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Benign Prostatic Obstruction

A Randomised Trial Comparing Holmium Laser Enucleation Versus Transurethral Resection in the Treatment of Prostates Larger Than 40 Grams: Results at 2 Years

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Abstract

Objective: To compare holmium laser enucleation of the prostate (HoLEP) with transurethral resection of the prostate (TURP) for treatment of men with bladder outflow obstruction (BOO) secondary to benign prostatic hyperplasia with a minimum of 24-month follow-up.

Patients and methods: Sixty-one patients were randomised to either HoLEP or TURP. All patients had BOO proven on urodynamic studies pre-operatively (prostate size 40–200 g). One patient died before treatment, which left 30 patients in each group. Perioperative data, as well as symptom scores, Quality of Life (QoL) scores, and maximum urinary flow rates (Q_{max}) were obtained at one, three, six,12, and 24 months. Post-void residual volumes, transrectal ultrasound (TRUS) volumes, and pressure flow studies were obtained six months post-operatively. Continence and potency data were also recorded.

Results: There were no significant differences between the two surgical groups pre-operatively. Mean pre-operative TRUS volume was 77.8 ± 5.6 g (42–152) in the HoLEP group and 70.0 ± 5.0 g (46–156) in the TURP group. Patients in the HoLEP group had shorter catheter times and hospital stays. More prostate tissue was retrieved in the HoLEP group. At six months, HoLEP was urodynamically superior to TURP in relieving BOO. At 24 months, there was no significant difference between the two surgical groups with respect to American Urology Association scores, QoL scores, or Q_{max} values; however, two patients in the TURP group required re-operation.

Conclusions: HoLEP has less perioperative morbidity and produces superior urodynamic outcomes than TURP, when treating prostates >40 g. At 24 months of follow-up, HoLEP is equivalent to TURP.

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1. Introduction

The surgical management of men with large prostates (>40 g) that cause bladder outflow obstruction (BOO) secondary to benign prostatic hyperplasia (BPH) is a challenging area. Traditional treatment such as transurethral electrocautery resection of the prostate (TURP) has increased risks of bleeding and TUR syndrome [1] when treating the larger prostate, and it is generally contraindicated for glands >100 g. These glands have often been treated with the more significant procedure of open prostatectomy, which often exposes elderly patients to increased perioperative morbidity.

The holmium laser, with a wavelength of 2,140 nm, conducts through saline and maintains the ability to precisely incise prostatic tissue, and has excellent haemostatic properties. This minimises the risks of perioperative bleeding and TUR syndrome, which are significant concerns when performing TURP. Holmium laser resection of the prostate (HoLRP) is as effectifve as TURP in the management of BOO and has less perioperative morbidity than TURP [2–4]. This procedure has been further refined with the development of the soft tissue morcellator to allow enucleation of whole lobes of the prostate. Holmium laser enucleation of the prostate (HoLEP) can treat any prostate size, with minimal risk of TUR syndrome because saline rather than iso-osmolar electrolyte-free irrigating solution is used. Transfusion rates are also extremely low.

To address the durability of HoLEP, this study reports the medium-term data from a randomised clinical trial that compared the postoperative outcomes of men with large prostates (40–200 g on ultrasound) that caused BOO, who underwent HoLEP compared to those who underwent TURP [5].

2. Patients and methods

2.1. Participants

After ethical approval was obtained, all patients who presented to the urology service at Tauranga Hospital between June 1997 and December 2000 and considered for surgical treatment for BOO secondary to BPH were invited by an independent research nurse to participate in this trial. At enrolment all patients were thoroughly evaluated by medical history and physical exam, digital rectal exam, prostate-specific antigen (PSA), urinalysis and urine culture, American Urological Association (AUA) symptom score, single question Quality of Life (QoL) score, transrectal ultrasound (TRUS) measurement of prostatic volume, post-void residual assessment (PVR), maximum urinary flow rate (Q_{max}) and pressure flow urodynamic assessment.

