Effect of Drastic Weight Loss after Bariatric Surgery on Renal Parameters in Extremely Obese Patients: Long-Term Follow-Up

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Obesity is a health problem that is reaching epidemic proportions. Extreme obesity (body mass index [BMI] ≥40 kg/m²) is a type of obesity that usually does not respond to medical treatment, with surgery being the current treatment of choice. Extreme obesity is associated with cardiovascular disease, type 2 diabetes, dyslipidemia, and hypertension. Recently, obesity has been related with high rate of renal lesions, but renal function and renal parameters in extreme obesity scarcely are documented. The objective of this study was to evaluate the effect of weight loss after bariatric surgery (BS) on BP, renal parameters, and renal function in 61 extremely obese (EO) patients after 24 mo of follow-up. A total of 61 EO adults (37 women) were studied prospectively before and 24 mo after surgery. Control subjects were 24 healthy, normal-weight adults (15 women). Anthropometric, BP, and renal parameters were determined. Presurgery weight, BMI, GFR, 24-h proteinuria, and 24-h albuminuria were higher in the EO patients than in control subjects (P < 0.001). All parameters improved at 12 mo after BS. However, during the second year of follow-up, only 24-h albuminuria (P = 0.006) and BMI (P = 0.014) continued to improve. At 24 mo after BS, obesity-related renal alterations considerably improved. This improvement was observed mainly in the first year after surgery, when the majority of weight loss occurred. However, 24-h albuminuria still improves during the second year of follow-up. It is possible that this decrease in 24-h albuminuria is not GFR related but rather is attributable to the persistence of the decrease in BMI and to the improvement of other weight-related metabolic factors.

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studies at both 12 and 24 mo after BS were included in our study. The mean age was 41 ± 9.07 yr, and the mean BMI was 53.62 ± 9.65 kg/m² (range 40.32 to 93.98 kg/m²). The surgical technique performed was gastric bypass according to the method described by Fobi et al. (24) (in 27 patients) and Salmon (25) (in 34 patients). Both interventions combined a permanent restriction in the volume ingested (gastroplasty) with moderate to mild malabsorption. This study was approved by the ethics committee of our hospital, and all of our patients gave their informed consent to participate in the study.

Twenty-one (35%) patients were smokers, and three (5%) had cardiovascular disease (two who had angina and had a normal coronary catheterism study and one who had undergone aortic-coronary bypass). None of the patients selected was being treated with insulin, oral antidiabetic drugs, or lipid-lowering drugs. Twenty-two patients were receiving treatment for hypertension (five with ACEI, four with AngII type I receptor blockers, three with diuretics, one with β blockers, and nine with ACEI in combination with other drugs). Medications were withdrawn 8 d before the analyses were performed. All patients in the study had normal levels of serum creatinine (normal values in our laboratory 44 to 106 μmol/L), and none had a history of renal disease.

Twenty-four healthy, normal-weight adults (nine men and 15 women) were included as a control group (mean BMI 23.52 ± 2.59 kg/m²; mean age 42.54 ± 11.39 yr). Only baseline studies were available for the control subjects.

Preoperative and postoperative (at 12 and 24 mo after bariatric surgery) blood samples were drawn between 8:00 and 9:00 a.m. after a minimum of 8 h of fasting. A 24-h urine sample was collected from all patients. Plasma creatinine, urea, and urinary creatinine were determined using a routine clinical chemistry laboratory analyzer. Creatinine clearance was calculated as 24-h urine (ml) × urinary creatinine concentration × 1000/plasma creatinine concentration × 1440 min. Twenty-four-hour proteinuria was measured by a spectrophotometric method (Pyrogallol Red), and 24-h albuminuria was determined by a method (Pyrogallol Red), and 24-h albuminuria was determined by a method (Pyrogallol Red), and 24-h albuminuria was determined by a method (Pyrogallol Red), and 24-h albuminuria was determined by a method (Pyrogallol Red), and 24-h albuminuria was determined by microdialysis with a modified version of the method described by Freitas et al. (26). Proteinuria was defined as SBP ≥140 mmHg and DBP ≥90 mmHg in two different measurements. Glomerular hyperfiltration was considered when the creatinine clearance was >140 ml/min (26) and microhematuria when there were four or more red blood cells per high-power field in the urinary sediment, according to routine values of our laboratory.

