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ORIGINAL CONTRIBUTIONS

Albuminuria in Patients with Morbid Obesity and the Effect of Weight Loss Following Bariatric Surgery

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Abstract

Background and Objectives Patients with morbid obesity are at an increased risk for cardiovascular and renal complications, which are not only linked to traditional cardiovascular risk factors. Thus, we evaluated (a) the prevalence of albuminuria in non-diabetic and diabetic morbidly obese patients and (b) the effect of weight loss following bariatric surgery.

Material and Methods We included 1307 patients (77% women, mean age 40 ± 12 years, BMI 45.6 ± 6.6 kg/m^2) in a cross-sectional study. A subgroup ($n = 318$) was followed up for 2 years after bariatric surgery. Weight, cardiovascular risk markers and a 75-g glucose tolerance test were determined. Albuminuria was assessed by collecting 24-h urine on three consecutive days.

Results In the cross-sectional study, the prevalence of microalbuminuria was 16.0% ($n = 209$), of macroalbuminuria 3.1% ($n = 41$). The chi-square for the association of albuminuria and diabetes was 31.937 ($p < 0.001$). Of all patients with albuminuria, 42.0% exhibited normal glucose tolerance. In a multivariate regression analysis, systolic blood pressure (beta = 0.236; $p < 0.001$), log fasting insulin (beta = 0.309; $p < 0.001$) and log 2-h postprandial insulin (beta = − 0.173; $p = 0.033$) were predictive risk factors for albuminuria. Longitudinally, albumin excretion decreased significantly from 11.1 (6.4, 18.4 mg/24 h) to 7.8 mg/24 h (4.9, 13.0 mg/24 h; $p < 0.001$). In the group with albuminuria preoperatively, albumin excretion decreased from 65.7 (38.2, 147.1 mg/24 h) to 13.5 mg/24 h (8.4, 36.8 mg/24 h; $p < 0.001$). After adjusting for age, sex and baseline albuminuria, patients with lower creatinine clearance showed a smaller decrease of albuminuria (beta = 0.117; $p = 0.021$).

Conclusion A substantial portion of patients with morbid obesity exhibits microalbuminuria, nearly half of those present with normal glucose tolerance. After weight loss, we found a significant decrease of albuminuria, potentially indicating or even contributing to the known reduction of cardiovascular mortality after bariatric surgery.

Keywords Albuminuria · Weight loss · Morbid obesity · Bariatric surgery

Introduction/Purpose

The prevalence of morbid obesity (MO) is rapidly increasing worldwide [1, 2]. Among several strategies, only bariatric surgery causes a substantial and sustainable weight loss [3, 4] leading to a significant decrease in diabetes, hypertension, cancer, cardiovascular complications and mortality [4–6].

In addition, MO has been linked to a sevenfold higher risk to develop end-stage renal disease, independent of the presence of hypertension or type 2 diabetes [7]. In that regard, a biopsy study in morbidly obese patients without clinical signs of renal disease revealed a higher frequency of increased mesangial matrix, podocyte hypertrophy, mesangial cell proliferation and glomerulomegaly compared with control patients [8]. Even though some patients showed a substantial increase in renal lesions, a follow-up study could show an excellent outcome regarding renal function 9 years after bariatric surgery [9]. Likewise, the Swedish Obese Subject Study demonstrated that weight loss by bariatric surgery results in a lower incidence of new-onset albuminuria [5, 10], and in a large cohort of patients after bariatric surgery, a slower decline

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in eGFR compared with control obese patients has been observed [11].

Data on the prevalence of albuminuria and the respective effect of weight loss in patients with MO are quite heterogeneous due to sample size [9, 12–20], duration of follow-up [9, 12–20] and characteristics of the study population [13, 15, 16, 20].

