Chronic kidney disease: use of statins

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A meta-analysis has found that statin therapy reduced the risk of cardiovascular events and death from any cause in people with chronic kidney disease of differing severity, with no apparent worsening of renal function. Although the study has limitations, it is consistent with the use of statin therapy outlined in the NICE clinical guideline on chronic kidney disease.

Overview and current advice

The term chronic kidney disease (CKD) describes abnormal kidney function or structure. It is common, frequently unrecognised and often exists together with other conditions (for example, cardiovascular disease and diabetes). When advanced, it also carries a higher risk of mortality. The risk of developing CKD increases with increasing age, and some conditions that coexist with CKD become more severe as kidney dysfunction advances. CKD can progress to established renal failure in a small but significant percentage of people.

The NICE clinical guideline on CKD (which is being updated; publication scheduled for July 2014) advises that the use of statin therapy for the primary prevention of cardiovascular disease in people with CKD should not differ from its use in people without CKD and should be based on existing risk tables for people with and without diabetes. People with CKD should be offered statins for the secondary prevention of cardiovascular disease irrespective of baseline lipid values.

See the Clinical Knowledge Summaries (CKS) topic and the NICE Evidence topic page for a general overview of CKD. The NICE Pathway: chronic kidney disease brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence

A systematic review and meta-analysis has assessed the effects of statin therapy on cardiovascular and renal outcomes in people with CKD. The 31 randomised controlled trials (RCTs) included 48,429 people with and without established cardiovascular disease. Study follow-up duration ranged from 6 months to 4.9 years. Some of the RCTs had been specifically conducted in people with CKD, others
had mixed populations. RCTs that included kidney transplant patients were excluded. The study authors used RCT-level data for the analysis.

For the composite outcome of major cardiovascular events (fatal or non-fatal myocardial infarction, fatal or non-fatal stroke, revascularisation procedures, cardiovascular death, or heart failure), statin therapy produced a statistically significant reduction in risk (relative risk [RR] 0.77, 95% confidence interval [CI] 0.70 to 0.85; p<0.001; 22 RCTs, n=44,096). However, there was evidence of statistically significant heterogeneity between trials for this outcome (p=0.002).

Subgroup analysis in a total of 23,513 patients (number of trials not specified) found that the benefit on major cardiovascular events differed by CKD stage (p<0.001 for between-stage differences). It was on the border of statistical significance for stage 5 patients on dialysis (RR 0.93, 95% CI 0.86 to 1.00; n=7289), not statistically significant for stage 5 patients not on dialysis (RR 0.82, 95% CI 0.60 to 1.11, n=1221), but statistically significant for people with stage 4 CKD (RR 0.78, 95% CI 0.63 to 0.96, n=2598) and stage 2–3 CKD (RR 0.69, 95% CI 0.63 to 0.77, n=12,405).

Statin therapy reduced the risk of death from cardiovascular causes (RR 0.91, 95% CI 0.84 to 0.99, 11 RCTs, n=31,859) and death from all causes (RR 0.92, 95% CI 0.85 to 0.99, 19 RCTs, n=39,722). There was no statistically significant effect on the risk of kidney failure (defined as a 25% decrease in estimated glomerular filtration rate, doubling of serum creatinine, or end-stage renal disease): RR 0.95, 95% CI 0.90 to 1.01 (6 RCTs, n=11,924).

Commentary

Commentary provided by the Medicines and Prescribing Centre

Although this meta-analysis had some limitations, its conclusions are consistent with NICE guidance. The authors conducted a thorough search process and careful data selection method, but they were hampered by not having patient-level data available to them: for example, in the analysis of effects of statins according to kidney function, the authors had to use the mean baseline GFR instead of individual patients' kidney function. In addition, although some of the included studies were specifically conducted in people with CKD, many others were not, so the authors had to rely on post hoc analyses. Furthermore, 18 RCTs used an open label design, which increases the risk of bias, and there was evidence of publication bias for the composite outcome of major cardiovascular outcomes as well as statistically significant heterogeneity in the results for this outcome.

The authors suggest possible reasons why the effects of statins on major cardiovascular events might be less in relative terms in people with poorer kidney function. These include the possibly different aetiology of cardiovascular events in people with severe CKD. However, as the authors point out, although the relative risk reduction is reduced, the comparatively higher baseline risk of cardiovascular events in people with more severe CKD means that the absolute benefits (events prevented per 100 people treated) are of a similar order. NICE guidance recommends the use of statins for primary prevention based on an estimate of cardiovascular risk. Unfortunately, this meta-analysis did not assess the benefits of statins in primary prevention compared with secondary prevention.
Study sponsorship

This systematic review and meta-analysis was supported by grants from the Major State Basic Research Development Program of China, National Natural Science Foundation of China, Natural Science Fund of China to the Innovation Research Group and Program for New Century Excellent Talents in University from the Ministry of Education of China.

References


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