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PHOTOSELECTIVE POTASSIUM-TITANYL-PHOSPHATE LASER VAPORIZATION OF THE BENIGN OBSTRUCTIVE PROSTATE: OBSERVATIONS ON LONG-TERM OUTCOMES

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ABSTRACT

Purpose: We present long-term observations on photoselective vaporization of the prostate in a prospectively studied cohort of men with obstructive benign prostatic hyperplasia.

Materials and Methods: Obstructive benign prostatic hyperplasia in 94 men was treated with transurethral near contact vaporization with potassium-titanyl-phosphate laser with the patient under general or spinal anesthesia. Baseline characteristics, perioperative data, postoperative outcomes and adverse events were recorded.

Results: Mean prostate volume was 45 ml (range 13 to 136). Mean lasing time was 47 minutes (range 10 to 99), and there was minimal blood loss and no evidence of fluid absorption. All 94 men were outpatients and all but 1 became catheter-free in less than 24 hours. Baseline mean American Urological Association symptom index score was 22, quality of life score 4.5, peak urinary flow rate 7.8 ml per second and post-void residual urine volume 197 ml. After surgery percentage changes from baseline in mean values of these parameters, reflecting significant ($p < 0.0001$) improvement at 1, 2, 3 and 5 years, ranged from 83% to 88%, 86% to 90%, 170% to 252% and 76% to 89%, respectively. Complications were mild, and included transient dysuria (6%), delayed hematuria (3%), bladder neck contracture (2%) and 2-day retention (1%). No patient had incontinence or newly developed impotence, but up to 26% of the sexually active men experienced retrograde ejaculation. Postoperatively, low stage prostate cancer was detected in 5% of the patients.

Conclusions: Despite limitations our long-term experience and the literature suggest that significant improvements in symptomatic and urodynamic outcomes of photoselective vaporization of the prostate are achievable and sustainable.

KEY WORDS: prostatic hyperplasia, laser surgery, potassium titanylphosphate, prostatectomy

Since its introduction just over a decade ago, laser prostatectomy (LP) has expanded to encompass a diversity of techniques applied with equally diverse laser wavelengths, each with a specific tissue interaction.[1–3] Consequently, the 3 principal types of LP, namely coagulative LP with the neodymium:YAG (Nd:YAG, visual laser ablation of prostate) or diode lasers (interstitial laser coagulation), cutting (enucleative) LP with the holmium:YAG (holmium laser prostate enucleation), and vaporization LP with the Nd:YAG (transurethral evaporation of prostate), holmium:YAG (holmium laser prostate ablation) or potassium-titanyl-phosphate (KTP) lasers, have produced rather variable outcomes.[1–3] Despite early setbacks with some of these diverse LP techniques, others such as high-power (60 to 80 W) KTP vaporization LP have met with some success.[2,3]

The efficiency of KTP laser in vaporizing tissue is due to selective absorption of photons by hemoglobin and the consequent release of superficially trapped vaporizing thermal energy.[2] Therefore, KTP vaporization LP has been called photoselective vaporization of the prostate (PVP).[2] In original short-term studies of PVP by Malek et al morbidity was minimal and outcomes were favorable.[4,5] Recently a 1-year prospective multicenter study of PVP confirmed these findings.[6] To better define the fundamentals and sequelae of PVP, we present our analysis of long-term outcomes in a prospectively studied cumulative cohort of men treated for obstructive benign prostatic hyperplasia.

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† Nothing to disclose.
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***Editor's Note*: This article is the fifth of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 1508 and 1509.**

MATERIALS AND METHODS

This study was approved by the Mayo Foundation Institutional Review Board and received no extra institutional funding. Patients underwent periodic reevaluation at their own expense.

