Holmium laser enucleation of prostate for patients with acute urinary retention due to benign prostate hyperplasia: Efficacy and safety

CURRENT STATUS: POSTED

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DOI: 10.21203/rs.2.16839/v1

SUBJECT AREAS
Urology & Nephrology

KEYWORDS
benign prostate hyperplasia, acute urinary retention, holmium laser enucleation of prostate
Abstract
Background Benign prostate hyperplasia (BPH) is a common disease in older men, and part of patients develop acute urinary retention (AUR) at the time of initial treatment. The aim of this study was to evaluate the effectiveness and safety of holmium laser enucleation of prostate (HoLEP) for patients with BPH in setting of AUR.

Methods The clinical data of 88 patients with BPH who underwent HoLEP surgery in our center were retrospectively analyzed. AUR existed in 34 patients and the other 54 patients had no AUR. The general information, prostate volume, urodynamic parameters and intraoperative parameters were recoed and compared. The outcome were recorded and analysed including the international prostate symptom score (IPSS), quality of life score (QoL), maximum urinary flow rate (Qmax), and post-voiding residual (PVR).

Results In both groups, the preoperative parameters were equivalent except for the white blood cell in urinalysis. All the HoLEP procedures were smoothly carried out. The intr- and post-operative complications were low in both groups and no difference were detected. All the patients were followed up for at least 6 months. IPSS, QoL, Qmax and PVR were all improved in both groups. No statistical differences were obtained in these parameters between groups.

Conclusion s HoLEP could be a safe and effective treatment for BPH patients either with or without AUR. The efficacy was immediate and sustained during the short-term follow-up session in both groups.

Background Benign prostate hyperplasia (BPH) is a common cause of lower urinary tract symptoms (LUTS) in elderly males worldwide; furthermore, BPH accounts for a considerable portion of hospital visits and substantial health related burden in elders. The incidence of histologic BPH in males ranges from approximately 50% in their 60s to nearly 90% in their 80s[1]. And a majority of elderly males have reported at least one LUTS. If untreated, BPH and associated LUTS may cause severe complications, including acute urinary retention (AUR), urinary tract infection (UTI), urinary tract calculi and chronic kidney disease (CKD). Therefore, BPH/LUTS adversely affects quality of life and may incur significant
morbidities in males.

AUR is one of the most disturbing complications of BPH/LUTS, which is estimated 0.6/100 to 1.8/100 patient-years according to the data from PLESS study and other population-based studies[2]. Although the occurrence of AUR is substantially decreased after effective medical therapy, AUR still accounts for 20% to 30% of BPH-related surgeries and considered as a definitive indicator of disease progression. Most patients with AUR are treated with catheterisation and subsequent medical therapy. However, the recurrence rate of AUR after removal of catheter is high and most patients are recommended to receive surgical treatment and thus enrolled in waiting lists. Although AUR caused by benign prostate obstruction (BPO) can be cured by surgery, considerable morbidity during and after surgery is associated with patients who are suffering from AUR compared with patients who present with other selective indications. In a study from Taiwan, transurethral resection of prostate (TURP) was used in BPH patients with or without AUR. The results have shown a significantly higher rate of blood transfusion during operation, UTI, septicaemia and subsequent LUTS after surgery, thereby entailing increased medical costs for patients with AUR[3].

Currently, several new minimally invasive techniques have been developed to treat BPH/LUTS including several kinds of laser techniques and bipolar techniques. Among these methods, holmium laser enucleation of prostate (HoLEP) has been demonstrated its superiority. This operation was originally developed by New Zealand urologist Peter Gilling using holmium laser as the energy source[4]. By imitating the open Millin’s procedure, this technique has equivalent short- and long-term efficacy with TURP and even open surgery. With excellent properties of holmium laser, this technique has diminished the occurrence of TURP syndrome and extremely reduced blood loss[5]. In addition, the penetrating depth of holmium laser is only 2 mm to 3 mm, resulting in less extravasation during operation and less LUTS post-operatively. Although the safety and efficacy of HoLEP has been well established, it is still absent of data about its use at the setting of BPH-related AUR. One authors reported holmium laser resection of prostate (HoLRP), a variation of holmium prostate surgery imitating TURP, was safe and effective in treating BPH-AUR[6]. And HoLEP was previously proved to be effective and safe in the setting of chronic urinary retention[7, 8]. Here in the present study, we
compared the efficacy and safety of HoLEP for treating BPH patients concurrent with or without AUR.

