Impact of sleeve gastrectomy on renal function in patients with morbid obesity: a 1-year prospective cohort study

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Abstract
Purpose Obesity is an independent risk factor for renal injury. A more favorable metabolic environment following weight loss may theoretically lead to improved renal function. We aimed to evaluate the evolution of renal function one year after sleeve gastrectomy in a large prospective cohort of patients with morbid obesity and assess the influence of fat-free mass (FFM) changes.

Methods We prospectively included obese patients admitted for sleeve gastrectomy between February 2014 and November 2016. We also included a historical observational cohort of patients undergoing sleeve gastrectomy between January 2013 and January 2014 who had FFM evaluation. Patients were systematically evaluated 1 year after surgery. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. The FFM was estimated by analyzing computerized tomography (CT) scan sections from CT systematically performed 2 days and 1 year after sleeve gastrectomy to detect surgery complications.

Results Five hundred sixty-three patients fulfilled the inclusion criteria. The mean age was 41.2 ± 0.5 years. The mean body mass index was 43.5 ± 0.3 kg/m² and 20.4, 30.5, and 30.7% of the included patients had type 2 diabetes, hypertension, and dyslipidemia, respectively. One hundred fifteen patients were excluded and four hundred forty-eight patients were finally included in the analysis. The eGFR was significantly higher 1 year after sleeve gastrectomy than before surgery (87.8 ± 0.9 versus 86.1 ± 0.9, p < 0.01). There was no difference in terms of post-surgery FFM loss between patients with an improved eGFR and those without (6.7 ± 0.3 kg versus 6.8 ± 0.5 kg, p = 0.9). Furthermore, post-surgery changes in the eGFR did not correlate with the amount of FFM loss (r = 0.1, p = 0.18).

Conclusion Renal function assessed by eGFR is significantly improved at 1-year post-sleeve gastrectomy, independent of changes in skeletal muscle mass.

Keywords Renal function · Sleeve gastrectomy · Fat-free mass · Morbid obesity
Introduction

The prevalence of obesity is increasing worldwide, and it is estimated that one-quarter of the world’s population will be overweight or obese by 2045. Among the complications of obesity, diabetes and hypertension account for half of kidney-failure cases. Nevertheless, obesity itself is an independent risk factor for renal injury [1, 2]. Obesity-related glomerulopathy is characterized by segmental and focal glomerulosclerosis associated with glomerulomegaly [3]. Chagnac et al. [4] showed that glomerular filtration and renal plasma flow are 51% higher in obese patients than healthy subjects. This may be due to vasodilatation of the afferent arteriole caused by insulin, together with vasoconstriction of the efferent arteriole favored by insulin resistance [5]. Thus, an increase in the glomerular filtration rate is an early manifestation of obesity-related renal injury.

A more favorable metabolic environment and a decrease in profibrotic factors following weight loss may theoretically lead to an improvement in renal function [6, 7]. Recent studies suggest that renal function may improve in morbidly obese patients undergoing bariatric surgery [8, 9], but data from large homogenous prospective cohorts are lacking. Furthermore, the available studies did not explore the influence of post-surgery skeletal muscle loss on the estimated glomerular filtration rate (eGFR) changes. We previously showed that morbidly obese patients lose 15% of their fat-free mass (FFM) at 1 year post-sleeve gastrectomy [10]. This FFM loss may theoretically decrease creatinine serum level and induce a false improvement of estimated GFR in these patients. Previous data show that renal function improvement occurs especially 1 year after bariatric surgery [11]. In this context, we aimed to evaluate the evolution of renal function one year after sleeve gastrectomy in a large prospective cohort of patients with morbid obesity. The secondary aims were to assess (1) the influence of baseline renal function and changes in FFM on the post-surgery evolution of renal function and (2) the effect of the renal function status on weight loss at one-year post-surgery.

