

# Prostate Cancer Survival and Mortality according to a 13-year retrospective cohort study in Brazil: Competing-Risk Analysis

*Sobrevida e mortalidade por câncer da próstata no Brasil por 13 anos em um estudo de coorte retrospectivo: Análise de riscos competitivos*

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**ABSTRACT:** *Objective:* To analyze cancer-specific mortality (CSM) and other-cause mortality (OCM) among patients with prostate cancer that initiated treatment in the Brazilian Unified Health System (SUS), between 2002 and 2010, in Brazil. *Methods:* Retrospective observational study that used the National Oncological Database, which was developed by record-linkage techniques used to integrate data from SUS Information Systems, namely: Outpatient (SIA-SUS), Hospital (SIH-SUS), and Mortality (SIM-SUS). Cancer-specific and other-cause survival probabilities were estimated by the time elapsed between the date of the first treatment until the patients' deaths or the end of the study, from 2002 until 2015. The Fine-Gray model for competing risk was used to estimate factors associated with patients' risk of death. *Results:* Of the 112,856 studied patients, the average age was 70.5 years, 21% died due to prostate cancer, and 25% due to other causes. Specific survival in 160 months was 75%, and other-cause survival was 67%. For CSM, the main factors associated with patients' risk of death were: stage IV (AHR = 2.91; 95%CI 2.73 – 3.11), systemic treatment (AHR = 2.10; 95%CI 2.00 – 2.22), and combined surgery (AHR = 2.30, 95%CI 2.18 – 2.42). As for OCM, the main factors associated with patients' risk of death were age and comorbidities. *Conclusion:* The analyzed patients with prostate cancer were older and died mainly from other causes, probably due to the presence of comorbidities associated with the tumor.

**Keywords:** Prostatic neoplasms. Survival. Mortality. Aged. Comorbidity. Unified Health System.

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**RESUMO:** *Objetivo:* Analisar a mortalidade câncer-específica (MCE) e a mortalidade por outras causas (MOC) em pacientes diagnosticados com câncer da próstata que iniciaram tratamento no Sistema Único de Saúde (SUS) entre 2002 e 2010, no Brasil. *Métodos:* Estudo observacional retrospectivo utilizando a “Base Nacional em Oncologia”, desenvolvida por meio de pareamento determinístico-probabilístico dos sistemas de informação do SUS: Ambulatorial (SIA), Hospitalar (SIH) e de Mortalidade (SIM). Probabilidades de sobrevivência específicas do câncer e por outras causas foram estimadas pelo tempo decorrido entre a data do primeiro tratamento até a morte do paciente ou o final do estudo, de 2002 a 2015. O modelo de riscos competitivos de Fine & Gray foi utilizado para estimar os fatores associados ao risco de morte do paciente. *Resultados:* Dos 112.856 pacientes estudados, a idade média foi de 70,5 anos, 21% foi a óbito devido ao câncer de próstata e 25% por outras causas. A probabilidade de sobrevida específica em 160 meses foi de 75% e a por outras causas de 67%. Na CSM, os principais fatores associados ao risco de óbito dos pacientes foram: estágio IV (AHR = 2,91; IC95% 2,73 – 311), tratamento sistêmico (AHR = 2,10; IC95% 2,00 – 2,22) e cirurgia combinada (AHR = 2,30; IC95% 2,18 – 2,42). Na MOC, os principais fatores associados ao risco de óbito do paciente foram idade e comorbidades. *Conclusão:* Os pacientes com câncer da próstata analisados mostraram-se mais velhos e faleceram principalmente por outras causas, provavelmente devido às comorbidades associadas ao tumor. *Palavras-chave:* Neoplasias da próstata. Sobrevida. Mortalidade. Idoso. Comorbidade. Sistema Único de Saúde.