Patient selection. From 1997 to 2003 obstructive benign prostatic hyperplasia was treated with PVP at Mayo Clinic in 94 men who were considered candidates for transurethral resection of the prostate (TURP). Preoperative evaluation included history, physical examination, assessment of symptoms according to the American Urological Association symptom index score (AUA-SI), patient satisfaction index, and later, quality of life score (QOL), peak urinary flow rate (Qmax), post-void residual urine volume (PVR), and determination of prostate size and appearance by transrectal ultrasonography (TRUS) and bladder status by cystoscopy. Laboratory studies included complete blood count, determination of values for serum chemistry and serum prostate specific

antigen (PSA), and urine culture. Criteria for inclusion in the study consisted of moderate to severe obstructive lower urinary tract symptoms as determined by AUA-SI 10 or greater, and Qmax 12 or less ml per second (voided volume greater than 120 ml) with or without considerable PVR. TRUS guided prostate biopsy was performed to rule out malignancy in patients with abnormality noted in 1 or more of the categories digital rectal examination (DRE), TRUS of the prostate or serum PSA. Patients with urethral stricture, urinary retention, neurogenic bladder, history of prostatic surgery (including minimally invasive techniques) or malignancy were excluded from analysis. Erectile and ejaculatory functions were assessed by direct questioning of patients.

Operative technique. The standard technique of PVP was described previously by Malek et al.[2,4,5] All procedures were performed by 1 surgeon (RSM) who had experience with KTP laser application to the prostate.[7–9] Near contact KTP laser vaporization was performed with a 600 μm side firing fiber with a quartz capsule over the 70-degree lateral deflecting fiber end. The laser fiber was introduced through the working channel of a 22Fr continuous flow laser cystoscope and sterile water was used as irrigant. KTP laser energy at 60 W was generated by a prototype generator and, later, with higher vaporization efficiency at 80 W by a new Laserscope GreenLight (San Jose, California) generator.[2] The end point of the procedure was to create a widely patent, hemostatically well controlled, TURP-like cavity surrounded by capsular fibers (fig. 1, *A* to *C*).

Perioperative management and followup. Patients received a general (91) or spinal (3) anesthetic and, despite sterile urine in all, they received 1 gm ampicillin or cephalosporin intravenously. At the conclusion of PVP an 18Fr Foley catheter (15 ml water in balloon) was left indwelling. All patients were dismissed receiving a 2-week prophylactic course of an antibacterial medication, and were instructed to refrain from strenuous physical activity for up to 8 weeks and sexual activity for 4 weeks. After surgery patients were asked to return for reevaluation immediately if they had any concerns, otherwise at 3 and 6-month intervals, and yearly thereafter for 5 years. They were contacted for each of the first 3 years and the 5th postoperative year. Those who declined to return cited long travel distances and financial constraints, and none indicated any problems to necessitate another urological visit. Reevaluation included determination of AUA-SI, QOL, Qmax, PVR and PSA, undergoing DRE, and inquiry about adverse events, status of erectile function and ejaculation. New, more mature followup data on our previous 55 patients plus data on the subsequent 39 patients are presented in this report.[5]

Data analysis. Calculations were made on a Microsoft Excel® spreadsheet with integrated statistical functions. Because of incremental inclusion of patients during a 5-year period, all outcome and improvement calculations used baseline numbers and mean values of the cohort of patients studied at each postoperative point up to which (6 months, 1 year, etc) they had matured rather than the numbers and baseline values for the entire group. Therefore, percentage evaluable represents the number of patients seen at each followup point divided by the total number of those who had matured to that point after PVP (table 1). The 5 patients who underwent treatment for prostate cancer and the 2 who died of unrelated infirmities of advanced age between 4 and 5 years after surgery were excluded from subsequent followup calculations. The 2-tailed Student t test was used to obtain p values with those less than 0.05 considered significant.

RESULTS

Baseline data are described in table 2. Lasing time ranged from 10 to 99 minutes (mean 47 ± 17), during which 32 to 477 kJ (mean 185 ± 78) of laser energy was delivered. PVP at 60 W was too laborious for glands 90 ml or greater (lasing time 48 minutes for 60 ml gland and 94.7 minutes for 90 ml). Therefore, the 80 W generator was used when introduced in 2001. However, there was no significant difference ($p=0.1383$) between mean lasing times at 60 and 80 W power

