PROSTATE CANCER AS INCIDENTAL FINDING IN TRANSURETHRAL RESECTION

Tristan Dellavedova, Rolando Ponzano, Laura Racca, Federico Minuzzi and Mariana Dominguez.

FUCDIM (Fundación Urológica Córdoba para la Docencia e Investigación Médica). Córdoba. Argentina.

Summary.- Prostate adenocarcinoma is found in surgical samples without prior diagnosis in 4 to 15% of the patients. In some of them, there is previous suspicion but in others this finding is completely incidental. We present 7 cases of prostate cancer detected in 100 patients who underwent bipolar transurethral resection (TUR) of the prostate due to regular indications. The aim of this paper is to describe patient’s characteristics, postoperative outcome, analyze TURP as a diagnostic tool and evaluate therapeutic options for prostate cancer (PCa).

METHODS: One hundred patients with bladder outlet obstruction due to benign prostatic hyperplasia (BPH) underwent TURP in FUCDIM between June 2007 and August 2009. In 7 of them, prostate adenocarcinomas were detected. None of the patients underwent TURP only because of increased prostate-specific antigen (PSA).

RESULTS: Mean preoperative PSA was 7.6 ng/ml (r= 0.72 -27 ng/ml), 39% of the patients had PSA < 4 ng/ml; 33 (40%) had undergone previous biopsies and 36% of them had 2 or more previous biopsies. Prostate cancer detection global rate was 7%, 3 cases were incidental findings (low PSA and low-risk tumors), 3 patients had increased PSA and several previous biopsies with negative results and 1 had low PSA and aggressive tumor (Gleason 4+3).

CONCLUSIONS: TURP patients with prostate cancer are a heterogeneous group. TURP can be both diagnostic and therapeutic when facing patients with obstructive symptoms, high PSA and negative prostate biopsies. There are several therapeutic alternatives for TURP patients with cancer, taking into consideration tumor grade and stage, age, life expectancy and will of the patient. Bipolar TUR, in selected patients, allows to offer optional active surveillance (in these patients PSADT is very useful) and if cancer is not found, it eases the follow up of these patients. Active treatment (surgery or radiotherapy) is indicated in T1a patients with life expectancy longer than 10 years, and in the majority of T1b patients.

Keywords: Prostate adenocarcinoma. Incidental tumor. Bipolar transurethral resection. Diagnostic TURP.

Resumen.- OBJETIVO: El hallazgo de adenocarcinoma prostático en piezas quirúrgicas sin diagnóstico previo de tumor se presenta en 4 a 15% de los pacientes.
En algunos, existe sospecha previa, en otros, el hallazgo es “incidental”. Presentamos 7 casos de cáncer de próstata detectados en 100 pacientes a quienes se les realizó resección transuretral (RTU) bipolar de próstata debido a indicaciones quirúrgicas habituales. El objetivo de este trabajo es describir las características de los pacientes en quienes se encontró cáncer en la resección transuretral y su evolución postoperatoria, analizar la RTU como herramienta diagnóstica y evaluar las opciones de tratamiento.

MÉTODO: Entre junio de 2007 y agosto de 2009, se realizaron en FUCDIM 100 RTU bipolares de próstata en pacientes con patologías obstructivas. En 7 se detectó adenocarcinoma de próstata. A ningún paciente se le realizó RTU solamente por elevación del antígeno prostático específico (PSA).

RESULTADOS: El promedio de PSA preoperatorio fue 7,6 ng/ml (r= 0,72-27 ng/ml), 39% de los pacientes tenían PSA <4 ng/ml; 33 (40%) pacientes tenían biopsias previas y 36% de ellos 2 o más biopsias previas. La tasa global de detección de cáncer de próstata fue de 7%, 3 fueron hallazgos “incidentales” (PSA bajo y tumor de bajo riesgo), 3 con PSA elevado y varias biopsias previas negativas y 1 con PSA bajo y tumor agresivo (Gleason 4+3).

CONCLUSIONES: Los pacientes con cáncer de próstata como hallazgo incidental durante la RTU constituyen un grupo heterogéneo. En pacientes con síntomas obstructivos, PSA elevado y biopsias negativas, la RTU es a la vez diagnóstica y terapéutica. Las alternativas terapéuticas ante el diagnóstico de CaP tras la RTU son variadas y se debe tener en cuenta el grado y estadío del tumor, edad, expectativa de vida y voluntad del paciente. La RTU bipolar permite plantear, en pacientes seleccionados, la posibilidad de ofrecer “active surveillance”(en este grupo es muy útil el PSADT) y de no encontrarse el tumor, facilita el seguimiento de estos pacientes. El tratamiento activo (cirugía o radioterapia) está indicado en pacientes T1a con expectativa de vida mayor a 10 años, y en la mayoría de pacientes T1b.

