Clinical value of the digital rectal examination and prostate-specific antigen in the opportune detection of prostate cancer in Hermosillo, Sonora

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KEYWORDS
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Abstract
Background: Opportune detection is essential for the prevention of metastatic prostate cancer (CaP). The use of prostate-specific antigen (PSA) and the digital rectal examination (DRE) has been the best alternative for CaP detection up to the present day. Unlike PSA, DRE sensitivity and specificity are strongly influenced by the level of training and experience of medical teams.

Methods: A descriptive, observational, cross-sectional study was conducted on male patients above the age of 50 years with no previous CaP diagnosis that were seen at the Jurisdicción Sanitaria Número I in Hermosillo, Sonora. All the patients had PSA determination and underwent DRE. Prostate biopsy was done on the cases suspected of CaP (PSA > 4 ng/mL and/or suspicious DRE). PSA and DRE sensitivity and specificity were evaluated and statistical significance was estimated through the chi-square test and the Pearson correlation.

Results: A total of 627 patients were included in the study and 73 of them were referred for prostate biopsy. DRE sensitivity and specificity were 64.8% and 2.7%, respectively. They were significantly lower (p ≤ 0.05) than the sensitivity and specificity of PSA, which were 92.3% and 98.3%, respectively.

Conclusions: The frequency of CaP in the population studied was similar to that found in studies carried out in other Mexican States (5.9%). In addition, the PSA results correlated with the prevalence of CaP histopathologic diagnosis. No correlation was observed between DRE and CaP diagnosis, suggesting the need to identify strategies for improving the training of medical teams that participate in the clinical evaluation of patients. PSA continues to be a highly useful diagnostic tool for CaP.
Introduction

In Mexico, prostate cancer (CaP) is the first cause of death by neoplastic disease in the male population according to a 2011 report by the National Statistics and Geography Institute (INEGI), and frequently responds to treatment even when it is generalized. 1,2 Approximately 70% of the cases are diagnosed in men above the age of 65 years, and of those cases, close to 90% are discovered in the local and/or regional stage. Survival at 5 years is close to 100% and overall survival calculated at 10 and 15 years is 92% and 61%, respectively. This improvement in survival is mainly attributed to earlier diagnosis and to some treatment advances. 3

Digital rectal examination (DRE) alone has not displayed an increase in the detection rate of early-stage CaP, 4 whereas prostate-specific antigen (PSA), as a tumor marker, has shown great usefulness at this level. Now that current studies report a tendency toward diagnosis in initial stages of the disease, to do so sooner.12 Detection is fundamental for preventing extraprostatic extension and metastatic dissemination of CaP because it facilitates the timely identification of localized tumors. Nevertheless, 12-core biopsy has been established as the minimum for achieving better detection. 9,10 Biopsy of the transitional zone, where benign hyperplastic pathology primarily presents, is suggested for patients with negative biopsies and suspected carcinoma. 11

Opportune detection is fundamental for preventing extraprostatic extension and metastatic dissemination of CaP because it facilitates the timely identification of localized tumors. 9,12 Knowing that early stage CaP is asymptomatic and that it is precisely this stage in which curative therapy can be applied, has given rise to the creation of detection regimens for early disease diagnosis. Although this is still controversial, the American Urological Association has suggested that men over 50 years of age have a yearly check-up, and in cases in which there is a family history of the disease, to do so sooner. 12 Detection is carried out through a DRE and total serum PSA determination. If one or both tests are suspicious, transrectal ultrasound (TRUS)-guided biopsy should be performed along with the histopathologic study of the samples.

Currently there are very few reports on CaP in the Mexican population and so only estimates have been made by the Sociedad Mexicana de Urología, which recognizes that the existing statistics are not fully available due to underreporting. The same holds true for the State of Sonora, and so it is important that new analyses be carried out. At the same time, it is also important to study the usefulness of PSA and DRE as massive detection means in our particular population and so only estimates have been made by the Sociedad Mexicana de Urología, which recognizes that the existing statistics are not fully available due to underreporting. The same holds true for the State of Sonora, and so it is important that new analyses be carried out. At the same time, it is also important to study the usefulness of PSA and DRE as massive detection means in our particular population and so only estimates have been made by the Sociedad Mexicana de Urología, which recognizes that the existing statistics are not fully available due to underreporting. The same holds true for the State of Sonora, and so it is important that new analyses be carried out. At the same time, it is also important to study the usefulness of PSA and DRE as massive detection means in our particular...
The aim of the present study was to evaluate whether PSA and DRE are effective tools in the massive detection of CaP in the population residing in Hermosillo.