Therefore, we designed a cross-sectional and a longitudinal study investigating the prevalence of microalbuminuria and early onset of chronic kidney disease (CKD) in MO patients before and after weight loss induced by bariatric surgery. We hypothesised that diagnosis of albuminuria, as a well-known predictor for cardiovascular and renal disease [21], might identify patients at high risk and thus influence the decision to perform bariatric surgery.

Materials and Methods

Study Population

The study was approved by the institutional ethics committee and complies with the Declaration of Helsinki including current revisions and the Good Clinical Practice guidelines. The procedures performed were in accordance with institutional guidelines and all subjects gave written informed consent before the study.

Study Design

We included 1307 patients aged from 18 to 60 years and a BMI of > 35 kg/m^2 in a cross-sectional study (77% women, mean age 40 ± 12 years, mean BMI 45.6 ± 6.6 kg/m^2). A total of 21.1% (n = 276) patients were suffering from type 2 diabetes and 6.5% (n = 85) had impaired glucose tolerance. A subgroup (n = 318) was followed up in a longitudinal intervention study over a period of 2 years after bariatric surgery. In this subgroup, 20.1% (n = 64) of the patients had type 2 diabetes and 19.8% (n = 63) impaired glucose tolerance. A total of 52.5% (n = 167) of the patients underwent laparoscopic Roux-en-Y gastric bypass surgery (RYGB), 35.2% (n = 112) sleeve gastrectomy and 12.3% (n = 39) gastric banding. Surgery was indicated according to the guidelines of the National Institutes of Health consensus statement for surgery in severe obesity (1992). Patients were treated by a multidisciplinary team for medical, psychological, nutritional and surgical treatment at the Outpatients Unit for Morbid Obesity. Patients on angiotensin-converting enzyme (ACE) inhibitor or angiotensin II (ATII) blocker for antihypertensive therapy were excluded from this study. In the longitudinal cohort, all patients presenting with albuminuria were treated with renin-angiotensin system (RAS) blockage medications according to standard of care. However, in the normal albumin excretion group, 29 patients were excluded from further analysis as they were on RAS blockage medication. Following a diagnosis of micro- or macroalbuminuria, patients with hypertension and/or type 2 diabetes were treated with ACE inhibitors or ATII blockers according to medical standards.

In the longitudinal study, all patients attended the postoperative care follow-up programme organised by the multidisciplinary team. All patients with severe renal or liver disease were excluded from this study. In the longitudinal cohort, two patients had to be excluded from the analyses due to the detection of renal disease.

Analyses

Peripheral venous blood samples were collected from all patients after an overnight fast for determination of basic laboratory characteristics. All patients without preexisting diabetes underwent a 75-g oral glucose tolerance test (0, 1 h and 2 h) for determination of glucose tolerance and insulin sensitivity. Renal, lipid and inflammatory parameters were assessed. All patients collected 24-h urine specimen on three consecutive days for determination of albumin excretion. In case of the presence of urinary tract infection, the assessment of albuminuria was repeated after appropriate treatment.

Measurement of Standard Laboratory Parameters

Blood glucose, cholesterol, HDL cholesterol and triglycerides were measured by enzymatic in vitro tests (Roche Diagnostics GmbH, Graz, Austria); the intra-assay and inter-assay coefficients of variation were 1.1% and 2.9%, 0.8% and 1.7%, 1.3% and 2.6% and 1.5% and 1.8%, respectively. Glycosylated haemoglobin was measured by high-performance liquid chromatography (Diamat, Bio-Rad, Hercules, CA). For quantification of insulin concentrations, an ELISA system was used (Enzymuntest Insulin, ES 600, Roche Corporation, Mannheim, Germany), for which the intra-assay and inter-assay coefficients of variation were 3.5% and 5.6%, respectively. Albuminuria was measured by an immunological turbidity test. Anti-albumin antibodies react with the antigen of the sample and to antigen/antibody complexes, which can be measured turbidimetric after agglutination (Cobas® Roche Corporation, Mannheim, Germany).

