



Improvements in Heart Rate Variability in Women with Obesity: Short-term Effects of Sleeve Gastrectomy

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Abstract

Purpose Obesity has been associated with reduced vagal function and increased sympathetic activity. Cardiac autonomic dysfunction has emerged as a major risk factor in the development of cardiovascular disease. Cardiac autonomic function (CAF) can be assessed by heart rate variability (HRV), an independent predictor of mortality based on changes in time intervals between adjacent heartbeats (RR). Bariatric surgery is considered the most effective treatment for obesity and its comorbidities, with sleeve gastrectomy (SG) being the most frequent bariatric procedure. There are few studies on HRV changes in women with obesity after SG. The aim of this study was to evaluate the short-term impact of SG on CAF and its relationship with weight loss.

Materials and Methods An observational cohort study was conducted. Twenty-three female patients were assessed before SG and at 1 and 3 months after surgery. CAF was evaluated by analyzing HRV from 5-min records of RR intervals while the subject was supine. HRV was analyzed in time and frequency domains and with a nonlinear method.

Results Patients (36.0 ± 11.1 years old, BMI 35.1 ± 3.4 kg/m²) presented higher HRV values, on average, in all domains both at 1 and 3 months after SG ($p < 0.05$). In addition, all anthropometric parameters improved ($p < 0.001$) although there was no relationship between HRV improvements and anthropometric changes.

Conclusion SG seems to be effective at reducing excess weight and improving HRV at the short term, and these changes are detectable as early as the first month after surgery. HRV assessment appears as a promising low-cost tool that deserves further research.

Keywords Obesity · Bariatric surgery · Autonomic nervous system · Weight loss

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Introduction

Obesity is a disease which affects over 650 million adults worldwide [1] with a higher prevalence in women [2]. It has been reported that obesity implies a greater cardiovascular disease (CVD) risk for women than men [3]. Obesity is associated with numerous comorbidities such as dyslipidemia, diabetes, osteoarthritis, some cancers [4], hypertension, atrial fibrillation, heart failure, stroke, and coronary heart disease [5–8]. CVD may occur due to structural and functional changes of the myocardium induced by the excess adipose tissue and other mechanisms related to obesity [5, 9].

Obesity is also characterized by autonomic dysfunction with elevated sympathetic and decreased parasympathetic system activity, leading to an autonomic imbalance across the cardiovascular system [10]. Hormonal changes observed in subjects with obesity, such as an increase in insulin and leptin plasmatic levels, have been established as factors that contribute to autonomic dysfunction and the development of obesity-related cardiac diseases [11, 12]. It has been described that a 10% increase in body weight is enough to decrease parasympathetic activity and to increase the activity of the sympathetic system; the latter would be an adaptive mechanism to increase the energy expenditure at rest and to promote the restoration of the previous weight [12].

Altered cardiovascular autonomic regulation resulting from obesity can be detected by assessing heart rate variability (HRV), the change in time intervals between adjacent heartbeats [13]. HRV has been widely described [14–19], proving to be an independent predictor of mortality [14, 20–24] associated with cardiac health [25].

HRV reductions in obese women have been previously reported [13], with a higher rate of sudden cardiac death among obese people, compared with those in adults with normal body weight [26–28].

Conventional obesity treatment has shown limited success in reducing body weight over time [29]. The number of bariatric procedures has increased over recent years [30] and more than 70% of these have been performed on women [31]. Although evidence exists regarding the efficacy of bariatric surgery on weight reduction and comorbidities [32–35], there is insufficient information on the changes that sleeve gastrectomy (SG), the most common bariatric procedure in the world [30], can induce on HRV. The aim of this study was to describe the short-term HRV changes following SG and their relationship to weight loss.

Materials and Methods

Study Design, Participants, and Procedures

In this analytical observational cohort study, participants were recruited over a 2-year period (2015 and 2016). The sample

size was calculated with an alpha error of 5% and a statistical power of 90%, considering previously reported high-frequency (HF) power data [36], which gave a required cohort size of 17 patients. The present study included 23 adult women with obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$) who were undergoing SG. Participants with arrhythmias, severe CVD, chronic renal insufficiency, chronic obstructive pulmonary disease, a smoking habit, used beta blockers, or a postmenopausal status or who had undergone previous bariatric surgery were excluded.