Patients and methods

Study population

We conducted an observational prospective cohort study that included 379 consecutive patients admitted to our institution to undergo sleeve gastrectomy between February 2013 and January 2014. The inclusion criteria and clinical pathway were the same, but patients from the historical cohort were excluded if they did not have a computerized tomography (CT) scan between 12 and 18 months after surgery. The objective of the historical cohort was to define a predictive score of sarcopenia occurrence 1 year after sleeve gastrectomy as previously described [10]. Therefore, estimation of fat-free mass starting from CT scan images before and 1-year post-surgery was available for all the patients included in the historical cohort and allowed us to assess the influence of FFM changes on the post-surgery evolution of renal function. As previously described [12], patients fulfilling the following criteria were considered to be eligible for this study: (i) severe obesity [body mass index (BMI) ≥ 35 kg/m²] with at least one comorbid condition or morbid obesity alone (BMI ≥ 40 kg/m²) not responsive to medical treatment; (ii) no medical or psychological contraindication for bariatric surgery; (iii) not currently an excessive drinker, as defined by a mean daily consumption of more than 20 g of alcohol per day for women or more than 30 g of alcohol per day for men; (iv) no long-term consumption of hepatotoxic drugs; and (v) negative screening results for chronic liver disease unrelated to obesity. All patients had a pre-operative evaluation including (i) clinical parameters; (ii) a biological assessment of renal function, lipid profile, nutritional status, and liver function tests; and (iii) liver ultrasound and transient elastography [12]. Hypertension was defined as a sustained elevation of systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg and/or ongoing antihypertensive drugs. Hypertension resolution was defined as normal blood pressure in the absence of antihypertensive drugs. Type 2 diabetes was defined as hemoglobin A1c (HbA1c) value ≥ 6.5% and/or fasting plasma glucose (FPG) ≥ 7 mmol/l (126 mg/dl) on two occasions and/or the use of any glucose-lowering drugs. At follow-up, diabetes remission was defined as HbA1c value < 6%, fasting plasma glucose < 5.6 mmol/l, and no use of glucose-lowering drugs. Dyslipidemia was defined as low-density lipoprotein (LDL) ≥ 4.14 mmol/l and/or high-density lipoprotein (HDL) < 1.03 mmol/l and/or triglyceride > 2.29 mmol/l and/or ongoing lipid lowering medication. Dyslipidemia resolution was defined as normal LDL, HDL, and triglyceride values in the absence of lipid lowering medication. All patients underwent a laparoscopic single-port sleeve gastrectomy. A liver biopsy was performed during the sleeve gastrectomy as previously described [13]. The indications for liver biopsy were (i) ultrasound results suggestive of liver steatosis or liver dysmorphism and/or (ii) abnormal liver tests and/or (iii) a macroscopically abnormal liver, as observed by the surgeons [12]. A CT scan was systematically performed two days and one year after sleeve gastrectomy to detect early and late complications of surgery. The clinical interest of routine postoperative CT scans has
been previously proven by our team [14]. We showed that a combination of clinical surveillance and early imaging allowed prompt management of complicated cases, avoiding further morbidity. In our patients, CT scans were performed on a targeted zone of interest using a limited number of phases, thus considerably decreasing radiation exposure. Written informed consent was obtained from all participants. The study did not include minors (patients under 18 years of age) and was conducted in accordance with the national law concerning medical investigations (Hurié Law) and the 1964 Helsinki declaration. The study protocol and consent procedure were approved by the ethics committee of the Bicètre Hospital.

**Follow-up**

All patients systematically received a convocation for an evaluation 1 year after the bariatric surgery during a 1-day hospital stay. Clinical parameters included the amount of weight loss [percentage of total weight loss (%TWL), percentage of excess weight loss (%EWL)], and persistence of comorbidities (hypertension, diabetes, dyslipidemia). Biological assessment included all parameters tested at inclusion (renal function, lipid profile, nutritional status, and liver function tests).

The primary outcome was the change in eGFR, calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation at 1-year post-surgery. A subgroup analysis of patients with hypofiltration (eGFR < 90 ml/min/1.73 m²) and hyperfiltration (eGFR > 120 ml/min/1.73 m²) was also performed. The secondary outcome was the evolution of the eGFR as a function of changes in FFM at 1-year post-sleeve gastrectomy.

**Renal function evaluation**

Renal function was assessed by calculating the eGFR. The use of eGFR equations that rely on total body weight, such as the Cockcroft and Gault formula, is not appropriate for extremely obese patients, as they overestimate the eGFR. A recent study from Guebre-Egziabher F et al. [15] showed that CKD-EPI equation is the most suitable way to estimate GFR in severely obese patients. Furthermore, deindexation of CKD-EPI equation worsened bias and decreased accuracy [16]. In our study, we used CKD-EPI equations, which do not include total body weight:

