RESEARCH COMMUNICATION

# Prostate Cancer Epidemiology in a Rural Area of North Western Greece

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## Abstract

**Epirus is a rural area of North-Western Greece. We reviewed data from 4 hospitals for 4.975 patients who underwent prostate biopsy in Epirus in the twelve year period from 1999 to 2010. Two six -year periods were compared (1999-2004 and 2004-2010). All cases of prostate cancer confirmed by biopsy were recorded and age-standardized incidence rates per 100,000 males were calculated. We also recorded the clinical stage for patients diagnosed in our hospital and correlated this with PSA and Gleason scores. Percentage of positive prostate biopsies was also calculated. There were a total of 1714 new cases during 1999-2010 and the mean annual age-adjusted incidence was 34/100.000. The mean incidences during 1999-2004 and 2005-2010 were 26/100,000 and 42/100,000, respectively. The mean age at diagnosis was 74. The most common Gleason score was 6 and the prevalent clinical stage was T2. Median PSA at diagnosis was 10.8 ng/ml. There was a significant difference between stage cT4 and all other stages regarding PSA value (p=0.000). A positive correlation was found between Gleason score and PSA (p=0.013). These results are in accordance with the incidence rise recorded in neighboring countries of South-East Europe. However we should keep in mind the risk of overdiagnosis and the detection of low-risk cancers that would not have caused morbidity or death during a man's lifetime anyway.**

**Keywords:** Prostate cancer - incidence - PSA - Greece

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## Introduction

Prostate cancer is the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males globally, accounting for 14% (903,500) of the total new cancer cases and 6% (258,400) of the total cancer deaths in males in 2008. Incidence rates vary by more than 25-fold worldwide, with the highest rates recorded primarily in the developed countries of Oceania, Europe, and North America. In contrast, males of African descent in the Caribbean region have the highest prostate cancer mortality rates in the world, which is thought to reflect partly difference in genetic susceptibility (CA, 2011). A general pattern of rising incidence is seen in most countries (Muir et al., 1991; Boyle et al., 2003; Bioteach, 2005)

Monitoring annual incidence trends in population subgroups provide useful information about environmental and socioeconomic influences and help to provide better screening practice, early detection and more successful treatment. Aim of this study is to evaluate the incidence for prostate cancer in the region of Epirus, northwest Greece on the basis of data collected from 4 tertiary hospitals. Also correlations are analyzed between Gleason score, clinical stage and PSA value.

## Materials and Methods

Research was conducted in four tertiary hospitals of Epirus (General Hospital Hatzikosta, University Hospital of Ioannina, General Hospital of Arta ,General Hospital of Preveza). The region has 336,392 inhabitants and 166,878 are men. We reviewed data from 4.975 patients who were submitted to prostate biopsy in the twelve year period 1999 to 2010. All cases of prostate cancer confirmed by biopsy were recorded, while benign and PIN (Prostate Intraepithelial Neoplasia ) cases were excluded. Two six-year periods were also compared (1999-2004 and 2004-2010). The number of prostate cancer cases was broken down by 5-year age group (0 - 4, 5 - 9,.., 80 - 84 and 85+ years)

Age-standardized incidence rates per 100.000 males were calculated, using the world as reference population. We also reviewed our own hospital data base in order

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to record clinical stage, Gleason score and correlations were made with PSA. A p value of 0.05 was considered statistically significant. Finally during 1999-2010 we calculated the percentage of positive prostate biopsies.

## Results

There were a total of 1714 new cases of prostate cancer in Epirus during 1999-2010. An increase was noted on prostate cancer incidence reaching a maximum of 52 new cases per 100.000 persons in 2009, while 22 new cases per 100.000 were diagnosed during the year 2000 (Table 1).

During 2005-2010, there was 59.3% increase in prostate cancer total incidence rate comparatively to 1999-2004 (Table 2). The greatest increase (threefold) was observed in the 55-59 age group. In both time periods incidence of prostate cancer was extremely low for men younger than 50 years old, reaching a peak in the 70-74 age group and decreasing thereafter (Figure 1)

Prevalence age group was 75-79, while almost half of the patients were between 70 and 79 age years old at diagnosis (Figure 2). The most common Gleason score was 6 (33% of the patients) (Figure 3).

Regarding our hospital the most common Gleason score was 6 (46% of patients) and the most common clinical stage was cT2 ( 57,3% of patients). Median PSA at diagnosis was 10.84 ng/ml, remaining almost stable in both the 6-year periods. The mean percentage of positive prostate biopsies was 33,9 %, showing an increasing trend in the last two years of our study (Figure 4).