All subjects followed the usual bariatric post-surgical diet indications [37] and were given recommendations for increasing physical activity levels.

Subjects were asked to fast for at least 3 h before each evaluation; they were also asked to wear comfortable clothes and to refrain from drinking caffeinated and alcoholic beverages and performing intense physical exercise over the preceding 24 h. All assessments were performed in the morning to avoid variations in the circadian rhythm.

A complete assessment of anthropometric parameters and HRV was conducted 7–14 days prior to surgery, as well as 1 month and 3 months following the SG.

All procedures were performed in accordance with the standards set out in the 1964 Helsinki declaration and its later amendments, and all patients signed an informed consent.

Anthropometrics

The body mass index (BMI) and the waist circumference (at the level of the iliac crests) were determined using a DETECTO 439 balance scale and a Rosscraft anthropometric tape, respectively [38]. Weight loss was expressed as the percentage of total weight loss (%TWL) and the percentage of excess weight loss (%EWL) [39].

Heart Rate Variability

The duration of RR intervals was recorded using a Polar RS800CX telemetry heart rate monitor (Polar Electro Oy, Kempele, Finland) [40–42]. After resting in the supine position for 5 min, the heart rate RR intervals were continuously recorded for 10 min in the same position in a quiet, temperature-controlled room (22–24 °C) while breathing at a controlled rate (14 breaths per minute) using a metronome [43]. The time domain, frequency domain, and nonlinear analysis of HRV were determined from the 5-min resting RR record with the lowest average heart rate.

RR data were analyzed with Kubios HRV Premium software (3.0.2 version) and preprocessed to remove abnormal intervals and artifacts [43, 44]. The time domain HRV variables analyzed were standard deviation of all RR intervals (SDNN), root mean square of successive differences in RR intervals (RMSSD), and percentage of consecutive RR intervals that differ by more than

50 ms (pNN50) [16, 23]. The frequency domain analysis was computed using the fast Fourier transform and the measures included the low-frequency (LF) power, HF power, and LF to HF power ratio (LF/HF) [14]. HF and LF were expressed in absolute and logarithm values (Ln).

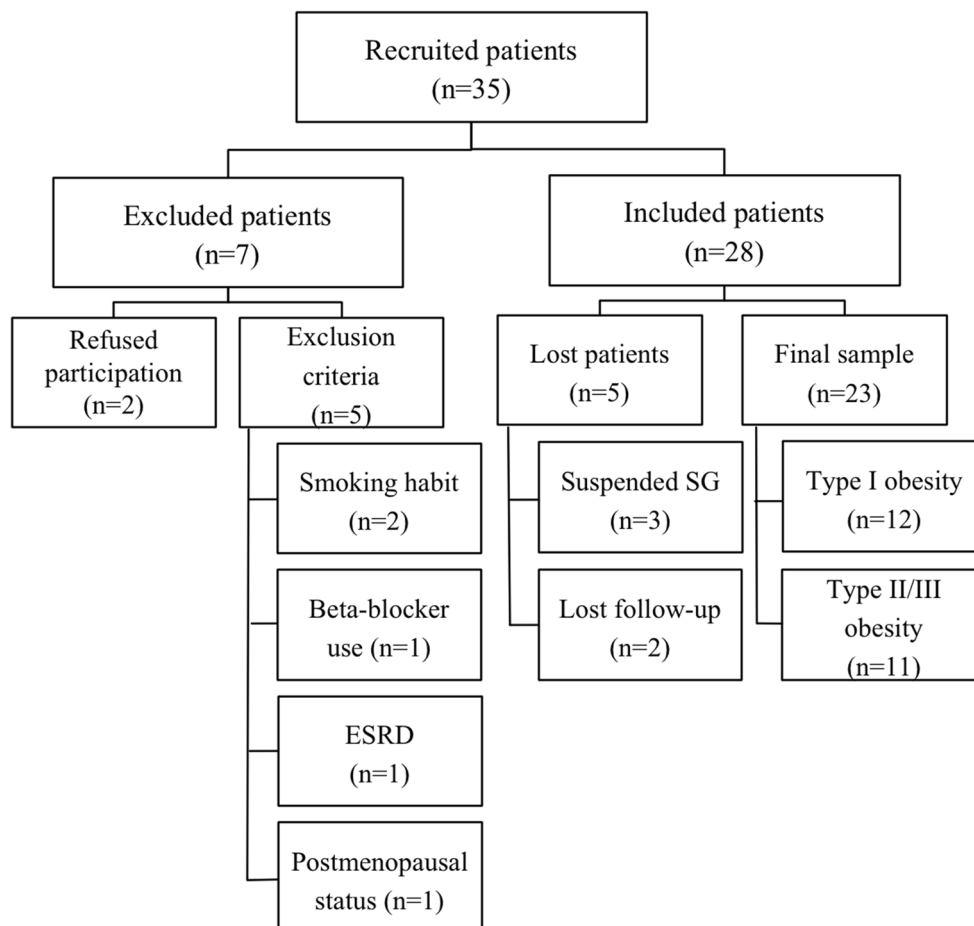
Nonlinear parameters included from Poincaré plot were standard deviation 1 (SD1), which represents short-term variability, the major axis which represents standard deviation 2 (SD2), meaning long-term variability (compared with SD1), and the sample entropy, which measures the regularity and complexity of a time series [18, 25].

