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Short title: Sympathetic activity after bariatric surgery

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Source of support: Allergan Inc. provided unrestricted research support for the study. This organization played no role in the design, analysis or interpretation of data described here, nor in the preparation, review, or approval of the manuscript.

Disclosure: EAL, TR, NE, NES and GAH have nothing to declare. JBD receives competitive research grant funding from Allergan Inc. He is a consultant for Allergan Inc, Bariatric Advantage, and Scientific Intake, and is a member of the Optifast® Medical Advisory Board for Nestle Health, Australia. He is on the speakers bureaus for Eli Lilly and iNova Pharmaceuticals, has developed educational material for Novartis and iNova Pharmaceuticals and received travel assistance from GI Dynamics for an educational meeting. MPS serves on scientific advisory boards for Abbott Pharmaceuticals, Novartis Pharmaceuticals and Medtronic and has received research support and
travel support, lecture fees and honoraria from Abbott, Novartis, Servier, Boehringer Ingleheim and Medtronic. GWL has acted as a consultant for Medtronic and has received honoraria from Medtronic, Pfizer and Wyeth Pharmaceuticals for presentations. The laboratories of JBD, GWL and MPS currently receive research funding from Medtronic, Abbott and Servier Australia. These organizations played no role in the design, analysis or interpretation of data described here, nor in the preparation, review, or approval of the manuscript.

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Word count: 4,532

Number of tables: 2

Number of figures: 2
Abstract

Objectives: Obesity is associated with elevated cardiovascular mortality which may be attributed, in part, to sympathetic nervous activation and an associated poor metabolic profile. Laparoscopic Adjustable Gastric Band (LAGB) surgery provides both short and long-term health-related beneficial effects. Methods: We sought to examine the effects of LAGB on sympathetic nervous system (SNS) activity, baroreflex function and cardiovascular profile following a predetermined weight loss of 10% in 23 severely obese non diabetic individuals. Results: The 10% weight loss was achieved at an average of 7.3±1.4 months (range 1.3 to 23.3 months). This was associated with significant improvement in office systolic and diastolic blood pressure (BP) (-12 mmHg and -5 mmHg respectively), a decrease in muscle SNA (33±3 to 22±3 bursts per minute), improvement in cardiac (16 ±3 to 31±4 ms.mmHg⁻¹) and sympathetic (-2.23±0.39 to -4.30±0.96 bursts/100 heartbeats.mmHg⁻¹) baroreflex function, total cholesterol (5.33±0.13 to 4.97±0.16 mmol/l), fasting insulin (29.3±2.4 to 19.6±1.1 mmol/l) and creatinine clearance (172±11 to 142±8 ml/min). None of the cardiovascular risk improvement related to the rate of weight loss. The change in systolic and diastolic BP correlated with change in waist circumference (r =0.46, p=0.04 and r=0.50, p=0.02 respectively). Conclusion: The initial 10% weight loss induced by LAGB was associated with substantial hemodynamic, metabolic, SNS and renal function improvements that did not depend on the rate of weight loss. Changes in waist circumference appear to be an important factor contributing to BP adaptation following LAGB surgery.

Condensed abstract

We examined the effects of Laparoscopic Adjustable Gastric Band (LAGB) surgery on cardiovascular risk profile and autonomic function following a fixed initial 10% weight loss in 23 severely obese non diabetic individuals. The achievement of the weight loss varied from 1.3 to 23.3 months. This was associated with significant improvement in systolic and diastolic blood pressure, autonomic function (sympathetic nervous activity and baroreflex function), total cholesterol,
fasting insulin and creatinine clearance. The initial 10% weight loss induced by LAGB was associated with substantial hemodynamic, metabolic, SNS and renal function improvements independent on the rate of weight loss.

