ORIGINAL ARTICLE

Transrectal biopsy of the prostate: experience at the Hospital Regional Lic. Adolfo López Mateos, ISSSTE

P. Cruz-G. a,*, M. Schroeder-U. a, M. Estrada-L. a, F. de la Torre-R. b and R. F. Velázquez-Macías c

a Urology Specialty Residency, Hospital Regional “Lic. Adolfo López Mateos”, ISSSTE, Mexico City, Mexico
b Pathology Service, Hospital Regional “Lic. Adolfo López Mateos”, ISSSTE, Mexico City, Mexico
c Urology Service, Hospital Regional “Lic. Adolfo López Mateos”, ISSSTE, Mexico City, Mexico

KEYWORDS
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Abstract

Background: Prostate cancer (CaP) in Mexico is the eighth cause of death by cancer in men above the age of 65 years. Transrectal biopsy of the prostate (TRBP) is regarded as the best diagnostic method for CaP.

Aims: To show the results of transrectal ultrasound-guided biopsies of the prostate obtained over a period of time at a regional hospital in Mexico City.

Material and methods: A descriptive study was conducted of all the transrectal biopsies of the prostate performed at our hospital over a 24-month period.

Results: TRBP was carried out in 420 patients. A total of 33.8% were positive for malignancy. A Gleason score of 7 predominated in 35%. Immunohistochemistry was done in 34 patients. The mean prostate specific antigen (PSA) value was 16 ng/ml. Complication incidence was analyzed. Seventy-seven percent of the patients received hormonal blockade.

Discussion: TRBP is the only method for diagnosing CaP. Sixty-five percent of CaP cases present in patients above the age of 65 years. According to a Mexican study conducted in 2011 in which TRBP was carried out in 145 patients, the overall cancer detection was 31%.

Conclusions: TRBP is the definitive method for CaP diagnosis and has a detection rate of 33%.
Introduction

According to figures from the Sistema Nacional de Información en Salud (SINAIS), prostate cancer (CaP) in Mexico is the eighth cause of death by cancer in men above the age of 65 years, with 4,435 deaths corresponding to the disease reported in 2007. In 2008, it was the twelfth cause of death by cancer in men of all ages, resulting in 1.7% of deaths in the male population. Of the total of deaths by CaP in the country, Mexico City is in first place with 478 deaths (15.7/100,000 inhabitants), followed by Jalisco with 473 (21/100,000 inhabitants), and the State of Mexico with 411 (12.2/100,000 inhabitants) 1.

An adequate screening method must have various characteristics, and among them it should be minimally invasive, simple to perform, available, accepted by the general population, have a low rate of false negative results, and have an important influence on mortality. Since 1991 when prostate specific antigen (PSA) emerged, it has become the only available CaP marker 2.

The PSA cut-off value is 4 ng/mL in most of Mexico. However, in other countries this cut-off point has gone down to 2.5 ng/mL, due to reports stating that the cancer incidence is from 24% to 26.3% in patients with a PSA between 2.6 and 4.0 ng/mL 3-6.

Transrectal biopsy of the prostate (TRBP) is considered an indication in those patients with an elevated PSA or digital rectal examination showing alterations in the surface and consistency of the prostate.

The present study is the first descriptive analysis to be conducted at the Hospital Regional “Lic. Adolfo López Mateos” of the ISSSTE that refers to TRBP results.

Methods

A retrospective, descriptive, cross-sectional study of all the ultrasound-guided TRBPs performed at the Urology Service of the Hospital Regional “Lic. Adolfo López Mateos” of the ISSSTE during the time frame of May 2010 to May 2012 was conducted.

All these biopsies were carried out on patients covered by the Urology Service of the ISSSTE, or from other peripheral ISSSTE clinics. Procedure indications were elevated PSA (> 4 ng/mL) or a clinical suspicion of CaP from the rectal examination. All the biopsies were performed using ESAOTE MyLab™Desk ultrasound equipment with a 12 Hz intracavitary transducer. The biopsies were taken with a 22G needle after anesthesia infiltration of the periprostatic segments with simple xylocaine at 2%. Twelve cores were taken in total, using the sextant regimen for each lobe. The biopsies were examined by pathologists from the hospital’s Pathology Service. The cases that were histologically regarded as suspicious or inconclusive were studied through immunohistochemistry.

