



Prostate Cancer

Nerve-Sparing Radical Retropubic Prostatectomy in Patients Previously Submitted to Holmium Laser Enucleation of the Prostate for Bladder Outlet Obstruction Due to Benign Prostatic Enlargement

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Abstract

Objectives: To evaluate the feasibility and safety of nerve-sparing radical retropubic prostatectomy (NSRRP) for localised prostate cancer after holmium laser enucleation of the prostate (HoLEP) for bladder outlet obstruction due to benign prostatic enlargement (BPE).

Methods: Fifteen consecutive patients with prostate cancer following HoLEP underwent NSRRP. They were matched with an equal number of patients who also underwent NSRRP following transurethral resection of the prostate (TURP group) or open prostatectomy (OP group). Patients were preoperatively assessed with validated questionnaires (International Prostate Symptom Score [IPSS] and International Index of Erectile Function-Erectile Function [IIEF-EF]). Intraoperative, perioperative, and follow-up functional data according to validated questionnaires (IPSS, IIEF-EF, International Consultation on Incontinence Questionnaire-Short Form [ICIQ-SF]) were evaluated with analysis of variance and χ^2 tests.

Results: At diagnosis, the prostate-specific antigen (PSA) level, clinical stage, Gleason sum distributions, body mass index, ICIQ-SF, and IPSS were not significantly different among the groups. IIEF-EF scores was higher in the HoLEP group ($p = 0.02$). Mean operative time was longer in the OP group ($p = 0.02$), but no difference was found in mean blood loss ($p = 0.5$). Final pathology showed no substantial differences among the groups, although a lower positive surgical margin rate was found in the HoLEP group ($p = 0.04$). Mean follow-up was 23.8 ± 10.5 mo. The groups showed no statistical differences in urinary continence rate ($p = 0.6$), IPSS ($p = 0.3$), or IIEF-EF ($p = 0.4$).

Conclusions: NSRRP is feasible in prostate cancer patients who previously underwent HoLEP for BPE and provides satisfactory functional outcomes.

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1. Introduction

Holmium laser enucleation of the prostate (HoLEP) is an effective, minimally invasive treatment modality for bladder outlet obstruction due to benign prostatic enlargement (BPE). It has been proposed as an alternative to transurethral resection of the prostate (TURP) [1] as well as to open prostatectomy (OP) [2–4]. Pathologic assessment of HoLEP specimens allows for the identification of both precancerous lesions and incidental prostate cancer (PCa) at rates equal to those of TURP specimens [5]. Patients with incidental PCa may be candidates for a nerve-sparing radical retropubic prostatectomy (NSRRP) [6,7]. It has been reported that RRP after previous prostatic surgery can be challenging [6,8,9]. Furthermore, to the best of our knowledge the feasibility of RRP in patients previously submitted to HoLEP has never been reported. Finally, there is no available report regarding the nerve-sparing technique in patients previously subjected to prostatic surgery for BPE. The aim of our study was to assess the surgical feasibility and oncologic plus functional outcomes of NSRRP in patients previously treated with HoLEP. We compared these results with those seen in two matched series of patients submitted to NSRRP for PCa who were treated with either TURP or OP prior to radical prostatectomy.

2. Patients and methods

Between January 2004 and March 2006, 206 consecutive patients underwent HoLEP at our institution for bladder outlet obstruction due to BPE. We used the surgical technique previously described by Gilling et al [10]. This included the morcellation of the enucleated prostatic lobes into fragments, which were subsequently retrieved from the bladder cavity. Holmium laser energy was delivered by a 360- μ m fibre placed in a 26F resectoscope. Enucleation of the prostate was performed with an energy of 2.0 J and a frequency of 50 Hz, for a total power of 100 W. Among the 206 patients, in 11 (5.3%) PCa was found in the HoLEP specimen and these men were considered as candidates for NSRRP. Another four patients demonstrated elevated serum prostate-specific antigen (PSA) levels despite benign pathology and were diagnosed with PCa on transrectal ultrasound (TRUS)-guided biopsies after HoLEP. All of these 15 patients were included in the HoLEP group.