The clinical value of DRE and PSA in diagnosing CaP was determined in 5 Primary Care Health Centers belonging to the Jurisdicción Sanitaria Número I in Hermosillo, Sonora, in the months of May and June 2010, for the purpose of estimating the usefulness of these 2 diagnostic tools in the opportune detection of CaP in our population. The results will aid in the development of strategies for improving new campaigns for opportune CaP detection.

Methods

Methodological design
A descriptive, cross-sectional, and observational study was conducted during the months of May and June 2010 within the framework of the campaign “Opportune Prostate Cancer Detection” carried out by the Health Department at the Jurisdicción Número I in the city of Hermosillo, Sonora.

Subject selection
Men older than 40 years of age that received medical attention at one of the 5 Primary Care Health Centers of the Jurisdicción Número 1 in Hermosillo, Sonora, Mexico, that had no previous CaP diagnosis, and that signed statements of informed consent in relation to their participation were included in the study. Patients under 40 years of age, those that lived outside of the study area, those that had a previous diagnosis of CaP, and/or patients that did not accept to participate, were not included in the study.

Data collection and blood sample obtainment
During the first medical consultation, the general data of all the patients were registered, as well as the clinical manifestations, through a Prostate Symptom Evaluation (PSE) questionnaire. In the same consultation, venous blood was drawn, using a vacuum tube extraction system with no anticoagulant. The samples were immediately sent to the Clinical Laboratory of the Hospital General del Estado for total PSA determination and quantification through electrochemoluminescence with the Elecsys 2010 Total PSA assay kit for in vitro quantitative detection in serum samples.

Digital examination of the prostate
The prostate was examined through a DRE, performed by the urologist to search for clinical signs of CaP. 2, 12

Prostate biopsy
TRUS-guided biopsy of the prostate was indicated for the patients that had a PSA value above 4 ng/mL and/or a CaP-suspicious DRE. This procedure was performed by radiologists from the Radiology Department of the Hospital General del Estado. The samples were labeled and placed in formaldehyde and then sent to the hospital’s Pathology Department to be processed. Diagnosis was confirmed through the histopathologic result of the biopsy. Twelve samples per region were taken under local anesthesia or intravenous sedation, as each case merited. The corresponding report was put in the clinical case record and given to each patient.

Data analysis
The data provided by the patient and the results of each test were analyzed through the chi-square test to determine the dependence of CaP on PSA and DRE, and the Pearson correlation analysis was employed to estimate the associations between the quantitative and qualitative variables (irritative or obstructive symptomatology).

Results

Population distribution
The study included a population of 627 patients and the majority of them were between the ages of 50 and 59 years. A total of 63% of the patients showed some type of urologic symptomatology that made them seek out medical attention (table 1). The remaining percentage of patients participated merely as a form of prevention. These results are similar to those reported in previous studies conducted on rural populations in New Zealand in which obstructive or emptying symptomatology were the most important and frequent clinical parameters in the diagnosis of advanced prostate tumors. 13

In relation to PSA distribution in the study population, 79% had PSA values below 2.4 ng/mL and required only watchful waiting when the DRE was not suspicious. A total of 7.6% of the patients had a PSA value between 2.5 and 4 ng/mL; a current consensus 14 as to the ideal management for this
group of patients exists, but not without urologic uncertainty. A PSA level between 4 and 10 ng/mL presented in 10% of the total study population; in this group of patients, biopsy was decided upon when the DRE was suggestive of CaP. A total of 2.7% of the study population presented with a PSA above 10 ng/mL and a prostate biopsy was performed with or without a suspicious DRE. In the present study, of the patients referred for biopsy due to a suspicious DRE (73 patients), 64.9% had a positive biopsy. This percentage is lower than that observed in the total population, which is probably due to bias from the fact that the patients with a histopathologic diagnosis of CaP had a significantly smaller prostate size than that of the total study population (data not shown); in other words, DRE is more useful when there is greater tumor growth. On the other hand, the remaining 35% of the patients than had an unsuspicious DRE with a positive CaP biopsy were in the group of patients for whom DRE was not useful; it is likely that the clinical value of this tool can be increased to the degree in which the training of the medical groups in our locality improves. The statistical analysis showed that DRE was associated with CaP diagnosis and that the sensitivity and specificity of the method were comparable with the reports of other studies (64.9% and 97.2 %, respectively). In conclusion, DRE was more useful in the general population, but its value was reduced when only patients with a histopathologic diagnosis of CaP were evaluated. Even so, its systematic use appears to be of great benefit in the population studied.