**Key words:** obesity, bariatric surgery, blood pressure, sympathetic nervous system, glomerular filtration

**Introduction**

Severe obesity is accompanied by increased mortality, medical morbidity, impaired quality of life and poor psychological well-being [1]. Type 2 diabetes, cardiovascular disease and many cancers dominate the morbidity, mortality and costs associated with obesity [2, 3]. The high prevalence of metabolic abnormalities including dyslipidemia, elevated blood pressure (BP), hyperinsulinemia and hyperglycemia are major issues contributing to increased cardiovascular (CV) risk associated with obesity.

It is well established that short and long-term weight reduction improves obesity-related cardiovascular risk factors, and in the severely obese reduces CV mortality [4, 5]. Current clinical guidelines emphasise the initial goal of weight loss therapy is to reduce body weight by approximately 10% from baseline [6]. Even when weight loss achieved is limited to 5-10% through diet and lifestyle interventions, marked improvements on BP [7] and all components of the metabolic profile [8] have been reported. Bariatric surgery is followed by a more pronounced and sustained weight reduction, with patients achieving 15 -30% weight loss at 20 years [5]. A recent systematic review of the data indicates that bariatric surgery leads to major reductions in CV risk factors with rates of remission or improvement for hypertension, diabetes and dyslipidemia being around 70% at a mean follow-up of 5 years [9]. Nevertheless, bariatric surgery has also been shown to have rapid beneficial effects as it improved metabolic and inflammatory parameters in high-risk obese patients who have lost about 20% of weight within 3 months [10].
While the exact mechanisms underlying improvement of CV risk are not completely understood, reduced abdominal fat mass and sympathetic nervous inhibition following weight loss may be crucial. Indeed, sympathetic nervous system (SNS) activation is strongly associated with abdominal visceral fat [11], and is evident even in individuals who are not hypertensive [12], and in those who are metabolically healthy [13]. Furthermore, we recently demonstrated that in young overweight individuals, SNS activity was directly related to the degree of cardiac, renal and vascular dysfunction [14], suggesting that sympathetic neural drive may be a major player in CV risk development. Life style intervention using calorie restriction with or without an exercise program have shown that the beneficial effects of moderate weight loss on CV risk are consistently accompanied by marked improvement in sympathetic neural drive [8, 15, 16].

Another factor that could contribute to improvement of CV risk is the rate of weight loss, as a pilot study recently suggested that slow weight loss may be more beneficial than rapid weight loss [17]. Studies investigating the effects of weight loss following bariatric surgery have mostly been conducted in patients who have lost substantial amount of weight (>20%); however, the effect of a more modest weight loss on markers of CV risk, such as the initial goal of 10% weight loss recommended by the clinical guidelines, has not been well investigated. Given that a moderate weight loss following life style changes is known to reduce SNS activity and improve CV risk, we hypothesized that severely obese patients reaching the initial goal of 10% weight loss following bariatric surgery would improve their CV risk profile and this may be associated with inhibition of the SNS activity, improvement of abdominal fat mass and the time required to achieve this initial goal.

Methods

Subjects

Twenty three severely obese patients (17 females, 6 males) with a BMI ranging from 36 to 51 kg/m² and aged from 19 to 53 years participated in the study. They were recruited at a medical
centre for bariatric surgery as eligible patients for laparoscopic gastric band (LAGB). For entry in the study, exclusion criteria included type 2 diabetes (fasting glucose ≥ 7 mmol/L or on drug treatment for elevated glucose), any medication for hypertension or for dyslipidaemia, a history of secondary hypertension, cardiovascular, cerebrovascular, renal, liver, thyroid or lung disease. The study protocol was approved by the Alfred Hospital Ethics Committee and all subjects gave written informed consent before participating in the study.

**Experimental protocol**

Participants were assessed at baseline (before surgery) and when they achieved approximately 10% weight loss. Participants were reviewed regularly, all had access to regular weighing and were well aware of their 10% testing weight target and were prioritized for study at this time. On both occasions, patients were studied in the morning following a 12-hour overnight fast. The studies were performed with the patients in the supine position.