A statistical analysis was performed in order to

**Table 1. Total Incidence Rates of Prostate Cancer in Epirus, 1999-2010**

| YEAR | NUMBER | INCIDENCE |
|---|---|---|
| 1999 | 113 | 23,33 |
| 2000 | 99 | 21,88 |
| 2001 | 131 | 30,75 |
| 2002 | 116 | 25,93 |
| 2003 | 100 | 23,03 |
| 2004 | 133 | 31,52 |
| 2005 | 155 | 37,37 |
| 2006 | 148 | 35,83 |
| 2007 | 150 | 36,94 |
| 2008 | 173 | 42,24 |
| 2009 | 215 | 52,07 |
| 2010 | 181 | 46,72 |

**Table 2. Age Adjusted Incidence Rates * of Prostate Cancer in Epirus, 1999-2004 and 2005-2010**

| AGE | 1999-2004 | | 2005-2010 | | % change |
|---|---|---|---|---|---|
| GROUPS | No. | Incidence | No. | Incidence | |
| 35-39 | 1 | 0,09 | 0 | 0,00 | N.A |
| 40-44 | 0 | 0,00 | 1 | 0,08 | N.A |
| 45-49 | 3 | 0,25 | 2 | 0,17 | -47 |
| 50-54 | 9 | 0,67 | 18 | 1,34 | 100 |
| 55-59 | 14 | 1,08 | 56 | 4,34 | 301,8 |
| 60-64 | 45 | 2,96 | 102 | 6,71 | 126 |
| 65-69 | 88 | 4,24 | 148 | 7,13 | 68,1 |
| 70-74 | 182 | 6,58 | 229 | 8,29 | 25,9 |
| 75-79 | 176 | 5,13 | 248 | 7,23 | 40,9 |
| 80-84 | 141 | 3,27 | 155 | 4,19 | 28,1 |
| 85+ | 53 | 2,01 | 63 | 2,39 | 18,9 |
| Total | 692 | 26,28 | 1022 | 41,87 | 59,3 |

*Per 100,000 person-years, age-adjusted using the world standard

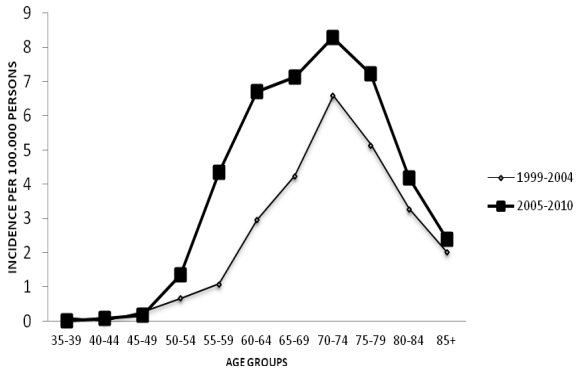


**Figure 1. Age-Adjusted Incidence Trends of Prostate Cancer during Time Periods, 1999-2004 and 2005-2010**

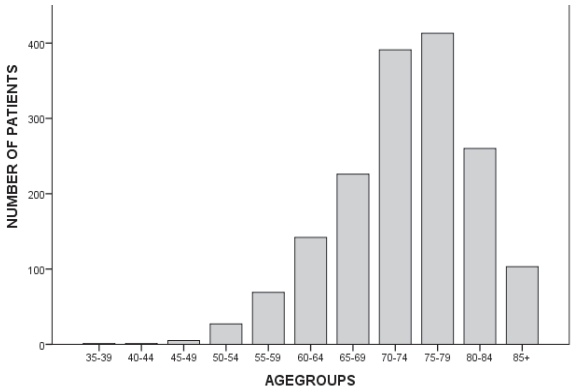


**Figure 2. Distribution of Patients According to Age**

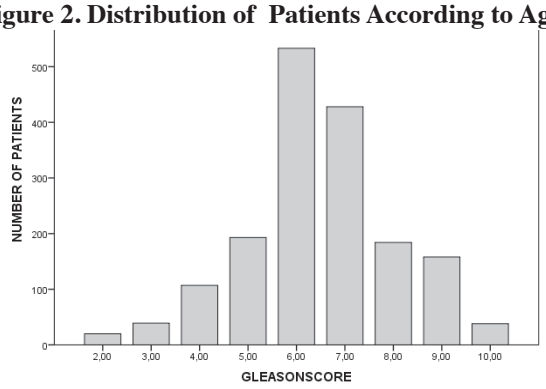


**Figure 3. Distribution of Patients According to Gleason Score**

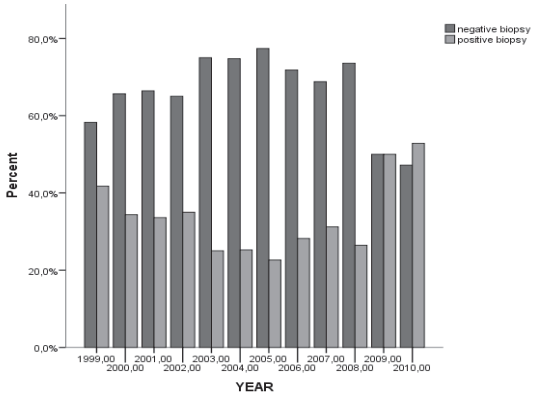


**Figure 4. Positive/Negative Biopsies Ratio**

correlate clinical stage and gleason score with PSA. There was a statistically significant difference between stage cT4 and all other stages regarding the PSA value (p=0,000). No difference was noted between clinical stages T1c, T2, T3. We also defined a positive correlation between Gleason score and PSA (p=0,013).

