U.PORTO

MESTRADO INTEGRADO EM MEDICINA

Impact of Kidney Function on Bariatric Surgery's Outcomes

João Miguel da Costa Martins Pereira

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2023

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João Miguel da Costa Martins Pereira

jpereira141999gmail.com

Mestrado Integrado em Medicina
Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto

Orientadora

Professora Doutora Mariana P. Monteiro

Professora Catedrática
Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto

Coorientadora

Professora Doutora Sofia S. Pereira

Professora Auxiliar
Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto

Junho, 2023

Porto, 1 de junho de 2023

Assinado por: **João Miguel da Costa Martins Pereira**
Num. de Identificação: 15487562
Data: 2023.06.01 01:43:31+01'00'

João Pereira

CHAVE MÓVEL

Assinado por: **LÍDIA MARIANA RODRIGUES PEREIRA MONTEIRO**
Num. de Identificação: 09782915

Mariana P. Monteiro

CHAVE MÓVEL

Assinado por: **Sofia Daniela da Silva Pereira**
Num. de Identificação: 13305686
Data: 2023.06.01 10:58:44+01'00'

Sofia S. Pereira

CHAVE MÓVEL

Ao avô, Joaquim;
Aos meus pais, António e Fernanda;
Ao meu irmão, Nélson;
À minha cara-metade, Andreia;
Aos meus melhores amigos, Diogo Rodrigues, Diogo Oliveira, João Silva e José Marques.

Acknowledgments | Agradecimentos

Antes de mencionar as pessoas que direta ou indiretamente contribuíram para este projeto, a primeira palavra tem de ser dirigida aos doentes. Assim, agradeço aos mesmos por terem aceitado participar neste estudo, num ato altruísta que visa contribuir para o conhecimento científico e para a melhoria da prática clínica.

Posto isto, gostaria de agradecer à minha orientadora, Professora Mariana Monteiro, por todo o apoio e acompanhamento durante o meu período de investigação e durante a escrita da minha dissertação. Para além de uma excelente professora, a Professora Mariana é um exemplo no que diz respeito à sua organização, liderança, perseverança e capacidade de orientação, qualidades que a fazem uma excelente cientista. Sem a professora, a elaboração desta dissertação teria sido muito mais complicada.

Adicionalmente, agradeço à minha coorientadora, Professora Sofia Pereira, pela sua omnipresença durante este período de investigação, bem como pela sua positividade, paciência e disponibilidade para esclarecer todas as minhas dúvidas. Foi um prazer trabalhar ao seu lado, num gabinete cheio de alegria e boa disposição, independentemente das adversidades que foram surgindo.

À Professora Marta Guimarães, expresso a minha gratidão pela sua disponibilidade para me auxiliar, quer na colheita de dados, quer no esclarecimento de dúvidas que foram surgindo, pela maneira como sempre me recebeu no Centro Hospitalar de Entre o Douro e Vouga e pelo contacto com os doentes visados neste estudo.

Ao Dr. Pedro Reis Pereira, um grande agradecimento pela amizade que criamos, pela sua preocupação e dedicação para com o meu trabalho e para com o meu bem-estar. Obrigado pelo auxílio na colheita de dados, pelas discussões de ideias e de temáticas que enriqueceram este trabalho.

À equipa multidisciplinar de tratamento de obesidade do Centro Hospitalar de Entre o Douro e Vouga, agradeço a disponibilidade em acompanhar os doentes, quer nas consultas, quer nos atos cirúrgicos em si.

Agradeço aos meus colegas de trabalho na UMIB, Sara, António, Sofia, Madalena e Ana, pelo companheirismo, camaradagem, espírito de equipa e de entreajuda que demonstraram ao longo deste período. Sinto-me grato pelo ambiente de trabalho que criaram e pela maneira como me receberam no Departamento de Anatomia do ICBAS.

Um agradecimento ao meu colega e melhor amigo Diogo Rodrigues, pelo seu apoio, críticas e ideias durante este período de investigação. Ademais, agradeço o seu rigor, persistência, carinho e auxílio durante estes últimos 6 anos, contribuindo para o meu crescimento pessoal, científico e profissional.

Agradeço também aos professores que mais me marcaram durante o meu percurso académico, pelo seu brio científico e médico, contribuindo também para a realização deste trabalho. Assim, destaco o papel do professores Dr. João Araújo Correia, Dr. Vital Domingues, Dra. Ana Campar, Dr. Rui Sarmento e Castro, Dr. Castro Poças, Dra. Luísa Lobato, Dr. João Chaves, Dr. Pedro Leuschner, Dr. Rui Henrique e Dr. Artur Águas.

Por último, um agradecimento final à minha família, à Andreia e aos meus amigos Diogo Oliveira, João Silva e José Marques por todo o apoio e suporte emocional, particularmente ao longo deste período de investigação e da realização deste trabalho.

Funding | Financiamento

Esta dissertação está integrada no plano estratégico da Unidade Multidisciplinar de Investigação Biomédica (UMIB/ITR - UIDB/00215/2020, UIDP/00215/2020 e LA/P/0064/2020) e nos objetivos do projeto de I&D "PTDC/MEC-CIR/3615/2021 Unravelling the molecular signatures and mechanisms associated with obesity surgery failure", ambos financiados pela Fundação para a Ciência e Tecnologia (FCT).

This dissertation is contemplated in the strategic plan of the Unit for Multidisciplinary Research in Biomedicine (UMIB/ITR - UIDB/00215/2020, UIDP/00215/2020 e LA/P/0064/2020) and in the objectives of the R&D project "PTDC/MEC-CIR/3615/2021 Unravelling the molecular signatures and mechanisms associated with obesity surgery failure", both financed by the FCT.

«Mistakes are also important to me. I don’t cross them out of my life, or memory. And I never blame others for them.»

Andrzej Sapkowski, *Blood of Elves*

Resumo

Introdução: A perda de peso obtida através da cirurgia bariátrica demonstrou ser eficaz na reversão da disfunção renal associada à glomerulopatia relacionada com a obesidade. No entanto, ainda existe pouca informação quanto ao impacto da função renal na eficácia da cirurgia bariátrica quanto à perda de peso.

