paper shredding material and an autoclaved glove box for nesting. All animals were kept on their assigned diet except for 24 h prior to surgery when they were switched to a rodent gel diet (Diet Gel Recovery, Clear H₂O) as well as for 48 h post-operatively when they were placed on the same gel diet until the HFD was re-introduced. Body weight and food intake were recorded daily. To account for any beneficial effects of weight loss on heart failure recovery, the sham group was pair fed on the average daily food intake of SG rats. For example, on post-operative day 7, SG rats averaged a daily food intake of 8.2 g; therefore, each PF rat was fed only 8 g of diet on their respective post-operative day 7.

Surgical Procedures

The described technique has been adapted from Bruinsma et al. based on our own personal experience with SG in rats [17]. All HFD animals were fasted from food overnight but had ad libitum access to water. A subcutaneous injection of enrofloxacin (10 mg/kg) was given pre-operatively. For SG animals, the abdomen was incised in the midline through the abdominal muscles from the xiphoid extending 2 cm inferiorly. The liver was retracted to the right exposing the stomach. The fibro-fatty tissue of the greater curvature was taken up to the gastroesophageal junction with scissors. An endoscopic stapling device (Endopath ETS-Flex, 45 mm white load; Ethicon, Cincinnati, OH) was used to remove the greater curvature

of the stomach including all of the non-glandular lateral stomach. A sizing device was not used. The abdominal muscles were closed with a running 4–0 polysorb suture. The skin was closed with interrupted vertical mattress 4–0 silk sutures. A saline injection was given subcutaneously to prevent dehydration (20 cm³/kg) on postoperative days 0 and 1. Buprenorphine SR was given via subcutaneous injection on day 0 for pain control. For sham animals, the same procedure was followed except the stomach was not divided. The animals were kept on a warmer until fully awake and then returned to their individual cages for the remainder of the study.

Cardiac Function Analysis

Rodent TTE was performed in anesthetized (2% isoflurane) rats at 13 weeks of age (1 week pre-operatively) and at 6 and 13 weeks post-operatively. Measurements and data analyses were performed as previously published by a small animal echocardiogram technician blinded to the study groups [18]. Animals were studied in the left lateral decubitus position with a commercially available echocardiographic system (Vivid 7, General Electric, with an 11-MHz M12-L linear array transducer, GE Healthcare, Waukesha, WI). TTE was performed from the cardiac short axis of the left ventricle at the papillary muscle level, using the anatomical M-mode feature of the Vivid 7 echo. A M-mode display was generated from raw data 2D images with the line selected passing through the anterior and inferior segments. Stroke volume (SV) was measured using left ventricular end diastolic volume (EDV) and end systolic volume (ESV) using the formula: $SV = EDV - ESV$. EF was measured using the formula: $EF = SV/EDV \times 100$. The LV mass was derived from the antero-septal thickness (AST) and (ILT) using the formula: $LV\ mass = 0.8 + (1.04[(ILT + LV\ internal\ diameter\ in\ diastole + AST)^3 - LV\ internal\ diameter\ in\ diastole^3]) + 0.6$. Diastolic function was measured by tissue Doppler including the isovolumetric relaxation time (IVRT), E wave, and mitral annulus (e') velocity. The A wave (late diastolic filling) is often merged with the E wave in rats and therefore was not measured. Three consecutive heart beats were measured and the average was used for analysis.

Hormone Analysis

Fasting glucose was measured immediately in duplicate using a handheld glucometer from a tail-vein blood sample. Additional fasting tail vein blood was collected in a EDTA collecting tube. Samples were kept on ice and then spun for 10 min at 4000 g with plasma collected for the measurement of insulin and BNP. Insulin concentrations were determined using a commercially available rat, sandwich enzyme-linked immunosorbent assay (ELISA) kit (EMD Millipore). QUICKI was measured after conversion to US standard units by the following calculation: $QUICKI = 1/[\log(\text{fasting insulin } \mu\text{U/mL}) + \log(\text{fasting glucose mg/dL})]$. BNP was measured using a sandwich ELISA kit (Rat BNP 45 ELISA kit, ab108816, Abcam) which is cross-reactive with BNP 45 and BNP 32.