Two matched cohorts were then obtained from our institutional databases for men who were underwent either TURP (TURP group) or OP (OP group) between 2003 and 2006. One-to-one matching starting from the most contemporary patients was used. Matching variables included PSA, clinical stage, body mass index, and preoperative Gleason sum. The preoperative PSA value and the Gleason sum were recorded at the time of diagnosis of PCa, both for patients diagnosed after surgery for bladder obstruction and for patients

submitted to prostatic biopsies. OP was performed through the transvesical approach [11]. Incidental PCa was found in 9 patients from the TURP group and in 10 patients from the OP group. All the others had a subsequent diagnosis of PCa.

All patients were assessed preoperatively with detailed medical history, physical examination, and scoring of subjective symptoms with validated questionnaires including the International Prostatic Symptoms Score (IPSS), the Erectile Function domain of the International Index of Erectile Function (IIEF-EF) [12], and the short form of the International Consultation on Incontinence Questionnaire (ICIQ-SF) [13].

All radical prostatectomies were performed under spinal anaesthesia and conscious sedation [14,15]. NSRRP was performed according to the anatomic technique described by Walsh [16] in the TURP and OP groups. In contrast, patients previously submitted to HoLEP underwent RRP with the same anatomic approach, with some modification during the isolation of neurovascular bundles, as described by Montorsi et al [17]. This technique basically implies incising the levator and prostatic fasciae high anteriorly (1 and 11 o'clock positions) over the prostate, developing the plane between the prostatic capsule and prostatic fascia, and displacing the neurovascular network localised between the two fasciae laterally. A pelvic lymph node dissection was performed in all patients, with retrieval of obturator and external iliac lymph nodes. All RRP was performed by senior urologic surgeons.

All intraoperative and perioperative parameters were recorded, including surgical time, blood loss, rate of bilateral nerve-sparing procedures, and complications, as well as postoperative hospital stay and length of catheterisation time.

Patients were followed up at 3, 6, and 12 mo. For the purpose of the current study, patients were evaluated at last follow-up during an office evaluation or via our mailing list-based follow-up database, and they were asked to complete the same questionnaires administered prior to RRP (ICIQ-SF, IPSS, and IIEF-EF). All the patients included in the study received the same counselling in terms of the use of phosphodiesterase type 5 inhibitors. No patient in the study was treated with prostaglandin E. Analysis of variance (ANOVA) and χ^2 tests were performed to test for significant differences among groups.

3. Results

The characteristics of the patients are reported in Table 1. Patients previously treated with OP were significantly older than those in the other two groups ($p = 0.01$). Preoperative body mass index ($p = 0.5$), PSA level ($p = 0.4$), clinical stage ($p = 0.3$), and Gleason sum distribution ($p = 0.5$) were not significantly different among the three groups. Preoperative erectile function, as quantified with the IIEF-EF score, was significantly better in the HoLEP group ($p = 0.02$), although no significant differences were noted in the ICIQ-SF ($p = 0.7$) or IPSS scores ($p = 0.2$) among the groups. Time between surgery for BPE and RRP was 5.8 ± 5.3 ,

Table 1 – Preoperative characteristics of the patients

	HoLEP (n = 15)	TURP (n = 15)	OP (n = 15)	p
Age, yr	64.29 ± 6.65	63.07 ± 5.31	71.13 ± 5.23	0.01
Body mass index, kg/m ²	25.75 ± 2.0	26.09 ± 3.30	27.0 ± 2.66	0.5
PSA, ng/ml	4.61 ± 4.62	3.45 ± 3.28	5.08 ± 3.61	0.4
Clinical stage				0.3
T1a	4 (26.7%)	3 (20%)	4 (26.7%)	
T1b	7 (46.6%)	6 (40%)	6 (40%)	
T1c	4 (26.7%)	6 (40%)	5 (33.3%)	
Biopsy Gleason sum				0.5
2–6	11 (73.3%)	11 (73.3%)	9 (60.0%)	
7	4 (26.7%)	3 (20%)	5 (33.3%)	
8–10	0 (0%)	1 (6.7%)	1 (6.7%)	
IPSS	10.3 ± 5.4	12.1 ± 4.5	9.7 ± 6.2	0.2
ICIQ-SF	0.2 ± 0.3	0.3 ± 0.1	0.5 ± 0.3	0.7
IIEF-EF	21.3 ± 5.6	17.6 ± 8.6	13.1 ± 13.0	0.02

HoLEP = holmium laser enucleation of the prostate; TURP = transurethral resection of the prostate; OP = open prostatectomy; PSA = prostate-specific antigen; IPSS = International Prostate Symptom Score; ICIQ-SF = International Consultation on Incontinence Questionnaire-Short Form; IIEF-EF = International Index of Erectile Function-Erectile Function.

