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RESEARCH

Are Histological Findings of Thulium Laser Vapo-Enucleation Versus Transurethral Resection of the Prostate Comparable?

Luca Carmignani[1] · Alberto Macchi[1] · Dario Ratti[1] · Elisabetta Finkelberg[1] · Stefano Casellato[1] · Giorgio Bozzini[1] · Serena Maruccia[1] · Carlo Marenghi[1] · Stefano Picozzi[1]

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Abstract We investigated if an adequate histological diagnosis can be made from tissue after Thulium laser vapo-enucleation of the prostate (ThuVEP) and whether it is comparable to transurethral prostate resection (TURP) tissue findings in patients with symptomatic benign prostatic hyperplasia. We analyzed 350 ThuLEP and 100 matched TURP tissue specimens from patients who underwent one of the two procedures between January 2009 and June 2014. Thulium Laser Enucleation of Prostate (ThuVEP) was combined with mechanical morcellation of the resected lobe. Each histological specimen was reviewed by two pathologists. Preoperative prostate ultrasound volume, total serum prostatic specific antigen and postoperative tissue weight were evaluated. Microscopic histological diagnosis was assessed by standard histological techniques and immunohistochemical evaluation. Patients were comparable in terms of age and preoperative total serum prostate specific antigen. Incidental adenocarcinoma and high grade PIN of the prostate were diagnosed in a comparable percent of specimens in the 2 groups (2.5 % in the ThuVEP group versus 3 % in the TURP group). Tissue thermal artifacts induced by the Thulium laser are mostly due to coagulation as that of the conventional monopolar diathermy in TURP. Tissue quality was maintained in the ThuVEP histological specimens. Tissue maintain histological characteristics and proprieties without modification for successive immunoistochemical analysis. The pathologist ability to detect incidental prostate cancer and PIN was maintained even if there is a quoted of vaporized tissue.

Keywords Prostate · Benign prostatic hypertrophy · Transurethral · Thulium · Laser

✉ Stefano Picozzi
stepico@tin.it

[1] Academic Urology Department, IRCCS Policlinico San Donato, University of Milan, Via Morandi 30, 20097 San Donato Milanese, Milan, Italy

Introduction

Benign Prostatic Hyperplasia (BPH) is one of the most common ailments affecting the elderly men. Surgical intervention is recommended for moderate to severe LUTS non-responsive to pharmacological treatments [1, 2].

Surgical treatment modalities have undergone a revolutionary change with minimally invasive techniques. The Trans-Urethral Resection of the Prostate (TURP) is considered the reference standard in the surgical therapy of symptomatic bladder outlet obstruction (BOO) secondary to BPH.

In recent years, laser prostatectomy is emerging as a replacement for the standard TURP [3]. To be at least comparable, laser should reduce or avoid the immediate and long-term complications of TURP and permit an adequate histological diagnosis of the retrieved tissue.

A recent technological advance for the surgical treatment of BOO has been the Thulium laser. This new surgical laser may have several advantages respect to the other laser including improved spatial beam quality, more precise tissue incision, and operation in continuous-wave/pulsed modes [4]. Since the first experience, Thulium laser has been proved capable of rapid vaporization and coagulation of prostate tissue [4].

The objective of the present study was to investigate if an adequate histological diagnosis can be made from tissue after Thulium laser vapo-enucleation of the prostate (ThuVEP) and whether it is comparable to transurethral prostate resection

(TURP) tissue findings in patients with symptomatic benign prostatic hyperplasia.

Material and Methods

Patients' Selection

From January 2009 to June 2014 we start a prospective study on patients who underwent ThuVEP. In this period, we analyzed 350 ThuVEP and 100 matched TURP tissue specimens from patients who underwent one of the two procedures between.

All these patients have LUTS refractory to medical management. According to the International Guidelines, also the following complications were considered strong indications for surgery: refractory urinary retention, recurrent urinary infection, and recurrent haematuria refractory to medical treatment with 5-alpha reductase inhibitors, renal insufficiency due to BPH and bladder stones [2]. Prostate carcinoma was ruled out by prostate specific antigen, digital rectal examination, Trans rectal ultrasonography (TRUS), and biopsies when necessary. Patients with prostate carcinoma were excluded from the study, as were those with concomitant urethral strictures and bladder tumors and those with a history of urethral or prostatic surgery. Written consent was obtained from each patient.

