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10-Year Experience in Performing Saturation Prostate Biopsy*

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Abstract

Objective: Identify the prostate cancer detection rate in patients in whom underwent a saturation prostate biopsy as a rebiopsy from January 2005 to February 2015 at San Ignacio Hospital. **Materials and methods:** In San Ignacio hospital were performed from January 2005 to February 2015, 114 saturation biopsies. The investigators made a univariate analysis of the variables. The association between the variable was evaluated based on the T-test and Wilcoxon test. $P < 0.05$ was considered statistically significant. Finally, a regression model was performed to predict significant variables for prostate cancer. **Results:** The cancer detection rate using saturation prostate biopsy was 16.7% of which 84% were categorized as significant. A mean of 19 cores were obtained. There were statistically significant differences between patients with prostate cancer and healthy patients in the number of previous biopsies, number of samples, prostate volume and PSA density. **Conclusion:** Saturation prostate biopsy in our study has a prostate cancer detection rate of 16.7% and 84% of them were significant in this cohort of patients.

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Key words: biopsy, diagnosis, prostate, prostatic neoplasms.

Título: Diez años de experiencia en la realización de biopsias por saturación

Resumen

Objetivo: Identificar la tasa de detección de cáncer de próstata en pacientes en quienes se realizaron biopsias por saturación en el Hospital Universitario San Ignacio desde enero del 2005 hasta febrero del 2015. **Métodos:** En el Hospital Universitario San Ignacio se han realizado 114 biopsias por saturación. Para este estudio se llevó a cabo un análisis univariado de las variables a estudio. Se obtuvo la asociación por medio del T-test y del test de Wilcoxon con una significancia de 0,05. Por último, se corrió un modelo de regresión para predecir un resultado positivo para cáncer de próstata. **Resultados**: La tasa de detección de cáncer de próstata fue del 16,7%, y de estos el 84% fueron categorizados como significativos. En promedio, se obtuvieron 19 muestras de tejido. El número de biopsias previas, el número de muestras, el volumen de la próstata y la densidad del PSA presentaron valores estadísticamente significativos. **Conclusiones**: La biopsia por saturación en Colombia presenta una tasa de detección de cáncer de próstata del 16,7%, de las cuales el 84% fueron significativas.

Palabras clave: biopsia, diagnóstico, próstata, tumores prostáticos.

Introduction

Prostate cancer, excluding non-melanoma skin cancer, is the most common cancer among men in the United States [1], and in Colombia it is also the most common cancer, and constitutes the second leading cause of mortality in men, according to the Ministry of Health of Colombia [2].

A positive prostate biopsy it´s required for diagnosing prostate cancer, allowing to stage and define treatment. An accurate biopsy scheme should be select, taking into account patient characteristics and medical history; in order to decrease the number of false negatives.

In the sextant method described by Hodge et al. in 1989, the investigators took cores of the apex, base and middle of the prostate, with a prostate cancer detection rate between 20% and 35% approximately [3]. Because of its low detection rate, an extended biopsy was proposed, which consists in obtaining 5 to 7 cores in each side [4]. Different authors have considered that increasing the number of cores, increases the detection rate; so that above 6 cores, the detection of positive cores increased in 5-30% [5-7]. In the extended biopsy scheme, 10 to 12 cores are taken; above this number of cores the concept of saturation biopsy is made, in which it is desired to acquire a greater amount of tissue for histopathological analysis, obtaining around 20 samples [8].

Saturation biopsy is considered as a diagnostic tool in prostate cancer; the 2013 guidelines of the health ministry of Colombia recommend the performance of a saturation biopsy in men

with persistently elevated PSA levels and multiple previous negative prostate biopsies [9].

It is important to know the impact that this diagnostic test has in our population, so we can define the utility and the target population. Knowing the detection rate for saturation prostate biopsy in Colombian men, allow us to compare our results with those reported in the literature.

Methods

Type of study: Analytical cross-sectional study.