5.5 ± 4.8, and 5.8 ± 4.3 mo in the HoLEP, TURP, and OP groups, respectively ($p = 0.9$).

Table 2 shows intraoperative and perioperative parameters. Operating time was significantly longer in the OP group ($p = 0.03$). No difference was found among the three groups in blood loss ($p = 0.6$). In one patient in the TURP group and in two patients in the OP group an anterograde approach was used [18] because of extensive fibrosis around the prostatic apex. A bilateral nerve-sparing procedure was completed in all patients in the HoLEP group (100%), 13 patients in the TURP group (86.6%), and 11 patients in the OP group (73.3%). Hospital stay and catheter removal after surgery were not significantly different among the three groups. No rectal, ureteral, or major vascular injuries occurred in any patients. Pelvic lymph node dissection was invariably performed in all patients. The mean number of pelvic lymph nodes removed at dissection was 12.3 (range: 6–34), and the number was not significantly different among the groups ($p = 0.1$).

Postoperative complications were also recorded. In one patient in the TURP group the postoperative course was characterised by pelvic lymphocele associated with temperature, and percutaneous

drainage was necessary. In the HoLEP, TURP, and OP groups the urethral catheter was removed 9.2 ± 4.5, 10.5 ± 6.2, and 11.2 ± 6.8 d after surgery, respectively ($p = 0.5$).

Table 3 shows the findings recorded on pathologic examination of the radical prostatectomy specimens. No patient showed absence of pCa at definitive pathologic examination (pT0). When the data were tabulated according to the type of previous surgery, the groups did not differ significantly with regard to rate of extracapsular extension, seminal vesicles invasion, or lymph node involvement ($p = 0.5$). However, the rate of positive surgical margins was significantly lower in the HoLEP group ($p = 0.04$).

The follow-up functional data is reported in Table 4. Mean follow-up was 20.0 ± 12.1 mo (range: 4–38 mo), 29.2 ± 7.9 mo (range: 11–38 mo), and 22.1 ± 9.4 mo (range: 5–36 mo) in the HoLEP, TURP, and OP groups, respectively. At last follow-up evaluation no statistical differences were found among the groups in terms of urinary continence, as measured with the first question of the ICIQ-SF ($p = 0.6$), the postoperative IPSS score ($p = 0.3$), or the IIEF-EF score ($p = 0.4$). Moreover, ANOVA was used to

Table 2 – Perioperative parameters

	HoLEP (n = 15)	TURP (n = 15)	OP (n = 15)	p
Operative time, min	126.0 ± 21.5	125.3 ± 34.6	156.0 ± 41.2	0.03
Blood loss, ml	1073.0 ± 576	1236.6 ± 507.9	1303 ± 457.2	0.6
Hospital stay, d	7.9 ± 4.33	8.5 ± 3.3	8.8 ± 2.5	0.8
Catheter removal, d	10.65 ± 5.98	11.52 ± 3.65	11.73 ± 4.86	0.5

HoLEP = holmium laser enucleation of the prostate; TURP = transurethral resection of the prostate; OP = open prostatectomy.

Table 3 – Findings on histopathologic evaluation

	HoLEP (n = 15)	TURP (n = 15)	OP (n = 15)	p
Pathologic Gleason sum				0.2
2–6	10 (66.6%)	9 (60.0%)	8 (53.3%)	
7	4 (26.7%)	6 (40.0%)	5 (33.4%)	
8–10	1 (6.7%)	0 (0%)	2 (13.3%)	
Pathologic T stage				0.5
pT0	0 (0%)	0 (0%)	0 (0%)	
pT2	13 (86.6%)	13 (86.6%)	12 (80%)	
pT3a	0 (0%)	1 (6.7%)	2 (13.3%)	
pT3b	2 (13.4%)	1 (6.7%)	1 (6.7%)	
pN1	0 (0%)	1 (6.7%)	0 (0%)	
Positive surgical margins	1 (6.7%)	5 (33.3%)	7 (46.7%)	0.04

HoLEP = holmium laser enucleation of the prostate; TURP = transurethral resection of the prostate; OP = open prostatectomy.