One day prior to the study, all participants underwent ambulatory BP monitoring over 24-26 hours using an oscillometric monitor (Model No. 90207, SpaceLabs Medical Inc, WA, USA) to measure brachial BP every 30-minutes. BP values were averaged over the total period of the recording.

**Biochemistry**

Venous blood was drawn for the measurements of the metabolic variables including electrolytes, glucose, insulin and c-peptides. Patients provided a 24-h urine collection on the day of the test. Creatinine clearance was calculated using the following formula: $C_{Cr} = (U_{Cr} \times V)/P_{Cr}$ where $U_{Cr}$ is the creatinine concentration in urine, $V$ the urine flow rate and $P_{Cr}$ is the creatinine concentration in plasma. HOMA-IR (an index of insulin resistance) was calculated as $(FIC \times FGC)/22.5$ where FIC is fasting insulin concentration and FGC is fasting glucose concentration.

**Muscle Sympathetic Nerve Activity (MSNA) recordings**

Recordings of multi-unit postganglionic MSNA were made from a tungsten microelectrode (FHC,
Bowdoinham, ME, USA) inserted directly into the right peroneal nerve at the fibular head, as previously described (6). A subcutaneous reference electrode was positioned 2 to 3 cm away from the recording site. Standard criteria were used to ascertain a MSNA site [18]. The nerve signal was amplified (X50,000), filtered (bandpass, 700 to 2000Hz), and integrated. During MSNA recording, BP was measured continuously using the Finometer system (Finapress Medical System BV, Amsterdam, The Netherlands) and heart rate (HR) was extracted from 3-lead ECG. All of these parameters were digitized with a sampling frequency of 1000Hz (PowerLab recording system, model ML 785/8SP, ADI Instruments). Resting measurements were recorded over a 15-minute period and averaged. Sympathetic bursts were counted manually and expressed as burst frequency (bursts/min) and burst incidence (bursts/100 heart beats).

**Spontaneous cardiac baroreflex sensitivity**

Baroreflex sensitivity was assessed using the sequence method [19]. This technique identifies series of three or more heart beats in which systolic blood pressure increased and cardiac interval lengthened (type 1 sequence) or in which systolic blood pressure decreased and cardiac interval shortened (type 2 sequence). The slope of the regression line between cardiac interval and systolic blood pressure within the sequence was computed when \( r > 0.85 \) to give an estimate of spontaneous baroreflex sensitivity. Measurements were taken at rest and averaged over a 10 minute recording period.

**Spontaneous arterial baroreflex control of MSNA**

Over a 5 to 8 min resting period, diastolic blood pressures associated with individual heart beats were grouped in intervals of 2 mmHg and, for each interval, the percentage of diastoles associated with a sympathetic burst was plotted against the mean of the pressure interval. Muscle sympathetic bursts were advanced by 1.3 sec to compensate for baroreflex delay [20]. The sensitivity of the sympathetic baroreflex gain was defined as the slope of the regression line and was expressed as bursts per 100 heartbeats.mmHg\(^{-1}\).

**Statistics**
Results

Anthropometric and metabolic characteristics of the participants at baseline

Of the 23 patients who underwent surgery, three did not return for follow-up assessment, therefore only the 20 subjects (6 males, 14 females) who completed the study were included in the analysis. At entry in the study, participants were on average 40±2 years, 121.1±3 kg and had a BMI of 42.2±0.8 kg/m². Four patients were current smokers and seven were ex-smokers. Five patients were taking antidepressant medication and one an antipsychotic drug. According to the Adult Treatment Panel–III for the clinical criteria defining the metabolic syndrome [21] seven patients (35%) fulfilled the criteria and on average patients had 2.10±0.25 metabolic abnormalities. Seven patients (35%) were hypertensive (office systolic BP >135 or diastolic BP >85 mmHg), four (20%) had elevated fasting glucose (≥6.1 mmol/L), 6 (30%) had elevated triglycerides (>1.69 mmol/L) and 5 (25%) had low HDL-cholesterol (<1.04 mmol/L in men and <1.29 mmol/L in women). None of the patients had microalbuminuria (albumin > 30 mg/l). Seven-teen patients (85%) presented with glomerular hyperfiltration (creatinine clearance above 140 ml/min).