Calculation and Statistics

Insulin resistance was calculated using the homeostatic model assessment (HOMA), and insulin sensitivity by the Matsuda index [22]. Creatinine clearance (CrCl) was calculated by using the Corcoran-Salazar formula, as this formula was especially derived for obese patients [23]: CrCl (males): [137 − age] × [(0.285 × weight) + (12.1 × height^2)] ÷ [51 × creatinine] and CrCl (females): [146 − age] × [(0.287 × weight) +

(9.74 × height^2)] ÷ [60 × creatinine]. Albuminuria was diagnosed when the mean albumin excretion in the 3-day 24-h urine samples exceeded 30 mg/24 h: microalbuminuria 30–300 mg/24 h and macroalbuminuria > 300 mg/24 h urine regarding KDIGO definitions.

Data are presented as mean ± SD or as median (25th–75th percentile) in case of non-normal distribution. If appropriate, parameters were logarithmized to gain normal distribution. Differences between patients were analysed by Student's paired and unpaired *t* tests and ANOVA or by Mann-Whitney *U* test, Wilcoxon or Kruskal-Wallis test or Kruskal-Wallis-H test, as appropriate. Data were tested for association within each other by univariate (Spearman) and multivariate regression analysis. For the multivariate regression analysis, the non-normally distributed parameters were logarithmized. An alpha level of $p < 0.05$ (two-tailed) was considered statistically significant. Statistical analyses were performed with SPSS 22.0 (IBM Corporation, Armonk, NY, USA).

Results

Cross-sectional Study

The prevalence of microalbuminuria was 16.0% ($n = 209$), and that of macroalbuminuria was 3.1% ($n = 41$). For the respective values in subgroups as well as clinical characteristics of all study participants, see Table 1.

Patients with micro- or macroalbuminuria presented with older age ($p = 0.004$) and higher BMI ($p < 0.001$), waist circumference ($p < 0.001$), systolic ($p < 0.001$) and diastolic ($p = 0.005$) blood pressure, fasting glucose ($p < 0.001$) and 1-h postprandial glucose levels ($p = 0.017$), HbA1c ($p < 0.001$), fasting ($p < 0.001$), 1-h postprandial ($p < 0.001$) and 2-h postprandial insulin levels ($p = 0.023$), HOMA-IR ($p < 0.001$) and triglyceride levels ($p < 0.001$), as well as lower HDL cholesterol levels ($p = 0.002$) than patients without albuminuria.

As type 2 diabetes and hypertension are the strongest known risk factors for albuminuria, we assessed the prevalence of diabetes and of hypertension in association with albuminuria (Fig. 1). The chi-square for the association with diabetes is 31.937 with a *p* value < 0.001. However, of all patients with albuminuria, 42.0% ($n = 105$) had a normal glucose tolerance. The chi-square test for the association of the prevalence of hypertension and albuminuria is weaker but still 13.728 ($p = 0.001$). A total of 20.4% ($n = 51$) of the patients with albuminuria had no hypertension.

To identify predictors for albuminuria, we performed a correlation analysis where we included age, weight, BMI and waist and hip circumference as well as waist to hip ratio (WHR), systolic and diastolic blood pressure, fasting glucose, 1-h and 2-h glucose, fasting insulin, 1-h and 2-h insulin, HOMA, Matsuda index, HbA1c, creatinine, CrCl, cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and C-reactive protein (CRP).

The correlation analysis is depicted in Table 2.

To identify the most important predictor, we performed a multivariate linear stepwise regression analysis, where we included all univariate parameters with significant correlation. In this multivariate linear stepwise backward regression analysis, systolic blood pressure (beta = 0.236; $p < 0.001$), log fasting insulin (beta = 0.309; $p < 0.001$) and log 2-h postprandial insulin (beta = − 0.173; $p = 0.033$) remained the best predictive parameters for albuminuria.

