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Research Article

Competing Risk of Specific Mortality in Prostate Cancer Patients in Brazil: A Retrospective Cohort Study

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Background: Prostate cancer is among the most common malignancies worldwide and a leading cause of premature mortality in men. Although survival rates have improved globally, disparities persist. Here, we aim to analyze the risk factors associated with prostate cancer-specific mortality among patients in a southeastern Brazilian state.
Methods: We conducted a retrospective cohort study using data from 10,556 patients diagnosed with prostate cancer between 2000 and 2016. Data were extracted from hospital-based cancer registries linked to the state Mortality Information System. Patients were followed up for a minimum of 5 years and classified as alive, deceased from prostate cancer, or deceased from other causes. Subdistribution hazard ratios (SHRs) were estimated using Fine–Gray competing-risks models.
Results: By the end of 2021, 6388 patients were alive, 1936 had died from prostate cancer, and 2232 had died from other causes. Older age increased prostate cancer-specific mortality (SHR per 10 year increment = 1.098; 95% CI: 1.024–1.176), while distant metastasis was the strongest clinical predictor (SHR = 5.315; 95% CI: 4.676–6.041). Higher educational attainment remained statistically associated with lower prostate cancer-specific mortality in the multivariable competing-risks model (SHR = 0.767; 95% CI: 0.629–0.935), although the protective effect was attenuated after adjustment. Surgery (SHR = 0.382; 95% CI: 0.309–0.471) and radiotherapy (SHR = 0.477; 95% CI: 0.396–0.575) were also associated with lower cancer-specific mortality, while hormone therapy remained associated with higher mortality, reflecting treatment selection among patients with a more advanced disease rather than a causal treatment effect.
Conclusion: Age, education, metastatic disease, and treatment modalities were significantly associated with prostate cancer-specific mortality. These findings reinforce the importance for equitable access to early diagnosis pathways and curative treatment options and highlight the value of competing-risks methods for accurately estimating prostate cancer outcomes in population-based settings.

Keywords: competing risks; mortality; neoplasms; prostate cancer; survival analysis

1. Introduction

Cancer is one of the leading causes of death worldwide and remains a major barrier to increasing life expectancy [1]. Among every 10 premature deaths attributed to chronic noncommunicable diseases, 3 are due to cancer [1]. In most countries, malignant neoplasms rank as the first or second leading cause of premature mortality before the age of 70 [2]. Globally, the burden of cancer incidence and mortality is rising rapidly. This trend reflects demographic shifts—particularly population aging and accelerated growth—as well as changes in the prevalence and

distribution of major cancer risk factors, many of which are linked to ongoing socioeconomic, epidemiological, and nutritional transitions [2, 3].

Prostate cancer, specifically, is among the most common malignancies globally and represents a significant cause of premature mortality in men [2, 3]. In Brazil, the National Cancer Institute (INCA) estimates nearly 72,000 new prostate cancer cases annually for the 2023–2025 period, with an estimated incidence rate of 67.86 and a mortality rate of 13.7 deaths per 100,000 men [4]. Although prostate cancer has a high incidence, the majority of cases are diagnosed at early stages, when the tumor remains confined to the prostate gland. The 5 year survival rate for prostate cancer in the United States is approximately 98% [5]. However, despite observed decreases in mortality in certain Brazilian regions during some years, projections indicate a 53.3% increase in prostate cancer deaths by 2025. This trend is largely attributed to population aging, increased life expectancy, and late-stage diagnoses [6].

Well-established risk factors for prostate cancer include advanced age, ethnicity, genetic predisposition, family history of cancer, and hormonal influences [3–5, 7]. Although robust evidence for the primary prevention of prostate cancer remains limited, modifiable lifestyle factors such as reducing dietary fat intake, increasing the consumption of fruits and vegetables, and engaging in regular physical activity may help lower the risk [7, 8].

While prior studies have investigated the risk factors associated with the development of prostate cancer [9–11], relatively few have focused on the predictors of prostate cancer-specific mortality [11–13]. This gap is particularly pronounced in low- and middle-income countries (LMICs) such as Brazil. Furthermore, estimating the risk of death due to specific versus noncancer causes has become an increasingly relevant component of public health surveillance [13]. Incorporating competing risk analyses in survival studies is essential for producing more accurate and unbiased mortality estimates [14, 15].

In this context, this study aims to analyze the risk factors associated with prostate cancer-specific mortality among patients in a southeastern Brazilian state.

2. Materials and Methods

2.1. Study Design and Patients. Brazil's Sistema Único de Saúde (SUS) is the world's largest publicly funded universal health system, providing healthcare to over 190 million users [16]. Recognized internationally for its scale and impact, the SUS spans all 5570 municipalities across the country and has significantly expanded healthcare access and reduced inequalities over its 30 years of existence [16].

Study was conducted in the State of Espírito Santo, located in southeastern Brazil, with a total area of 46,098.1 km^2 and an estimated population of 4.02 million, unevenly distributed across 78 municipalities and 10 microregions. Approximately half the population resides in the Metropolitan Region of Vitória, which includes the capital, Vitória, and six neighboring municipalities: Cariacica, Fundão, Guarapari, Serra, Viana, and Vila Velha. Espírito Santo borders the Atlantic Ocean (east), Bahia (north), Minas Gerais (west/northwest), and Rio de Janeiro (south) (Figure 1) [17].

We performed a retrospective observational cohort study using secondary data from the state's hospital-based cancer registries (HCR) (RHC, Registros Hospitalares de Câncer) linked to the state Mortality Information System. Access to these databases was authorized by the Cancer Surveillance Division of the Espírito Santo State Health Secretariat (SESA/ES).

The Oncology Care Network of Espírito Santo is structured into three health regions—North/Central, Metropolitan, and South—and includes one High Complexity Oncology Center (CACON), the Santa Rita de Cássia Hospital (Vitória), and seven High Complexity Oncology Units (UNACONs): the Evangelical Hospital of Cachoeiro de Itapemirim (Cachoeiro de Itapemirim), Vila Velha Evangelical Hospital (Vila Velha), Antônio Cassiano de Moraes University Hospital, Santa Casa de Vitória Hospital, and Nossa Senhora da Glória State Children's Hospital (all in Vitória), São José Hospital (Colatina), and Rio Doce Hospital (Linhares). All oncology hospitals maintain structured RHCs, with annual submissions to the National Cancer Registry Integrating System (SIS-RHC) [17–20] (Figure 1).