Antibodies against protein 63 (4A4 DAKO clone, 1:100) and racemase (P504S) (13H4 DAKO clone, 1:100) were used. During the study time frame, 34 immunohistochemistry studies were carried out from the total of the prostate biopsy samples. For the present study, only 18 cases corresponding to patients of our Unit were regarded as having complete information.

Results

Biopsies performed at the Urology Service over a 24-month period (May 2010 to May 2012) were retrospectively...
reviewed. TrBP was done on 420 patients. The mean age was 66 (range 42-89) years. Of the patient total that underwent TrBP, 142 had a positive result for malignant prostate tumor, corresponding to 33.8% (table 1).

Of the 278 patients (66.2%) with a negative result for malignancy, 60% showed data of fibromuscular hyperplasia, 22% chronic prostatitis, 16% had no alterations, and 2% presented with glandular atrophy (fig. 1).

Of the total of patients with malignant disease results, 50 patients (35.2%) had a Gleason score of 7, 45 patients (34.5%) had a Gleason score of 6, 20 patients (14%) a Gleason score of 8, 11 patients (8.4%) a Gleason score of 5, 5 patients (3.5%) a Gleason score of 9, 4 patients (3.5%) a Gleason score of 4, and one patient (0.7%) had a Gleason score of 10 (fig. 2).

An additional analysis was done according to the sum of the differentiation patterns for each Gleason score, which is illustrated in figure 3.

Of the 420 biopsied patients, it was necessary to carry out immunohistochemistry for p63 markers for basal cells and racemase (P504S) of the cores in 34 (8%) cases, because of doubt in the histopathologic diagnosis. Of the 34 patients, 50% presented with stains consistent with adenocarcinoma.

From the total number of patients that underwent biopsy in our Institution, it was possible to conduct a retrospective review of the information of 163 cases. Of these patients

### Table 1 Result analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66 (42-89)</td>
</tr>
<tr>
<td>Family history</td>
<td>3.1% (5)</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>16 (2.78-100)</td>
</tr>
<tr>
<td>Digital rectal examination</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>24%</td>
</tr>
<tr>
<td>-</td>
<td>76%</td>
</tr>
<tr>
<td>TRBP +</td>
<td>33.8% (142)</td>
</tr>
<tr>
<td>TRBP -</td>
<td>66.2% (278)</td>
</tr>
<tr>
<td>IHC</td>
<td>8% (34)</td>
</tr>
<tr>
<td>+</td>
<td>50%</td>
</tr>
<tr>
<td>-</td>
<td>50%</td>
</tr>
<tr>
<td>Prostate volume (g)</td>
<td>80.9 ± 42.5</td>
</tr>
<tr>
<td>Post-TRBP hematuria</td>
<td>69%</td>
</tr>
<tr>
<td>Post-TRBP urinary retention</td>
<td>2.4%</td>
</tr>
<tr>
<td>Post-TRBP hospitalization</td>
<td>2.9%</td>
</tr>
<tr>
<td>Radical prostatectomy</td>
<td>15%</td>
</tr>
<tr>
<td>Hormonal blockade</td>
<td>77%</td>
</tr>
<tr>
<td>Orchietomy</td>
<td>5.3%</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

PSA: prostate specific antigen; TRBP: transrectal biopsy of the prostate; IHC: immunohistochemistry

Figure 1 Patients with a negative result for malignancy.

Figure 2 Patients with a positive transrectal biopsy of the prostate.
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Data was collected related to age, a family history of CaP, the PSA for which biopsy was indicated, suspicious rectal examination, ultrasound prostate volume, number of biopsy cores, complications, immunohistochemistry data, and the therapeutic decision in those cases with positive malignancy.

In 3.1% (n=5) of these patients there was some family history of CaP. The mean PSA value was 16 ng/mL, with a range from 2.78 to 100 ng/mL.

The mean ultrasound-measured prostate volume was 80.9 ± 42.5 g. The mean number of biopsy cores was 11.45.

