The longer-term effects of Roux-en-Y gastric bypass surgery on sodium excretion

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ABSTRACT

Background:
Obesity is an independent risk factor for hypertension and chronic kidney disease. During the first months after bariatric surgery, an improvement of sodium excretion has been described. The aim of this work was to study the influence of bariatric surgery on sodium excretion at more than a year after the intervention.

Methods:
Patients who have undergone Roux-en-Y gastric bypass (RYGB) and who had collected a 24-h urine sample before surgery more than 12 months ago were asked to participate. A second 24-h urine sample was collected. Blood pressure and weight were measured. The difference in sodium excretion before and after surgery was calculated, and the relationship with blood pressure and weight loss was investigated.

Results:
We included 33 patients; the median follow-up time was 21 months (range 14-41). Sodium excretion was high before surgery (median 195 mmol/day, IQR range 167-247) and decreased by 18% after surgery (median 160 mmol/day, IQR range 118-205, p= 0.015), while there were significant improvements in body weight (% EWL 80.9 ± 21.8), systolic blood pressure (126 to 120 mmHg, p=0.02), and diastolic blood pressure (84 to 77 mmHg, p=0.002), even with a reduced number of antihypertensive drugs.

Conclusions:
After RYGB and considerable weight loss, sodium excretion remains high in the longer term. The profound improvement in blood pressure cannot be explained by reductions in sodium excretion after RYGB.
INTRODUCTION

Obesity is a steadily growing problem as a global epidemic [1]. Obesity increases the prevalence of chronic kidney disease through renal damage associated with type-2 diabetes and hypertension [2]. However, obesity is also an independent risk factor for chronic kidney disease [3-6], and it is associated with an increased risk of microalbuminuria [7-11]. There appears to be a graded association between the severity of obesity and the magnitude of urinary albumin excretion (UAE), especially in the case of a higher salt intake [11,12]. Several studies have shown that metabolic syndrome enhances blood pressure response to sodium intake [2,9,13]. Reduction in sodium intake could be an especially important component in reducing cardiovascular risk factors in obese patients [2,14-17].

There is scarce information on the mean salt intake in the obese and about their eating patterns after weight loss, for example, after bariatric surgery [18,19]. The improvements in blood pressure have been attributed at least partially to reductions in salt intake [2,14-17,20]. Urinary sodium excretion is often used as a parameter for salt intake [21,22]. A significant decrease in sodium excretion has been described a few months after bariatric surgery. In the studies, a mean absolute difference of 80-90 mmol/day after 4-6 months was observed [18,19]. However, the longer-term effects of bariatric surgery on sodium excretion are unknown.

We hypothesized that in concert with the reduced food intake and weight loss, sodium intake will remain considerably lower than before surgery, also when weight has stabilized, as one of the contributors to improvements in blood pressure and albuminuria. Therefore, we set out a study in which we compared sodium excretion for more than a year after bariatric surgery to excretion before surgery. We evaluated whether changes in sodium excretion were related to weight loss and improvements in blood pressure.

MATERIALS AND METHODS

Study population
Patients who had laparoscopic Roux-en-Y gastric bypass (RYGB) surgery at the Slotervaart Hospital at least one year before the start of the study and who had collected a 24-h urine sample before surgery were eligible. Patients whose 24-h urinary samples before surgery were missing or incomplete were excluded. All eligible patients were contacted
by telephone to ask whether they would participate in the study. Approval for the study was obtained from the local ethical committee of Slotervaart Hospital (Amsterdam, the Netherlands) and the study was performed in accordance with the guidelines of the Declaration of Helsinki. All patients provided written informed consent.

**Data collection and measurements**

Patients were asked for one study visit at the outpatient clinic of our hospital for the registration of predefined items (gender, ethnicity, smoking status, alcohol intake, comorbidity, complications, current medication) and physical examination. Weight, height and blood pressure were measured. Blood pressure was measured using an automated Vital Signs Monitor, 300 series device (Welch Allyn Protocol Inc., Beaverton, Oregon USA). Five consecutive readings were taken at 3-min intervals, and the mean systolic and diastolic blood pressure values of the fourth and fifth measurement were recorded (in mmHg). Blood pressure cuff was chosen based on the circumference of the arm. Medical information before surgery was retrieved from the electronic patient files (24-h urine results, weight, blood pressure, smoking status, alcohol intake, comorbidity, medication). During the first visit, participants were asked to fill out the informed consent form and submit 24-h urinary sodium specimens after the visit on another day.

