Variability of the urological clinical practice in prostate cancer in Spain

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Abstract
Objectives: To study the opinion of the Spanish urologists regarding the main points in the diagnosis, prevention, quality of life and treatment of prostate cancer.

Material and methods: An anonymous questionnaire was administered to 290 specialists who represented the urological professional group involved in the management of prostate cancer in Spain. The following were considered in their definition: grade of professional experience, work setting, contractual relation with patient and academic character of the center. The statistical analysis was based on the study of relative frequencies for qualitative variables. The results were interpreted in 2009–2010 and the final report of them was done in 2011.

Results: Response rate collected and correctly transcribed from the forms was 96.9% (n = 281). This accounts for 10–15% of the national group. Median age was 47.7 (29–69) years and 92% were men. Mean years of professional experience were 19.1 (1–43). Responses collected regarding 153 questions were analyzed. These dealt with: (a) how the diagnosis of the disease was carried out in the setting of the surveyed; (b) the opinions given on the disease prevention; (c) treatment of the localized treatment; (d) treatment of the advanced disease; and (e) the definition of the fields of interest for the professional.

Conclusion: This survey showed important variability in some points of clinical practice in regard to the recommendations of the experts. It also shows the principal concerns of the professional, defines opportunities for training improvements and detects needs in the national urological group.

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Introduction

Prostate cancer is the most common solid tumor, responsible for 11% of all cancer deaths, but only 20% of the men who have it die from it. Its clinical approach has been modified in recent years by continuous relevant advances that include aspects related to the prevention and detection of the disease, minimizing the impact on quality of life of the patient due to the disease and its treatment, and the increasingly complex decision-making among the numerous treatment options available. This continuous development generates a growing uncertainty in many aspects. In addition, the urologist finds it increasingly complex to maintain a level of knowledge and skills updated as the disease evolves and new treatment options are introduced.

Like it or not, the actual approach of prostate cancer in Spain is currently undergoing a major variability of professional standards and not well evaluated clinical practice, whose existence deserves special consideration and deep corporate reflection of the urological association. The aim of exploring the profile of professional skills and clinical habits in managing prostate cancer in urological practice, and identifying possible opportunities for improvement in this area (disclosure, education, training, provision of equipment, optimization of the doctor-patient relationship), a survey posed to a representative portion of the urological association of our country, which addresses the most controversial aspects of the disease and some of the practices most subject to variability in the approach of the disease, has been conducted.

Materials and method

In 2009, we conducted a prospective observational, descriptive and transversal study, through an autofilled survey by a group of Spanish urologists practicing regularly involved in the diagnosis and treatment of prostate cancer in its healthcare environment. The questionnaire posed 137 elements or direct questions. In order to ensure the relevance of the questions and the objectivity of the responses, the questionnaire was submitted to consideration by a group of specialists in the field, several of them signatories of this manuscript, which defined the definitive questions and the keys of the final questionnaire. The specialists involved in conducting the surveys did so voluntarily and anonymously. All the questions were conducted trying for the answers to be dichotomous, what happened in 85 questions (62% of the questionnaire). Only 3 questions (2.2%) had more than 4 possible answers, where possible reducing the dispersion in the analysis of answers. The answers were structured in 14 specific thematic sections, at the end of which an inquiry was made as to the degree of interest that the professional would have to delve into that topic, obtaining a comparative panel that distinguishes the relative interest depending on the ranges of response and the confidence intervals of the same. Thus, relative differences are established between some topics that may be interpreted as of more or less interest.

The 290 specialists surveyed represent the urological professional association involved in the clinical approach of prostate cancer in Spain. In its definition, the degree of professional experience, scope of work, the contractual relationship with the patient, and the academic nature of...
the center were taken into account. The response rate collected and correctly transcribed of the forms was 96.9% (n = 281). This sample allows for the main estimates of the study with sufficient accuracy, assuming a maximum error of ±5.8% for a 95% confidence interval (95% CI) and supposing the most unfavorable distribution of responses to dichotomous survey variables (p = q = 0.5).

**Results**

The mean age of the participants was 46.9 ± 9.6 years (median: 47; range: 29–69), and in the distribution by homogeneous age groups, 258 (91.8%) were men and 23 (8.2%) women. The age of women was lower (39 years; range: 29–69) than that of men (48 years; range: 29–69). The mean practice time was 19.1 ± 9.5 years (range: 1–43). Depending on the type of medical practice, 127 (45.3%) worked in a first-level healthcare environment, and 154 (54.7%) in specialized centers. Regarding the type of practice, 115 (40.9%) worked in public healthcare, 10 (3.6%) in private healthcare, and 156 (55.5%) in a mixed environment. Not all the respondents answered all the questions, extrapolating the results for each specific question to theoretical 100%.