Objetivo: Avaliar o impacto da função renal pré-operatória nos resultados da perda de peso até um ano após a cirurgia bariátrica.

Métodos: Doentes com obesidade candidatos a serem submetidos a cirurgia de *bypass* gástrico (N=127) realizaram uma colheita de urina de 24 horas no pré-operatório para avaliar a taxa de depuração de creatinina, taxa de filtração glomerular estimada (TFGe), proteinúria e albuminúria. Os dados antropométricos foram recolhidos para calcular o índice de massa corporal (IMC), a perda de peso total (PTE) e a perda de excesso de IMC (PEIMC) aos 6 e 12 meses após a cirurgia.

Resultados: Os participantes tinham uma média de IMC pré-operatório de 39.6 ± 3.0 kg/m2. Destes, 56.7% apresentavam uma taxa de depuração de creatinina superior a 130 mL/min, 23.6% proteinúria > 150 mg/24h e 15.0% albuminúria > 30 mg/24h. Não foram encontradas correlações significativas entre as métricas de perda de peso e a taxa de depuração da creatinina pré-operatória, proteinúria ou albuminúria. Os doentes com valores mais elevados de TFGe apresentaram valores mais elevados de PTE e PEIMC durante o período de seguimento. Apenas um doente não atingiu os critérios de sucesso do PEIMC aos 12 meses após a cirurgia.

Conclusão: Os resultados do nosso estudo sugerem que o estado da função renal pré-operatória não parece ter um impacto negativo clinicamente relevante na perda de peso após a cirurgia bariátrica.

Palavras-chave: Cirurgia Bariátrica; Obesidade; Glomerulosclerose Segmentar Focal; Proteinuria; Perda de Peso.

Abstract

Introduction: Weight loss, as achieved through bariatric surgery, was demonstrated to be effective at reversing kidney dysfunction associated with obesity-related glomerulopathy. However, robust data on how does pre-operative kidney status impacts on bariatric surgery weight loss outcomes is still lacking.

Aim: The aim of this study was to evaluate the impact of pre-surgical kidney function on weight loss outcomes up to one year after bariatric surgery.

Methods: Patients with obesity to be submitted gastric bypass surgery (N=127) underwent a pre-operative 24-hour urine collection to evaluate creatinine clearance rate, eGFR, proteinuria and albuminuria. Anthropometric data was collected to calculate body mass index (BMI), total weight loss (TWL) and excess BMI loss (EBMIL) at 6 and 12 months after surgery.

Results: Patients had a mean pre-operative BMI of 39.6 ± 3.0 kg/m^2. Among these, 56.7% had a creatinine clearance rate greater than 130 mL/min, 23.6% had proteinuria > 150 mg/24h and 15.0% had albuminuria > 30 mg/24h. No significant correlations were found between weight loss metrics and pre-operative creatinine clearance rate, proteinuria or albuminuria. Patients with higher values of eGFR had higher values of TWL and EBMIL during follow-up period. Only one patient did not achieve the EBMIL success criteria at 12 months after surgery.

Conclusion: Our data suggests that pre-operative kidney status does not seem to have a clinically relevant negative impact on bariatric surgery weight-loss outcomes.

Keywords: Bariatric surgery; Obesity; Focal Segmental Glomerulosclerosis; Proteinuria; Weight Loss.

List of abbreviations

BMI	Body Mass Index
BSA	Body Surface Area
CKD	Chronic Kidney Disease
CKD-EPI	Chronic Kidney Disease
EBMIL	Excess Body Mass Index Loss
eGFR	estimated Glomerular Filtration
ESRD	End Stage Renal Disease
GFR	Glomerular Filtration Rate
HbA1c	Glycated Haemoglobin
ORG	Obesity Related Glomerulopathy
RAAS	Renin Angiotensin Aldosterone System
TWL	Total Weight Loss

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Introduction

The number of patients with obesity or overweight is increasing at a rapid pace worldwide, as well as the risk of obesity related complications, leading to a substantial social-economic burden[1].

Obesity is associated with a form of glomerular involvement coined obesity-related glomerulopathy (ORG). In the absence of histological confirmation, slowly progressive proteinuria within the subnephrotic range in a patient with obesity can be used as a surrogate diagnostic marker for ORG, provided other causes of renal are not suspected[2]. Histologically, ORG characteristic features include glomerulomegaly and focal segmental glomerulosclerosis, which is typically perihilar, although it can affect any portion of the glomerulus[3]. Studies suggest that the predominance of perihilar sclerosis could be explained by the increased filtration demands and dilation of the afferent arteriole, which leads to an increase in ultrafiltration pressure[4]. As the disease progresses, glomeruli enlarge and podocytes' density decreases, aggravating the segmental sclerosis and the overall renal function[5, 6, 7]. Although most patients have stable or slowly progressive proteinuria, up to one-third of individuals can develop progressive renal failure and end-stage renal disease (ESRD)[3, 8, 9, 10]. Notwithstanding, studies have shown that hyperfiltration and proteinuria can be improved, provided sustained weight loss is achieved either with medical interventions, or with bariatric surgery[2].

Bariatric surgery is an effective intervention to achieve significant and sustained weight loss in patients with obesity and obesity related disorders, in whom other conservative interventions have proved to be ineffective[11, 12, 13, 14]. The weight loss achieved through bariatric surgery and obesity comorbidities improvements are known to be influenced both by pre-operative and post-operative patient characteristics[15]. The pre-operative factors recognized to have the greatest impact on weight loss are: pre-operative body weight and body mass index (BMI), presence of eating disorders, such as binge eating or food addiction[16, 17], presence of type 2 diabetes mellitus[17], residual β-cell function[18], glycated haemoglobin (HbA1c) and fasting blood glucose levels[15]; additionally, genetic, dietary and anatomic factors were also shown to have a potential impact on bariatric surgery weight loss outcomes[17, 19].

