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Original article

Trends in prostate cancer incidence and mortality in a mid-sized Northeastern Brazilian city☆

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A B S T R A C T

Objective: International data have reported prostate cancer as the most frequent among men, and the third highest in mortality. A rise in incidence has been observed in the course of recent decades, probably influenced by early detection, mainly in asymptomatic men, through regular screening with prostate-specific antigen (PSA) testing. The purpose of this study was to contribute to information on trends in prostate cancer incidence and mortality using population-based data.

Methods: This was an exploratory ecological study of time trends, aiming at describing changes in prostate cancer incidence and mortality in Aracaju, Sergipe, Brazil, from 1996 to 2006. Rates were calculated from data of the Registro de Câncer de Base Populacional de Aracaju. Trends were calculated using the Joinpoint Regression Program.

Results: For the study period, 1,490 incident cases and 334 deaths were included. Incident cases were more common after 50 years of age, and deaths after 55 years. Age-standardized incidence rates of 46.6 and 50.0/100,000 were observed in the early years of the series, and then progressively increased, with rates higher than 100.0/100,000 in later years. For mortality, age-standardized rates varied from 21.6 and 16.6/100,000 to 24.1 and 28.9/100,000 in later years. Joinpoint analysis identified one joinpoint for the incidence series, resulting in two trends, the first with annual percent change of 34% and the second with 5.8%; for the mortality series no joinpoint was identified, and the annual percent change was 2.1%.

Conclusion: There was a sharp increase in incidence rates during the study period, probably due to screening. Mortality rates had a small upward trend, and did not show major changes during the study period.

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Tendências temporais de incidência e mortalidade por câncer de próstata em uma cidade de médio porte do nordeste brasileiro

Palavras-chave:
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RESUMO

Objetivo: Dados internacionais apontaram o câncer de próstata como o mais incidente e o terceiro em mortalidade entre os homens. O aumento da incidência tem sido observado nas últimas décadas, provavelmente por causa da detecção precoce, principalmente em homens assintomáticos, através do rastreamento regular com dosagem do antígeno prostático específico (PSA). O objetivo do estudo foi contribuir com as informações sobre as tendências de incidência e mortalidade por câncer de próstata a partir de extratos populacionais.
Métodos: Tratou-se de um estudo ecológico exploratório de tendências temporais, visando descrever as mudanças de incidência e mortalidade por câncer de próstata em Aracaju, SE, Brasil, no período de 1996 a 2006. As taxas foram calculadas a partir dos dados do Registro de Câncer de Base Populacional de Aracaju e as tendências temporais foram determinadas pelo Joinpoint Regression Program.
Resultados: No período do estudo, 1490 casos incidentes e 334 mortes foram incluídos. Os casos incidentes foram mais frequentes a partir de 50 anos de idade e as mortes a partir de 55 anos. Taxas padronizadas de incidência de 46,6 e 50,0/100.000 foram observadas nos primeiros anos da série, e um aumento progressivo acima de 100,0/100.000 foi observado nos últimos anos. Para a mortalidade, as taxas padronizadas variaram de 21,6 e 16,6/100.000 para 24,1 e 28,9/100.000. A análise do Joinpoint identificou duas tendências para a incidência, a primeira com percentual de mudança de 34,0% e a segunda com percentual de 5,8%; para a mortalidade, a análise resultou em uma tendência com percentual de 2,1%.
Conclusão: Houve um grande aumento nas taxas de incidência, provavelmente devida ao rastreamento, durante o período de estudo. A mortalidade, entretanto, mesmo com uma pequena tendência de aumento, não apresentou grandes mudanças no tempo estudado.
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Introduction

International data have reported prostate cancer as the most frequent among men, and the third highest in mortality.[1] In Brazil, prostate cancer has been the most incident cancer and the second most common cause of cancer-related death in men.[2,3] A rise in incidence has been observed in the course of recent decades, probably influenced by early detection, mainly in asymptomatic men. Published data in Europe have shown an increase in prostate cancer incidence since the 1990s, with figures higher than 7% yearly.[4] Despite this increase in incidence being related to early detection, a negative impact in mortality rates has not been consistent.[4,5]

Prostate cancer risk has increased with age, due to individual factors and diminished antitumor mechanisms, and has rarely been diagnosed under the age of 50. Prostate cancer five-year survival rates have been rising in high income countries, surpassing 70%, while in low income countries it has usually been below 50%.[6]

The aim of screening has been to identify men in the general population who have had no suspicion of prostate cancer; however, this approach has been controversial because prostate cancer mortality rates have remained stable, and have not shown differences between screened and non-screened groups. Another feature of this disease has been that it has often followed an indolent form that would not progress to aggressive forms if left untreated. Others, on the contrary, have stated that there should be a subset of lethal disease and, for that subset, screening could provide a chance for cure.[1,4,5]

In the 1990s, the concept of screening adult men for prostate-specific antigen (PSA) was introduced, aiming at decreasing morbidity and mortality caused by advanced disease. Since then, increased incidence has been observed and asymptomatic tumors have been detected.[4] As to the mortality rates, some studies have not shown significant changes after the advent of PSA testing,[4,6] while others have.[7,8]

In Brazil, screening has not been conducted systematically, and PSA testing has been applied opportunistically, usually at the suggestion of the patient or his physician; however, there has been growing awareness that screening should be performed.

