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Controversies in Bariatric Surgery

Longitudinal assessment of renal function in native kidney after bariatric surgery

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Abstract The epidemic of obesity parallels that of chronic kidney disease (CKD). Obesity worsens the course of CKD, mainly defined by an abnormal glomerular filtration rate (GFR). Patients with severe obesity stages (II and III with body mass index >35 kg/m^2) are eligible for bariatric surgery (BS), which is the most efficient method of achieving durable weight loss. BS may reverse glomerular hyperfiltration and albuminuria, improve adipocytokine profile, and relieve diabetes and hypertension. Obesity remission after BS might prevent the progression of renal failure in populations with morbid obesity. However, evidence for the beneficial effect of BS on renal function is scant. This lack of knowledge is mainly due to methodologic reasons, which are addressed in this review. The reversibility of hyperfiltration due to the presence of functional renal reserve hampers the interpretation of changes in true GFR after BS. This true GFR is only obtained with the renal clearance of an exogenous filtration marker. Estimation of GFR is generally provided by prediction equations, namely by modification of diet in renal diseases or by chronic kidney disease–epidemiology collaborative group. These equations are not accurate because the serum levels of both creatinine and cystatin C depend on extrarenal factors, which are modified by BS. Comparing the slopes of measured GFR according to various durations of exposure with morbid obesity would be critical in providing reliable data. Herein, we review the current knowledge on the effects of BS on kidney function; we specify the methodologic issues and particularities of the dietary management of CKD patients to propose reliable directions for future clinical research. (Surg Obes Relat Dis 2018;xxx:xxx–xxx.) © 2018 American Society for Bariatric Surgery. Published by Elsevier Inc. All rights reserved.

Keywords: Morbid obesity; Bariatric surgery; Chronic kidney disease; Hyperfiltration; Functional renal reserve; Glomerular filtration rate

Chronic kidney disease (CKD) is defined by an abnormal glomerular filtration rate (GFR) and/or signs of renal injury such as albuminuria, hematuria, leukocyturia, morphologic, and/or histologic changes [1]; CKD stages are defined by the level of GFR (Table 1). Hyperfiltration has

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Table 1
GFR levels define CKD stages.

Stage 1	Normal GFR 90–120 mL/min/1.73 m^2
Stage 2	Mildly decreased GFR 60–89 mL/min/1.73 m^2
Stage 3	Moderately decreased GFR 30–59 mL/min/1.73 m^2
Stage 4	Severely decreased GFR 15–29 mL/min/1.73 m^2
Stage 5	Kidney failure: GFR <15 mL/min/1.73 m^2

GFR = glomerular filtration rate; CKD = chronic kidney disease.

a GFR >120 mL/min/1.73 m^2. Normal GFR is 120 to 90 mL/min/1.73 m^2. Renal failure is characterized by a GFR <90 mL/min/1.73 m^2 (stages 2, 3, and 4), and end-stage renal disease has a GFR <15 mL/min/1.73 m^2 (stage 5). The kidneys present a definite number of nephrons that cannot increase after birth. Patients with preterm and low birth weights have a decreased number of nephrons. Women have a slightly lower number of nephrons compared with men. In a healthy kidney, every single nephron has a functional filtration reserve [2]. In obesity, the functional renal reserve is recruited, as demonstrated by the diminution of GFR after bariatric surgery (BS), which is due to recovery from hyperfiltration. Recruitment of functional renal reserve occurs in transplanted kidneys as well because this depends on visceral obesity [3,4]. Functional renal reserve decreases with the presence of CKD, with hypertension, and with age, leading to glomerulosclerosis [2]. Moreover, long-lasting hyperfiltration causes renal lesions called secondary focal segmental glomerulosclerosis [5] and reduces GFR [4,6,7].

Obesity is a risk factor for kidney disease, independently from diabetes and hypertension, because the kidneys have to cope with hyperfiltration in the context of a deleterious adipocytokine profile. Currently, 1 in every 2 CKD patients is obese, and this trend is not expected to reverse [8]. Obesity (class I–III) may accelerate the decline of renal function in patients with prior kidney diseases [9,10]. Obesity class II (BMI 35–40 kg/m^2) and III (BMI >40 kg/m^2) increase the risk for end-stage renal disease by 6- and 7-fold, respectively [11]. Clinical care in nephrology aims at correcting hyperfiltration, preventing renal function decline in stages 1 to 4, and replacing insufficient kidney function with maintenance dialysis and/or kidney transplantation in stage 5.

There has been an exponential increase of BS in recent years in concomitance with the obesity epidemic and the adaptation of the laparoscopic technique with bariatric procedures. The 3 main bariatric procedures that are currently performed worldwide include gastric banding, the Roux-en-Y gastric bypass, and the sleeve gastrectomy. BS can achieve dramatic and durable weight loss [12]. The beneficial effect of BS on the progression of renal disease may be expected because it reduces hyperfiltration [13,14], decreases albuminuria [15,16], allows positive changes in adipocytokine profile [17], and improves the control of diabetes and hypertension [18,19], which are major causes of end-stage renal disease.

Characterizing the renal function of morbidly obese patients and studying its evolution after BS are real challenges and critical issues. The gold-standard method to assess GFR is the measurement of the renal clearance of an exogenous filtration tracer (inulin, ^{51}Cr-EDTA, ^{125}I-iothalamate, iohexol). However, most studies have used estimations of GFR obtained with prediction equations (Table 2), mainly modification of diet in renal diseases and CKD-EPI (chronic kidney disease–epidemiology collaboration). In this review, our purpose was to discuss the results of the most relevant studies considering GFR changes in the same patients before and after BS (Table 3). Most particularly, we addressed the technical aspects and the limits of the methods used to assess GFR (Tables 4 and 5) to provide a useful background for designing future studies.

Assessment of kidney function

Kidney function is best defined by GFR, which is the main limiting factor for soluble waste disposal. The gold-standard method to obtain GFR is the measurement of the renal clearance of an exogenous filtration tracer. This measure gives the true GFR or the measured GFR (mGFR). After a single injection or during the continuous infusion of inulin, ^{51}Cr-EDTA, ^{125}I-iothalamate, or iohexol, blood and urine samples are drawn regularly at predefined time intervals to calculate the mean value of the renal clearance (Table 2). Before this procedure, hydration level and concomitant medications are standardized [20–22]. These precautions are usual and of paramount importance when comparing mGFR before and after BS because various drugs have profound hemodynamic effects on the glomerulus (i.e., insulin, diuretics, and renin angiotensin aldosterone system blockers may be stopped after remission and/or improvement of diabetes and/or blood pressure after BS) [19,23]. Measurement of the renal clearance of an exogenous filtration marker is adapted for cohort studies but not for everyday practice because it is time-consuming and costly.

Prediction equations have been obtained by regression analysis in various populations where GFR was measured by the gold-standard method. The following variables were used to coin the equations: the serum level of creatinine or cystatin C (endogenous filtration markers), age, sex, and ethnicity [24,25]. These equations give an estimated GFR (eGFR) indexed to body surface area (BSA; mL/min/1.73 m^2). Indeed, weight was not entered in the formulas because their main purpose is to allow the comparison of the filtration capacity between people with diverse corpulences. The BSA of 1.73 m^2 is "standard" of a 70-kg and 160-cm adult (Table 2). In fact, to have a normal GFR of 100 mL/min/1.73 m^2, a very small patient with half the mean standard BSA would only require a GFR of 50

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