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The Worldwide Epidemiology of Prostate Cancer: Perspectives from Autopsy Studies

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Abstract

Introduction—Prostate cancer is the most frequently diagnosed non-skin cancer in the United States and the third leading cause of cancer deaths. International trends in the incidence, mortality and prevalence of prostate cancer are assessed.

Methods—Data bases from the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute and the International Agency for Research on Cancer (IARC), and the literature on autopsy studies on prostate cancer were reviewed and summarized in the article.

Results—Prostate cancer remains an important public health concern in Western countries and an emerging malignancy in developing nations. Prostate cancer incidence is dependent on efforts to detect the disease. Autopsy studies provide accurate and useful information regarding comparative prevalence rates of the disease among regions of interest.

Conclusions—Improved cancer registration is needed in developing nations. The prevalence of prostate cancer must be established to predict the expected incidence of the disease and in order to plan rational detection and treatment strategies. Clinically significant disease should be distinguished from insignificant disease which may pose little or no biological danger to the patient.

INTRODUCTION

Prostate cancer is a disease of increasing significance worldwide. In many industrialized nations such as the United States, it is one of the most common cancers and among the leading causes of cancer deaths.[1] In developing countries it may be less common, however its incidence and mortality has been on the rise.[2] It is tempting to judge the public health significance of a disease by its incidence or mortality, but when it comes to prostate cancer this dogma is confounded by the very high prevalence of occult disease.[3] Incidence is therefore influenced by the intensity of diagnostic efforts, and the mortality figures reported for any particular geographic area depend on the reliability of cancer registries. The United States has one of the most active prostate cancer early detection programs in the world, and also the highest incidence. Once prostate specific antigen (PSA) tests became available for prostate cancer screening, the US has experienced a huge increase in prostate cancer incidence.[4] Therefore, it is very important to understand the actual prevalence of prostate cancer in given areas of the world if we wish to compare incidence and mortality figures for various age and racial groups, or between different geographical regions.

ESTIMATION OF PROSTATE CANCER PREVALENCE

Prevalence is the number of cases of a particular condition that exists in a given population and consists of diagnosed cases plus those cases that are present but yet undetected. Prostate cancer prevalence can be estimated from a variety of sources. Several decades ago, many prostate cancers were discovered during the pathological examination of specimens from transurethreal prostatectomies. These patients were operated for suspected benign prostatic hyperplasia (BPH), but up to 25 per cent were found to have malignancy.[5,6] However, the frequency of finding such incidental cancers has precipitously dropped since PSA came into existence, as most of the men undergoing surgery for BPH have their PSA tested and those with elevation are worked up.

Several authors investigated the prevalence of prostate cancer in cystoprostatectomy specimens, an operation usually carried out for the treatment of invasive bladder cancer. 25% to 40% of prostates were found to contain unsuspected prostate cancer.[7-10] However, we have since then discovered that prostate and bladder cancers may share a common pathway of carcinogenesis, and therefore the association of prostate and bladder cancers may not be coincidental.[11-14] Nevertheless, these clinical studies demonstrated that prostate cancer is present in many patients unsuspected of harboring the disease, and the more thoroughly one examines the specimens, the more cancers will be discovered.

A very important clinical trial performed by Thompson and associates further elucidated the high prevalence of prostate cancer in the general population. The results of the Prostate Cancer Prevention Trial were published in the New England Journal of Medicine in 2003.[15] In this trial, men with normal PSA and digital rectal examination results were biopsied at the end of the study. 15% of men were found to have prostate cancer. Sextant biopsies were performed in this study, had the authors utilized a mote extensive biopsy regimen, most likely additional cancers would have been discovered. Even men with very low PSA values were at some risk for harboring prostate cancer.[16]