**Disease diagnosis**

This section addressed epidemiological aspects, the relevance of population screening, the use of PSA and other markers, the use of various imaging studies, and the indication and ways to perform a prostate biopsy. 64.4% of the respondents believe that the data on incidence and mortality of prostate cancer in our environment should be interpreted as reliable, and a ratio as high as 97.9% assume that it is possible to improve the currently available record. On the other hand, 64.2% know the existence of some records of prostate cancer in the autonomous community in which they work.

With regard to population screening programs, 49.6% of the professionals believe necessary to carry out a systematic screening for prostate cancer, and even 23.2% carry it out actively. In fact, 65.5% assume that the routine PSA performance can reduce mortality from the disease. However, 71.1% agree not to practice PSA routinely in the elderly. Interestingly, only 63% report their patients adequately of the risks and benefits involved in getting a PSA. On the other hand, the routine use of PSA ranges (85.4%, 95% CI: 81.2–89.3) and the free PSA fraction (89%, 95% CI: 84.9–93.1) has definitely shifted in the routine care of our country to the PSA density (48.4%; 95% CI: 41.6–55.2) as an element of consideration before the indication of prostate biopsy (p < 0.001). With regard to the new imaging modalities, 34.9% use FDG-PET, 19.5% choline PET in their work environment, and 75.4% use MRI. Only 12.8% know the multiparametric study of the prostate by means of endorectal MRI. 25.1% routinely use duplex ultrasound. Only 14.6% of the respondents use bone resorption markers. 38.5% (95% CI: 32.8–44.6) believe that the most promising marker is PC3A versus 14.4% (95% CI: 10.6–19.2) who consider the GDPH methylation study (p < 0.05) for this role.

With regard to the technique of biopsy performance, before an initial biopsy, 32.2% usually conduct a sextant biopsy (6 cylinders), 26.3% also include the transitional zone (8 cylinders), and 41.5% practice extended biopsy (with 10–12 cylinders, depending on whether a sample of the transitional zone is taken or not, or more). But, when it comes to a repeat biopsy, the rate of urologists performing sextant biopsy falls to 7%, that of sextants with transitional zone to 19.6%, and that of extended biopsy rises to 73.4% (Fig. 1). 39.7% use local anesthetic infiltration, and 20.5% take into account the patient’s age and the prostate volume to decide the number of cylinders obtained.

**Disease prevention**

29.5% of the respondents believe that it is possible to carry out drug prevention strategies for prostate cancer, and 21.7% believe that the dutasteride is the appropriate drug for these chemoprophylaxis strategies. 32% believe it is possible to carry out prevention strategies for prostate cancer based on nutritional care. The main candidates are presented and recommended in a non-exclusive manner (Fig. 2).

**Treatment of the localized disease**

With respect to the main therapeutic decision of the localized disease, the professionals take into account the patient’s age (97.1%), the overall comorbidity (92.1%), and the patient's age (97.1%), the overall comorbidity (92.1%), and...
the urologists surveyed believe in the benefits of robot-assisted laparoscopic radical prostatectomy (RALRP), only 1.4% practice it. As for the concept of cost-benefit, 33% (95% CI: 27.7–38.7) and 92.1% (95% CI: 88.35–94.74) of the respondents consider that LRP and RALRP, respectively, are expensive in terms of the alternative of open surgery \((p < 0.0001)\). 10 and 38.27%, respectively, consider that LRP and RALRP should be financed in our health system by the patient holistically.

With regard to the effects of the treatment, 85% of the specialists define themselves as concerned about the sexual sphere of the patient with prostate cancer. In this sense, 88.9% take into account the patient’s opinion about their sex life when deciding about treatment of the localized disease. Even in the treatment of disseminated disease, 49.7% consider the patient’s opinion in this regard to the point of delaying the indication of hormone treatment if necessary. 68.6% of the respondents practice prostatectomy with erector preservation, and 98.6% of the professionals are involved in the search for the treatment that solves the effect (56.3% actively, and 43.7% only if the patient demands it). 84.9% are concerned about the continence of the patient with prostate cancer, so much so that when this effect occurs, 99.3% participate in the search of the treatment (82.4% actively, and 17.6% only if the patient demands it). 74.3% always recommend pelvic floor exercises, 78.4% consider placing sphincter prosthesis and 63.9% male sling

68.2% of the respondents believe that it is easy to define biochemical recurrence, both for patients operated and for those treated with radiotherapy, and 75% believe that this situation must be treated actively and early. The treatment decisions collected vary depending on whether it is a failed surgery (radiotherapy 36.8%, hormone therapy 20.7%, combination of both 42.5%) or failed radiotherapy (hormone therapy 96%, salvage surgery 2.5%, and salvage cryotherapy 5.4%). No respondents chose expectant management, or for patients operated or radiated.