The ratio of change of the HRV variables was expressed as a percentage and was calculated by subtracting the pre-surgical value from the post-surgical data and dividing it by the pre-surgical values.

Surgical Technique

The surgical procedures were performed by three certified bariatric surgeons. All the patients underwent laparoscopic SG, as described previously [45], leaving an estimated stomach capacity of 120–150 ml.

Fig. 1 Flow diagram of patient recruitment. ESRD end-stage renal disease



Statistical Analysis

For data distribution, the Shapiro-Wilk normality test was used. All HRV values were expressed as medians [minimum–maximum] whereas the anthropometric values were expressed as means \pm standard deviation (SD). Differences in HRV over the three time points were analyzed using the Friedman test, with the Wilcoxon test being employed for pairwise comparison. To compare the anthropometric measurements over the three assessments, we used ANOVA with Bonferroni post hoc analysis. The Spearman test was applied for correlation analysis. Statistical analysis was performed using SPSS 21.0 software (SPSS Inc., Chicago, IL, U.S.). A *p* value of < 0.05 was considered statistically significant.

Results

Thirty-five women with an indication for SG were recruited; however, five of them were excluded and two patients did not consent to participate in the study. Of the 28 patients initially included, five were lost during the study (Fig. 1).

The study finally included 23 women (36.0 ± 11.1 years old; excess weight 26.0 ± 9.2 kg; BMI 35.1 ± 3.4 kg/m²), two of which did not participate in the 1-month postoperative evaluation. Regarding comorbidities, 2 of them had controlled arterial hypertension, 7 had controlled hypothyroidism, and 14 had non-alcoholic fatty liver disease.

There was a significant improvement in all the anthropometric measurements at both the first and the third month after surgery (Table 1). Regarding the HRV analysis, an improvement in all time domain variables was observed among the three assessments, SDNN ($p = 0.003$; Cohen's $d = 0.68$), RMSSD ($p = 0.006$; Cohen's $d = 0.87$), and pNN50 (Fig. 2) (Cohen's $d = 0.80$), with all the improvements being statistically significant from the first month post-surgery (Table 2). In the frequency domain analysis, there was an improvement in HF power from the preoperative to postoperative assessments (both in absolute and Ln values, $p = 0.015$; a Cohen's d for absolute HF power = 0.75), with a higher spectral power from the first month following SG (Table 2). On the other hand, the LF power showed a tendency to improve among the three assessment points ($p = 0.076$), with a significant change only between the preoperative assessment and the third month in absolute values ($p = 0.030$; Cohen's $d = 0.22$) and Ln values ($p = 0.007$; Cohen's $d = 0.58$) (Table 2). There were no significant changes in the LF/HF ratio ($p = 0.201$).

