Cochrane for Clinicians

Putting Evidence into Practice

Low-Protein Diets for Adults Without Diabetes Mellitus Who Have CKD

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Clinical Question

In patients without diabetes mellitus who have chronic kidney disease (CKD), is a low-protein diet effective at preventing progression to end-stage renal disease (ESRD) or the need for dialysis?

Evidence-Based Answer

There is moderate-quality evidence that compared with low-protein diets (0.5 to 0.6 g per kg per day) or normal-protein diets (0.8 g per kg per day or more), very low-protein diets (0.3 to 0.4 g per kg per day) reduce the number of patients with advanced kidney disease (CKD stage 4 or 5) who progress to ESRD (i.e., the need for dialysis or transplant; relative risk [RR] = 0.65; 95% CI, 0.49 to 0.85). However, in patients with less advanced disease (CKD stage 3 or lower), low-protein diets do not appear to reduce the progression to ESRD compared with normal-protein diets (RR = 1.05; 95% CI, 0.73 to 1.53; low-certainty evidence).[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

CKD is defined as abnormalities of the structure or function of the kidneys present for three months or more, often diagnosed initially by a glomerular filtration rate of less than 60 mL per minute per 1.73 m^2.[2] In 2016, an estimated 37 million adults in the United States had CKD, representing 15% of all U.S. adults.[3] CKD is associated with a number of adverse health outcomes, including increased all-cause and cardiovascular-related mortality.[2] Identifying interventions that may halt the progression of CKD to ESRD may lead to improved clinical outcomes and lower costs. Protein-restricted diets are thought to have nutritional benefits in patients with CKD, particularly in correcting metabolic acidosis and reducing the adverse effects of phosphate and sodium retention. This Cochrane review aimed to investigate whether low-protein or very low-protein diets were effective in preventing the progression of CKD and delaying the need for dialysis and/or transplant.[1]

This updated review included 17 randomized and quasi-randomized controlled trials.[1] The total number of participants was 2,996 adults without diabetes who had moderate to severe CKD (stage 3 or higher). Participants were 15 to 75 years of age, and the study duration ranged from 12 to 50 months. The review found no difference in the number of patients reaching ESRD when comparing a low-protein diet with a normal-protein diet (RR = 1.05; 95% CI, 0.73 to 1.53; low-certainty evidence). However, when comparing a very low-protein diet to a normal- or low-protein diet, there appeared to be moderate-quality evidence demonstrating a reduction in the number of people reaching ESRD (RR = 0.65; 95% CI, 0.49 to 0.85). It was unclear whether very low-protein diets impacted or changed the glomerular filtration rate compared with normal- or low-protein diets (very low-certainty evidence). There were no significant differences in death rates among participants who followed a low-protein diet (five studies, 1,680 participants; RR = 0.77; 95% CI, 0.51 to 1.18) or very low-protein diet (six studies, 681 participants; RR = 1.26; 95% CI, 0.62 to 2.54).

Adherence to the protein-restrictive diet was measured at regular intervals in all studies and largely reported to be satisfactory. However, no study formally assessed the impact of the dietary restriction on quality of life. Data on adverse effects were limited. Three studies reported that body weight declined during the first few months of the low-protein diet, but then stabilized. Of the 15 studies that assessed for protein energy wasting (malnutrition), 12 found no evidence of malnutrition, and three showed small amounts of wasting.

These are summaries of reviews from the Cochrane Library.

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Current clinical guidelines do not support restricting protein intake to less than 0.8 g per kg per day, the recommended daily intake for the general population, as part of standard treatment to slow the progression of CKD.[2,4] Further studies are needed to better understand the potential benefits of reduced protein intake, as well as adverse effects and impact on quality of life. A 2009 Cochrane review found that very low- or low-protein diets reduced the composite outcome of death and ESRD.[5] This review provides low- to moderate-certainty evidence that for patients with advanced CKD, clinicians should assess dietary protein intake and engage in shared decision-making regarding dietary protein restriction.

The practice recommendations in this activity are available at http://www.cochrane.org/CD001892.

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Beta Blockers for Suspected or Diagnosed Acute Myocardial Infarction

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Clinical Question

Is beta-blocker administration beneficial in the setting of acute myocardial infarction (MI)?