Study Population: Male who underwent saturation prostate biopsy at the San Ignacio Hospital, from January 2005 to February 2015. Inclusion criteria: patients that were in the INTRANET database and in whom saturation biopsy was performed by the Urology Department. Exclusion criteria: biopsies with less than 16 cores and patients who had already a diagnosis of prostate cancer.

Data collection: Was performed by searching medical records in the electronic database (INTRANET), of the San Ignacio hospital from January 2005 to February 2015, containing as a keyword prostate and biopsy (Performed by the unit of Urology). From this research the investigators obtained 177 medical records, and after applying inclusion and exclusion criteria, 114 medical records were classified for data collection. The principal investigator was in charge of reviewing each of the medical records, and collected the following data: age, saturation biopsy indication, initial PSA, number of previous biopsies, histology of previous biopsies, number of cores obtained in the saturation biopsy, prostate volume, and the histologic result of the saturation biopsies.

Statistical analysis: The investigators made a univariate analysis of the variables. Mean was obtained for the quantitative variables, with their respective standard deviation or range. Frequencies and proportions were obtained for the qualitative variables. The association between the variable were evaluated based on the T-test and Wilcoxon test. $P < 0.05$ was considered statistically significant. Finally, a regression model was made to predict prostate cancer.

Ethical considerations: The study was approved by the Ethics Committee of the Pontificia Universidad Javeriana and complied with the provisions of the Best Clinical Practice Guidelines, the Declaration of Helsinki, and local regulations. Following the guidelines of the resolution 8430 of 1993 of the Colombian Health Ministry, the following research protocol is classified as a safe

investigation under Article 11. Therefore, and in compliance with the first paragraph of Article 16 of the same resolution, it is not required a written informed consent because of the low risk of the investigation.

Funding source: San Ignacio Hospital.

Conflicts of interest: The authors declare that they have no conflict of interest.

Results

We analyzed 114 clinical records, the average age was 61.7 years (SD = 7.1), with a minimum age of 44 and a maximum of 84 years. 55.8% of the patients had an initial PSA greater than 10 mg/dl and 83.5% had two previous biopsies. The principal indications for biopsy were a persistent elevated PSA greater than 4 ng/ml (92%), followed by atypia and multifocal high grade prostatic intraepithelial neoplasia on previous biopsy with a 4.9% and finally a 3% for histology on previous biopsy (atypia and multifocal high grade prostatic intraepithelial neoplasia) and persistent elevated PSA. The mean for cores taken were 19 (SD = 2.75).

The cancer detection rate using saturation prostate biopsy was 16.7% of which 84% were categorized as significant, where the predominant variable for categorization was the PSA density greater than 0.15 ng/ml in 13 patients, followed by the number of positive cores ≥ 3 (10 patients). Of the patients with adenocarcinoma Gleason score was 6 in 61.1%, 7 in 27.7%, and 8 in 11.1%. Age and initial PSA, didn't have an association with cancer. The number of previous biopsies, number of cores, the prostate volume and the PSA density had a statistically significant association ($p<0.05$) with prostate cancer (Table 1). In those with adenocarcinoma, the prostate volume was lower (40.78 vs. 50.25) and less cores (18.42 vs. 19.69) were taken.

Table 1. Data

	Cancer		Normal		p-value
	Mean	SD	Mean	SD	
Age	63.52	6.94	61.44	6.94	0.125*
Initial PSA	16.44	12.90	12.70	12.89	0.150*
Number of previous biopsies	2.28	1.13	1.71	1.06	0.022+
Number of cores	18.42	2.69	19.69	2.72	0.032+
Prostate Volume	40.78	15.16	50.25	18.42	0.049+
PSA Density	0.40	0.44	0.19	0.24	0.036+

* T-test; + = Wilcoxon test.

The PSA density was used to develop a ROC curve (Figure 1), and the area under the curve was 0.63 [95% CI (0.47 to 0.80)]. A logistic regression model was developed using the continuous variables which had a $p<0.05$ to predict prostate cancer. The investigators found that in this model none of the variables were sufficient as a single predictor for prostate cancer.