Longitudinal Study

In the whole group ($n = 318$), 17.6% ($n = 56$) of the patients had albuminuria pre-surgery, after surgery the prevalence decreased to 8.5% ($n = 27$). There was a significant decrease of albumin excretion from 11.1 (6.4, 18.4 mg/24 h) to 7.8 mg/24 h (4.9, 13.0 mg/24 h; $p < 0.001$) in the entire population; in patients with normal albumin excretion and without RAS blockage medication ($n = 233$), we could demonstrate a decrease in albumin excretion from 10.3 (6.7, 16.8) to 7.6 mg/24 h (5.0, 12.7; $p < 0.001$). In the group with albuminuria preoperatively, albumin excretion decreased from 65.7 (38.2, 147.1 mg/24 h) to 13.5 mg/24 h (8.4, 36.8 mg/24 h; $p < 0.001$; see Fig. 2). In Table 3, albumin excretion levels are depicted in the different subgroups.

The median of the CrCl was 149.5 ml/min (128.2, 181.3) before surgery; it decreased after surgery to 132.5 ml/min (116.6, 155.2). When splitting the whole group of patients into patients with higher and lower CrCl, we used the pre-surgery median of the CrCl as cut-off value. Patients with higher CrCl had a higher baseline albumin excretion 12.1 (7.2, 23.8) decreasing to 7.8 mg/24 h (5.0, 12.7) after bariatric surgery compared with 9.7 (6.3, 16.1) decreasing to 7.9 mg/24 h (4.9, 13.7) after surgery in the lower CrCl group ($p = 0.046$). However, if only selecting patients with albuminuria before surgery, albumin excretion dropped from 43.5 (35.5, 81.6) to 10.2 mg/24 h (6.8, 17.5) in the high-CrCl group and from 64.7 (38.2, 113.4) to 13.8 mg/24 h (11.5, 36.7) in the low-CrCl group ($p = 0.003$). Patients in the high-CrCl group were initially more obese (BMI 46.2 kg/m^2 vs 43.3 kg/m^2; $p < 0.001$) and lost more weight after bariatric surgery (decrease of BMI − 15.7 kg/m^2 vs − 13.4 kg/m^2; $p < 0.001$) compared with patients in the lower CrCl group.

After adjusting for age and sex, patients with lower CrCl had a smaller decrease of albumin excretion (beta = 0.117; $p = 0.021$). After further adjustment for the change of BMI and HOMA as well as the baseline parameter, this association remains significant (beta = 0.107; $p = 0.043$).

Patients with lower CrCl had a 24% decrease (95% CI 9–37%) of albumin excretion of the geometric mean after surgery. Patients with higher CrCl had a 42% decrease (95% CI

Table 1 Baseline characteristics stratified by albuminuria

	Normoalbuminuria	Microalbuminuria	Macroalbuminuria	*p* value
Age, years	40 ± 12	42 ± 12	45 ± 13	0.004
Weight, kg	127 ± 23	137 ± 24	136 ± 39	< 0.001
BMI, kg/m^2	45 ± 6	47 ± 7	46 ± 9	< 0.001
Waist circumference, cm	133 ± 16	141 ± 14	139 ± 18	< 0.001
Systolic BP, mmHg	141 ± 16	147 ± 16	155 ± 25	< 0.001
Diastolic BP, mmHg	90 ± 11	92 ± 11	95 ± 15	0.005
Creatinine, μmol/l	71 ± 18	71 ± 18	80 (62–89)	< 0.001
C-reactive protein, nmol/l	10.5 ± 7.6	11.4 ± 8.6	10.5 ± 8.6	0.297
Glucose fasting, mmol/l	5.5 ± 1.7	6.2 ± 2.6	6.6 ± 2.7	< 0.001
Glucose 1-h postprandial, mmol/l	8.9 ± 2.7	9.5 ± 2.4	9.4 ± 2.9	0.017
Glucose 2-h postprandial, mmol/l	6.5 ± 2.3	6.9 ± 2.6	6.2 ± 2.3	0.091
HbA1c, %	6.0 ± 1.0	6.5 ± 1.5	7.0 ± 1.7	< 0.001
Insulin fasting, pmol/l	181 ± 118	228 ± 188	215 ± 139	< 0.001
Insulin 1-h postprandial, pmol/l	1035 ± 611	1271 ± 896	1326 ± 597	< 0.001
Insulin 2-h postprandial, pmol/l	708 ± 576	861 ± 799	764 ± 597	0.023
HOMA-IR	5.1 (3.5–7.5)	6.2 (4.0–10.2)	6.2 (5.0–9.7)	< 0.001
Total cholesterol, mmol/l	5.3 ± 1.4	5.1 ± 1.0	5.3 ± 1.2	0.312
HDL cholesterol, mmol/l	1.3 ± 0.4	1.2 ± 0.4	1.1 ± 0.4	0.002
LDL cholesterol, mmol/l	3.0 ± 0.9	3.0 ± 0.8	3.1 ± 1.1	0.595
Triglycerides, mmol/l	1.8 ± 1.1	2.1 ± 1.3	2.4 ± 1.4	< 0.001