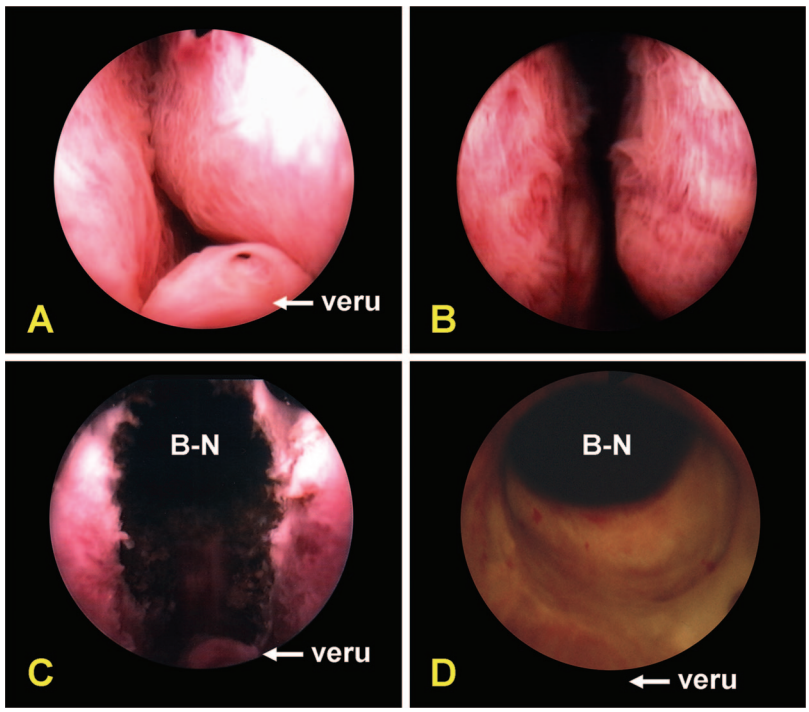

FIG. 1. Cystoscopic appearance of obstructive prostatic urethra. *A*, distal view. veru, verumontanum. *B*, mid prostatic view. *C*, immediate postoperative appearance. Note widely patent channel and bladder neck (B-N) viewed from level of external sphincter and verumontanum. *D*, appearance of well healed, functioning bladder neck (B-N) and prostatic urethra during micturition around cystoscope 2 years after PVP. Patient maintained antegrade ejaculation.

TABLE 1. *Symptomatic and urodynamic outcome variables*

	Baseline	6 Mos	1 Yr	2 Yrs	3 Yrs	5 Yrs
Total/evaluable pts (%)	94/94 (100)	94/76 (81)	79/66 (83)	63/48 (76)	50/32 (64)	24/14 (58)
Mean ± SD AUA symptom score (p value):	22 ± 6	4.6 ± 2.3 (<0.0001)	3.8 ± 2.4 (<0.0001)	3.7 ± 2.2 (<0.0001)	3.4 ± 1.7 (<0.0001)	2.6 ± 1.6 (<0.0001)
Range	10–35	0–10	0–12	0–10	1–8	0–5
% Improvement		82	83	83	85	88
Mean ± SD QOL score (p value):	4.5 ± 1.2	0.3 ± 0.7 (<0.0001)	0.4 ± 0.6 (<0.0001)	0.6 ± 1.0 (<0.0001)	0.4 ± 0.5*	0.1 ± 0.4*
Range	3–6	0–2	0–1	0–2	0–3	0–1
% Improvement		93	90	86	*	*
Mean Qmax ± SD ml/sec (p value):	7.8 ± 2.3	26.4 ± 9.5 (<0.0001)	27.1 ± 10.6 (<0.0001)	26.6 ± 11.3 (<0.0001)	23.6 ± 9.2 (<0.0001)	22.2 ± 9.0 (<0.0001)
Range	2.4–12	7.0–47.1	9.2–56.3	7.6–55.3	8.5–44.7	12.7–42.5
% Improvement		246	252	242	201	170
Mean PVR vol ± SD ml (p value):	197 ± 143	37 ± 34 (<0.0001)	43 ± 52 (<0.0001)	18 ± 28 (<0.0001)	23.6 ± 28 (<0.0001)	25 ± 26 (<0.0001)
Range	17–684	0–150	0–202	0–121	0–106	0–86
% Improvement		82	76	89	84	84

Total number of patients reflects the cohort that had matured to that point in followup. All patients at 1, 2, 3 and 5 years were treated at 60 W.
* QOL scores are not comparable to preoperative nonnumerical old satisfaction index used for early entries into the study cohort.

