

The Impact of COVID-19 on the Diagnosis and Treatment of Prostate Cancer in Paraná

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O Impacto da Covid-19 no Diagnóstico e Tratamento do Câncer de Próstata no Paraná

El Impacto del COVID-19 en el Diagnóstico y Tratamiento del Cáncer de Próstata en Paraná

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ABSTRACT

Introduction: The impact of the COVID-19 pandemic on various health areas is undeniable, yet little is known, in numbers, about the effects that the disease and the ensuing isolation had on oncological patients. **Objective:** To analyze the impact of the pandemic on the diagnosis and treatment of prostate cancer in specialized hospitals in the North and Northwest of Paraná, comparing the pre-pandemic and pandemic periods (years 2019, 2020, and 2021). **Method:** Cross-sectional, qualitative and quantitative, *ex-post-facto* study. Men aged 50 to 70 with diagnosis of prostate cancer were selected, and subsequently, a data collection instrument was used to determine if there was a significant difference in the number of diagnoses, health complications, clinical outcomes, and failure in treatment adherence. Data analysis was conducted using Pearson's chi-squared test and *post hoc* analysis with *p*-value correction. **Results:** It was observed that the pandemic significantly affected the number of consultations, especially in 2020, but there was no detriment regarding other variables. **Conclusion:** No failure in treatment adherence was found for these patients, which contributed to many positive outcomes in the course of the disease. **Key words:** COVID-19; Prostatic Neoplasms/diagnosis; Neoadjuvant Therapy; Antineoplastic Protocols; Cancer Care Facilities.

RESUMO

Introdução: É inquestionável o impacto que a pandemia da covid-19 teve sobre as mais diversas áreas da saúde, porém pouco sabe-se, ainda, em números, sobre o efeito que a doença e o isolamento causaram nos pacientes oncológicos. **Objetivo:** Analisar o impacto da pandemia no diagnóstico e tratamento do câncer de próstata em hospitais especializados do Norte e Noroeste do Paraná, comparando os períodos pré-pandêmico e pandêmico (anos de 2019, 2020 e 2021). **Método:** Estudo transversal, quali e quantitativo, de caráter *ex-post-facto*. Foram selecionados homens de 50 a 70 anos com o diagnóstico de câncer de próstata e, posteriormente, o instrumento de coleta de dados foi utilizado para identificar se houve diferença significativa no número de diagnósticos, agravos de saúde, desfechos clínicos e falha na adesão do tratamento. Para a análise de dados, foram utilizados o teste qui-quadrado de Pearson e a análise *post hoc* com correção no valor de *p*. **Resultados:** Observou-se que a pandemia afetou de forma significativa o número de consultas, principalmente em 2020, porém, em relação a outras variáveis, não houve prejuízo. **Conclusão:** Não houve falha na adesão ao tratamento desses pacientes, o que contribuiu para que muitos tivessem desfechos positivos em relação ao curso da neoplasia. **Palavras-chave:** COVID-19; Neoplasias da Próstata/diagnóstico; Terapia Neoadjuvante; Protocolos Antineoplásicos; Institutos de Câncer.

RESUMEN

Introducción: Es incuestionable el impacto que la pandemia de COVID-19 ha tenido sobre las más diversas áreas de la salud, sin embargo, aún se conoce poco, en cifras, el efecto que la enfermedad y el aislamiento causaron en los pacientes oncológicos. **Objetivo:** Analizar el impacto de la pandemia en el diagnóstico y tratamiento del cáncer de próstata en hospitales especializados en el Norte y Noroeste de Paraná, comparando los períodos pre pandémico y pandémico (años 2019, 2020 y 2021). **Método:** Estudio transversal, cuali y cuantitativo, de carácter *ex post facto*. Se seleccionaron hombres de 50 a 70 años con diagnóstico de cáncer de próstata y, posteriormente, se utilizó un instrumento de recolección de datos para determinar si hubo una diferencia significativa en el número de diagnósticos, agravamientos de salud, desenlaces clínicos y fallo en la adhesión al tratamiento. Para el análisis de datos se utilizaron la prueba ji al cuadrado de Pearson y el análisis *post hoc* con corrección en el valor *p*. **Resultados:** Se observó que la pandemia afectó de manera significativa el número de consultas, especialmente en 2020, sin embargo, en relación con otras variables, no hubo perjuicio. **Conclusión:** No hubo fallo en la adhesión al tratamiento de estos pacientes, lo que contribuyó a que muchos tuvieran desenlaces positivos en relación con el curso de la neoplasia. **Palabras clave:** COVID-19; Neoplasias de la Próstata/diagnóstico; Terapia Neoadjuvante; Protocolos Antineoplásicos; Instituciones Oncológicas.