A previous retrospective study has shown that patients with advanced chronic kidney disease (CKD) (stages 4 and 5) experienced worse weight loss outcomes at 6 and 12 months of follow-up after bariatric surgery, when compared to patients with other stages of CKD[20]. In contrast, another retrospective study that compared bariatric surgery weight loss outcomes across patients with CKD stages 1, 2, 3a and 3b, did not find any significant differences at 6 and 12 months of follow-up[21]. However, both of these studies relied on CKD-EPI equations indexed to body surface area to

estimate glomerular filtration rate (GFR), which is not the most reliable surrogate measure for kidney function in patients with obesity[2, 22]. Additionally, in these studies, albuminuria or proteinuria were not evaluated and they included patients with type 2 diabetes mellitus, two features that could have impacted on data interpretation.

This being said and in order to contribute to fill this knowledge gap, the aim of this study was to evaluate the impact of pre-operative kidney function on weight loss outcomes after bariatric surgery, utilising the creatinine clearance rate, estimated glomerular filtration rate (eGFR), proteinuria and albuminuria.

Methods

Study population

Subjects enrolled in this study were recruited at a single academic public centre among obesity surgery candidates from 2019 to 2022, after approval by the institutional ethical review board (approval number: CA-014/20 0t_MP/CC). Patients with obesity were considered eligible for bariatric surgery if presented a BMI higher than 40 kg/m^2 or a BMI higher than 35 kg/m^2 in the presence of obesity-related comorbidities, provided there were no contraindications for the procedure. Obesity surgery candidates who accepted to participate (n=236) underwent a 24-hour urine analysis to assess urinary creatinine, albumin and total proteins' values, in addition to the pre-established pre-operative routine evaluations, which included complete blood count, fasting blood glucose, HbA1c, lipid profile, creatinine, urea, albumin and total proteins serum levels.

Patients who have had a prior bariatric intervention, candidates for revision surgery procedures, or submitted to any bariatric surgery procedure other than gastric bypass (n=84) were excluded from the study. Patients with a previous history of gestational diabetes, or current diagnosis of diabetes defined as having an HbA1c ≥ 6.5% or treated with anti-diabetic drugs, regardless of the HbA1c levels (n=15), were also excluded, since these conditions were demonstrated to have a negative impact on bariatric surgery weight loss outcomes. Additionally, in order to avoid the potential bias of inadequate 24h urine sample collection, patients with a 24-urine collection volume under 800 mL were also excluded (n=10), leading to the final number of patients in this study for data analysis (n=127) **(Figure 1)**.

Data collection

Data concerning preoperative body weight, height, BMI, comorbidities, ongoing medications, blood pressure, complete blood count, fasting blood glucose, HbA1c, lipid profile, creatinine, urea, albumin and total proteins serum levels was collected and registered. The patients were given oral and written instructions regarding the 24-hour urine collection.

The 24-hour creatinine clearance [(urine creatinine concentration [mg/dL] $\times$ total urine volume [mL/24]) $\div$ (serum creatinine concentration [mg/dL] $\times$ 1440)], along with the eGFR, calculated with the 2021 CKD-EPI creatinine equation[23], were used to assess kidney function.

Anthropometric data was used to calculate BMI [weight (kg) $\div$ height^2 (m2)], percentage of EBMIL [(preoperative BMI - postoperative BMI) $\div$ (preoperative BMI - 25) $\times$ 100] and percentage of TWL [(preoperative weight – postoperative weight) $\div$ preoperative weight $\times$ 100].

After bariatric surgery, patients were followed by a multidisciplinary team which included surgeons, endocrinologists, psychologists and nutritionists. At 6 and 12 months after surgery, patients underwent a revaluation of the aforementioned parameters during routine follow-up visits. The primary outcome of this study was the % of total weight loss (%TWL) and the % of excess BMI loss (%EBMIL).

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) and categorical values as percentage, unless otherwise specified. The Kolmogorov-Smirnov test was used to determine the normality of the continuous variables. Comparison of two independent variables was performed by using either the Pearson correlation coefficient, or the Spearman correlation coefficient, as appropriate depending on the normality. A correlation coefficient value of 0-0.19 is defined as very weak, 0.2-0.39 as weak, 0.40-0.59 as moderate, 0.6-0.79 as strong and 0.8-1 as very strong correlation. To compare two non-parametric variables, the Mann-Whitney test was used, while the unpaired T-Test was used to compare two parametric variables. To compare three or more variables, the One-way ANOVA test or the Kruskal-Wallis test was performed according to the normality distribution of the variables. A P-value < 0.05 was considered statistically significant. Statistical analysis was carried out using GraphPad (Prism; Version 9.5.1) and SPSS (IBM; Version 27.0) for Windows.

Results

Subjects

Our final patient cohort (n=127) encompassed predominantly females (n=104; 81.9%) over males (n=23; 18.1%), in parallel to the sex proportion attending our obesity clinic, as previously reported[24, 25]. There were no follow-up dropouts reported. At the time of surgery, the patients' mean age was 42.7 ± 10.9 years, and the mean BMI was 39.6 ± 3.0 kg/m^2. Detailed patients' clinical and biochemical characteristics are depicted on **Table I**.

Preoperative kidney function markers

Patients had an average serum creatinine of 0.8 ± 0.1 mg/dL and average serum urea of 30.9 ± 7.6 mg/dL. The mean creatinine clearance was 145.3 ± 39.2 mL/min, with the average eGFR being 105.0 ± 12.9 mL/min/1.73 m^2. Creatinine clearance was higher than 130 mL/min in 56.7% (n=72) of patients and higher than 170 mL/min in 27.6% (n=35). Creatinine clearance was lower than 130 ml/min in 43.3% (n=55) of patients, and lower than 90 mL/min in 3.2% (n=4). According to the eGFR, the majority of patients (85.8%, n=109) were classified as CKD stage G1, with the remaining (14.2%, n=18) being classified as stage G2[26]. Proteinuria was higher than 150 mg/24h in 23.6% (n=30) of patients, while albuminuria was higher than 30 mg/24h in 15.0% (n=19) of patients[26] **(Table I).**

Postoperative anthropometric characteristics

After bariatric surgery, there was a statistically significant reduction in body weight and BMI during the follow-up period (39.6 kg/m^2 pre-operatively, 27.7 kg/m^2 at 6 months, 25.0 kg/m^2 at 12 months, p<0.0001), yielding a TWL of 29.9 % and 36.6 % and EBMIL of 83.1 % and 101.8 % at 6 and 12 months after surgery, respectively. Additionally, only 3 patients (2.4%) did not achieve an EBMIL greater than 50% at 6 months and only 1 patient (0.8%) at 12 months after surgery **(Table II).**