Table 4 – Functional follow-up data

	HoLEP (n = 15)	TURP (n = 15)	OP (n = 15)	p
IPSS	12.1 ± 3.2	11.4 ± 5.2	13.4 ± 4.1	0.3
ICIQ-SF	2.3 ± 2.9	5.3 ± 5.6	3.8 ± 4.5	0.6
IIEF-EF	14.0 ± 6.5	11.9 ± 7.5	11.0 ± 4.40	0.4
3-mo continence	80.0%	73.3%	66.6%	0.3
6-mo continence	93.3%	93.3%	80.0%	0.1
Patients reporting satisfactory sexual intercourse at last follow-up	53.3%	40.0%	33.3%	0.2

IPSS = International Prostatic Symptoms Score; ICIQ-SF = International Consultation on Incontinence Questionnaire-Short Form; IIEF-EF, Erectile Function domain of the International Index of Erectile Function. Continence was defined as the need of no more than 1 small pad/d.

compare the mean change between preoperative and postoperative IIEF-EF scores, and no difference was found among the HoLEP, TURP, and OP groups ($p = 0.27$). Two patients in each group (13.3%) developed an anastomotic stricture.

4. Discussion

Incidental adenocarcinoma of the prostate can be retrieved in up to 10% of patients who had surgery for BPE, despite an appropriate preoperative PCa assessment [5]. Radical prostatectomy is a commonly used treatment for patients with primary localised PCa [19]. In addition, it may be considered as a viable alternative for selected patients with incidental PCa or for disease diagnosed following surgery for an obstructive benign disease [6]. In our institution we are offering radical prostatectomy to all patients with T1b diseases. Patients with T1a disease are usually counselled about a watchful waiting program. However, the final decision for many patients is surgical treatment.

Several reports indicated that radical prostatectomy may be performed safely with an acceptable morbidity rate following TURP and OP, although

postoperative urinary incontinence and erectile dysfunction are more frequent as compared to primary cases [8,9]. Performing NSRRP in patients who previously had surgery for urinary obstruction can present some unexpected difficulties. Recently, Colombo et al [9] demonstrated that better surgical skills may be needed to perform radical prostatectomy in these cohorts of patients.

HoLEP represents a valid alternative to both TURP and OP for bladder urinary obstruction secondary to BPE. This technique has been gaining popularity due to its long-term efficacy, which is associated with reduced blood loss and shorter duration of postoperative catheterisation time [3,4,20].

To the best of our knowledge, the present study is the first to address the feasibility and the safety of NSRRP in patients previously undergoing HoLEP. In our series of 15 consecutive procedures performed by a single surgeon, a bilateral nerve-sparing technique was always completed. We noticed significantly greater difficulty in the dissection of the neurovascular bundles in RRP performed in patients previously treated by HoLEP as compared to primary cases. This finding was not unexpected, if we consider the reports describing RRP after TURP [6,9,21]. Rossignol et al [6] described a higher

perioperative morbidity while performing RRP in patients with A1/A2 stage PCa, with a 5% incidence of early complications, but with good oncologic and functional outcomes. Ramon et al [21] compared patients who had radical prostatectomy after TURP with patients who underwent RRP as the first surgical approach to the prostate. They concluded that, although radical prostatectomy sometimes is more difficult after previous prostate surgery, operative complication rates, patient morbidity, and the opportunity for surgical cure are not much different from those seen in patients with no history of previous prostate operations. In the current study, blood loss was higher than expected in primary cases in all the groups. Again, this could be because NSRRP is more difficult to perform than primary cases. Colombo et al also reported a high mean blood loss in patients undergoing radical prostatectomy as second prostatic surgery [9]. Unfortunately, the other previous studies reporting RRP after previous prostatic surgery did not report on blood loss.