Inclusion criteria were TRUS volume of 40–200 g, Q_{max} of 15 ml/s or less, AUA symptom score of 8 or greater, PVR of less than 400 ml, and urodynamic Schaffer grade 2 or greater. TRUS biopsies were performed to exclude cases of prostatic carcinoma. Catheterised patients and those with a history of previous urethral or prostatic surgery were excluded.

2.1.1. *HoLEP*

All procedures were performed by one of two surgeons (PJG or MRF), who used the technique previously described [6]. Maximum power was set at 100 W for each case and a Versacut morcellator (Lumenis, Inc., Tel Aviv, Israel) was used. Post-operative Foley catheter irrigation was performed if deemed necessary; most patients were treated with a standard Foley catheter, which was normally removed the day after surgery.

2.1.2. *TURP*

Standard TURP was performed with a tungsten cutting wire at 160 W cutting and 80 W coagulating current by one of three surgeons (PJG, MRF, AMW), all of whom had performed more than 500 TURPs. An irrigating Foley catheter was inserted and bladder irrigation was used as necessary until haematuria had settled sufficiently to remove the catheter.

2.2. Outcomes

2.2.1. *Primary outcomes*

Post-operative primary outcomes were AUA symptom scores, QoL score, and Q_{max} at one, three, six, 12, and 24 months.

2.2.2. *Secondary outcomes*

Secondary outcomes included a pressure flow urodynamic assessment, PVR, and TRUS volume measurement at six months of follow-up. Continence and potency were assessed with a questionnaire that involved standard questions that we have employed in each of our studies over the last 10 years [2,5]. These predated current standardised questionnaires, but are useful in that they allow internal comparison. Continence questions involved separate questions about stress, urge, and overflow incontinence, and post-void dribbling. Re-operation and recatheterisation rates were recorded and patients with less than 50% improvement in Q_{max} or symptom score had flexible cystoscopy to ensure the absence of urethral strictures.

A sample size calculation that used $\alpha = 0.05$ and $\beta = 0.20$ based on previous work [2] showed that 30 individuals would be required per group to show a 10% difference. A balanced blocked randomisation schedule (block of six patients) was used to allocate patients to one or the other treatment arm. Any patient who met the inclusion criteria was allocated the next available envelope and allocated accordingly to a treatment arm. If the patient refused to participate in the study, his envelope was not reused. Data distribution for all primary and secondary outcomes did not fit with standard normality assumptions, so the two procedures were compared with a non-parametric Mann-Whitney *U* test.

Table 1 – Baseline patient characteristics

	Mean ± SE HoLEP[a] (range)	Mean ± SE TURP[a] (range)
Age (range)	71.7 ± 1.1 (54–84)	70.3 ± 1.0 (59–83)
AUA[a] Symptom Score	26.0 ± 1.1 (14–35)	23.7 ± 1.2 (9–35)
QoL[a] Score	4.8 ± 0.2 (2–6)	4.7 ± 0.2 (2–6)
Q_{max}[a] (ml/s)	8.4 ± 0.5 (2–14)	8.3 ± 0.4 (3–12)
TRUS[a] vol (cc)	77.8 ± 5.6 (42–152)	70.0 ± 5.0 (46–156)
PdetQ$_{max}$ (cmH20)	76.2 ± 4.4 (44–137)	85.8 ± 5.4 (46–156)
Schaffer Grade	3.5 ± 0.2 (2–6)	3.7 ± 0.2 (2–6)

[a] HoLEP: holmium laser enucleation of the prostate; TURP: transurethral resection of the prostate; AUA: American Urological Association; QoL: Quality of Life; Q_{max}: maximum urinary flow rates; TRUS: transrectal ultrasound.

3. Results

3.1. Baseline data

Sixty-one men participated in this study: 31 in the HoLEP arm and 30 in the TURP arm. Table 1 shows the preoperative patient characteristics of each arm. There was no significant difference between the two groups. One patient from the HoLEP arm died preoperatively, which left 30 in each arm of the study. A total of 48 patients reached the 24 month follow-up, 26 following TURP and 22 following HoLEP. Four patients were lost to follow-up between 12 and 24 months. One died and three could not be contacted.