Correlations between kidney function markers and weight-loss measures

A weak positive correlation between pre-operative eGFR and the percentage of TWL at 6 months (r=0.238, p=0.008) and at 12 months (r=0.261, p=0.004), as well as with the percentage of EBMIL at 12 months after surgery (r=0.244, p=0.008) was found. Very weak and weak positive correlations between pre-operative creatinine clearance rate and the percentage of TWL at 6 months (r=0.189, p=0.035) and at 12 months (r=0.201, p=0.029), respectively, were also found,

while no statistically significant correlation was found with the percentage of EBMIL, neither at 6 nor 12 months after surgery. No statistically significant correlations were found between pre-operative 24h proteinuria or albuminuria and the percentage of TWL and EBMIL at 6 and 12 months after surgery **(Table III).**

There were no statistically significant differences in the percentages of TWL and EBMIL at any time point of the follow-up, when comparing patients with different creatinine clearance categories **(Table IV)**. The same was observed when comparing patients with greater creatinine clearance rates (higher than percentile 75 [>172.6 mL/min]), with those with lower creatinine clearance rates (lesser than percentile 25 [<113.9 mL/min]) **(table V)**.

When compared to patients without pre-operative CKD (stage G1), patients with pre-operative stage G2 CKD had statistically lower average percentages of TWL (25.9 ± 5.2% *versus* 30.5 ± 5.7%, p=0.0006, at 6 months; 32.8 ± 5.5% *versus* 37.2 ± 6.3%, p=0.0016, at 12 months), and of EBMIL (73.1 ± 14.4% *versus* 84.8 ± 18.1%, p=0.0104, at 6 months; 93.1 ± 21.1% *versus* 103.2 ± 20.2%, p=0.0037, at 12 months) (**Table VI; Figure 2**). When compared to patients with greater eGFR values (higher than percentile 75 [>114.2 mL/min]), patients with smaller eGFR values (lesser than percentile 25 [<98.3 mL/min]) also had lower percentages of TWL (27.6 ± 5.7% *versus* 31.8 ± 5.1%, p=0.0031, at 6 months; 34.4 ± 5.8% *versus* 39.4 ± 4.9%, p=0.0007, at 12 months) and of EBMIL (76.3 ± 17.5% *versus* 85.1 ± 17.5%, p=0.0478, at 6 months; 94.8 ± 19.8% *versus* 106.1 ± 19.1%, p=0.0061, at 12 months) (**Table VII; Figure 3**).

There were no significant correlations between weight loss metrics and pre-surgical albuminuria's or proteinuria's categories (**Table VIII**).

Discussion

Obesity plays an important role in the development and progression of CKD, along with diabetes mellitus, being one of its leading causes and an independent risk factor for ESRD[27, 28, 29]. Approximately 50% of patients with ORG are estimated to have mild lesions in histological examination that are characteristic of diabetic nephropathy, despite not having any clinical evidence of glucose intolerance[3]. The coexistence of biopsy proven lesions, such as focal or diffuse increases in mesangial matrix, thickening of the glomerular basement membrane, as well as accumulation of intracellular lipid vacuoles in mesangial cells, podocytes and proximal tubular epithelial cells, in both entities is consistent with previous findings that indicate shared molecular pathways in ORG and diabetic nephropathy[3].

Several pre-operative determinants of weight loss and obesity related comorbidities remission induced by bariatric surgery have been identified, with diabetes mellitus being one of them[15, 17]. Despite previous studies demonstrating worse bariatric surgery weight loss outcomes only on patients with eGFR lower than 30 mL/min/1.73m^2, their study designs had some limitations that could have impacted on data interpretation[20, 21]. Therefore, we aimed to investigate whether creatinine clearance rate, eGFR, proteinuria and albuminuria, without the concomitant presence of dysglycaemia, influenced bariatric surgery weight-loss outcomes.

In our study population, over half of the patients (56.7%, n=72) presented a pre-surgical creatinine clearance rate greater than 130 mL/min. Despite not existing any universally accepted creatinine clearance rate threshold to define glomerular hyperfiltration, several studies suggest this threshold falls within the interval from 125 to 175 mL/min/1.73m^2 [30]. Therefore, if this creatinine clearance rate is considered, this suggests that approximately half of our patient population of obesity surgery candidates are likely to have glomerular hyperfiltration, which puts them at particular risk for kidney injury, even in the absence of diabetes[2].

Glomerular hyperfiltration plays a central role in the development and progression of ORG[2]. In patients with obesity, there is a documented overactivation of the renin-angiotensin-aldosterone system (RAAS)[31], in part due to the increased production of its components in adipocytes[32, 33], and also an overactivation of the renal sympathetic nervous system[34]. In turn, these lead to excessive tubular reabsorption of sodium and water[35, 36] that is positively correlated with BMI and waist circumference[37], decreased distal solute delivery, lower activation of tubuloglomerular feedback and vasodilation of the afferent arteriole, leading to an increased transcapillary hydraulic pressure gradient and consequent glomerular hyperfiltration[38].

Additionally, in our study, proteinuria higher than 150 mg/24h and albuminuria higher than 30 mg/24h were identified in 23.4% and 15.0% of the patients, respectively. The prevalence of

proteinuria and albuminuria observed in our patient population is consistent with previous reports in patient cohorts with comparable clinical features[39].

With time, the increased transcapillary hydraulic pressure and glomerular hyperfiltration induces glomerulomegaly through an increase in circumferential and axial capillary wall stress, glomerular tuft enlargement and expansion of the glomerular basal membrane[40]. In turn, this causes a fluid shear stress on podocytes, prompting maladaptive hypertrophy and leading to foot effacement, podocyte detachment and apoptosis with consequent glomerulosclerosis[40]. These structural changes[41], combined with the low circulating adiponectin[42] and the glomerular permselectivity effect of angiotensin II[43], were appointed as contributing factors to the increased prevalence of albuminuria and proteinuria (essentially sub-nephrotic) seen in patients with obesity[44]. Therefore, our data shows that patients with obesity, and without the confounding effect of diabetes, depict not only signs of glomerular hyperfiltration, but also start to show signs of its consequences on renal structure and physiology.