The nonlinear analysis showed an improvement in SD1 and SD2 (Fig. 3), and no changes in sample entropy ($p = 0.217$), with higher variability in the Poincaré plot from the first month in SD1 and SD2 (Table 2) (Cohen's d for SD1 = 0.87).

There was no relationship between the weight changes and HRV improvements observed in our patients.

Discussion

This study showed that SG is effective at inducing significant weight loss and improving HRV indices, beginning as soon as the first month after surgery.

Only three previous studies have reported the effect of SG on HRV [36, 46, 47]. The study by Casellini et al. (on 56 patients with SG) showed an improvement in the HRV time domain 6 months after bariatric surgery. Unfortunately, the authors did not include either a frequency domain analysis or a nonlinear HRV analysis [46].

The work of Kokkinos et al. (on 23 patients with SG) showed similar results to our study related to improved HF and LF power both 3 and 6 months after SG, with no changes in the LF/HF ratio. The authors did not include time domain or nonlinear analysis results. There was also no information regarding the gender distribution of the sample [36].

Finally, in the work by Wu et al. on a sample of 18 patients with SG (50% women), the authors found statistically significant HRV improvements 6 months after SG, both in terms of the time and frequency domain analyses, although these changes were not apparent 3 months after surgery. Moreover, they found no changes in the nonlinear analysis. The findings of Wu et al. clearly differ from our results and theirs is the only work that showed changes in the LF/HF ratio after SG [47].

The increase in the RMSSD and pNN50 following SG that we observed in our study, which is directly related to vagus nerve activity [19], indicates enhanced parasympathetic activity [48]. The spectral power in HF, which increased in our patients from the first month following SG, is a well-known marker of parasympathetic tone [19]. In contrast, the LF, which only increased 3 months after SG in our study, reflects both sympathetic and vagal influences [19]. Likewise, the improvement we observed in the Poincaré plot indexes, SD1 and SD2, has been described as a reliable indicator of better parasympathetic system functioning [17].

Moreover, the SDNN, which also increased from the first month post SG in our study, is negatively influenced by the sympathetic component of the autonomic nervous system [15, 19]. This might be due to the fact that, after bariatric surgery, there is a severe caloric restriction, mainly in the first months. It has been reported that these dietary changes produce a

Table 1 Anthropometric characteristics at baseline and during follow-up after SG

	Pre-surgery ($n = 23$)	1 month after surgery ($n = 21$)	3 months after surgery ($n = 23$)	p value
Height (m)	1.61 ± 0.06	-----	-----	-----
Weight (kg)	90.6 ± 10.7	$80.8 \pm 10.5^*$	$73.0 \pm 9.3^*$	< 0.001
EW (kg)	26.0 ± 9.2	$16.6 \pm 9.4^*$	$8.4 \pm 8.3^*$	< 0.001
%EWL	-----	39.7 ± 13.6	72.2 ± 21.9	$< 0.001^{\text{Y}}$
%TWL	-----	10.6 ± 2.4	19.2 ± 4.2	$< 0.001^{\text{Y}}$
BMI (kg/m ²)	35.1 ± 3.4	$31.5 \pm 3.6^*$	$28.3 \pm 3.2^*$	< 0.001
WC IC (cm)	109.0 ± 7.3	$102.6 \pm 7.2^*$	$94.6 \pm 8.2^*$	< 0.001

Data are presented as means \pm SD

SG sleeve gastrectomy, EW excess weight, %EWL percentage excess weight loss, %TWL percentage total weight loss, BMI body mass index, WC IC waist circumference at the level of the iliac crests

ANOVA p value. * $p < 0.001$ compared with preoperative values. ^Y T test p value

