Original Article:

CKD.QLD: Effect of bariatric procedures on renal and non-renal parameters in obese CKD patients

I Ismail,[1,2] SK Venuthurupalli,[1,2,3] A Cameron,[2,3] W.E. Hoy [2,3]

[1]Renal Services, Toowoomba Hospital, Darling Downs Hospital and Health Service [DDHHS], QLD, Australia; [2]NHMRC CKD.CRE & CKD.QLD and [3]Centre for Chronic Disease, The University of Queensland, Brisbane, Australia

ABSTRACT

Background: Obesity has an adverse impact on metabolic parameters including CKD. Bariatric procedures produce significant weight loss compared to non-surgical means and have a positive effect on renal and non-renal parameters. The present study retrospectively evaluated the effect of bariatric procedures and weight loss on renal function, proteinuria, hypertension, lipid profile and diabetic status in chronic kidney disease (CKD) patients in Queensland, Australia.

Methods: Of the 880 patients who consented to the CKD Registry, data of patients who underwent bariatric procedures were analysed. Changes in anthropometric measures, renal functions, lipid profile, glycosylated haemoglobin A_{1c} (HbA_{1c}) (%), proteinuria and requirement for blood pressure medications and insulin dose were noted during follow-up.

Results: Eight patients (1%) (mean age 48 years: there were 5 men) underwent bariatric procedures (gastric banding - four, gastric sleeve - three and gastric bypass - one). Mean follow-up duration was 10 years. During follow-up a trend towards reduction was noted in weight (kg) (163 - 115 p = 0.01), proteinuria (g/mol) (381 - 65 p = 0.302), HbA_{1c} (%) (8.1 to 6.7 p = 0.03) and total cholesterol (mmol/L) (4.7 to 4.0 p = 0.33). The estimated glomerular filtration rate (eGFR) (mL/min/1.73m^2) did not change significantly (58.1 - 54.1 p = 0.426). Reductions of anti-hypertensive medications (1.8 - 0.75, p = 0.08) and insulin dose (IU) (61.3 - 25 p = 0.37) were also noted. One patient developed complications requiring removal of the gastric band. One patient progressed to end-stage renal disease.

Conclusions: There was significant weight loss leading to improvement in multiple metabolic parameters. There was a trend towards a slow progression of CKD post-bariatric surgery during the follow-up. Although the numbers are small bariatric procedures appears to have a significant role in the management of obesity associated with CKD and related metabolic conditions.

Key words: *Obesity, Renal insufficiency chronic, Bariatric surgery*

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INTRODUCTION

The World Health Organization (WHO) officially recognised obesity as a 'global epidemic' in 1997.[1] According to WHO, obesity is defined as a body mass index (BMI) of > 30 kg/m^2.[1] Obesity is a growing public health problem in Australia as well, with a reported 28% of Australians aged ≥18years being obese in 2014-2015.[2] Adults living in the lowest socio-economic areas were more likely to be overweight or obese than those in the highest socioeconomic areas (66% Vs 58 %).[2] Obesity is the second largest contributor to the burden of disease in Australia.[3] Obesity is an independent risk factor for progression of chronic kidney disease (CKD).[4] There has been a parallel increase in the prevalence of CKD with the rise in obesity.[5] An epidemic of obesity-related kidney disease has been predicted.[6]

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Corresponding author: Dr S.K. Venuthurupalli, Director, Renal Serices, Toowoomba Hospital, Darling Downs Hospital and Health Service, Australia.
e-mail: sree.venuthurupalli@health.qld.gov.au

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The rising popularity of bariatric surgery is attributed mainly to its beneficial effects on obesity related conditions such as insulin resistance, hypertension, obstructive sleep apnoea and reduction of mortality, that are maintained up to 18 years postoperatively.[4] These related conditions play a key role in development and progression of CKD. Non-surgical weight loss regimens (calorie restriction, exercise, and/or anti-obesity drugs) also have potential renal benefits of reduced proteinuria and stabilisation of renal function.[5] However, bariatric surgery has been shown to not only reduce proteinuria but also normalise glomerular hyperfiltration.[5] There are three main types of bariatric procedures conducted in Australia. These include sleeve gastrectomy and laparoscopic adjustable gastric banding, which are "restrictive" type of surgical procedures, and Roux-en-Y gastric bypass which is classed as a "mal-absorptive" procedure.