Statistics

All values are presented as the mean $\pm$ SD. Comparisons of results between the two experimental groups over time (body weight, food intake, repeated TEE measures) were performed using a two-way repeated measures ANOVA. Glucose, insulin, BNP, QUICKI, and LFD vs. HFD comparisons for the same time point were done using a student's *t* test.

Cardiac recovery was compared to non-recovery in SG and PF rats by a chi-square test. Values were determined statistically significant if $p < 0.05$.

Results

SG and PF Rats Had No Difference in Body Weight or Food Intake Post-operatively

Ten weeks of HFD feeding induced a significant increase in body weight, 558 ± 56 g compared to low-fat rats, 482 ± 49 g, $p = 0.005$. Twelve, 14-week-old HFD Wistar rats then underwent SG and eight underwent sham surgery after matching for EF. Our survival rate for SG rats was 75% ($n = 9$). The survival rate for sham PF rats was 100%. There was no post-operative day when there was a statistically significant difference in body weight (Fig. 1a) or food intake (Fig. 1b) between SG and PF, sham rats. As per study design, PF sham rats received the averaged food intake of SG rats to the nearest gram for their matched post-operative day.

SG Decreases Fasting Blood Glucose and BNP Concentrations

At 10 weeks postoperatively, SG rats had a significantly lower fasting glucose concentration, 62.2 ± 6.1 mg/dL, compared to PF rats, 72.9 ± 3.4 mg/dL, $p = 0.006$ (Fig. 2a). There was no difference between the two groups in the fasting insulin concentrations or QUICKI as a surrogate marker of insulin resistance (Fig. 2b, d). As shown in Fig. 2c, plasma BNP levels were significantly lower in SG rats compared to PF rats (915 ± 467 vs. 1694 ± 959 pg/mL, $p = 0.05$). This is indicative of a decreased cardiac disease burden in SG rats despite similar weight loss from caloric reduction.

SG Induces LV Remodeling at 13 weeks Post-Op

Baseline echocardiograms performed 10 weeks after a HFD revealed significant reductions in systolic function as determined by fractional shortening (FS) compared to LFD rats ($49.7 \pm 5.3\%$ HFD compared to $55.4 \pm 5.2\%$ LFD, $p = 0.02$) and EF (85.0 ± 4.3 HFD compared to $89.4 \pm 3.6\%$ LFD, $p = 0.03$). The decreased LV function was associated with significant increases in LV internal diameter in systole (LVIDs) and ESV in HFD rats compared to a LFD (Table 1). Baseline preoperative echocardiograms did not reveal any differences in LV dilation, hypertrophy, diastolic, or systolic function between the SG and PF groups before surgery (Table 2).

At 13 weeks postoperatively, both SG and PF rats had similar echocardiogram mean indexes without significant differences between the two groups (Table 2). A large amount of variability in the cardiac parameters was seen in the SG group. No recovery of EF was observed in either the SG or PF groups ($82.2 \pm 8.5\%$ for SG rats and $80.8 \pm 6.4\%$ for PF rats, $p = 0.71$). There was also no statistical difference in LV mass or LV dilation between the two HFD fed groups post-operatively.

After setting the threshold for normal EF to 89.4%, which is the average EF from the pre-operative LFD group, we then examined the EFs from each HFD rat individually. Four out of the nine (44%) SG rats had a EF at or above normal at 13 weeks post-operatively (“responders”) whereas the remaining five rats had no improvement in EF (“non-

responders”). In the PF group, none of the rats had a normal EF ($p = 0.03$). There were a significant number of SG responders compared to PF responders ($p = 0.03$).