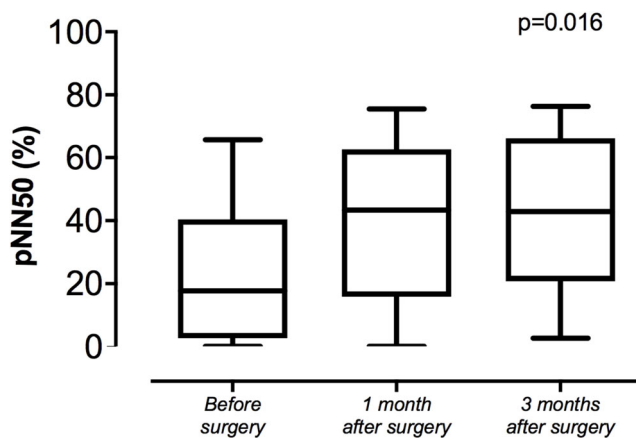


Fig. 2 Improvement in pNN50 after sleeve gastrectomy. pNN50 percentage of RR intervals with differences above 50 ms. Friedman p value

global reduction in sympathetic activity [49, 50] with implications regarding resting energy expenditure as an adaptive response to a caloric restriction [50, 51].

The improvement in parasympathetic tone following SG that we observed in our patients may be beneficial to their cardiovascular system, as previously reported [52–54], although it has not yet been established how much the vagal activity markers need to increase to provide protection for the heart.

Few studies have reported beneficial effects on cardiac function after SG. One study showed an improvement in systolic function and global longitudinal strain on the left ventricle that correlated with weight loss [55]. Also, after SG, a

reduction in the interventricular septum, the thickness of the posterior wall, and the mass of the left ventricle has been demonstrated [56].

A recent meta-analysis showed that SG has a greater effect on the parasympathetic tone than the gastric bypass procedure [57]. The SG surgical technique preserves the vagal trunk of the stomach's lesser curvature [57], and it has been suggested that the effects of bariatric surgery on the brain-gut axis could be influenced by the surgically induced anatomical alterations [12].

In our patients, we observed improved HRV in the time and frequency domains, as well as in the nonlinear analysis, with no additional intervention. In contrast, it has been previously reported that patients who have undergone a gastric bypass may only show improved HRV if there is a physical training program, with no change in those patients who only received the surgery [58]. This differs from the studies carried out by Bobbioni-Harsch et al., who found improvements in the time domain [59], and by Kokkinos et al., who reported improvements in the frequency domain. In both cases, there was no physical exercise training following surgery [36].

Our results suggest a recovery in cardiac autonomic function and a reversal of vagal impairment following weight loss [19]; this was demonstrated by the increase in SDNN, RMSSD, pNN50, HF, LF, SD1, and SD2, with a predominantly large or medium effect size. However, a difference in HRV between men and women has been described [60] so our results cannot be applied to the male bariatric population. It is also important to consider that age and initial BMI of our participants are lower than mean values previously reported

Table 2 HRV at baseline and during follow-up after SG

HRV variable		Pre-surgery ($n = 23$)	1 month after surgery ($n = 21$)	p value (a)	3 months after surgery ($n = 23$)	p value (b)
Time domain	Heart rate (bpm)	70 [57–85]	62 [51–89]	0.003	61 [49–91]	0.008
	SDNN (ms)	33.1 [8.7–96.2]	59.6 [13.3–128.4]	0.013	49.3 [22.2–125.9]	0.012
	RMSSD (ms)	38.4 [7.8–116.0]	76.7 [12.7–175.4]	0.006	58.7 [22.4–172.1]	0.002
	pNN50 (%)	17.7 [0.0–65.7]	43.4 [0.0–75.5]	0.006	42.9 [2.6–76.3]	0.004
Frequency domain	LF power (ms^2)	237 [38–3693]	425 [38–1980]	0.289	734 [96–2096]	0.030
	Ln LF power (ms^2)	5.46 [3.64–8.21]	6.05 [3.64–7.59]	0.131	6.60 [4.56–7.65]	0.007
	HF power (ms^2)	675 [30–6454]	1506 [95–14,559]	0.017	1241 [296–11,635]	0.010
	Ln HF power (ms^2)	6.51 [3.40–8.77]	7.32[4.55–9.59]	0.016	7.12 [5.69–9.36]	0.011
	Ratio LF/HF	0.39 [0.07–3.34]	0.34 [0.05–1.58]	0.122	0.55 [0.07–1.60]	0.648
Nonlinear analysis	SD1 (ms)	27.2 [5.5–82.2]	54.3 [9.0–124.2]	0.006	41.5 [15.8–121.9]	0.002
	SD2 (ms)	39.6 [11.0–108.4]	64.3 [16.6–132.4]	0.035	55.9 [25.9–130.1]	0.018
	Sample entropy (au)	1.61 [1.28–2.02]	1.52 [1.09–2.14]	0.848	1.68 [1.06–2.17]	0.121

