

# Weight reduction in obese patients with chronic kidney disease

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## GUIDELINES

- a. Obese patients with proteinuric nephropathy should be encouraged to reduce their weight while ensuring adequate nutrition. (Level II evidence – no long-term studies)
- b. The potential metabolic and cardiovascular benefits that may arise from weight reduction in obese patients should not be ignored (Level I evidence)

## SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV sources)

In patients with obesity, weight reduction can be an important adjunct to anti-hypertensive interventions, insulin sensitivity and lipid control.<sup>1</sup> Such improvements arising from weight reduction should have beneficial effects in slowing the progression of chronic kidney disease (CKD). There is some evidence that obese patients (body mass index (BMI) > 30 kg/m<sup>2</sup>) have increased rate of progression of kidney disease compared with non-obese (but well-nourished) probands. In addition, reductions in proteinuria (>1 g/day) have been reported following weight loss over-and-above improvements in blood pressure and metabolic control (Level III–IV evidence: uncontrolled series and case reports):

- Palomar *et al.*<sup>2</sup> reported that bilio-pancreatic diversion in individuals with morbid obesity significantly reduced microalbuminuria decreased and eliminated proteinuria disappeared after weight loss.
- Chagnac *et al.*<sup>3</sup> studied eight subjects with severe obesity undergoing weight loss programmes. A decrease in body mass was associated with reduced hyperfiltration and a reduced albumin excretion rate.
- Ohashi *et al.*<sup>4</sup> investigated the effect of weight reduction on blood pressure, microalbuminuria and renal function in 25 hypertensive patients with obesity. In 10 patients achieving weight loss of at least 5% over 12 months of follow-up, albumin excretion rate was significantly decreased, while the further 15 patients having no significant weight loss or gain, had no change in albuminuria. Overall, urinary albumin excretion rate significantly correlated with weight reduction and a decrease in blood pressure.
- In a cross-sectional study of 73 patients undergoing unilateral nephrectomy, Praga *et al.*<sup>5</sup> found that among the 14 obese patients, 13 (92%) developed proteinuria/

renal insufficiency. In contrast, among the 59 patients with BMI < 30 kg/m<sup>2</sup>, only seven (12%) developed these complications.

- In obese patients with type 2 diabetes, albuminuria can also be reduced by weight loss, over and above effects on metabolic control<sup>6</sup> and improve renal function.<sup>7</sup>

However, while obesity is a strong risk factor for morbidity and mortality in the general population, some recent studies suggest that obesity may be associated with increased survival on haemodialysis<sup>8</sup> and peritoneal dialysis.<sup>9</sup> In one study of 131 African-American patients,<sup>8</sup> the relative risk for dying after a year of dialysis was reduced with an increase in BMI beyond the higher end of 'normal' BMI after adjusting for the biochemical markers of nutrition. The authors hypothesize a survival advantage for obese uraemic patients, possibly by virtue of excess adipose tissue, rather than the absence of malnutrition.

However, a larger survey of the ANZDATA registry demonstrated that obesity at the commencement of renal replacement therapy is a significant risk factor for death, peritonitis and technique failure.<sup>10</sup> There is some evidence that obese patients experienced more complications following renal transplantation and have a higher mortality resulting from an excess of cardiac events.<sup>11,12</sup> Despite the apparent reverse causality that exists in patients receiving renal replacement therapy, the weight of evidence suggests that obese patients with CKD should be encouraged to reduce their weight, while ensuring adequate nutrition. Weight reduction in obese patients into the high end of normal BMI range may also help to reduce the high cardiovascular mortality and morbidity in uraemic patients.

## How much weight to lose?

The initial goal of weight loss initiatives in obese patients should be to reduce body weight by approximately 10% from baseline in line with NHLB guidelines.<sup>1</sup> With success, further weight loss can be attempted, if indicated, through further assessment. Therapeutic weight loss should not be confused with catabolism with increasing

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uraemia and requiring RRT and appropriate renal diets should be recommended.<sup>13</sup>

## BACKGROUND

Obesity represents a significant problem in patients with CKD. Obesity is a risk factor for focal and segmental glomerulosclerosis. In addition, there is some evidence that obesity *per se* may influence the progression of renal damage because of other causes, including diabetic kidney disease. The objective of this guideline was to evaluate the available clinical evidence pertaining to the impact of weight reduction in patients with obesity on renal functional decline in patients with CKD. This guideline does not address the potential metabolic and cardiovascular benefits that may arise from weight reduction in obese patients.<sup>1</sup>

## SEARCH STRATEGY

**Databases searched:** MeSH terms and text words for CKD were combined with MeSH terms and text words for obesity. The search was carried out in Medline (1966 to November Week 2, 2004).

