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NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of Holmium Laser Prostatectomy

Introduction

This overview has been prepared to assist members of IPAC advise on the safety and efficacy of an interventional procedure previously reviewed by SERNIP. It is based on a rapid survey of published literature, review of the procedure by Specialist Advisors and review of the content of the SERNIP file. It should not be regarded as a definitive assessment of the procedure.

Procedure name

Holmium laser resection of the prostate (HoLRP)
Holmium Laser Enucleation of the Prostate (HoLEP)

SERNIP procedure number

138

Specialty society

British Association of Urological Surgeons

Executive Summary

The evidence regarding holmium laser prostatectomy is limited and of poor quality. There were three RCTs comparing HoLRP and TURP and two RCTs comparing HoLEP with TURP. All were characterised by short follow-up periods and small sample sizes.

Compared to TURP, HoLRP/HoLEP appears to result in less blood loss, and shorter catheterisation times. No other conclusions about safety could be made, and no differences in patient outcomes were detected between the two procedures.

Patient outcomes, whether objective urodynamic outcomes, or subjective outcomes do not appear to show an advantage for the holmium procedures.

Indication(s)
Benign Prostatic Hyperplasia (BPH).

Benign prostatic hyperplasia (BPH), a non-malignant enlargement of the prostate, is a common cause of lower urinary tract symptoms in men older than 40 years of age and a widely accepted antecedent of bladder outlet obstruction.[1] Although the aetiology of BPH is still poorly understood, it is nonetheless prevalent in men over 50 years of age to the extent that two out of ten males will eventually require an operation to relieve the symptoms of BPH.[2,3 4,5]Increasing resistance to urinary flow caused by the enlarged prostate gland results in bladder hypertrophy and progressively higher voiding pressure, which in turn produces obstructive symptoms such as a weak stream, hesitancy and incomplete voiding. The irritative symptoms such as frequency, nocturia and dysuria are generally attributed to the increasing instability of the hypertrophied bladder. A syndrome of bladder decompensation can eventually develop if the bladder is unable to adapt.[6] This can manifest as an accumulation of residual urine, which can lead to recurrent urinary tract infections and the formation of bladder calculi.[5] In severe cases, acute urinary retention can occur and obstructive nephropathy can develop if high voiding pressures are transmitted back to the kidneys.[6]

BPH can be managed medically or surgically. The gold-standard surgical treatment is Transurethral Resection of the Prostate (TURP). However, relatively high morbidity for this procedure has led to the development of a range of minimally invasive techniques, some of which utilise thermal energy. HoLRP is one such minimally invasive technique utilising a Holmium: Yttrium-Aluminium-Garnet laser.

Summary of procedure
HoLRP utilises the holmium laser exclusively at high powered settings of 60 to 80W.[7] The procedure is performed with a modified 26F continuous flow resectoscope that has been fashioned with a circular fibre guide in the tip of the scope. An end-firing laser fibre is used as a precise cutting instrument to resect large pieces of prostate.[7] Initially a bilateral bladder neck incision is made to define the margins of resection. The median and lateral lobes are then individually undermined and peeled off the prostate capsule in a retrograde direction until only a bridge of tissue remains at the bladder neck. The laser is then used to cut the resected tissue into smaller pieces prior to their release into the bladder. These are then removed with a modified resectoscope loop.[7]

A primary advantage of HoLRP over other laser prostatectomy techniques is that it can rapidly create a large “TURP-like” cavity by immediately removing obstructing tissue, rending it suitable for large prostates of up to 100 grams.[8] The coagulative ability of the holmium laser effectively seals tissue planes as the operation progresses, which makes HoLRP a relatively bloodless operation with a concomitant reduction in transfusion requirement, and also avoids the dangers of systemic fluid absorption.[9] Other postulated advantages include a reduced need for bladder irrigation, shorter postoperative catheterisation period and length of hospital stay, and the ability to retrieve

tissue for histological examination.[10-12] However, HoLRP is associated with a steep learning curve that requires the development of significant endoscopic skill and longer procedure times, particularly for larger prostates.[13] A further evolution of the HoLRP procedure is holmium laser enucleation of the prostate (HoLEP) in which the entact prostatic lobes are removed with the holmium laser and then passed into the bladder where they are morcellated with a specially designed mechanical morcellator for evacuation.

Literature review

A systematic search of MEDLINE, PREMEDLINE, EMBASE, Current Contents, PubMed, Cochrane Library and Science Citation Index using Boolean search terms was conducted, from the inception of the databases until October 2002. The York Centre for Reviews and Dissemination, Clinicaltrials.gov, National Research Register, SIGLE, Grey Literature Reports, relevant online journals and the Internet were also searched in October 2002. Searches were conducted without language restriction.

Articles were obtained on the basis of the abstract containing safety and efficacy data on holmium laser resection of the prostate in the form of randomised controlled trials (RCTs), other controlled or comparative studies, case series and case reports. Since a systematic review has recently been completed comparing HoLRP with TURP this comprised the majority of the included data. However, 2 additional studies comparing HoLRP with visual laser ablation of the prostate (VLAP) were also obtained, and though excluded from the systematic review, were included in this overview.