## INTRODUCTION

Prostate cancer is the second most frequent cancer and the fifth leading cause of cancer death in men worldwide. In 2018, the incidence and mortality estimates registered about 1.3 million new cases and 358,989 deaths in the world<sup>1,2</sup>. In Brazil, 68,220 new prostate cancer cases and 15,391 deaths were estimated in 2018<sup>3</sup>. The incidence and mortality rates of prostate cancer worldwide are strongly related to age, with the highest incidence observed in older men, and almost 55% of all deaths occurred in men aged over 65 years<sup>4</sup>. The increase in incidence in Brazil is also related to population aging and, as in other countries, to the spread of Prostate-Specific Antigen (PSA) in the 1990s in the diagnosis of this neoplasm<sup>4-6</sup>.

In the medical literature, well-established risk factors for prostate cancer are advanced age, ethnicity, genetics, and family history<sup>4</sup>. Age is the main risk factor for prostate cancer; approximately 60% of diagnosed cases occurred in men aged over 60 years<sup>7</sup>. Considering that prostate cancer mainly affects older adults, they may present comorbidities in the diagnosis<sup>4-7</sup>. Consequently, the risk of dying from the prostatic neoplasms may be difficult to be observed due to other causes<sup>8-13</sup>. The event that hinders or modifies the possibility of observing the main event is named competitive event<sup>8-13</sup>. By interpreting the results of survival studies, in which death is the event of interest, competitive risks are an important issue to be assessed. Therefore, methods specifically designed for such analyses should be employed, such as Fine and Gray's method for competitive risks<sup>13-17</sup>, whereas many studies use traditional methods such as the Kaplan-Meier estimator and Cox's proportional hazards model<sup>18,19</sup>.

Analytical studies are needed to assess survival in different countries. Such studies can use information produced by their health systems such as cancer registries or administrative databases<sup>19,20</sup>. There is a growing trend toward the use of large administrative databases (big data) to investigate health outcomes. These datasets allow to identify many patients across a broad spectrum of comorbidities, providing information regarding disparities in care and outcomes, such as mortality and survival, at local, state, and national levels in the countries<sup>20,21</sup>. Cancer survival analysis based on big data supports the public health system for preventing new cases, extending survival after cancer diagnosis, and reducing inequalities in access to cancer treatment<sup>17-21</sup>.

To date, to the best of the authors' knowledge, there are no population-based studies that investigate the factors associated with the survival probability of patients diagnosed with prostate cancer in Brazil. In addition, a survival model best suited to the case of prostate cancer was used, the competitive risk model. The advantage of using this model is that the other causes of death are considered in the estimates of the model parameters, in such a way the risks are more accurately estimated. A better understanding about the survival probability of patients diagnosed with prostate cancer and the associated factors may enable us to develop actions aiming to improve the health care, besides contributing to the current scientific knowledge. Thus, the aims of this study were to analyze the survival probability of patients diagnosed with prostate cancer in the Brazilian Unified Health System (SUS), who have initiated oncologic treatment from 2002 to 2010, and factors associated with risk of death by prostate cancer and other causes according to SUS information systems in Brazil.

## METHODS

### DATA SOURCE

This is an observational retrospective cohort study evaluating time elapsed between the onset of oncologic treatment at SUS and the death of the prostate cancer patient. The data source was the National Oncological Database, a national population-based cohort that comprises all records of patients under oncological treatment in the SUS, between 2001 and 2015. This database is a subset from the National Database of Health and was developed by record-linkage techniques used to integrate data from the major SUS Information Systems: the Outpatient Information System (from Portuguese, *Sistema de Informações Ambulatoriais* – SIA-SUS), the Hospital Information System (*Sistema de Informações Hospitalares* – SIH-SUS), and the Mortality Information System (*Sistema de Informações sobre Mortalidade* – SIM-SUS), from 2000 to 2015, in order to enable the cohort follow-up. The SIA-SUS contains data on the national provision of outpatient care, such as chemotherapy, radiotherapy, exceptional drugs, and renal replacement therapy in SUS. The SIH-SUS deals with information about hospital admissions in the SUS, with data from the national provision of all care in the hospital. The SIM-SUS deals with population-based information on mortality in Brazil<sup>22</sup>.