Data are presented as medians [minimum–maximum]

SG sleeve gastrectomy, SDNN standard deviation of RR intervals duration, RMSSD root mean square of successive differences in RR intervals, pNN50 percentage of RR intervals with differences above 50 ms, LF low frequency, Ln natural logarithm, HF high frequency, SD standard deviation (from Poincaré plot), au arbitrary units

p value (a): comparison of HRV variation from pre-surgery to 1 month after surgery; p value (b): comparison of HRV variation from pre-surgery to 3 months after surgery

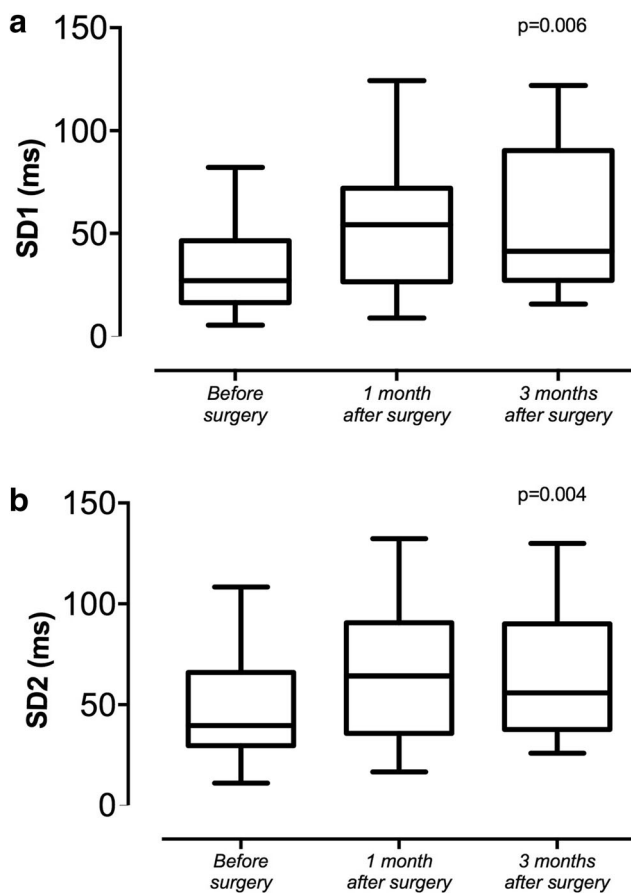


Fig. 3 Improvement in SD1 and SD2 after sleeve gastrectomy. SD1 standard deviation from 45° axis on Poincaré plot, SD2 standard deviation from 135° axis on Poincaré plot. Friedman *p* value

worldwide [31] and might have influenced these positive results.

As HRV is a predictor of cardiovascular disease and early mortality [24] and considering the physiological changes that SG induces on autonomic function, repeated measurements of HRV may provide the data necessary for evaluating cardiac risk and other post-surgical complications [61]. However, we suggest additional research involving larger cohorts (ideally with higher BMI and including older patients and male population), with at least a 12-month follow-up, to confirm our findings and assess the utility of including HRV assessment in the routine practice of bariatric patients.

We should acknowledge that the main limitation of this study is its inability to determine whether weight loss and HRV improvements will be permanent due to the short-term nature of the follow-up. In addition, had we included a control group made up of obese patients who had not undergone surgery, or diet-induced weight loss patients, it would have enabled us to compare the results. Regarding the study's main strength, we would like to point out that, so far, this is the most comprehensive HRV analysis conducted on a sample of women who have undergone exclusively SG.

Compliance with Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (registered number 149-2014) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of Interest The authors declare that they have no competing interests.

Informed/Written Consent Informed consent was approved by the institutional research ethics committee and was obtained from all individual participants included in the study.

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