List of studies found (HoLRP)

Systematic Review comparing HoLRP and TURP: 1
- Randomised controlled studies – 3
- Non-randomised comparative studies – 1
- Case series – 12

RCTs comparing HoLRP and VLAP: 1
Non-RCT comparative studies: 1 (HoLRP vs VLAP vs TULIP)

List of studies found (HoLEP)

Systematic Review comparing HoLEP and TURP: 1
- Randomised controlled studies – 2
- Non-randomised comparative studies – 1
- Case series – 8

RCTs comparing HoLEP and open enucleation: 1

Abbreviations

BPH	Benign Prostatic Hyperplasia
DVT	Deep Vein Thrombosis
HoLRP	Holmium laser resection of the prostate
RCT	Randomised controlled trial
TRUS	Transrectal ultrasound
TULIP	Transurethral ultrasound guided laser induced prostatectomy
TUR	Transurethral
TURP	Transurethral resection of the prostate
VLAP	Visual laser ablation of the prostate

Study	Key efficacy findings	Key safety findings	Validity and generalisability
Systematic Review			
Tooher *et al.* 2002[14] **Comparator TURP** **Studies included:** RCTs – 3 Gilling et al 1999, 2000 Hammad et al 2002 Kitigawa 1997 non-RCT comparative – 1 Matsuoka & Noda (2001) case series - 12	Operative time and duration of catheterisation shorter in HoLRP than in TURP Both TURP and HoLRP are effective at improving urodynamic obstruction, symptom scores and quality of life. No differences could be detected in terms of urodynamic outcome (Qmax) or patient subjective report (symptom score and quality of life) Durability of HoLRP could not be determined	Blood loss appears to be lower in HoLRP than in TURP. No other differences could be detected between HoLRP and TURP.	*Potential for bias*: • RCTs of poor quality, with little information regarding randomisation, allocation concealment or blinding • length of follow-up short • losses to follow-up large *Outcome measures and their validity*: A large variety of outcome measures were reported, and primary or secondary outcomes not defined. Not all subjective outcomes were validated. *Other comments:* Much of the evidence regarding HoLRP is in the form of case series, 2 of the 3 RCTs were only published in abstract form and thus had little detail regarding study methodology and limited outcomes reported

Study	Key efficacy findings			Key safety findings			Validity and generalisability
Randomised controlled trials – comparator not TURP							
Gilling *et al.*[8] 1998, NEW ZEALAND N=44 HoLRP – {22} VLAP – {22} Dates not stated. *Follow-up:*12 months *Selection criteria:* Exclusion: >85yrs, TRUS>100mL Qmax>15ml/s AUA < 8 Schafer Grade < 2	Mean (range) – at 12 months	HoLRP	VLAP	Number of patients	HoLRP	VLAP	*Potential for bias*: • no information regarding randomisation, allocation concealment or blinding of patients or outcome assessors • relatively short follow-up period • small sample size limited power to detect differences *Outcome measures and their validity*: Q_{max} – peak flow at maximum pressure PVR – post void residual volume AUA – American Urological Association Symptom Score – validated patient symptom rating scale *Other comments:* Gilling is the inventor of the HoLRP procedure
	Q_{max} (mL/sec)	22 (8 – 41)[pns]	18 (10 – 33)	urinary tract infection	NR	3	
	AUA symptom score	4 (0 – 9)[pns]	5 (1 – 18)	blood transfusions	0	0	
	Operative time (mins)	52 (30 –100)[†]	41 (25 – 75)	haematuria	0	0	
	Catheter time (days)	1.4 (1 – 8)[§]	11.6 (3 – 46)	urinary retention	NR	3	
	Estimated resection weight (g)	21 (10 – 60)	24 (5 –60)	submeatal stricture	1	NR	
	PVR volume (mL)	40 (5 – 163) [pns]	73 (20 –211)				
	Number of patients						
	reoperation	1	3				
	recatheterisation	2	8				
	new incontinence	0	0				
	new impotence	0	0				
	retrograde ejaculation (% sexually active patients)	68%	45%				
Non-randomised comparative trials – comparator not TURP							
Kitigawa *et al.*[15] 1998, JAPAN Retrospective comparative study May 1995- August 1996 N= 60 HoLRP – 20 TULIP – 20 VLAP – 20 *Follow-up:* 3 months *Selection criteria:* none stated	Mean[SD] – at 3 mths	HoLRP	TULIP	VLAP	Number of patients	HoLRP	TULIP	VLAP	*Potential for bias*: • use of historical comparative groups • short length of follow-up • no indication of how patients were allocated to different treatments • some loss to follow-up for HoLRP patients • statistical comparisons made using paired t-test when almost no control over possible confounding variables *Outcome measures and their validity*: Q_{max} – peak flow at maximum pressure PVR- post void residual volume IPSS – International Prostate Symptom Score – validated patient symptom rating scale QoL – quality of life – validation unknown
	IPSS	4.1[1.5]	6.2[3.4]	6.1[2.7]	Blood transfusion	0	0	0	
	QoL	1.4[0.6]	1.9[0.7]	1.8[0.8]	TUR syndrome	0	0	0	
	Q_{max}(mL/sec)	21.6[8.3]	14.1[5.7]	16.0[6.3]	Incontinence	0	0	0	
	Prostate volume(cm^3)	21.1[8.5]	34.5[12.6]	26.2[13.0]	Epididymitis	0	1	1	
	PVR volume (cm^3)	18.7[20.1]	13.1[13.7]	13.8[12.6]	External meatal stricture	3	0	0	
	Operative time (min)	88.9[39.1]	41.5[11.4]	68.0[23.7]	Urethral stricture	0	0	1	
	Resected tissue (g)	8.3[4.7]	NR	NR	Postoperative bleeding	0	1	1	
	Catheter duration(d)	1.9[0.9]	12.8[5.4]	9.0[3.2]	Retrograde ejaculation	9	0	0	
	Q_{max} for patients undergoing HoLRP statistically significantly higher ($p<0.05$) at 3 months compared to VLAP and TULIP. All measures showed significant improvement at 3 months from preoperative baselines ($p<0.0001$).								

