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Incidence of prostate cancer and net survival by grade in a geriatric population: A population-based study in a French administrative entity from 1991 to 2013

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ABSTRACT

Background: Prostate cancer is the leading type of cancer among men in more developed countries. Incidence trends and survival rates could differ by age groups considering potential differences in the frequency of PSA testing, types of cancers and medical management. Our objective was to compare incidence trends and survival rates of prostate cancer between men aged ≥75 and 60–74 years.

Method: We analyzed data from a population-based cancer registry in Isère, France. All men aged ≥60 years diagnosed with an incident prostate cancer during the 1991–2013 period were included. Incidence and mortality rates were computed as well as net survival rates.

Results: In 2013, observed incidence rates were 557.6 and 568.7 per 100,000 for men aged 60–74 and ≥75, respectively, with high grades cancers more frequent among elderly men. The incidence and mortality trends among men aged ≥75 included a period of stability followed by a decreasing trend from 2003, whereas a peak of incidence was observed in 2005 for men aged 60–74. For both age groups, net survival rates increased with period of diagnosis and 8-year net survival remained higher than 70% for cases diagnosed in the 2000–2004 period. Lower survival rate of 51% (95%CI: 42%; 60%) was observed for high grades cancers diagnosed among men aged 75–84 in 2000–2004.

Conclusion: The epidemiology of prostate cancers among men aged ≥75 include a decrease of incidence and mortality rates from 2003, an important proportion of high grade cancers and a relatively good prognosis except for high grade cancers.

1. Introduction

Prostate cancer is the second most common cancer in men worldwide and the leading type of cancer among men in more developed countries [1]. In 2011, nearly 54,000 cases were diagnosed in France corresponding to a world standardized incidence rate of 97.7 per 100,000 person-year [2]. An increase of incidence rates was observed until the 1990's in North America [3] and until the 2000's in European countries [4] in relation to the diffusion of Prostate Specific Antigen (PSA) testing. In France, the world standardized incidence rates per 100,000 persons increased from 24.8 in 1980 to 127.1 in 2005, followed by a decrease to 99.4 in 2009 [5]. Prostate cancer belongs to the good prognosis group of cancers. Data from French cancer registries for cases diagnosed during the 1989–1998 period showed 10-year net survival rates of 73% (95%CI: 71%–75%) and 71% (95%CI: 69%–73%) for men aged 55–64 and 65–74, respectively [6,12,13,16]. Survival rates increased with calendar period in most countries, from 79.4% at 5 years for cases diagnosed in France during the 1995–1999 period to 90.5% during the 2005–2009 period [7,8].

Incidence trends and survival rates could differ by age groups considering potential differences in PSA testing, types of cancers [9,10] and medical management [11]. For example, prostate cancers among elderly patients included more high-grade forms categorized as Gleason 8–10 and 48% of cases had metastases at diagnosis [9], involving many deaths even with aggressive therapy [12,13].

The description of the epidemiology of prostate cancer among men aged 75 and over is of particular interest considering the importance of prostate cancer among this age group. Indeed, incidence rates of prostate cancer increase with age [5] and the proportion of individuals aged over 75 years among men diagnosed with prostate cancer has

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rapidly increased due to the increase of the life expectancy. Twenty nine percent of cases were diagnosed after 75 years in 2009 in France whereas 78% of prostate cancer deaths occurred among men aged over 75 years [5]. Although older-people do not lose as many years of life than younger patients due to their shorter remaining life expectancy, patients aged over 75 years still lose three quarters of their life expectancy [9].

The increase of the number of elderly patients contributed to the development of geriatric oncology [14] whose purpose is to improve the management of patients aged over 75 years [15] to minimize toxicity and maximize the effectiveness of different treatment options taking into account their specificity [16–21]. This approach could result in changing survival rates [14].

Surprisingly, few studies computed incidence and survival rates of prostate cancer in a population of men aged 75 and over. Moreover, the characteristics of prostate cancers in geriatric population were not frequently studied, especially the severity of cancer and few data are available on incidence trends and survival rates depending on prognostic grades, based on the Gleason grading system.

Therefore, our primary objective was to compare incidence trends and survival rates of prostate cancer among two age groups: an onco-geriatric population aged 75 and over, and a younger group of patients aged 60–74. Our secondary objective was to compare incidence trends and survival rates by the prognostic grades of the cancers based on the Gleason grading system.

2. Material and methods

2.1. Study design and setting

We analyzed data from an ongoing population-based cancer registry in Isère, a French administrative entity with nearly 1.2 million inhabitants.