Anthropometry, metabolic and clinical variables

Patients achieved 10 % weight loss after 7.3±1.4 months; however, the time to achieve this weight loss ranged from 1.3 to 23.3 months.

Changes in the metabolic variables are summarised in table 1. Total cholesterol concentration was significantly reduced while HDL and LDL cholesterol, triglycerides and fasting glucose remained
unchanged following the 10% weight loss. Insulin decreased markedly from 29.3±2.3 to 19.6±1.2 mmol/L (P<0.001), HOMA-IR was reduced from 7.16±0.69 to 4.50±0.25 (P<0.001) and c-peptides decreased from 1.12±0.10 to 0.92±0.07 pmol/ml (P<0.01).

Changes in BP, HR and creatinine clearance are summarised in table 2. Supine SBP and 24-hour ambulatory SBP were significantly decreased (-12 mmHg, P = 0.005 for supine SBP and -5 mmHg, P=0.025 for 24-hour ambulatory SBP). Supine DBP decreased by 6 mmHg (P<0.01), however 24-hour supine DBP was not significantly reduced. Both supine HR and 24-hour ambulatory HR were reduced (-7 bpm, for supine HR and -8 bpm, for ambulatory P<0.05 for both) (table 1). Only two patients remained hypertensive (out of 7) following the weight loss.

For the entire cohort, creatinine clearance significantly decreased (172±11 to 142±8 ml/min, P=0.005). When considering only those patients who presented with glomerular hyperfiltration at baseline, creatinine clearance significantly decreased following the weight loss (from 184±10 to 145±8 ml/min, P=0.002). Nine subjects (45%) still presented with glomerular hyperfiltration after weight loss. The prevalence of glomerular hyperfiltration was significantly less following surgery (45 vs 85%, P=0.02).

**Sympathetic nervous system activity and baroreflex function**

Microneurographic recordings were successfully obtained in 16 patients before and after LABG. Following the 10% weight loss, the burst frequency decreased from 33±3 to 22±3 bursts per minute (-30%, P=0.004) and the burst rate from 49±4 to 36±3 bursts per 100 heartbeats (-21%, P=0.008) (figure 1). Cardiac and sympathetic baroreflex function were both significantly improved following 10% weight loss; the slope of the cardiac baroreflex increased from 16±3 to 31±4 ms.mmHg⁻¹ (P=0.019) and the slope of the sympathetic baroreflex function improved from -2.23±0.39 to -4.30±0.96 bursts / 100 heartbeats.mmHg⁻¹ (P=0.03).

**Association analysis**

None of the improvements in hemodynamic, metabolic and sympathetic and renal functions bore
an association with the time required to lose 10% weight loss.

When controlled for baseline BMI, age, gender and baseline waist, the change in office SBP and DBP at 10% weight loss were associated with the change in waist circumference ($r=0.46$, $P=0.042$ for SBP and $r=0.50$, $P=0.024$) (figure 2)

**Discussion**

In this study, we explored the clinical, hemodynamic, metabolic, and SNS activity changes associated with 10% weight loss following LABG in severely obese individuals. The key finding is that this initial 10% weight loss was associated with substantial decrease in SNS activity, marked improvement in the cardiac and sympathetic baroreflex function, a decrease in arterial BP, and an improvement in total cholesterol concentrations, insulin sensitivity and renal function. All the CV and metabolic improvements were observed regardless of the time required to achieve the 10% weight loss.

