Systematic review of surgical treatments for benign prostatic hyperplasia and presentation of an approach to investigate therapeutic equivalence (non-inferiority)

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CRD summary
The review found no proof that non-standard surgery was superior to standard surgery for reducing symptoms of benign prostatic hyperplasia. An indication of additional benefit was found only for holmium and thulium laser resection of the prostate. These conclusions require cautious interpretation, mainly due to the poor quality of the included trials.

Authors’ objectives
To assess the therapeutic superiority or equivalence of non-standard surgical treatment compared with standard treatment for reducing the symptoms of benign prostatic hyperplasia. The full report was published in German (see Other Publications of Related Interest).

Searching
MEDLINE (from 1966), EMBASE (from 1980) and The Cochrane Library were searched in October 2009 for full-text studies in any language. Search terms were reported. The reference lists of systematic reviews and health technology assessments were checked, and a manufacturers’ association was approached for unpublished studies.

Study selection
Randomised controlled trials (RCTs) were eligible if they evaluated treatments for symptomatic benign prostatic hyperplasia, by comparing standard surgery, such as transurethral resection of the prostate or open prostatectomy, with non-standard surgery, such as minimally invasive techniques, and if they reported patient-relevant outcomes. Controlled clinical trials were eligible in some circumstances, such as if no RCTs were found. If a specific type of non-standard surgery was not inferior in symptom reduction, other outcomes were considered (quality of life, hospital stay, catheterisation, or adverse effects). Inferiority was defined as an effect size of 0.25 standard deviations or more below that of the control intervention. Trials of outdated interventions (listed in the review) and trials with insufficient data (less than 70% of sample analysed) were excluded.

The mean age of participants in the included trials ranged from 60 to 76 years. Most participants had severe symptoms at baseline and a slightly to moderately enlarged prostate. Nine types of non-standard surgery were included; the most common types were holmium laser enucleation and visual laser ablation of the prostate. Standard surgery was often not fully described in the trials. The included trials defined adverse events in different ways. The mean follow-up ranged from six to 84 months, but only data up to 24 months were included in the review.

Two reviewers independently selected trials for inclusion. Disagreements were resolved through consensus.

Assessment of study quality
The following aspects of study quality were assessed: allocation concealment, blinding, statistical power, use of intention-to-treat analysis, losses to follow-up and data consistency. Trials were assessed as having no, minor, or major deficiencies. Evidence based on trials with major deficiencies was classed as indicative rather than proof.

The quality assessment was conducted by one reviewer and checked by a second reviewer, with disagreements resolved by consensus.

Data extraction
Standardised mean differences (Hedges’ g) were calculated for continuous outcomes, with 95% confidence intervals. Data from intention-to-treat analyses were used if possible. Statistical data on adverse events were not available and an alternative method (defined in the review) was developed post-hoc to assess this outcome. Findings were reported at five to eight, nine to 17, and 18 to 24 months of follow-up.

Data extraction was conducted by one reviewer and checked by a second reviewer, with disagreements resolved by
Methods of synthesis
Trial data were combined to calculate pooled effect sizes with 95% confidence intervals, using a random-effects model. Heterogeneity was assessed using I² and if this was over 50%, pooling was not conducted and ranges were presented.

Results of the review
Forty-three trials were included and all were RCTs (4,539 patients). Of these, 41 had major deficiencies, such as insufficient information on allocation concealment (30 RCTs), failure to blind outcome assessment (37 RCTs) and lack of clearly reported intention-to-treat analysis (20 RCTs).

No evidence was found for the superiority of non-standard compared with standard surgery in reducing symptoms.

Non-standard surgery was not inferior to standard surgery for holmium laser of the prostate at six months (SMD -0.29, 95% CI -0.67 to 0.10; one RCT) and at 18 months (SMD -0.30, 95% CI -0.71 to 0.11; one RCT) and for thulium laser resection at 12 months (SMD -0.31, 95% CI -0.66 to 0.04; two RCTs). When these two interventions were combined (viewing them as one technology), they were not inferior at six months (SMD -0.05, 95% CI -0.29 to 0.19; three RCTs) and at 12 months (SMD -0.21, 95% CI -0.49 to 0.07; three RCTs).

Both interventions were associated with shorter duration of catheterisation and length of hospital stay; holmium laser resection was also associated with improved quality of life. These findings were defined as indicative only, due to major deficiencies in the trials. There was no evidence of a difference between the groups in adverse event rates, but reporting was poor. Other outcomes were reported in the review.

Authors’ conclusions
There was no proof that non-standard surgery was superior to standard surgery for reducing the symptoms of benign prostatic hyperplasia. Indications of additional benefit were found only for holmium and thulium laser resection of the prostate.

CRD commentary
The initial objective was to assess whether non-standard surgery was superior to standard surgery. If no evidence was found to support this, the outcome was broadened to include non-inferiority in symptom reduction, and a post-hoc definition of non-inferiority was constructed. Relevant sources were searched for trials, but the restriction to full-text articles meant that there might have been publication bias and this was not assessed.

Steps were taken to minimise the risk of bias in the processes of study selection, quality assessment and data extraction, and heterogeneity between the trials was assessed and addressed appropriately. As the authors noted, the review had limitations, which included post-hoc changes to the review methods and difficulty in classifying procedures as standard or non-standard.

The conclusions may require cautious interpretation, mainly due to the poor quality of the included trials.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that future studies should define a non-inferiority threshold before starting. Indirect comparisons could be used to compensate for the lack of data comparing non-standard and standard treatment. The procedural advantages of non-standard treatment should be taken into account when balancing the benefits and harms.

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