The SG responders had a decreased LV internal diameter in diastole (LVIDd) and EDV, compared to non-responder SG rats at 6 weeks (LVIDd 0.84 ± 0.03 vs. 0.90 ± 0.04 cm, $p = 0.03$; EDV 1.27 ± 0.17 vs. 1.57 ± 0.16 mL, $p = 0.03$, respectively). The responders also had significantly less LV mass (hypertrophy) at 6 weeks, 1.61 ± 0.11 g, compared to non-responders SG rats, 1.89 ± 0.14 g, $p = 0.01$. These trends continued throughout the study so at 13 weeks SG responders had statistically smaller LVIDs and ESV and increased systolic function by measurement of both EF as shown in Fig. 3 and FS (EF 90.7 ± 1.7 vs. $75.4 \pm 3.6\%$, $p < 0.001$; FS 57.1 ± 2.9 vs. $39.8 \pm 3.1\%$, $p < 0.001$, respectively) compared to SG non-responders (Table 3). There was no significant difference in responders compared to SG non-responders for fasting glucose, insulin, or BNP concentrations.

Discussion

In this first proof of concept study, a SG in Wistar rats with diet-induced obesity and cardiac dysfunction significantly improved systolic function in 44% of rats independent of weight loss at 13 weeks after surgery. None of the PF rats had preserved or recovered EF at this time point. The improvement in LV systolic function was associated with a decrease in LV dilation and hypertrophy at 13 weeks. This suggests beneficial, reverse cardiac remodeling without systolic changes as early as 6 weeks after surgery. SG rats also had significantly lower fasting glucose and plasma BNP concentrations compared to HF rats. As there was no difference in body weight or food intake, only weight-loss independent changes as a result of the alteration in gastric anatomy are responsible for the differences in functional improvement between the two groups.

In this study, we utilized a 60% HFD to induce cardiac dysfunction in male Wistar rats. We have found the Wistar rat to be obesity-prone, and multiple authors have published the Wistar rat to be a susceptible rodent strain to cardiac dysfunction of a HFD [19–22]. Samniang et al. found 12 weeks of a HFD fed to male Wistar rats induced significantly increased body weight, plasma insulin, HOMA index, total cholesterol, and LDL levels as well as significant reductions in FS% and systolic blood pressure. Extension of the HFD to 20 weeks induced significant diastolic and mean arterial blood pressure changes [20]. Recently, Pongkan et al. documented significant reductions in left ventricular function by both %FS and %EF at 8 and 12 weeks after initiation of a high fat diet in Wistar rats compared to a standard chow diet. A HFD also induced cardiac autonomic imbalance, cardiac myocardial dysfunction, and increased circulating and cardiac tissue oxidative stress [21]. Many of these metabolic derangements are shared with patients who are morbidly obese with cardiac metabolic disease including hypertriglyceridemia, hypertension, glucose intolerance, and hyperleptinemia [22]. However, the relationship between obesity and heart failure development in humans is complex involving multiple different pathways that ultimately affect cardiac function. Morbid obesity has directly toxic adverse effects on the cardiac myocyte which is confounded by the accumulating effects of hypertension, hypoxia, metabolic syndrome, coronary artery disease, and type 2 diabetes mellitus [23, 24]. Importantly, this rodent model is distinct from overtly diabetic, hypertensive, and ischemic

cardiac dysfunction models. Relatively acute induction of cardiac dysfunction (10 weeks) with a HFD alone in male rats cannot capture the multiple complex mechanisms at play in clinical obesity cardiomyopathy but allows for the scientific exploration of potential beneficial mechanisms involved in cardiac recovery after SG.

The mechanisms for LVEF improvement after bariatric surgery are unknown but weight-loss independent mechanisms generated from the gastrointestinal tract likely play a role. As early as 1 week after SG and RYGB, meal-induced insulin and glucagon-like peptide-1 (GLP-1) secretion are increased. Enhanced post-operative GLP-1 is believed to be one of the primary mechanisms for the dramatic resolution of type 2 diabetes after SG. Active GLP-1 exerts its actions via the GLP-1 receptor on the pancreas, brain, kidney, immune cells, intestine, and heart of rodents and humans [25]. Myocardial GLP-1 receptor activation increases cardiac muscular contractions and heart rate, increases myocardial glucose uptake, and decreases apoptosis [26, 27]. In patients with heart failure, chronic GLP-1 infusion significantly improved left ventricular ejection fraction, physical stamina and aerobic capacity, and heart failure related quality of life [28]. Future studies are needed to determine if enhanced post-operative GLP-1 mediates the beneficial impact of SG on cardiac function independent of weight loss.