No major complications occurred, and anastomotic strictures occurred at a rate similar to those reported by other studies in patients who had radical prostatectomy as the first prostatic surgery [22].

The urethral catheter was removed earlier in the HoLEP group. However, the differences among the three groups failed to reach statistical significance ($p = 0.5$). The routine catheter removal time in our institution is on postoperative day 8. However, at the end of each single operation the surgeon decides whether or not a patient should keep the catheter for a longer period based on anatomic characteristics of the membranous urethra and the degree of watertightness of the anastomosis as assessed intraoperatively. Furthermore, any additional postoperative complication can push the surgeon to maintain the catheter in place longer.

In our series we found a lower rate of positive surgical margins in the HoLEP group. This could be due to the different surgical technique used in this patients subgroup. However, the small number of patients in each cohort does not allow a definitive statistical analysis. In addition, the proportion of positive surgical margins is high as compared to the most recently reported series, especially if we consider the low rate of pT3 diseases. This finding supports the higher grade of difficulty in performing RRP as a second prostatic surgery.

Our data show that continence recovery is not compromised in patients undergoing a second prostatic surgery, and this result is in agreement with those reported by other series [9,21]. Both the IPSS and the ICIQ-SF findings indicated a satisfac-

tory urinary symptom outcome after RRP, although we did not analyse precisely the time needed to achieve full continence recovery, which can have a negative impact on patients' quality of life.

Although preoperative erectile function was higher in the HoLEP group, no difference was found postoperatively among the groups in terms of IIEF-EF scores. Thus, it could be argued that radical prostatectomy had a more influential impact on erectile function in the HoLEP group. However, when we compared the mean changes between preoperative and postoperative IIEF-EF scores, we found no significant differences among the three groups.

Although most of the patients underwent NSRRP, in some of them we recorded postoperative erectile dysfunction. These findings are not surprising because previous reports indicated that the most negative impact of previous prostate surgery for BPH on outcome after RRP concerns postoperative erectile function [9]. This may be related to the fact that a nerve-sparing procedure does not guarantee optimal results in RRP after previous surgery for BPE. However, no significant differences were found among the groups, and the majority of our patients with high preoperative IIEF-EF scores reported satisfactory sexual activity at follow-up. Based on the consideration that erectile function can be negatively affected by NSRRP as second prostatic surgery, we strongly recommend strict evaluation (PSA, digital rectal examination, and ultrasound) in patients undergoing surgery for BPE, especially in those who are interested in sexual activity, as well as a discussion of the risk of an incidental diagnosis of cancer and its related outcomes on quality of life. Finally, because our study and previous ones [6,8,9] demonstrated that NSRRP can be challenging after previous prostate surgery, we recommend that this procedure be performed by expert surgeons. We encourage further studies to show the feasibility of NSRRP in these patients with laparoscopic and robotic approaches.

Several limitations may apply to our study. First, although this is the first report of RRP after HoLEP, the cohort of patients was small. The inclusion of a more consistent number of patients in each group could change some of our results. Second, our control groups were obtained in a retrospective fashion, but we feel that a randomised and prospective study could hardly be conducted when patients are undergoing RRP as a second surgery. Third, operations in the TURP and OP groups were performed by different surgeons, which may have affected the outcomes. Fourth, our database did not allow us to match the patients in the HoLEP group with a similar number of patients who underwent

OP at a comparable age, resulting in the older age in patients in the OP group. This could have led to different outcomes, especially in erectile function recovery evaluation. Finally, the small number of patients in each group did not allow us to stratify patients according to time between the two procedures. However, no single patient underwent NSRRP within the first 4 mo after the BPH procedure. Based on our personal experience, we consider this period as necessary to diminish the periprostatic inflammation due to the first intervention.

5. Conclusions

NSRRP is a feasible procedure in patients diagnosed with PCa who previously underwent HoLEP for BPE, although it may require higher surgical skills than in patients never having previous prostate surgery. It provides satisfactory oncologic and functional outcomes, without any significant differences compared with patients undergoing RRP after TURP or OP.

Conflicts of interest

The authors have nothing to disclose.

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