Pathological Characteristics of Prostate Cancer in Elderly Men

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Purpose: Recent guidelines recommend that men older than 75 years should not be screened for prostate cancer. However, increased life expectancy and the development of less invasive treatments have led to an interest in characterizing prostate cancer in elderly men. We determined how prostate cancer pathological characteristics differ in men older vs younger than 70 years.

Materials and Methods: We studied differences in prostate cancer pathological characteristics in autopsied glands from men 70 years old or older and compared findings to those in men younger than 70 years. All men died of causes unrelated to prostate cancer. Prostates were whole mounted at 4 mm intervals. Histological analysis was done to identify and characterize each cancer focus observed. Tumor volume was measured by computerized planimetry. Cancer was defined as clinically significant or insignificant based on established histological characteristics.

Results: Of 211 prostates evaluated 74 were from men 70 years old or older. We identified cancer in 33 men (45%) in this age group vs in 26 of 137 (19%) younger than 70 years ($p < 0.001$). Men older than 70 years had significantly larger cancer and more clinically significant cancer (64% vs 23%, $p < 0.005$). Older men had more advanced stage cancer and greater Gleason scores ($p < 0.001$).

Conclusions: In an autopsy study of men with no history of prostate cancer those older than 70 years were more likely to have larger and higher grade prostate cancer than younger men.

Key Words: prostate, prostatic neoplasms, aged, diagnosis, autopsy

Abbreviations and Acronyms

ITV = index tumor volume

PCa = prostate cancer

PSA = prostate specific antigen

TTV = total tumor volume

Submitted for publication December 29, 2008.

Study received institutional review board approval.

Supported by National Institute on Aging AG021389 (GPH) and National Cancer Institute CA097751 (GPH).

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One of 6 American men will have PCa in his life.[1] The disease incidence is increasing in the United States, Europe and many other nations.[2] However, because of the slow growth of malignant prostate cells, many cancers remain latent and a significant proportion of patients may not need radical, possibly morbid treatment. Men with a life expectancy of less than 10 years may not have any consequences of the disease. If these men are not candidates for treatment, they should not be candidates for screening. Based on these observations the Task Force for Preventive Medicine suggested that PCa screening should stop after age 75 years.[3]

The decision to screen should probably not be based on age alone but also on comorbidities and cancer aggressiveness. As suggested recently, potentially curative treatment may lead to significant gains in health outcomes in elderly men with poorly differentiated cancer.[4] PCa local and systemic spread is closely associated with its pathological characteristics. Tumor volume and Gleason score are directly related to the risk of capsular penetration, seminal vesicle invasion and microscopic metastasis to the pel-

0022-5347/09/1823-0927/0
THE JOURNAL OF UROLOGY®

Vol. 182, 927-930, September 2009
Printed in U.S.A.
DOI:10.1016/j.juro.2009.05.018

vic lymph nodes.[5,6] If small, well differentiated cancer is not considered an immediate threat, so-called clinically significant tumors, defined as an index volume of greater than 0.5 cm^3 and a Gleason score of 7 or higher,[7,8] may have an impact on health outcomes even in elderly men.

Little information is currently available on the pathological characteristics of PCa in elderly men.[9] With the development of watchful waiting strategies and nonsurgical treatments such as brachytherapy, external beam radiotherapy, cryosurgery and high intensity focused ultrasound therapy few men older than 70 years are recommended to undergo radical prostatectomy. A high proportion of men older than 70 years do not undergo prostate biopsy and men in whom prostate biopsy fails to detect cancer do not undergo surgical verification. Thus, prostate tissues are lacking to accurately evaluate PCa prevalence and its pathological characteristics in elderly men.

The histological prevalence of PCa has been studied in autopsied material in several populations.[10–12] We characterized PCa in elderly men and determined how PCa pathological characteristics differ in men older vs younger than 70 years.