We found a heterogeneous cardiac response even when groups were matched for strain, sex, age, diet, and etiology of heart failure (HFD). It is possible that the inciting mechanisms generated from the entero-cardiac axis after SG are variable, and in the “cardiac responders” those mechanisms are more robust. Prior studies examining the variance in the weight loss outcome suggest that the degree of positive hormonal change after bariatric surgery impacts the metabolic outcome [29, 30]. Dirksen et al. found a larger release of GLP-1 and greater suppression of ghrelin during a meal test in good weight loss responders (excess weight loss >60%) compared to poor weight loss responders (<50%). Both glucagon-like-peptide (GLP)-1 and GLP-2 exertion are significantly correlated with satiety after Roux-en-Y gastric bypass [31]. It is also possible that cardiac responsiveness is not due to variability in the hormonal response but due to downstream differences in receptor responsivity or sensitivity. Habegger et al. published variable diabetes resolution in Long-Evans rats after Roux-en-Y gastric bypass related to GLP-1 receptor sensitivity [32]. Future studies are needed to determine if a similar phenomenon can explain the variability in cardiac recovery after SG in HFD fed rats.

This study is limited by a small sample size in the setting of a heterogeneous cardiac response. Further, this study does not have a sham surgical group who was fed ad lib to determine the weight-loss dependent effects of SG or PF. Future studies with larger animal numbers that include an ad lib sham group will highlight what affects calorie restriction has on the natural history of diet-induced cardiac dysfunction in rats. We would expect that there are some clinical benefits to substantial weight loss alone on cardiac function as has been published after vertical banded gastroplasty, a non-metabolic procedure [33].

This study provides the initial evidence for a positive, direct effect of a SG on cardiac function independent of any changes in calorie restriction, weight loss, or dietary changes in a rodent model of cardiac dysfunction. This novel finding suggests that a SG acts as a

cardiac metabolic intervention, beyond the benefits of weight loss, by manipulating the entero-cardiac axis to preserve recovered function or reverse dilation, hypertrophy, and impaired systolic function in the setting of obesity.

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Fig. 1. Body weight (a) and food intake (b) for 10 weeks post-operatively between high-fat fed sleeve gastrectomy and pair-fed, sham Wistar rats

Fig. 2. Fasting plasma parameters of glucose homeostasis. **a** Glucose. **b** Insulin. **d** QUICKI as well as cardiac function. **c** BNP at 10 weeks after surgery in SG or PF rats. Data are mean $\pm$ SD. Statistical significance determined at $p < 0.05$ (*)

Fig. 3. Individual ejection fraction % curves for sleeve gastrectomy responders (EF > 89.4%, *solid lines*) or sleeve-gastrectomy non-responders (EF < 89.4%, *dotted lines*)

Table 1

The effect of a x on cardiac structure and function

	LFD	HFD	p value
BW (g)	482 ± 48.5	558 ± 55.8	0.005
IVSd (cm)	0.19 ± 0.02	0.19 ± 0.02	0.47
LVIDd (cm)	0.82 ± 0.05	0.83 ± 0.04	0.52
LVPWd (cm)	0.18 ± 0.01	0.18 ± 0.02	0.52
LVIDs (cm)	0.37 ± 0.05	0.42 ± 0.05	0.03
EDV (mL)	1.21 ± 0.20	1.26 ± 0.17	0.52
ESV (mL)	0.13 ± 0.06	0.19 ± 0.07	0.05
EF (%)	89.4 ± 3.6	85.0 ± 4.3	0.03
FS (%)	55.4 ± 5.2	49.7 ± 5.3	0.02
SV (mL)	1.08 ± 0.18	1.07 ± 0.13	0.86
LV mass (g)	1.53 ± 0.09	1.60 ± 0.14	0.29
IVRT (ms)	10.6 ± 2.4	11.3 ± 2.4	0.56
E (m/s)	1.24 ± 0.17	1.22 ± 0.12	0.82
e' (m/s)	0.09 ± 0.02	0.10 ± 0.02	0.43
E/e'	14.8 ± 4.2	13.4 ± 3.8	0.44
Heart rate (beats/min)	380 ± 29.0	381 ± 25.1	0.85