2.2. Procedures. A total of 10,560 records of prostate cancer diagnoses (ICD-10 code C61) from 2000 to 2016 were extracted from the HCR of Espírito Santo. All records of men aged over 18 who received care within the state's oncology network and were registered with a diagnosis of malignant neoplasm of the prostate (ICD-10: C61) during this period were included. Four records were excluded due to invalid age entries (0 or 999), resulting in a final sample of 10,556 men treated in oncology units across the state (Figure 2). The follow-up period extended until death from any cause or censoring on December 31, 2021.

Data were collected from June to October 2023 through the deterministic linkage [21] of the HCR and the state Mortality Information System (SIM). Standardization and deduplication procedures were applied, including formatting of dates, names, and municipality fields. Matching variables included patient and mother's names (and their phonetic codes), date of birth, sex, and municipality. Manual review used residence address, diagnosis date, and death date to confirm true matches.

The HCR uses a standardized Tumor Registration Form, developed by INCA and endorsed by IARC/WHO, comprising 44 variables (35 mandatory), covering sociodemographic, clinical, treatment, and outcome data. This form enables systematic extraction of medical record information and integration into the SIS-HRC database [22].

Baseline variables collected included age at diagnosis, race/skin color (white/nonwhite), marital status (married/not married), education level (none, elementary, secondary/higher), state of residence, referral source (Public Health System (SUS)/Private/Insurance), and history of prior diagnosis or treatment. Tumor-specific variables included diagnostic basis, histological type, multiple primaries, TNM stage, distant metastasis, first treatment modality (e.g.,

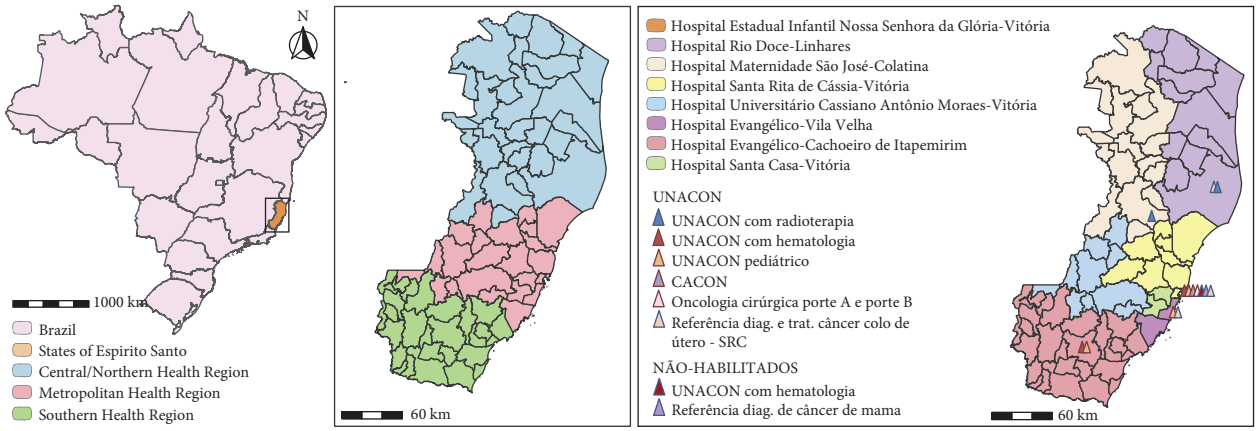

Figure 1: Geographic location.

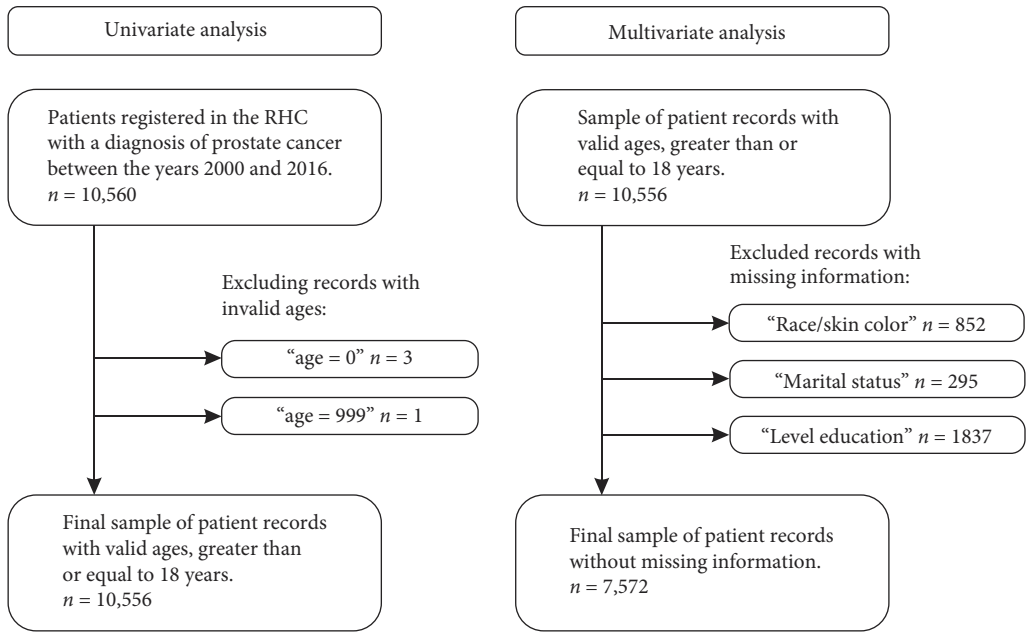

Figure 2: Flowchart of sample selection for univariate and multivariate analyses.

surgery, radiotherapy, hormone therapy), treatment outcome, cause of death, and date of death.