TABLE 2. *Baseline characteristics*

	Mean ± SD (range)
Pt age	68 ± 8 (46–87)
AUA symptom score	22 ± 6 (10–35)
QOL score	4.5 ± 1.2 (3–6)
Peak flow (ml/sec)	7.8 ± 2.3 (2.4–12)
Post-void residual vol (ml)	197 ± 143 (17–684)
Prostate vol (ml)	45 ± 17 (13–136)
PSA (ng/ml)	2.35 ± 1.51 (0.3–6.7)

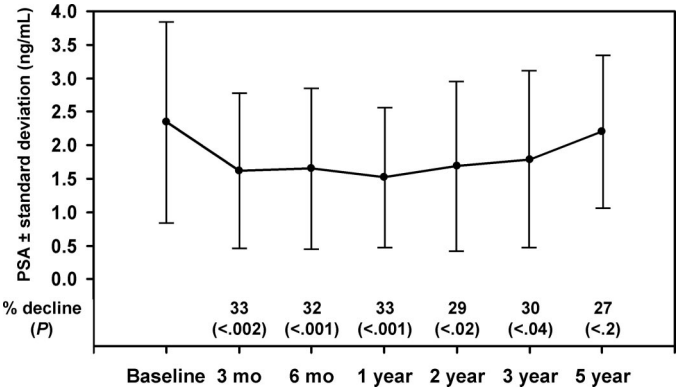

FIG. 2. Postoperative decrease in mean PSA ± standard deviation at 3 months to 5 years compared with baseline.

(45.6 ± 17.2 and 52.9 ± 16.8 minutes, respectively) due to the significantly (p=0.002) larger prostatic volumes (57.2 ± 27 and 42.6 ± 13.6 ml) of the last 15 patients treated at 80 W compared with the 79 treated at 60 W. All patients had sterile urine and normal renal function, and none had any clinical or hyponatremic evidence of fluid absorption intraoperatively. Immediate postoperative serum sodium values were normal (range 133 to 144 mEq/l). Estimated perioperative blood loss was no more than approximately 200 ml only in patients with large prostates (90 ml or greater) while others had generally clear drainage during and after surgery. No patient required blood transfusion. All patients were treated as outpatients (within 23 hours). Only 8 patients stayed for 23 hours because of slow recovery or other postanesthesia sequelae. The remaining 86 patients left the hospital within 6 to 8 hours after surgery. None of the catheters required irrigation and all were removed 18 to 21 hours (mean 20) after surgery. One patient failed to void and required recatheterization for 2 additional days (72 hours).

After surgery mean serum PSA decreased from baseline by approximately 30% (fig. 2). However, after these decreases 23 patients had an increase in PSA. In 11 of these patients PSA decreased to low-normal postoperative values after a 6-week course of antibiotic therapy. Another 12 patients whose PSA did not decrease after antibiotic therapy underwent prostate biopsy. Of these 12 patients 6 had negative biopsy results, 1 had prostatic intraepithelial neoplasia with PSA decrease, staying low after biopsy, and 4 had localized adenocarcinoma of the prostate. The remaining patient declined biopsy. In another patient with decreased PSA, a prostatic nodule developed 2 years later and he was also diagnosed with prostatic carcinoma. Altogether 5 patients (5%) had prostate cancer diagnosed within 6 months to 3 years after surgery, 4 underwent uncomplicated radical retropubic prostatectomy and 1 received external beam radiation therapy.

Subjective and objective outcomes. Symptomatic and urodynamic outcomes at 6 months to 5 years postoperatively (mean 3.5) in patients who returned for evaluation showed significant improvement (p <0.0001, table 1). Only 8 of 15 patients who entered the study during its last 9 months and who underwent PVP at 80 W returned for just a 6-month followup. Except for prostatic volumes, no significant difference was found between baseline values (p=0.139–0.935) or outcomes (p=0.073–0.840) in these patients vs those treated at 60 W. A majority of the patients followed achieved at least 50% improvement in AUA-SI and 100% improvement in Qmax (table 3).