Surgical Technique

Thulium laser prostatectomy was performed by Quanta Cyber TM Thulium Laser. The operative technique adopted for ThuVEP was that described by Herrmann et al in 2010 [5]. All the patients were in lithotomy position, and epidural or general anesthesia was achieved. This technique include five steps: circumferential incision of the verumontanum, incision to reach the prostatic capsule at 5 and 7 o clock and removal of the median lobe, apical incision of the lateral lobes, removal of the lateral lobes and morcellation. The level of tissue dissection was between the adenomatous tissue and the prostatic capsule. The result was an open prostatic fossa. A Quanta Cyber TM (Thulium:YAG) laser was used at three different energy levels, 120 W for incision and enucleation, 70 W for coagulation of the large capsular artery and 150 W for vaporization of small residues of adenoma at the end of the procedure. Laser energy was transmitted through a 15 times reusable 800 μm laser fiber.

A Wolf resectoscope with a separate operative channel for the fiber was used, with a 10° optic. Isotonic saline solution (NaCl 0.9 %) at room temperature was used for irrigation. Morcellation was performed by a Wolf 2303 Power Stick morcellator drawn towards the blades by suction due to a Wolf Piranha 2208 suction peristaltic pump. The use of morcellator allows the retrieval of tissue to a specimen container suitable for histologic analysis. A standard 3-way 20Fr Foley catheter is routinely used. Irrigations were stopped in the first postoperative day and after two hours; catheters were removed if the urine color was satisfactorily light. All patients were kept two hours in hospital after catheter removal and discharged.

Histological Analysis

Each histological specimen was reviewed by two pathologists. Preoperative prostate ultrasound volume, total serum prostatic specific antigen and postoperative tissue weight were evaluated.

Postoperative tissue weight, histological analysis of each specimen and immunohistochemical evaluation were assessed and compared between the two groups.

Microscopic histological diagnosis was assessed by standard histological techniques and immunohistochemical evaluation. Briefly, surgical specimens were fixed in buffered formaldehyde and embedded routinely in paraffin. The 4 μm sections were stained with hematoxylin and eosin. Immunohistochemical studies were performed on paraffin sections using antibody CK34_E12 (Dako, Glostrup, Denmark) (1:10) against high molecular weight cytokeratin.

Data Analysis

The primary outcomes measured included the tissue weights, the percentage of incidental cancer or PIN detection, the feasibility of tissue treatment, the presence of tissue artefacts due to laser damage on the tissue. Also we investigated if with the improvement of the learning curve the amount of tissue varied.

Results

Three hundred fifty patients performed the surgical treatment with Thulium laser. This patients were matched with 100 patients underwent to standard TURP. Table 1 lists the baseline characteristics of all men undergoing to the two treatments.

The patients' mean age was 67.9 and 65 years respectively in the thulep and in the TURP group. Mean preoperative prostatic adenoma volume, as measured by trans-rectal ultrasound (TRUS) was 77.05 mL and 76 respectively.

Table 2 lists perioperative data in the two groups.

Mean total operative time, including cystoscopy, enucleation and morcellation was 82 min. In the TURP group, the men operatory time was of 65 min. Average of 18.5 g of tissue was retrieved in the ThuVEP group. The variation of the percentage of adenomatous tissue retrieved in time was reported in Fig. 1.

Table 1 Baseline characteristics of all men undergoing to the two treatments

	ThuVEP			TURP		
Parameter	Mean	Range	SD	Mean	Range	SD
Age (y)	67.91	48–88	8.1	68.38	40–85	7.72
BMI	25.94	18.3–36.3	3.29	26.71	20.20–47.66	4.06
Vol Prostate (ml)	77.05	14–235	41.04	61.35	13–167	29.46
Vol Adenoma (ml)	45.15	7–167	30.22	31.03	4–80	17.84
PSA (ng/ml)	3.67	0.124–24	3.35	3.07	0.173–8.5	3.31

Here, it has to be kept in mind, that tissue retrieval in the ThuVEP group is underestimated, due to the amount of vaporization during the procedure.

Table 3 reported the diagnosis of incidental prostate cancer and PIN and the characteristics of these patients in the ThuVEP group. Incidental adenocarcinoma and high grade PIN of the prostate were diagnosed in a comparable percent of specimens in the 2 groups (2.5 % in the ThuVEP group versus 3 % in the TURP group).