Much of what we know today about the prevalence of prostate cancer in various parts of the world comes from autopsy studies. If a representative cross section of a population is evaluated with post-mortem examination, one can determine the frequency of prostate cancer in that particular group. Autopsy studies of prostate cancer have been reported since the 1950s when some of the classical work has been performed by Franks.[17] This is the reference to the supposition that if a man lives to age 100, he will have a nearly 100% likelihood of developing prostate cancer. Breslow et al.[18] investigated the incidence, mortality and autopsy prevalence of prostate cancer in a wide geographical area and concluded that while incidence and mortality rates varied greatly, the differences in prevalence were small. Similar conclusions were drawn by Yatani et al.[19] who compared Japanese and American men. Guileyardo et al.[20] compared an African American and Caucasian cohort of men, and concluded that despite major racial disparities in cancer incidence and mortality, prostate cancer prevalence was similar among the two groups.

These studies differed in their method of tissue processing, thoroughness of examination, and even in the selection of subjects. It is difficult to provide head-to-head comparisons among the reports. However, since the early 1990s, several investigators from very distinct geographical regions of the world utilized similar techniques of analyzing step-sectioned autopsied prostate specimens to report the prevalence of prostate cancer in their particular region.[3] Despite minor differences in their techniques, these authors contributed a wealth of data that can be used to draw meaningful comparisons about the epidemiology of prostate cancer around the world.

WORLDWIDE INCIDENCE OF PROSTATE CANCER

Prostate cancer has no national boundaries and may be found on all continents Table 1 is adapted from the database of the International Agency for Research on Cancer (IARC), and represents the most up to date information on the incidence of prostate cancer around the world. The highest rates are from the United States, particularly among African American men. China has some of the lowest incidence rates. Among European countries, the incidence in Austria is notable, because there is wide variation within the country. Incidence rates are very high in the region of Tyrol compared to those reported from the eastern region. Tyrol has an organized, very thoroughly conducted screening program for prostate cancer. Incidence rates in the United States fluctuated during the last decade (Figure 1). We postulate that the great increase in incidence between the late 1980s and the mid 1990s were due to the large number of cases detected once PSA became available and widely utilized. This increase was followed by a dip in the curves as most detectable tumors were identified. The current slow rise in incidence, during the first half of the new century may be due to increased detection efforts with lower PSA thresholds and increased numbers of biopsy cores taken[21].

WORDLDWIDE MORTALITY OF PROSTATE CANCER

Table 2 shows prostate cancer mortality rates around the world. Mortality remains highest in Scandinavian countries. In many areas of the world, but particulary in the United States, a steady decline in mortality has been noted during the last decade (Figure 1). There is a great deal of controversy surrounding the role of prostate cancer screening on the reduction of mortality. Advocates attribute the reduction in mortality over the last several years to the delayed effect of early detection initiatives[22]. Some even believe that men who come to attention during prostate cancer screening or treatment are likely to benefit from additional medical attention for unrelated but potentially hazardous conditions, the treatment of which will result in an overall increase in survival[23]. Others believe that prostate cancer screening leads to overtreatment of disease which is of low biological risk, therefore creating unnecessary morbidity and cost.[24-28] While it is beyond the scope of this work to resolve the issue, it is apparent that advocates of either side of the argument need reliable data not only of the incidence and mortality, but on the actual prevalence of prostate cancer and its various biological subtypes.

When national trends in mortality are contrasted against the incidence figures, a large disparity is noted for the United States, where large numbers of men are diagnosed with prostate cancer, and relatively few die of the disease (Fig. 1). In contrast, many Asian and African countries, where the incidence rates may be lower, most men will eventually succumb to prostate cancer. This suggests that American men may be either diagnosed earlier, in a more curable state of the disease, or that they may be diagnosed with many more biologically insignificant disease. In contrast, Asian and African men may be diagnosed later, with advanced stage, incurable disease.

PREVALENCE OF PROSTATE CANCER ARROUND THE WORLD

Based on autopsy material, prostate cancer prevalence information according to age has been published by several authors (Table 3). [3,19,29-31] Prostate cancer prevalence is highest among American men of Caucasian and African origin, but the trends are similar among all countries reporting. Prostate cancers are identified at a much younger age than would be expected based on incidence data, and most men in the older age groups are effected. It appears that some prostate cancers may pass through a period of latency of up to 15 to 20 years, during which the disease is histologically present but has not come to attention yet.. It is uncertain if this is equally true for aggressive, high risk prostate cancers.

