# Participation in a Structured Weight Loss Program and All-Cause Mortality and Cardiovascular Morbidity in Obese Patients With Chronic Kidney Disease



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**Objective:** To determine if participation in a weight loss program impacted upon a composite end point of all-cause mortality and cardiovascular morbidity in obese patients with chronic kidney disease (CKD).

Design: Retrospective cohort study.

**Subjects:** All patients with a body mass index (BMI) >30 kg/m<sup>2</sup> or >28 kg/m<sup>2</sup> with at least 1 comorbidity (hypertension, diabetes, or dyslipidemia) referred to an established weight management program (WMP) from 2005 to 2009 at a metropolitan tertiary teaching hospital were eligible for inclusion in the study cohort.

Intervention: Twelve-month structured weight loss program.

**Main Outcome Measures:** Combined outcome of all-cause mortality, myocardial infarction, stroke, and hospitalization for congestive heart failure; kidney transplantation waitlisting.

**Results:** A total of 169 obese patients with CKD commenced the WMP and 169 did not—becoming the observational control group (CON). There were no significant differences between groups for age, BMI, sex, ethnicity, smoking, hypertension, or kidney function at baseline, although CON included more patients with diabetes than WMP (49% vs. 38%, P = .03). Kaplan–Meier survival analysis with log-rank test differed between groups for the combined outcome (P = .03). Cox regression analysis with adjustment for age, sex, ethnicity, hypertension, diabetes, kidney function, baseline BMI, and smoking status, indicated that patients in WMP had a significantly longer event-free period for the combined outcome, than those in CON (adjusted hazard ratio 0.53; 95% confidence interval [CI] 0.29-0.97; P = .04). Participation in the WMP did not increase the likelihood of kidney transplantation waitlisting (odds ratio [OR] 1.06; 95% CI 0.39-2.87; P = .9). Lower baseline BMI and greater weight loss over 12 months were the only factors related to kidney transplantation waitlisting (adjusted  $R^2 = 0.426$ ).

**Conclusions:** Participation in a structured weight loss program may be associated with improved outcomes in obese patients with CKD. Crown Copyright © 2015 Published by Elsevier Inc. on behalf of the National Kidney Foundation, Inc. All rights reserved.

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#### Introduction

BESITY IS A risk factor for both the development of chronic kidney disease (CKD) and the decline in kidney function leading to end-stage kidney failure. 1-3 Weight loss of 5% to 10% in the overweight and obese general population is associated with decreased blood pressure, improved blood lipid profile, and reduced insulin resistance leading to improved glycemic control.<sup>4</sup> However, the effect of weight loss on cardiovascular morbidity and mortality in overweight and obese populations in observational studies indicates that overall, the impact of weight loss on mortality is unclear. Weight loss has been associated with increased all-cause and cardiovascular mortality, decreased mortality, and no association with mortality in observational and experimental studies, although intentionality of weight loss and comorbidities may be confounding factors.<sup>6-8</sup>

Intentional weight loss achieved via specific weight loss programs in populations of patients with existing comorbidities, such as diabetes and cardiovascular disease, is

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associated with a lower likelihood of mortality, 9,10 or cardiovascular morbidity.<sup>11</sup> The relationship between intentional weight loss and mortality and cardiovascular morbidity has not previously been explored in obese patients with CKD. Obesity, cardiovascular disease, and diabetes are all risk factors for the development and progression of CKD,<sup>2,12,13</sup> yet studies on the long-term outcomes of weight loss interventions in obese patients with CKD are lacking. We have previously demonstrated the efficacy and effectiveness of our renal weight management program (WMP) for weight loss and reported an association between compliance and a reduction in systolic blood pressure. 14,15 Recent evidence also suggests that 50% of overweight and obese patients with CKD have actively attempted weight loss, f6 indicating that weight loss treatments are being sought by this patient population.

This study aimed to determine if participation in a weight loss program impacted upon a composite end point of: all-cause mortality, myocardial infarction, stroke, and hospitalization for congestive heart failure, and secondly, kidney transplantation waitlisting, in obese patients with CKD.