## STUDY POPULATION

According to the National Oncological Database, 317,484 men with prostate cancer were identified, who received outpatient oncological treatment at SUS between 2001 and 2015. Following the criteria adopted in this study, patients who initiated outpatient cancer treatment at SUS between January 1<sup>st</sup>, 2002 and July 31, 2015; with ages from 19 to 100 years were included.

In data analysis, patients without information on staging (n = 91,711), with stage 0 (n = 13,291), follow-up time, in days, less than one (n = 99), and with first treatment date prior to January 1<sup>st</sup>, 2002 and after December 31, 2010 (n = 99,527) were excluded. In the end, 112,856 patients were studied.

## DEFINITION OF VARIABLES

The response variable consisted in the time elapsed from the date of the first oncological treatment to the date of death by prostate cancer or other causes or the final date of the studied follow-up (July 31, 2015).

The variables analyzed were: age at the beginning of follow-up, age group (19–59, 60–69, 70–79, or ≥80 years old), geographic region of the patient's residence (Southeast, Northeast, South, Midwest, and North) in the first register, cancer stage at the moment of diagnosis (I, II, III, or IV), first treatment received by patients (radiotherapy, systemic treatment, radiotherapy and systemic treatment, combined surgery with systemic treatment or radiotherapy), number of the Elixhauser Comorbidity<sup>23</sup> (0, 1-3, or ≥4), and number of hospital admissions (0, 1, 2, 3, 4, or ≥5). The patients' length of stay ranged from 1 to 2,920 days during the entire period of the cohort follow-up. Cancer stage was measured at the start of treatment and classified according to the TNM classification of malignant tumors by the Union for International Cancer Control (UICC)<sup>24</sup>. To calculate the number of comorbidities as proposed by Elixhauser<sup>23</sup>, all codes of the International Classification of Diseases (ICD-10) registered in the National Database of Health were retrospectively investigated. The look-back period was extended until the oldest date of the database records (01/01/2000). Therefore, all patients had at least one complete year as look-back period to register comorbidities. Deaths were computed using the ICD-10 code C61.

## STATISTICAL ANALYSIS

Demographic and clinical characteristics of the patients included in the study were described with proportions, measures of position, and variability. In the analysis of cancer-specific mortality (CSM), death by prostate cancer (C61) should be present in the primary cause of the death certificate, but also in one of the underlying causes. On the other hand, other ICDs not related to malignant prostate neoplasms were considered as competitive events. Concerning

the analysis of other-cause mortality (OCM), death from other causes was considered the event of interest, whereas death from prostate cancer (C61) was deemed the competitive event. In both analyses, patients who did not experience the event of interest or the competitive event, or who were not found on the SIM-SUS database until July 31, 2015, were excluded.

In order to estimate cancer-specific and other-cause survival probabilities at each time period, the Aalen-Johansen nonparametric estimator<sup>25</sup>, which considers the presence of competitive events, was used. Probabilities of death from prostate cancer or other causes at a specific time period of 163 months were obtained through Cumulative Incidence Function (CIF)<sup>26</sup>, which considers the presence of competitive risks, thus being equivalent to the Aalen-Johansen estimator. The test of Gray<sup>27</sup> was used to verify accumulated equality incidences among categories of evaluated covariates on the presence of competitive risks. All covariates with p-value on Gray's test associated with a significance level lower than 0.10 were included in the Fine-Gray multiple regression model<sup>28</sup>, which allows to model risk subdistribution through covariates in order to estimate the factors associated with patients' mortality risk.

The proposition of proportionality among failure rates over time according to the Fine-Gray<sup>28</sup> model was verified using the proportionality test<sup>29</sup>. This test evaluates whether there are evidences in Pearson correlation between times and standardized Schoenfeld residuals for each covariate different from zero, as correlations close to zero indicate there is no evidence for rejecting the hypothesis of proportional failure rates. Furthermore, graphical analyses of standardized Schoenfeld residuals against time were conducted for each covariate from the final model. Residuals with lack of patterns over time reinforce the validity of failure rate proportionality.