Although the current report does not contain contemporary African sources, earlier reports by Jackson and coworkers[31] documented similar trends from several African countries. Clearly, there is a great need to update this information.

Prostate cancer prevalence rates were lowest among men of Mediterranean origin.[29,30] One of the authors postulated that it is a diet rich in antioxidants from cereals, vegetables, olive oil, etc. which may be responsible for a diminished prostate cancer risk[29].

Only one study reported an increase in the frequency of latent cancers between two time periods for the same location.[19] Therefore comparisons between time-related trends in incidence or mortality versus prevalence can not be established based on these data.

Most of the autopsy detected tumors in younger men are small volume, relatively well differentiated lesions. Histological criteria have been developed based on radical prostatectomy specimens regarding differences between clinically significant versus insignificant prostate cancers.[33,34] Clinically significant cancers are defined as having a volume greater than 0.5 ml or have Gleason grades >6, or are locally invasive. Tumors that do not meet any of these criteria are thought to represent clinically insignificant, low biological risk tumors that are unlikely to cause risk to the health of the patient. These definitions do not take into consideration patient factors such as age or existing comorbidities, which clearly influence not only the influence of the cancer over survival and life-expectancy, but greatly impact on treatment decisions as well. Since the men investigated in the autopsy studies, by inclusion criteria, died of unrelated causes not knowing that they had prostate cancer, technically speaking, all of the specimens would have clinically insignificant disease.

In our most recent autopsy study, prostate cancer prevalence increased with age.[21] We first detected prostate cancer in a 42 year old man. Although overall 43% of the tumors were clinically significant by histological definition, all but one of the tumors in men under the age of 60 were insignificant, and clinical significance correlated with age thereafter (Fig. 2). Half the cancers were multifocal, the majority were Gleason sore of 6 or less. It was the larger tumors which were also less well differentiated, while 80 % of tumors less than 0.5 ml were of Gleason score of 6 or less. This data should not be interpreted that younger man would not be diagnosed with clinically significant or high risk disease; we simply did not encounter this variety of prostate cancer in our autopsy study. Possibly men with such more aggressive disease would have presented with an elevated PSA or clinical manifestations of prostate cancer and could have been selected out.

Our data also provided useful information for clinicians by mapping out the location of the tumors and indicating the recommended biopsy regimen to identify most of the clinically significant tumors.[21]

CONCLUSIONS

The clinical incidence, mortality, and to a lesser degree prevalence of prostate cancer varies among various geographical regions of the world. The approach to screening, early detection initiatives, and availability of treatment modalities has a major impact on disease epidemiology. The differing role of genetic and environmental factors in prostate cancer carcinogenesis is yet to be elucidated. Autopsy studies provide important information toward the understanding of the prevalence of the disease, data which will lead to the rational design of diagnostic initiatives, and the diagnosis of those tumors which need to be identified and treated. There is a paucity of clinical and epidemiologic data from African populations, and this will need to be remedied in the immediate future as attention is focused on cancer care in Africa.

