Heart failure

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High-risk people: ACE inhibitors

ACE inhibitors in people at high risk of heart failure

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Summary

Mortality

Compared with placebo ACE inhibitors may be more effective at reducing all-cause mortality in people with asymptomatic left ventricular systolic dysfunction, and in people with vascular disease without known evidence of left ventricular dysfunction or heart failure, and at reducing fatal MI in people with left ventricular systolic dysfunction (low-quality evidence).

Hospitalisation

Compared with placebo ACE inhibitors are more effective at reducing all-cause hospitalisations, cardiovascular hospitalisations and heart-failure hospitalisations in people with heart failure, asymptomatic left ventricular dysfunction, or other risk factors for heart failure (moderate-quality evidence).

For GRADE evaluation of interventions for heart failure, see table.

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Benefits

ACE inhibitors in people with asymptomatic left ventricular systolic dysfunction:

We found one systematic review [77] and three additional RCTs, [78] [79] [80] one of which [79] reported the 12-year follow-up of one of the RCTs included in the review. [81] The systematic review included three RCTs of people with vascular disease, but no heart failure or left ventricular dysfunction (29,805 people,) and five RCTs of people with left ventricular systolic dysfunction or heart failure (12,763 people). [77] In the people with vascular disease, ACE inhibitors significantly reduced all-cause mortality (OR 0.86, 95% CI 0.79 to 0.94; P = 0.0004), non-fatal myocardial infarction (OR 0.82, 95% CI 0.75 to 0.91; P = 0.0001), and heart failure hospitalisation compared with placebo (OR 0.77, 95% CI 0.67 to 0.90; P = 0.0007). In people with left ventricular systolic

dysfunction or heart failure, ACE inhibitors also significantly reduced all-cause mortality, non-fatal myocardial infarction, and heart failure hospitalisation compared with placebo (all-cause mortality: OR 0.80, 95% CI 0.74 to 0.87; P less than 0.0001; non-fatal myocardial infarction: OR 0.77, 95% CI 0.67 to 0.88; P = 0.0001; heart failure hospitalisation: OR 0.66, 95% CI 0.60 to 0.74; P less than 0.0001). In the combined analysis, ACE inhibitors also significantly reduced all-cause mortality (OR 0.83, 95% CI 0.79 to 0.88; P less than 0.0001), non-fatal myocardial infarction (OR 0.80, 95% CI 0.74 to 0.87; P less than 0.0001), and heart failure hospitalisation compared with placebo (OR 0.70, 95% CI 0.64 to 0.76; P less than 0.0001). There was no heterogeneity between groups. The first additional RCT in asymptomatic people after myocardial infarction with documented left ventricular systolic dysfunction, found that an ACE inhibitor (captopril) significantly reduced the risk of all ischaemic events, all myocardial infarctions, and fatal myocardial infarctions compared with placebo (all ischaemic events: 29% with captopril *v* 33% with placebo, RR 0.86, 95% CI 0.74 to 1.0; all myocardial infarctions: 12% with captopril *v* 15% with placebo, RR 0.75, 95% CI 0.60 to 0.95; fatal myocardial infarctions: 5% with captopril *v* 7% with placebo, RR 0.68, 95% CI 0.49 to 0.96). [78] The second additional RCT [79] was a 12-year follow-up of one of the RCTs included in the review. [81] It found that enalapril given for 3–4 years significantly reduced all-cause mortality and cardiac deaths compared with placebo (all-cause mortality: HR 0.86, 95% CI 0.79 to 0.93; cardiac death: HR 0.85, 95% CI 0.77 to 0.94). [79] The third additional RCT (1749 people with left ventricular dysfunction, ejection fraction 35% or less) compared trandolapril versus placebo given 3–7 days after myocardial infarction. [80] The RCT found that, over 12 years, trandolapril significantly reduced the risk of all-cause mortality (RR 0.89, 95% CI 0.80 to 0.99; P = 0.03), all-cause hospitalisations (RR 0.92, 95% CI 0.88 to 0.96; P less than 0.001), cardiovascular hospitalisations (RR 0.95, 95% CI 0.91 to 1.00; P less than 0.047), and heart failure hospitalisations (RR 0.85, 95% CI 0.77 to 0.93; P less than 0.001) compared with placebo. [80]

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Harms

ACE inhibitors in people with asymptomatic left ventricular systolic dysfunction:

The review gave no information on adverse effects. [77] The first additional RCT over 40 months found that a high proportion of people in both groups reported adverse effects (76% with enalapril *v* 72% with placebo; significance not reported). [81] Dizziness or fainting (46% with enalapril *v* 33% with placebo) and cough (34% with enalapril *v* 27% with placebo) were reported more often in the enalapril group (significance not reported for any outcome). The incidence of angio-oedema was the same in both groups (1%). Study medication was permanently discontinued by 8% of the people in the enalapril group compared with 5% in the placebo group (significance not reported). The second additional RCT (12-year follow-up of the first RCT) did not report on adverse effects. The third additonal RCT gave no information on adverse effects. [80]

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Comment

Asymptomatic left ventricular systolic dysfunction is prognostically important, but we found no prospective studies that evaluated screening to detect its presence.

References

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