Overall, this study results corroborate our previous report in a larger patient cohort that deterioration of kidney function occurs in a considerable proportion of patients with obesity undergoing bariatric interventions[25]. The prevalence of kidney dysfunction identified in these patients reinforces the need of considering the inclusion of a 24-hour urine analysis on pre-operative routine assessment. This simple measure would allow a more comprehensive assessment of obesity related comorbidities to categorize patient risk, enable a timely diagnosis of kidney dysfunction and ultimately contribute towards improving patient care. For instance, by monitoring renal function markers in the long-term, renoprotective measures could be adopted[3, 8], reducing proteinuria[2].

In order to address our study's primary aim, we assessed whether the abovementioned kidney function markers had a significant impact on weight loss outcomes after bariatric surgery. Our data showed that there were no significant correlations between pre-operative creatinine clearance and any of the weight-loss metrics evaluated, as well as no significant differences when comparing patients with and without glomerular hyperfiltration. This being said, it seems that in a population of patients with obesity and without concomitant diabetes submitted to gastric bypass surgery, pre-operative creatinine clearance and hyperfiltration do not seem to have any clinically relevant effect on weight loss outcomes achieved by bariatric surgery, at least up to 12 months after the procedure. Nevertheless, this observation does not preclude that no differences will be observed over follow-up, for which mid and long-term studies are still needed.

Of particular notice, is the fact that despite no strong correlations were identified between eGFR, and TWL or EBMIL at 6 and 12 months after bariatric surgery, there were statistically significant differences when these parameters were compared between patients with different CKD

stages (G1 and G2), and between the patients with the highest eGFR values and the ones with the lowest values eGFR values. Our results showed that patients with higher eGFR values presented greater TWL (30.5 % *versus* 25.9 % at 6 months; 37.2 % *versus* 32.8 % at 12 months) and EBMIL (84.8 % *versus* 73.1 % at 6 months; 103.2 % *versus* 93.1 % at 12 months) within the first year after bariatric surgery. However, despite these weight-loss differences, at 12 months of follow-up, with the exception of a sole patient without any abnormality in kidney function markers, all patients fulfilled the Halverson and Koehler 50% EBMIL criteria to define successful weight loss after bariatric interventions[45]. Overall, these findings suggest that regardless the statically significant differences, a decreased eGFR or at least CKD stage 1 and 2 is unlikely to have a clinically relevant negative impact on weight-loss achieved through bariatric surgery, at least up to 12 months after the procedure, corroborating the data from literature[21].

Moreover, our data does not show any correlation between preoperative proteinuria and albuminuria values and weight-loss, even when comparing patients with different albuminuria and proteinuria categories. These findings suggest that in our population, even patients with clinically significant albuminuria (greater than 30 mg/24h) or proteinuria (greater than 150 mg/24h), which are a frequent finding in ORG[8], benefit from the weight loss achieved with gastric bypass surgery, in addition to kidney function improvements that were documented in previous studies[46, 47, 48, 49, 50, 51, 52, 53].

This study presents some limitations that must be acknowledged, since these could have impacted on our data interpretation. The eGFR was calculated with the 2021 CKD-EPI creatinine equation, which is indexed for body surface area (BSA) and, therefore is not the best marker to estimate kidney function and GFR in a population of patients with obesity, as pointed by previous studies[2, 22]. Additionally, since our sample size was rather limited, although sufficiently large to disclose some robust statistical differences, these findings require confirmatory studies in larger patient populations.

Nonetheless, our study design also holds some strengths that bolster its accuracy on the proposed objectives, when compared to previous studies[20, 21]. Creatinine clearance rate calculation was not corrected for BSA, in order to prevent the underestimation of GFR in a population of patients with obesity which would conceal glomerular hyperfiltration[22]. Therefore, we are confident that our findings reveal a more accurate estimate of glomerular filtration for this patient population. In addition, we evaluated proteinuria and albuminuria through a 24-hour urine sample, increasing our ability to analyse small variations in albumin and protein excretion rates, as opposed to the alternative use of a spot urine analysis, and we also excluded patients with concomitant diabetes, which could have impacted on our data interpretation.

Conclusion

In summary, this study allowed to demonstrate that the presence of hyperfiltration, proteinuria or albuminuria, does not seem to have a clinically relevant negative impact on bariatric surgery's weight loss outcomes. These findings, if consistent over a longer follow-up period, suggest that even patients with obesity and deterioration of kidney function can achieve good bariatric surgery's outcomes, while potentially benefiting from the improvements in renal function previously reported.

Appendix

Table I – Patients' Preoperative Characterization.

		Total (n=127)
Age (years)		42.7 ± 10.9
Sex	**Male (n, %)**	23 (18.1%)
	Female (n, %)	104 (81.9%)
Weight (kg)		106.4 ± 13.2
BMI (kg/m^2)		39.6 ± 3.0
Hypertension	**No (n, %)**	94 (74.0%)
	Yes (n, %)	33 (26.0%)
Dyslipidemia	**No (n, %)**	93 (73.2%)
	Yes (n, %)	34 (26.8%)
ACE-i	**No (n, %)**	115 (90.6%)
	One (n, %)	12 (9.5%)
ARB	**No (n, %)**	111 (87.4%)
	One (n, %)	16 (12.6%)
CCB dihydropyridine	**No (n, %)**	118 (92.9%)
	One (n, %)	9 (7.1%)
Diuretics	**No (n, %)**	111 (87.4%)
	One (n, %)	14 (11.0%)
	Two (n, %)	2 (1.6%)
Systolic Blood Pressure (mmHg)		132.7 ± 11.8
Diastolic Blood Pressure (mmHg)		79.8 ± 9.0
Glucose (mg/dL)		93.5 ± 27.3
Glycated Hemoglobin (%)		5.4 ± 0.8
Serum Urea (mg/dL)		30.9 ± 7.6
Serum Creatinine (mg/dL)		0.8 ± 0.1
Total Cholesterol (mg/dL)		195.5 ± 34.7
HDL-c (mg/dL)		50.0 ± 11.6
LDL-c (mg/dL)		132.9 ± 35.4
VLDL-c (mg/dL)		26.2 ± 12.8
Triglycerides (mg/dL)		130.9 ± 64.4
Total Proteins (mg/dL)		7.0 ± 0.3
Total Bilirrubin (mg/dL)		0.6 ± 0.3