Methods
A total of 88 patients diagnosed with BPH with or without AUR were included in this retrospective study from July 2016 to June 2017 in the First Affiliated Hospital of Nanjing Medical University. All of the patients aged between 55 and 80 years; these patients also exhibited moderate to severe LUTS because of BPH. None of these patients manifested absolute contraindications to the proposed surgery. Under general anaesthesia, all of the patients received HoLEP performed by one consulting surgeon (MXX). The surgeon had more than 700 surgical cases before this study was carried out.

The indication of HoLEP was moderate to severe LUTS (with or without AUR) with demonstrable prostate enlargement and bladder outlet obstruction (BOO). Histories were carefully recorded to exclude other potential causes of LUTS. The international prostate symptom score (IPSS) and quality of life score (QoL) were obtained by experienced residents. Each patient was subjected to digital rectal examination to exclude evident prostate cancer. Baseline PSA level was determined at least three weeks before the surgery was performed. Patients who had elevated PSA more than 4 ng/L were further examined by biopsy. All of the prostate cancer cases were excluded from this study.

Transrectal ultrasonography was performed to determine prostate volume and intravesical protrusions of the prostates were also recorded. Urinalysis was routinely performed before surgery. Midstream urine culture was also performed when necessary. All of the patients were subjected to pressure-flow studies one day before operation, in which detrusor pressure at maximum urinary flow rate (PdetQmax) and Qmax were recorded. Bladder outlet obstruction index (BOOI) and bladder contractility index (BCI) were calculated as follows: BOOI = PdetQmax—2(Qmax) and BCI = PdetQmax + 5(Qmax)[9].

Patients with detrusor acontractile were excluded in this study. Post-voiding residual volumes (PVR) were also determined by urodynamic studies. A single dose of third-generation cephalosporin was administered 3 d before surgery to catheterised patients suffering from AUR; otherwise, a single dose of third-generation cephalosporin was administered before induction. Oral antibiotics were administered for one week after operation. Intake of any anticoagulants was terminated for at least 3
with low molecular heparin substitution. HoLEP was performed as previously described[10,11,12]. In brief, a 550-nm Holmium laser fibre (Lumenis, Yokneam,Israel) with a 26 Fr continuous-irrigating resectoscope (Karl-Storz, Tuttlingen, Germany) were inserted into the urethra. The urethra and the bladder were inspected under direct vision. The energy was set to 80 watts (2.0 J/pulse × 40 Hz). The initial resection was made in at either side proximal to the verumontanum, then an anatomical plane was formed. Using the tension of the resectoscope and the burst of the laser, the plane was developed between surgical capsule and hyperplastic gland till the bladder neck. The same method was employed to strip the lateral and middle lobes. The anterior fibrous tissue was removed directly to the bladder neck until all lobes were resected from the bladder neck. Usually, the first sally port to the bladder neck was made at 11 o’clock to 1 o’clock, and then continuously resection was performed on either side, carefully avoiding penetration into bladder neck at 5 o’clock to 7 o’clock. After resection, all lobes shed into the the bladder. A tissue morcellator (Lumenis, Yokneam, Israel) was introduced and the excisional adenoma was crushed and removed by aspiration under direct viewing.

Haemoglobin level was determined 2 h after operation. The patient was kept under closed-continuous irrigation for the first 24 h. The catheter was removed at 2 d post-operation if no further complications were observed. Patients who could not urinate after removal of the catheter were re-catheterised and subjected to a bladder training program for one week before the catheter was removed for the second time. All of the patients were then instructed to visit the hospital one, three and six months after the operation to undergo a follow-up procedure with an assistant. IPSS, QoL, PVR, Qmax and urinalysis parameters were determined during the follow-up session; any related medication was also recorded. Data were analysed using Student’s t, Mann-Whitney U, Chi-square, or Fisher’s exact tests according to their distribution. Results were expressed as mean with standard deviation (SD) or median with interquartile range (IQR). Statistical analyses were performed using Stata 14.0 (Texas, USA).