MATERIALS AND METHODS

Tissue Collection

We prospectively collected 261 consecutive prostate glands from deceased men that were provided by University Hospital and the Onondaga County Medical Examiner, Syracuse, New York, and the National Disease Research Interchange, Philadelphia, Pennsylvania. This study was approved by the institutional review board and tissue suppliers obtained informed consent from the next of kin. All samples were de-identified to protect individual identity. Age, race and cause of death were recorded. The decedents had no known history of PCa. At autopsy the entire prostate with the seminal vesicles was excised and placed in 10% neutral buffered formalin. Prostatic tissue was not entirely removed in 50 autopsied prostates (20%). These subjects were excluded, leaving 211 prostate glands available for analysis.

Prostate Processing and Histological Evaluation

After fixation in formalin for at least 72 hours the glands were separated from any surrounding tissue and volume was measured. The glands were cut into 4 mm sections perpendicular to the posterior plane. The blocks were labeled, embedded in paraffin and sectioned to produce 5 μm whole mount sections that were stained with hematoxylin and eosin. A single pathologist (GdlR) analyzed the sections in blinded fashion. Each tumor focus detected was outlined. Immunohistochemical studies using a cocktail containing basal cell marker p63 and P504S/α-methylacyl-coenzyme A racemase were performed in cases that were not unequivocally considered cancerous on morphology alone. The total number of tumor foci and their sites were recorded. An area of carcinoma was considered a separate focus when it was separated from the nearest adjacent focus by a low power field diameter (4.5 mm), as previously reported.[13] Each tumor focus was graded according to the modified Gleason grading system.[14]

Digital Reconstruction and Tumor Volume

The surface of each tumor focus was determined by computerized planimetry using an image analysis program.[12,15] Tumor volume was calculated by multiplying each tumor surface by section thickness (4 mm) and by 1.5 to compensate for tissue shrinkage.[16] ITV was the volume of the largest carcinoma focus. TTV was calculated as the sum of the volumes of the individual foci. Tumors were considered clinically insignificant when they were organ confined (less than pT3) with an ITV of less than 0.5 cm^3 and a Gleason score of 6 or less.[7,8]

Statistical Methods

We distinguished 2 groups of autopsied glands according to subject age at death (70 years old or older vs younger than 70). The Mann-Whitney Wilcoxon rank test was used to compare tumor foci and Gleason score distributions. Pathological stage distribution was analyzed by the Mann-Whitney Wilcoxon rank test or Fisher's exact test when the number was small. Pearson's chi-square test was applied to compare the frequency of clinically significant tumors and the 2-sided Student t test was used to compare tumor volumes. Statistical analysis was done using Stata® 9.0.

RESULTS

The 211 autopsied glands analyzed were from white American men with a median age of 64 years (range 22 to 92). At death 74 men (35%) were 70 years old or older (median 76, IQR 73–81) and 137 (65%) were younger than 70 years (median 57, IQR 50–64). Of men older vs younger than 70 years 33 of 74 (45%) vs 26 of 137 (19%) had cancer identified ($p < 0.001$). The table lists pathological characteristics. Although the difference in ITV was not significant, TTV was greater in the older group ($p < 0.05$). Gleason score ($p < 0.001$) was also significantly higher in men older than 70 years. Although the pathological stage distribution was not significantly different ($p = 0.086$), the elderly group appeared to have more pT3 tumors (2-sided Fisher's exact test $p = 0.067$). Cancer in men older than 70 years was more commonly clinically significant ($p < 0.005$).

DISCUSSION

Considerable controversy surrounds the optimal treatment in elderly patients with localized PCa. The 3 main treatments are radical prostatectomy, radiotherapy and watchful waiting. Men younger than 60 years who have clinically localized disease are 25 times more likely to undergo radical prostatectomy than men 70 years old or older.[17] A 75-year-old man with moderately differentiated tumor is offered radical prostatectomy 3,000 times less fre-