Data are depicted in mean ± SD or median (25th–75th percentile) as appropriate. In normal distributed data, an ANOVA was used; in non-normally distributed data, a Kruskal-Wallis-H test was used to determine differences

BP blood pressure

31–51%) of albumin excretion of the geometric mean after surgery. Comparing both groups, patients in the lower CrCl group had a 30% (95% CI 4–65%) reduction of albumin excretion after bariatric surgery compared with patients in the higher CrCl group in the geometric mean ($p = 0.021$).

We performed a stepwise backward regression analysis and included the pre-post-surgery change (delta) of all variables. We found the delta triglycerides (− 0.171; $p = 0.042$) and the delta Matsuda index (beta = − 0.231; $p = 0.008$) to be the most predictive parameters for the change in albumin excretion.

Operation Techniques

We performed an ANCOVA-adjusted mean delta albumin excretion to identify possible difference between operation techniques. After adjustment for age and sex and pre-surgery albuminuria, patients with gastric bypass (beta = − 0.185; $p = 0.008$) and patients undergoing sleeve gastrectomy (beta = − 0.156; $p = 0.035$) had a stronger decline of albumin excretion compared with patients undergoing gastric banding.

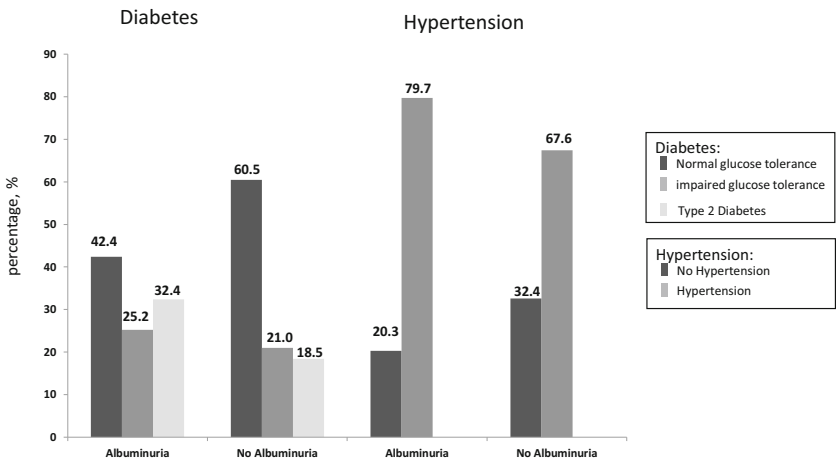

Fig. 1 Albuminuria in association with diabetes and hypertension

Table 2 Predictors of albuminuria

Variables	*R* value	*p* value
Age	*0.63*	*0.041*
Weight	*0.155*	*< 0.001*
BMI	*0.112*	*< 0.001*
Waist circumference	*0.205*	*< 0.001*
Hip circumference	0.080	0.150
Waist/hip ratio	*0.113*	*0.041*
Systolic blood pressure	*0.176*	*< 0.001*
Diastolic blood pressure	0.049	0.107
Fasting glucose	*0.090*	*0.003*
1-h glucose	*0.092*	*0.004*
2-h glucose	0.042	0.197
Fasting insulin	*0.133*	*< 0.001*
1-h insulin	*0.113*	*0.001*
2-h insulin	*0.081*	*0.013*