Results
A total of 88 patients with BPH and who were treated with HoLEP were included in the study. Among these patients, 34 (38.6%) suffered from BPH with AUR and 54 (61.4%) exhibited moderate to severe
LUTS with selected indications. The mean age of the AUR group (71.2 ± 9.5 years) was greater than that of the non-AUR group (69.4 ± 6.3 years). However, no statistical difference was observed between the two groups (P = 0.14). All of the baseline parameters are listed in Table 1. In terms of the severity of LUTS, patients with AUR exhibited a significantly higher IPSS score (21 vs. 17, P = 0.02) and QoL score (5 vs. 4, P < 0.010) than non-AUR patients.

The volume and intravesical protrusion of the prostate were pre-operatively determined. PSA levels were also recorded before surgery and AUR. No significant difference was observed in these parameters between the two groups (Table 1), although the mid-lobe was protruded into bladder at a higher extent in the AUR group than in the non-AUR group. At 1 d before the surgery, all of the patients were subjected to urodynamic assessment. Qmax and BCI were significantly lower in the AUR group than in the non-AUR group; BOOI was similar in both groups (Table 1). Thus, we confirmed that all of the patients manifested bladder outlet obstructions. As a result, PVR evaluated from urodynamic studies was significantly higher in the AUR group than in the non-AUR group (Table 1).

HoLEP procedures were completed smoothly. The average operation time was similar in both groups (Table 1). No transfusion was conducted in both groups. The average haemoglobin losses after surgery were 0.97 and 0.79 g/dL in AUR and non-AUR groups, respectively, but the difference was not significant. The median durations of catheterisation after surgery were 3.5 and 2.5 days in AUR and non-AUR groups, respectively; this result was significantly different. The success rates of first attempt of removal catheter, were not significantly different between the two groups, although the patients in AUR group did confront with more failures.

Long term complication rates, including incontinence, urethral stricture/bladder neck contracture, and persistent LUTS, were similar in both groups after HoLEP was performed (Table 1). Fortunately, the overall complication rate was low except persistent LUTS (14.3% and 7.4% in AUR and non-AUR groups, respectively).

All of the patients completed the six-month follow-up visit. During follow-up sessions, IPSS and QoL scores notably decreased and then remained constant (Figure 1). No significant differences were observed between the two groups at each follow-up point. Qmax and PVR were also recorded during
the follow-up sessions, in which Qmax was significantly higher than pre-operative level; PVR was decreased (Figure 2). No statistical differences were obtained in these parameters between the two groups. In the first follow-up session (one month after surgery), the respective median IPSS and QoL were 13.5 and 3.5 in the AUR group while 11 and 3 in non-AUR group. At the same point, Qmax was 10.4 ± 5.3 mL/s in AUR group and 12.1 ± 4.4 mL/s in non-AUR group, and PVR was 64.6 ± 82.9 mL in AUR group and 40.7 ± 45.8 mL in non-AUR group. Obviously, the IPSS, QoL score, Qmax and PVR shown a faster improvement in AUR group than in non-AUR group during follow-up, and at 6 month after surgery these parameters almost reached to the same level.

Discussion
In this study, we showed that HoLEP could be effectively and safely applied to treat patients with BPH-AUR. Post-operative IPSS and QoL decreased significantly in both groups compared with pre-operative levels. During the first month, Qmax increased by 120% and 35% in AUR and non-AUR groups, respectively. PVR also decreased remarkably and remained constant thereafter. To our knowledge, this was the first study of HoLEP in this subgroup of BPH patients. Our results support that HoLEP could be used as a definitive treatment for patients with AUR.

AUR is significantly detrimental to the quality of a patients’ life and may even cause severe complications in patients with BPH. The recurrence of AUR is very common; thus, surgical treatments are highly recommended[1]. However, patients were initially treated with catheterisation and then subjected to maintenance medication. In the waiting period, patients may suffer from recurring AUR and other complications.