Adverse events and sexual function. Adverse events are summarized in table 4. There was no significant postoperative hematuria despite the fact that at least half the patients were receiving antiplatelet medications and 1 had untreated factor VII deficiency. Two patients (2%) with sterile urine became febrile, 1 had pneumonia and 1 had an allergic response to sulfonamide. In 6 patients (6%) mild sterile dysuria developed but it resolved within 2 to 3 weeks without any treatment. Delayed complications included transient, self-limiting gross hematuria in 3 patients (3%) 6 to 8 weeks postoperatively as a result of strenuous physical activity, soft vesical neck contracture that responded to simple dilation in

TABLE 3. *Percentage of patients with at least 50% improvement in AUA symptom score or 100% improvement in peak flow rate compared with baseline*

Postop Time	% AUA Symptom Score	% Peak Flow Rate
6 Mos	99	91
1 Yr	99	88
2 Yrs	100	83
3 Yrs	100	74
5 Yrs	100	79

TABLE 4. *Adverse events*

	No. Pts (%)
Dysuria (sterile)	6 (6)
Hematuria (delayed)	3 (3)
Bladder neck contracture (dilated)	2 (2)
Fever (nonurological*)	2 (2)
Epididymitis	1 (1)
Retention (recatheterization)	1 (1)
Retrograde ejaculation	† (26 or less)
Impotence	0 (0)
Incontinence	0 (0)

* One patient had pneumonia and 1 had reaction to sulfonamide.
† Number of patients with retrograde ejaculation varied at different followup points.

2 patients (2%) with small prostate volumes (13 ml treated at 60 W and 30 ml treated at 80 W) 3 months postoperatively, and epididymitis that subsided promptly after antibiotic therapy in 1 patient (1%). None of the patients had urinary incontinence or newly developed impotence, and none, including those who declined to return for long-term followup, to our knowledge, has required reoperation. However, among sexually active men retrograde ejaculation developed in 9 of 37 (24%) at 1 year, 8 of 31 (26%) at 2 years, 5 of 21 (24%) at 3 years and in 0 of 9 (0%) at 5 years.

DISCUSSION

Frequency doubling of the 1,064 nm Nd:YAG laser creates the 532 nm KTP laser with different tissue effects. Histopathological studies of the healed prostatic cavity after LP show the remarkably benign nature of KTP laser injury.[8,9] In contrast to the vaporization Nd:YAG laser induced small (1.4 cm)[8] cavity walled by much collagenous scar tissue (fig. 3, *A*), KTP laser PVP results in a larger (2.4 cm), practically collagen-free unscarred prostatic channel (fig. 3, *B*).[8,9] All forms of transurethral prostatic surgery cause thermal injury. One may speculate that the outcomes of these procedures depend not only on the caliber of the newly created channel but also on the degree of postoperative scarring. A combination of unscarred, elastic bladder neck and an open and pliable prostatic channel may perform better than a scarred, rigid, albeit open, pipe. This may be the crux of the rather impressive urodynamic outcomes of PVP compared with the best of those of some of the contemporary TURP series with longest reported followup of up to 3 years.[5,10] In comparison, equally significant improvements in subjective and objective outcomes were sustained for 5 years in our patients with a similar rate of attrition (table 1).[5,10]

The learning curve for PVP is short and 15 procedures on smaller (50 ml or less) prostates are usually adequate. That multiple investigators with no prior PVP experience have achieved excellent results indicates that the technical ability to perform this procedure successfully is readily within reach of all urologists who adhere to the established principles of PVP.[2,5,6] However, despite similar landmarks and goals, the techniques for PVP and TURP are substantially different and, just as with TURP, incomplete PVP may lead to early recurrent obstruction in 2% to 3% of patients.[11,12] Although tissue effects of the KTP laser have been demonstrated to be the same irrespective of the power used, vaporization speed increases significantly with increase in power under otherwise equal circumstances of similar exposure time and spot size.[8,9] However, statistically we could not demonstrate a significant difference between the lasing times of our 2 groups treated at 60 and 80 W because of the significantly larger prostatic volumes of the 80 W group. Nevertheless, a lasing time of 99 minutes for the largest prostate of 136 ml treated at 80 W was faster than 94.7 minutes for the largest prostate of 90 ml treated at 60 W. Collective experience indicates that PVP is safe despite some lengthy operative times for larger prostates,[2,6,11] therefore, it is eminently suitable for high risk cases.[12] Generally patients do not require irrigation and are treated as outpatients.[2,5,6] Some with well functioning bladders require no catheterization at all,[2,6,11,12] and many others become catheter-free in less than 24 hours and return to nonstrenuous work in 2 to 3 days with minimal loss of productivity, thus reducing the health care costs despite the additional cost of a single use laser fiber and the onetime initial cost of a laser generator.[13]