2.3. Statistical Analysis. Descriptive statistics were presented as absolute and relative frequencies. The Gray test was used to estimate the cumulative incidence function (CIF) in the presence of competing risks [23], comparing the incidence of prostate cancer-specific mortality versus other causes of death [23, 24]. Variables with statistically significant differences between groups were included in univariate and multivariate Fine–Gray subdistribution hazard models to assess factors associated with prostate cancer-specific mortality [25, 26]. Subdistribution hazard ratios (SHRs) and 95% confidence intervals (CIs) were reported. Given the high proportion of missing values for some clinical variables, and because the patterns of missingness were likely not at random, no imputation methods were applied, as they would require strong and unverifiable assumptions about the missing data mechanism. Instead, we used complete-case analysis for the multivariable Fine–Gray model while acknowledging the potential for selection bias and loss of precision. All analyses were performed using RStudio (version 2023.06.2) and R (version 4.3.1). Statistical significance was set at $\alpha = 0.05$. The full variable selection process for the multivariate model is illustrated in Figure 2.

3. Ethical Statement

This study was approved by the Research Ethics Committee of the Federal University of Espírito Santo (Approval No. 5.533.541). Authorization to access secondary and restricted data were granted by the Espírito Santo State Health Department based in Vitória. The requirement for informed consent was waived due to the use of secondary data from a historical cohort spanning 15 years, with many patients already deceased at the time of the study.

4. Results

4.1. Baseline Characteristics. The study sample included 10,556 cases of malignant prostatic neoplasms registered in the HCR (RHC) of Espírito Santo, Brazil, diagnosed between 2000 and 2016.

Table 1 summarizes the sociodemographic and clinical characteristics of the cohort. The mean age at diagnosis was 69.2 years (SD = 9.1), with 70.4% of patients aged 65 or older. Most patients identified as nonwhite (63.4%) were married (65.9%) and had no formal education or only primary education (63.6%).

Regarding clinical characteristics, 66.8% were referred through the Unified Health System (SUS) and 95.2% presented with a single primary tumor located in the prostate. Most patients (62.1%) had no prior treatment at the time of diagnosis. Adenocarcinoma was the predominant histological type (98.5%), and 91.7% showed no evidence of distant metastasis at diagnosis.

Initial treatments administered in hospital settings included surgery (23.7%), hormone therapy (22.0%), radiotherapy (19.5%), and combined radiotherapy and hormone therapy (15.2%). Data on clinical TNM staging and disease status following initial treatment were missing in 48.9% and 51.7% of cases, respectively. At the end of follow-up, 60.5% of patients were alive, while 18.3% had died from prostate cancer and 21.1% from other causes.

4.2. Univariate Analysis of Risk Factors for Patients With Prostate Cancer. Table 2 presents the cumulative incidence of death due to prostate cancer and other causes in the presence of competing risks. Prostate cancer-specific mortality was significantly higher ($p < 0.05$) among older patients; those self-identified as Black, multiracial, Asian, or Indigenous; not married; illiterate; referred from the private healthcare system; undiagnosed and untreated at admission; diagnosed with stage IV disease; presenting with distant metastases; treated with hormone therapy; or not undergoing surgery or radiotherapy.

Regarding noncancer mortality, higher cumulative incidence was observed among older patients; those self-identified as White; not married and illiterate individuals; patients without a prior diagnosis or treatment; those with stage IV disease or distant metastases; those treated with hormone therapy or combined hormone therapy and radiotherapy; and those who did not undergo surgery ($p < 0.05$ for all).

Figures 3, 4, 5 illustrate the CIFs for prostate cancer-specific and noncancer mortality, stratified by sociodemographic and clinical variables, in the presence of competing risks.

Visual inspection of the CIF curves (Figures 3, 4, 5) highlights the largest separations between exposure groups among older patients and those with distant metastasis, who exhibited markedly higher cumulative incidence of prostate cancer-specific death. In contrast, patients who underwent surgery or radiotherapy demonstrated substantially lower cumulative incidence curves for cancer-specific mortality. These graphical contrasts reinforce the direction and magnitude of the associations identified in both univariate and multivariate Fine–Gray analyses.

The Fine–Gray univariate regression analysis confirmed that age, race, education, referral source, TNM staging, presence of distant metastases, surgery, radiotherapy, and hormone therapy were significantly associated with prostate cancer-specific mortality ($p < 0.05$). Age at diagnosis, modeled as a continuous variable, indicated a 34% increased risk of death for every 10 year increase in age, as shown in Table 3.

Variables such as "prior diagnosis and treatment" and "combined radiotherapy and hormone therapy" were excluded from the univariate Fine–Gray analysis due to violation of the proportional hazard assumption, as evident in Figures 3, 4, 5. In contrast, age at diagnosis met the proportionality assumption, as supported by the Schoenfeld residuals test ($p = 0.2699$; see Supporting Information 1).

4.3. Multivariate Analysis of Risk Factors for Specific Mortality in Prostate Cancer Patients. In the Fine–Gray multivariate regression analysis, referral source and TNM clinical staging were excluded due to high levels of missing data. The final model included 7572 patients after excluding records with missing values for race/skin color, marital status, and educational level.

As presented in Table 4, age at diagnosis was significantly associated with increased prostate cancer-specific mortality; for every 10-year increase in age, the risk rose by nearly 10% (SHR = 1.098; 95% CI: 1.024–1.176). The presence of distant metastases was a strong predictor of mortality (SHR = 5.315; 95% CI: 4.676–6.041), as was treatment with hormone therapy (SHR = 1.318; 95% CI: 1.166–1.490).

Conversely, patients with intermediate or higher educational attainment had a significantly lower risk of prostate cancer-specific death compared to those with no formal education (SHR = 0.767; 95% CI: 0.629–0.935). Similarly, those who underwent surgery (SHR = 0.382; 95% CI: 0.309–0.471) or radiotherapy (SHR = 0.477; 95% CI: 0.396–0.575) showed a markedly reduced risk of death from prostate cancer.

5. Discussion

In this study, we applied the Fine–Gray proportional hazards model to investigate factors associated with prostate cancer-specific mortality, accounting for the presence of competing risks. The cohort comprised patients diagnosed between 2000 and 2016 and followed until death or censoring. Our findings indicate that age at diagnosis, educational level, presence of distant metastases, surgery, radiotherapy, and hormone therapy were independently associated with specific mortality. The use of a competing risks framework is essential to obtain unbiased survival estimates when alternative causes of death may preclude the event of interest [14, 15].

Prostate cancer remains the second most frequently diagnosed cancer and the fifth leading cause of cancer death

Table 1: Baseline characteristics of all included participants ($n = 10{,}556$).