Previously, Chen and colleagues reported their experience with transurethral resection of prostate (TURP) in the setting of AUR[3]. But their results did not support the use of TURP during AUR for increased peri-operative risks. Nevertheless, other authors promoted immediate surgery by HoLRP and HoLEP as a definitive treatment in these settings[6-8]. Our results also showed that HoLEP could be a safe alternative method to treat patients with BPH associated with AUR. Although catheterisation were prolonged, the overall efficacy was the same as in non-AUR patients. Moreover, peri-operative complications and long term complications were not increased. Although the patients in the AUR
group exhibited a greater proportion of positive urinary white blood cells, but no urosepsis occurred in both groups after HoLEP was performed. Furthermore, intra-operative bleeding was not significantly different between groups because of excellent coagulation properties of HoLEP. In HoLEP, procedures similar to open-prostate surgery are performed; thus, resection develops at the true surgical plane, or the layer between the inner adenoma and the outer peripheral zone. At the same time, holmium laser exhibits an enhanced coagulation property; therefore, reports on holmium prostate surgeries have indicated reduced blood losses and very low transfusion rates, as demonstrated in our study[13,14]. The overall complication rate was similar in both groups. In the AUR group, the patients experienced a prolonged period of catheterisation after surgery, resulting in a prolonged hospital stay. We also showed that patients with AUR suffered from impaired bladder contractility (BCI > 100). Although urodynamic test, which was performed one day before operation, could be undermined by continuous catheterisation in the AUR group, the results could still represent the actual situation to some extent. These results may also be accounted for the failed first post-operative voiding in the AUR group compared with the non-AUR group. Bladder decompensation, caused by overfilling of the bladder, may lead to AUR in patients with BPH. These patients required more time for the recovery of bladder detrusor function.

In contrast to a previous study in patients with BPH related to AUR treated with holmium laser resection, our study revealed that persistent LUTS was more frequent in the AUR group (14.3%) than in the non-AUR group (7.4%), although this result did not reach statistical significance. This finding may be attributed to pre-operative irritating bladder symptoms masked by AUR in the AUR group. Nonetheless, most patients in both groups exhibited evidently reduced objective symptoms and satisfactory quality of life after three months.

During follow-up sessions, the patients in both groups underwent a similar process of recovery, as delineated by IPSS, QoL, Qmax and PVR except the initial post-operative months. In general, the main motivation for requesting surgical treatment is to improve the symptoms, particularly for patients with AUR. Our results showed that HoLEP could alleviate urinary symptoms and increase quality of life of patients with BPH either with or without AUR. Furthermore, no significant difference in the final
efficacy was observed between the two groups within follow-up period. However, this preliminary study is retrospective and non-randomised in nature. The number of patients was relatively small. The follow-up period was only short term. Considering these drawbacks, we could not provide a definitive recommendation for the setting of BPH with AUR.

Conclusions
HoLEP could be a safe and effective treatment for BPH patients either with or without AUR. The efficacy was immediate and sustained during the short-term follow-up session of both groups. Further prospective studies with long-term follow-up periods are necessary to reach a definitive conclusion.

Declarations

Ethics approval and consent to participate
This study was approved by Institutional Review Board (IRB) of the First Affiliated Hospital of Nanjing Medical University, and was done in accordance with Declaration of Helsinki of ethical principles for medical research involving human participants. Informed consent of written format was obtained from all individual participants included in the study.

Consent for publication
The results presented in this paper have not been published previously in whole or part. All authors agree to publish the paper in BMC Urology.

Availability of data and material
The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests
The authors declare that they have no competing interests.

Funding
This study was funded by the National Natural Science Foundation of China (grant number 81302217).

Authors’ contributions
P. L. and X. M. conceived and designed the experiments; P. L., J. T. and X. M. performed the operations; M. T. and C. W. analyzed the data; P. L. and J. T. drafting the article; X. M. critical review of manuscript. All authors read and approved the final manuscript.

Acknowledgements

Acknowledgments: This work was supported by the by the National Natural Science Foundation of China.

References

1. Oelke, M., et al., EAU guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. Eur Urol, 2013. 64(1): 118-40.

2. Roehrborn, C. G., et al., Urinary retention in patients with BPH treated with finasteride or placebo over 4 years. Characterization of patients and ultimate outcomes. The PLESS Study Group. Eur Urol, 2000. 37(5): 528–36.

3. Chen, J. S., et al., Acute urinary retention increases the risk of complications after transurethral resection of the prostate: a population-based study. BJU Int, 2012. 110(11 Pt C): p. E896–901.

4. Gilling, P. J., et al., Holmium laser resection of the prostate: preliminary results of a new method for the treatment of benign prostatic hyperplasia. Urology, 1996. 47(1): 48–51.

5. Gilling, P. J. and A. K. Williams, Holmium laser enucleation of the prostate is the single best treatment for benign prostatic hyperplasia refractory to medication. J Endourol, 2008. 22(9): 2113–5.

6. Anderson, C. B., B. T. Helfand, and K. T. McVary, Holmium laser prostatic resection for patients presenting with acute urinary retention. BJU Int, 2008. 102(11): 1623–8.

