National Prostate Cancer Registry 2010 in Spain

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Abstract
Objectives: To estimate the 2010 incidence of PCa in Spain and describe the clinical profile of newly diagnosed cases using a nationwide hospital-based registry.
Material and methods: National epidemiological study in 25 public hospitals with a specific reference population according to the National Health System. Sociodemographic and clinical variables of all newly diagnosed, histopathological confirmed PCa cases were collected in 2010, in the area of influence of each center. The age-standardized PCa incidence was determined based on the age distribution of the Spanish population in Spain and in 3 regions: Andalusia, Catalonia and Region of Madrid.
Results: 4087 new cases of PCa were diagnosed for a reference population of 4,933,940 men (21.8% of the Spanish male population). The estimated age-standardized PCa incidence was 82.27 cases per 100,000 men in Spain, 70.38 in Andalusia, 85.70 in Catalonia and 92.29 in the Region of Madrid. Mean age at diagnosis was 69 years. Median PSA was 8 ng/ml. Gleason score was ≥6 in 56.5%, 7 in 26.7% and >7 in 16.8% of patients. At diagnosis, 90% had localized disease.
Conclusions: In the 3 Regions analyzed, around 80–90% of the cases are diagnosed in a clinical localized stage. The incidence rates in Andalusia, Catalonia and Region of Madrid show a great difference between them due to several factors.
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Registro nacional de cáncer de próstata 2010 en España

Resumen

Objetivo: Estimar la incidencia del cáncer de próstata (CaP) en España para el año 2010 y describir el perfil clínico de los nuevos casos diagnosticados, mediante un registro de base hospitalaria y ámbito nacional.

Material y métodos: Estudio epidemiológico en 25 hospitales públicos con área de población de referencia según el Sistema Nacional de Salud. Se recogieron variables sociodemográficas y clínicas de todos los casos de nuevo diagnóstico en 2010, con confirmación histopatológica en el área de influencia de cada centro. Se estimó la tasa de incidencia estandarizada a población española en función de la distribución etaria de la población española a nivel nacional y en Andalucía, Cataluña y Comunidad de Madrid.

Resultados: Se diagnosticaron 4.087 nuevos casos de CaP, cubriendo el 21,8% de la población masculina española. La tasa de incidencia estimada estandarizada a población española es de 82,27 por 100.000 varones. La estimación de la tasa de incidencia en Andalucía es de 70,38, en Cataluña de 85,70 y en la Comunidad de Madrid de 92,29. La edad media fue de 69 años (8,15). La mediana de PSA fue de 8 ng/ml. El 56,5% presentaron Gleason total ≤ 6, el 26,7% = 7 y el 16,8% > 7. Según la clasificación D’Amico el 90% presentaban enfermedad localizada.

Conclusiones: En las 3 Comunidades Autónomas estudiadas, entre el 80–90% de los casos son clínicamente localizados, alrededor del 50% son de riesgo intermedio o alto. Las tasas de incidencia encontradas en Andalucía, Cataluña y Comunidad de Madrid reflejan una gran diferencia entre ellas de causa multifactorial.

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Introduction

Prostate cancer (PCa) represents, approximately, 12% of the newly diagnosed cancer cases in Europe.1 It is one of the most prevalent tumors in Spain and one of the most frequently diagnosed in the developed world.2,3 Since the introduction of the measure of the levels of prostate specific antigen (PSA) as an early screening test for PCa, the diagnosis rate has increased significantly, and specific mortality has also been reduced in most Western countries.4,5 Although the impact of mass screening in reducing mortality has been proven in time, its recommendation has not been agreed by the risk of over-diagnosis and overtreatment in a significant number of patients.6 This is due to the high average age at diagnosis and the migration of the new cases detected to early stages.7

Knowing the incidence is crucial to measure the impact of the disease and set priorities for action, both in the fields of politics and healthcare and in the lines of research.