Variable	N	%
Age at diagnosis (in years)		
Mean (Standard Deviation)	69.2 (9.10)	—
Median (Interquartile Range)	70 (63–76)	—
Age range at diagnosis		
18–64 years	3126	29.61
65 years or older	7430	70.39
Race/Skin color		
White	3010	28.51
No-White	6694	63.41
Missing data	852	8.07
Marital Status		
Married	6959	65.92
Not married	3065	29.04
Missing data	532	5.04
Education Level		
No education	1213	11.49
Basic Education	5505	52.15
Middle or High Education	1238	11.73
Missing data	2600	24.63
State of residence		
Espírito Santo	10,279	97.38
Other state	277	2.62
Referral Source		
Public Health System (SUS)	7047	66.76
Private/Insurance	1835	17.38
Missing data	1674	15.86
Previous diagnosis and treatment		
No Diag/No Treat	2174	20.59
With Diag/No Treat	6555	62.10
With Diag/WithTreat	1673	15.85
Missing data	154	1.46
Most important basis for tumor diagnosis		
Histology of the primary tumor	10,321	97.77
Other	175	1.66
Missing data	60	0.57
Histological type of primary tumor		
Adenocarcinoma	10,400	98.52
Other	156	1.48
Occurrence of more than 1 primary tumor		
No	10,049	95.20
Yes	320	3.03
Uncertain	28	0.27
Missing data	159	1.51
Clinical tumor staging by group (TNM)		
Stage I	735	6.96
Stage II	2545	24,11
Stage III	1017	9.63
Stage IV	1095	10.37
Missing data	5164	48.92
Distant Metastasis		
No	9675	91.65
Yes	881	8.35
Surgery		
No	8053	76.29
Yes	2503	23.71
Radiotherapy		
No	8501	80.53
Yes	2055	19.47
Hormone Therapy		
No	8237	78.03

Table 1: Continued.

Variable	N	%
Yes	2319	21.97
Radiotherapy e Hormone Therapy Combined		
No	8957	84.85
Yes	1599	15.15
Disease status at the end of the first hospital treatment		
No evidence of disease (complete remission)	1880	17.81
Partial remission	243	2.30
Stable disease	1576	14.93
Disease progression	355	3.36
Oncologic supportive care	258	2.44
Death	785	7.44
Missing data	5459	51.71
Outcomes		
Survived at the end of the follow-up period	6388	60.52
Died of Prostate Cancer	1936	18.34
Died of other causes	2232	21.14

Table 2: Cumulative incidence rate (5 years) of death factors in patients with prostate cancer by Gray's test for prostate cancer death and other deaths ($n = 10{,}556$).

Variables	N	PCa death			Other deaths		
		CIF	95% CI	p value	CIF	95% CI	p value
Age range at diagnosis	**10,556**			**< 0.001**			**< 0.001**
18–64 years	3126	7.6	6.7–8.5		4.8	4.1–5.6	
65 years or older	7430	13.5	12.7–14.3		11.9	11.2–12.6	
Race/Skin color	**9704**			**0.025**			**0.036**
White	3010	11.1	10.0–12.2		10,4	9.4–11.6	
No-White	6694	12.2	11.5–13.0		9,1	8.4–9.8	
Marital Status	**10,024**			**0.041**			**0.013**
Married	6959	11.2	10.4–11.9		9.1	8.4–9.8	
Not married	3065	13.0	11.8–14.2		11.3	10.2–12.4	
Education Level	**7956**			**< 0.001**			**0.002**
No education	1213	15.7	13.8–17.9		11.7	10.0–13.6	
Basic Education	5505	11.6	10.8–12.5		9.5	8.7–10.3	
Middle or High Education	1238	9.1	7.6–10.8		6.0	4.7–07.4	
Referral Source	**8882**			**0.043**			0.760
Public Health System (SUS)	7047	10.9	10.2–11.6		9.8	9.1–10.5	
Private/Insurance	1835	13.1	11.6–14.7		8.7	7.5–10.1	
Previous diagnosis and treatment	**10,402**			**0.005**			**< 0.001**
No Diag/No Treat	2174	15.0	13.5–16.5		10.7	9.4–12.0	
With Diag/No Treat	6555	11.1	10.4–11.9		10.5	9.7–11.2	
With Diag/WithTreat	1673	10.0	8.6–11.5		5.1	4.1–6.2	
Clinical tumor staging by group (TNM)	**5392**			**< 0.001**			**< 0.001**
Stage I	735	3.4	2.3–4.9		7.9	6.1–10.0	
Stage II	2545	6.6	5.7–7.6		10.7	9.5–11.9	
Stage III	1017	7.9	6.3–9.6		9.6	7.9–11.5	
Stage IV	1095	46.3	43.3–49.2		13.1	11.1–15.1	
Distant Metastasis	**10,556**			**< 0.001**			**< 0.001**
No	9675	7.9	7.4–8.5		9.7	9.2–10.3	
Yes	881	53.8	50.4–57.0		10.4	8.5–12.6	
Surgery	**10,556**			**< 0.001**			**< 0.001**
No	8053	13.9	13.2–14.7		11.0	10.3–11.6	
Yes	2503	4.8	4.0–5.6		6.1	5.2–7.1	
Radiotherapy	**10,556**			**< 0.001**			0.340
No	8501	13.5	12.8–14.3		10.4	9.8–11.1	
Yes	2055	4.4	3.6–5.4		7.1	6.0–8.3	
Hormone Therapy	**10,556**			**< 0.001**			**< 0.001**
No	8237	9.2	8.6–9.8		8.5	7.9–9.1	
Yes	2319	21.0	19.3–22.6		14.5	13.1–16.0	

Table 2: Continued.

Variables	N	PCa death			Other deaths		
		CIF	95% CI	p value	CIF	95% CI	p value
Radiotherapy e Hormone Therapy Combined	**10,556**			0.300			**0.002**
No	8957	12.0	11.4–12.7		9.8	9.2–10.4	
Yes	1599	10.3	8.8–11.8		9.9	8.5–11.5	

Note: The bold values in Column N indicate only the sample size for each specific variable, whereas the *p* values shown in bold correspond exclusively to those that reached statistical significance (i.e., values lower than 0.05).
Abbreviations: CI, confidence interval; CIF, cumulative incidence function.

among men worldwide [3]. Its incidence continues to rise, particularly in LMICs, where it is the most commonly diagnosed cancer in 112 countries and the leading cause of cancer-related deaths among men in 48, according to GLOBOCAN estimates [2, 3].

