Weight loss interventions in chronic kidney disease: a systematic review and meta-analysis
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CRD summary
The authors concluded that weight loss might have beneficial effects on chronic kidney disease and cardiovascular risk, but supporting evidence was modest and further research was needed. The authors' conclusions appear suitably cautious, but the poor quality of the included studies and their different weight loss approaches should be borne in mind.

Authors' objectives
To assess the effects of weight loss interventions on patients with non-dialysis-dependent chronic kidney disease and obesity related glomerular hyperfiltration.

Searching
MEDLINE (1966 to November 2008) and SCOPUS (November 2008) were searched for studies published in English. Search terms were reported. Abstracts presented at the annual meetings of three main renal associations were searched from 2004 to 2007. Bibliographies of relevant studies were handsearched. Web of Knowledge's Cited References list and the Related Articles link in PubMed were used to identify additional studies.

Study selection
Randomised controlled trials (RCTs) and observational studies that assessed the effects of surgical or nonsurgical weight loss interventions in overweight or obese patients (aged 18 years or older) with non-dialysis-dependent chronic kidney disease and glomerular hyperfiltration were eligible for inclusion. Studies in patients with chronic kidney disease were required to report post-intervention changes in glomerular filtration rate or creatinine clearance and proteinuria as the primary outcome. Studies in patients with glomerular hyperfiltration were required to report the post-intervention change in glomerular filtration rate or creatinine clearance using a measured value (inulin or iothalamate studies, 24-hour urinary creatinine clearance) as the primary outcome. Secondary outcomes for all patients were post-intervention changes in body mass index (BMI), systolic and diastolic blood pressure, glycosylated haemoglobin and/or fasting blood glucose levels, and lipid profile. Studies were excluded if they were case reports or case series, used low-protein diets or assessed the impact of weight loss on albumin excretion in patients with normoalbuminuria. Studies that included both non-dialysis-dependent and dialysis patients and studies of both patients with normoalbuminuria and microalbuminuria were eligible if data on non-dialysis patients and patients with microalbuminuria could be extracted separately.

Included studies of non-surgical interventions assessed hypocaloric diet with or without exercise or anti-obesity agents in patients with chronic kidney disease. Control groups received usual dietary intake or captopril. Surgical interventions assessed gastric bypass, end-to-side jejunoileostomy, gastroplasty or biliopancreatic diversion in patients with glomerular hyperfiltration. Where reported, BMI in non-surgical patients ranged between 30.4 and 47.6 kg/m² and in surgical patients ranged between 46.9 and 53.6 kg/m². Comorbidities included (borderline) diabetes, metabolic syndrome, hypertension, coronary artery disease, obstructive sleep apnoea and retinopathy.

Two reviewers independently screened studies for inclusion to reach consensus.

Assessment of study quality
The quality of RCTs was assessed according to Cochrane Renal Group criteria on allocation concealment, intention-to-treat (ITT) analysis, completeness to follow-up and blinding. Observational studies were assessed according to the Newcastle-Ottawa Scale, based on selection of study participants, quality of the adjustment for confounding and ascertainment of the exposure (case-control) or outcome of interest (cohorts) to a maximum score of nine [A: Two reviewers assessed the quality].

Data extraction
Two reviewers extracted mean changes between pre- and post-intervention periods and their standard deviations to
calculate mean differences and 95% confidence intervals. Discrepancies were resolved through discussion. Authors were contacted for clarification, where necessary.

Methods of synthesis
Weighted mean differences and 95% confidence intervals were combined using the DerSimonian and Laird random-effects model, where appropriate. Statistical heterogeneity was assessed using $X^2$ and $I^2$ statistics. Where pooling was not appropriate, data were presented as a narrative synthesis.

Subgroup analyses were undertaken by study design. Sensitivity analyses were performed to test the robustness of the primary outcomes.

Results of the review
Two RCTs and 11 observational studies (n=528, range eight to 94) met the inclusion criteria. The quality of observational studies ranged between 3 and 8 (low to moderate quality). There were no drop-outs in the two RCTs, but allocation concealment was unclear and neither study was blinded or used ITT analysis. Follow-up ranged between four weeks and one year in the non-surgical studies and between one and two years in the surgical studies (one study reported follow-up up to 13 years).

For non-surgical interventions, weight loss did not statistically significantly change glomerular filtration rate or creatinine clearance (two RCTs, three observational studies); there was some evidence of statistical heterogeneity among the three observational studies for glomerular filtration rate ($I^2=57\%$).

Weight loss interventions statistically significantly reduced proteinuria (WMD -1.65g/24hours, 95% CI -3.21 to -0.08, $I^2=0\%$; two RCTs and WMD -1.05g/24hours, 95% CI -2.08 to -0.01, $I^2=67\%$; two observational studies).

Compared with controls, non-surgical weight loss interventions reduced BMI significantly, but this involved the pooling of two RCTs and three observational studies and there was evidence of significant statistical heterogeneity ($I^2=90\%$).

Systolic blood pressure and total cholesterol were also reduced with non-surgical interventions. Triglycerides and HDL cholesterol levels did not change significantly. Findings for other secondary outcomes were reported in the review.

For surgical interventions, weight loss normalised glomerular filtration rate in patients with glomerular hyperfiltration (WMD -25.56mL/min, 95% CI -36.23 to -14.89; three observational studies) without evidence of statistical heterogeneity ($I^2=0\%$). BMI was statistically significantly reduced with weight loss (WMD -16.53kg/m\(^2\), 95% CI -19.59 to -13.48; three observational studies), but with evidence of statistical heterogeneity ($I^2=78\%$). Systolic blood pressure was reduced (results reported in the review), but with statistical heterogeneity ($I^2=86\%$).

Subgroup and sensitivity analyses did not significantly alter the results.

Authors’ conclusions
Weight loss might have beneficial effects on chronic kidney disease and cardiovascular risks, but the evidence to support the use of weight loss interventions for patients with mild-to-moderate chronic kidney disease was modest at best and further research was needed.

CRD commentary
This review addressed a clear question and was supported by clearly defined inclusion criteria. The literature search was satisfactory and included a search for both published and unpublished studies. The search was limited to English-language studies, language bias could not be ruled out. Publication bias was not assessed formally; the authors acknowledged potential for publication bias. Study quality was assessed using appropriate criteria, but most studies were observational and quality was generally poor (acknowledged by the authors). Study selection and data extraction were performed in duplicate; it was unclear whether this was true for quality assessment [A: Study quality was assessed by two reviewers]. There was some evidence of significant statistical heterogeneity among the observational studies. Combining observational studies and RCTs for some analyses (for example, BMI) did not seem appropriate and the findings from these analyses should be interpreted with caution. The authors acknowledged the short duration of the
studies and inadequate power. The authors also highlighted the skewed distribution for proteinuria, which limited the interpretation of the findings.

The authors’ conclusions appeared suitably cautious, but interpretation must take into consideration the limitations highlighted above and the differences between surgical and non-surgical approaches to weight loss.

Implications of the review for practice and research

**Practice:** The authors stated that most of the included studies were of patients with stages one to three chronic kidney disease and the findings might not be generalisable to patients with more severe forms of kidney disease.

**Research:** The authors stated that further research was needed using consistent measures to investigate whether intentional weight loss with bariatric surgery or diet and exercise affected renal function, development of end stage renal disease (ESRD) and mortality in patients with kidney disease, independent of its effect on diabetes, hypertension and hyperlipidaemia. Future studies might also benefit from assessing the impact of weight loss on inflammation, insulin resistance and oxidative stress.

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