HOMA	*0.152*	*< 0.001*
Matsuda index	*0.153*	*< 0.001*
HbA1c	0.059	0.055
Creatinine	− 0.018	0.557
Creatinine clearance	*0.087*	*0.005*
Cholesterol	0.009	0.781
LDL cholesterol	− 0.32	0.307
HDL cholesterol	*− 0.73*	*0.018*
Triglycerides	*0.114*	*< 0.001*
C-reactive protein	0.039	0.207

Data were calculated by a Spearman rho test; all significant variables are depicted in italicized fashion

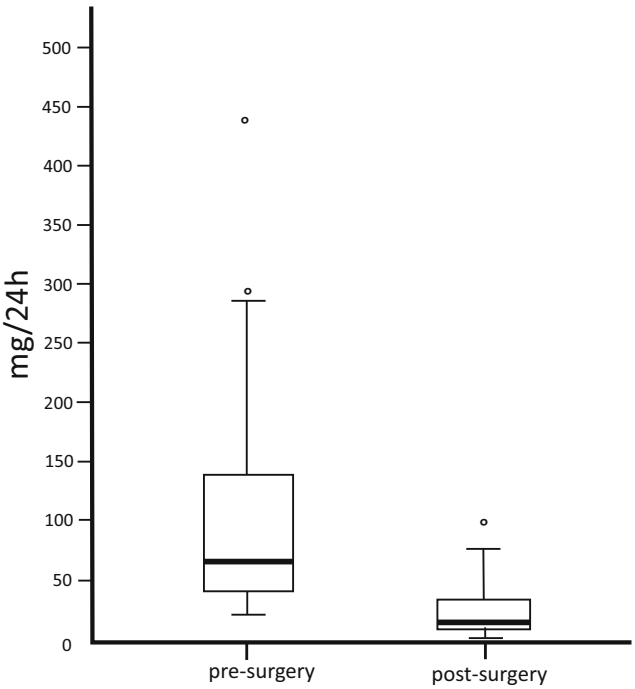

Fig. 2 Decrease of albuminuria after bariatric surgery in patients with preoperative albuminuria

After further adjustment for pre-surgery BMI and HOMA, only patients with gastric bypass have a significantly steeper decline of albumin excretion compared with patients with gastric banding (beta = − 0.163; $p = 0.020$). In another step, we adjusted for weight loss and the improvement of insulin resistance (delta HOMA). The steeper decline in albumin excretion after gastric bypass compared with gastric banding still remained borderline significant (beta = − 0.155; $p = 0.051$).

After sex and age adjustment, patients with gastric bypass had a reduction of albumin excretion in the geometric mean of 40% (95% CI 29–49%) compared with patients undergoing sleeve gastrectomy (36%; 95% CI 22–47%) and patients undergoing gastric banding (8%; 95% CI − 23–31%; overall $p = 0.030$).

When comparing the different procedures, patients undergoing gastric banding had a 43% (95% CI 2–100%; $p = 0.035$) lower decline of albumin excretion compared with patients undergoing sleeve gastrectomy. Additionally, patients with gastric banding differ from gastric bypass patients with a 53% (95% CI 12–109%; $p = 0.008$) lower decrease of albumin excretion. There were no significant differences between gastric bypass and sleeve gastrectomy. All percentages are calculated as the geometric mean after age and sex adjustment.