AST (U/L)		21.6 ± 10.8
GGT (U/L)		29.3 ± 20.3
Alkaline Phosphatase (U/L)		71.8 ± 19.1
24h Diuresis (mL)		1566.0 ± 534.8
24h Albuminuria (mg/24h)		21.3 ± 32.0
24h Proteinuria (mg/24h)		120.2 ± 66.2
24h Urine Creatinine (mg/24h)		1582.2 ± 509.7
eGFR (2021 CKD-EPI Creatinine[23])		105.0 ± 12.9
CKD Category	**G1, n (%)**	109 (85.8%)
	G2, n (%)	18 (14.2%)
	G3a, n (%)	0 (0%)
	G3b, n (%)	0 (0%)
	G4, n (%)	0 (0%)
	G5, n (%)	0 (0%)
Creatinine Clearance (mL/min)		145.3 ± 39.2
Creatinine Clearance Category	**< 90 mL/min, n (%)**	4 (3.2%)
	90 - 130 mL/min, n (%)	51 (40.2%)
	130 - 170 mL/min, n (%)	37 (29.1%)
	> 170 mL/min, n (%)	35 (27.6%)
24h Proteinuria Category	**<150 mg/24h, n (%)**	97 (76.4%)
	>150 mg/24h, n (%)	30 (23.6%)
24h Albuminuria Category	**<30 mg/24h, n (%)**	108 (85.0%)
	>30 mg/24h, n (%)	19 (15.0%)

Continuous variables are presented in mean ± standard deviation.

Abbreviations: BMI, body mass index; ACE-i, angiotensin conversing enzyme inhibitors; ARB, angiotensin II receptor blockers; CCB, calcium channel blockers; HDL-c, high density lipoprotein; LDL-c, low density lipoprotein; VLDL-c, very-low density lipoprotein; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; eGFR, estimated glomerular filtration rate; CKD-EPI, chronic kidney disease-epidemiology; CKD, chronic kidney disease.

Table II – Patients' anthropometric characteristics and evolution.

		Pre-Op	6 Months	12 Months	p-value
Weight (kg)		106.4 ± 13.2	74.5 ± 9.2	66.9 ± 9.7	**<0.0001**
BMI (kg/m²)		39.6 ± 3.0	27.7 ± 2.8	25.0 ± 2.8	**<0.0001**
TWL (%)		-	29.9 ± 5.8	36.6 ± 6.4	**<0.0001**
EBMIL (%)		-	83.1 ± 18.1	101.8 ± 20.5	**<0.0001**
EBMIL Failure/ Success Criteria	**Missing Values**	-	2 (1.6%)	9 (7.1%)	-
	EBMIL < 50 % Failure	-	3 (2.4%)	1 (0.8%)	-
	EBMIL > 50 Success	-	122 (96.1%)	117 (92.1%)	-

Variables are presented in mean ± standard deviation.

P values refer to all possible comparisons between the three different follow-up stages. Significant differences are highlighted in bold.

The "missing values" of EBMIL success criteria refer to patients who skipped the corresponding clinical evaluation.

Abbreviations: BMI, body mass index; TWL, total weight loss; EBMIL, excess BMI loss.

Table III – Correlations between weight loss metrics and kidney function markers.

	2021 CKD-EPI Creatinine - eGFR	Creatinine Clearance	Proteinuria	Albuminuria
TWL 6 Months (%)	R = 0.238 (**p = 0.008**)	R = 0.189 (**p = 0.035**)	R = -0.029 (p = 0.749)	R = 0.136 (p = 0.129)
EBMIL 6 Months (%)	R = 0.171 (p = 0.057)	R = 0.063 (p = 0.482)	R = 0.012 (p = 0.898)	R = 0.126 (p = 0.161)
TWL 12 Months (%)	R = 0.261 (**p = 0.004**)	R = 0.201 (**p = 0.029**)	R = -0.117 (p = 0.208)	R = -0.084 (p = 0.364)
EBMIL 12 Months (%)	R = 0.244 (**p = 0.008**)	R = 0.062 (p = 0.508)	R = 0.025 (p = 0.786)	R = -0.006 (p = 0.950)

"R" correlation's coefficient, Pearson or Spearman, as applicable.

Significant differences are highlighted in bold.

Abbreviations: TWL, total weight loss; EBMIL, excess BMI loss; CKD-EPI, chronic kidney disease-epidemiology; eGFR, estimated glomerular filtration rate.

Table IV – Weight Loss according to pre-operative creatinine clearance's categories.

	Creatinine Clearance Category				p-value
	< 90 mL/min	**90 - 130 mL/min**	**130 - 170 mL/min**	**> 170 mL/min**	
% TWL 6 Months	24.1 ± 6.4	29.4 ± 5.1	30.1 ± 5.9	31.0 ± 5.4	> 0.05
% EBMIL 6 Months	65.3 ± 32.4	83.9 ± 16.2	81.8 ± 17.9	85.3 ± 18.5	> 0.05
% TWL 12 Months	29.6 ± 17.9	36.4 ± 5.3	36.1 ± 6.4	38.3 ± 5.2	> 0.05
% EBMIL 12 Months	80.2 ± 46.7	103.3 ± 18.3	98.4 ± 17.0	106.0 ± 21.8	> 0.05

Variables are presented in mean ± standard deviation.
P values refer to all possible comparisons between the four different categories.
Abbreviations: TWL, total weight loss; EBMIL, excess BMI loss.

Table V – Weight loss according to pre-operative creatinine clearance extreme values.

