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Impact of bariatric surgery–induced weight loss on heart rate variability

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Abstract

Obesity is associated with an increased risk of sudden death that may be due to abnormal cardiac vagal modulation reflected by reduced heart rate variability (HRV). Few studies have been conducted analyzing the effect of bariatric surgery–induced weight loss on HRV assessed by 24-hour Holter monitoring. The aim of this study was to assess weight loss effect after bariatric surgery on HRV and ventricular size and function. Ten morbidly obese patients, 6 women and 4 men aged 24 to 47 years, underwent bariatric surgery. Seven morbidly obese patients without active obesity treatment were used as controls. Twenty-four–hour Holter monitoring and echocardiogram were obtained before and at 6 to 12 months after surgery or at follow-up in control patients. Changes in minimal, maximal, and mean heart rate along with HRV during daytime and nighttime were compared before and after surgery. Baseline characteristics in the control group did not differ significantly from the treatment group. Average weight in the treatment group was 141 ± 31 kg (mean ± SD) at baseline and decreased to 101 ± 18 kg at follow-up, corresponding to a body mass index of 52.3 ± 7.6 kg/m^2 at baseline and 37.7 ± 5.3 kg/m^2 at follow-up. There was a decrease in minimal heart rate (48 ± 10 vs 40 ± 6 beats per minute, $P = .021$) and mean heart rate (82 ± 7 vs 66 ± 10 beats per minute, $P < .001$) during the Holter monitoring. Spectral analysis showed a significant enhancement in HRV parameters (high- and low-frequency power) because there was an increase in the standard deviation of normal to normal R-R intervals (116 ± 25 vs 174 ± 56 milliseconds, $P < .001$), the standard deviation of the mean R-R intervals calculated over a 5-minute period (104 ± 25 vs 148 ± 45 milliseconds, $P < .001$), the square root of the mean of the squared differences between adjacent normal R-R intervals (25 ± 8 vs 50 ± 20 milliseconds, $P < .001$), and the percentage of differences between adjacent normal R-R intervals exceeding 50 milliseconds (5% ± 5% vs 22% ± 13%, $P < .001$). Echocardiographic measures remained unchanged when comparing the groups. Weight loss after bariatric surgery enhances HRV and decreases mean and minimal heart rate during Holter monitoring through a better cardiac parasympathetic modulation.

1. Introduction

In a search for a better assessment of risk factors of cardiovascular (CV) mortality, several studies have reported altered heart rate variability (HRV) to be an independent risk factor of cardiac death after myocardial infarction [1,2] or in patients with conventional CV risk factors [3]. Hence, lower HRV in different clinical settings (obesity, after myocardial infarction, population studies) revealed itself as a risk marker for total mortality, sudden death, and CV death [1,3-5]. Lower HRV is also a risk marker for ventricular arrhythmias [6,7].

Heart rate variability refers to the variation in intervals between heartbeats and reflects cardiac autonomic modulation, which is influenced in a favorable way by increased parasympathetic activity [8]. As stated, in asymptomatic subjects, lesser HRV is associated with a greater incidence of cardiac events [9]. Obesity is independently associated with an increased risk of CV death [10,11], as it is also associated with sudden cardiac death [10,11]. Altered autonomic

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nervous system activity has been reported in patients with obesity [12-14]. Indeed, sympathetic overactivity has also been described in association with obesity [15,16]; and spectral analysis showed decreased HRV with weight gain [17-19].

Weight loss after diet or gastroplasty in morbidly obese patients has been shown to reverse the deleterious impacts of obesity on cardiac autonomic nervous system modulation, with subjects showing enhanced HRV after reduction in body mass index (BMI), through increased cardiac vagal modulation [20,21]. Biliopancreatic diversion with duodenal switch (BPD-DS) surgery may not only cause a more prominent weight loss than other surgeries; the malabsorption created by the anatomical modifications in the gastrointestinal tract by BPD-DS brings a unique metabolic state. To our knowledge, no study has reported the influence of BPD on HRV. On the other hand, obesity is associated with cardiomyopathy, with increased left ventricular wall stress, left ventricular hypertrophy, diastolic dysfunction that can evolve to left ventricular dilatation, and left ventricular systolic dysfunction [22]. Furthermore, it was reported that diastolic dysfunction is associated with altered HRV in subjects with uncomplicated diabetes [23].