Rectal examination was done on all patients before the biopsy and was classified as suspicious or non-suspicious. Some type of alteration was found in the rectal examination of 24% (n=40) of the patients.

Of the patient total whose records could be reviewed (n=163), 34% had a positive result for malignancy. A total of 34 immunohistochemistry studies were done, corresponding to 8% of the patients. In 18 of the 163 patients with complete information, the immunohistochemical assay with P63 and P504S was done to determine the definitive histopathologic result; of these, 8 (5%) were consistent with adenocarcinoma of the prostate.

After TRBP, 69% of the patients presented with hematuria, 2.4% with urinary retention, and only 2.9% required hospitalization for some motive after the procedure.

In regard to therapy in the patients with positive malignancy, retropubic radical prostatectomy was performed in 15%, androgen blockade was initiated in 78%, radiotherapy in 1.8%, and orchietomy in 5.3%.

Discussion

Today, TRBP is the only means available for making the definitive diagnosis of CaP. In order to carry out TRBP, previous screening in a particular population must be done. In Mexico it is currently recommended to have an annual PSA test and rectal examination from the ages of 45-50 years. It has been proposed to begin at a lower age in other countries. A man with a family history of CaP has a 2 to 2.5 times higher risk for presenting with CaP during his lifetime. If there is a history of CaP in a first-degree relative, screening is recommended starting at the age of 40 years. The mean age in our study population was 66 ± 9.3 years. A total of 65% of CaP cases presents in patients older than 65 years. If there is a persistent PSA elevation or a rectal examination alteration, TRBP is indicated. According to some meta-analyses, the positive predictive value of the rectal examination is 18% to 28%. PSA as a screening method can exclude up to 20% of positive cases. Therefore, the joint use of PSA and rectal examination improves the detection rate. According to a Mexican study conducted in 2011, in which TRBP was done on 145 patients, the overall cancer detection was 31%. In their study, Roehl, Antenor, and Catalona reported a cancer incidence of 29% in the patients that had undergone TRBP because they had presented with a PSA above 4 ng/mL. Other large studies have reported positive TRBPs in 33% of patients with a PSA above 4 ng/mL, and one third of them also presented with abnormal rectal examination results.

In our case series, we reported a percentage that was very close to that of other studies with a 33.8% incidence of TRBPs that were positive for CaP.

In the Prostate Cancer Prevention Trial (PCPT), 23% of men with a PSA between 3 and 4 ng/mL presented with CaP. In some countries the present PSA cut-off point is 2.5 ng/dL. In the PCPT, the CaP detection rate through TRBP was 16.2% in those patients with a PSA value between 2.6 and 4.0 ng/mL.

PSA continues to be of great value in detecting those patients at high risk for presenting with CaP. One of the limitations of PSA is its relatively low specificity of 60% to 70%. It is true that an important percentage of patients with a high antigen value will not present with prostate malignancy, which is explained by factors that condition an inflammatory response.
prostatic state or by a simple increase in the number of fibromuscular stroma cells. Prostatic hyperplasia is the main cause of elevated PSA, followed by inflammation, trauma, and urinary retention. In our study, we found that of the 60.9% of the patients whose TRBP was negative, 22.9% of them had histopathologic data related to fibromuscular hyperplasia and chronic prostatitis. Chronic prostatitis is defined as a state of persistent inflammation of the prostate gland lasting more than 3 months and that clinically manifests with lower obstructive urinary symptoms, such as poorly localized pain, as well as PSA elevation. In contrast, fibromuscular hyperplasia refers to an increase in the number of fibromuscular stromal cells with a subsequent PSA elevation as a consequence of an increase in its production.

In comparing the results of our Gleason scores with a study by Catalona, we found that in that study a Gleason score of 2 to 4 corresponded to 8% of the patients, a score of 5 to 6 to 6%, a score of 7 to 19%, and a score of 8 to 10 to 4%. We also found a different distribution: 3.5% for patients with a Gleason score of 2 to 4, 43% for a score of 5 to 6, 35.2% for a score of 7, and 18% for a score of 8 to 10. This difference may be due to the fact that the Catalona study was conducted 10 years ago. Currently, pathologists have greater experience in CaP diagnosis and Gleason classification. In our study there was a predominance of tumors with a Gleason score of 7 with the 3+4 sum.

