A systematic review of holmium laser prostatectomy

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CRD summary
This well-conducted review compared the safety, efficacy and durability of holmium laser prostatectomy techniques with transurethral resection of the prostate (TURP). Holmium laser procedures were at least as effective as TURP in the short term, although the operations took longer. However, comparative safety could not be determined in relation to mortality or other complications. The conclusions are reliable.

Authors’ objectives
To compare the safety, efficacy and durability of holmium laser prostatectomy, both holmium laser resection (HoLRP) and holmium laser enucleation (HoLEP), with transurethral resection of the prostate (TURP).

Searching
The following sources were searched: MEDLINE (from 1966 to 2002), Current Contents (from 1993 to 2002), EMBASE (from 1980 to 2002), the Cochrane Library (Issue 1, 2002), PREMEDLINE (August 2002), PubMed (August 2002), the Science Citation Index (from 1995 to 2002), SIGLE (Issue 6, 2002), a clinical trials database (USA; August 2002), and NHS Centre for Reviews and Dissemination and NHS HTA databases (August 2002). Searches for studies with a TURP arm were only performed from 1995 onwards. In addition, the National Research Register (Issue 2, 2002) was searched for studies on holmium laser treatment. The search terms were stated and no language limitations were applied. The bibliographies of all publications were manually searched for additional studies.

Study selection

Study designs of evaluations included in the review
For HoLRP and HoLEP, randomised controlled trials (RCTs), historical and/or non-randomised comparative studies and case series were eligible. Abstracts and conference proceedings with sufficient data were included. The HoLRP and HoLEP arms of studies that did not include a TURP arm were included as case series data. Data from the TURP study arms (with at least 50 patients) of RCTs that compared TURP with non-TURP treatment were used as a source of benchmark data for TURP.

Specific interventions included in the review
Studies that compared HoLRP or HoLEP performed with the Ho:YAG laser with TURP were eligible for inclusion. Studies that combined either of the holmium laser techniques with other methods were only included if the results for HoLRP or HoLEP could be separated from the combined data. Studies that used any additional non-prostate surgery were excluded.

Participants included in the review
Studies of patients with outflow obstruction secondary to benign prostatic hypertrophy (BPH) were eligible. Studies of patients with malignant tumour were only included if the results could be separately analysed for patients with BPH.

Outcomes assessed in the review
Studies that reported at least one of the following safety or efficacy outcomes were eligible: peri- and post-operative mortality; subjective symptom improvement using standard symptom scores; objective symptom improvement; peri- and post-operative morbidity; peri- and post-operative factors; evaluation of treatment durability; and measures of patient convalescence. The review assessed: blood loss or bleeding, generally using surrogate measures such as secondary haemorrhage, transfusion rates, haematuria, bladder irrigation, TUR syndrome, fluid absorption, reduction of haemoglobin, duration of catheterisation and hospitalisation; mechanical complications such as perforations and strictures; other adverse events such as mortality, cardiopulmonary complications, urinary tract and other infections; urodynamic obstruction, i.e. peak urinary flow rate, detrusor pressure at maximum flow, Schafer grade, post-void residual volume and post-operative prostate volume; symptom relief, i.e. American Prostate Association Database of Abstracts of Reviews of Effects (DARE) Page: 1 / 5
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(AUAI)/International Prostate Symptom Score (IPPS) scores, quality of life, transient urinary retention, incontinence and dysuria/irritative symptoms; sexual function;

peri-operative factors such as operating time, tissue retrieval and prostate cancer; durability, i.e. re-catheterisation rate, re-operation rate, symptoms and obstruction over time; and cost-effectiveness.

How were decisions on the relevance of primary studies made?
Two researchers independently selected the studies and resolved any differences through discussion.

Assessment of study quality
Study validity was assessed by considering the quality of the study reporting, method of randomisation and allocation concealment (for RCTs), blinding of patients and outcome assessors, attempts to minimise bias, sample size and power, generalisability of results, and the statistical methods used to analyse the data. The author does not state how the papers were assessed for validity. However, the validity of the included studies was discussed using a hierarchical of evidence framework.

Data extraction
One reviewer extracted the data onto a specially designed data extraction form, while a second reviewer checked the results. The tabulated information included the year of publication, study location, study design, intervention, the number of patients per treatment arm, patient characteristics, type of analysis and results. Relative risks (RRs) or weighted mean differences (WMDs), along with 95% confidence intervals (CIs), were calculated for individual RCTs when appropriate.