## **Methods**

### **Study Population**

All patients, aged 18 to 80 years, under the care of a nephrologist and with a body mass index (BMI) of >30 kg/m<sup>2</sup> or >28 kg/m<sup>2</sup> with at least one comorbidity (hypertension, diabetes, or dyslipidemia) referred to the Renal Weight Management Program at King's College Hospital, London, from 2005 to 2009 were eligible for inclusion in the study cohort. Patients were invited to attend a 60minute session outlining the program and were then given a 7-day food and activity record to complete and return in a preaddressed, postage-paid envelope. Return of the food and activity record indicated consent to participate in the WMP group. Patients who either did not attend the information session or did not return the food and activity record, were entered into the contemporaneous observational control (CON) group. Study data were recorded at either WMP visits or standard nephrology care visits. The King's College Hospital Research Ethics Committee approved the study.

## **Weight Loss Intervention**

The WMP has been described previously. 14,17 Briefly, the WMP is a 12-month weight loss program including a low-fat, energy-reduced renal diet, regular exercise, and use of the anti-obesity medication, orlistat (120 mg three times daily, Xenical; Roche Products, Basel, Switzerland), with motivational interviewing 18 and behavioral therapy techniques to address barriers to lifestyle change. A low-fat energy-reduced renal diet was negotiated with each patient based on food preferences and each patient's CKD stage. 14 Protein intake was optimized for the stage of CKD for each patient, and sodium was modified to 80 to 100 mmol/day. 19 Potassium and phosphorus intake were

adjusted according to serum biochemistry and kidney function. <sup>20,21</sup> Adherence to dietary recommendations was monitored from continuous daily written food intake records. Personal exercise plans were developed based on the patient's individual current level of exertion and comorbid conditions and incorporated aerobic and muscular endurance activities to improve functional capacity and increase energy expenditure. <sup>17</sup>

### **Study End Points**

The primary end point of the study was a composite variable for a combined event, consisting of all-cause mortality, or the first occurrence during the study period of a cardio-vascular event. A cardiovascular event was defined as myocardial infarction, stroke, or congestive heart failure requiring hospitalization and treatment with inotropes, vasodilators or diuretics. The secondary end point was placement on the waiting list for kidney transplantation.

#### **Measurements and Definitions**

Demographic data including age, sex, ethnicity, smoking status (never smoked, previous smoker, current smoker), weight history, estimated kidney function (estimated glomerular filtration rate [eGFR]), or dialysis modality were collected at the baseline visit in the WMP group. Height was measured to the nearest 0.01 m using a fixed stadiometer. Body weight was measured to the nearest 0.1 kg in light clothing on a digital scale, and BMI was calculated as weight (kg)/height (m<sup>2</sup>). For dialysis patients, estimated edema-free body weight was used. Resting sitting blood pressure was recorded using an automated sphygmomanometer and an appropriate-sized cuff. Kidney function was assessed by eGFR, for all patients except those undergoing dialysis, and was calculated with the four-variable modification of diet in renal disease study equation using serum creatinine, age, and sex, and corrected for ethnicity.<sup>22,23</sup> Body weight, blood pressure, and 12month weight change were recorded prospectively at WMP visits. Baseline for patients in the CON group was defined as the date of the initial information session each patient was invited to attend. Body weight, height, BMI, smoking status, eGFR (for nondialysis patients), and body weight 12 months after baseline, were extracted retrospectively from electronic medical records.

Hypertension was defined as systolic blood pressure greater than 140 mm Hg or diastolic blood pressure greater than 90 mm Hg; or greater than 130/80 mm Hg in patients with proteinuria or diabetes; or the patient was prescribed at least 1 of the following classes of antihypertensive agents: angiotensin-converting-enzyme inhibitors, angiotensin receptor II blockers, beta receptor blockers, calcium channel blockers, and thiazide-type diuretics. Hypertension was actively treated with multiple agents in WMP and CON groups; and during follow-up, attending physicians could openly modify antihypertensive agents. Diabetes status was defined as the presence of type 1 or type 2 diabetes

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