	Creatinine Clearance Percentile		p-value
	< P25	**> P75**	
% TWL 6 Months	28.7 ± 6.2	31.0 ± 5.5	0.0876
% EBMIL 6 Months	81.2 ± 19.7	85.2 ± 18.9	0.4427
% TWL 12 Months	34.9 ± 8.0	38.0 ± 5.2	0.0615
% EBMIL 12 Months	98.5 ± 24.4	105.4 ± 22.4	0.4102

Variables are presented in mean ± standard deviation. P25: 113.9 mL/min; P75: 172.6 mL/min.
Abbreviations: TWL, total weight loss; EBMIL, excess BMI loss.

Table VI – Weight loss according to pre-operative CKD stages (according to eGFR).

	CKD stage		p-value
	G1	G2	
% TWL 6 Months	30.5 ± 5.7	25.9 ± 5.2	**0.0006**
% EBMIL 6 Months	84.8 ± 18.1	73.1 ± 14.4	**0.0104**
% TWL 12 Months	37.2 ± 6.3	32.8 ± 5.5	**0.0016**
% EBMIL 12 Months	103.2 ± 20.2	93.1 ± 21.1	**0.0037**

Variables are presented in mean ± standard deviation.
Significant differences are highlighted in bold.
Abbreviations: TWL, total weight loss; EBMIL, excess BMI loss.

Table VII – Weight loss according to pre-operative eGFR percentile.

	eGFR Percentile		p-value
	< P25	**> P75**	
% TWL 6 Months	27.6 ± 5.7	31.8 ± 5.1	**0.0031**
% EBMIL 6 Months	76.3 ± 17.5	85.1 ± 17.5	**0.0478**
% TWL 12 Months	34.4 ± 5.8	39.4 ± 4.9	**0.0007**
% EBMIL 12 Months	94.8 ± 19.8	106.1 ± 19.1	**0.0061**

Variables are presented in mean ± standard deviation. P25: 98.3 mL/min; P75: 114.2 mL/min.
Significant differences are highlighted in bold.
Abbreviations: TWL, total weight loss; EBMIL, excess BMI loss.

Table VIII – Weight loss according to pre-operative albuminuria's and proteinuria's classification.

	Albuminuria Classification			Proteinuria Classification		
	< 30 mg/24h	**> 30 mg/24h**	**p-value**	**< 150 mg/24h**	**> 150 mg/24h**	**p-value**
% TWL 6 Months	29.9 ± 5.3	29.7 ± 8.5	0.6820	30.0 ± 5.3	29.3 ± 7.3	0.6721
% EBMIL 6 Months	82.7 ± 17.1	85.0 ± 23.6	0.3472	82.4 ± 16.5	85.3 ± 22.8	0.5430
% TWL 12 Months	40.0 ± 6.5	34.4 ± 5.4	0.0712	37.1 ± 6.5	35.3 ± 5.5	0.0702
% EBMIL 12 Months	102.3 ± 21.1	98.8 ± 16.9	0.7314	101.8 ± 21.5	101.6 ± 17.4	0.7140

Variables are presented in mean ± standard deviation.
Abbreviations: TWL, total weight loss; EBMIL, excess BMI loss.

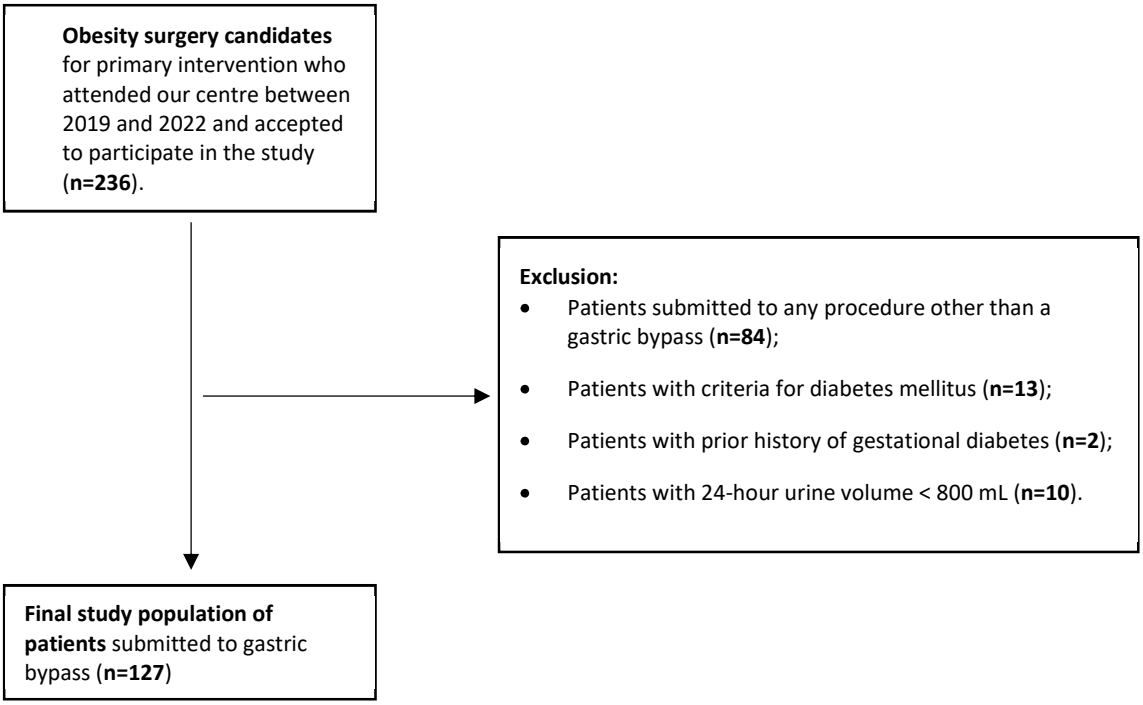

Figure 1 – Patients' selection criteria.