The statistical procedures were executed in the R software, version 3.5.1. The Survival, Chron, Cmprsk, and RiskRegression libraries were used.

## RESULTS

The population of this study consists in 112,856 patients who initiated oncological treatment at SUS in Brazil between 2002 and 2010 (Supplementary Material Table 1). From these patients, 23,167 (20.5%) died from prostate cancer and 27,382 (24.3%) from other causes, and 62,307 (55.2%) were censored. The total time of follow-up was 163 months, an average time of 70.7 months ( $SD \pm 40.3$ ), and a median of 70 months.

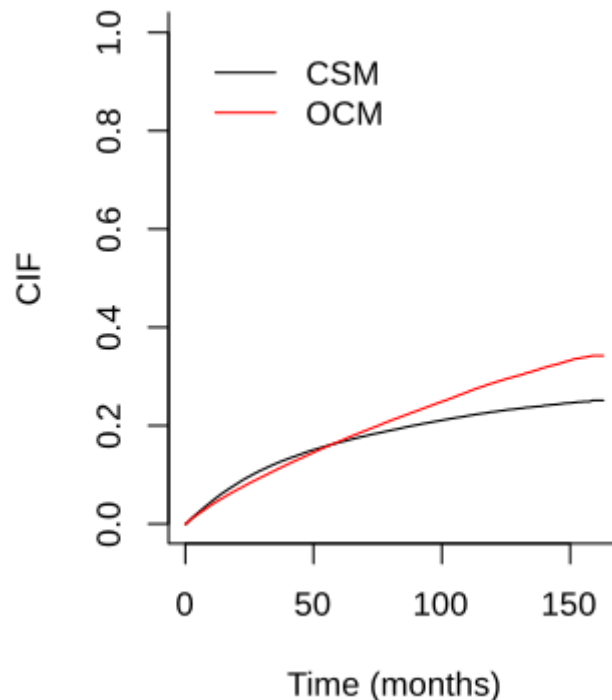
According to the demographic characteristics, the average age of the patients was 70.5 ( $SD \pm 9.0$ ) years and most patients aged between 60 and 80 years or over (88.7%), and over half patients (53.2%) resided in the Southeast region. Regarding clinical and treatment characteristics, 56.4% of patients were diagnosed in advanced stages (III and IV). Most treatment modalities were systemic treatment (32.6%), most patients presented one to four comorbidities (87.8%), and 63.4% required one or more hospital admissions (Supplementary Material Table 1).

Supplementary Material Table 2 presents the cancer-specific and other-cause survival probabilities and survival time. The general specific survival probability in 160 months was 75% (0.75), and from other causes, 67% (0.67). Specific and other-cause survival decreased as patients' age

advanced. Among those aged from 70 to 79 years, and 80 years or over, specific survival probability was 75% (0.75) and 69% (0.69) respectively; as for other-cause survival probability, 61% (0.61) and 55% (0.55) respectively. The South region presented the lowest survival probabilities, 69% (0.69) for cancer-specific and 64% (0.64) for other-cause. The probability of cancer-specific survival decreased with advancing stages of the disease, presenting 60% (0.60) in stage-IV patients. Patients who underwent systemic treatment or combined surgery had lower probabilities compared with other treatment modalities. Concerning survival from other causes, tumor stage and treatment modalities did not present clear tendencies in the estimations.

Figures 1 and 2 present the curves from the Cumulative Incidence Function (CIF), which calculated failure probability from an event of interest, considering the presence of competitive risks. In Figure 1, in curves up to 50 months of follow-up, the death probability from prostate cancer is similar to death from other causes; however, risk of death from other causes is higher until the end of follow-up.

Figure 2 presents the CIF according to the categories of the exposure variables considered in the study. For every category, both regarding death from prostate cancer and death from other causes, comparison among every curve showed statistically significant differences in the test of Gray ( $p < 0.05$ ).



CSM: Cancer-specific mortality; OCM: Other-cause mortality.