7. Elzayat, E. A., E. I. Habib, and M. M. Elhilali, Holmium laser enucleation of prostate for patients in urinary retention. Urology, 2005. 66(4): 789–93.

8. Peterson, M. D., et al., Holmium laser enucleation of the prostate for men with urinary retention. J Urol, 2005. 174(3): 998–1001.

9. Han JH, Yu HS, Lee JY, et al. Simple Modification of the Bladder Outlet Obstruction Index for Better Prediction of Endoscopically-Proven Prostatic Obstruction: A Preliminary Study. PLoS One. 2015,10(10):e0141745. doi: 10.1371/journal.pone.0141745.
10. Kahokehr, A. and P. J. Gilling, Enucleation techniques for benign prostate obstruction: which one and why? Curr Opin Urol, 2014. 24(1): 49–55.

11. Kim, M., H. E. Lee, and S. J. Oh, Technical aspects of holmium laser enucleation of the prostate for benign prostatic hyperplasia. Korean J Urol, 2013. 54(9): 570–9.

12. Li P, Wang C, Cao Q, et al. Prostatic Arterial Embolization Followed by Holmium Laser Enucleation of the Prostate as a Planned Combined Approach for Extremely Enlarged Benign Prostate Hyperplasia. Urol Int. 2017. 99(4):422–28.

13. Cynk, M., Holmium laser enucleation of the prostate: a review of the clinical trial evidence. Ther Adv Urol, 2014. 6(2): 62–73.

14. Michalak J, Tzou D, Funk J. HoLEP: the gold standard for the surgical management of BPH in the 21(st) Century. Am J Clin Exp Urol. 2015. 3(1): 36–42.

Tables

Table 1 Comparison of the baseline parameters, intraoperative parameters, postoperative complications between BPH patients with or without AUR

| Factors                      | with AUR | without AUR | P value |
|------------------------------|----------|-------------|---------|
| Number of cases (n, %)       | 34(38.6) | 54(61.4)    |         |
| Pre-operative                |          |             |         |
| Age                          | 71.2(9.5)| 69.4(6.3)   | 0.14    |
| Prostate volume (ml)         | 72.4(23.5)| 72.9(24.9)| 0.46    |
| Intravasical protrusion (mm) | 14.2(8.8)| 11.9(9.0)  | 0.12    |
| Preoperative PSA (ng/mL)     | 3.1(3.8) | 2.9(2.4)    | 0.38    |
| PVR (mL)                     | 122.3(113.9)| 61.5(53.8)| 0.01    |
| IPSS                         | 21(4.5)  | 17(11.25)   | 0.02    |
| QOL                          | 5(1.0)   | 4(1.0)      | < 0.01  |
| Qmax (ml/s)                  | 4.7(2.4) | 8.9(2.7)    | < 0.01  |
| BOOI                         | 61(34.25)| 62(34)      | 0.30    |
| BCI                          | 94.5(35) | 124(46.5)   | < 0.01  |
| Peri-operative               |          |             |         |
| Operative duration (min)     | 89.3(15.8)| 91.1(16.7)| 0.31    |
| Change of hemoglobin at the first postoperative day (g/dL) | -0.97(0.64) | -0.79(0.44) | 0.06 |
| Blood transfusion (n)        | 0        | 0           | /       |
| Duration of catheterization (days) | 3.5(2.5) | 2.5(2.0)    | 0.02    |
| Success on the first void (n) | 24(70.6) | 47(87.0)    | 0.08    |
| Long term complications (n, %) |         |             |         |
| Incontinence lasting > 1 month | 0(0)    | 1(1.9)      | 0.98    |
| Urethral stricture/bladder neck contracture | 1(2.9) | 2(3.7)      | 0.89    |
| Persistent LUTS              | 5(14.3)  | 3(7.4)      | 0.33    |

Figures
Trend of QoL score and IPSS during follow-up postoperatively. There were no significant difference between AUR- and AUR+ groups. And the improvements were immediate and lasting during the short term follow-up. At the first 3 months, patients without AUR might show lower IPSS and better QoL, but after 3 months the scores were similar in both groups.
Figure 2

Trend of Qmax and PVR during follow-up postoperatively. There were no significant difference between AUR- and AUR+ groups. Both groups had a significant improvement at the first months and continuing progress with the time.