The aim of this study was to assess the weight loss effect after BPD-DS surgery on HRV assessed with a 24-hour Holter monitoring. Secondly, echocardiographic study was performed on subjects before and after surgery to verify the presence of such a cardiomyopathy and to assess left ventricular size and function.

2. Materials and methods

Ten patients submitted for BPD-DS, 6 women and 4 men aged 24 to 47 years, were enrolled in the treatment arm of this study; and 7 morbidly obese patients without active obesity treatment were enrolled as controls. Inclusion criteria were patients with a BMI >40 kg/m^2 or > 35 kg/m^2 with comorbid conditions before bariatric surgery. Data were collected before and after bariatric surgery. The time elapsed between the 2 evaluations varied from 6 to 12 months (mean, 6.8 ± 1.8 months). Twenty-four–hour Holter monitoring was performed at baseline and after surgery. Heart rate variability was established throughout numerous indices [24]. Parameters from the time domain and from the spectral domain were calculated from the Holter monitoring. Subanalysis of daytime and nighttime recordings was performed, as well as analysis for the full recording period [19]. In the time domain, R-R interval, standard deviation of R-R interval (SDNN), standard deviation of the mean R-R calculated over a 5-minute period (SDANN), square root of the mean squared difference of successive R-R intervals (rMSSD), number of adjacent N-N differing by more than 50 milliseconds (NN50), and NN50 divided by total number of N-N intervals (pNN50) were analyzed. The rMSSD and pNN50 indices are associated with high-frequency power (HF) and hence parasympathetic activity. In the spectral domain, low-frequency power (LF; 0.04-0.15 Hz), which is an index of both sympathetic and parasympathetic activity, and HF (0.15-0.4 Hz), representing the most efferent vagal (parasympathetic) activity to the sinus node, were analyzed. The LF/HF ratio, representing the sympathovagal balance, was also calculated [20].

All patients had an echocardiogram performed before and after surgery. Left ventricular mass, volume, and parietal thickness as well as ejection fraction (EF) and diastolic function were assessed. Biochemical analysis was performed post hoc on blood drawn before and after surgery, which was stored at −80°C. Fasting plasma glucose concentration, insulin levels, serum total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were analyzed. Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula. Insulin sensitivity was calculated using the homeostasis model assessment (HOMA) [25].

The bariatric procedure can be described as a combination of a restrictive procedure (gastric volume reduction) and a malabsorptive procedure (duodenal switch). The gastric volume is reduced by ablation of a portion of the gastric wall along the greater curvature to create a gastric tube along the lesser curvature, commonly referred to as a *sleeve gastrectomy*. The duodenal switch diverts the flow of nutrients to the last 250 cm of the ileum through a duodenoileal anastomosis placed proximal to the Vater ampulla. The biliopancreatic secretions from the Vater ampulla are transported along the jejunum to meet the nutrients at an anastomosis created 100 cm from the ileocecal valve on the alimentary limb. Weight loss ensues over time to reach maximal effect at 18 months after operation [22].

3. Statistical analysis

Parameters were compared in both groups using a Student paired t test. Data are expressed as mean ± SD unless specified otherwise. A 2-way analysis of variance was used to compare the impact of surgery. P value < .05 was considered statistically significant. The spectral domain data from the Holter monitoring have been log-transformed to allow normal distribution.