Most of the PCa incidence data are obtained from the information from cancer population registries that often do not cover the entire population. The effect of the non-homogeneous geographical distribution in national estimates has been discussed before.8,9

Studying the real incidence from direct estimates on a significant proportion of the population of a country is a task that involves a great effort but it can provide added data that are not obtained from the population registries, such as descriptive epidemiological information of the characteristics of newly diagnosed patients or the quality of diagnostic care, for their suitability to current clinical practice guidelines. In this sense, there are very few well-known initiatives that attempt to systematize the collection of descriptive data of the patients registered. One of these initiatives is the EUROCARE-4 project,10 which includes data of tumor type and morphology following the third revision of the International Classification of Diseases for Oncology, in order to better estimate the survival of patients.

From the Spanish Association of Urology, based on the organizational structure of the Spanish National Health System, distributed in well-defined health areas,11 we decided to carry out a registry of hospital-based PCa in order to know not only the incidence of the disease, but also the clinical profile of newly diagnosed PCa patients.

Materials and methods

An epidemiological study, nationwide in the context of the National Health System, was designed in order to collect all the newly diagnosed cases of PCa in 2010 in areas covering in total at least 20% of the Spanish population, to from them estimate the national incidence. Additionally, it was intended to collect information of the clinical variables at the time of diagnosis, as well as describe the incidence rates in the various participating regions and how to analyze the heterogeneity in the PCa diagnostic processes across the various participating regions.

The study protocol was approved by the Clinical Research Ethics Committee of the Hospital Virgen de las Nieves in Granada, and all the patients gave written informed consent.

A total of 25 public hospitals with known health area took part in the study, selected ensuring that the age distribution...
of the reference population of each hospital was very similar to the national average.\textsuperscript{12}

In each center, the data from all the patients with newly diagnosed PCa by histopathologic confirmation, at any stage, between January 1 and December 31, 2010, were included, according to the routine clinical practice. We excluded from the study the cases diagnosed at the center, but which did not belong to the reference population of each hospital. Thus, the study population included 4,933,940 males belonging to the reference area of the participating hospitals, representing 21.8% of the male population of Spain.

For each patient, we collected in a data collection logbook specific to the study, sociodemographic variables (age, ethnicity, geographic area), clinical variables (weight, height, BMI, family history of PCa, the patient’s symptoms, comorbidities, DRE, total PSA, prostate volume by ultrasound), and histopathological variables for confirmation of the diagnosis of PCa (number of cylinders, Gleason score, and TNM clinical stage) according to standard practice at each center. The data were obtained from medical registries and registries of histopathologic confirmation of Pathological Anatomy Services. To ensure the quality and homogeneity of the data collected, intensive monitoring was conducted by an independent external person in each of the participating centers.

For the classification of clinical stage, we considered the 2009 TNM classification,\textsuperscript{13} and for the distribution according to the risk of progression, we considered the D’Amico classification.\textsuperscript{14}

The data collected in the DCL were tabulated in a database specific to the study, created using the SPSS 14.0 statistical software. Internal consistency rules and ranges to control inconsistencies and/or corrections to the data collection and tabulation were applied. In the statistical analysis, we used absolute and relative frequencies for the description of the qualitative variables, and the median and interquartile range or mean and standard deviation for the quantitative variables.

The calculation of the national incidence was made taking into account the weight of each area depending on its reference population (obtained by the most recent available hospital memory, 2009 or 2010). The distribution of males within the area of influence was carried out assimilating it to the estimates of the relevant province.\textsuperscript{12} The data were standardized according to the European and Spanish standard distribution.\textsuperscript{15}

Results

We diagnosed a total of 4087 new PCa cases with histological confirmation in the 25 centers in the study period, for a reference population of 4,933,940 men, which would correspond to 19,107 new cases of PCa yearly (18,713–19,504) in public health (adjusted to the Spanish population). The estimated incidence rate (95% CI) from these data standardized to Spanish population is 82.27 per 100,000 males (95% CI: 80.57–83.97). In Andalusia, Catalonia, and Madrid, 2147 patients were diagnosed, 52.5% of the patients included in the study. The estimated incidence rate in Andalusia is 70.38 (95% CI: 65.33–75.36), 85.70 in Catalonia (95% CI: 78.95–92.88), and in the Community of Madrid it is 92.29 (95% CI: 85.72–99.24). On the other hand, the estimated incidence rate adjusted to the European standard population is 70.75 cases per 100,000 males (95% CI: 68.71–73.17).