Reported complications have been relatively mild and scarce.[2,5,6,11,12] Hematuria was negligible or nonexistent perioperatively despite the use of antiplatelet medications by many patients and untreated factor VII deficiency in 1. Indeed a multitude of patients receiving warfarin anticoagulation have undergone PVP without risking substantial blood loss or receiving transfusion[2,12] as we initially described.[5] However, as noted in some patients after TURP, delayed hematuria due to premature strenuous physical activity occurred in a few patients (3%). Sterile dysuria was uncommon (6%), transient and mild, and required no treatment. Despite a deliberate attempt to widely resect the bladder neck à la TURP, the incidence of retrograde ejaculation in our study (26% or less) was similar to that reported in the multicenter study (36%)[6] and lower than that expected after TURP. Vis-à-vis at least a 100% improvement in Qmax in 74% to 91% of our patients (table 3), it is likely that a combination of some surviving muscle fibers[6] resulting in a functional bladder neck plus a pliable and unobstructed prostatic channel (fig. 1,

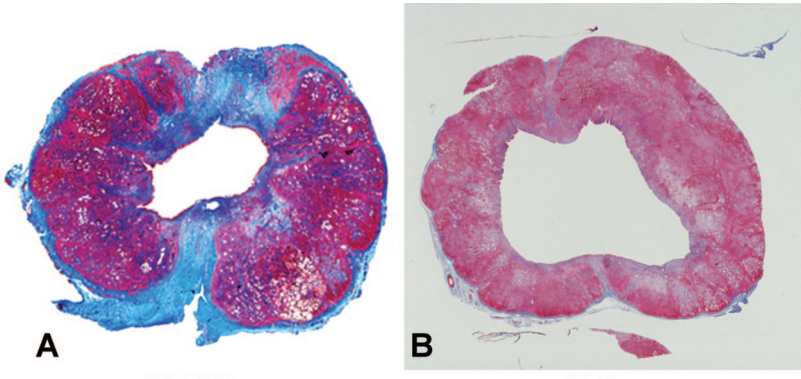

FIG. 3. Photomicrographs of canine prostates 8 weeks after laser prostatectomy. *A*, Nd:YAG laser vaporization. Note extensive, deep blue submucosal periurethral and periprostatic collagenous fibrosis, and small prostatic urethral channel created. *B*, KTP laser vaporization. Note absence of collagenous fibrosis and large prostatic urethral channel created. Masson trichrome stain, reduced from ×1. Reprinted with permission.[8]

D), rather than limited removal of prostatic tissue, may explain this outcome. Bladder neck contracture in 2 patients (2%) with a small prostate was soft and responded to 1 dilation as noted by others.[6]

PVP yields no tissue for pathological examination. Therefore, it is mandatory to continue postoperative PSA and DRE surveillance. A sustained reduction in serum PSA of approximately 30% or more occurs postoperatively (fig. 2).[6] Failure of PSA to decrease or a sustained increase after surgery is suspect. By following these criteria, early localized prostatic carcinoma was detected and treated in 5 (5%) of our patients.

CONCLUSIONS

PVP has a well established record for safety, low morbidity, rapid recovery and short-term durability.[2,5,6,11,12] Despite expected attrition, as in long-term studies of other forms of LP or TURP,[10,14] our 5-year observations suggest that significant improvements in outcomes are sustainable in the long term. However, as with TURP, PVP is not a panacea. Incomplete tissue removal is a recipe for poor outcomes hallmarked by recurrent obstruction.[11,12]

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