Figure 1. Cumulative Incidence Function (CIF) for data of patients diagnosed with prostate cancer and treated between 2002 and 2010 in the Brazilian Public Health System (SUS), Brazil.

Table 1 presents the models of Fine and Gray for Cancer-Specific Mortality (CSM) and Other-Cause Mortality (OCM) in prostate cancer patients. The risk of death from prostate cancer increased 2% as the patients' age advanced, and 3% in in relation to death from other causes. Patients who lived in the South region showed risk increased by 13% (Adjusted Hazard Ratio [AHR] = 1.13; 95%CI 1.10 – 1.17) in prostate cancer death and 7% (AHR = 1.07; 95%CI

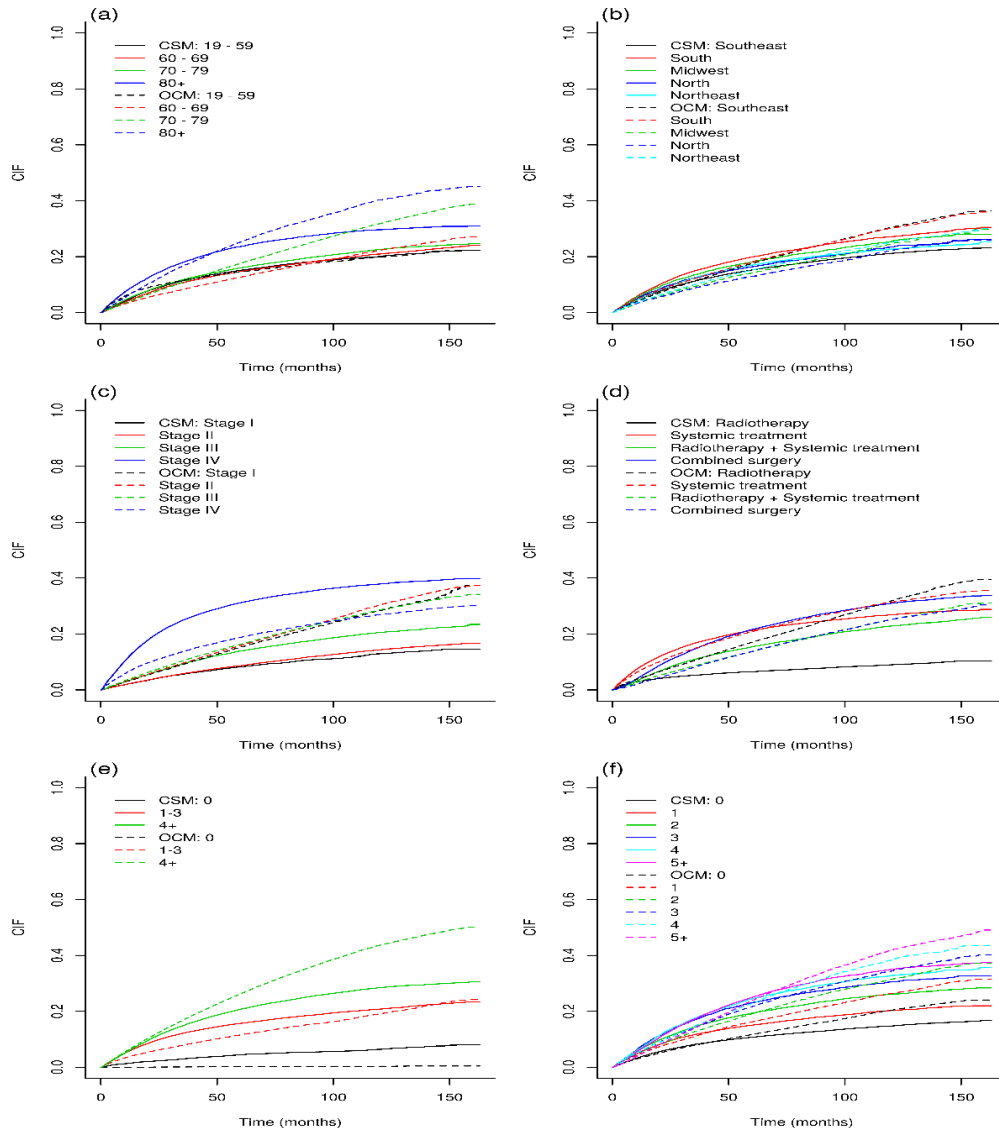


Figure 2. Cumulative Incidence Function (CIF) concerning cancer-specific mortality (CSM) and other-cause mortality (OCM) according to the categories of the exposure variables of patients diagnosed with prostate cancer and treated between 2002 and 2010 in the Brazilian Public Health System (SUS): (a) age range; (b) region of residence; (c) cancer stages; (d) first treatment; (e) number of Elixhauser comorbidity; and (f) number of hospital admissions.

Table 1. Estimates obtained for the Fine-Gray model adjusted to the data of patients diagnosed with prostate cancer and treated between 2002 and 2010 in the Brazilian Public Health System (SUS), Brazil.

Predictors	Cancer-Specific Mortality (Csm)		Other-Cause Mortality (Ocm)	
	Simple	Adjusted	Simple	Adjusted
	HR (95%CI)	HR (95%CI)	HR (95%CI)	HR (95%CI)
Age in years	1.02 (1.02 – 1.02)**	1.02 (1.01 – 1.02)**	1.03 (1.03 – 1.03)**	1.03 (1.02 – 1.03)**