Current evidence has been questioning the routine use of screening for prostate cancer with PSA testing.[9] Due to its growing incidence, this cancer has inflicted a great burden on society, especially with population aging.

The purpose of this study has been to contribute with information on trends in prostate cancer incidence and mortality using population-based data from 1996 to 2006 in the municipality of Aracaju, capital of the Northeastern Brazilian state of Sergipe, and to provide means to implement control strategies for this common cancer.

Methods

This was an exploratory ecological study of time trends, aimed at describing changes in prostate cancer incidence and mortality in Aracaju, Sergipe, Brazil. Incidence data were obtained from the database of the Registro de Câncer de Base Populacional de Aracaju (Cancer Registry). The Cancer Registry actively collected cancer cases from public and private sources such as hospitals, diagnostic and treatment clinics, pathology laboratories, units that provide comprehensive cancer treatment, and from governmental databases such as: the mortality system, the systems of information on hospital and outpatient procedures, and the system of information on breast and cervical cancer. The Cancer Registry followed the rules organized by the International Agency for Research on Cancer (IARC) as defined by the Brazilian National Cancer Institute (Instituto Nacional do Câncer – INCA). All cases of invasive prostate cancer diagnosed in the years of reference were included for analysis. The means of diagnosis considered were: histology, cytology, imaging, clinical and laboratory evidence, and surgical findings. Duplicity of cases was managed by Cancer Registry software, which verified available information in the several sources and databases. Classification and coding were performed according to the International Classification of Diseases for Oncology, 2nd edition (ICDO-2) until 2004, and the 3rd edition (ICD-3) from 2005 on. For publication reference, the International Classification of Diseases, 10th edition (ICD-10) was used. For mortality, the ICD-10 was also used. The topography considered was C61. The database prepared for analysis contained all invasive cancer cases, except non-melanoma skin cancer. Mortality data were retrieved from the Mortality Database of the State of Sergipe, which provided information for the National Mortality Database. The Cancer Registry, as a branch of the State Health Agency, had full access to the mortality database, including the digitalized death certificates.

All invasive prostate cancer cases and all prostate cancer deaths identified from 1996 to 2006 were included for analysis. Crude rates (CR) and age-standardized rates (ASR), adjusted by the world population,[10,11] were calculated using the official software of the Cancer Registry.[12] Trends in incidence and mortality were calculated using the Joinpoint Regression Program,[13] version 3.5.2, which was developed for non-commercial use by the National Cancer Institute, USA. This software has been broadly used to estimate future trends of time series based on the calculation of the annual percent change (APC). This program assumed the model based on a minimal number of joinpoints where statistically significant changes in time trends would occur, enabling to test whether an apparent change in trend would be statistically significant. A logarithmic linear regression model added join points from 0 to 5, and calculated the difference up to a statistically significant value, using the Monte Carlo permutation test.[14] Thus, the APC was calculated to define time trends in prostate cancer incidence and mortality. A significant increase of a trend was defined as the slope of the curve being statistically significant ($p < 0.05$).

Results

From 1996 to 2006, 1,490 cases of invasive prostate cancer were identified by the Cancer Registry of Aracaju, and 334 deaths were retrieved from the mortality database for analysis.

Table 1 shows the incidence and mortality data of the time series. Age-standardized incidence rates of 46.6 and 50.0/100,000 were observed in the early years; incidence progressively increased over the subsequent years, with rates higher than 100.0/100,000. Age-standardized mortality

Table 1 – Prostate cancer incidence, mortality, and mortality-to-incidence ratio in Aracaju, Sergipe, Brazil, for the period of 1996 to 2006.