Methods of synthesis
How were the studies combined?
The studies were grouped according to the study design (comparative and case series), intervention and outcome, and a narrative synthesis (with or without a meta-analysis) was undertaken. Data from the RCTs were only combined when the outcomes were comparable and there was no apparent heterogeneity, and the pooled RR or WMD with 95% CIs were calculated. The level of evidence was classified on the basis of study design (see Other Publications of Related Interest): systematic review of all relevant RCTs (level 1); at least one properly designed RCT (level 2); well-designed pseudo-RCTs (level III-1); comparative studies with concurrent controls, cohort studies, case-control studies, or interrupted time-series with control group (level III-2); comparative studies with historical control, one or more single arm studies or interrupted time series with no parallel control group (level III-3); and case series, either after test or before-and-after test (level IV).

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test and differences were discussed in the text.

Results of the review
Three RCTs (230 patients), one comparative study with historical controls (132 patients) and 13 case series (between 2,188 and 2,569 patients) assessed HoLRP. Two RCTs (182 patients), one comparative study with historical controls (111 patients) and 10 case series (847 patients) assessed HoLEP. Nineteen RCTs provided TURP study arms (1,682 patients).

The evidence-base was rated as average.

Quality.

Four of the 5 RCTs were of poor quality. Methodological flaws included: inadequate description of the methods used for randomisation, allocation concealment and blinding; no power calculations; no estimates of outcome effect sizes or CIs; limited information on the inclusion and exclusion criteria; and a lack of reporting the losses to follow-up in 3 RCTs.
The comparative studies suffered from several methodological flaws: a lack of detail about the methods used to select the sample; no inclusion or exclusion criteria; a lack of reporting the adverse events in one study; no actual outcome data reported; and a lack of clarity in reporting data and whether there were any losses to follow-up.

The case series suffered from a number of problems: the difficulty in establishing the extent of overlap in samples between reports; the wide variety of pre-, peri- and post-operative outcomes; inadequate reporting of the outcomes; and considerable losses to follow-up (up to 50% for some series) without reasons.

Safety.

The holmium laser procedures were considered at least as safe as TURP in terms of blood loss, rate of stricture and urinary tract infection. The relative safety of the holmium laser could not be determined with respect to mortality, perforation rate and other complications.

Both HoLRP and HoLEP reduced several indicators of blood loss (transfusion rates, post-operative bladder irrigation, and duration of catheterisation and length of hospital stay) compared with TURP.

Transfusion rates (3 RCTs): holmium laser treatment significantly reduced transfusion rates compared with TURP (RR 0.2, 95% CI: 0.0, 0.9). No significant heterogeneity was found (P=0.87).

Post-operative bladder irrigation (1 RCT): patients having HoLRP required significantly less post-operative irrigant compared with TURP (WMD 27.5 mL, 95% CI: 21.7, 33.3). Duration of catheterisation: patients required a significantly shorter period of catheterisation after HoLRP compared with TURP; the mean duration (2 RCTs) was -0.8 days (95% CI: -1.0, -0.7). Borderline significant heterogeneity was found (p=0.096). Another 3 RCTs (not included in the meta-analysis) found similar results favouring holmium laser treatment: 1.9 days with HoLRP versus 3.2 days with TURP; a difference of -1.2 days (95% CI: -2.0, -0.4) in favour of HoLEP; and a median duration of catheterisation of 1.0 days with HoLP versus 2.0 days with TURP (p less than or equal to 0.001).

Duration of hospital stay: in comparison with TURP, patients had a significantly shorter hospital stay after HoLRP: the mean duration (2 RCTs) was -0.9 days (95% CI: -1.1, -0.7, p=0.79). Two other RCTs (not included in the meta-analysis) found similar results: a difference of -1.2 days (95% CI: -2.0, -0.4) in favour of HoLEP; and a median stay of 2.0 days with HoLEP versus 3.0 days with TURP (p<0.001).