Statistical Analyses

Data first were tested for normal distribution using the Kolmogorov-Smirnov test. Variables with normal distribution were expressed as mean ± SD. Nonparametric variables such as proteinuria and albuminuria were expressed as median (25th and 75th percentiles). The significance of differences between the control group and the obese patients was evaluated with unpaired t test or χ² test, as appropriate. Differences within the obese group before and after BS were evaluated with paired t test or the McNemar test, as appropriate. The t test was applied to the nonparametric data after log transformation.

All statistical analyses were made with the statistical software package SPSS (version 12.0; SPSS, Chicago, IL). Statistical significance was considered at P < 0.05.

Results

Study Population

Table 1 shows the general characteristics of the 61 EO patients compared with the 24 healthy normal-weight control subject, with no differences in the distribution for age or gender. Before undergoing BS, the EO patients presented with a statistically significant elevation in BP (both SBP and DBP) compared with the control group. Although there were no differences in urea and blood creatinine between the two groups, the EO patients had a greater creatinine clearance, 24-h proteinuria, and 24-h albuminuria and a greater percentage of microhematuria than in the control group.

Table 1. General characteristics of the EO patients and control group

<table>
<thead>
<tr>
<th></th>
<th>EO Group at Baseline</th>
<th>Control Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>61</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>24 (39.3%)/37 (60.7%)</td>
<td>9 (37.5%)/15 (62.5%)</td>
<td>NSb</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>41.10 ± 9.07</td>
<td>42.54 ± 11.39</td>
<td>NSc</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>150.55 ± 39.88</td>
<td>66.07 ± 11.05</td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>53.62 ± 9.65</td>
<td>23.52 ± 2.59</td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>137.69 ± 15.50</td>
<td>81.77 ± 10.35</td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>144.61 ± 17.28</td>
<td>112.67 ± 16.53</td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>85.28 ± 16.45</td>
<td>72.38 ± 10.61</td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>81.18 ± 11.60</td>
<td>83.15 ± 20.19</td>
<td>NSc</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>4.76 ± 1.16</td>
<td>5.34 ± 1.50</td>
<td>NSc</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min)</td>
<td>140.09 ± 40.96</td>
<td>104.56 ± 15.19</td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>Proteinuria (g/24 h)</td>
<td>0.08 (0.07 to 0.10)</td>
<td>0.08 (0.07 to 0.10)</td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>Albuminuria (mg/24 h)</td>
<td>14.20 (7.95 to 92.2)</td>
<td>6.45 (4.72 to 9.32)</td>
<td>&lt;0.001c</td>
</tr>
<tr>
<td>Microhematuria (yes/no)</td>
<td>26.2%/73.8%</td>
<td>8.3%/91.7%</td>
<td>&lt;0.05b</td>
</tr>
</tbody>
</table>

aBMI, body mass index; DBP, diastolic BP; EO, extremely obese; SBP, systolic BP; WC, waist circumference.

bχ² test.

cUnpaired t test.
Changes Observed 12 Mo after BS

In comparing the group of obese patients before and 12 mo after BS (Table 2), a mean weight loss of 56.3 kg and a mean decrease in BMI of 20 units was found. There also was a significant decrease in SBP and DBP. In regard to renal parameters, a decrease in creatinine clearance, 24-h proteinuria, 24-h albuminuria, and microhematuria is shown.

Changes Observed 24 Mo after BS

At 24 mo after surgery (Table 2), the patients continued to lose weight, although in a smaller proportion than during the first year (weight loss was 37% during the first year and 3% during the second). However, there were no significant differences in the decrease of SBP, DBP, creatinine clearance, 24-h proteinuria, and microhematuria before and 24 mo after BS. A significant decrease in all of the variables studied is shown after 2 yr of weight loss, with the exception of microhematuria, which showed a tendency toward decreasing but without reaching statistical significance ($P = 0.33$).

In comparing the group of EO patients at 24 mo of follow-up with the control group (Table 4), we found that there still were significant differences between the anthropometric parameters (weight, BMI, and waist circumference). SBP was significantly lower in the control group, whereas DBP did not show statistically significant differences between the two groups, although the postoperative EO patients continued to present higher 24-h albuminuria than the control group. Although EO patients showed a decrease in creatinine clearance at 24 mo after BS, it still was significantly lower in the control group.

Discussion

This study demonstrates that after BS, there is a significant improvement in the renal alterations that are associated with extreme obesity (glomerular hyperfiltration, proteinuria, high albuminuria, and microhematuria), as well as in the values of SBP and DBP. This improvement occurred mainly in the first year after surgery, because this is when the majority of weight loss takes place. Furthermore, we demonstrate for the first time that albuminuria continued to improve despite the discrete level of weight loss observed in the second year after BS.