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INTRODUCTION

Cancer is considered one of the greatest public health issues in the world due to it affecting millions of people, being among the top causes of death in several countries. The number of cancer cases and deaths increases every year, being responsible for three out of ten premature deaths. In 2022, there was approximately 20 million new cancer cases in the world, followed by 9.7 million deaths by the disease, with prostate cancer being the fifth main cause of death among men in 2022¹.

According to the National Cancer Institute (INCA)², in Brazil, 704,000 new cancer cases will be reported annually from 2023 to 2025. Excluding non-melanoma skin cancer, breast and prostate cancer are each responsible for approximately 15% of new cases, followed by colon and rectum cancer (9.4%). Moreover, when analyzing the distribution of cases per geographical region, it was observed that 48.4% of new cases were found in the Southeast Region of the country, followed by 22.8% in the Northeast, and 17.1% in the South.

The most prevalent cancer types targeting the male sex (excluding non-melanoma skin cancer) are prostate (30% of cases), colon and rectum (9.2%), trachea, bronchus and lung (7.5%) and stomach (5.6%)². Additionally, when it comes to malign neoplasms, the prognosis can be quite varied and depend on multiple factors, like neoplasm type and location, disease stage, presence or absence of metastasis, among other aspects³. In prostate cancer, the most common among men, the probability of survival is 87.7% in five years, with factors such as old age and metastasis reducing this perspective⁴. These data show that an early diagnosis and a rapid initiation of treatment are determining factors for a good prognosis.

According to the Brazilian Society of Urology (SBU) and INCA⁵, the main method for investigating prostate cancer is the rectal examination and PSA dosage check, the last one having a key role in prognosis assessment and recurrence of this type of neoplasm. Diagnosis is confirmed through biopsy and, later, the tumor receives a staging classification through the Gleason score, which determines the more adequate treatment and prognosis for the patient, whose approach at the disease is completely individual for each patient⁵.

The coronavirus pandemic was decreed by the World Health Organization (WHO) on March 11, 2020, with one of the first cases of the disease in Paraná confirmed in the Northwest Region of the State, one day after the decree⁶. Soon after cases were confirmed, the first isolation measures were taken, and hospitals started preparing to deal with the situation⁷. According to data from *Projeto Brasil.io*, March 2021 was the month with the most deaths by COVID-19 in the whole State of Paraná⁸.

It is known that patients undergoing cancer treatment such as chemotherapy and radiotherapy are immunosuppressed and, therefore, more susceptible to infections. With the pandemic, it was proved that oncological patients, whether under treatment or not, are more prone to be infected by SARS-CoV-2 and are at greater risks of developing complications due to the virus⁹. With that, hospitals and oncological treatment centers faced difficulties in establishing protocols that minimized the risk of contracting the disease while maintaining effective follow-up appointments and treatments.

In a descriptive study developed by Ribeiro et al.¹¹, using the databases from the Brazilian National Health System (SUS), it was observed that from 2019 to 2020 in Brazil, there was a decrease in the monitoring (45%), diagnosis (35%) and cancer treatment procedures (about 15% less oncological surgeries were performed). It is worth highlighting that cancer monitoring and diagnosis were the most affected procedures, which shows the main gap left by the pandemic.