DRE evaluation

Different authors suggest that close to 30% of patients with first-stage prostate tumors had apparently normal DREs and therefore the clinical usefulness of this diagnostic tool depends as much on the experience of the examiner as it does on the intrinsic difficulty of detecting small nodules. Other authors have been able to demonstrate the positive predictive value of this examination, which varies in the different studies between 1.5% and 39%. The American Urological Association (AUA) recommends the DRE as a yearly routine examination method in men above the age of 40 years.

Figure 1A shows the percentages found in the survey total (n=627). Twenty-seven cases, representing 72.9% of the patients that were referred for biopsy due to a suspicious DRE -for an increase in consistency in one or both of the prostatic lobes- were positive for CaP (much higher than that reported); on the other hand, 544 cases (92%) with a normal DRE did not present with cancer (benign pathology), demonstrating the great usefulness of DRE in the population studied.

The debate in relation to the value of DRE continues in the era in which PSA has a widely validated use. This is partially due to the fact that DRE has been seen independently from the PSA value, and so the PSA test continues to be the cornerstone for opportune CaP detection. In the present study, of the patients referred for biopsy due to a suspicious DRE (73 patients), 64.9% had a positive biopsy. This percentage is lower than that observed in the total population, which is probably due to bias from the fact that the patients with a histopathologic diagnosis of CaP had a significantly smaller prostate size than that of the total study population (data not shown); in other words, DRE is more useful when there is greater tumor growth. On the other hand, the remaining 35% of the patients than had an unsuspicious DRE with a positive CaP biopsy were in the group of patients for whom DRE was not useful; it is likely that the clinical value of this tool can be increased to the degree in which the training of the medical groups in our locality improves. The statistical analysis showed that DRE was associated with CaP diagnosis and that the sensitivity and specificity of the method were comparable with the reports of other studies (64.9% and 97.2 %, respectively). In conclusion, DRE was more useful in the general population, but its value was reduced when only patients with a histopathologic diagnosis of CaP were evaluated. Even so, its systematic use appears to be of great benefit in the population studied.

PSA evaluation

PSA was approved by the U.S. Food and Drug Administration (FDA) in 1994 as a marker for detecting CaP when its effectiveness together with DRE was demonstrated. The probability of CaP detection in men with a PSA value < 4 ng/mL and a suspicious DRE has been estimated at 20%; it is 30% in men with a normal DRE and PSA between 4 and 10 ng/mL, and 50% when the PSA value is > 10 ng/mL. Although the use of total PSA for early CaP diagnosis is still a matter of debate, more and more studies suggest that this method should be used as a routine examination for CaP.
prevention in all men above the age of 40 years. Values above 10 ng/mL are the most precise indicators of CaP, which is why it was used as the cut-off point in the present study. Figure 2A shows the results of total PSA. Ten of the patients of the general population that were referred for prostate biopsy had a histopathologic CaP diagnosis, indicating that 27.1% had a PSA value above the cut-off point.

In regard to PSA values of the patients that were referred for biopsy after evaluation of the marker, we observed that 92.3% (n=59) of the patients that had an abnormal PSA value also had a positive biopsy, confirming CaP. In contrast, 98.3% (n=59) of the patients with a normal PSA value presented with benign prostatic hyperplasia that was corroborated by biopsy (fig. 2B). These results suggest to us the merit of PSA as a marker of CaP progression and its outcome, as well as its great usefulness for reducing the need for repeat or confirmation biopsies.

At the same time, in our study, PSA was useful for discriminating between the patients with cancer and hyperplasia. Finally, it demonstrated the statistically significant (p=0.05) direct relation between PSA and CaP diagnosis, as well as a sensitivity of 92.3% and a specificity of 98.3% for the test. These results show the usefulness of measuring total PSA in patients at risk for CaP.