Region of residence				
Southeast	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
South	1.34 (1.29 – 1.38)**	1.13 (1.10 – 1.17)**	1.00 (0.97 – 1.03)	1.07 (1.03 – 1.10)**
Midwest	1.22 (1.15 – 1.29)**	0.99 (0.93 – 1.04)	0.77 (0.73 – 0.81)**	0.84 (0.80 – 0.89)**
North	1.10 (1.02 – 1.18)*	1.05 (0.97 – 1.12)	0.69 (0.64 – 0.75)**	0.82 (0.76 – 0.89)**
Northeast	1.10 (1.06 – 1.14)**	1.00 (0.97 – 1.04)	0.81 (0.79 – 0.84)**	0.90 (0.87 – 0.93)**
Cancer stages				
Stage I	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Stage II	1.12 (1.04 – 1.19)**	1.06 (0.99 – 1.13)	1.07 (1.02 – 1.12)*	1.11 (1.06 – 1.16)**
Stage III	1.70 (1.59 – 1.82)**	1.37 (1.28 – 1.47)**	1.04 (0.99 – 1.09)	1.13 (1.07 – 1.18)**
Stage IV	3.89 (3.65 – 4.15)**	2.91 (2.73 – 3.11)**	1.06 (1.01 – 1.11)*	1.09 (1.04 – 1.15)**
First treatment				
Radiotherapy	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Systemic treatment	2.61 (2.48 – 2.74)**	1.99 (1.88 – 2.09)**	0.77 (0.74 – 0.80)**	0.72 (0.69 – 0.74)**
Radiotherapy + systemic treatment	3.43 (3.27 – 3.60)**	2.10 (2.00 – 2.22)**	1.09 (1.05 – 1.12)**	1.00 (0.97 – 1.04)
Combined surgery	3.76 (3.57 – 3.95)**	2.30 (2.18 – 2.42)**	0.78 (0.75 – 0.81)**	0.63 (0.61 – 0.66)**
Number of Elixhauser comorbidity	1.06 (1.05 – 1.06)**	1.01 (1.01 – 1.02)**	1.13 (1.12 – 1.13)**	1.15 (1.14 – 1.15)**
Number of hospital admissions	1.07 (1.07 – 1.07)**	1.06 (1.05 – 1.06)**	1.08 (1.07 – 1.08)**	0.98 (0.97 – 0.98)**

\*Estimated mean time in relation to 163 months of follow-up; \*\*no 95%CI and SD have been added to the means.