Darling Downs-Maranoa region, west of Brisbane, has the highest rate of obesity, at 44%, in the country.[7] The aim of this study was to evaluate the effect of bariatric procedures on both renal and non-renal parameters in CKD patients from this region.

MATERIAL AND METHODS

All patients who attended public renal clinics in Darling Downs Hospital and Health Service (DDHHS) in Queensland, Australia were offered enrolment into the Chronic Kidney Disease in Queensland (CKD.QLD) Registry, with informed consent. Among a total of 880 patients recruited, between June 2011 and June 2016, those who underwent any bariatric procedures were identified from this registry database and included in this retrospective study. BMI was classified per WHO classification (Table 1). Renal function was measured using Modification of Diet in Renal Disease (MDRD) initially (2006-2012) and Chronic Kidney Diseases Epidemiology Collaboration (CKD-EPI) formula from 2012 onwards.[8] Random urine protein: creatinine ratio was used to assess for degree of proteinuria. Renal function was classified as per CKD stages based on Kidney Disease Outcomes Quality Initiative (KDOQI) classification.[9] Diabetic status was defined by HbA_{1c} status and number of antihypertensive medication was noted as an indication of blood pressure control. Total cholesterol and triglycerides were also reviewed.

Table 1: WHO classification of underweight, overweight and obesity by BMI

Classification	BMI, kg/m^2
Underweight	<18.5
Ideal	18.5 - 24.9
Overweight	25.0 - 29.9
Obesity	> 30
Class I	30 - 34.9
Class II	35.0 - 39.9
Class III	≥ 40

BMI = body mass index

A detailed chart review for all relevant clinical data during clinic review was performed for the patients selected. Relevant pathology results were obtained from both public and private laboratories for pre-defined parameters pre/post-bariatric procedures. Some data missing from patient charts were obtained from patients during follow-up visits prospectively.

Statistical analysis

A p-value < 0.05 was considered significant. All variables with a normal distribution are expressed as the mean ± standard deviation. A paired-samples t-test was conducted to compare renal and non-renal parameters before and after bariatric procedures. The Statistical Package for Social Sciences (IBM SPSS version 22.0) was used to perform the statistical analysis.

RESULTS

Among 880 patients enrolled in the CKD.QLD registry, eight patients underwent bariatric procedures. There were four gastric banding, three gastric sleeves and one gastric bypass procedure performed (Figure 1). Mean age was 48 ± 12 years and three were female. Five patients had type 2 diabetes. Three patients were CKD stage 1, one patient CKD stage 2, one patient had CKD stage 3A and three patients had CKD stage 4 pre-bariatric procedure.

Mean post-procedure follow-up was 9.8 ± 2 years. During follow-up a trend towards reduction was noted in weight (kg) (163.4 to 114.7, $p = 0.01$), proteinuria (g/mol) (381 to 64.8 $p = 0.302$), HbA_{1c} (%) (8.1 to 6.7, $p = 0.03$) and total cholesterol (mmol/L) (4.7 to 4.0, $p = 0.33$). eGFR (mL/min/1.73m^2) did not change significantly (58.1 mL/min/1.73m^2 to 54.1 mL/min/1.73m^2, $p = 0.426$), Reduction of anti-hypertensive medication use (1.8 to 0.75, $p = 0.08$) and insulin dose (IU) (61.3 to 25, $p = 0.37$) were also noted. These details are shown in Table 2.