The variables gender, ethnicity, smoking, alcohol, frequency of dietary consultation, and sports were categorized. Comorbidity like diabetes and hypertension before surgery were registered. Type 2 diabetes was defined as an HbA1c >6.5% and/or being on antidiabetic drugs. Diabetes resolution was defined as the percentage of those with diabetes at baseline that had an HbA1c <6.5% and no use of antidiabetic drugs anymore after surgery. Hypertension was defined as a blood pressure of above 140/90 mmHg and/or being on antihypertensive drug. Medication after surgery was categorized as still using or stopped. Body mass index (BMI) was calculated as weight divided by the height squared (kg/m2). % Excess weight loss (EWL) was defined with the following formula: (weight before surgery-weight after surgery) / (weight before surgery – ideal weight) x 100%. Ideal weight was defined as a BMI of 25 kg/m2. Total weight loss (TWL) was defined as the percent difference between the weight before and after surgery. The frequency of dietetic consultation after surgery was noted. Urinary sodium and creatinine were determined by indirect potentiometry on a clinical chemistry analyzer (Synchron® LX20, Beckman Coulter Inc, Fullerton CA, USA), and urinary excretion of albumin was determined using rate nephelometry with a threshold of 1.9 mg/dL by Immage Immunochemistry System (Beckman Coulter Inc, Brea CA, USA).
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The 24-h urine sodium excretion and UAE values are shown in mmol/day. Microalbuminuria was defined as UAE of 20-300 mg/day. Creatinine clearance, as a measure of renal function, was calculated with the MDRD formula [23].

**Power considerations and statistical analysis**

First of all, the mean urinary sodium excretion before surgery of 200 patients was calculated for the sample size calculation for this study. Our hypothesis was that the sodium intake would be at least 20% lower at more than a year after bariatric surgery. To detect this difference, we needed at least 32 patients for the study to have enough power (80%). Initially, we intended to study patients undergoing different types of bariatric surgery. However, since 85 to 90% of the patients in our hospital undergo RYGB, and the type of surgery may influence salt intake, we decided to study RYGB only. The baseline characteristics of the patients were summarized using descriptive statistics. Data were first tested for normal distribution using the Kolmogorov-Smirnov and Shapiro and Wilk tests of normality. Data were expressed as mean and/or median with a range depending on the distribution. For the dependent variables, the Wilcoxon signed ranks test or paired t-test were used when applicable. Changes in the variables sodium excretion, UAE, weight, BMI, comorbidity, medication, blood pressure, pulse, and waist circumference were computed and shown as absolute and relative differences from the baseline. Correlations between variables were tested using univariate analyses (Pearson’s or Spearman’s correlations where appropriate). All tests were two-tailed and a p value <0.05 was considered as statistically significant. Statistical analyses were performed using SPSS software package (version 18.0).