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\text{For women: } \begin{cases} 
\text{eGFR} (\text{ml/min}/1.73 \text{m}^2) = 144 \times (\text{creatinine}/0.7)^{-0.329} \times (0.993)^{\text{age}} \\
(> 62 \mu\text{mol/l} \leq 7 \text{mg/dl}) \\
\text{eGFR} (\text{ml/min}/1.73 \text{m}^2) = 144 \times (\text{creatinine}/0.7)^{-1.209} \times (0.993)^{\text{age}} \\
(> 62 \mu\text{mol/l} > 7 \text{mg/dl}) \\
\end{cases} \\
\text{For men: } \begin{cases} 
\text{eGFR} (\text{ml/min}/1.73 \text{m}^2) = 141 \times (\text{creatinine}/0.9)^{-0.411} \times (0.993)^{\text{age}} \\
(> 80 \mu\text{mol/l} \leq 7 \text{mg/dl}) \\
\text{eGFR} (\text{ml/min}/1.73 \text{m}^2) = 141 \times (\text{creatinine}/0.9)^{-1.209} \times (0.993)^{\text{age}} \\
(> 80 \mu\text{mol/l} > 7 \text{mg/dl}) \\
\end{cases}
\]

In young and middle-aged adults, normal eGFR values are considered to be between 90 and 120 ml/min/1.73 m² [17]. In our cohort, the mean age of patients was 41 years. We therefore used these ranges to define renal filtration status. An eGFR value < 90 ml/min/1.73 m² was considered to indicate impaired renal function (or hypofiltration). An eGFR value > 120 ml/min/1.73 m² was considered to be representative of glomerular hyperfiltration [17].

**Fat-free mass evaluation**

Fat-free mass (FFM) estimation starting from CT scan was available for the 184 patients included in the historical cohort. It was previously showed that skeletal muscle cross-sectional area measured on CT-scan images at the third lumbar vertebrae (SMA, cm²) is linearly related to whole-body muscle mass [18 19]. The SMA was measured on the CT scan according to the method of Prado et al. [20]. The SMA was identified and quantified using Hounsfieeld unit thresholds (−29 to +150) [18]. The third lumbar vertebrae region contains psoas, paraspinal muscles (quadratus lumborum and erectorspiniae), and abdominal wall muscles (external and internal obliques, transversus abdominus, and rectus abdominus). Measurements were performed 2 days and 1 year after sleeve gastrectomy, by a single reader blinded to patient details, as previously described by our team [10]. The FFM was estimated starting from SMA and using the following regression equation previously validated by Moutzarkis et al. [19]: FFM (kg) = 0.3 × SMA (cm²) + 6.06.

**Statistical analysis**

The \( \chi^2 \) test was used for comparisons between qualitative variables, which are described by the frequency and percentage of each class. Student \( T \) tests were used to compare normally distributed quantitative variables and
Mann–Whitney and Wilcoxon tests for those for which the distribution did not follow a normal distribution. Comparison of data before and after surgery was performed with the use of a paired sample Student T test or Wilcoxon test adequately. The distributions of the quantitative variables are described by the mean ± the standard error of the mean (SEM). All comparisons were performed using bilateral tests with an alpha risk of 5%. Simple correlations between variables were evaluated using Spearman Correlation Tests. An analysis of the different groups of patients was performed before and after the bariatric surgery to evaluate (1) the evolution of renal function according to the initial eGFR and (2) the weight loss and evolution of the comorbidities based on whether or not there was pre-existing renal insufficiency. We used multiple linear regression to investigate the influence of the amount of FFM loss on the evolution of eGFR. We used Number Cruncher Statistical Systems Software version 9.0.14 (Statistical Systems, Kaysville, UT).

Results

Characteristics of the patients

In total, 563 patients with an indication for sleeve gastrectomy fulfilled the inclusion criteria (prospective cohort: 379 patients; historical cohort: 184 patients). The mean age of the patients was 41.2 ± 0.3 years; historical cohort: 184 patients). The mean age of the patients was 41.2 ± 0.3 (18 to 74 years old) years and a large majority were women (77.1%). The mean BMI was 43.5 ± 0.3 kg/m² and 20.4, 30.5, and 30.7% of the included patients had type 2 diabetes, hypertension, or dyslipidemia, respectively. A preoperative liver biopsy was available in 82% of the included patients. Steatosis, nonalcoholic steatohepatitis (NASH), or advanced fibrosis (F ≥ 3) were present in 81, 38, and 4.8% of the included patients, respectively. Postoperative complications occurred in thirty-seven patients (6.5%): intraabdominal bleeding (21 patients), staple-line leak (14 patients), and death (2 patients). The characteristics of the study population are described in Table 1.

Baseline characteristics were similar across the prospective and historical cohorts (Table 1).