Wistar rats were assigned either to a 35% kcal from fat low-fat diet (LFD, $n = 6$) or 60% kcal from fat high-fat diet (HFD, $n = 20$) for 10 weeks. Echocardiograms were performed on anesthetized rats at 13 weeks of age. Data are expressed as mean ± SD. Statistical significance determined at $p < 0.05$

BW body weight, *IVDs* inter-ventricular septum in diastole, *LVIDd* left ventricular internal diameter in diastole, *LVPWd* left ventricular posterior wall in diastole, *LVIDs* left ventricular internal diameter in systole, *EDV* end diastolic volume, *ESV* end systolic volume, *EF* ejection fraction, *FS* fractional shortening, *SV* stroke volume, *LV* left ventricle, *IVRT* isovolumetric relaxation time

Table 2

The effect of sleeve gastrectomy or calorie restriction on cardiac structure and function

	Pre-op		13 weeks Post-op	
	HFD SG	HFD PF	HFD SG	HFD PF
BW (g)	546 ± 50	564 ± 53	601 ± 80	604 ± 62
IVSd (cm)	0.19 ± 0.01	0.19 ± 0.02	0.18 ± 0.02	0.17 ± 0.02
LVIDd cm	0.84 ± 0.04	0.83 ± 0.05	0.87 ± 0.08	0.85 ± 0.05
LVPWd cm	0.19 ± 0.02	0.18 ± 0.01	0.19 ± 0.01	0.18 ± 0.02
LVIDs cm	0.42 ± 0.07	0.41 ± 0.06	0.46 ± 0.11	0.46 ± 0.07
EDV (mL)	1.29 ± 0.17	1.23 ± 0.19	1.44 ± 0.34	1.31 ± 0.19
ESV (mL)	0.20 ± 0.09	0.18 ± 0.07	0.27 ± 0.15	0.26 ± 0.11
EF (%)	84.9 ± 5.4	85.3 ± 4.5	82.2 ± 8.5	80.8 ± 6.4
FS (%)	49.9 ± 6.6	50.0 ± 5.8	47.5 ± 9.5	45.2 ± 6.3
SV (mL)	1.09 ± 0.11	1.05 ± 0.15	1.17 ± 0.24	1.05 ± 0.13
LV Mass (g)	1.62 ± 0.11	1.55 ± 0.17	1.64 ± 0.17	1.53 ± 0.11
IVRT (ms)	11.7 ± 2.5	10.9 ± 2.9	14.5 ± 2.8	15.2 ± 3.4
E (m/s)	1.21 ± 0.12	1.25 ± 0.11	1.12 ± 0.15	1.20 ± 0.08
e' (m/s)	0.10 ± 0.03	0.10 ± 0.02	0.09 ± 0.02	0.11 ± 0.02
E/e'	13.0 ± 4.8	13.9 ± 3.6	12.2 ± 2.8	11.7 ± 2.0
Heart rate (beats/min)	375 ± 22	382 ± 27	380 ± 20	381 ± 24

Echocardiograms were performed on anesthetized sleeve gastrectomy (SG) or pair fed (PF) rats pre-operatively and at 13 weeks post-operatively. Data are mean ± SD. Non-significant for all comparisons (between groups and over-time)

BW body weight, *IVD* inter-ventricular septum in diastole, *LVIDd* left ventricular internal diameter in diastole, *LVPWd* left ventricular posterior wall in diastole, *LVIDs* left ventricular internal diameter in systole, *EDV* end diastolic volume, *ESV* end systolic volume, *EF* ejection fraction, *FS* fractional shortening, *SV* stroke volume; *LV* left ventricle; *IVRT* isovolumetric relaxation time