Evidence-Based Answer

Compared with placebo, beta-blocker use in patients with acute MI reduces short-term (less than three months) risk of MI (number needed to treat [NNT] = 196; 95% CI, 143 to 333) and long-term (more than three months) risk of cardiovascular mortality (NNT = 83; 95% CI, 48 to 500) and all-cause mortality (NNT = 91; 95% CI, 48 to 1,000). There are no significant harms.[1] (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

Heart disease was the leading cause of death in the United States in 2018, according to data from the Centers for Disease Control and Prevention.[2] Among the contributors to death from heart disease are the acute coronary syndromes, which include ST elevation MI (STEMI), non–ST elevation MI (NSTEMI), and unstable angina. This Cochrane review examined whether beta-blocker administration in the acute or subacute phase after MI impacts morbidity and/or mortality.[1]

The authors included 63 randomized controlled trials and 85,550 patients and evaluated the use of beta blockers compared with placebo or no intervention in people with suspected or acute MI. Trials were conducted between 1966 and 2018 in 31 countries, including 15 trials in the United Kingdom and four in the United States. The mean patient age was 57.4 years (range = 45.9 to 70.0 years), and 25.5% of participants were women. Fifty-six trials examined beta-blocker use in the post-MI acute phase (within 48 hours of symptom onset), whereas the remaining seven trials considered the subacute phase (three days to 21 days after symptom onset). Selective and nonselective beta blockers were used; the most common was propranolol, which is nonselective. Most trials included all acute coronary syndromes, whereas seven focused only on the use of beta blockers in patients with STEMI. Primary outcomes were all-cause mortality and major adverse cardiovascular events (MACE, encompassing cardiovascular mortality and nonfatal MI), as well as risk of other serious adverse events. Secondary outcomes included quality of life, angina, cardiovascular mortality, and recurrent MI. Each outcome was considered in the short term (less than three months) and long term (six to 60 months).

This Cochrane review demonstrated a significant reduction in long-term all-cause and cardiovascular mortality with beta blockers. They also reduced the short-term risk of MI. Use of beta blockers did not reduce the risk of angina, and there was insufficient evidence to determine if their use altered quality-of-life scores, MACE, or other serious adverse events. It is notable that most trials were conducted before the introduction of what is now standard reperfusion therapy. However, a reassuring subgroup analysis

SUMMARY TABLE

Beta Blockers vs. Placebo or No Intervention for Patients with Suspected or Confirmed MI

Outcomes	Probable outcome with beta-blocker administration	Probable outcome with placebo or no treatment	NNT (95% CI)	Participants (studies)	Evidence quality
Short-term MI risk (within three months)	23 per 1,000 (98% CI, 21 to 25)	28 per 1,000	196 (143 to 333)	67,562 (18 RCTs)	Moderate
Long-term MI risk (six to 60 months)	83 per 1,000 (98% CI, 69 to 99)	92 per 1,000	NA	6,825 (14 RCTs)	Low
Long-term cardiovascular mortality risk (six to 24 months)	112 per 1,000 (98% CI, 103 to 122)	124 per 1,000	83 (48 to 500)	22,457 (14 RCTs)	Moderate
Long-term all-cause mortality risk (six to 60 months)	138 per 1,000 (97.5% CI, 127 to 147)	148 per 1,000	91 (48 to 1,000)	25,210 (21 RCTs)	Moderate

MI = myocardial infarction; NA = not applicable (no statistical difference in outcomes); NNT = number needed to treat; RCT = randomized controlled trial.

found that the above conclusions were statistically valid for patients who had and had not received reperfusion therapy (coronary artery bypass grafting, percutaneous coronary intervention, or thrombolytics).

Current guidelines for the management of STEMI and NSTEMI acute coronary syndromes (including unstable angina) recommend initiation of beta-blocker therapy within the first 24 hours of presentation and continuation after hospitalization for patients without contraindications.[3,4] Family physicians should continue to incorporate beta-blocker therapy in the care of patients with a history of MI.

The practice recommendations in this activity are available at http://www.cochrane.org/CD012484.

Editor's Note: The numbers needed to treat and CIs reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

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