According to the PCPT, the most appropriate PSA value for carrying out biopsy is 2.5 ng/mL. In a study of 24,000 men, the same percentage of CaP was found in the group with PSA values of 2.6 to 4.0, as well as in the group with PSA values of 4.0 to 10 ng/mL. When the cancers detected with a PSA between 2.6 and 4.0 ng/mL were compared with those cancers with a PSA of 4.0 to 10 ng/mL, it was observed that the former cases had less volume, were equally significant, and had a greater probability of being organ-confined.

At the beginning of 2012, the U.S. Preventive Services Task Force (USPSTF) recommended that PSA stop being used as a CaP diagnostic tool, stating that the screening would only benefit a small number of men and would be harmful for a larger number. This recommendation was based on the results obtained in 2 randomized studies, the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial and the European Randomized Study of Screening for Prostate Cancer (ERSPC). In both studies, the screening groups had a higher CaP incidence than those that were not evaluated with PSA and they presented a mortality rate that was very similar to the control group. Due to these results, the USPSTF decided that the reduction in the cancer-specific mortality rate for CaP was not greater than the risks and complications of screening and diagnosis, as well as the complications related to CaP treatment. The USPSTF gave PSA a grade D recommendation, meaning that this tool should not be used, given that it offered no benefit or its benefit did not exceed the risks involved.

Different international associations and researchers have expressed their disagreement with this recommendation. They argue that the USPSTF has misinterpreted the results of these studies due to “contamination” of the results in both studies. In other words, that there were important biases in patient selection and methodology of these studies and so their results cannot be used as references for such a radical decision. The urologic community has not accepted this recommendation, because there is currently no other validated tool or marker that is sufficiently sensitive and specific for replacing PSA. The low cost of PSA makes it an adequate and available screening method. It is in the selection of patients where more care should be taken in order to prevent over-diagnosis, and in some cases, the complications inherent in the medical and/or surgical treatment of CaP.

Markers such as proPSA and PCA3 are being studied and used in an attempt to improve the PSA detection rates. Some studies have reported a higher sensitivity in proPSA than in PSA.

Immunohistochemistry markers for aiding in the diagnosis of adenocarcinoma have been utilized since 1998. The most widely used markers have been high molecular weight cytokeratin (CKH), cytokeratin 5/6 (CK 5/6), cytokeratin 5 (CK 5), cytokeratin 14 (CK 14), and protein 63 (p63). These markers highlight the presence of basal cells in benign glands and their absence in suspicious glands, supporting their malignant nature. They can be used alone or in double or triple stains. Racemase overexpression (α-methylacyl-CoA racemase [AMACR], P504S) is a characteristic of the prostate adenocarcinomas and their expression is an equally strong malignancy indicator. Eighty percent of the biopsied adenocarcinomas are positive but there can be positivity in benign glands. In addition, the lack of p63 positivity is not a definitive datum, given that between 5% and 23% of benign glands can show negativity, and some adenocarcinomas can be positive for CKH and p63. Immunohistochemical support correlates the histologic characteristics of the abnormal glands with the clinical information.

Therefore, it is important for the urologist to be completely familiarized with the different therapeutic options for CaP management that are currently available, and to have the necessary criterion for identifying those cases in which the benefit from diagnosis and treatment will exceed the risks and complications following a positive CaP diagnosis.

Conclusions

The use of PSA as a screening method in the male population continues to be an extremely useful tool for diagnosing CaP. TRBP in patients with suggestive or suspicious CaP data may provide the definitive diagnosis in approximately one third of these patients. Today, TRBP is the definitive method for CaP diagnosis. It is important to know the CaP detection data of each institution in order to have a better follow-up of CaP behavior at the national level. In Mexico, PSA, together with digital rectal examination, continue to be the main elements for requesting TRBP and thereby detecting prostate cancer.

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Conflict of interest

The authors declare that there is no conflict of interest.
References