4. Results

Ten patients with a baseline weight of 141 ± 30 kg and a BMI of 52.3 ± 7.6 kg/m^2 were included in the study (Table 1). Two had diabetes. Seven obese patients without any intervention were analyzed as controls. Baseline characteristics were similar between the control and treatment groups, and no significant changes were noted in the control group between the initial and follow-up data. Weight loss after surgery was on average 40 kg (P < .001), a relative reduction of 28.3%, corresponding to a difference in BMI of

Table 1
Patient and control characteristics at baseline and after follow-up

	Treatment		Control	
	Pre (n = 10)	Post (n = 10)	Pre (n = 7)	Post (n = 7)
Age (y)	37.7 ± 8.5		44.7 ± 10.8	
Weight (kg)	141 ± 31	101 ±18***	151± 42	150 ± 42
BMI (kg/m^2)	52.3 ± 7.6	37.7 ± 5.3***	54.3 ± 10.9	54.0 ±10.5
Heart rate (beats/min)				
Minimal	48 ± 10	40 ± 6*	44 ± 12	47 ± 12
Maximal	132 ± 15	126 ± 19	129 ± 19	115 ± 16
Mean	82 ± 7	66 ± 10***	79 ± 10	76 ± 12
Total cholesterol (mmol/L)	5.1 ± 0.8	3.4 ± 0.6***	5.3 ± 0.8	5.0 ± 0.7
HDL (mmol/L)	1.1 ± 0.2	0.9 ± 0.2***	1.2 ± 0.2	1.2 ± 0.2
LDL (mmol/L)	3.0 ± 1.0	1.9 ± 0.6***	3.1 ± 0.7	2.9 ± 0.7
Triglycerides (mmol/L)	2.1 ± 0.7	1.4 ± 0.8***	2.0 ± 0.4	2.2 ± 0.9
Total cholesterol–HDL ratio	4.7 ± 1.2	4.0 ± 1.2	4.4 ± 0.5	4.4 ± 0.6
Apo A-I (g/L)	1.5 ± 0.3	1.2 ± 0.2***	NA	NA
Apo B (g/L)	1.0 ± 0.2	0.7 ± 0.2***	NA	NA
Glucose (mmol/L)	6.6 ± 1.7	4.9 ± 0.3**	7.9 ± 2.1	7.7 ± 2.2
Insulin (pmol/L)	156 ± 64	45 ± 32***	NA	NA
HOMA [25]	44.8 ± 24.8	9.6 ± 6.5***	NA	NA

Data are means ± SD. NA indicates not applicable.
* $P < .05$ vs pre.
** $P < .01$ vs pre.
*** $P < .001$ vs pre.

15 kg/m^2. Mean heart rate and minimal heart rate decreased, whereas maximal heart rate did not change significantly compared with baseline ($P = .209$). The number of premature ventricular or supraventricular complexes was not influenced by weight loss. Total cholesterol, LDL cholesterol, and HDL cholesterol were significantly reduced by weight loss, as was blood glucose and insulin levels (Table 1). Total cholesterol was reduced by 34%, LDL cholesterol by 37%, apolipoprotein (apo) B by 32%, triglycerides by 35%, fasting glucose by 25%, and fasting insulin by 71%. The ratio of total cholesterol to HDL cholesterol did not change significantly. In the control group, the total cholesterol was significantly lower after follow-up. All other analyzed biochemical values remained unchanged. The HOMA score, assessing insulin resistance, was decreased by 78% after weight loss. Significant relations were observed between changes in lipid profile and HRV. More specifically, correlations were found between delta rMSSD daytime, SDNN daytime, and cholesterol (rMSSD, $r = -0.64$; SDNN, $r = -0.69$; all Ps < .05); delta rMSSD daytime, SDNN daytime, and LDL (rMSSD, $r = -0.67$; SDNN, $r = -0.73$; all Ps < .05); and SDNN 24 hours and triglycerides ($r = 0.65$, $P < .05$). However, there was no significant correlation between HRV parameters and HOMA. The 2 diabetic patients at study entry were no longer diabetic. Charts were reviewed; and none of the patients took insulin, oral glucose-controlling agents, or lipid-lowering drugs at the control postoperative blood draw.