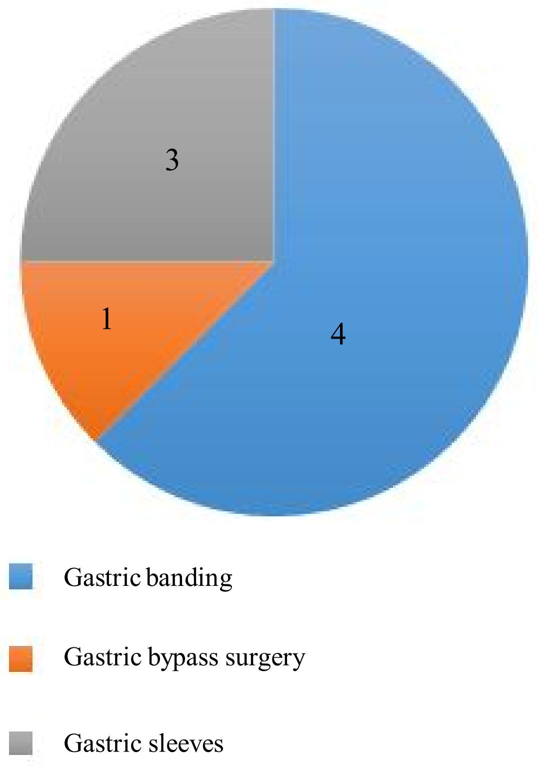


Figure 1: Types of bariatric procedures performed

Table 2: Mean change in parameters post-bariatric procedures

	Pre-bariatric procedure			Post-bariatric procedure			
Variable	**Mean**	**Min**	**Max**	**Mean**	**Min**	**Max**	**p-value***
Urea (mmol/L)	12.36	4.60	27.00	10.36	5.90	16.20	0.22
Serum creatinine (µmol/L)	141.63	70.00	254.00	187.25	60.00	600.00	0.39
eGFR (ml/min/1.73m^2)	58.13	17.00	92.00	54.25	7.00	90.00	0.43
Weight (kg)	163.38	139.00	200.00	114.67	78.30	134.70	0.01
BMI (kg/m^2)	53.21	44.00	60.90	37.13	31.00	41.00	0.01
Number of antihypertensive medications	1.75	0.00	6.00	0.75	0.00	2.00	0.09
Total cholesterol (mmol/L)	4.69	3.40	8.50	4.21	2.80	6.00	0.33
LDL cholesterol (mmol/L)	3.39	2.06	5.71	2.26	1.74	3.00	0.46
Triglycerides (mmol/L)	2.40	1.10	4.60	1.80	0.70	4.10	0.83
High Density Lipoprotein cholesterol (mmol/L)	1.00	0.80	1.23	1.10	1.01	1.16	0.54
HbA1c (%)	8.18	5.7	9.7	6.7	5.7	8.2	0.03
Urine Prot:Cr ratio (g/mol)	381.00	6.00	1200.00	64.83	13.00	180.00	0.30

eGFR = estimated glomerular filtration rate test; BMI = body mass index; LDL = low density lipoprotein; HbA_{1c} = glycosylated haemoglobin

The procedures performed are shown in Figure 1. Change in obesity class post-bariatric procedure is shown in Figure 2. Change