Table 3

Cardiac function between responders and non-responders after sleeve gastrectomy

	Pre-operatively		6 weeks post-operatively		13 weeks post-operatively	
	R	SG	R	SG	R	SG
BW (g)	524 ± 54	563 ± 45.4	508 ± 58	545 ± 58	584 ± 95	616 ± 75
IVSd (cm)	0.19 ± 0.01	0.20 ± 0.01	0.20 ± 0.02	0.23 ± 0.02	0.19 ± 0.02	0.18 ± 0.03
LVIDd cm	0.84 ± 0.03	0.84 ± 0.06	0.84 ± 0.04	0.90 ± 0.04*	0.83 ± 0.05	0.91 ± 0.07
LVPWd cm	0.18 ± 0.01	0.19 ± 0.02	0.18 ± 0.01	0.18 ± 0.03	0.19 ± 0.01	0.18 ± 0.01
LVIDs cm	0.39 ± 0.06	0.45 ± 0.07	0.40 ± 0.11	0.53 ± 0.07	0.35 ± 0.03	0.55 ± 0.03*
EDV (mL)	1.27 ± 0.11	1.30 ± 0.22	1.27 ± 0.17	1.57 ± 0.16*	1.22 ± 0.22	1.62 ± 0.32
ESV (mL)	0.16 ± 0.06	0.23 ± 0.10	0.19 ± 0.13	0.37 ± 0.12	0.12 ± 0.03	0.39 ± 0.5*
EF (%)	88.0 ± 4.1	82.6 ± 5.5	85.6 ± 9.4	76.6 ± 8.1	90.7 ± 1.7	75.4 ± 3.6*
FS (%)	53.5 ± 5.9	47.0 ± 6.1	51.8 ± 11.6	41.5 ± 7.7	57.1 ± 2.9	39.8 ± 3.1*
SV (mL)	1.12 ± 0.06	1.07 ± 0.15	1.08 ± 0.17	1.20 ± 0.18	1.10 ± 0.20	1.23 ± 0.28
LV mass (g)	1.57 ± 0.09	1.67 ± 0.11	1.61 ± 0.11	1.89 ± 0.14*	1.56 ± 0.15	1.71 ± 0.18
IVRT (ms)	10.5 ± 1.0	12.7 ± 3.0	12.4 ± 2.8	12.7 ± 3.5	13.8 ± 2.9	15.1 ± 2.9
E (m/s)	1.12 ± 0.06	1.27 ± 0.12	1.11 ± 0.17	1.21 ± 0.12	1.09 ± 0.15	1.14 ± 0.16
e' (m/s)	0.09 ± 0.03	0.11 ± 0.02	0.10 ± 0.02	0.11 ± 0.02	0.10 ± 0.02	0.09 ± 0.02
E/e'	13.9 ± 6.8	14.7 ± 12.3	12.7 ± 5.6	10.9 ± 2.1	10.7 ± 1.6	13.4 ± 3.1
Heart rate (beats/min)	366 ± 25	382 ± 21	373 ± 7	379 ± 19	373 ± 18	385 ± 22

Echocardiograms were performed on anesthetized rats pre-operatively and at 6 and 13 weeks post-operatively. Data are mean ± SD. Statistical significance determined at $p < 0.05$ (*) between responders (R) vs. non-responders (NR) after sleeve gastrectomy (SG) for the same time point

BW/body weight, *IVDs* inter-ventricular septum in diastole, *LVIDd* left ventricular internal diameter in diastole, *LVPWd* left ventricular posterior wall in diastole, *LVIDs* left ventricular internal diameter in systole, *EDV* end diastolic volume, *ESV* end systolic volume, *EF* ejection fraction, *FS* fractional shortening, *SV* stroke volume, *LV* left ventricle; *IVRT* isovolumetric relaxation time