Discussion

In our study, we were able to show a high prevalence of albuminuria in unselected patients with MO as well as a significant decline after weight loss induced by bariatric surgery. This prevalence is higher than that reported in the population based HUNT2 study in women ($n = 5061$). Compared with our study, the prevalence was 12.0% vs 19.1% for the entire cohort and 22.4% vs 32.4% in patients with diabetes [24]. These numbers are in line with another population study performed in over 30-year-old Korean subjects, where the overall prevalence of albuminuria was 5.1% [25]. Our higher prevalence in a relatively young (40 ± 12 years) population could be either specific to our patients, which is rather unlikely, or indicate that the 24-h urine collection for albumin excretion used in the present study might be more accurate than its determination from spot urine.

Albumin excretion is a marker not only for deterioration of kidney function but also for the risk of cardiovascular events. A follow-up study in 37,000 patients showed that even slightly elevated albumin levels within the normal range (< 30 mg/g) predict a higher risk for cardiovascular events and hypertension [26]. Accordingly, normotensive non-diabetic patients with a preserved glomerular filtration rate in the highest tertile of low-grade albumin excretion (in men > 9.6 mg/g, in women > 12.4 mg/g) had an increased incidence of hypertension and cardiovascular mortality during a follow-up period of almost 6 years [27]. The association between low-grade albuminuria

Table 3 Pre- and post-surgery albuminuria in different subgroups

Albuminuria in:	Pre-surgery	Post-surgery	*p* value
Total cohort ($n = 318$), mg/24 h	11.1 (6.4, 18.4)	7.8 (4.9, 13.0)	< 0.001
Diabetes ($n = 64$), mg/24 h	13.3 (7.6, 35.9)	9.7 (6.2, 16.9)	0.002
Diabetes and albuminuria ($n = 18$), mg/24 h	82.7 (38.7, 304.1)	26.4 (8.5, 34)	0.001
Hypertension ($n = 228$), mg/24 h	12.3 (6.9, 22.3)	8.7 (5.0, 14.7)	< 0.001
Hypertension and albuminuria ($n = 42$), mg/24 h	49.1 (35.0, 119.2)	11.7 (7.2, 24.6)	< 0.001
Diabetes and hypertension ($n = 52$), mg/24 h	12.1 (7.5, 21.8)	9.3 (6.0, 16.8)	0.016
No diabetes and no hypertension ($n = 54$), mg/24 h	8.5 (5.4, 13.8)	7.0 (5.3, 11.5)	0.059

Subgroups are specified pre-surgery

and elevated cardiovascular risk in non-diabetic and non-hypertensive has also been shown in the Framingham Heart Study [28].

Thus, the high prevalence of albuminuria in our relatively young cohort might reflect and predict the elevated risk for cardiovascular disease. While we have not demonstrated a relation between elevated albumin excretion and cardiovascular endpoints in our follow-up study due to its design, one could speculate that determination of albuminuria could identify patients at high risk and serve as a selection criterion for performing bariatric surgery.

In our study, patients with macroalbuminuria were less obese, which can be interpreted as a finding by chance or as a consequence of older age and more comorbidities such as hypertension and diabetes, which could serve as a marker for earlier referral to bariatric surgery.

Obesity is associated with the early onset of glomerulomegaly, hemodynamic changes of a hyperfiltrating kidney and increased albumin excretion, which are potentially reversible by weight loss [29]. However, the pathologic lesions of focal segmental glomerulosclerosis in experimental mouse models of obesity, and in obese human subjects presenting with massive proteinuria, are different from those of classic diabetic nephropathy [30]. Accordingly, observational studies have confirmed obesity as an independent risk factor for chronic kidney disease regarding onset and deterioration of kidney function even after adjustment for confounding comorbidities such as diabetes and hypertension [7, 31, 32].

The cause for the higher prevalence of albuminuria in patients with MO is considered multifactorial, and the exact link between kidney disease and obesity has not yet been identified.