**RESULTS**

**Population and surgery**

A total of 33 patients who had RYGB between December 2007 and December 2010 were included. A total of 93 patients were eligible for the study. There were 60 patients excluded because of incomplete urine samples (n=25) or not being willing to participate (n=35). Mean age at the time of surgery was 45.2 ± 8.5 years and 30 were female (91%). At baseline, hypertension was present in 15 patients (45%) and diabetes in 10 patients (30%). The mean weight of the patients before surgery was 126.2 ± 18.1 kg and the BMI 44.6 ± 5.4 kg/m2. The median follow-up time for the study population was 21 months (range 14-41 months). The characteristics of the whole study group are presented in table 1.
Table 1. Baseline patient characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Age, years</th>
<th>Smoking</th>
<th>Sex, n (%)</th>
<th>Ethnicity, n (%)</th>
<th>Alcohol</th>
<th>Sports</th>
<th>Comorbidity, n (%)</th>
<th>Surgery</th>
<th>Medication</th>
<th>Follow up time (months)</th>
<th>%EWL</th>
<th>%TWL</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>45.2 ± 8.5</td>
<td>Current smoker 4 (13)</td>
<td>30 (91%)</td>
<td>Dutch native 21 (64)</td>
<td>Never/seldom 19 (59)</td>
<td>Average (2-3 times a week) 8 (28)</td>
<td>Hypertension 15 (45)</td>
<td>RYGB 33 (100)</td>
<td>Beta blockers 5 (15)</td>
<td>21 (14-41)</td>
<td>108 ± 35</td>
<td>80.9 ± 21.8</td>
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<td></td>
<td></td>
<td>Stopped smoking 15 (48)</td>
<td></td>
<td>Surinamese 3 (9)</td>
<td>Social 12 (38)</td>
<td>Sometimes/ stopped 17 (59)</td>
<td>Type 2 diabetes 10 (30)</td>
<td></td>
<td>ACEi &amp; ARBs 8 (24)</td>
<td></td>
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<td></td>
<td></td>
<td>Never 12 (39)</td>
<td></td>
<td>Other/unknown 7 (21)</td>
<td></td>
<td></td>
<td>Dyslipidemia 10 (30)</td>
<td></td>
<td>Diuretics 8 (24)</td>
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<td>OSAS 6 (18)</td>
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Data are presented as mean ± standard deviation, median (range), or number of patients (%). OSAS=Sleep apnea hypopnea syndrome; ACEi=Angiotensin-converting-enzyme inhibitor; ARBs=Angiotensin receptor blocker; RYGB=Roux-en-Y Gastric Bypass; EWL=Excess weight loss; TWL=Total weight loss.

Weight loss, blood pressure, and diabetes after surgery

The mean weight and BMI loss after RYGB were 42.8 ± 10.9 kg (p<0.001) and 15.2 ± 3.9 kg/m² (p<0.001), respectively. There were significant improvements for the systolic blood pressure (p=0.02) and diastolic blood pressure (p=0.002) (Table 2). The heart rate decreased from 83 to 67 per minute (p<0.001). As expected, the prevalence of diabetes and hypertension decreased after bariatric surgery, and the use of antihypertensive medication declined after surgery, especially the use of diuretics (Table 2). There were 12 patients using antihypertensives before surgery and 6 patients after surgery (p=0.014). Five patients with
Table 2. Differences in the parameters after bariatric surgery.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before surgery</th>
<th>After surgery</th>
<th>Relative difference (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>126.2 ±18.1</td>
<td>83.4 ± 16.1</td>
<td>33.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>44.6 ± 5.4</td>
<td>29.4 ± 4.9</td>
<td>34.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidity (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>15(45)</td>
<td>7 (21)</td>
<td>53.3</td>
<td>0.005</td>
</tr>
<tr>
<td>Diabetes type 2</td>
<td>10 (30)</td>
<td>3 (9)</td>
<td>60</td>
<td>0.008</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>10 (30)</td>
<td>5 (15)</td>
<td>50</td>
<td>0.025</td>
</tr>
<tr>
<td>Type anti-HT drugs (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta blockers</td>
<td>5(15)</td>
<td>2 (6)</td>
<td>60</td>
<td>0.083</td>
</tr>
<tr>
<td>ACEi/ARBs</td>
<td>8(24)</td>
<td>6 (18)</td>
<td>25</td>
<td>0.157</td>
</tr>
<tr>
<td>Diuretics</td>
<td>8 (24)</td>
<td>3 (9)</td>
<td>63</td>
<td>0.025</td>
</tr>
<tr>
<td>Other</td>
<td>3 (9)</td>
<td>3 (9)</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>Any</td>
<td>12 (37)</td>
<td>6 (18)</td>
<td>50</td>
<td>0.014</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>126 (115-148)</td>
<td>120 (113-136)</td>
<td>4.8</td>
<td>0.02</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>84 (73-91)</td>
<td>77 (71-85)</td>
<td>8.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Heart rate (min)</td>
<td>83 (76-92)</td>
<td>67 (63-74)</td>
<td>19.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>121 (113-132)</td>
<td>97 (87-109)</td>
<td>19.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24h sodium (mmol/day)</td>
<td>195 (167-247)</td>
<td>160 (118-205)</td>
<td>18</td>
<td>0.015</td>
</tr>
<tr>
<td>&lt;150 mmol/day, n (%)</td>
<td>6 (18)</td>
<td>16 (48)</td>
<td>63</td>
<td>0.002</td>
</tr>
<tr>
<td>&lt;100 mmol/day, n (%)</td>
<td>2 (6)</td>
<td>4 (12)</td>
<td>50</td>
<td>0.157</td>
</tr>
<tr>
<td>24hr UAE mg/day</td>
<td>7.6 (4-16)</td>
<td>9 (6-14)</td>
<td>15</td>
<td>0.877</td>
</tr>
<tr>
<td>&lt;300 mg/day, n (%)</td>
<td>30/32 (94)</td>
<td>31/31 (100)</td>
<td>6</td>
<td>0.180</td>
</tr>
<tr>
<td>&lt;30 mg/day, n (%)</td>
<td>29/32 (91)</td>
<td>28/31 (90)</td>
<td>1</td>
<td>0.655</td>
</tr>
<tr>
<td>&lt;20 mg/day, n (%)</td>
<td>25/32 (78)</td>
<td>24/31 (77)</td>
<td>1</td>
<td>0.655</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation, median (IQR range), or as percentage patients (%).