**Treatment of the advanced disease**

With regard to hormonal blockade, 69.7% (95% CI: 62.1–74.8) prefer maximum androgen blockade (MAB) versus 30.3% (95% CI: 26.1–34.5) supporter of simple androgen blockade with LHRH analogue alone \((p < 0.001)\). As for the best time for the onset of hormone therapy in disseminated disease, 89.5% consider appropriate to start it as early as possible, compared to 10.5% who think that it should be started in a delayed way when there are data of progression or pain. When prescribing a LHRH analogue, the respondents consider that LRP and RALRP, respectively, are expensive in terms of the alternative of open surgery \(p < 0.0001\). 10 and 38.27%, respectively, consider that LRP and RALRP should be financed in our health system by the patient holistically.
In the locally advanced disease, there are differences in the use of neoadjuvant hormone therapy according to the type of definitive treatment: 92.8% (95% CI: 89.5–96.1) systematically consider it before radiotherapy, compared with 35.3% (95% CI: 29.2–41.4) before surgery ($p < 0.001$). Even 21.3% (95% CI: 16.4–26.1) use neoadjuvant treatment in apparently localized tumors that will undergo surgery ($p < 0.05$). Regarding the use of adjuvant hormone therapy, 48.9% (95% CI: 43.4–54.4) consider it after surgery in the cases that prove to be locally advanced in the histopathologic specimen, and 83% (95% CI: 79.1–86.9%) after radiotherapy for high-risk cases ($p < 0.001$). There is great variability about what the appropriate duration of adjuvant hormone therapy is (Fig. 6).

In order to detect treatment failures, 82.9% perform regular testosterone controls in patients with hormone blockade, although 34.2% only do it before the PSA increase. 69.9% believe that it is easy to define the castration-resistant disease. In this circumstance, 45.7% (95% CI: 39.2–52) consider giving up the hormonal blockade, 78.8% (95% CI: 75.2–82.4) believe that docetaxel and prednisone are the best treatments, and 77.6% (95% CI: 72.4–82.8) use strategies of second-line hormone therapy, but only 34.4% refer having updated information on new drugs which act that way. In addition, 45.7% (95% CI: 39.9–51.6) use a bisphosphonate routinely in patients with refractory disease. These practices show that secondary hormone manipulation (removing or adding antiandrogen) and initiating docetaxel with prednisone are the most used attitudes to remove LHRH analogue or establish bisphosphonates ($p < 0.001$).

**Defining areas of interest to the professional**

The degree of relative interest is collected by the Likert scale for each of the main headings covered by the survey. The main usefulness of this representation is to group the points of different degree of interest according to the overlap of the confidence intervals of the same. This analysis may be seen graphically in Fig. 7, and relatively in Table 1, providing levels of interest from 1 (maximum interest) to 5 (minimum interest).

**Discussion**

The variability in clinical practice may be determined by lack of awareness of the official recommendations, or because the professionals involved in the analysis of the opinions and views do not agree with the theoretical lines supported and recommended in the documents used as reference. So, if there are any deviations in the different fields analyzed, their magnitude will be evaluated with the aim of defining improvement opportunities and analyzing the needs of the national urological association represented by the respondents.

The clinical practice guidelines are very sophisticated documents due to the exhaustive search of data in the literature and the systematization of the same to establish conclusions. The fundamental aspects on which clinical guidelines are currently based are the quality of the evidence and the strength of the recommendations. The *Guía de Práctica Clínica sobre Tratamiento de Cáncer de Próstata*, published in 2008 by the National Health System, the European Association of Urology Guidelines on Prostate Cancer [http://www.uroweb.org/professional-resources/](http://www.uroweb.org/professional-resources/).

**Table 1** Levels of relative interest for the different topics from 1 (maximum) to 5 (minimum).

<table>
<thead>
<tr>
<th>Topic</th>
<th>Levels of relative interest</th>
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<tbody>
<tr>
<td>1. Development of new therapies</td>
<td></td>
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<tr>
<td>3. Dilemmas in the treatment decision of localized cancer – current role of hormone blockade</td>
<td></td>
</tr>
<tr>
<td>5. Robotic radical prostatectomy – chemoprophylaxis strategies</td>
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</tbody>
</table>
Medians and confidence intervals of the degree of interest that the different topics arise in the respondents.