Palabras clave: Adenocarcinoma de próstata. Tumor incidental. Resección transuretral bipolar. Resección transuretral diagnóstica.

INTRODUCTION

Most prostate carcinomas are currently diagnosed by biopsies indicated for elevation of prostate-specific antigen (PSA), widely used these days(1). However, adenocarcinomas are still found in histopathological exams of surgical samples of patients without previous diagnosis. This is not surprising, since many patients have the surgery indicated for symptomatic benign prostate hyperplasia with elevated PSA and negative preoperative biopsies. A different situation occurs with incidental finding of tumors that would never have been detected if the surgery had not been indicated; they would not have produced symptoms or increased PSA values.

Treatment options have to be tailored according to patients and tumors and include: active surveillance, local surgery or external radiotherapy, and androgen deprivation in patients with advanced disease, aged or those who prefer a non-invasive approach.

We present 7 of 100 patients who underwent bipolar transurethral resection of the prostate (TURP) due to regular indications, in whom prostate adenocarcinomas were detected.

The aim of this paper is to describe cancer patient’s characteristics, postoperative outcome, analyze TURP as diagnostic tool and evaluate treatment options for prostate cancer (PCa).

MATERIAL AND METHODS

Retrospective and descriptive study of 100 bipolar TURPs performed by the same endoscopic surgeon. All the procedures were performed in FUCDIM between June 2007 and August 2009. All the patients had obstructive diseases, and those with prior diagnosis of prostate cancer were excluded.

All the samples were analyzed by the same uropathologist. A database was elaborated including name, age, prostate volume, PSA, previous biopsies, indication of surgery, International Prostate Score of Symptoms (IPSS) and flowmetry, surgical data (amount of prostatic tissue removed, operative time, histopathological results) and postoperative information (PSA, complications, functional outcome).

Patients with diagnosis of prostate cancer were staged with CT-scan of the abdomen and pelvis and bone scan. Follow-up was performed independently of the selected therapy.

RESULTS

Main indications for surgery were low urinary tract symptoms (LUTS) (58%), acute urinary retention, recurrent infections, bladder lithiasis and iterative hematuria. No TURPs were performed due only to increased PSA values, but in some cases prostatic
symptoms, elevated PSA values and previous negative biopsies coexisted. Characteristics of patients with and without cancer are presented in Table I.

The patients of PCa group were older, had smaller prostates, lower preoperative PSA levels, higher percentage of preoperative negative biopsies, less amount of tissue resected, equal hospitalization time and no complications when compared with the non-cancer group.

Global PCa detection rate was 7%, 4% corresponded to patients without previous biopsies and 12% to those who did have prior biopsies.

No reoperations were needed and there was no perioperative mortality. Postoperative functional outcomes were satisfactory (estimated by symptoms score, quality of life, flowmetry), and average postoperative PSA was 1 ng/ml. Sixty-one percent of the patients had preoperative PSA higher than 4 ng/ml, none of them presented values within this range after surgery, not even those with cancer.

None of the patients had previous diagnosis of cancer, and in 7 cases the disease was detected by histopathological analysis of the fragments. In the rest of them, no malignancies were found and 2 patients had granulomatous prostatitis.

### Table I. Pre, intra and postoperative characteristics (average) of the patients with and without prostate cancer in RTU.

<table>
<thead>
<tr>
<th>Grupo</th>
<th>Nº</th>
<th>Age</th>
<th>Preoperative weight</th>
<th>Preoperative PSA</th>
<th>Previous biopsies</th>
<th>RTU grams</th>
<th>Surgical time</th>
<th>Hospitalization time</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without CaP</td>
<td>93</td>
<td>65</td>
<td>99,2</td>
<td>7,6</td>
<td>39%</td>
<td>78,6</td>
<td>81</td>
<td>16</td>
<td>18%</td>
</tr>
<tr>
<td>With CaP</td>
<td>7</td>
<td>69</td>
<td>74,5</td>
<td>6,4</td>
<td>57%</td>
<td>71,4</td>
<td>60</td>
<td>16</td>
<td>-</td>
</tr>
</tbody>
</table>

PCa: prostate cancer.