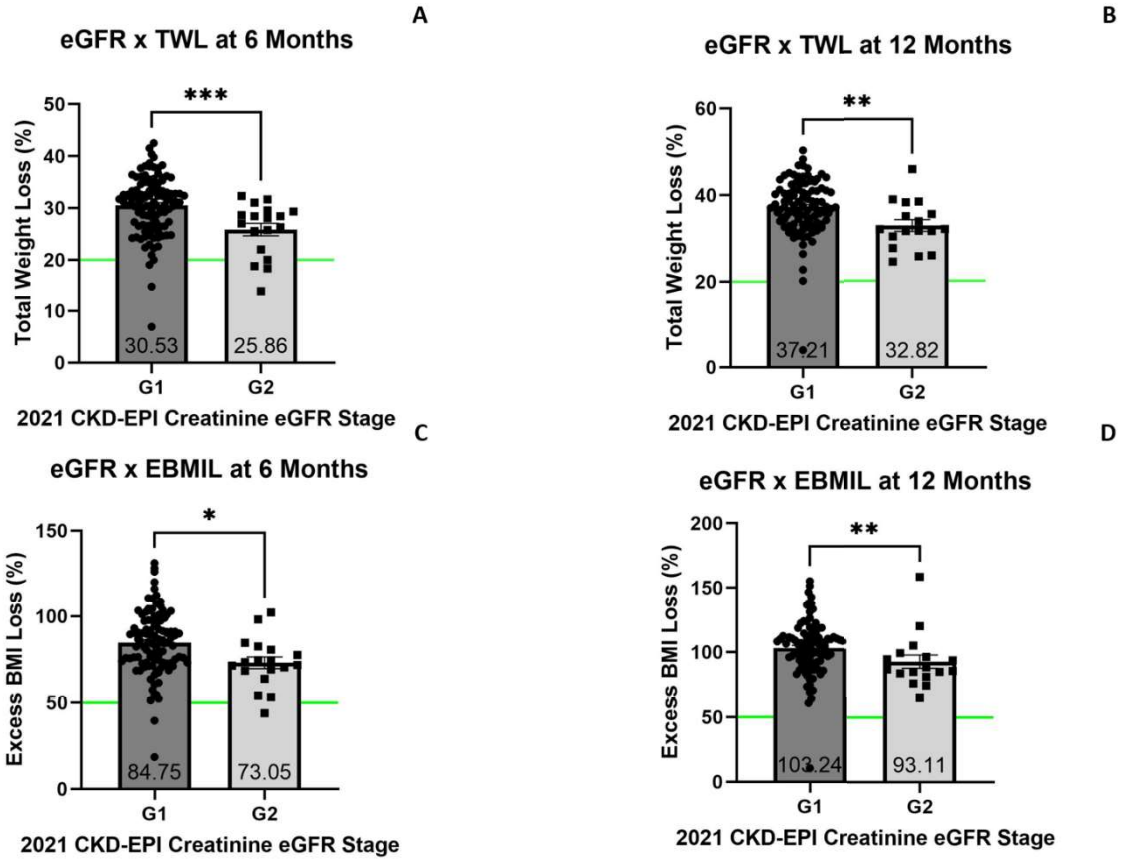

Figure 2 – Anthropometric evolution according to eGFR: A – TWL 6 months after surgery; B – TWL 12 months after surgery; C – EBMIL 6 months after surgery; D – EBMIL 12 months after surgery.

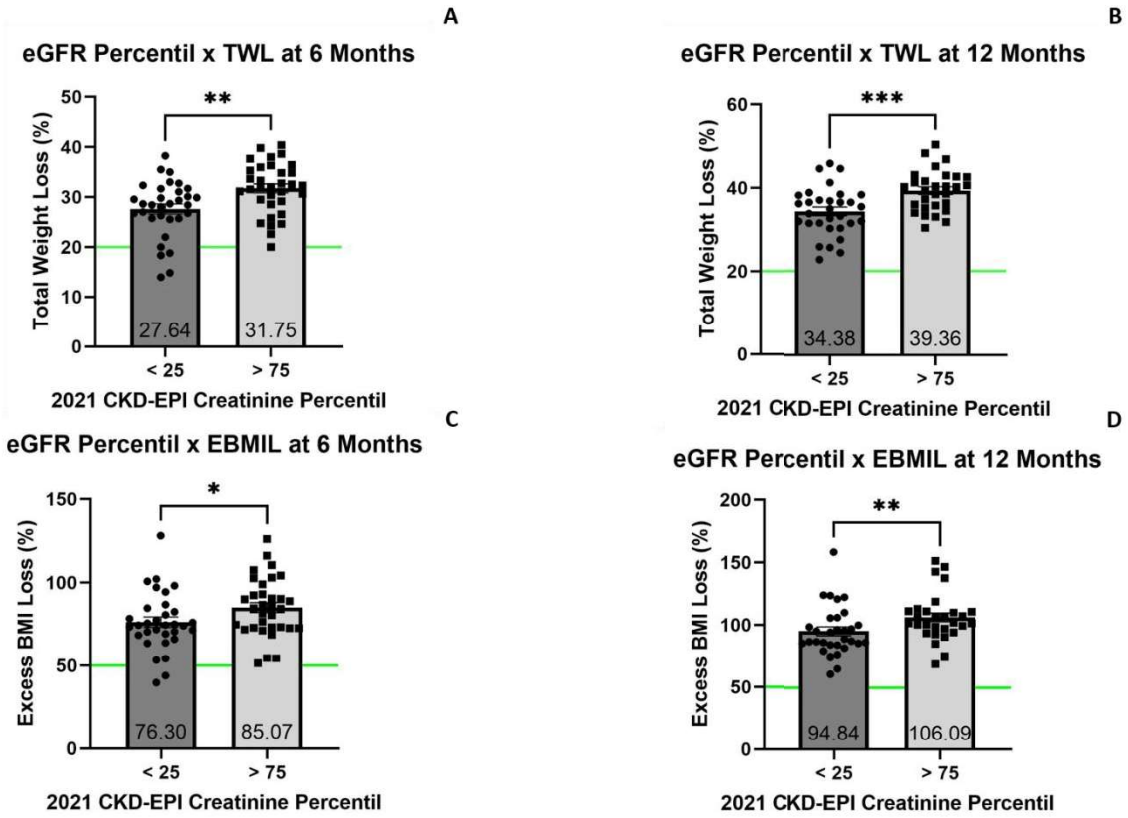

Figure 3 – Anthropometric evolution according to eGFR percentiles (P25: 98.3 mL/min; P75: 114.2 mL/min): A – TWL 6 months after surgery; B – TWL 12 months after surgery; C – EBMIL 6 months after surgery; D – EBMIL 12 months after surgery.

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