	Incidence			Mortality			M:I
Year	n	Crude rate	ASR	n	Crude rate	ASR	
1996	52	26.0	46.6	23	11.5	21.6	0.44
1997	53	26.1	50.0	18	8.9	16.3	0.34
1998	88	42.7	79.3	23	11.2	20.7	0.26
1999	124	59.5	113.5	33	15.8	28.0	0.27
2000	139	64.4	114.8	35	16.2	26.2	0.25
2001	126	57.5	97.7	31	14.2	23.3	0.25
2002	148	66.8	113.6	35	15.8	24.8	0.24
2003	155	69.1	117.9	27	12.0	18.0	0.17
2004	191	84.1	139.8	32	14.1	23.6	0.17
2005	223	95.6	165.2	35	15.0	24.1	0.16
2006	191	80.8	145.1	42	17.8	28.9	0.22
Total	1,490	–	–	334	–	–	–
Average	–	61.0	107.6	–	13.8	23.2	–

ASR, age-standardized rate (world population); M:I, mortality-to-incidence ratio.

rates showed variation from 21.6 and 16.6/100,000 to 24.1 and 28.9/100,000 in the later years of the series. The mortality-to-incidence ratio, which expresses the risk of dying of prostate cancer, had a mean value of 0.25.

Age-standardized incidence and mortality rates increased with age. Higher incidence rates were observed for the following age groups: 50 to 54 years = 70.5/100,000; 55 to 59 years = 195.0/100,000; 60 to 64 years = 376.2/100,000; 65 to 69 years = 786.0/100,000; 70 to 74 years = 1112.6/100,000; 75 to 79 years = 1462.6/100,000; 80 to 84 years = 1901.0/100,000; and 85 years and above = 1935.7/100,000. Higher mortality rates were identified for the following age groups: 55 to 59 years = 23.3/100,000; 60 to 64 years = 42.9/100,000; 65 to 69 years = 94.6/100,000; 70 to 74 years = 187.6/100,000; 75 to 79 years = 473.4/100,000; 80 to 84 years = 655.3/100,000; and 85 years and above = 1042.1/100,000.

Joinpoint analysis identified one joinpoint for the incidence series, separating two trends: 1996 to 1999, and 1999 to 2006 (Table 2). For incidence, the 1996 to 1999 trend had a sharp significant increase with an APC of 34%; the 1999 to 2006 trend showed a less steep slope (Fig. 1), still with a significant APC of 5.8%, which was equal to the average annual percent change (AAPC) of the last five years the series, the latter correlating better with future trends. For the mortality series, the number of joinpoints was zero, and the whole series was considered as a single trend. The APC of the single trend and the AAPC of the last five years was 2.1% (the confidence interval included 0, thus not being significantly different from the 0 joinpoint at alpha = 0.05) (Table 2), showing a less steep slope of the mortality trend (Fig. 1).

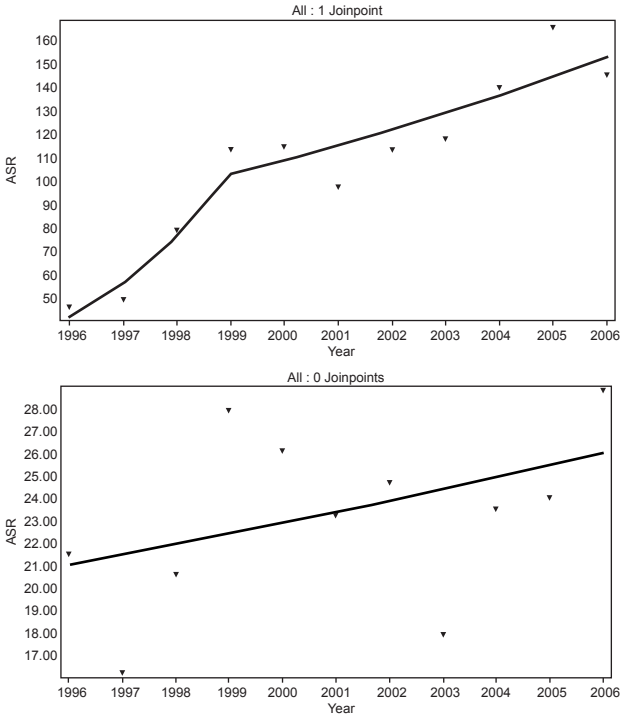

Fig. 1 – Joinpoint for prostate cancer incidence and mortality in Aracaju, Sergipe, Brazil, 1996-2006. ASR, age-standardized rate (world population).

Discussion

Prostate cancer incidence has been showing increasing rates in Western countries but conversely lower rates in Asia;[15] however, there has been a trend of rising incidence rates globally, mainly because early tumors have been diagnosed more often.[4,16] In Brazil, reports have shown incidence rates of 112.1/100,000 in Brasilia DF, 99.3/100,000 in Goiania, and 86.4/100,000 in São Paulo.[17] In the present study, ASIRs of 46.6 and 50.0/100,000 in the early years of the series might reflect two points: first, that these were the beginning years of the Cancer Registry of Aracaju and case collection was not comprehensive; and second, that PSA testing was not systematically used at that time. Increasing ASIRs have been observed over time. Aracaju had a comparatively high incidence rate of prostate cancer with an average ASR of 107.6/100,000, and even higher if the last eight years of the series are considered, with an average rate of 125.9/100,000.