1.03 – 1.10) in other causes compared with patients living in the Southeastern region. In the remaining regions, the patient's risk of death from cancer and other causes is smaller than in Southeastern region. In terms of tumor staging, there was increased risk of death from prostate cancer as tumor stage increased, almost tripling in stage IV (AHR = 2.91; 95%CI 2.73 – 3.11) compared with stage I. The risk increased from stage II to III, but decreased in stage IV, showing an inconclusive pattern of tumor staging regarding death from other causes. Among treatment modalities the patients underwent, systemic treatment or combined surgery showed more expressive risks of death due to prostate cancer when compared with radiotherapy, with combined surgery having the worst prognosis (AHR = 2.30; 95%CI 2.18 – 2.42). Concerning death from other causes, treatment modalities demonstrated better prognosis, that is, decreased risk of death when compared with radiotherapy at the end of follow-up. The number of Elixhauser comorbidity showed a 1% increase (AHR = 1.01; 95%CI 1.01 – 1.02) in risk of death from prostate cancer for each additional comorbidity affecting the patients, and a 15% increase (AHR = 1.15; 95%CI 1.14 – 1.15) in risk of death from other causes. Regarding number of admissions, risk of death from prostate cancer increased 6% (AHR = 1.06; 95%CI 1.05 – 1.06) after each admission, although there is a reduction in mortality due to other causes.

The Pearson correlation between time and standardized Schoenfeld residuals were all close to zero, indicating proportionality among subdistribution failure rates of death from prostate cancer and other causes (Supplementary Material Table 3). The graphical analysis of Schoenfeld residuals reinforced the proportionality hypothesis.

## DISCUSSION

### KEY RESULTS

This study analyzed the survival probability of 112,856 patients diagnosed with prostate cancer, who started oncologic treatment in SUS, accounting for more than 13 years of follow-up. On average, a patient diagnosed with prostate cancer survived about 8.5 years after receiving the first treatment. The probability of cancer-specific survival at 160 months was 75%, and that of other causes, 67%. The risk of specific death from prostate cancer increased with advancing age; residing in the South region; being classified with a higher tumor stage (almost tripling in stage IV); having undergone systemic treatment or surgery combined with other treatments as the initial modality of treatment; having some comorbidity; and increased number of hospital admissions. The risk of death from other causes increased with patients' advancing age and having some comorbidity.

### INTERPRETATIONS

Regarding the event of interest, death due to prostate cancer, the proportion of patients dying from other causes (24.3%) was higher than death from prostate cancer (20.5%). Furthermore, a

proportion of 89% was verified for patients aged over 60 years (average age of 70.5 years), demonstrating a profile of older patients, with most of them (88%) presenting more than one comorbidity. Similarly, many studies have shown that prostate cancer affects older men, who have other diseases in addition to the tumor, thus affecting survival and risk of death in these individuals<sup>6-13</sup>.

Moreover, many studies have shown that due to the long natural history of prostate cancer, a many patients might succumb to other causes, as verified in studies conducted by Daskivich et al.<sup>8</sup> and Abdollah et al.<sup>9,10</sup> analyzing mortality from prostate cancer and other causes in the United States of America, with data from the SEER-Medicare linked database (Surveillance, Epidemiology and End Results – SEER); Briganti et al.<sup>30,31</sup>, according to the European Multicenter Prostate Cancer Clinical and Translational Research Group (EMPaCT), and Boehm et al.<sup>32</sup>, using SEER data, analyzed the OCM in individuals treated with radical prostatectomy, brachytherapy, external beam radiation therapy, and androgen deprivation therapy. The authors stated that most patients, analyzed for 10 years of follow-up, have died from other causes rather than from prostate cancer. Likewise, these authors have used competitive risk of death in their methodology as well.