**Date of searches:** 11 November 2004.

## WHAT IS THE EVIDENCE?

There have been two small randomized controlled trials of weight reduction in patients with chronic proteinuric nephropathy:

- Morales *et al.*<sup>14</sup> randomly assigned 30 overweight patients with diabetic and non-diabetic proteinuric nephropathies to either follow a low-calorie normoproteinc diet (weight loss) or maintain their usual dietary intake for 5 months. Proteinuria was decreased by 31% in the diet group whereas it tended to increase in the control group (diet *vs* control,  $P < 0.05$ ). Renal function remained stable in the diet group, but worsened in the control group, although overall changes in renal function did not differ significantly between groups. However, this small short-term study was not designed to address the effect of weight loss on renal function decline.
- Praga *et al.*<sup>15</sup> studied 17 obese patients with proteinuria  $>1$  g/day. Nine patients were treated with hypocaloric diets (protein intake not noted) and eight were treated with captopril, without dietary changes. Both weight loss and captopril reduced proteinuria to a similar extent. Moreover, there was a significant correlation between body weight loss and decrease in proteinuria.

## SUMMARY OF THE EVIDENCE

Weight loss in patients with proteinuric nephropathies ( $>1$  g/day) is able to reduce urinary protein excretion. The impact of these changes on long-term preservation of renal function remains to be established in Level I–II clinical trials. The utility of weight loss in obese patients with non-proteinuric nephropathies has not been formally tested.

Nonetheless, the potential metabolic and cardiovascular benefits that may arise from weight reduction in obese patients should not be ignored.<sup>1</sup>

## WHAT DO THE OTHER GUIDELINES SAY?

**Kidney Disease Outcomes Quality Initiative:** There are no guidelines for the management of obesity specifically in patients with pre-end-stage kidney disease (ESKD).

**UK Renal Association:** There are no guidelines for the management of obesity specifically in patients with pre-ESKD.

**Canadian Society of Nephrology:** There are no guidelines for the management of obesity specifically in patients with pre-ESKD.

**European Best Practice Guidelines:** There are no guidelines for the management of obesity specifically in patients with pre-ESKD.

## INTERNATIONAL GUIDELINES

For the general population:

**National Heart, Lung, and Blood Institute/National Institute of Diabetes and Digestive and Kidney Diseases. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults:**<sup>1</sup>

Weight loss is recommended to lower elevated blood pressure in overweight and obese persons with high blood pressure.

Weight loss is recommended to lower elevated levels of total cholesterol, low-density lipoprotein cholesterol, and triglycerides and to raise low levels of high-density lipoprotein cholesterol in overweight and obese persons with dyslipidaemia.

Weight loss is recommended to lower elevated blood glucose levels in overweight and obese persons with type 2 diabetes.

The initial goal of weight loss therapy should be to reduce body weight by approximately 10% from baseline. With success, further weight loss can be attempted, if indicated, through further assessment.

**Obesity in Scotland: Integrating Prevention with Weight Management 1996:**<sup>16</sup>

The priority in obesity management should be weight management with risk factor reduction, rather than major weight loss.

The goal should be modest weight loss rather than a return to ideal or normal weight

**Recommendations on obesity and weight loss, Canadian Consensus Conference on the Non-Pharmacologic Treatment of Hypertension, 4 May 1999:**<sup>17</sup>

All overweight hypertensive patients (BMI  $> 25$ ) should be advised to reduce their weight.

## IMPLEMENTATION AND AUDIT

No recommendation.

## SUGGESTIONS FOR FUTURE RESEARCH

The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) to record and review patients with increased BMI and pre-ESKD outcomes. As cardiovascular risk tracks with waist circumference and not BMI in the general population, this parameter should be added to data collection.

## CONFLICT OF INTEREST

Merlin Thomas has a Level II b conflict of interest according to the conflict of interest statement set down by CARI.

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