Among the qualifying patients, 115 were excluded due to a loss to follow-up (80 patients), an early follow-up evaluation between 3 and 9 months after surgery (25 patients), an incomplete evaluation 1 year after surgery (8 patients), and death (2 patients). Finally, 448 patients were included in the analysis. The patients lost to follow-up were younger (37.3 ± 1.3 versus 42.2 ± 0.6, p < 0.0001), had a lower frequency of dyslipidemia (23.5% versus 32.6%, p = 0.05), and a higher baseline eGFR (94.3 ± 2.3 versus 86.1 ± 2.3, p < 0.0001) than those returning for the 1-year post-surgery evaluation. The baseline characteristics of patients who returned for the 1-year follow-up and those who did not are reported in Table 2.

Evolution of renal function one year after sleeve gastrectomy

The eGFR, as estimated by the CKD-EPI equation, significantly improved 1 year after sleeve gastrectomy relative to the value before surgery (87.8 ± 0.9 versus 86.1 ± 0.9, p < 0.01). The mean weight lost at the 1-year follow-up was 27.1 ± 0.4% of total body weight. We further retrospectively collected creatinine values at 5-year post-surgery to calculated eGFR. The eGFR was still significantly improved 5 years post-bariatric surgery relative to the value before intervention (91.6 ± 1.7 versus 86.1 ± 0.9, p = 0.05).

We then assessed the post-operatory evolution of the eGFR as a function of the baseline renal status. The eGFR significantly increased for patients with impaired renal function (hypofiltration) at baseline by 1-year post-sleeve gastrectomy (78.8 ± 1 ml/min/1.73 m² versus 74.3 ± 0.9, p < 0.001), where it decreased for those with baseline renal hyperfiltration (114.1 ± 2.8 ml/min/1.73 m² versus 124.7 ± 1.2, p < 0.01) (Fig. 1). Furthermore, the %TWL was lower for patients with a low eGFR at baseline than for those with a normal baseline eGFR (26.3 ± 0.6% versus 28.2 ± 0.6%, p = 0.03) (Fig. 2). The hyperfiltrating patients were younger (27.9 ± 1.6 versus 46.3 ± 0.6 years; p < 0.0001), had lower rate of hypertension (16.7 versus 38.8%; p < 0.001), diabetes (4.2 versus 23.3%; p < 0.0001) and dyslipidemia (16.7 versus 35.3%; p < 0.01) than those with baseline hypofiltration. There was no difference in term of body mass index.

Fat-free mass and estimated glomerular filtration rate evolution 1 year after sleeve gastrectomy

FFM values 2 days and 1-year post-sleeve gastrectomy, estimated from the SMA measured by CT, were available for the 184 patients included in the historical cohort. FFM was significantly lower 1-year post-surgery (43.6 ± 0.7 kg versus 50.3 ± 0.8 kg, p < 0.0001). However, there was no difference in terms of post-surgery FFM loss between patients for whom the eGFR improved and those for whom it did not (6.7 ± 0.3 kg versus 6.8 ± 0.5 kg, p = 0.9). The post-surgery changes in eGFR did not correlate with the amount of FFM loss (r = 0.1, p = 0.18). Furthermore, the absolute weight loss (32.6 ± 0.7 kg versus 32.4 ± 0.9 kg, p = 0.9) and %TWL (27.4 ± 0.6% versus 26.8 ± 0.7%, p = 0.48) were not significantly different between patients with an improved eGFR and those for whom it did not improve 1-year post-surgery. We then assessed the amount of FFM loss according
to baseline eGFR. Patients with baseline hypofiltration, normofiltration, or hyperfiltration had similar post-surgery FFM loss (6.57 versus 6.92 versus 6.91 kg, \(p = 0.8\)). Furthermore, changes in eGFR did not correlate with the amount of FFM loss in these three subgroups of patients \(r = 0.16 (p = 0.1), r = 0.03 (p = 0.8), \) and \(r = 0.14 (p = 0.5)\), respectively. In a multiple linear regression analysis (dependent variable: eGFR evolution) simultaneously taking into account FFM loss and baseline eGFR, the post-surgery FFM loss do not independently correlated with eGFR evolution.

### Patient outcome 1 year after sleeve gastrectomy

The rate of diabetes, hypertension, and dyslipidemia significantly improved 1 year after sleeve gastrectomy (Table 3). Nevertheless, there was no difference in terms of hypertension (36.3% versus 30.8%, \(p = 0.32\)), diabetes (46.4% versus 45.7%, \(p = 0.28\)), or dyslipidemia (39.6% versus 30.9%, \(p = 0.58\)) remission rate between patients for whom renal function improved and those for whom it did not at one-year post-sleeve gastrectomy. Bariatric surgery also induced