Strictures and urinary infection: HoLRP and HoLEP appeared to have similar rates of stricture and urinary infection in comparison with TURP. The RR was 3.0 (95% CI: 0.1, 76.4) for urethral stricture (1 RCT of HoLEP), 5.2 (95% CI: 0.2, 110.0) for bladder neck stricture (1 RCT of HoLEP), 0.5 (95% CI: 0.0, 5.4) and 0.8 (95% CI: 0.2, 3.1) for meatal stricture (1 RCT of HoLEP and 1 RCT of HoLRP, respectively), and 0.3 (95% CI: 0.0, 8.0) and 0.4 (95% CI: 0.0, 5.1) for bulbar or penile (1 RCT of HoLEP and 1 RCT of HoLRP, respectively). There was no significant difference between holmium laser and TURP for urinary infections; the RR (2 RCTs) was 0.4 (95% CI: 0.1, 1.5, p=0.55).

Other: there was insufficient good quality data to compare mortality and rates of perforation and other complications between HoLRP or HoLEP with TURP.

Efficacy.

The holmium laser procedure was at least as efficacious as TURP in the short term, but long-term efficacy could not be determined.

HoLRP and HoLEP appeared to produce similar levels of symptom relief compared with TURP. There was no significant difference in symptom scores between holmium laser and TURP at 6 or 12 months post-operatively; the WMD was -0.9 (95% CI: -2.1, 0.2, p=0.07) at 6 months (3 RCTs) and -0.4 (95% CI: -1.8, 1.1, p=0.69) at 12 months (2 RCTs).

Both holmium laser treatment and TURP retrieved sufficient tissue for the detection of undiagnosed prostate cancer, although no studies directly compared holmium laser with TURP for this outcome. One RCT detected prostate cancer in 11.8% of patients having TURP, compared with 0% of those having HoLRP. One comparative study found prostate
cancer in 5.5% of patients having HoLEP. Seven case series of HoLRP detected prostate cancer in between 0 and 11.4% of the patients. Ten case series of TURP detected prostate cancer in between 1.7 and 21% of the patients.

TURP reduced operating time in comparison with holmium laser treatment; the WMD (2 RCTs) was 19.3 minutes (95% CI: 13.5, 25.1). There was insufficient long-term follow-up data to compare the durability of HoLRP or HoLEP and TURP.

Results were also reported for all the outcomes listed in the 'Outcomes Assessed' section.

Cost information
Yes. One RCT suggested that HoLRP may be more cost-effective than TURP: NZ$2,012 for each HoLRP compared with $2,663 for each TURP, assuming equivalent clinical outcomes at 12 months.

Authors' conclusions
In comparison with TURP, holmium laser prostatectomy reduced blood loss according to several indicators of blood loss. The two techniques appeared to have similar rates of stricture and urinary tract infection, but no conclusion could be reached about mortality or other complications. Holmium laser prostatectomy and TURP appeared to have an equivalent effect on symptoms, and both procedures provided adequate tissue to allow the detection of prostatic cancer. No conclusions could be reached about the durability of holmium treatment in comparison with TURP.

CRD commentary
This was a well-conducted review in which the aims were stated and the inclusion criteria were defined in terms of the participants, study design, outcome and interventions. Several relevant sources were searched, details of the literature search were provided, and no language restrictions were applied. Two reviewers assessed validity, and the data were extracted by one reviewer and checked by a second. This reduced the potential for bias and errors. Validity was assessed using defined criteria, but the methods used were not described. The methodological flaws were summarised according to study design. Relevant information on the primary studies was tabulated. The studies were appropriately grouped according to outcome, and the results from comparative studies and case series were summarised separately. Only RCTs reporting similar outcomes were pooled in a meta-analysis. Statistical heterogeneity was assessed and attention was drawn to better quality sources of evidence in the review. Tissue retrieval for the detection of cancer was based on results from only two studies that used different methods. Excluding the conclusion relating to the adequacy of tissue retrieval, the evidence presented appears to support the author's conclusions.

Implications of the review for practice and research
Practice: The author states that surgeons undertaking holmium laser treatment should have adequate experience in transurethral resection methods and, preferably, experience in laparoscopic and laser surgery.

Research: The author states that the priority is to provide long-term follow-up and to tackle the problem of losses to follow-up. In addition, further research would strengthen the evidence for holmium laser methods, and that longer-term follow-up and studies in other setting are required to confirm results from the one cost-effectiveness analysis that was identified.

Bibliographic details

Original Paper URL
Other publications of related interest

Indexing Status
Subject indexing assigned by CRD

MeSH
Holmium /therapeutic use; Laser Therapy; Male; Prostatectomy; Prostatic Diseases /surgery

AccessionNumber
12003008492

Date bibliographic record published
31/10/2003

Date abstract record published
31/10/2003

Record Status
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.