Angiotensin-receptor blockade and risk of cancer: meta-analysis of randomised controlled trials
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CRD summary
This generally well-conducted review concluded that angiotensin receptor blockers were associated with a modestly increased risk of new cancer diagnosis. It was not possible to draw conclusions about the exact risk of cancer associated with each particular drug. These conclusions are likely to be reliable.

Authors' objectives
To assess whether angiotensin-receptor blockers affect cancer occurrence.

Searching
Medline, Scopus (including EMBASE and other journal groups), the Cochrane Library, and the US Food and Drug Administration website were searched to November 2009 for studies published in English. Search terms were reported; additional details were available as a web appendix.

Study selection
Randomised controlled trials (RCTs) of angiotensin receptor blockers that had median or mean follow-up of at least 12 months and included at least 100 patients were eligible for inclusion. Trials had to report data of cancer occurrence on death. Trials where all groups received an angiotensin receptor blocker were excluded.

Angiotensin receptor blockers assessed in the included trials were losartan, telmisartan alone or combined with ramipril, candesartan, and valsartan alone or combined with captopril. Five trials compared angiotensin receptor blockers with placebo; other comparator agents were atenolol, ramipril, and captopril. Patients in the included trials had pre-hypertension/hypertension, cardiovascular disease, diabetes, recent ischaemic stroke, heart failure, and year acute myocardial infarction. The mean age of participants ranged from 48 to 67 years; the proportion of men ranged from 46 to 74%.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
The authors did not formally assess trial quality.

Data extraction
Two reviewers independently extracted data to populate 2x2 tables. These data were used to calculate relative risks (RRs) and 95% confidence intervals (CIs). Where reported, hazard ratios (HRs) were extracted.

Methods of synthesis
Summary relative risks and 95% confidence intervals were estimated using random-effects models if heterogeneity could not be ruled out, otherwise fixed-effect models were used. Summary hazard ratios and 95% confidence intervals were also estimated. Heterogeneity was assessed using the Q and I² statistics.

Sensitivity analysis was carried out by restricting the analysis to patients without a history of cancer at baseline. The number needed to harm (NNH) was estimated using background cancer incidence for people aged 65 to 69 years (the mean age of patients n the included trials) and the summary relative risks.

Publication bias was assessed using funnel plots and the Begg test.

Results of the review
Nine RCTs were included in the review (n=94,570 patients). All trials reported adequate concealment of treatment allocation.

Angiotensin receptor blockers were associated with an increased risk of new cancer (RR 1.08, 95% CI 1.01 to 1.15; five RCTs). The association was similar when the analysis was restricted to trials in which cancer was a pre-specified endpoint (three RCTs). The only specific solid organ cancer to show a significant association with angiotensin receptor blocker use was lung cancer (RR 1.25, 95% CI 1.05 to 1.49). There was no evidence of heterogeneity for these analysis ($I^2=0\%$). Other cancers investigated which showed no association with angiotensin receptor blocker use were prostate and breast cancer. There was no significant difference in the risk of cancer related death (eight RCTs).

There was no evidence of publication bias (p>0.80).

**Authors’ conclusions**

Angiotensin receptor blockers were associated with a modestly increased risk of new cancer diagnosis. Given the limited data, it was not possible to draw conclusions about the exact risk of cancer associated with each particular drug.

**CRD commentary**

The review addressed a focused question supported by clearly defined inclusion criteria. The literature search was adequate for published studies, but restriction of the review to studies published in English meant that there was a possibility of language and publication bias; this was assessed in the review and no evidence was found. Appropriate steps were taken to minimise bias and errors when extracting data, but it was unclear whether such steps were also taken when selecting studies.

Trial quality was not formally assessed, but details on adequate concealment of treatment allocation were reported. Methods used to pool data were appropriate. The results were clearly presented.

This was generally a well-conducted review. The authors’ conclusions, which take account of the small number of included trials, are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that their findings warrant further investigation, but did not specify further details on how this should be done.

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