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**Table 1** Baseline characteristics of the study population

|                     | Total population \((N=563)\) | Prospective cohort \((N=379)\) | Historical cohort \((N=184)\) | \(p\) |
|---------------------|-------------------------------|-------------------------------|-------------------------------|------|
| **Age (years)**     | 41.2 ± 0.5                   | 41.1 ± 0.7                   | 41.4 ± 0.9                   | ns   |
| **Male**            | 124 (22%)                    | 89 (23.2%)                   | 35 (19.4%)                   | ns   |
| **BMI (kg/m²)**     | 43.5 ± 0.3                   | 43.7 ± 0.3                   | 43 ± 0.5                     | ns   |
| **Hypertension**    | 170 (30.5%)                  | 110 (28.8%)                  | 60 (34.1)                    | ns   |
| **Type 2 diabetes** | 115 (20.4%)                  | 82 (21.4%)                   | 33 (18.2%)                   | ns   |
| **Dyslipidemia**    | 171 (30.7%)                  | 118 (30.9%)                  | 53 (30.3%)                   | ns   |
| **Urea (mmol/L)**   | 5.1 ± 0.1                    | 5 ± 0.1                      | 5.2 ± 0.2                    | ns   |
| **Creatinine (µmol/L)** | 83.1 ± 2.5                 | 85 ± 3.5                     | 78.8 ± 1.5                   | ns   |
| **Uric acid (mmol/L)** | 350.1 ± 3.5                | 350.3 ± 4.3                  | 349.7 ± 5.9                  | ns   |
| **Fasting blood glucose (mmol/L)** | 6 ± 0.1                     | 6.2 ± 0.2                    | 5.8 ± 0.1                    | ns   |
| **HbA1c (%)**       | 5.9 ± 0.1                    | 5.9 ± 0.1                    | 5.8 ± 0.1                    | ns   |
| **Insulin (mmol/L)** | 25.3 ± 0.7                  | 26.2 ± 0.8                   | 23.1 ± 1.5                   | ns   |
| **AST (IU/L)**      | 30.7 ± 0.9                   | 30.8 ± 1.1                   | 30.4 ± 1.6                   | ns   |
| **ALT (IU/L)**      | 43.4 ± 1.5                   | 44.7 ± 1.9                   | 40.7 ± 2.4                   | ns   |
| **GGT (IU/L)**      | 46.4 ± 2.3                   | 44.5 ± 1.7                   | 50.2 ± 6.3                   | ns   |
| **Albumin (g/L)**   | 40.7 ± 0.1                   | 40.5 ± 0.1                   | 41.1 ± 0.3                   | ns   |
| **Cholesterol (mmol/L)** | 5.3 ± 0.07                  | 5.29 ± 0.05                  | 5.36 ± 0.18                  | ns   |
| **Serum triglycerides (g/L)** | 1.47 ± 0.04             | 1.50 ± 0.05                  | 1.42 ± 0.07                  | ns   |
| **HDL (mmol/L)**    | 1.29 ± 0.2                   | 1.29 ± 0.03                  | 1.31 ± 0.03                  | ns   |
| **LDL (mmol/L)**    | 3.38 ± 0.06                  | 3.37 ± 0.05                  | 3.40 ± 0.15                  | ns   |
| **CRP (mg/L)**      | 12.4 ± 0.4                   | 12 ± 0.5                     | 13.2 ± 0.8                   | ns   |
| **Ferritin (ng/L)** | 145.5 ± 6.20                 | 128.3 ± 7.8                  | 114.7 ± 9.9                  | ns   |
| **TE (kPa)**        | 7.7 ± 0.3                    | 7.7 ± 0.3                    | 7.5 ± 0.8                    | ns   |
| **CAP (dB/m)**      | 309.8 ± 4.4                  | 313.9 ± 4.1                  | 310 ± 4.2                    | ns   |
| **Steatosis**       | 776 (81%)                    | 281 (82.4%)                  | 95 (77.2%)                   | ns   |
| **NASH**            | 177 (38.3%)                  | 140 (41.1%)                  | 37 (30.6%)                   | 0.04 |
| **Fibrosis**        | 0–No fibrosis                | 84 (18.3%)                   | 55 (16.3%)                   | 29 (23.6%)  | 0.04 |
|                     | 1–peri-sinusoidal or periportal fibrosis | 276 (60%)                  | 218 (64.7%)                  | 58 (47.2%)  | 0.001  |
|                     | 2–Peri-sinusoidal and periportal fibrosis | 78 (20%)                   | 50 (14.8%)                   | 28 (22.8%)  | ns   |
|                     | 3–Septal fibrosis            | 17 (3.7%)                    | 11 (3.3%)                    | 6 (4.9%)    | ns   |
|                     | 4–Cirrhosis                  | 5 (1.1%)                     | 3 (0.9%)                     | 2 (1.6%)    | ns   |