*The relative differences for albumin excretion are corrected because of not measuring urinary albumin in two patients after surgery and one case before surgery.

BMI= body mass index; ACEi= angiotensin-converting-enzyme inhibitor, ARBs= angiotensin receptor blocker; anti-HT=anti-hypertensive, WC= waist circumference; 24h sodium= 24 hours urinary sodium excretion, UAE=urinary albumin excretion.

monotherapy and one of the two patients with two antihypertensive medications stopped all antihypertensives after surgery. Four patients continued with at least one of the three drugs. Only one patient used five drugs, of which four had to be continued.
Figure 1. Sodium intake before and after bariatric surgery, presented per patient. The dotted lines present patients whose sodium excretion was increased after bariatric surgery.

Sodium excretion
The median sodium excretion decreased from 195 mmol/day (IQR range 167-247) to 160 (IQR 118–205) after surgery, a statistically significant improvement of 18% (p=0.015). Figure 1 shows that there is considerable variation in sodium excretion before and after surgery. Sodium excretion decreased in 22 patients (67%) after surgery (figure 1), but increased in others. We calculated which proportion of patients reached prespecified sodium excretion.
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Figure 2. Relation between %excess weight loss (EWL) and the change in sodium excretion after bariatric surgery. Positive values in sodium excretion present patients whose sodium excretion decreased after bariatric surgery.

levels. Six patients were below the arbitrary chosen level of 150 mmol/day (18%), and only 2 were below 100 mmol/day (6%) before the operation. These percentages increased to 48 and 12% after surgery (table 2).

Albumin excretion

The median albumin excretion did not change after surgery (median of 7.6 mg/day before and 9.0 after surgery) (table 2). Urine albumin was not measured in two patients after surgery and one before surgery (table 2). Because it is expected that the reduction of UAE will not be significant in subjects with normoalbuminuria, the study population was divided in two groups; patients with an UAE of ≥ 20 mg/day (n=7) and below 20 mg/day (n=25). In this last mentioned group of 7 patients with a median UAE of 28 mg/day, no reduction was seen in the UAE after surgery.
Relation between the sodium excretion differences and weight, blood pressure, and albuminuria

Using changes in sodium excretion before and after surgery as the dependent variable, only the positive change in %EWL was a significant (p=0.045) determinant for the decline in sodium excretion with a correlation coefficient of 0.351 (figure 2). Vice versa, the absolute decline in sodium excretion was not accompanied with a significant decline in the systolic or diastolic blood pressure, pulse, and antihypertensive use. Nor was the frequency of dietary consultation of influence on the changes in sodium excretion. There was no significant correlation between the decrease in sodium intake and improvement of UAE ($r_s$ -0.242, p= 0.198), also not when the search was limited to patients with an UAE of >20 mg/day ($r_s$ -0.179, p=0.702).