The SNS plays a major role in both cardiovascular and metabolic regulation, influencing glucose and lipid metabolism as well as energy expenditure. As sympathetic neural overdrive characterises the state of obesity [15], any disturbances in its function may play a major role in the CV and metabolic risk. Indeed, sympathetic activation has been shown to be closely associated with insulin sensitivity [8] and we previously reported that in obese patients with the metabolic syndrome baseline sympathetic drive was an important prognostic marker for calorie restriction weight loss outcome [22]. Our recent studies emphasised the potential deleterious effects of sympathetic activation in obesity as we documented that MSNA was associated with target organ damage as evidenced by the presence of cardiac, vascular and renal dysfunction in young overweight individuals [14]. This is the first study documenting the change in sympathetic nervous function following bariatric surgery. We observed that MSNA was markedly decreased (-30%) when patients achieve the initial weight loss target of 10%. In addition, the baroreceptor modulation of
heart rate and MSNA, that has been reported to be blunted in obesity, suggesting a baroreflex impairment as a possible cause of the obesity-related sympathetic activation [23], are also improved following the weight loss. These changes in autonomic function observed following LABG are similar to those observed after weight loss induced by a low calorie diet program in obese individuals [15] and in individuals with the metabolic syndrome [8]. Decreased SNS is likely to be associated with multiple humoral changes including improvement of insulin sensitivity [24], as indicated by a decrease in HOMA index, decreased plasma renin activity [25], leptin [26] as well as changes in gut hormones [27].

The study cohort included 7 hypertensive individuals, 5 of whom could be classified as normotensive following the surgery. While hypertensive individuals displayed the highest change in BP (-19.5 mmHg for clinic SBP), the change in BP in the normotensive subgroup was also highly significant (-6.4 mmHg for clinic SBP). Previous observations indicated that bariatric surgery improved BP in obese hypertensive subjects while normotensive subjects displayed small [28] or no BP changes [25]. While BP was only measured prior to and following the achievement of 10% weight loss, a previous study reported that similar reductions in clinic BP occurred as early as one week post laparoscopic Roux-en-Y gastric bypass surgery and were maintained for the 12 month follow-up, and that this early impact on BP occurred before any significant weight loss was achieved [29]. Whether such an early drop in BP also occurs in our participants undergoing LABG is uncertain. While reduction in sympathetic tone may likely induce a decrease in BP, diet-induced decrease in sympathetic activity as assessed by plasma noradrenaline concentrations has been shown to occur before any significant weight loss and BP reduction [30]. Furthermore the decrease in MSNA following the weight loss was similar in the normotensive (-29%) and hypertensive sub-groups (-33%). Improvement of central adiposity is also likely to play a role in the regulation of BP. The Olivetti Heart Study indicated that in middle-aged men, a central distribution of body fat as assessed by the waist circumference was associated with increased BP, independently of BMI and insulin resistance [31], and waist circumference was also found to be the only clinical index of
adiposity that is associated with 24-h and conventional BP independent of other adiposity indices in a community with a high prevalence of obesity [32]. Waist circumference is as such a recommended marker of abdominal fat content [6, 33]. The achievement of 10% WL was accompanied by changes in waist circumference ranging from 0 to -16 cm. Interestingly, the decrease in BP observed was largely driven by the changes in waist circumference supporting the view that loss of abdominal fat mass rather than the amount of total weight lost is the key factor in improving the BP. The association between abdominal fat and BP may involve hyperinsulinemia [34] and enhanced SNS activity [23]. However, the changes in waist circumference observed following LABG did not relate to the changes in MSNA, but tended to correlate with the improvement of insulin sensitivity as assessed by the HOMA index (R=0.446, P=0.055).