Figure 7

Prostate cancer epidemiology in Spain -
PSA-based screening -
News in molecular diagnosis -
News in imaging -
Technical optimization of the biopsy -
Strategies for chemoprophylaxis -
Sex life of patients with prostate cancer -
Continenence associated with treatment -
Dilemmas of treatment decision in localized cancer -
Laparoscopic radical prostatectomy -
Robotic radical prostatectomy -
Attitude to biochemical failure -
Current role of hormone blockade -
Development of new therapies -

Little interest
Enough interest
Much interest

Guidelines) updated in 2011,7-9 and the National Comprehensive Cancer Network Guidelines (http://www.nccn.org/professionals/physician_gls/f_guidelines.asp)10 are the main consensus documents in our clinical practice environment for this disease. It is not intended to compare opinions with recommendations, but to collect the variability detected among the majority opinions and what we accept as consensus, which reflects the view of the experts and the critical reflection of the current literature.

A national registry of prostate cancer that will be used to have own and current data on the prevalence, incidence, and mortality of prostate cancer in Spain is currently being carried out. This point is regarded as one of the topics of greatest relative interest to the respondents. The technical optimization of prostate biopsy is another key point in the diagnosis of the disease. The criteria used are adjusted to a rational pattern, which takes into account whether it is initial or repeat biopsy and, to a lesser extent, the prostate volume and age of the patient. There is little interest in those surveyed in developing new markers and imaging techniques. PCA3 could be useful to identify cancer in men with initially negative biopsies despite an elevated PSA.11 The detection of TMPRSS2-erg fusion genes or the study of abnormal methylation of promoters of various genes in the urine sediment obtained after a prostatic massage.12,13 The multiparametric study of the prostate by means of MRI with endorectal antenna is also under-considered.14 All these issues are of little interest to specialists in our environment.

The survey includes the areas on which the therapy decision is based in a patient with localized prostate cancer, taking into account a balance between the hypothetical benefit in results in favor of surgery and the different severity of the effects and risks, age and comorbidity, in favor of radiotherapy. We describe the expectant management practices for localized cancer in our environment, as well as the relative proportions for surgery, radiotherapy, brachytherapy, cryotherapy, HIFU, and even hormone blockade in these patients. The still low penetration of PRL, in 1:3 ratio compared to open surgery, is once more evidenced.15 Professionals appreciate the advantages thereof, and even more of the RALRP, although they are very aware of the economic implications that these approaches entail. Concern over issues related to the quality of life of the patients is very high. Erection sparing surgery is one of the points of special interest to the healthcare professional, and it is one of the areas of continuous improvement in the management of these patients. And so is the proper management of patients with biochemical recurrence after failed surgery or radiotherapy.

The data on the use of hormone blockade are very interesting. The professional surveyed overwhelmingly supports the BAM versus monotherapy with LHRH analogue, early hormone treatment, and the use of neoadjuvant and adjuvant hormone therapy for operated patients, and especially for those who are oriented to radiotherapy. It is curious to know how there are also strong preferences regarding the characteristics inherent to the preparation and properties of the different forms of LHRH analogues.16 For the first time, the practices of intermittent hormone blockade are described in our country.

The main point of concern is the development of new therapies for prostate cancer. The professionals may perceive their role in the advent of new forms of secondary hormone manipulation, and they may be aware of their increasingly important role in the treatment decision at all stages of the disease, including castration-resistant prostate cancer.1,17 On the contrary, the least worrying point revealed in this survey is constituted by robotic surgery and disease prevention.

In summary, this survey shows a significant variability in some points of clinical practice with regard to the recommendations of experts,7-10 highlights the main concerns of professional training, defines opportunities for training improvement, and detects needs in the national urological associations.
Family of the urological clinical practice in prostate cancer in Spain

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Conflict of interest

The survey UROQUEST, which supports this work, was conducted by Luzán 5 Inc. under the auspices of Abbott Laboratories Inc., taking the opinion of a sample of urologists based on their practice.

The results derived therefrom have been critically analyzed by Drs. Núñez, Javier Angulo, Manuel Sánchez-Chapado, José Antonio Portillo, and Humberto Villavicencio, without any conflict of interest and without receiving any fees for the completion of this work.

Dr. Sara Alonso works at the Medical Department of Abbott Laboratories Inc., Spain.

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References