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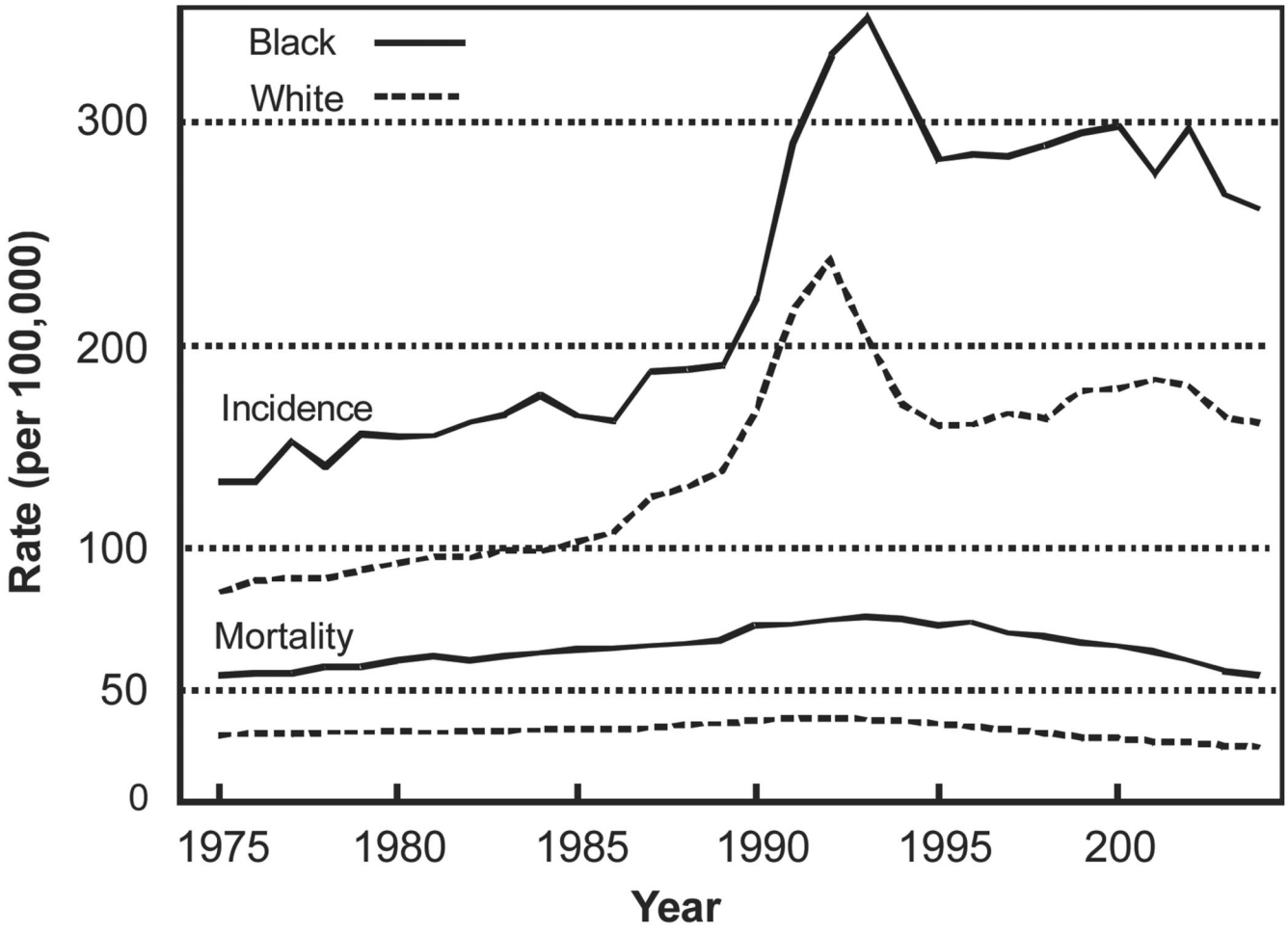

Fig. 1.
Age-adjusted total US incidence and mortality rates for prostate cancer, all ages.. 1995-2004.
Age-adjusted to the 2000 US Std Population