The achievement of 10% weight loss was accompanied by a significant improvement in plasma total cholesterol concentration and a trend for TG to improve. This resulted in 6 patients out of 13 to become free of hyperlipidemia. This data is in agreement with a previous study reporting that a moderate weight loss induced by LABG (about 10-20% of the initial body weight) was able to produce the maximal effect on lipid levels in patients with morbid obesity, despite the fact that as with our study, these patients remained obese. More pronounced degrees of weight reduction (>30%) did not add additional benefits to the lipid profile [35]. Our previous observation that females with dyslipidemia presented with higher sympathetic activation and worse endothelial function [36], and observations from a longitudinal study following LAGB therapy[37], support the view that improvement of the lipid profile is likely to confer improved CV risk.

Obesity is an important factor in the progression and perhaps the initiation of chronic kidney disease and activation of the SNS activity is likely to be a crucial factor mediating obesity-related renal injury. Glomerular hyperfiltration, which may be seen as a compensatory response to achieve sodium balance [38] is a common occurrence in obesity. Hyperfiltration may lead to a subsequent increase in urinary albumin excretion which over time progresses to microalbuminuria, proteinuria
and, in the worst case scenario, end-stage renal failure [39]. Obesity-associated glomerular hyperfiltration was shown to lead to increased postglomerular oncotic pressure and enhanced proximal tubular sodium reabsorption suggesting that glomerular hyperfiltration may play a role in the pathogenesis of hypertension in obesity [40]. The vast majority of our obese patients presented with glomerular hyperfiltration before undergoing LABG. The achievement of 10% weight loss was strongly associated with an improvement of hyperfiltration as creatinine clearance decreased by 12%. This is similar to previous studies indicating substantial improvement in glomerular filtration following gastroplasty [41] or gastric bypass [42-44]. However the improvement noted in these other studies was observed at a weight loss of more than 30%. Our study therefore indicates that bariatric surgery may have beneficial effects on renal function as early as when a weight loss of 10% is achieved. Improvement of glomerular filtration has been proposed to lead to the decrease in BP [41] and slow the evolution towards irreversible renal damage [42].

Another important finding of this study is that the time taken to lose this amount of weight did not dictate the extent of hemodynamic, metabolic and renal improvements. Only one small study has looked at the effect of rapid versus slow weight loss following a low calorie diet and found that a slower weight loss was associated with better improvement in the metabolic risk profile, in particular with regards to the triglycerides level and resting diastolic BP [17]. Our finding that the rate of the weight loss has no effect on the beneficial effects is in agreement with our previous study indicating that LABG produced, in association with weight loss, sustained improvements in lipid profile that are independent of the time or weight loss achievement [37].

This small observational study has important limitations. The relatively low number of participants allows for the detection of only large effect sizes to be detected. There are no independent controls with patients acting as their own controls.

In summary, LAGB induced 10% weight loss was associated with substantial hemodynamic, metabolic, SNS and renal function improvements. The initial 10% weight loss as recommended by the guidelines for the treatment of obesity are likely to confer beneficial CV effects that are not
dependent on the rate of weight loss. Changes in waist circumference seem to an important factor contributing to BP adaptation following LAGB surgery.

References

10. Shargorodsky M, Fleed A, Boaz M, Gavish D, Zimlichman R. The effect of a rapid weight loss induced by laparoscopic adjustable gastric banding on arterial stiffness, metabolic and


Table 1: Anthropometric and metabolic characteristics of the patients at baseline and after 10 percent weight loss (n=20)

