Meta-analysis: risk for hypertension in living kidney donors

CRD summary
This review investigated the risk for hypertension after kidney donation and concluded that healthy kidney donors may have a 5-mmHg increase in blood-pressure over that expected with normal ageing 5 to 10 years after donation. This was a good review despite the poor quality of the available evidence. Further research is required before definitive conclusions can be drawn.

Authors' objectives
To assess whether normotensive adults who donate a kidney develop higher blood-pressure (BP) and risk of hypertension than healthy non-donors.

Searching
MEDLINE and EMBASE were searched from inception to November 2005; the search terms were reported. The Science Citation Index, results of the 'Related Articles' facility on PubMed, reference lists of previous reviews, included studies and citations provided by primary study authors were also searched. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Inclusion criteria for study design were not specified other than that the study had to have at least 10 participants. The included studies were prospective and retrospective cohort studies, and some used a non-donor control group. The median length of follow-up was 6 years (range: 1 to 25).

Specific interventions included in the review
Studies of living kidney donation were eligible for inclusion. No included study described the use of laparoscopy for kidney removal.

Participants included in the review
Studies of healthy normotensive adults who had donated a kidney were eligible for inclusion. The mean donor age of the participants in the included studies was 41 years (range: 26 to 59), the mean systolic BP was 121 mmHg (range: 107 to 132) and the mean diastolic BP was 77 mmHg (range: 66 to 85). Very few participants in the included studies were black or had no genetic relationship with the recipient. The control participants (where present) in the included studies were healthy volunteers or people being evaluated as potential donors who were of similar age, gender, race or height.

Outcomes assessed in the review
Studies that assessed BP in terms of systolic or diastolic BP or hypertension at least one year following the procedure were eligible for inclusion; studies only reporting mean arterial pressure were excluded. The outcomes of interest were change in systolic and diastolic BP after donation and the proportion of donors who developed hypertension. The included studies varied in how hypertension was defined.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for relevance, except for non-English language articles which were assessed by a single reviewer with the help of a translator.

Assessment of study quality
Quality was assessed on the basis of whether studies were prospective, the proportion of donors lost to follow-up, the duration of follow-up and the method used to assess BP. Two reviewers independently extracted these data.
Data extraction
Two reviewers independently extracted the data, except for non-English language papers which were extracted by one reviewer with the help of a translator. Attempts were made to contact the authors of all included studies to validate the extracted data and obtain missing data. Where variance estimates for changes in BP were not available, they were derived from t-statistics or the correlation between pre- and post-donation BP. Control group data were excluded for two studies because participants were younger than the donors or had to fulfil further criteria. The mean difference in systolic and diastolic BP and relative risk for hypertension, along with the associated 95% confidence intervals (CIs), were calculated for controlled studies.

Methods of synthesis
How were the studies combined?
The study findings were reported in tables and in a narrative synthesis. In addition, studies with a control group and appropriate data were pooled in a meta-analysis using a random-effects model to estimate the weighted mean difference (WMD) and relative risk for the outcomes of interest.

How were differences between studies investigated?
The Q statistic, using a P-value of less than 0.1 to indicate statistical significance, and the I-squared statistic were used to investigate statistical heterogeneity. Univariate and multivariate meta-regression were used to investigate diversity in the outcomes.

Results of the review
Forty-eight studies (n=5,145) were included: 11 were prospective and the remaining were retrospective. Twelve studies had a control group.

The majority of the studies were retrospective and an average of 31% of participants were lost to follow-up. The majority of studies defined how BP was measured, provided a definition of hypertension and described the donors from which the sample was selected. The control group participants were not assembled and were followed along with donors in the majority of the studies. The studies were underpowered.

BP was higher in donors than controls at least 5 years after donation: the WMD was 6 mmHg (95% CI: 2, 11) for systolic BP (4 studies) and 4 mmHg (95% CI: 1, 7) for diastolic BP (5 studies). There was no evidence of statistical heterogeneity. The data on hypertension (6 studies) were not pooled because of evidence of statistical heterogeneity; an increased risk of hypertension in donors was noted in one study.

The authors commented that the thresholds used to define hypertension in many of the studies were different to those currently used; this has implications for generalisability.

Authors' conclusions
Kidney donors may have a 5-mmHg increase in BP over that expected with normal ageing 5 to 10 years after donation. However, the studies had limitations and prospective controlled studies with long follow-ups are required to provide better information on safety.

CRD commentary
There was a clearly stated review question. Some relevant databases were searched and non-English language studies were included, though unpublished studies were not sought; relevant studies might therefore have been missed. Appropriate procedures were used to reduce errors and bias in the review procedures. This included the sending of data to primary study authors for verification, to which there was a good response. The analysis seemed appropriate and included sensitivity analyses to investigate the assumptions used for imputing missing data. The main limitation was the poor quality of the primary studies available and the authors took this into consideration in their conclusions, which were appropriately tentative.
Implications of the review for practice and research

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

Research: The authors stated that a large, prospective multicentre cohort study that uses modern criteria to define hypertension, and that includes racially diverse, older and genetically unrelated donors and appropriate control participants, is required.

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Other publications of related interest

This additional published commentary may also be of interest. Hsu CY. Review: healthy kidney donors may have a long-term increase in blood pressure beyond that associated with normal aging. ACP J Club 2006;145:79.

Indexing Status

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.