Obesity is associated with glomerular hyperfiltration, which favors the occurrence of microalbuminuria and/or proteinuria in patients without known renal disease (7,27,28). Brochner et al. (20) demonstrated for the first time in the 1980s that GFR decreased in EO patients who had undergone intestinal bypass surgery. Only two studies support these results after 12 mo of follow-up (12,19), and there are no studies on GFR in patients who undergo BS and are followed over a longer period of time. In our study, an important percentage of EO patients had glomerular hyperfiltration before undergoing BS. This percentage decreased at 12 mo after BS in a similar way to patients in previous studies, including one from our group (12,19). However, this percentage of EO patients with high GFR did not improve significantly between 12 and 24 mo, even though there was a discrete weight loss during this time. That a few patients still had glomerular hyperfiltration at 24 mo after BS could be attributed to these patients’ still having type 1 obesity. The value of GFR was estimated using creatinine clearance as measured by 24-h urine sample, without correcting for body surface area, because the correction would underestimate considerably the real value of the GFR (29). For the same reason, we did not use other types of formulas to estimate the GFR (Cockcroft-

Table 2. Anthropometric, BP, and renal parameter changes in EO patients observed 12 and 24 mo after BS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EO Group (Baseline; $n = 61$)</th>
<th>$P$ (Baseline versus 12 mo)</th>
<th>EO Group (12 mo after BS; $n = 61$)</th>
<th>$P$ (12 versus 24 mo)</th>
<th>EO Group (24 mo after BS; $n = 61$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>150.55 ± 39.88</td>
<td>$&lt;0.001^b$</td>
<td>94.25 ± 18.68</td>
<td>0.011$^b$</td>
<td>91.74 ± 20.00</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>53.62 ± 9.65</td>
<td>$&lt;0.001^b$</td>
<td>33.66 ± 6.45</td>
<td>0.014$^b$</td>
<td>32.81 ± 7.19</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>137.69 ± 15.50</td>
<td>$&lt;0.001^b$</td>
<td>104.17 ± 14.07</td>
<td>NS$^b$</td>
<td>104.40 ± 15.54</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>144.61 ± 17.28</td>
<td>$&lt;0.001^b$</td>
<td>126.36 ± 18.66</td>
<td>NS$^b$</td>
<td>123.40 ± 18.78</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>85.28 ± 16.45</td>
<td>$&lt;0.001^b$</td>
<td>75.90 ± 12.77</td>
<td>NS$^b$</td>
<td>72.73 ± 10.69</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>81.18 ± 11.60</td>
<td>$&lt;0.001^b$</td>
<td>72.92 ± 12.72</td>
<td>NS$^b$</td>
<td>73.91 ± 11.37</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>4.76 ± 1.16</td>
<td>NS$^b$</td>
<td>4.92 ± 1.60</td>
<td>NS$^b$</td>
<td>5.04 ± 1.24</td>
</tr>
<tr>
<td>Creatinine clearance (ml/min)</td>
<td>139.51 ± 41.90</td>
<td>0.001$^b$</td>
<td>119.59 ± 44.24</td>
<td>NS$^b$</td>
<td>117.96 ± 33.99</td>
</tr>
<tr>
<td>Proteinuria (g/24 h)</td>
<td>0.14 (0.09 to 0.32)</td>
<td>$&lt;0.004^b$</td>
<td>0.11 (0.08 to 0.14)</td>
<td>NS$^b$</td>
<td>0.11 (0.07 to 0.13)</td>
</tr>
<tr>
<td>Albuminuria (mg/24 h)</td>
<td>14.20 (7.95 to 92.2)</td>
<td>$&lt;0.001^b$</td>
<td>13.00 (9.25 to 25.25)</td>
<td>0.006$^b$</td>
<td>12.55 (6.47 to 19.92)</td>
</tr>
<tr>
<td>Microhematuria (yes/no)</td>
<td>26.2%/73.8%</td>
<td>0.035$^c$</td>
<td>11.5%/88.5%</td>
<td>NS$^c$</td>
<td>16.4%/83.6%</td>
</tr>
</tbody>
</table>

$^a$BS, bariatric surgery.
$^b$Paired $t$ test.
$^c$McNemar test.
Gault and Modification of Diet in Renal Disease), because these formulas are designed for patients with chronic renal failure and, if applied to our study population, also would underestimate the real value of GFR (30,31).