[ ] = standard deviation { } = measure of variability not stated pns = not significant * = $p < 0.05$ † = $p<0.01$ ‡ = $p < 0.001$ § = $p<0.0001$

Study	Key efficacy findings	Key safety findings	Validity and generalisability
Systematic Review	**HoLEP**		
Tooher *et al.* 2002[14] **Comparator TURP** **Studies included:** RCTs – 2 Gilling et al (2002) (2001) Kuntz et al (2001) non-RCT comparative – 1 (Stephenson et al 2001) case series - 12	Duration of hospital stay and duration of catheterisation shorter in HoLEP than in TURP HoLEP was found to be inferior to TURP in terms of operative times, weight of tissue retrieved an volume of irrigant used. No differences could be detected in terms of urodynamic outcome (Qmax) or patient subjective report (symptom score and quality of life) HoLEP procedure has allowed for quite significant prostate tissue retrieval	No significant difference was found between HoLEP and TURP in either blood loss or transfusions .	*Potential for bias*: • RCTs of poor quality, with little information regarding randomisation, allocation concealment or blinding • length of follow-up short • losses to follow-up large *Outcome measures and their validity*: A large variety of outcome measures were reported, and primary or secondary outcomes not defined. Not all subjective outcomes were validated. *Other comments:* Much of the evidence regarding HoLEP is in the form of case series,
Randomised controlled trials – comparator not TURP			
Kuntz and Lehrich [16](2002) **GERMNAY** N=120 Prostate greater than 100gm HoLEP 60 Open 60 January 1999 and March 2001 Follow-up: 6 months	Outcome / HoLEP / Open Peak urinary flow rate: 3.8 ±3.6 / 3.6 ±3.8 PVR volume (cm^3): 280 ±273 / 292 ±191 AUA symptom score: 22.1 ±3.3 / 21.0 ±3.6 Operating time was significantly longer in the HoLEP group. Effects on continence and potency were similar in both groups	Complication / HoELP / Open Blood transfusion: 0 / 8 Recatheterization: 3 / 3 Reoperation: 6 / 5 Myocardial infarction: 0 / 1	*Potential for bias*: • 104 completed 6 month follow-up • relatively short follow-up period • small sample size limited power to detect differences *Outcome measures and their validity*: PVR – post void residual volume AUA – American Urological Association Symptom

Specialist Advisor's opinion / Advisors' opinions

Specialist advice was sought from the British Association of Urological Surgeons

Specialist comments were provided by three urologists. All three rated the procedure as either no longer new or a variation on an established procedure (TURP), and suggested that no more than 25% of urologists are likely to be using this technique. Specialist Advisor opinion regarding the impact of the procedure on the NHS was split. One of the Advisors suggests that the procedure would be used in a minority of specialist centres (mainly district general hospitals) and that the impact was likely to be moderate, whereas another Advisor felt that the impact was likely to be minor at present, as the cost of the holmium laser would be likely to restrict its purchase within the NHS. A third Specialist Advisor stated that the procedure is likely to be done in most district general hospitals, and would be ideal for new short stay treatment centres. There were no major concerns regarding the safety and efficacy of the procedure. However one Specialist Advisor was concerned about bladder damage occurring through the use of a mechanical morcellator after renucleation. All three Advisors were in agreement that there is a significant learning curve and that a training program is required for this procedure, although one Advisor felt that the learning process should be rapid for experienced urological surgeons.

Issues for consideration by IPAC

Holmium laser resection of the prostate has a steep learning curve, although for surgeons who are experienced in resection techniques it is not expected to be very long. It is recommended that a minimum of 30 procedures on small prostates (less than 50g) are performed before the technique is used on larger prostates.

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