Mean follow-up was of 14 months (range 3–24 months). No one of the patients in the ThuLEP group whit a negative histology required a prostatic biopsy due to a rising PSA.

Histological Evaluation of the Specimens

The thermal alterations found in histological preparations of patients undergoing ThuLEP appeared similar to those observed in endoscopic trans-urethral resection of the prostate. These artifacts, including the nuclear ipercromasia and the alteration of the glandular architectural components, appear for either confined to the most peripheral smaller fragments or even negligible in larger fragments (Fig. 2). Therefore, the interpretation of histological preparation stained with hematoxylin-eosin and immunohistochemical methods, in particular in the identification of prostate incidental neoplasia, do not show significant differences.

Discussion

In the last decade, various new technologies have been developed in transurethral surgery in an effort to decrease the existing morbidity of TURP. The new technique need to show a shorter bladder catheterization and washout. In addition, they will reduce the possible complications including catheter blockage by blood clots or unevacuated prostate chips, lower urinary tract infections, hemorrhage requiring transfusion, extraperitoneal fluid collection and do not permit TURP syndrome [6].

In this clinical picture, laser treatment of benign prostatic enlargement is gaining acceptance in daily urologic practice. Particularly Greenlight vaporization (PVP: photoselective vaporisation), Holmium laser enucleation (HoLEP) and ThuLEP have been studied and challenge the widely accepted treatment options as TURP [3].

This article will resolve a simple question: the ThuVEP method with morcellation provides an adequate tissue samples for a correct histological examination, comparable to TURP samples, to result in the same findings in terms of incidental adenocarcinoma of the prostate. In literature on ThuVEP there are no information regarding this issue.

A characteristic of the lasers are the capacity to vaporize and coagulates tissue. Tissue thermal artifacts induced by the laser were mostly due to coagulation, which may explain why alterations induced by the laser are similar to those after TURP. Due to the procedure, a moderate loss of tissue are

Table 2 Lists of perioperative data lists in the two groups

	ThuVEP			TURP		
Parameter	Mean	Range	SD	Mean	Range	SD
Operative Time (min)	82	25–220	20	65	35–95	17
Resected Weight (g)	18.54	5–80	15.64	21	2–60	13.1
Pre-Op Haemoglobin (g/dl)	14.12	9.3–17.3	1.19	13.75	10–16.5	1.45
Post-Op Haemoglobin (g/dl)	12.78	8.3–16.1	1.43	12.07	7.8–15.3	1.58
Haemoglobin Decrease (g/dl)	−1.23	(−6.9–2.2)	1.06	−1.67	(−3.6–0.4)	1.13
Catheterization time (day)	1.63	1–8	1.23	2.71	2–7	1.18
Hospital Stay (day)	2.62	1–11	1.7	5.06	3–6	2.01

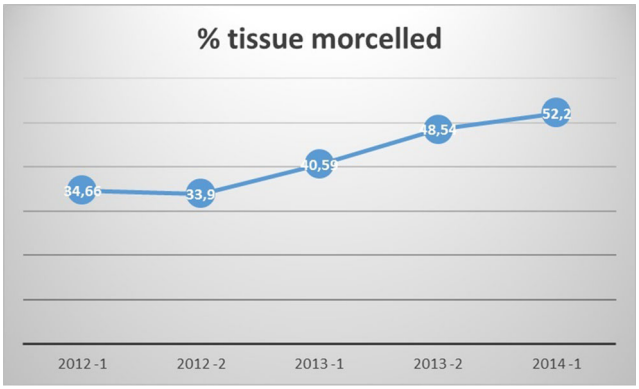

Fig. 1 Variation of the percentage of adenomatous tissue retrieved in time

due to vaporization. The amount of tissue recovered depend also from the learning curve of the surgeon. In fact as reported in Fig. 1 the percentage of tissue retrieved increased with the experience due in part to a reduction of the vaporized tissue for the increase expertize in the individuation of the correct plane between the adenoma and the prostatic capsule and he reduction of prostatic tissue that need to be regularized in the prostatic fossa at the end of the procedure. In addition, surgeon with the increased experience treats larger prostate that permit to increase the tissue retrieved by morcellation. Also in this difference, we need to take into account the well-known preoperative ultrasound overestimation of prostatic volume.