Excessive consumption of animal protein as well as a high-salt intake by morbid obese patients might play a role in the development of renal alterations, since high-salt intake increases blood pressure and oxidative stress [33], whereas elevated protein intake might impede glomerular autoregulation by afferent vasodilatation. This increases the glomerular filtration rate and allows the transmission of elevated systemic pressure to the glomerular capillary [31]. Consecutively, the higher pressure leads to a barotrauma of the glomerular capillaries. In addition, due to the vasodilatation, podocytes need to cover a larger surface which could also increase their permeability.

Obesity-related glomerulopathy has been recognised as an own entity, different to focal segmental glomerulosclerosis [29]. It is characterised by glomerulomegaly and hypertrophy of podocytes and mesangial cells, and these structural changes might be present even before albuminuria, as shown in kidney biopsies of morbid obese patients [8].

In the longitudinal study, we found a significant decline in albumin excretion, irrespective of the presence of diabetes mellitus. The first study investigating albuminuria after gastroplasty was performed by Chagnac et al. in 9 patients [19]. Subsequently, a decline of albumin excretion after bariatric surgery, which was associated with baseline albumin excretion and the change of HbA1c, has been shown in a pilot study [13]. However, the follow-up after bariatric surgery was only 1 year, 34% of the patients were suffering from type 2 diabetes as compared with 20.1% in our cohort and the patients were older compared with our sample. In our study, neither baseline albumin excretion nor the change of HbA1c was a predictor for the decrease in albumin excretion, which may be at least partly explained by the relative short duration of diabetes. In fact, in most cases, diabetes was diagnosed at the baseline visit by the glucose tolerance test. In another study with a small sample size ($n = 38$), a prevalence of albuminuria of 39% was shown in non-diabetic patients [18]. After bariatric surgery, a decrease of microalbuminuria was demonstrated (35.3 ± 66.6 vs 12 ± 10.3 mg/g, $p = 0.029$). However, the cut-off point for albumin excretion was set lower than in our study (20 mg/dl) and different from accepted standards for the definition of microalbuminuria. Furthermore, the postoperative assessment was median 30 days after bariatric surgery. At that time point, patients consumed a very special liquid diet, which can influence the results of the study.

In our study, patients undergoing gastric bypass had a steeper decline of albumin excretion compared with patients who underwent sleeve gastrectomy. This is in line with many studies which demonstrated a slightly better outcome for gastric bypass compared with sleeve gastrectomy regarding diabetes remission or other cardiovascular risk factors [6].

A limitation of the study might be the measurement of CrCl, which has not been performed from 24-h urine but has been estimated by the Corcoran-Salazar formula, which, however, is validated in obese subjects [23]. In addition, due to the design of the study, we were not able to demonstrate any reduction in renal and cardiovascular events related to the decrease in albumin excretion. The strengths of the study are the high number of subjects, the longer observation period than reported by other studies and the measurement of albumin excretion in urine collected over 24 h, which makes false positive results very unlikely.

In conclusion, we were able to demonstrate a rather high prevalence of albuminuria in a large patient cohort, irrespective of the presence of diabetes in our study. Furthermore, we showed a significant decline of albumin excretion after bariatric surgery over a sufficiently long follow-up period. Albuminuria is an early predictor for renal and for cardiovascular disease. This corresponds to a threefold higher risk for the development of end-stage renal disease in patients with BMI > 30 kg/m^2 compared with patients with normal weight [7], which encourages screening for albuminuria also in non-diabetic patients with MO and might identify patients at high risk and potentially allow reduction of renal and cardiovascular risk by bariatric surgery.

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Compliance with Ethical Standards

The study was approved by the institutional ethics committee and complies with the Declaration of Helsinki including current revisions and the Good Clinical Practice guidelines. The procedures performed were in accordance with institutional guidelines and all subjects gave written informed consent before the study.

Conflict of Interest The authors declare that they have no conflict of interest.

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