5. Heart rate variability

5.1. Time domain

Increments in all measures of the time domain of the Holter monitoring, SDNN, SDANN, rMSSD, and pNN50 were encountered after weight loss (Table 2). The difference reached statistical significance in all measures but nighttime SDANN. Enhancement in HRV parameters was more pronounced during daytime in comparison with nighttime (increase in SDNN of 85% vs 39%, in SDANN of 79% vs 22%, in rMSSD of 153% vs 88%, and in pNN50 of 750% vs 192%, respectively); but the changes were statistically significant for both the daytime and nighttime data ($P <$ .01), except for SDANN at night. No difference was found in the control group.

5.2. Spectral domain

Table 3 shows spectral domain indices of the Holter monitoring. Low- and high-frequency power increased significantly after weight loss ($P < .001$). However, the LF/HF ratio did not change because both high- and low-frequency signals were increased in the same proportion. As with time domain data, enhancement in HRV was more prominent during daytime. Statistically significant enhancement in HRV occurred with weight loss, and the difference was maintained even when men and women were divided and after exclusion of the diabetic patients (data not shown).

6. Echocardiography

Echocardiographic variables are depicted in Table 4. After weight loss, left ventricular diameter in diastole

Table 2
Heart rate variability indices in the time domain in the treatment and control groups

	Treatment (n = 10)		Control (n = 7)	
	Pre	Post	Pre	Post
24 h				
SDNN	116 ± 25	174 ± 56***	117 ± 40	114 ± 32
SDANN	104 ± 25	148 ± 45***	101 ± 48	98 ± 39
rMSSD	25 ± 8	50 ± 20***	32 ± 17	32 ± 19
pNN50	5 ± 5	22 ± 13***	10 ± 13	11 ± 13
Daytime				
SDNN	82 ± 16	152 ± 71**	82 ± 39	96 ± 30
SDANN	72 ± 15	129 ± 59**	67 ± 31	78 ± 28
rMSSD	17 ± 5	43 ± 23**	26 ± 23	31 ± 23
pNN50	2 ± 2	17 ± 15**	8 ± 17	11 ± 17
Nighttime				
SDNN	92 ± 30	128 ± 39**	108 ± 54	96 ± 34
SDANN	65 ± 24	79 ± 26	67 ± 52	70 ± 37
rMSSD	33 ± 12	62 ± 22***	40 ± 19	30 ± 12
pNN50	12 ± 9	35 ± 17***	16 ± 14	10 ± 11

Data are mean ± SD.
* $P < .05$ vs pre.
** $P < .01$ vs pre.
*** $P < .001$ vs pre.

Table 3
Heart rate variability indices in the frequency domain

	Treatment (n = 10)		Control (n = 7)	
	Pre	Post	Pre	Post
24 h				
Ln LF (ms^2)	5.81 ± 0.83	6.95 ± 0.69***	6.17 ± 0.69	6.18 ± 0.46
Ln HF (ms^2)	4.60 ± 0.71	5.91 ± 0.88***	4.90 ± 1.00	5.04 ± 0.76
LF/HF	1.21 ± 0.55	1.04 ± 0.47	1.27 ± 0.62	1.14 ± 0.64
Daytime				
Ln LF (ms^2)	5.16 ± 0.72	6.70 ± 0.91***	5.30 ± 1.06	5.94 ± 0.66
Ln HF (ms^2)	3.78 ± 0.74	5.59 ± 1.08***	4.10 ± 1.40	4.86 ± 1.13
LF/HF	1.35 ± 0.48	1.11 ± 0.53	1.19 ± 0.71	1.08 ± 0.78
Nighttime				
Ln LF (ms^2)	6.37 ± 1.13	7.26 ± 0.59**	6.80 ± 0.94	6.11 ± 0.87
Ln HF (ms^2)	5.36 ± 0.83	6.38 ± 0.85**	5.53 ± 1.13	5.04 ± 0.63
LF/HF	1.00 ± 0.73	0.87 ± 0.54	1.28 ± 0.72	1.08 ± 0.70

Data are mean ± SD. LF and HF data are log-transformed.
** $P < .01$ vs pre.
*** $P < .001$ vs pre.