As for the cancer-specific and other-cause survival probability estimated at 13.5 years, patients presented survival rates of 75% and 67%, respectively. These results are similar to the study of Abdollah et al.<sup>9,10</sup>, conducted in the USA, with specific and other-cause survival rates being 73% and 69%, respectively, in 10 years. The authors used a database with health registers from diverse localities throughout the USA, similar to the database used in the present study. Hospital-based studies or treatment centers may differ in relation to the survival probability. The study conducted by Stone and Stock<sup>33</sup> analyzed the survival of 1,669 patients in the USA by estimating specific and other-cause survival probabilities over 10 years of follow-up, accounting for 98.1% and 86.8% respectively. Prognosis was much better than those presented by the patients in this study. Such differences can be attributed to the origin of the data used in such studies – hospital-based data *versus* population-based cancer registries and the methodology used in data analysis. Hospital-based records refer to cases treated in an institution. They ensure the monitoring of these patients and also contribute to the patients' individual care<sup>11</sup>. Huang et al.<sup>34</sup> state that population-based cancer registries play an important role in improving care programs aimed at cancer patients, assessing care patterns, estimating survival, and providing evidence-based results for physicians, researchers, and public health policymakers.

Considering both estimated events, on average, patients have survived for 8.5 years from total follow-up time. This aspect reinforces the long natural history of this cancer compared with other types of cancer, considering that patients might live with the disease for a long time and, depending on the age and clinical conditions, they may be followed up in active surveillance in many cases<sup>31,35,36</sup>.

The competitive risk model was used to estimate patients' mortality. In both models, CSM and OCM, the risk of death increased 2% and 3%, respectively, as the patients' age advanced. Abdollah et al.<sup>9,10</sup> found an increase in risk of death of 4% and 10%, respectively. Hoffman<sup>7</sup> has found an increase of 4% in risk of death and Boehm et al.<sup>32</sup>, 0an increase of 7% regarding OCM as the patients' age advanced.

The South region had a higher risk of death in CSM and OCM compared with other regions. The incidence and mortality rates are the highest in the country<sup>3</sup>. This could overestimate survival and risk of death among patients from this region in the present study.

Risk of death in CSM increased as tumor stage increased, tripling in stage IV, although this pattern was not observed for OCM; in this case, the risk decreased for stage-IV patients, which indicates staging is more important for death due to prostate cancer. Hsiao et al.<sup>37</sup> developed a study in the USA, in which they found stage-IV patients with a 60% specific cancer survival in a 10-year period, most of whom received systemic treatment, and differences in survival mainly depended on the patients' age. Similarly, patients in stage IV of this study showed 60% of specific survival in a 10-year period and most of them were treated with systemic treatment. However, in OCM, patients' risk of death in other treatment modalities was smaller compared with those undergoing radiotherapy. Finally, patients with many comorbidities had higher risk of death, mainly in OCM. Briganti et al.<sup>30,31</sup>, when investigating CSM and OCM risks in patients with prostate cancer, reported that age and comorbidities were the main determinants of OCM, whereas their impact on CSM was negligible. Regarding CSM, hospitalized patients had increased risk of death, whereas for OCM there was a smaller risk, which could indicate patients would be more closely monitored for presenting other diseases.

Limitations in the use of an administrative database must be mentioned, such as failures in filling out clinical information, difficulty in coding procedures, absence of socioeconomic and demographic variables, and also in the use of the death certificate as a source of cause of death. Attention to underreporting and inadequate data filling must be paid, considering that the percentage of ill-defined causes may imply an overestimation of the survival probability. In this study, it was not possible to include patients who underwent exclusive surgery due to their lack of information of cancer stage at the onset of treatment. The lack of data from these patients must be mentioned, taking into account that surgery is commonly the treatment modality recommended for patients on early stages of prostate cancer. However, these limitations are overcome by the benefits of using a large database that includes the entire population of patients treated for cancer in SUS.

Furthermore, deaths of patients from other causes were higher than deaths from prostate cancer, which was related to the higher proportion of older patients and the greater number of comorbidities in this population. The risk factors associated with patients' deaths were age, comorbidities, and tumor staging, considering that most patients were diagnosed in stages III and IV and were mainly treated with systemic therapy. These results highlight the need for diagnosing prostate cancer patients at earlier stages, so that they receive curative and non-palliative treatments at the appropriate time in the Brazilian Unified Health System.

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