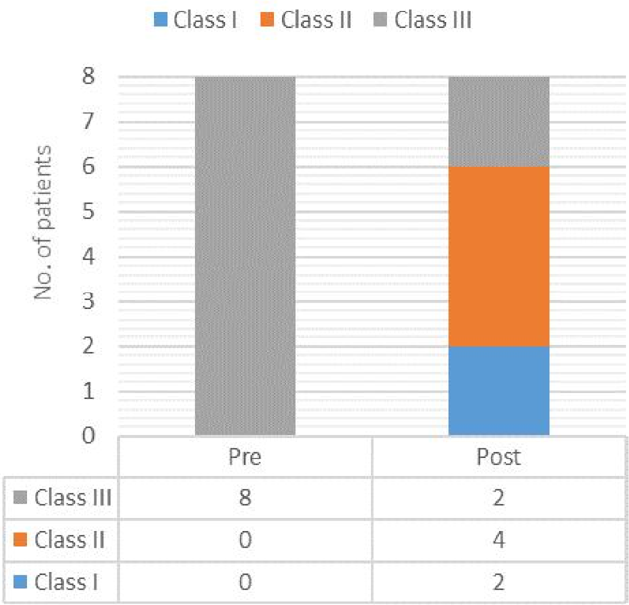


Figure 2: Change in obesity class post-bariatric procedures

observed in various parameters after bariatric procedures are shown in Figure 3. Change in CKD stage and eGFR in relation to reduction in BMI are depicted in Figures 4 and 5 respectively. One patient developed complications requiring removal of the gastric band. One patient progressed to end-stage kidney failure requiring haemodialysis.

For subgroup analysis of correlation of weight loss and change in renal function, our patients were sub-divided into three groups (Figure 5). Group A (n=2) included patients who had improved renal function (eGFR), group B (n =2) had stable renal function (eGFR) and group C (n=4) had reduction in renal function (eGFR) post bariatric procedures. Patients in the latter group on average had a longer duration post bariatric surgery (Group A = 6 years, Group B = 2 years and Group C 16 years), more advanced CKD represented as stage 4

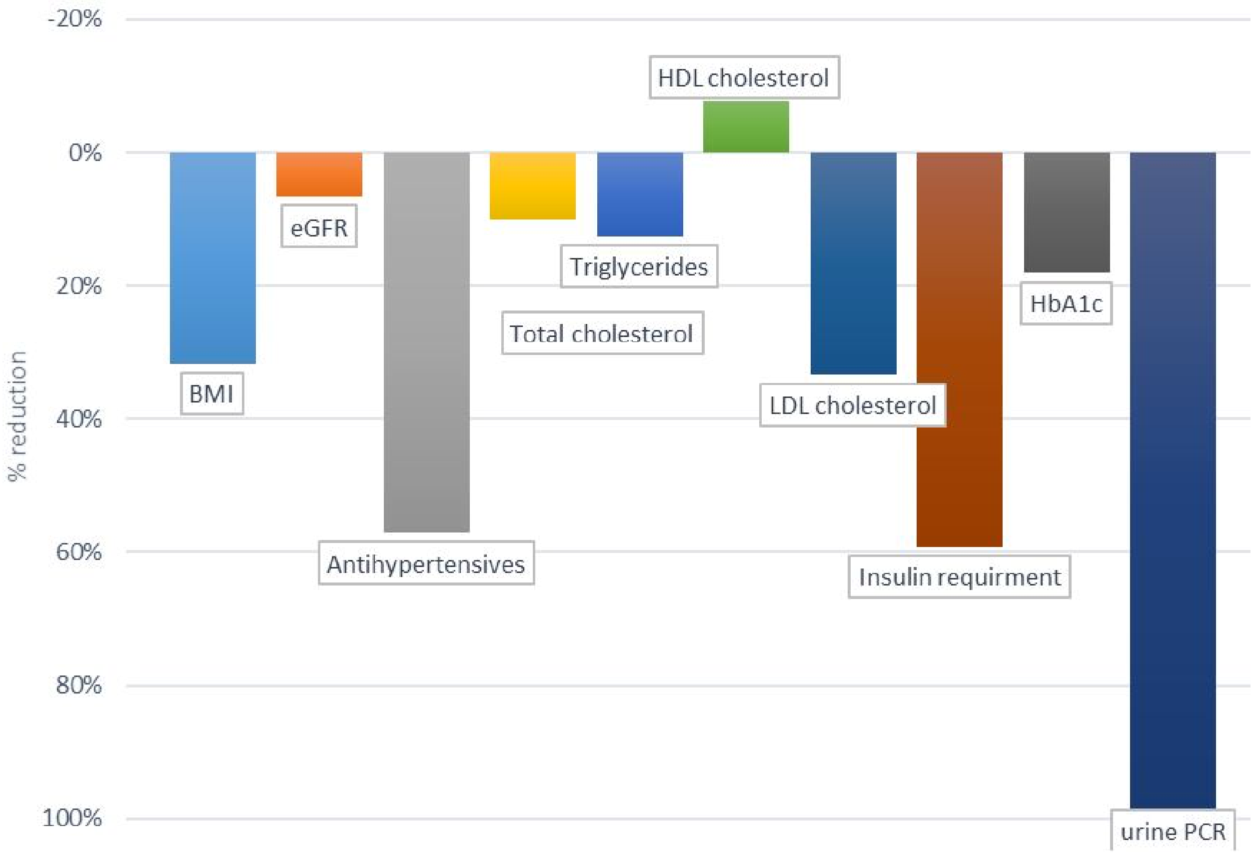
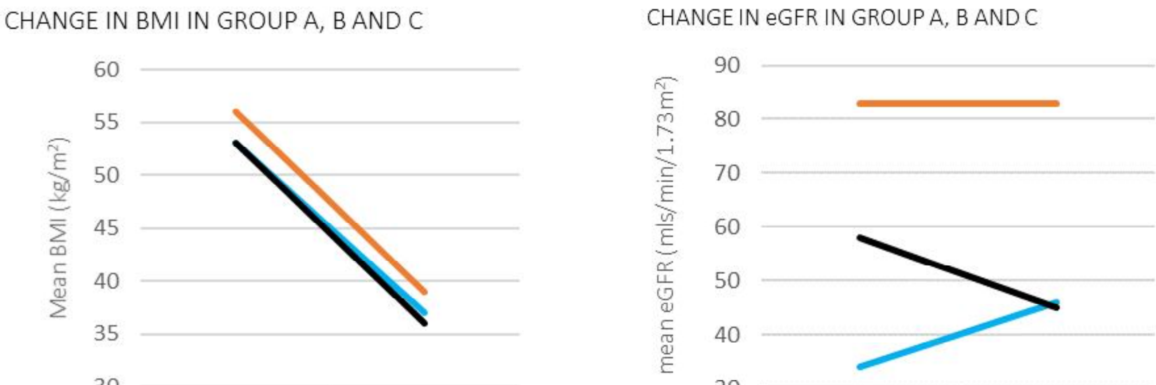