Regarding prostate cancer, specifically, data from the Ministry of Health¹² point that, comparing 2019 and 2020, the number of SUS urological appointments dropped 33.5%. In addition, the collection of prostate-specific antigen (PSA) and prostate biopsy decreased 27% and 21%, respectively. The number of surgeries for prostate cancer removal also dropped 21.5% from 2019 to 2020¹².

A study conducted in England¹³ analyzed the impact of postponing oncological surgeries in the survival rates of the most varied types of cancer and concluded that, in more aggressive cancer cases, even the short delays (three months) have a significant impact in the survival rate. For favorable cancer prognoses, a six-month delay would result in a significant number of deaths, since many of these neoplasms are common. These delays also resulted in more advanced tumors, which means that the surgical or chemotherapeutic treatment ended up being less effective and more expensive.

It is evident that the Brazilian health system has countless challenges ahead and, thus, one of the necessary measures is to identify the profile of men whose health issues worsened during the pandemic due to lack of oncological treatment. Moreover, it is important to acknowledge those who failed to perform monitoring exams, thus receiving a tardy diagnosis and, consequently, being more prone to having worse outcomes.

Considering what has been discussed, the objective of this study is to make a quantitative and qualitative analysis of the impact of COVID-19 on prostate cancer treatments in specialized hospitals in the North and Northwest Paraná State, comparing the pandemic and

pre-pandemic periods, in addition to identifying if there was a significant difference in the number of diagnoses, lack of treatment adherence, worsening of health status and deaths.

METHOD

Cross-sectional, qualitative and quantitative, *ex-post-facto* study. The research project was sent to two reference hospitals in the North and Northwest Paraná State that treat oncological diseases. The research was conducted in two phases. The first consisted of an initial selection of patients diagnosed with prostate cancer neoplasm. The second phase consisted of applying the Informed Consent Form (ICF). The hospital and its Ethics Committee were responsible for scheduling the dates and defining the method for data collection to not disturb the work in the facilities. The data collection instrument was adapted from the study by Araújo et al.¹⁴ and the PECO Strategy was used for systematizing the research.

The collected data correspond to the periods of March through May 2019 (pre-pandemic), 2020, and 2021 (active pandemic) and gathered information according to medical records regarding patient identification, date of first appointment, start of treatment, type of interventions adopted, evolution of the clinical condition (if there was some kind of worsening during the analyzed period and outcome) and number of follow-up appointments. The impact was characterized if, during the pandemic, there was a postponing of appointments, if patients have abandoned or delayed treatment, if they have contracted COVID-19 or died due to the disease. The criteria for sample inclusion were men diagnosed with prostate cancer in the 50-70 years old age group, of all ethnicities and any education level. There were no exclusion criteria.

The data were compiled in a Microsoft Excel spreadsheet. Then, the categorical variables were described in terms of absolute and relative frequency, being later analyzed regarding association to the years 2019, 2020, 2021 through Pearson's chi-square test and *post-hoc* analysis with a *p*-value correction according to Bonferroni¹⁵. The age variable was described through measures of central tendency and dispersion, with the mean of this variable compared, between hospitals, using the Kruskal-Wallis's test and normality analyzed using the Kolmogorov-Smirnov test. The analyses were performed in the R software¹⁶ platform.

This study has been approved by the Research Ethics Committee, report number 6425089 (CAAE (submission for ethical review): 74632823.1.0000.5539). Researchers collected data from medical records, in compliance with ethical guidelines recommendations related to studies that involve human beings according to Resolution n. 466/2012¹⁷ of the National Health Council.

RESULTS

According to the data analysis, by tracing a profile of the studied patients, it can be observed that the age of patients presents the same tendency, regardless of the studied year or hospital, varying between 50 and 71 years-old, with a median around 64 years-old (Table 1). The *p*-value of the Kolmogorov-Smirnov test for the age variable for hospitals 1 and 2 is < 0.001 and < 0.055 , respectively. Thus, the null hypothesis that the age variable of patients in hospital 1 follows a normal distribution is rejected. From the Kruskal-Wallis's test ($p = 0.0185$), the hypothesis that measurements are different considering a significance level of 5% is rejected.