**PSA and DRE usefulness in our population and its relation to other studies**

PSA is an essential study in the evaluation of the prostate, but it is not sufficient on its own for establishing the prostatic differential diagnosis; it has been said that it is not a substitute for DRE because that examination evaluates prostate consistency, providing clinical information that no other laboratory test or imaging study can provide. Nevertheless, the clinical skill needed to perform the DRE has an undeniable impact on the final result, and depending on the circumstances, could modify the diagnostic possibilities. In our study, we established that both DRE and PSA were of great use in the evaluation. There have been other similar reports in Mexico; a study conducted in Monterrey, Nuevo León, differed only slightly, reporting a sensitivity of 93% for PSA and a specificity of 82% for DRE. In another study carried out at the Hospital de Alta Especialidad del Bajío, they reported the usefulness of PSA as a progression marker. In addition, in the present study conducted in Hermosillo, Sonora, the predictive usefulness of DRE and PSA for CaP detection was evaluated in a population of 627 patients (table 2). The results showed no significant difference in the percentage of patients referred for biopsy whose CaP diagnosis was finally confirmed (86.4%), compared with the 86.1% of patients whose diagnosis was benign prostatic hyperplasia. It should be pointed out, however, that such a high percentage of patients with prostatic growth shows the need to implement efficient detection programs that would reduce the potentially negative impact on the quality of life of adult men in Sonora. On the other hand, in the patients with a PSA value above 10 ng/mL, as shown in table 3, tenesmus was the only symptom in which there was a statistically significant correlation.

Early detection programs for the population are becoming an attractive alternative for dealing with the problem of the high prevalence of CaP in contemporary populations, from the perspective of the public health services of different countries, especially since the appearance and availability of serum PSA determination in the biochemical laboratories. Nevertheless, the results have not been as encouraging as imagined, and different institutions have made evaluation reports on this and other alternatives aimed at reducing the incidence and mortality rates of CaP and improving patient results. In this sense, our study showed that 40% of the CaP detected in patients in Sonora was limited to the prostate, resulting in a good number of patients receiving radical treatment. Being aware of the usefulness of PSA and DRE is definitely instrumental in

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**Figure 2** Representation of the total PSA behavior. A) In the total population (n= 627), B) In the population referred for biopsy. The behavior is presented in the form of percentages and separately, according to the prostate biopsy result, reporting a sensitivity of 92.3% and a specificity of 98.3% with a p=0.05.
realizing the need for providing more resources for large-scale detection programs. And the knowledge that many of these patients will be candidates for curative management makes it obvious that the cost/benefit of such programs is positive.

Likewise, the results show that PSA usefulness is definitely good, in other words, despite the fact that on its own it does not guarantee CaP detection, its use over the past years has increased, because when it is used together with DRE its clinical value increases. Finally, the histopathologic diagnosis for 60% of the patients that had PSA levels above 10 ng/mL was CaP that was not limited to the prostate, showing that the PSA test can provide better detection for this subgroup of patients.

Histologic studies of size, extension, and pathologic differentiation suggest that only one third of these tumors detected through PSA determination shows signs of clinically important aggressiveness, even though it cannot be predicted which of these cases will progress. Over-detection and/or under-detection would be produced in the rest of the cases. Intuitively, it could be expected that through early detection, more cancers would be found before extending outside the prostate gland, leading to more cures through aggressive treatments.

In fact, the majority of detected tumors are localized and not extended. The general dilemma in relation to cancers that are discovered through detection programs involves those that are found in the early stages: they might not need intervention due to their slow progression and very low mortality rate, even though they are curable, whereas the advanced cases that need treatment often are incurable. To evaluate the effectiveness of early treatment, the majority of authors underline the high level of existing uncertainty, given that no controlled and randomized studies are available or any other type of study with a design that guarantees detection 100%. And currently there is no unanimous agreement as to making an early CaP diagnosis in asymptomatic individuals.

Conclusions

DRE continues to be an important detection examination for making CaP diagnosis. Even though PSA has a margin of error, when its figures surpass 10 ng/mL, there is a great possibility that the patient presents with CaP. Although the sample has not been randomized, it is important to point out the high frequency of CaP (5.9%) shown by the opportune detection campaign at the Jurisdicción Sanitaria I in Hermosillo, Sonora. This frequency is at the upper limit of the reported national mean value (5.2% to 5.9%). PSA was abnormal in 92% and DRE was abnormal in 64%, which clearly shows that when PSA and DRE are analyzed separately, especially in those patients referred for biopsy, PSA produced better results. And rigorously discriminating between the two, at least in this study, PSA was more capable of detecting cases and was stronger, when the patients with prostate biopsy were analyzed. No correlation was observed between DRE and CaP diagnosis, which suggests the need for identifying strategies to improve the training of the medical teams that participate in patient clinical evaluation.

The current consensus is that detection continues to have its limitations. Nevertheless, both PSA and DRE continue to be useful as diagnostic tools despite their limitations. In favor of those that support opportune detection, up to 40% of localized tumors are able to be diagnosed; and in favor of
the detractors of opportune detection, more studies are needed to determine whether PSA and DRE, on their own, will be effective, if they continue to be the only tools for opportune CaP diagnosis.  

Conflict of interest

The authors state that there is no conflict of interest.

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