Almost half of the EO patients in our study presented with albuminuria and/or proteinuria before undergoing BS. This improved significantly at 12 mo after BS, although it did not disappear completely, which confirms previously published reports by other authors (12,19). During the second year of follow-up, albuminuria continued to decrease even though GFR did not decrease. Other weight-related factors, such as improvement of lipid alterations and hyperinsulinemia or decrease in plasma leptin levels, may contribute to the persistence of this improvement (our unpublished observations, 2005).

This is the first study to demonstrate that EO patients present with a greater percentage of microhematuria compared with the control group and that these alterations in urinary sediment improve within 12 mo of drastic weight loss. To evaluate these results further, we would have had to carry out subsequent histologic studies, which are difficult to justify for ethical reasons.

Although the cause-and-effect relationship of glomerular hyperfiltration in obesity is not fully understood, we do know that in these patients, there is an increase in the tubular reabsorption of sodium in the loop of Henle. As such, the macula densa receives less salt, which leads to vasodilatation of the afferent arterioles and a subsequent increase in GFR (3). This retention of sodium could be the physiopathologic mechanism of the arterial hypertension that is associated with obesity. This study shows that drastic weight loss and the subsequent decrease in glomerular filtration leads to a decrease in SBP and DBP, as shown in previous studies (12,18,19,21). SBP and DBP did not decrease more between the first and the second years, probably because of the lack of change in the GFR.

**Conclusion**

After the drastic weight loss 24 months after BS, parameters of renal function and BP considerably improved, although a small percentage of patients still had glomerular hyperfiltration, proteinuria, and/or microalbuminuria, given that at 2 yr of follow-up the patients changed to type 1 obesity. The decrease in albuminuria that took place during the first year after

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**Table 3.** Percentage of EO patients with glomerular hyperfiltration, hypertension, high 24-h albuminuria, 24-h proteinuria, and microhematuria before and 24 mo after BS

| Parameter                        | EO Group (Baseline) | EO Group (24 mo after BS) | Decrease (%) | p  
|----------------------------------|---------------------|---------------------------|--------------|-----
| Glomerular hyperfiltration (%)   | 39.3                | 16.4                      | 58           | 0.04  
| High SBP (%)                    | 59                  | 19.7                      | 67           | <0.001  
| High DBP (%)                    | 49.2                | 11.5                      | 77           | 0.001  
| 24-h albuminuria (%) ≥30 mg/24 h| 42.6                | 14.8                      | 76           | <0.001  
| 24-h proteinuria (%) >0.15 g/24 h| 47.5                | 11.5                      | 65           | <0.001  
| Microhematuria (%)              | 26.2                | 16.4                      | 37           | NS    

*a *McNemar test.

**Table 4.** Anthropometric parameters, renal function, and BP values in EO patients 24 mo BS compared with the control group

| Parameter                | EO Group (24 mo after BS) | Control Group | P  
|--------------------------|---------------------------|---------------|-----
| n                         | 61                         | 24            |     
| Weight (kg)              | 94.25 ± 18.68             | 66.07 ± 11.05 | <0.001  
| BMI (kg/m²)              | 33.66 ± 6.45              | 23.52 ± 2.59  | <0.001  
| WC (cm)                  | 104.40 ± 15.54            | 81.77 ± 10.35 | <0.001  
| SBP (mmHg)               | 126.36 ± 18.66            | 112.67 ± 16.53| <0.002  
| DBP (mmHg)               | 75.90 ± 12.77             | 72.38 ± 10.61 | NS    
| Creatinine (µmol/L)      | 72.92 ± 12.72             | 83.15 ± 20.19 | 0.025  
| Urea (mmol/L)            | 4.92 ± 1.60               | 5.34 ± 1.50   | NS    
| Creatinine clearance (ml/min) | 119.59 ± 44.24           | 104.56 ± 15.19| 0.01  
| Proteinuria (g/24 h)     | 0.11 (0.08 to 0.14)       | 0.08 (0.07 to 0.10)| NS    
| Albuminuria (mg/24 h)    | 13.00 (9.25 to 25.25)     | 6.45 (4.72 to 9.32)| <0.001  
| Microhematuria (yes/no)  | 11.5%/88.5%              | 8.3%/91.7%    | NS    

*a Unpaired *t* test.

*b *χ² test.
BS could be attributed mainly to the drastic weight loss that took place during this time, whereas during the second year, other metabolic factors may have played a more important role. Only weight loss decreases GFR and stops the cascade of events that are caused by glomerular hyperfiltration, which could slow the evolution toward irreversible renal damage.

References