Most patients had an intermediate risk neoplasm (based on the Gleason score) and stage II cancer following TNM classification¹⁸. In terms of percentages, there is a rise of stage II cases starting at 4.3% in 2019, growing to 25% in 2020 and reaching 35.5% in 2021.

Under a less detailed perspective, between the hospitalization, worsening and outcome variations in the years 2019, 2020 and 2021, there was little difference among the proportions, with a highlight in the low number of hospitalizations in every year of the studied period, as shown in Tables 2 and 3. Additionally, these hospitalizations were mostly related to biopsy or prostatectomy procedures, with no reports of hospitalization due to COVID-19 in the analyzed period.

In hospital 1 (Table 2), 12.1% were affected in some way by the pandemic, either from COVID-19 infection or the need to reschedule appointments. There was also a subtle drop in abandoning follow-up appointments. There were no records of death by the disease.

The application of Pearson's chi-square test concluded that there was in fact differences in the proportion of worsening conditions, outcomes, staging, Gleason score, and pandemic impact in the years 2019, 2020 and 2021, for both hospitals. According to Table 4, there are significant differences, at a 5% significance level, between the pandemic impact proportions.

By applying Pearson's chi-square test involving variables with three or more categories, the *post hoc* analysis applying a *p*-value correction becomes necessary, according to Bonferroni¹⁶. Significant relations after *post hoc* are presented in Table 5 with the respective confidence intervals and odds ratio.

Though the number of people affected by the pandemic was not apparently so expressive, given the number of patients treated, according to Table 5, there are significant differences between 2019 and 2020 and mostly between 2020 and 2021, with the patients treated in 2020 being five times more affected. However, it is worth noting that there were no significant differences in worsening and outcomes, that is, the pandemic was not a predominant factor for treatment success.



Table 1. Measurements of central tendency and dispersion of the age of patients

Variable	Number of observations	Minim.	25%	Mean	Mean CI	Median	75%	Maxim.	Standard deviation
Ages in 2019 – Hospital 1	162	50	60	62.8	[61.9, 63.7]	62	68.7	70	5.8
Ages in 2020 – Hospital 1	140	50	60	62.9	[62, 63.9]	63	69	70	5.9
Ages in 2021 – Hospital 1	161	50	61	62.7	[61.9, 63.5]	63	65	71	5.3
Ages in 2019 – Hospital 2	23	56	63.5	64.9	[63.3, 66.5]	66	68	69	3.7
Ages in 2020 – Hospital 2	28	55	61.5	64.5	[62.7, 66.3]	65	68.2	70	4.7
Ages in 2021 – Hospital 2	45	52	60	64.2	[62.6, 65.7]	66	69	70	5.2

Caption: CI = confidence interval.

Table 2. Variables frequency for the years 2019, 2020 and 2021 in hospital 1

Variables	2019	2020	2021	p
Hospitalization				0.504
No	133 (82.1%)	111 (79.2%)	136 (84.4%)	
Yes	29 (17.9%)	29 (20.7%)	25 (15.5%)	
Worsening				0.530
Metastasis	13 (8%)	10 (7.1%)	8 (4.9%)	
None	149 (91.9%)	130 (92.8%)	153 (95%)	
Outcome				0.159
Abandoned follow-up	28 (17.2%)	11 (7.8%)	10 (6.2%)	
Abandoned treatment	2 (1.2%)	1 (0.7%)	1 (0.6%)	
Still following-up	68 (41.9%)	64 (45.7%)	82 (50.9%)	
Discharged	9 (5.5%)	7 (5%)	6 (3.7%)	
Palliative care	4 (2.4%)	4 (2.8%)	5 (3.1%)	
Unknown	30 (18.5%)	25 (17.8%)	22 (13.6%)	
Death	2 (1.2%)	3 (2.1%)	0 (0%)	
Still in treatment	14 (8.6%)	20 (14.2%)	26 (16.1%)	
Interrupted treatment	5 (3%)	4 (2.8%)	8 (4.9%)	
Disease stage				0.853
Unknown	30 (18.5%)	15 (10.7%)	25 (15.5%)	
I	5 (3%)	5 (3.5%)	5 (3.1%)	
II	60 (37%)	58 (41.4%)	61 (37.8%)	
III	25 (15.4%)	23 (16.4%)	29 (18%)	
IV	42 (25.9%)	39 (27.8%)	41 (25.4%)	