The mean age (standard deviation) of the sample studied was 69 (8.15) years, 14.6% of the participants were under 60 years, 41.3% were between 60 and 70, 20.3% were between 70 and 75, and 23.1% were older than 75 years. The distribution by age groups and Communities is shown in Fig. 1. Of the total study population, almost all (98.6%)
the cases studied were of Caucasian ethnicity. Two hundred and thirty-two patients (5.7%) had a family history of PCa, and in 93% of these cases the relatives were parents and/or siblings.

Of all the patients, 475 (11.6%) had symptoms associated to the tumor at the time of diagnosis and 39.5% lower urinary tract symptoms (LUTS). A total of 2541 patients (62.2%) had one or more comorbidities.

With regard to the histopathological variables in the diagnosis of PCa, in 34.5% of the patients, the DRE was abnormal. In 4035 cases (98.7%), the diagnosis was reached by transrectal prostate biopsy, obtaining 8 or more cylinders in 81.8% of the cases, and in the other cases through the study of the tissue obtained by TUR, adenomectomy, or radical cystectomy. Fig. 2 shows the number of cylinders taken per biopsy according to the Autonomous Community of the centers.

With regard to the Gleason classification, 56.5% of the patients had a score lower than or equal to 6, 26.7% equal to 7, and 16.8% a rate greater than 7. Fig. 3 shows the distribution according to the Gleason classification.

**Figure 2**  Frequency of cylinders taken per biopsy.

**Figure 3**  Distribution according to the Gleason classification.
distribution according to the Gleason classification in the various Autonomous Communities.

The results of prostate ultrasound showed a mean volume (standard deviation) of 44.43 cc (23.02). The median PSA value was 8 ng/ml (Pc25 = 5.63; Pc75 = 13.55; min = 1.01; max = 2254). In terms of the distribution in groups according to the PSA level, 62.9% of the cases had a PSA level ≤10 ng/ml and 36.2% above 10 ng/ml. The distribution according to PSA levels in Andalusia, Madrid, and Catalonia is shown in Fig. 4.

Regarding the risk groups, 37.5% of the patients were low risk, 23.1% intermediate risk, and 28.6% high risk (Fig. 5; details by Autonomous Communities).

**Discussion**

This is the first national registry of PCa in Spain in which the incidence is calculated by direct estimation in hospital registries that collectively cover a very substantial
proportion of the male population of the country, of 82.27 cases per 100,000 men. The organization of the National Health System of our country in health areas, with a well-defined assigned population results in the reliability of estimates of cases. The incidence rates found in Andalusia, Catalonia, and Madrid reflect a great difference among them of multifactorial cause.

The differences in the incidence rates among different Autonomous Communities may be attributable basically to real differences in the incidence of PCa, to differences in the age distribution of the population of each Autonomous Community, and to differences in the diagnostic protocols used in routine clinical practice among the different Communities.

Assuming that the proportional distribution of cases among the different age groups remains constant in the different Autonomous Communities, the rates of each of them should be similar (changes in the number of subjects of an age group would cause changes in the number of patients diagnosed in this age group, the ratio remaining stable).

Catalonia has a similar percentage of the population in the older age groups (aged over 65 years or over 75 years) than the Spanish average, and the diagnosed cases in these groups maintain the same proportion with regard to the total cases in the whole of Spain.