## Discussion

Our research has showed that in Epirus-north west Greece prostate cancer incidence was doubled during the last 6 years, reaching a mean number of 42 new cases per 100.000. In the rest countries of South-East Europe (Italy, Slovenia, Serbia, Romania, Croatia, Bosnia Herzegovina, FYROM, Bulgaria, Cyprus, Albania) there is also a marked increase of prostate cancer incidence with an average incidence of almost 34/100.000. Slovenia has the highest incidence rate with 63 new cases per 100.000 population followed by Italy and Cyprus with 58 and 47 new cases per 100.000 respectively. Serbia and Romania are in the last place with incidence rates of 19 and 20 cases per 100.000 respectively. Western Europe countries have the largest incidence of prostate cancer with 93 new cases per 100.000 (Ferlay et al., 2010).

In an effort to interpret time trends in prostate cancer incidence, two types of factors must be discussed. First, there may be a real increase in incidence due to increased exposure to one or more risk factors. The only well-established risk factors for prostate cancer are age, race/ethnicity and family history (Larranaga et al., 2010). Modifiable risk factors include diet, obesity and screening history (Soral et al., 2008). Prostate cancer is androgen sensitive and it is well confirmed that steroid hormones play a role in carcinogenesis. Secondly, there may be increased detection of existing tumours by transurethral resection (TURP) (Potosky et al.,1990; Merrill et al., 1999) and the prostate-specific antigen test (Potosky et al., 1995).

The greatest role in prostate cancer incidence increase should be attributed to PSA screening. However on October 2011, the U.S. Preventive Services Task Force (USPSTF) released a new draft recommendation against PSA-based screening for prostate cancer, asserting that there is "moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits," and discouraged the use of the test by issuing it a Grade D rating. This recommendation was based on the results from two high quality trials. The U.S. Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer trial reported that screening was associated with increased prostate cancer incidence (relative risk [RR], 1.2 [95% CI, 1.2 to 1.3]) but no effect on prostate cancer-specific (RR, 1.1 [CI, 0.75 to 1.7]) or all-cause (RR, 0.98 [CI, 0.92 to 1.0]) mortality. The European Randomized Study of Screening for Prostate Cancer (ERSPC) showed that prostate cancer incidence was higher in the screened group (net increase, 34 per 1000 men), but there was no statistically significant difference in prostate cancer–specific mortality (RR, 0.85 [CI, 0.73 to 1.0]) (Chou et al., 2011). Patients and physicians should now be encouraged to consider engaging in shared and informed decision process concerning screening for prostate cancer.

Population in Greece has better access to health services across years. The introduction into routine clinical practice of therapeutic modalities such as TURP and diagnostic procedures such as echo-guided biopsy, transrectal ultrasonography and PSA testing, can be assumed to have made a greater contribution to the incidence increase as a result of an enhanced capability to detect incidental cancers that would otherwise be latent (Potosky et al., 1990; Potosky et al., 1995; Merrill et al., 1999). Thus, incidence may be distorted by the inclusion of varying numbers of so-called latent cancers.

Epirus is a rural area of North-Western Greece. Prostate cancer incidence rate is 55% lower compared to countries of Western Europe were population is mainly urban. It has been observed that rural residents have lower rates of cancer screening, which results in decreased incidence but increased late-stage disease and a higher proportion of unstaged cancer (Higginbotham et al., 2001). However, research on rural-urban disparities has produced mixed and conflicting findings that question whether rural residents are disadvantaged in late-stage risk. A recent study has shown that the risk of late stage cancer was highest in the most highly urbanized area and decreased as rurality increases, following a J-shaped progression that included a small upturn in risk in the most isolated rural areas (McLafferty et al., 2009).

In the near future, incidence in Greece will show if it either remains stable or increases partly depending on our policy in pursuing early diagnosis. However we should keep in mind the risk of overdiagnosis and the detection of low-risk cancers that would not have caused morbidity or death during a man's lifetime anyway. The following overtreatment would expose men to unnecessary morbidity .Anyhow prostate cancer will remain a significant health problem requiring a great amount of health funds.

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