3.2. Outcomes

Perioperative data and flow diagram out to 12 months have been previously published [5]. This showed that HoLEP was superior to TURP with respect to catheter time and hospital stay, but took longer to perform. However, significantly more tissue was removed by HoLEP than TURP.

3.3. Primary outcome data

The primary outcome data at one, three, six, 12, and 24 months are shown in Table 2. There was no difference in post-operative Q_{max}, AUA, or QoL scores between the two groups at six, 12, and 24 months.

3.4. Secondary outcome data

Secondary outcome data are shown in Table 3.

In the 18 TURP patients who had complete PSA data before and after, a 65% reduction was seen (a mean of 5.2 micromol/l to 2.3 micromol/l) and in the 10 HoLEP patients with PSA measured post-operatively in 87% reduction was noted: (8.7 micromol/l to 1.2 micromol/l).

There was no significant difference in post-operative PVR between the two groups. However, there were statistically significant differences in favour of HoLEP with regard to improvements in post-operative TRUS volume, PdetQmax, and Schaffer Grade at six months of follow-up.

Table 2 – Post–operative data

	HoLEP	TURP
1 month ($n = 60$)		
AUA	8.6 ± 1.2	5.7 ± 1.1*
QoL	2.7 ± 0.4	1.6 ± 0.3
Q_{max} (ml/s)	22.3 ± 2.3	18.4 ± 1.6
3 months ($n = 56$)		
AUA	4.8 ± 0.8	2.4 ± 0.9
QoL	1.8 ± 0.4	1.9 ± 0.6
Q_{max} (ml/s)	24.2 ± 1.7	18.9 ± 1.9*
6 months ($n = 54$)		
AUA	6.0 ± 1.0	4.8 ± 0.7
QoL	1.6 ± 0.3	1.5 ± 0.2
Q_{max} (ml/s)	21.3 ± 2.1	18.9 ± 2.8
12 months ($n = 52$)		
AUA	4.6 ± 0.7	4.7 ± 0.9
QoL	1.5 ± 0.5	1.4 ± 0.3
Q_{max} (ml/s)	21.3 ± 2.1	18.9 ± 2.8
24 months ($n = 48$)		
AUA	6.1 ± 1.0	5.2 ± 0.8
QoL	1.25 ± 0.2	1.25 ± 0.2
Q_{max} (ml/s)	21.0 ± 2.0	19.3 ± 2.2

* $p < 0.05$.

3.5. Continence and potency

Forty-three percent of HoLEP patients and 39% of TURP patients had potency sufficient for intercourse pre-operatively. At 12 months, two patients had improved potency (3.9%) and two (3.9%) had deterioration in potency. At 24 months, two patients in each group had new onset of erectile dysfunction (erections insufficient for penetration) compared to their pre-operative state. Retrograde ejaculation

Table 3 – Data at six months post-procedure (including pre-op. PdetQmax)

	HoLEP	TURP
PVR* (mls)	33.7 ± 5.5	51.8 ± 14.5
TRUS vol (ml)	28.4 ± 1.8**	46.6 ± 4.4
PdetQmax (cmH20) preop	73.2 ± 4.4	85.8 ± 5.4
PdetQmax (cmH20) 6 mos	20.8 ± 2.8**	40.7 ± 2.7
Schaffer Grade	0.2 ± 0.09**	1.2 ± 0.2

* PVR: post-void residual.
** $p < 0.001$.

Table 4 – Total adverse events at 24 months

	HoLEP	TURP
Blood transfusion	–	1
Re-catheterisation	5	4
Re-operation	–	2
Documented urinary tract infections	–	2
Strictures	1 (submeatal)	3 (2 submeatal, 1 bulbar)
Deaths	–	1 at 15 months post-op

was seen in 12 of 16 patients in the Holmium group and eight of 13 in the TURP group.