By employing a competing risks model, our study provides a nuanced analysis of mortality dynamics in prostate cancer. This approach allows for more accurate estimation of cause-specific mortality by distinguishing deaths attributable to prostate cancer from those due to other causes [26, 27]. In this context, older age and the presence of distant metastases increased the risk of prostate cancer-specific death, while higher educational attainment, surgery, and radiotherapy were associated with reduced mortality. Hormone therapy, in contrast, was associated with an increased risk, possibly reflecting its use in more advanced or less surgically treatable cases. These findings emphasize the importance of early detection and access to curative treatments such as surgery and radiotherapy. They also underscore how social determinants, such as educational level, influence cancer outcomes, reinforcing the need for equity-oriented public health strategies in LMICs.

Being diagnosed with prostate cancer at age 65 or older was identified as a significant risk factor for disease-specific mortality in our cohort. Similar findings have been consistently reported in studies incorporating competing risk models for prostate cancer mortality, reinforcing the increased vulnerability of older patients [28–30]. In broader cohort studies, marital status has been recognized as a predictor of prostate cancer-specific mortality [31, 32]. Married men tend to have lower mortality risk and higher survival rates compared to single, divorced, or widowed individuals [33]. This survival advantage may reflect enhanced social support, greater awareness of disease-related symptoms, and improved adherence to treatment—often facilitated by spouses' involvement in caregiving [34, 35]. However, in contrast to previous evidence, marital status did not emerge as a significant predictor in our analysis.

Race/skin color is a critical variable in prostate cancer research, as individuals of African or Asian descent have been shown to experience higher incidence and mortality rates [7, 8]. Beyond biological factors, this variable often reflects structural disparities, including differential access to timely diagnosis and effective treatment [36–38]. Despite race/skin color being a well-established factor associated with prostate cancer disparities in high-income countries, this association was not statistically significant in our multivariate analysis. This finding may reflect contextual elements of Brazil's universal publicly funded health system (SUS), which reduces direct financial barriers to diagnosis and treatment when compared to insurance-based care models. Therefore, the effect of structural inequities may be partially attenuated in this setting, with clinical severity variables—particularly presence of metastasis—exerting a stronger influence on disease-specific mortality. Similar attenuations in racial gradients have been previously reported in analyses conducted in universal coverage contexts [37].

Lower educational attainment has been consistently associated with delayed diagnosis and treatment of prostate cancer, reducing the likelihood of curative outcomes and increasing mortality [39]. Barriers related to health literacy, limited access to care, and inadequate understanding of disease symptoms often contribute to advanced-stage diagnoses among individuals with lower education and income levels [40]. Men in these groups are also at a higher risk of prostate cancer-related mortality [41]. Although the protective effect of higher educational attainment was attenuated after adjustment, it remained statistically significant in the multivariable competing-risks model. This pattern suggests that the observed association between education and prostate cancer-specific mortality may be mediated through social determinants that are correlated with educational level—such as health literacy, early recognition of symptoms, timeliness of diagnostic entry, and access to curative treatment options. In this sense, education functions as an upstream marker of socioeconomic status and care navigation capacity, rather than an independent biological determinant of risk. Similar findings have been reported in other international population studies evaluating socioeconomic inequalities in prostate cancer outcomes [41].

Additionally, in the context of LMICs, educational attainment captures multiple axes of structural inequality, including differential access to information, screening, early recognition of symptoms, and speed of integration into oncology care pathways, which ultimately shape cancer outcomes and survival inequities [42].

Tumor grade and stage are well-established prognostic indicators in prostate cancer, with advanced stages correlating with poorer survival [5, 7]. In our univariate Fine–Gray analysis, patients diagnosed at stages II, III, and IV had significantly higher mortality risks compared to those diagnosed at stage I, highlighting the critical importance of early detection, as emphasized in prior study [43]. Metastatic prostate cancer remains incurable and is associated with substantial morbidity, often requiring palliative care and resulting in reduced quality of life [44]. In our cohort, the