Regarding the mechanic alterations, the macroscopic and homogenized aspect of the prostatic fragments, which are smaller than TURP fragments do not seem to influence the successive pathological analysis (Fig. 2).

Major histological alterations resulting from thermal damage at the periphery of the tissue are limitated (Fig. 3). This is due to the fact that the technique leave to the circumferential of the lobe these artefacts, that became limited, and not to every chip as in TURP.

Architectural and cytological artifacts were observed in ThuVEP and TURP tissue specimens without significant differences.

The limitation of this study is the non-randomization of the patients, between the two techniques. We matched in terms of preoperative parameters such as age, total serum PSA and preoperative prostatic volume, thus, decreasing patient selection bias. However, the primary study objective was to assess

Table 3 The diagnosis of incidental prostate cancer and PIN and the characteristics of these patients in the ThuLEP group

Incidental prostate cancer histology	9
GPS 3+3 (pT1 A)	6
GPS 3+4 (pT1 A)	1
GPS 5+3 (pT1 A)	1
GPS 5+4 (pT1 A)	1
ASAP	1
PIN	1

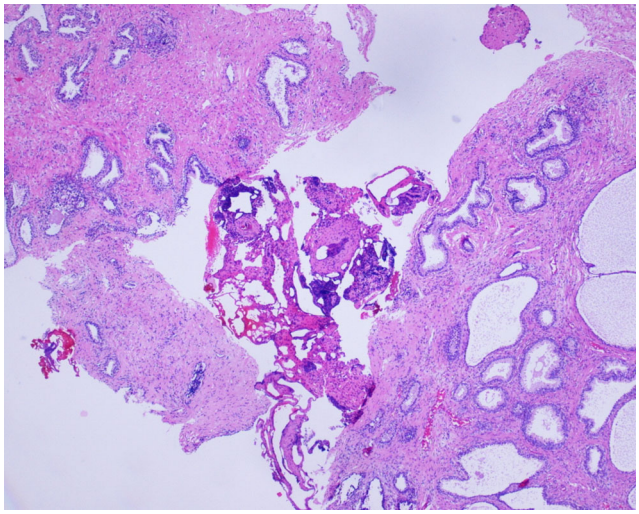

Fig. 2 The macroscopic and homogenized aspect of the prostatic fragments smaller than TURP fragments (HeE 10×)

the feasibility and reproducibility of Thulium laser impact on tissue evaluation, in particular cancer detection, from a pathological point of view.

The analysis of the patients' follow-up with negative histology findings, to date no patient has undergone needle biopsy for increased PSA or has had prostate cancer. Furthermore, patients at high risk, that is those with high PSA, or positive or doubtful digital rectal examination or TRUS findings, undergo preoperative TRUS biopsies to rule out any potential oncological risk.

Conclusion

Tissue quality was maintained in the ThuVEP histological specimens. Tissue maintain histological characteristics and proprieties without modification for successive

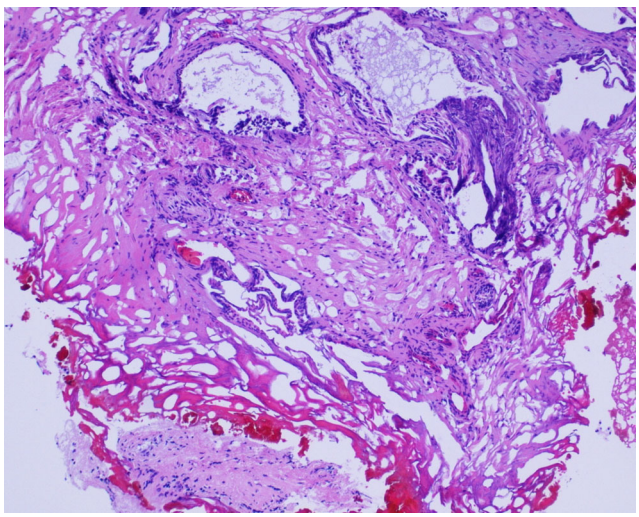

Fig. 3 Major histological alterations resulting from thermal damage at the periphery of the tissue are limitated (HeE 20×)

immunoistochemical analysis. The pathologist ability to detect incidental prostate cancer and PIN was maintained even if there is a quoted of vaporized tissue.

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