increased from 50 ± 5 to 53 ± 4 mm ($P = .002$); and septal as well as posterior thickness decreased significantly ($P < .01$). No change was noted in left ventricular diameter in systole, left atrial diameter, aortic diameter, right ventricular diameter in diastole, EF, and ejection volume. Calculated left ventricular mass decreased 16 ± 26 g without reaching statistical significance ($P = .084$). Diastolic dysfunction was present in one patient before and in 2 patients after weight loss. No difference was seen in A and E waves, as well as in S and D waves (data not shown). Isovolumetric relaxation time also remained unchanged. All echocardiographic parameters remained unchanged in the control group.

7. Discussion

The principal findings of this study confirm our hypothesis, demonstrating an increase in HRV following weight loss after BPD. Higher HRV has been shown to be associated with increased survival in previous studies [1,3,9]. We found that the 28% weight loss achieved after bariatric surgery improved HRV expressed by SDNN, SDANN, rMSSD, pNN50, LF, and HF. The differences observed before and after weight reduction remained significant even if the analysis was performed separately for men and women. The best improvement in HRV was observed during the daytime period. However, the overall HRV enhancement was not only driven by this period because the nighttime period analysis also demonstrated statistically significant enhancement in HRV parameters. Moreover, HRV parameters measured initially were abnormally low; and weight loss not only increased but normalized HRV parameters [20,24]. This suggests that normalization of HRV can occur with weight loss even if normalization of body weight does not occur because patients at the time of study were still considered obese after surgery (BMI, 37.7 ± 5.3 kg/m^2). On the basis that mortality and sudden death rates are higher than expected in cohorts of obese subjects [10,11,26] and that lower HRV is a risk factor for mortality, sudden death, and arrhythmia, we can postulate that the normalization of HRV observed in our study could lower patient's CV risk.

Others have reported similar findings with diet-induced weight loss and weight-reducing gastroplasty showing improvement in autonomic cardiac modulation [20,21]. However, the bariatric procedure performed herein may interfere differently from a metabolic standpoint. It may not only cause a more prominent weight loss than other surgeries, but the malabsorption created and the associated vitamin supplements make BPD-DS a unique metabolic state. Weight loss through starvation, liquid protein diets, very low calorie diets, or even obesity surgery can be associated with prolongation of the corrected QT interval, which may induce ventricular arrhythmias. To some extent, it is irrespective of the biological value of the constituent protein or the addition of mineral and trace supplements [22]. Therefore, it seems to us that extrapolating data obtained from other weight-reducing strategies and applying them to our cohort of subjects could be inappropriate because of the many differences in techniques and in the resulting nutrient absorption.

The absence of improvement in echocardiographic parameters may be explained by the short time duration of our study, as structural modification of the heart is a mid- to long-term adaptation and may not be measured after a few months, except if the underlying condition is extreme. Although not statistically significant, left ventricular mass decreased after weight loss. Controls had comparable parameters except for the EF, which was significantly lower in comparison with the treatment group. Of note,

Table 4
Echocardiographic characteristics of subjects in the control and treatment groups

	Treatment (n = 10)		Control (n = 7)	
	Pre	Post	Pre	Post
LV mass (g)	207 ± 59	191 ± 55	232 ± 91	244 ± 69
LV end diastole (mm)	50 ± 5	53 ± 4***	56 ± 8	56 ± 11
LV end systole (mm)	31 ± 4	32 ± 7	37 ± 10	39 ± 11
Septal thickness (mm)	12 ± 2	10 ± 2**	10 ± 1	12 ± 2
Posterior thickness (mm)	10 ± 1	9 ± 1***	10 ± 2	10 ± 1
Left atrium (mm)	39 ± 5	40 ± 4	42 ± 5	42 ± 4
EF (%)	64.7 ± 3.6	65.6 ± 8.3	54 ± 10	55 ± 13
E/A	1.36 ± 0.2	1.49 ± 0.3	1.49 ± 0.50	1.45 ± 0.49
E/A Valsalva	1.36 ± 0.2	1.44 ± 0.4	1.14 ± 0.42	1.16 ± 0.45
Isovolumetric relaxation time (s)	0.08 ± 0.01	0.08 ± 0.01	0.08 ± 0.02	0.08 ± 0.01