### Table II. Patients with incidental finding of prostate cancer in TURP.

<table>
<thead>
<tr>
<th>Patient Nº</th>
<th>Age</th>
<th>PSA</th>
<th>Bx (-)</th>
<th>Location of tumor</th>
<th>Gleason</th>
<th>Percent of (+) tissue</th>
<th>1st postop PSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>10</td>
<td>2</td>
<td>Peripheral</td>
<td>3+3</td>
<td>&lt;5%</td>
<td>0,5</td>
</tr>
<tr>
<td>2</td>
<td>69</td>
<td>18</td>
<td>5</td>
<td>Peripheral bilateral</td>
<td>3+3</td>
<td>&lt;5%</td>
<td>0,1+</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>7,7</td>
<td>4</td>
<td>Transitional and Peripheral</td>
<td>3+3</td>
<td>&lt;5%</td>
<td>0,58</td>
</tr>
<tr>
<td>4</td>
<td>70</td>
<td>5,4</td>
<td>1</td>
<td>Transitional and Peripheral “incidental”</td>
<td>3+3</td>
<td>&lt;5%</td>
<td>0,26</td>
</tr>
<tr>
<td>5</td>
<td>82</td>
<td>0,9</td>
<td>-</td>
<td>Transitional, “incidental”</td>
<td>3+3</td>
<td>&lt;5%</td>
<td>0,1</td>
</tr>
<tr>
<td>6</td>
<td>67</td>
<td>1,2</td>
<td>-</td>
<td>Transitional, “incidental”</td>
<td>3+3</td>
<td>&lt;5%</td>
<td>0,47</td>
</tr>
<tr>
<td>7</td>
<td>77</td>
<td>2,6</td>
<td>-</td>
<td>Transitional and Peripheral</td>
<td>4+3</td>
<td>90%</td>
<td>0,1 *</td>
</tr>
</tbody>
</table>

* Received androgen deprivation after diagnosis
+ Received androgen deprivation after diagnosis, and subsequent radiotherapy
Bx: biopsy
Resected tissue was stored in 4 different flasks, identified as right and left transitional and peripheral, excepting those unusual cases where very little part of the prostate was resected (in all cases of cancer, we extracted more than 30 g and all samples were submitted separately).

The characteristics of the 7 patients with cancer are shown in Table II. Six of them had normal rectal exam. The staging studies performed in 6 patients were compatible with localized tumors. The only case that was not staged was the eldest patient, who had complications due to previously diagnosed leukemia and died 8 months after the surgery.

The fourth patient was diagnosed while being operated due to urothelial cancer of the bladder, with bladder wall and prostatic infiltration. Bladder wall and prostatectomy were performed and urethelial cancer (confirmed by immunohistochemical analysis) largely compromising the prostate was found, as well as incidental finding of prostatic adenocarcinoma. As previously mentioned, all patients, even those with initial increased PSA values, had postoperative values lower than 1 ng/ml and only two of them received androgen deprivation. Median follow-up was 20 months (12 to 29). Patients number 5 and 7 died (the first one had incidental finding of prostate cancer and the second an extended tumor) 8 and 15 months after the surgery respectively, due to causes unrelated to the surgery or the prostate cancer. From the other patients, 3 are still under active surveillance with PSA doubling time (PSADT) of 13, 17 and 20 months respectively; other received external radiotherapy (case n° 2) and the patient with muscle-invasive urothelial carcinoma received chemo-radiotherapy. All patients received detailed information about benefits and risks of each option and they agreed with the chosen alternative.

The seventh patient had suspicious rectal exam but also severe prostatism (permanent indwelling urethral catheter) and other comorbidities. TUR was performed to release the urinary tract and to obtain biopsy samples.

**DISCUSSION**

Within surgeries due to benign obstructive prostatic diseases, adenocarcinomas can be unintentionally detected. In some cases, TURP is used for patients with symptomatic bladder outlet obstruction (BOO), to detect tumors suspected by elevation of the PSA, which had not been revealed by transrectal biopsies (diagnostic TURP). In other cases, these tumors are incidentally found and probably, if these patients had not required a surgery to release their urinary tract, the tumors would never have been detected (incidental tumors). The third situation presented is the diagnosis of an aggressive tumor (Gleason score 7, 4+3) in a patient in whom cancer was suspected after rectal examination and who had severe obstructive symptoms.