Results are shown as the mean ± standard error of the mean or n (%). (SEM, standard error of the mean)

**BMI** body mass index, **HbA1c** glycated hemoglobin, **AST** aspartate aminotransferase, **ALT** alanine aminotransferase, **GGT** γ-glutamyl transferase, **HDL** high-density lipoprotein, **LDL** low-density lipoprotein, **CRP** C reactive protein, **CAP** controlled attenuation parameter, **NASH** nonalcoholic steatohepatitis
when stratified by baseline renal status, eGFR was significantly higher by the 1-year follow-up only for patients with impaired renal function (eGFR < 90 ml/min/1.73 m²) before surgery. Our results are in accordance with those of previously published studies showing that the glomerular filtration rate improves mainly for obese patients with impaired baseline renal function [2 6 21 22]. In a retrospective study of 149 obese patients undergoing gastric by-pass or sleeve gastrectomy, Holcomb et al. [6] showed a post-surgery increase of the eGFR for patients with a baseline eGFR < 90 ml/min/1.73 m². A significant increase in eGFR was also found during the first year following bariatric surgery by Neff et al. [21] in a prospective cohort of 461 patients with morbid obesity. In their study, changes in eGFR correlated with %TWL and %EWL. The authors also showed progressive improvement of the eGFR over a 5-year follow-up in a subgroup of 19 patients with impaired renal function at baseline. In our cohort, the mean increase of eGFR was 1.7 ml/min/1.73 m² and 4.5 ml/min/1.73 m² in the entire group and in the subgroup of patients with impaired baseline renal function, respectively. This eGFR improvement may seem low as absolute value but clinically important. In fact, morbidly obese patients have faster degradation of renal function compared to normal weight individuals [23]. Therefore, the increase of eGFR following bariatric surgery translates a stabilization of renal function in patients with morbid obesity.

In our study, the eGFR was lower at 1-year post-surgery for patients with baseline glomerular hyperfiltration (eGFR > 120 ml/min/1.73 m²). Our results confirm those of the study of Clerte et al. [2] who showed a post-bariatric surgery decrease in the measured GFR, using the plasma iohexol clearance test, for a small group of morbidly obese patients with baseline renal hyperfiltration [2]. Previous biopsy studies showed that nephron hypertrophy and an increased number of glomerular capillaries are early events in obesity-related renal injury [24 25]. Rebelos et al. [26] recently reported that morbidly obese patients without chronic kidney disease show higher renal blood flow and cortical perfusion than lean controls, which reverses 6 months after bariatric surgery. Obesity-associated systemic hypertension increases glomerular blood flow through afferent arteriole dilation, thus partially explaining glomerular hyperfiltration in obese patients [27]. This phenomenon promotes arteriosclerotic changes and further progressive renal damage. Glomerular hyperfiltration can therefore be considered as an early signal of renal injury in obese patients. Thus, the decrease of the eGFR observed following sleeve gastrectomy in our subgroup of obese patients with baseline glomerular hyperfiltration translates into an improvement in renal function and probably slower degradation of the renal reserve. In accordance with this hypothesis, a recent study showed that obesity is associated with degradation of

**Table 2** Baseline characteristics of patients with versus without a follow-up evaluation at one year post-bariatric surgery

|                        | One-year evaluation (N=448) | Lost to follow-up (N=115) | p     |
|------------------------|-----------------------------|---------------------------|-------|
| Age (years)            | 42.2±0.6                    | 37.3±1.3                  | <0.0001|
| Male                   | 92 (20.5%)                  | 32 (27.8%)                | ns    |
| BMI (kg/m²)            | 43.3±0.3                    | 44.4±0.7                  | ns    |
| Hypertension           | 137 (30.9%)                 | 33 (28.7%)                | ns    |
| Type 2 diabetes        | 91 (20.5%)                  | 22 (19.1%)                | ns    |
| Dyslipidemia           | 144 (32.6%)                 | 27 (23.5%)                | 0.05  |
| Creatinine (µmol/L)    | 82.8±2.2                    | 84.2±8.5                  | ns    |
| Uric acid (mmol/L)     | 349.4±7.5                   | 352.7±7.5                 | ns    |
| eGFR (ml/min/1.73 m²)  | 86.1±2.3                    | 94.3±2.3                  | <0.0001|
| Fasting blood glucose (mmol/L) | 6±2.0          | 5.9±0.2                  | ns    |
| HbA1c (%)              | 5.9±0.1                     | 5.9±0.1                   | ns    |
| Insulin (mmol/L)       | 24.9±0.4                    | 26.7±0.4                  | ns    |
| AST (IU/L)             | 31.1±1.3                    | 29.1±1.3                  | ns    |
| ALT (IU/L)             | 43.2±2.8                    | 44.3±2.8                  | ns    |
| GGT (IU/L)             | 46.7±3.6                    | 44.9±3.6                  | ns    |
| Cholesterol (mmol/L)   | 5.36±0.09                   | 5.12±0.09                 | ns    |
| Serum triglycerides (g/L) | 1.48±0.07                 | 1.43±0.07                 | ns    |
| TE (kPa)               | 7.6±0.4                     | 7.8±0.5                   | ns    |
| CAP (dB/m)             | 306.3±0.5                   | 319.1±7.5                 | ns    |
| Steatosis              | 297 (81.2%)                 | 79 (80.6%)                | ns    |
| NASH                   | 144 (39.6%)                 | 33 (33.7%)                | ns    |
| Significant fibrosis (F ≥ 2) | 79 (21.7%)            | 21 (21.9%)                | ns    |