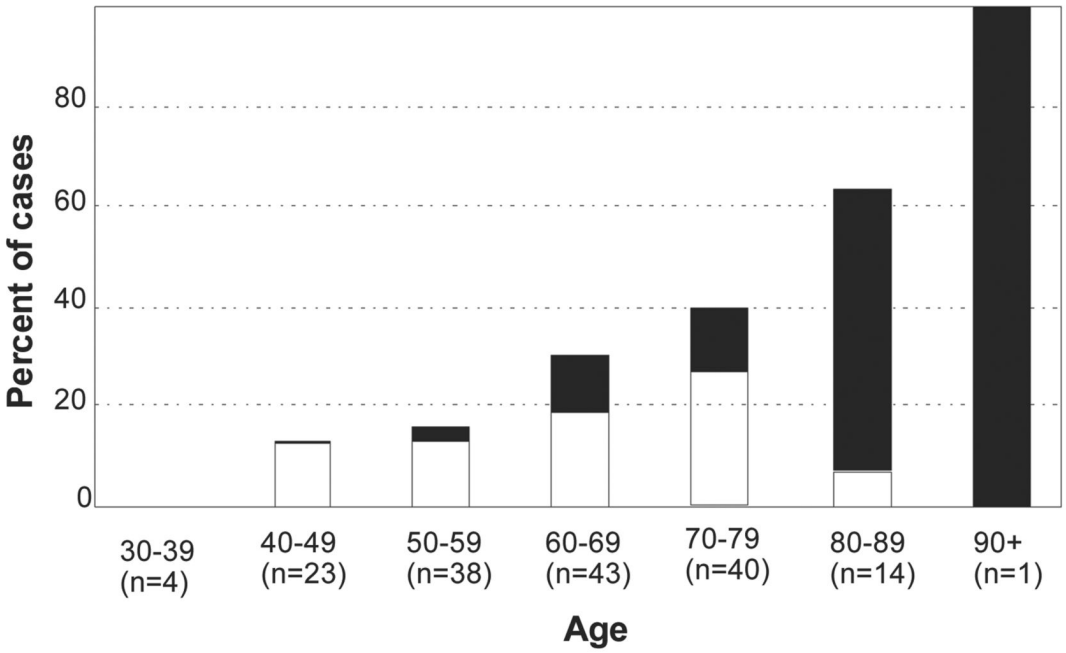

Fig. 2.
Prevalence of prostate cancer in autopsy cases with increasing age[34].

Table 1

Age-standardized incidence of prostate cancer (per 100,000) in the world

Africa	Congo	29.0
	Kenya	16.6
	Senegal	7.5
	Uganda	38.0
	Zimbabwe	27.4
North America	Canada	78.2
	US	124.8
	US, White	107.8
	US, Black	185.4
Asia	China	1.7
	Taiwan	3.0
	Israel	47.5
	Japan	12.6
	Korea	7.6
	Thailand	4.5
Europe	Austria	71.4
	Austria, Tyrol	100.1
	Austria, Vorarlberg	66.4
	France	59.3
	Hungary	34.0
	Iceland	75.2
	Norway	81.8
	Spain	35.9
	Sweden	90.9
	Switzerland	77.3
	UK	52.2
Oceania	Australia	76.0
	New Zealand	100.9

Note: Rates are age-adjusted to the WHO world standard population.

Sources: http://www-dep.iarc.fr/

Table 2

Age-standardized mortality of prostate cancer (per 100,000) in the world

Africa	South Africa	22.6
	Uganda	32.5
	Senegal	6.5
	Zimbabwe	23.5
Asia	China	1.0
	Israel	13.4
	Japan	5.7
Europe	Austria	18.4
	France	18.2
	Germany	15.8
	Hungary	18.4
	Iceland	23.0
	Italy	12.2
	Norway	28.4
	Spain	14.9
	Sweden	27.7
	UK	17.9
North America	US	15.8
	Canada	16.6
Oceania	Australia	17.7
	New Zealand	20.3

Note: Rates are age-adjusted to the WHO world standard population.

Sources: http://www-dep.iarc.fr/.

Table 3

Autopsy prevalence of prostate cancer in the world

Age	US White[3]	US Black[3]	Japan[19]	Spain[28]	Greece[29]	Hungary[30]
21-30	8	8	0	4	0	0
31-40	31	31	20	9	0	27
41-50	37	43	13	14	3	20
51-60	44	46	22	24	5	28
61-70	65	70	35	32	14	44
71-80	83	81	41	33	31	58
81-90			48		40	73