TUR of the prostate is not currently considered as a diagnostic tool for prostate cancer, except in special cases. Bipolar surgery is a new technique, in use for less than 10 years, that allows the removal of prostatic tissue with continuous irrigation of saline solution, which is isotonic with plasma; this avoids the risk of absorption syndrome, the most dreaded complication of monopolar TURP (2). Neither in the literature nor in our series, we found differences between monopolar and bipolar TUR in terms of cancer detection (2,3). However, the bipolar option offers the possibility of using more endoscopic resection time to tackle larger prostates without risking morbidity from the effect of water reabsorption and TURP syndrome. A TURP is considered appropriate when at least a third of the gland has been resected. In our series, the mean size of preoperative prostates was 99.2 g and the total resected grams were 78.6, this means that a mean of 78% of the glands were resected.

For patients with increased or increasing PSA and negative transrectal biopsies, Bratt recommends to repeat biopsies including the transitional area and afterwards saturation biopsies of 24 to 48 samples with general anesthesia. Magnetic resonance spectroscopy is under study, with promising results to detect suspicious areas and direct biopsies; in the last place, diagnosis TUR can be used for a small number of patients with large prostates and continuously rising PSA when all other diagnostic measures have been used (5).

On the other side, the “National Comprehensive Cancer Network” of the United States proposes the following algorithm: first, a 12-sample biopsy, if negative, it can be repeated including the transitional area, if negative again in a high-risk patient, consider saturation biopsy (6).

Performing TURP only to detect cancer is not accepted as formal indication, only in those cases with negative prostatic biopsies and obstructive symptoms that validate the intervention. van Renterghem studied asymptomatic patients with BPH with urodynamical studies detecting BOO in most of them; for this reason, he proposed to perform diagnostic surgeries with the triple objective of relieving obstruction (even if asymptomatic), making extended biopsies and decreasing PSA values (7).
In spite of the scarce arguments that support TURP as diagnostic alternative, more evidence is arising:

• Asymptomatic patients with increased PSA may have significant obstructions and may benefit from the surgery (7,8). High PSA values are associated to increased risk of urinary retention (9).

• Patients with increasing PSA who may have a transitional zone tumor are better sampled with TURP rather than transrectal biopsies (8,10).

• TURP has low rate of complications that can be reduced with limited resections, in order to avoid apical resection and capsular perforation (8).

• Tumors of the transitional area are more often low grade and less prone to penetrate capsule and metastasize, and there is a fair chance of cure even if the PSA is well above 20 ng/ml (8,11).

• PSA decreases to normal values in most patients (4).

• The remnant prostate is more easy and completely biopsied in subsequent biopsies, increasing the chances to detect cancer in postoperative biopsies (4).

• Radical prostatectomy after TURP may present some technical difficulties but in experienced hands it has excellent oncological and functional outcomes (8).

Those who do not support this technique believe that after a second negative biopsy, the rate of cancer detection is very similar, indicating a third biopsy (10% detection), with “diagnostic TURP” (9-12% detection), or only with follow up during 7 years and a newer biopsy in case of PSA elevation (11% detection) (8).

Paolo Puppo proposes as an alternative for cases with at least 2 negative biopsies, to perform TURP and transrectal biopsy at the same time. From 43 patients studied, he detected cancer in 8 (18.6% detection rate), 6 with RTU (75%), 1 with biopsy (12.5%) and 1 with both (12). A recent publication of Ploussard showing different results includes 113 asymptomatic patients with at least 2 negative biopsies of 21 samples each, performed in patients that received a newer 21-sample biopsy and immediate TURP. The rate of global detection was 23.9%, being 63% reached by biopsy only, 22% by TURP and 15% by the combination of both (4).

The detection of adenocarcinoma in patients who undergo TURP ranges between 4 and 15% in the literature (13-15). According to the International Union Against Cancer classification (2002), a difference between T1a (finding of incidental tumor in 5% or less of the resected tissue) and T1b (finding of an incidental tumor in more than 5% of the resected tissue) was established (16). This is based on the progression risk, which is only 5% at 5 years for T1a (although 50% progress after 10 to 13 years) and is present in most of the T1b patients in that period of time (16); this allows to classify the first ones as “insignificant tumors” and the second ones as “clinically significant” (17).