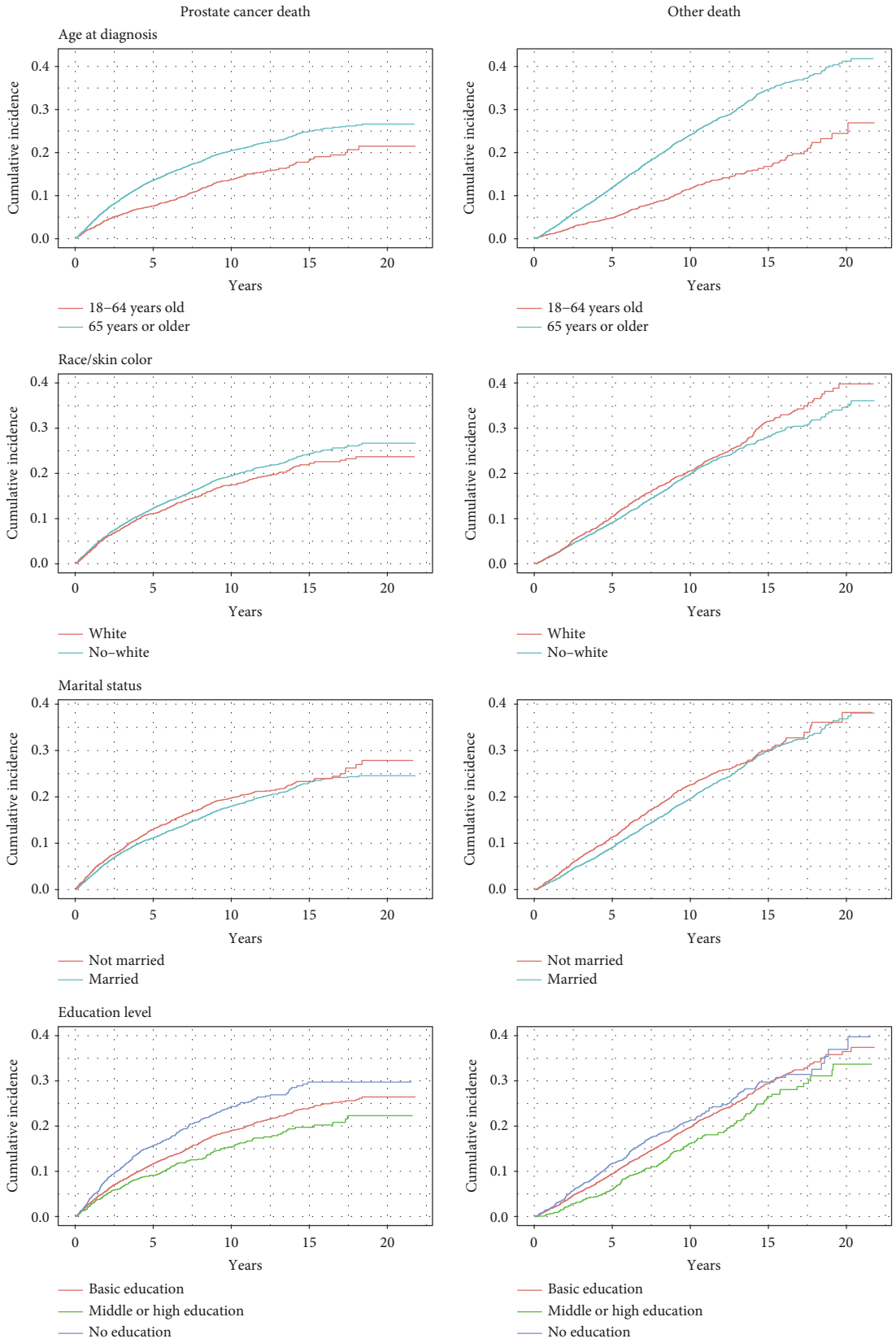

Figure 3: Cumulative incidence function (CIF) related to death from prostate cancer and other deaths stratified by exposure variables age, race/skin color, marital status, and education level of patients diagnosed with prostate cancer between 2000 and 2016 in the Espírito Santo, Brazil ($n = 10{,}556$).

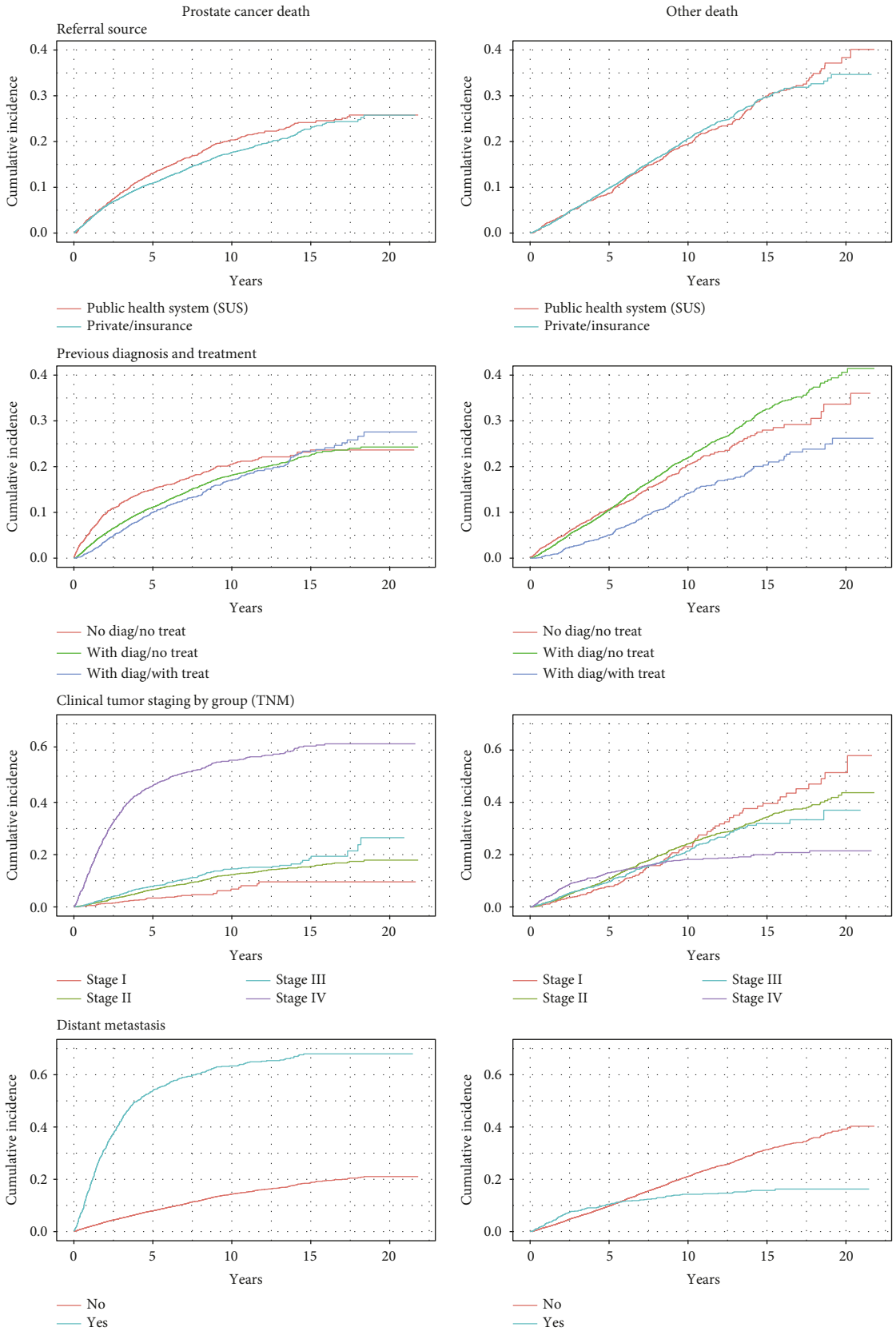

Figure 4: Cumulative incidence function (CIF) related to death from prostate cancer and other deaths stratified by exposure variables referral source, previous diagnosis and treatment, clinical tumor staging by group (TNM) and distant metastasis of patients diagnosed with prostate cancer between 2000 and 2016 in the Espírito Santo, Brazil ($n = 10{,}556$).