<table>
<thead>
<tr>
<th></th>
<th>BASELINE</th>
<th>10% Weight Loss</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight, kg</strong></td>
<td>121.2±2.7</td>
<td>109.8±2.6</td>
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<tr>
<td><strong>BMI, kg/m²</strong></td>
<td>42.2±0.9</td>
<td>38.2±0.8</td>
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<tr>
<td><strong>Waist, cm</strong></td>
<td>121.4±2.7</td>
<td>113.9±2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hip, cm</strong></td>
<td>135.1±2.0</td>
<td>127.9±1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Total Cholesterol, mmol/l</strong></td>
<td>5.33±0.13</td>
<td>4.97±0.16</td>
<td>0.014</td>
</tr>
<tr>
<td><strong>Triglycerides, mmol/l</strong></td>
<td>1.62±0.17</td>
<td>1.35±0.15</td>
<td>0.050</td>
</tr>
<tr>
<td><strong>HDL cholesterol, mmol/l</strong></td>
<td>1.54±0.14</td>
<td>1.29±0.08</td>
<td>0.071</td>
</tr>
<tr>
<td><strong>LDL cholesterol, mmol/l</strong></td>
<td>3.10±0.17</td>
<td>3.06±0.14</td>
<td>0.330</td>
</tr>
<tr>
<td><strong>Fasting glucose, mmol/l</strong></td>
<td>5.38±0.25</td>
<td>5.21±0.11</td>
<td>0.271</td>
</tr>
<tr>
<td><strong>Fasting insulin, mmol/l</strong></td>
<td>29.3±2.4</td>
<td>19.6±1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>HOMA-IR</strong></td>
<td>7.16±0.69</td>
<td>4.50±0.25</td>
<td>&lt;0.001</td>
</tr>
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<td><strong>C-peptide</strong></td>
<td>1.12±0.10</td>
<td>0.92±0.07</td>
<td>0.005</td>
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<tr>
<td><strong>Number of metabolic abnormalities</strong></td>
<td>2.10±0.24</td>
<td>1.80±0.20</td>
<td>0.137</td>
</tr>
<tr>
<td><strong>Metabolic Syndrome prevalence</strong></td>
<td>7 (35%)</td>
<td>4 (20%)</td>
<td>0.479</td>
</tr>
<tr>
<td><strong>Prevalence of hyperlipidemia</strong></td>
<td>13 (65%)</td>
<td>7 (35%)</td>
<td>0.114</td>
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</table>

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate
Table 2: Blood pressure, heart rate and creatinine clearance of the patients at baseline and after 10 percent weight loss (n=20)

<table>
<thead>
<tr>
<th></th>
<th>BASELINE</th>
<th>10% Weight Loss</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine SBP, mmHg</td>
<td>125±3</td>
<td>113±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Supine DBP, mmHg</td>
<td>72±2</td>
<td>65±2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Supine HR, bpm</td>
<td>68±3</td>
<td>60±2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ambulatory SBP (24-hour), mmHg</td>
<td>120±2</td>
<td>115±2</td>
<td>0.025</td>
</tr>
<tr>
<td>Ambulatory DBP (24-hour), mmHg</td>
<td>69±2</td>
<td>67±1</td>
<td>0.211</td>
</tr>
<tr>
<td>Ambulatory HR (24-hour), bpm</td>
<td>81±2</td>
<td>74±2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prevalence of hypertension</td>
<td>7 (35%)</td>
<td>2 (10%)</td>
<td>0.127(Fisher)</td>
</tr>
<tr>
<td>Creatinine clearance, ml/min</td>
<td>172±11</td>
<td>142±8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prevalence of glomerular hyperfiltration</td>
<td>17 (85%)</td>
<td>9 (45%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate
Legends to the figures

**Figure 1**: Changes in muscle sympathetic nerve activity (MSNA) (expressed as bursts per minute: A, and bursts per 100 heartbeats, B), cardiac baroreflex (C) and sympathetic baroreflex (D) function following 10 % weight loss (WL). *:P<0.05, **:P<0.01

**Figure 2**: Relation between changes in systolic blood pressure (SBP) (left panel) and diastolic blood pressure (DBP) (right panel) before and after weight loss and changes between waist circumference. r=0.46, P=0.042 for SBP, r=0.50, P=0.024 for DBP
FIGURE 2

Waist change (cm) vs. Change in SBP (mmHg)

Waist change (cm) vs. Change in DBP (mmHg)