Radical prostatectomy for these two early stages poses the risk of not finding cancer in the specimen (pT0) in 4 to 21% of cases. However, as we previously mentioned, the long term risk of progression is high for T1a, so surgery is offered for patients with life expectancy greater than 15 years. According to the 2010 European Society of Urology Guidelines, watchful waiting is standard therapy for T1a and active treatment for T1b (particularly in patients with longer life expectancy), grouping this last category with palpable tumors that occupy a prostate lobe (T2a-T2b) (16).

Monda proposes that the regular use of PSA is not really useful to decrease the prevalence of T1a tumors, since it does not differentiate these tumors from prostatic hyperplasia, but it can decrease the prevalence of T1b lesions, which generally increases PSA values (18). In our series there were no T1b cases.

It is believed that many patients with previous negative biopsies have tumors located in the transitional zone, especially in the frontal area. These are usually low grade tumors, not very aggressive and with high possibilities of cure (8,11). However, other authors think that these lesions can be aggressive and that they are frequently associated to bigger satellite tumors in the peripheral area, of higher grade (4,19).

Some authors report an actual low incidence of pure transitional tumors (0.6%) and do not consider that performing biopsies in this area can be useful (20). On the other hand, Ploussard reports 19% of tumors exclusive of the transitional area (4). In our patients, among those suspected to have PCA, none had exclusively transitional tumor, and in 2 of the incidental cases the tumor was located only in the transitional area (PSA were 0.9 and 1.2 ng/ml, respectively).

In patients with cancer found after endoscopic surgery, post TURP transrectal biopsies could be useful to detect residual tumor, non-diagnosed peripheral
cancer or to achieve a more appropriate tumor grading (16). Among our cases, none was biopsied, since only 2 had exclusive transitional tumor, one of them died and the other has a PSA doubling time (PSADT) of 17 months.

The finding of incidental tumors is also described in the literature and its frequency is related to the patient’s age (21). These tumors are not life-threatening, since they are usually low-grade and low volume. In our series, the 3 tumors catalogued as incidental had Gleason score of 6 and were found in 1, 2 and 3 fragments (less than 1% of tissue with cancer), respectively. Usually, these tumors do not require active therapy. From our 3 patients with incidental lesions, 2 did not have increased PSA, were T1a and did not require any therapy, the third one had a tumor of the bladder that infiltrated the prostate, which could explain PSA values of 5.4 ng/dl and the negative results of previous biopsies. In this case, we found a great volume of the prostate involved within the urothelial tumor and only 3 fragments of the TUR (less than 5%) with adenocarcinoma, meaning that low volume of adenocarcinoma would not have raised PSA or prompted a biopsy.

The third scenario of our cohort was special; it was an aged patient with several other diseases, PSA: 2.61 ng/ml, rectal exam clearly abnormal, enlarged prostate and severe obstructive symptoms that did not respond to therapy. We felt urged to make a decision: either indicate biopsy with the consequent events that follow diagnosis in addition to his clinical condition, or to perform diagnostic and therapeutic TURP to release the obstruction, obtain samples for biopsy and to decrease the PSA values (postoperative PSA at 3 months: 0.1 ng/ml). His life expectancy was limited and as a matter of fact, he died 15 months later due to a cardiovascular event unrelated to his urological problem; for this reason, we considered that his oncological care was a secondary matter. The studies revealed a localized tumor and the patient had very good functional outcome after the surgery.

**CONCLUSIONS**

Patients with prostate cancer found in TURP are a heterogeneous group, including some with high preoperative suspicion of neoplasia and others with incidental tumors.

TURP as diagnostic tool is useful in selected cases: high PSA values, obstructive symptoms and negative biopsies. Many lurk cancer in the transitional zone, although not exclusively. It poses the advantage of relieving urinary flow and at the same time obtains a good amount of tissue for histopathological analysis. This should not be performed in the absence of obstruction.

The finding of prostate cancer after bipolar TURP points out different situations regarding the management of this disease, in which volume, grade and stage of the tumor should be considered, as well as age, life expectancy and motivation of the patient. PSADT is a useful marker of tumoral activity in patients with active surveillance and can help to identify patients who require active therapy.

Detection of cancer by bipolar TURP allows proposing, in selected cases, active surveillance, and if any kind of active treatment is chosen, the available options include external radiotherapy, radical prostatectomy and androgen deprivation.

In case of not finding any tumor, TUR eases the follow-up of these patients, smoothing the symptoms, decreasing PSA values and improving outcome of possible subsequent biopsies.

**REFERENCES AND RECOMMENDED READINGS**

(*of special interest, **of outstanding interest)


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