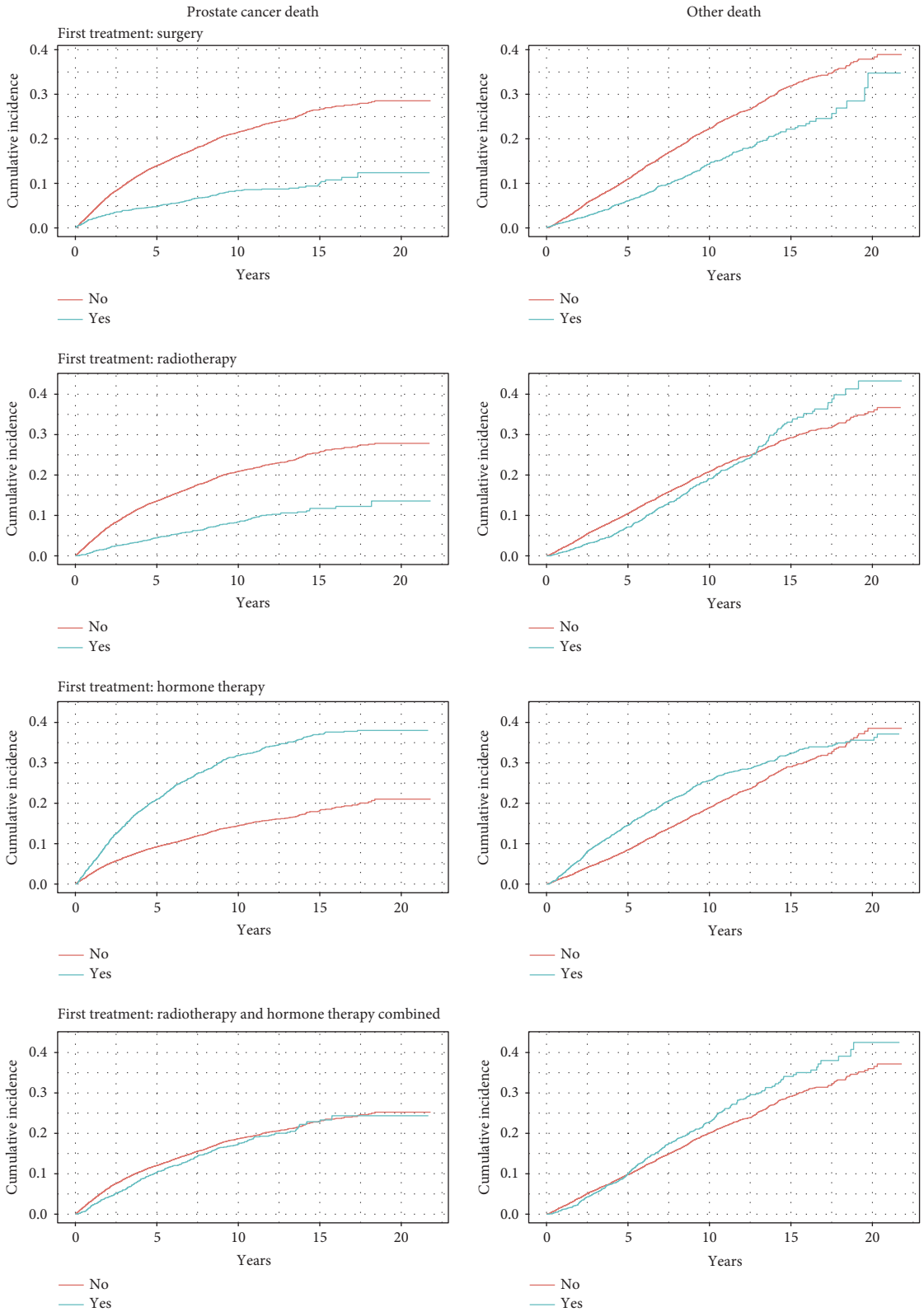

Figure 5: Cumulative incidence function (CIF) related to death from prostate cancer and other deaths stratified by exposure variables first treatment: surgery, radiotherapy, hormone therapy and radiotherapy + hormone therapy combined, of patients diagnosed with prostate cancer between 2000 and 2016 in the Espírito Santo, Brazil ($n = 10{,}556$).

Table 3: Univariate analysis of the risk factors of the specific mortality in patients with prostate cancer for competing risks ($n = 10{,}556$).

Variables	SHR	95% CI	*p* value
Age at diagnosis			
every 10 years increment	1.34	1.27–1.42	< **0.001**
Age range at diagnosis			
18–64 years	1	—	—
65 years or older	1.56	1.40–1.74	< **0.001**
Race/Skin color ($n = 9704$)			
White	1	—	—
No-White	1.11	1.01–1.23	**0.036**
Marital Status ($n = 10{,}024$)			
Married	1	—	—
Not married	1.10	1.00–1.22	**0.050**
Education Level ($n = 7956$)			
No education	1	—	—
Basic Education	0.77	0.68–0.88	< **0.001**
Middle or High Education	0.62	0.52–0.74	< **0.001**
Referral Source ($n = 8882$)			
Public Health System (SUS)	1	—	—
Private/Insurance	1.15	1.03–1.29	**0.017**
Clinical tumor staging by group (TNM) ($n = 5392$)			
Stage I	1	—	—
Stage II	2.13	1.53–2.97	< **0.001**
Stage III	2.51	1.76–3.56	< **0.001**
Stage IV	14.39	10.42–19.88	< **0.001**
Distant Metastasis			
No	1	—	—
Yes	7.10	6.4–7.89	< **0.001**
Surgery			
No	1	—	—
Yes	0.35	0.30–0.40	< **0.001**
Radiotherapy			
No	1	—	—
Yes	0.38	0.33–0.44	< **0.001**
Hormone Therapy			
No	1	—	—
Yes	2.43	2.22–2.66	< **0.001**

Note: The *p* values shown in bold correspond exclusively to those that reached statistical significance (i.e., values lower than 0.05).
Abbreviations: CI, confidence interval; SHR, subdistribution hazard ratio.

presence of distant metastases at diagnosis increased the risk of prostate cancer-specific death by more than fourfold, consistent with findings from other population-based studies [31, 32, 45]. Although TNM staging showed strong associations with prostate cancer-specific mortality in univariate analyses, it was excluded from the multivariate model due to nearly 50% missingness. Because this missingness was not random, imputation was not considered appropriate, as it could artificially increase precision and bias effect estimates. Therefore, complete-case analysis was prioritized to preserve internal validity, although this analytical choice may have attenuated the inclusion of staging-related prognostic variation in the final model.