Mean ± SD. LV indicates left ventricle.
* $P < .05$ vs pre.
** $P < .01$ vs pre.
*** $P < .001$ vs pre.

both groups had mean EF within the normal limits. Beneficial improvements in biochemistry parameters were observed after weight loss. Total cholesterol, LDL cholesterol, apo B, and HDL cholesterol as well as triglycerides were all greatly reduced, without the use of medication. Part of these changes can be attributed to malabsorption induced by the surgery, but weight loss alone has a beneficial effect on lipid profile. Because BPD leads to weight loss largely because of malabsorption, the effects on lipid profile of this surgery could have been different from the effect of other weight loss strategies, although other studies using gastric bypass or gastric banding have reported similar results [27,28]. The net clinical impact of these changes on lipid profile is yet to be measured in a long-term cardiac event study. High-density lipoprotein was lowered after BPD-DS surgery in our cohort of patients. Total cholesterol and LDL cholesterol were also lowered significantly, but the ratio of total cholesterol to HDL was lowered in a nonsignificant way. In numerous studies, the ratio of total cholesterol to HDL was the best predictor of CV disease; hence, the diminution in HDL cholesterol seen in our study can be expected to have minimal effects on CV risk considering the fact that the ratio of total cholesterol to HDL is similar and shows a trend toward diminution after surgery. The concomitant reduction in HDL cholesterol and hence the absence of changes in the ratio of total cholesterol to HDL, a parameter that has been shown in the past to be associated with CV disease, may however mitigate the beneficial impact of LDL reduction over the long term [29-31]. The significant relations observed between surgery-induced lowering in cholesterol, triglycerides, LDL, and HRV parameters suggest that lipid profile positive changes possibly contribute to improvement in HRV parameters through a better vascular compliance.

Glucose metabolism was improved, with a 3-fold diminution in fasting insulin and normalization of fasting glucose levels. The greater magnitude of change occurring with insulin levels compared with glucose reflects a reduction in insulin resistance. The HOMA was also significantly reduced, providing further support for a lower insulin resistance state after weight loss. Hyperinsulinemia has been shown to favor sympathetic dominance over vagal tone in measurements of cardiac autonomic regulation [19]. The results of our study show a significant diminution in fasting insulin concentrations. The overall improvement in HRV seen after surgery and weight loss was not found to be attributable to the lowering of the insulin levels. Moreover, we did not observe any significant correlations between changes in HOMA and HRV parameters. These findings may be related to the fact that our study included subjects with type 2 diabetes mellitus, where insulin levels could be modulated at the same time by medication and/or insulin resistance state.

Inclusion of subjects with diabetes could have induced a bias because diabetes is indeed associated with cardiac dysautonomy [23]. However, statistical analysis has been performed with and without inclusion of the 2 diabetic patients: all measured HRV parameters showing significant improvement remained significantly improved after surgery whether diabetic subjects were included or not. The ratio of low frequency to high frequency was not improved in a statistically significant way whether subjects with diabetes were or were not part of the analysis. Although one may be very cautious following a statistical analysis that included a small number of subjects, we do not think that our conclusion that weight loss after bariatric surgery improves HRV is influenced by inclusion of the subjects with diabetes. The small number of subjects and the short period over which data were collected prevent us from having any mortality data. Moreover, if bariatric surgery would be proven to improve survival, it would be difficult to assess the relative contribution of reduction in HRV in contrast with the lowering of blood pressure, the improvement of glucose metabolism, and other physiologic effects of weight loss. To obtain such data, longer studies with more patients would be necessary.

8. Conclusion

These results suggest that weight loss after BPD-DS improves HRV and hence cardiac autonomic modulation.

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