DISCUSSION

This study shows that there is only a limited decrease in sodium excretion two years after RYGB. The observed sodium excretion indicates that salt intake remains relatively high, especially in comparison with the large improvements in BMI and the prevalence of diabetes and blood pressure. The improvement of blood pressure was independent of the reduction in sodium excretion.

Previous studies indicated improvements of sodium excretion after bariatric surgery. In a study of Borne et al. [18] gastric restrictive surgery decreased 24-h urine excretion of sodium from 185 ± 13 to 98 ± 10 mmol/day 4 months after the operation. The 24 hour urine analysis in the study of Kumar et al. [19] showed a decrease in the sodium excretion from 170.3 ±103.8 to 93.5 ± 39.6 6 months after RYGB in 11 patients (p=0.04). However, it was observed that the reduction in sodium excretion was less pronounced on the longer term, and in studies on the effect of very low caloric diets or sodium restriction the decrease in sodium excretion was also limited [15, 24].

We know that salt intake in the general population is high as well [22,25], especially in the obese [26-29]. A nutritional status survey in 1997 among Dutch people showed a mean salt intake of about 9 g (150 mmol) a day [25]. The mean sodium excretion after surgery in our study reflects a salt intake which is still somewhat higher than the normal population. The WHO advises to reduce the salt intake to below 6 g a day [18, 25]. However, many (bariatric)
dietary guidelines that present recommendations about sodium intake remain vague on this issue [30].

An explanation for the relatively small difference in the sodium excretion 2 years after bariatric surgery is not clear. The lower sodium excretions in the initial months after surgery probably reflect the enormous reduction in intake in these months. Food intake increases in the subsequent months to a steady but lower level compared to before surgery. We speculate that changes in eating patterns play a role. These may be caused by changes in the taste [31] or because of physical complaints, like dumping syndrome, whereby patients can avoid sweet food products and prefer savory foods. The fact that the persons who lost most weight more often had an increase in sodium excretion is in line with this hypothesis. The observed relationship between the change in sodium excretion and %EWL indicates that patients whose urinary sodium excretion decreases after surgery, are not especially more conscious in their eating patterns. In this study, we did not perform a dietary assessment. Although a dietary assessment is notoriously difficult to assess accurately, it may help to explain the observed limited improvement in sodium excretion.

Despite the small change in sodium excretion, the reduction of weight/BMI and blood pressure was significant. Other studies have already shown that weight reduction is an important factor in the improvement of blood pressure [15, 32-36] and microalbuminuria [10, 34, 35, 37-40]. However, our study does not exclude a positive effect of salt reduction on blood pressure. It is still possible that the effect of bariatric surgery on blood pressure could be more pronounced with a lower sodium excretion on the longer term [14,16,17,20].

There are some limitations in our study which require comment. The primary focus of the study was to check sodium excretion as an indicator of salt intake. The study was not powered to draw definitive conclusions about the interactions of sodium excretion and albuminuria and other parameters. Furthermore, a single 24-hour urine sample cannot represent usual sodium intake at the individual level. Therefore, the results have to be interpreted with caution. In addition, we did not use food questionnaires to get more insight in the mean salt intake of patients after bariatric surgery.

The knowledge that sodium excretion remains high on the long term after bariatric surgery is important. Although weight loss is considerable after surgery, a large proportion of patients are still in the obese or overweight range. The chance that blood pressure may
increase again in the future is conceivable. The efficacy of ACE inhibitors and ARBs is significantly reduced in patients with a high salt intake [41]. Studies evaluating the effect of interventions to reduce salt intake in patients after bariatric surgery are needed. It is conceivable that salt intake and sodium excretion may differ after different types of bariatric surgery, especially when there is more malabsorption. This should be investigated in future studies.

In conclusion, sodium excretion as an indicator of salt intake remains high in the vast majority of post-RYGB patients on the long term. This subject requires extra attention in obese patients, because they remain a risk group for cardiovascular morbidity and mortality, even after their operation.

CONFLICT OF INTEREST

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.
REFERENCE LIST