Conversely, nonmetastatic prostate cancer poses distinct challenges in clinical decision-making due to its generally favorable prognosis, with 10-year cancer-specific survival rates exceeding 98%. However, this favorable outlook must be balanced against the potential morbidity of treatment, particularly urinary incontinence and sexual dysfunction [46]. As such, the standard of care ranges from active surveillance to more aggressive multimodal therapies involving surgery, radiation, and hormonal treatment [46]. Patients must navigate complex trade-offs between the side effects of treatment and the long-term risk of progression to metastatic disease or cancer-specific death within a 10–20 year timeframe [46, 47].

In our study, multivariate analysis accounting for competing risks demonstrated that patients who underwent surgery or radiotherapy had significantly lower risks of prostate cancer-specific mortality compared to those who did not receive these treatments. These findings are consistent with the literature, including Robinson et al. [48], who found no significant difference in prostate cancer-specific survival between surgery and radiotherapy, highlighting that treatment decisions should be guided primarily by expected side effects and patient preferences rather than survival outcomes alone [48].

In contrast, patients treated with hormone therapy exhibited a 33.9% higher risk of death from prostate cancer compared to those who did not receive this treatment. This finding should be interpreted cautiously, as hormone therapy is more frequently indicated in advanced or metastatic disease and in patients who are not suitable

Table 4: Multivariate analysis of the risk factors of the specific mortality in patients with prostate cancer for competing risks ($n = 7572$).

Variables	SHR	95% CI	*p* value
Age at diagnosis			
Every 10 year increment	1.098	1.024–1.176	**0.008**
Race/Skin color			
White	1	—	—
No-White	1.073	0.952–1.209	0.250
Marital Status			
Married	1	—	—
Not married	1.021	0.907–1.149	0.730
Education Level			
No education	1	—	—
Basic Education	0.874	0.755–1011	0.070
Middle or High Education	0.767	0.629–0.935	**0.009**
Distant Metastasis			
No	1	—	—
Yes	5.315	4.676–6.041	< **0.001**
Surgery			
No	1	—	—
Yes	0.382	0.309–0.471	< **0.001**
Radiotherapy			
No	1	—	—
Yes	0.477	0.396–0.575	< **0.001**
Hormone Therapy			
No	1	—	—
Yes	1.318	1.166–1.490	< **0.001**

Note: The *p* values shown in bold correspond exclusively to those that reached statistical significance (i.e., values lower than 0.05).
Abbreviations: CI, confidence interval; SHR, subdistribution hazard ratio.

candidates for curative interventions, such as surgery or radiotherapy. Thus, the increased risk associated with hormone therapy likely reflects treatment selection bias and the unfavorable prognostic baseline of this subgroup, rather than a harmful causal effect of endocrine therapy itself. This interpretation is consistent with current international guideline recommendations, which indicate androgen deprivation therapy primarily for advanced, metastatic, or noncurative settings, and with recent evidence highlighting the prognostic profile of patients selected for endocrine therapy in prostate cancer management [49, 50]. Therefore, the association between hormone therapy and higher cancer-specific mortality observed in this study should be interpreted as reflecting the advanced disease severity of the patients selected to receive endocrine therapy, rather than a direct detrimental causal effect of hormonal treatment.

These associations should not be interpreted as causal treatment effects. Treatment choices in prostate cancer are strongly driven by unmeasured clinical factors such as disease stage, PSA levels, Gleason score, comorbidities, metastatic burden, and performance status—variables not available in our dataset. Therefore, the observed SHRs predominantly reflect treatment selection patterns and underlying disease severity, rather than the intrinsic efficacy of each treatment modality.

5.1. Strengths and Limitations of the Study. To the best of our knowledge, this is among the few studies in Latin America to apply a competing risk methods to prostate cancer-specific mortality. The use of a competing risk framework enhances the accuracy of risk estimates by accounting for the influence of alternative causes of death, thus avoiding overestimation. Nevertheless, as with most studies based on secondary databases, the analysis was constrained by missing data in key variables, which limited their inclusion in the final models. Because complete-case analysis retains only individuals with fully documented variables, it may preferentially select patients with more complete or better-recorded care episodes, which can introduce selection bias and limit generalizability.

6. Conclusions

This study identified age, educational level, presence of distant metastases, surgery, radiotherapy, and hormone therapy as significant factors associated with prostate cancer-specific mortality. These observed associations, particularly those related to treatment modalities, should not be interpreted as causal effects. Surgery and radiotherapy were associated with lower prostate cancer-specific mortality, likely reflecting treatment selection among patients with more favorable clinical profiles and earlier-stage disease. These findings underscore the potential for developing personalized diagnostic and treatment strategies to improve outcomes for prostate cancer patients. Moreover, they offer a framework for other Latin American countries to design equitable health policies within universal health systems, aiming to reduce disparities in cancer care.

Improving access to treatment must be coupled with efforts to enhance early detection, ensuring that patients are diagnosed when therapies are most effective. Finally, this study highlights the growing importance of linking secondary data sources—such as HCR—to estimate cancer outcomes in settings where population-based cancer registries are unavailable.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Disclosure

All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Wesley Rocha Grippa and Luís Carlos Lopes-Júnior designed the research; Wesley Rocha Grippa and Luís Carlos Lopes-Júnior conducted the research; Wesley Rocha Grippa and Luís Carlos Lopes-Júnior analyzed data; Wesley Rocha Grippa and Luís Carlos Lopes-Júnior wrote this article. Wesley Rocha Grippa had primary responsibility for the final content.

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The authors have nothing to report.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. *(Supporting Information)*

Schoenfeld's test for continuous variable "age at diagnosis." This figure displays the Schoenfeld residuals for the continuous covariate age at diagnosis in the Cox proportional hazards model. The residuals are plotted against time to visually inspect deviations from proportionality. The graphical inspection shows no systematic departure from proportionality, as the smoothed line fluctuates randomly around zero without discernible trends. This is further supported by the formal global test, which yielded a non-significant result ($p = 0.2699$), indicating that the proportional hazards assumption holds for age at diagnosis.

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