Results are shown as the mean± standard error of the mean or n (%). (SEM, standard error of the mean)

*BMI* body mass index, eGFR estimated glomerular filtration rate, *HbA1c* glycated hemoglobin, AST aspartate aminotransferase, ALT alanine aminotransferase, GGT gamma-glutamyl transferase, TE transient elastometry, CAP controlled attenuation parameter, NASH non-alcoholic steatohepatitis

Significant improvement of liver function tests (Table 3). Furthermore, the degree of liver steatosis and fibrosis as assessed by controlled attenuation parameter (CAP) (225.3±5.2 versus 307.3±5.4 dB/m; p < 0.0001) and transient elastometry (7.6±0.4 versus 5.9±0.2 kPa; p < 0.0001), respectively, significantly decreased post-surgery. Serum markers of low-grade chronic inflammation (C-reactive protein and ferritin) and metabolic parameters significantly improved at 1-year post-surgery (Table 3). The evolution of comorbidities and main biologic parameters are presented in Table 3.

**Discussion**

In this homogenous prospective cohort of 448 morbidly obese patients undergoing sleeve gastrectomy, renal function assessed by eGFR globally improved 1-year post-surgery.
the eGFR during a 3-year follow-up of kidney transplant recipients [28].

Accurate evaluation of renal function by plasma creatinine-based eGFR is problematic in obese patients, especially when surgery could lead to a reduction of muscle mass. Radiolabel- and non-radiolabel-based methods for measuring GFR are the gold standard but are complicated to perform in routine practice and are expensive [29]. Plasma creatinine alone is a poor marker of renal function impairment, as it depends on the rate of creatinine production by the muscles. Therefore, methods to estimate the GFR using plasma creatinine and anthropometric data, such as the Cockcroft and Gault formula, have been developed. However, morbidly obese patients have a disproportional amount of fat mass relative to lean mass [30], and these methods overestimate the GFR. The use of equations that do not include total body weight may theoretically overcome the issue of fat mass over-representation in obesity. Friedman et al. [31] showed...
that the CKD-EPI creatinine-cystatin C equation accurately estimates the GFR of morbidly obese patients. However, the CKD-EPI creatinine equation also performed adequately in this patient group and we therefore used it in our study in the absence of routine cystatin C level assessment. Furthermore, a recent study suggests that CKD-EPI equation is the best method to estimate GFR in severely obese patients in the absence of measured GFR [15].

Aside from the loss of fat mass, sleeve gastrectomy also induces a decrease in skeletal muscle mass, as previously shown using CT cross-sections to estimate FFM [10]. Muscle mass loss influences plasma creatinine levels and may therefore falsely increase the eGFR in the absence of a true modification. In our study, patients whose eGFR increased 1 year post-sleeve gastrectomy showed similar absolute weight loss and %TWL as those whose eGFR did not. Furthermore, post-surgery changes in the eGFR did not correlate with the amount of skeletal muscle loss as evaluated on CT-scan images. Overall, these data suggest that the post-bariatric surgery changes of eGFR described in our cohort of morbidly obese patients is not related to FFM loss and may reflect a true improvement in renal function. Sleeve gastrectomy is a highly effective treatment for weight-loss and therefore induces a more favorable metabolic environment with hypertension and diabetes regression. Furthermore, our study showed a significant improvement in markers of chronic low-grade inflammation (meta-inflammation) such as C reactive protein and ferritin which may also contribute to renal function stabilization. Therefore, weight loss is necessary to slow degradation of renal function in morbidly obese patients but insufficient in some of them.