2.2. Study population

We included all men aged 60 years and over diagnosed with an incident primary invasive prostate cancer between January 1, 1991 and December 31, 2013 to analyze incidence trends. This period was chosen to have an exhaustive database including data from the most recent period. For survival analyses, active search for the vital status at June 30, 2013 was carried out for all cases diagnosed in 1991–1994 and 2000–2004. The information was collected for individuals with a birthplace known by electronic request to the Répertoire National d'Identification des Personnes Physiques which collects data on deaths in France. In case of missing birthplace, other sources of information on the vital status were used such as medical records.

2.3. Data collection

Data were collected by the Isère Cancer Registry, which collects incident cancer cases from different sources including histopathology laboratories, oncology departments, social security offices and medical databases. Due to regulatory constraints, death certificate only cases are not included in French registries. Notification of cases is not mandatory in France but the high number of sources transmitting information to the Isère Cancer registry and regular assessment by national authorities suggest a high level of completeness.

Cancer site was defined according to the International Classification of Diseases for Oncology (third edition) and the prostate cancer was defined by topography code C619.

Prostate cancer deaths were obtained using a database from the Centre d'épidémiologie sur les causes médicales de décès (CépiDc).

The number of person-years at risk in each age group and calendar year were calculated using population data estimated by the French national institute of statistics (INSEE).

The following variables were used: age at diagnosis, year of diagnosis, Gleason grading system of tumor and year of death from prostate cancer. From the Gleason grading system, we defined three categories corresponding to different grades and prognoses: score $\leq$ 6 corresponding to a well-differentiated carcinoma with a good prognosis (low-grade), score of 7 corresponding to a moderately differentiated carcinoma with intermediate prognosis (intermediate-grade) and score $\geq$8 corresponding to a poorly differentiated carcinoma with poor prognosis (high-grade) [22,23].

3. Theory/calculation

We compared incidence, mortality trends and survival among men aged 75 years and over, and among men aged 60–74.

Annual standardized incidence and mortality rates were computed for each calendar year from 1991 to 2013, for the 2 age groups considered using a truncated world standard population aged 60–74 and aged over 75. Incidence rates were also computed for the 3 different grades (low, intermediate and high). We then applied the Joinpoint regression model [24] to identify breakpoints in the trend of age-standardized rates and to estimate average rates of change. Basically, the Joinpoint model finds the best-fit line through several years of data using algorithm that tests whether a multi-segmented line is a significantly better fit then a straight or less-segmented line. The program starts with the minimum number of joinpoint (0 joinpoint, which is a straight line) and tests whether more joinpoints are statistically significant and must be added to the model.

Net survival rates, i.e. the survival that would be observed if the prostate cancer was the only possible cause of death, were computed. To quantify survival associated with prostate cancer, net survival is much more relevant than observed survival since mortality rates due to other causes than prostate cancer among men aged over 75 years is relatively high. The net survival estimates were obtained from the Pohar-Perm method which included a weighting procedure to correct biases due to the informative censoring mechanism induced by the life-table variables [25,26]. This method required the expected mortality from the general population that was obtained from life tables provided by the INSEE. Net survival rates were computed by age group and grade, separately for cases diagnosed in 1991–1994 and 2000–2004: the first period corresponded to a rather low level of incidence whereas the second period included the peak of incidence. For survival analyses, patients aged over 85 years were excluded because 8-years survival is not relevant among a group of patients with a short life expectancy. Survival rates were computed each year since diagnosis until 8 years after diagnosis. No results were reported for a specific time after diagnosis when unstable estimates were observed resulting in increasing survival rates with time. A log-rank-type test was realized to compare net survival distributions.

Finally, we realized two separate multivariable analyses based on a Cox model for men aged 60–74 and 75–84 years to assess if changes in survival rates observed in more recent periods could be explained by a severity shift caused by PSA dissemination.

Analyses were performed using Stata version 13.0 (Stata Corporation, College Station, TX, USA) and the R package Relsurv.

4. Results

From 1991–2013, the Isère Cancer Registry collected 15,462 invasive prostate cancer cases among men aged 60 years and over: 9805 between 60 and 74 years and 5657 over 75 years. There were 1786 (11.1%) cases with missing data about the Gleason grading system, 713 (7.1%) for cases diagnosed among men aged 60–74 and 1073 (17.9%) for cases diagnosed among men aged 75 and over. Considering 8-year follow-up, the proportion of individuals lost to follow up were 1.3% and 2.0% for diagnostic periods 1991–1994 and 2000–2004, respectively.