Figure 3: Change observed in various parameters after bariatric procedures
BMI = body mass index, eGFR = estimated glomerular filtration rats, LDL = low density lipoprotein, HbA_{ic} = glycosylated haemoglobin, PCR = protein creatinine ratio

	Pre-bariatric procedure	Post-bariatric procedure
CKD Stage 5	0	1
CKD Stage 4	3	2
CKD Stage 3	1	0
CKD Stage 2	1	4
CKD Stage 1	3	1

Figure 4: Change in CKD stage post-bariatric procedures
CKD = Chronic kidney disease



	Pre-bariatric	Post-bariatric
Group A (n=2)	53	37
Group B (n=2)	56	39
Group C (n=4)	53	36

	Pre-bariatric	Post-bariatric
Group A (n=2)	34	46
Group B (n=2)	83	83
Group C (n=4)	58	45

Figure 5: Change in renal function (eGFR) in relation to reduction in weight (BMI)
eGFR = estimated glomerular filtration rate test; BMI = body mass index

Group A = patients with improved eGFR, **Group B** = patients with no change in eGFR and **Group C** = patients who had a reduction in eGFR post-bariatric procedures (group A =1, group B = none, group C = 2). There were complications requiring surgical revision in one patient. Age, change in weight loss and other co-morbidities were similar in three groups. Pearson's correlation did not show a significant correlation with weight loss and change in renal function (eGFR) for the entire cohort ($r = -0.35$. $p = 0.40$).