Our study had a number of strengths, including its prospective design and the high number of included patients undergoing sleeve gastrectomy as the only bariatric surgery procedure. Another strength was the availability of FFM evaluation before and after surgery, which allowed us to assess the relationship between FFM loss and evolution of the eGFR.

Our study also had several limitations. First, we used the CKD-EPI equation to estimate the GFR rather than cystatin C, as it was not routinely performed at our institution. However, the use of the CKD-EPI creatinine equation has already been validated in morbidly obese patients and post-surgery changes of skeletal muscle mass did not appear to influence the evolution of the eGFR in our cohort. Second, a measured GFR was not available in our cohort. Nevertheless, the available methods to measure the GFR are too laborious to be used in clinical practice. Third, we only had follow-up data at 1-year post-surgery. However, the rate of

| Table 3 Evolution of comorbidities and biologic parameters at one year post sleeve gastrectomy |

| Parameter                        | Pre sleeve (N=448) | Post sleeve (N=448) | p     |
|----------------------------------|--------------------|---------------------|-------|
| eGFR (ml/min/1.73 m²)            | 86.1±0.9           | 87.8±0.9            | <0.01 |
| BMI (kg/m²)                      | 43.3±0.3           | 31.5±0.3            | <0.0001 |
| Hypertension (%)                 | 138 (30.9%)        | 51 (11.5%)          | <0.0001 |
| Type 2 diabetes (%)              | 92 (20.5%)         | 48 (10.6%)          | <0.0001 |
| Dyslipidemia (%)                 | 146 (32.6%)        | (9.8%)              | <0.0001 |
| Creatinine (µmol/L)              | 82.8±2.2           | 81.2±2.5            | 0.012 |
| Uric acid (mmol/L)               | 349.8±4            | 291.2±3.8           | <0.0001 |
| Fasting blood glucose (mmol/L)   | 6±0.2              | 4.8±0.1             | <0.0001 |
| HbA1c (%)                        | 5.9±0.1            | 5.4±0.1             | <0.0001 |
| Insulin (mmol/L)                 | 25±0.8             | 8.9±0.3             | <0.0001 |
| Cholesterol (mmol/L)             | 5.36±0.08          | 5.6±0.17            | ns    |
| HDL cholesterol (mmol/L)         | 1.28±0.03          | 1.52±0.03           | <0.0001 |
| Serum triglycerides (g/L)        | 1.48±0.05          | 0.99±0.03           | <0.0001 |
| CRP (mg/L)                       | 11.9±0.6           | 7.6±0.9             | <0.0001 |
| Ferritin (ug/L)                  | 124.8±7.3          | 107.5±5.6           | 0.003 |
| AST (IU/L)                       | 31.1±1.3           | 22.2±0.5            | <0.0001 |
| ALT (IU/L)                       | 43.2±2.8           | 24.2±1.3            | <0.0001 |
| GGT (IU/L)                       | 46.7±3.6           | 27±1.3              | <0.0001 |
| TE (kPa)                         | 7.6±0.4            | 5.9±0.2             | <0.0001 |
| CAP (db/m)                       | 307.3±5.4          | 225.3±5.2           | <0.0001 |

Results are shown as the mean ± standard error of the mean or n (%). (SEM, standard error of the mean)

eGFR estimated glomerular filtration rate, BMI body mass index, HbA1c glycated hemoglobin, HDL high-density lipoprotein, CRP C reactive protein, AST aspartate aminotransferase, ALT alanine aminotransferase, GGT gamma-glutamyl transferase, TE transient elastometry, CAP controlled attenuation parameter
loss to follow-up was only around 20%, similar to previous results from tertiary centers. Furthermore, improvement of the eGFR mainly occurs during the first year after bariatric surgery. It should also be mentioned that measurement of albuminuria is not systematically performed in patients requiring bariatric surgery and therefore was not available in our study.

In conclusion, our results show that renal function of morbidly obese patients is significantly improved at 1-year post-sleeve gastrectomy. This improvement was defined by an increase in the eGFR in the sub-group with a low baseline GFR and a decrease in the eGFR of those with baseline renal hyperfiltration. The post-sleeve evolution of the eGFR was independent of changes in skeletal muscle mass.

Authors’ contributions CSV, SN, and GP performed study conceptualization and design. DS, AL, SS, SN, and CSV performed data collection. CV and SN performed data analysis. All authors were involved in the interpretation of the data. DS and CSV edited the manuscript. PL, HT, KL, SP, MN, MG, MZ, AB, and ID provided revision. All authors approved the final version to be published.

Declarations

Competing interests The authors declare no competing interests.

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