Incontinence was present in 48% of HoLEP patients and 38% of TURP patients pre-operatively (not including post-micturition dribbling). Six of the 15 incontinent patients in the HoLEP group and eight of 11 in the TURP groups regained continence post-operatively. Only one patient (in the HoLEP group) had new onset stress incontinence noted at 12 months, which had resolved by 24 months. One patient in the TURP group had urge incontinence at 24 months that did not require protection.

3.6. *Adverse events*

Adverse events at 24 months are documented in Table 4. Similar numbers required recatheterisation in the two groups. One TURP patient required blood transfusion. Aside from recatheterisation, the only other adverse event in the HoLEP group was a urethral stricture that required dilatation in the office. Three patients in the TURP group developed strictures.

4. Discussion

Many treatments have been offered as alternatives to TURP. Most have not approached TURP with respect to durability or efficacy, although morbidity is often improved. In men with larger prostates, the alternatives are even more limited. The characteristics of the holmium laser wave length determine its versatility and provide an endoscopic alternative to both TURP and open prostatectomy when used for enucleation [6].

In our study, HoLEP was equivalent to TURP with respect to symptom score improvement, QoL improvement, and Q_{max} at 24 months of follow-up, although two TURP patients required re-operation. This study also demonstrated that HoLEP was superior with regard to perioperative morbidity, with reduced bladder irrigation and catheter times and reduced hospital stay, even though more prostate tissue was retrieved [5].

The goal of this paper is to demonstrate HoLEP's medium-term durability compared to TURP. TRUS volume reduction post-operatively is superior, and urodynamic relief of obstruction is greater; thus, HoLEP is likely to be at least as effective as TURP in long-term follow-up.

HoLEP has been proven to be a valid alternative in small (<40 g) [7], large (>40 g) [8–11], and very large [12] (>100 g) prostates compared to TURP or open prostatectomy. Kuntz et al., in a well-designed study, demonstrated reduced perioperative morbidity for HoLEP compared to open prostatectomy, with equal outcome measures [12]. Gilling et al. [2] demonstrated similar findings when they compared HoLRP with TURP for smaller glands. There is potentially no limit to the size of a prostate that can be treated with HoLEP [13]; the largest gland treated in our institution is 450 g and open prostatectomy has been eliminated.

Two issues, apart from appropriate marketing, prevent HoLEP from rapidly becoming a more widespread procedure: the learning curve and the financial outlay. The learning curve [14] can be minimised with appropriate case selection and a short period of structured supervision. Anecdotally, the opinion of our trainees is that the anatomical nature of enucleation makes it inherently easier to master than TURP. The initial outlay for a holmium laser is significant, but a previous study at our institution [15] demonstrated that HoLRP was cost effective compared to TURP. The multi-use nature of the holmium laser for stones and other soft tissue applications further improves its cost effectiveness.

The only other minimally invasive procedure that may challenge HoLEP is laparoscopic retropubic prostatectomy [16]. In this recent series from Brazil, the mean prostate size was 144 g on ultrasound, the catheter time was 4.6 days, and the hospital stay 3.5 days. In a contemporary HoLEP series the prostate size was greater and the operative, hospital, and the catheter times were significantly shorter [17]. Individual expertise will likely determine which approach for enucleation is employed, but the transurethral route (HoLEP) appears superior in comparable series in every respect.

No case of TUR syndrome was seen in either group. None would be expected in the HoLEP arm as normal saline is the irrigant; however, 26% of patients do absorb a mean of 459 ml of fluid [18]. The incidence of TUR syndrome is slight in modern TURP series.

5. Conclusions

HoLEP is an efficient technique performed with a versatile energy source. It represents a paradigm shift in the endoscopic management of BPH and can be used to treat prostates of all sizes. This study addresses the question of durability of HoLEP and suggests that it will be at least as durable as TURP in the long term as more tissue is surgically removed and by 24 months fewer re-operations were required.

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