Incidence time trends presented APC of 34.0% for the 1996 to 1999 period and then a less steep pattern of ascension with APC of 5.8%. International data have shown that future estimates can be more precisely performed using data from the most recent years. The AAPC based on the five last observations also showed an increasing tendency of 5.8%. This pattern of ascension is remarkable compared to international data, despite the great variance of the reported data.[15,18,19]

The trend of diagnosing prostate cancer in earlier stages has been observed worldwide; it has also been shown that the average age at diagnosis has decreased.[20] The increasing incidence rates might be due to several diagnostic means resulting in discovering early tumors; however, in population-

Table 2 – Joinpoint analyses of prostate cancer incidence and mortality with the annual percent change (APC), the average annual percent change (AAPC) and 95% confidence interval (CI).

	Trend 1			Trend 2			Last five years	
	Years	APC	CI	Years	APC	CI	AAPC	CI
Incidence	1996-1999	34.0[a]	2.1-75.0	1999-2006	5.8[a]	0.8-11.1	5.8[a]	0.8-11.1
Mortality	1996-2006	2.1[b]	-1.3-5.7	_	_	–	2.1[b]	-1.3-5.7

[a]The APC and AAPC are significantly different from zero at alpha = 0.05;
[b]The APC and AAPC are not significantly different from zero at alpha = 0.05.

based studies, staging has not been broadly referred.[18] Despite the uncertainty about the impact of PSA testing over mortality, there has been no doubt about its effect on incidence.[21] Some studies have not only reported advances in other diagnostic means such as echography and biopsy material, but also have demonstrated great development in medical and surgical therapy.[2,18]

It cannot be said that the mortality rates have remained unchanged over the last decades; actually, there has been a slight decreasing tendency.[18] The present study showed that age-standardized mortality rates had an increasing trend with APC of 2.1%, which is contrary to data observed in high-income countries,[4,8,16] but still comparable with Brazilian reports.[3] An average ASR of 23.2/100,000 was calculated, considering the whole series of 1996 to 2006. The mortality-to-incidence ratio of 0.25 is a good predictor of survival and is similar to data observed in high income countries.[22]

Another point to be discussed is the actual benefit derived from screening and subsequent treatment, since prostate cancer has been diagnosed predominantly in older men with comorbidities, as confirmed by the present data. In a study of PSA testing, it was estimated that 1,410 men needed to be screened and 48 treated in order to avoid one death.[23] Conversely, other studies have stated that in countries where screening was systematic there has been remarkable decreases in mortality rates.[8,24] This should be taken into account since prostate cancer often shows favorable outcomes.

PSA screening for prostate cancer has been a matter of discussion worldwide. Evidence has been provided that screening may lead to over-diagnosis and consequently to over-treatment of indolent disease. Current means of diagnosis and treatment could lead to undesirable morbidity and mortality. Since the benefit of the test has been controversial, especially in older men, most guidelines have not supported population screening; however, testing should be available upon physician and patient request. Early diagnosis of high-risk tumors might lead to more effective treatments and improved survival, but it has not been easy to select those patients needing treatment from those who could be observed. Mortality rates have declined in high-income countries since the initiation of PSA screening, but it has been debated whether this was the actual reason and alternative factors have been proposed, such as the use of hormonal treatment for asymptomatic bulky disease.[25] There has been growing evidence that screening has little impact on mortality, and effort should be made to identify high-risk patients that could benefit from early diagnosis and treatment.

Limitations

The Cancer Registry of Aracaju has collected cancer cases for the whole state of Sergipe to select the cases from the capital, Aracaju. This practice, although comprehensive for case identification, has resulted in delay to close the annual data base, and case ascertainment has been more tedious. Since several sources of information have been used, cases could be found in more than one source, and thus, extra care has been exercised to avoid duplication. There has been a number of cases where place of residency could not be determined; after consulting all sources and databases, a few cases still had to be excluded. Mortality rates have been calculated from the official State Mortality Database; cause of death has been called into question and could jeopardize conclusions.

Conclusion

Worldwide prostate cancer incidence rates have increased sharply, as also observed in the present study, probably due to a screening effect. For mortality rates, differently from international data, a slight increasing trend has been observed. This study did not aim to analyze the causes of the increase in incidence rates and the impact on mortality rates; more research needs to be conducted to determine which patients might benefit from screening and treatment without unnecessary interventions, and to better design strategies to reduce prostate cancer mortality.

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Conflict of interest

All authors declare to have no conflict of interest.

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