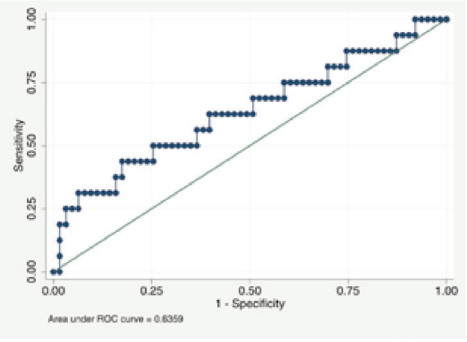

Figure 1. ROC Curve PSA density for Prostate Cancer

Discussion

According to the Centers for Disease Control and Prevention (CDC) in 2010 the most common cancer in the United States among men was prostate cancer (PC) with 126.1 cases per 100,000 population [10]. In Colombia there are few sources of information about the epidemiology of the disease, however according to the National Cancer Institute [2] in 2006 about 7,957 new cases of PC were estimated for each year, which represents an age-adjusted incidence rate of 47.8 cases per 100,000 men, and leading cause of mortality in 2,379 cases in 2011.

Saturation Biopsy is one of the current diagnostic tools for PC. International guidelines currently recommend performing saturation biopsy in patients with persistently elevated PSA levels, multiple previous negative prostate biopsies, atypical small acinar proliferation of prostate and multifocal high grade prostatic intraepithelial neoplasia, patients in active survey and candidates to focal therapy [8,9,11-14]. It is estimated that around a 25% of patients with prostate cancer are identified after a negative biopsy [15].

There are controversial issues in performing saturation biopsy such as: the number of cores required and it´s relationship between the cancer detection rate and prostate volume [8]. Our study found that patients with prostate cancer had a lower volume (40.78 ml) and required fewer number of cores (18.42), while patients in whom no cancer was detected, the prostate volume was higher (50.25 cm^3) and higher number of cores were taken (19.69); both differences were statistically significant. However, the study couldn't find out a cutoff to define how many samples are required for prostate cancer detection in relationship with the prostate volume; more studies are required for this type of analysis.

Stewart et al. [16] and Scattoni et al. [7] reported prostate cancer detection rates between 30-34%. In our study the detection rate was 16.7%. This differences are explained by the fact that the populations were different. In the two studies cited above the saturation biopsy was performed in patients who had an initial sextant prostate biopsy, and in our population they had an initial biopsy with an average of 12 cores. By increasing the number of cores, the initial detection rate increased; so that above 6 cores, the detection rate for PC increased in 5-30% [5-7].

Another scenario for saturation biopsy is the detection of significant prostate cancer, defined as the one who has an effect on patient mortality and the capacity to develop metastatic disease. Epstein et al [17] in 1994 defined insignificant cancer and these standards still apply, such as: PSA density <0.15 ng/ml, biopsy Gleason ≤6, the presence of cancer in less than 3 samples and the presence of ≤50% commitment of sample. Zaytoun et al. [18], showed a detection rate of significant prostate cancer of 33.3% with saturation biopsy. In our study, the detection rate for significant cancer was 84%. The predominant variable in patients with significant prostate cancer was PSA density, which correlates with the data obtained in Table 1. However, as a diagnostic tool is not useful because of its low area under the curve obtained in the ROC curve.

Nonetheless, prostate biopsy guided by ultrasound has limitations as false negatives, risk of and incorrect stratification, detection of insignificant prostate cancer and the need of multiple biopsies [19].

Today there are new techniques to offer to these patients, such as the MRI guided biopsy. Its detection rate is between 39-59% [20-23], with high detection rate in significant cancer [20]. However, MRI-guided biopsy could not be implemented in daily use by the urologist, due to lack of studies [19].

Saturation biopsy is a diagnostic study sustained by international and national guidelines in the study of prostate cancer. Our study showed a high detection rate in significant prostate cancer, and found that variables such as number of previous biopsies, number of cores, prostate volume and density of PSA are associated with prostate cancer detection. A greater number of studies are required in saturation biopsy to define their diagnostic utility.

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