DISCUSSION

Obesity is a well-known risk factor for increased cardiovascular disease, diabetes mellitus, hypertension and obstructive sleep apnoea.[10] All of them in turn have adverse impacts on progression of CKD. The relationship between obesity and proteinuria has been described more than two decades ago and increasing literature has supported harmful renal effects of obesity.[11,12] Many potential factors, including hormonal factors, oxidative stress, inflammation and endothelial dysfunction have been implicated as causes of CKD in patients with obesity.[13] Hence, there is a growing interest in offering bariatric surgery to these patients to halt the progression of CKD. The results of our study showed a trend in improvement in all the renal and non-renal parameters (Table 2).

Though gastric banding was the most common procedure performed in this cohort (Figure 1), this procedure has not been favoured in recent times in comparison with the gastric sleeve, currently the most common bariatric procedure.[14,15] The decrease in gastric banding is reported to be due to its relatively modest amount of weight loss and long-term complications requiring removal or revision surgery.[10,16,17] One of our patients had the gastric band removed in our study.

There was a significant mean weight loss following bariatric procedures in our study. Every patient had significant and sustained weight loss throughout follow-up (Figure 2). Bariatric procedures are one of the fastest growing procedures performed worldwide and are superior to non-surgical interventions in achieving sustained weight loss.[10,11,18]

A mean reduction of HbA_{1c} and total insulin dose following bariatric surgery noted in this study is similar to previous studies that have shown that bariatric surgery in combination with medical therapy achieved significantly better glycaemia control in uncontrolled type 2 diabetic patients.[19] Nearly 20% reduction in HbA_{1c} and 60% reduction in insulin requirements post-bariatric procedures were noted in this cohort (Figure 3).

Obesity worsens proteinuria and accelerates the progression of CKD.[20-23] Results of two meta-analyses evaluating renal outcomes has shown that for every kilogram of weight loss there was an average reduction of 110 mg in proteinuria and a 1.1 mg decrease in microalbuminuria and surgical procedures normalized GFR.[5,24] There was a reduction of proteinuria and slowed progression of CKD (majority CKD stage 2) in our cohort during follow-up after bariatric procedures (Figure 4).

There was a trend towards improvement in blood pressure control as demonstrated by a reduction in number of antihypertensive medications and an improvement in lipid profile, with reductions in total cholesterol, LDL cholesterol and triglycerides, and a rise in HDL cholesterol, consistent with numerous other studies.[10,25]

The major limitation is the small study size and observational nature, which has its inherent bias. Renal function (eGFR) calculated from current formulae are not validated in morbidly obese patients which may be a limitation of this method to assess renal function in this setting. However, recent literature suggests that eGFR calculated from CKD-EPI formula has a good correlation with the gold standard using inulin or iohexol clearance in patients with eGFR ≤ 60 mL/min per 1.72 m^2 with a BMI range up to 40kg/m^2.[26] It has also been shown that waist circumference and waist-to-hip ratio (WHR) as indices of visceral obesity are probably more sensitive predictors of renal injury than BMI.[27,28] However, this data was not available for our patients. One of the major strengths of this study is the mean follow-up of our patients at 9.8 years. This is also the first study to look at this subject in an Australian setting. We also reported all the documented complications associated with the bariatric procedures such as kidney stones and revision surgeries.

Nephrologists are hesitant to initiate a referral for bariatric procedures, despite literature supporting renal benefits, possibly due to misconceptions and safety concerns including fear of worsening renal function.[29] Furthermore, some studies have shown a paradoxical neutral effect or even benefit with obese patients on dialysis.[30-32] Given there is no consensus on weight management strategies in CKD patients with obesity, analysis of individual centre data and reflection on the results is paramount in moving forward in this important area that affects an increasing number of CKD patients.

The present study has shown that bariatric procedures have an impact on multiple metabolic parameters in CKD patients, including slowing the progression of renal disease. Larger prospective trials on the impact of these procedures on CKD progression including looking at barriers for bariatric procedures in the CKD population is important.

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