Andalusia and Madrid have a lower population rate than the Spanish average in the older age groups; if so, they should have fewer cases in these age groups to maintain the rate similar to the national average. However, it is not so in Andalusia, where the rate is lower, or in Madrid, where the rate is higher. These differences would be explained by a lower proportion of cases diagnosed in these age groups in Andalusia with regard to the national average, which would make the rate to decrease, and by a greater proportion of cases diagnosed in those age groups in Madrid with regard to the national average, which would make the rate increase.

In Madrid, there are data from a hospital registry of PCa conducted by Herranz to estimate the incidence of PCa in this Community in 2000. If we take the cases collected in the 4 hospitals included in the National Prostate Cancer Registry and the data of the same centers in the PCa Madrid 2000 study, and we make a projection and estimation of the incidence to 2010, the estimated incidence is 89.34, very similar to that obtained in our study 92.29.

In addition, this national incidence study collects the clinical profile of the newly diagnosed patients in our country, a very useful tool to assess the impact of the disease and its social and health management.

Our estimate for the PCa incidence rate standardized to European population, 70.75 cases per 100,000 men, is lower than those obtained by other authors, based on population registries (86.6 per 100,000 men and year in 2004 and 77.2 in 2006[2,8] and lower than the indirect estimates based on mortality and survival data available (86 per 100,000 men and year for 2006 and 98 for 2012). This may be due to the differences in the estimation methods, the different geographical distribution of the participating centers in this study with respect to the population registries and the fact that the cases diagnosed in private healthcare were not reflected in this study.

Although the population registries in principle should provide more accurate information, the population covered by the institutions participating in this study is 21.8% of the Spanish male population, including important areas such as the province of Barcelona and Madrid, which are not covered in population registries. Moreover, and as a limitation in the study, it should be mentioned that the data obtained do not take into account the cases diagnosed in private healthcare, although the National Health System has universal coverage.

Another limitation could be the difference in diagnostic methods or inhomogeneous biopsy techniques, although a high percentage of centers meet the standards of the EAU guidelines. To our knowledge, there are no prospective studies nationwide that provide additional information to the incidence on the type of diagnosed patients. However, these data are of great importance when forecasting and planning healthcare resources, as well as for the development of research policies.

At the time of diagnosis, 71% of the patients were over 65 years, with a low percentage of cases diagnosed in patients younger than 60 years (14.6%). This is consistent with what was described in previous studies. The results show that the mean age for the diagnosis of PCa is 69 years. Given that life expectancy in Spain at the age of 70 is 14, a considerable number could be candidate for some kind of therapeutic action. The mean age for the diagnosis is similar to that recorded in the U.S. in the SEER and CaPSURE databases.

The percentage of patients with localized disease (89.8%) is slightly higher than that found in the U.S. for the SEER database (81%), the percentage of metastatic cancer being similar (around 4%).

Moreover, the study detects a risk of overtreatment, as 37% of the diagnosed ones are clinically low risk and comorbidity associated patients, in which the advantage provided by the treatments with curative intent is minimized by the impact of life expectancy in this group. The percentage of low-risk patients found is somewhat lower than that reported in the U.S. in the CaPSURE database (37 vs 46%), possibly as a result of a less aggressive screening policy.

The policies for early diagnosis and/or opportunistic screening appear to be effective, given the decline in mortality in those countries with these practices. In fact, our study shows that 51.7% of the newly diagnosed patients belong to the intermediate-risk (23.1%) and high-risk (28.6%) groups, in which the disease will potentially compromise their life. The percentages of patients with intermediate and high risk found in the CaPSURE database are similar (27 and 25%, respectively).

The availability of incidence data, along with the associated sociodemographic and clinical data, makes it possible, thus, to estimate resource consumption and associated costs. Finally, we must note that the results found in terms of practice of indications and method of biopsies show a good adaptation to the recommendations of the current European and American Clinical Practice Guidelines.

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Conflict of interest

Arancha Cantalapiedra and Dr. Emilio Pedrosa are employees of Astellas Pharma, Inc.

The remaining authors declare that they have no conflicts of interest.

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