to be continued



Table 2. continuation

Variables	2019	2020	2021	p
Gleason score				0.959
Unknown	7 (4.3%)	5 (3.5%)	10 (6.2%)	
High risk	39 (24%)	37 (26.4%)	39 (24.2%)	
Low risk	30 (18.5%)	24 (17.1%)	28 (17.3%)	
Intermediate risk	86 (53%)	74 (52.8%)	84 (52.1%)	
Pandemic				<0.001
Impacted	0 (0%)	17 (12.1%)	3 (1.8%)	
Not impacted	161 (99.3%)	123 (87.8%)	158 (98.1%)	

Table 3. Variables frequency for the years 2019, 2020 and 2021 in hospital 2

Variables	2019	2020	2021	p
Hospitalization				0.382
No	22 (95.6%)	28 (100%)	42 (93.3%)	
Yes	1 (4.3%)	0 (0%)	3 (6.6%)	
Worsening				0.865
Metastasis	3 (13%)	2 (7.1%)	4 (8.8%)	
None	20 (86.9%)	25 (89.2%)	40 (88.8%)	
Outcome				0.279
Abandoned treatment	2 (8.7%)	2 (7.1%)	4 (8.8%)	
Still following-up	3 (13%)	10 (35.7%)	20 (44.4%)	
Palliative care	1 (4.3%)	0 (0%)	0 (0%)	
Death	5 (21.7%)	2 (7.1%)	3 (6.6%)	
Still in treatment	11 (47.8%)	13 (46.4%)	17 (37.7%)	
Interrupted treatment	1 (4.3%)	1 (3.5%)	1 (2.2%)	
Disease stage				0.058
Unknown	2 (8.7%)	0 (0%)	4 (8.8%)	
I	1 (4.3%)	1 (3.5%)	0 (0%)	
II	1 (4.3%)	7 (25%)	16 (35.5%)	
III	1 (4.3%)	3 (10.7%)	6 (13.3%)	
IV	18 (78.2%)	17 (60.7%)	19 (42.2%)	
Gleason score				0.835
Unknown	1 (4.3%)	0 (0%)	1 (2.2%)	
High risk	7 (30.4%)	5 (17.8%)	10 (22.2%)	
Low risk	2 (8.7%)	2 (7.1%)	3 (6.6%)	
Intermediate risk	13 (56.5%)	21 (75%)	31 (68.8%)	
Pandemic				0.443
Impacted	0 (0%)	2 (7.1%)	2 (4.4%)	
Not impacted	23 (100%)	26 (92.8%)	43 (95.5%)	

DISCUSSION

In the analyzed hospitals, there was little interference by the pandemic in the treatment and clinical condition

of patients, with the greater rates of appointment and treatment rescheduling being in 2020, at the beginning of the pandemic. Data found in this study differ from the data by Gouveia et al.¹⁹, who found a reduction in



Table 4. Chi-square test for analyzing the investigated variables proportion

Variable	p*
Hospitalization	0.595
Worsening	0.705
Outcome	0.148
Disease stage	0.530
Gleason score	0.938
Pandemic impact	0.000013**

(*) Pearson's chi-square test.

(**) From the observation of $p \leq 0.05$ in the "pandemic impact" variable, it is possible to conclude that there was a significant difference in frequencies comparing the years 2019, 2020 and 2021 in both hospitals.

the numbers of radiotherapy and radical prostatectomy performed in prostate cancer patients in Brazil during the pandemic.

It was not possible to analyze the number of postponed diagnoses since the first appointment data are varied and do not fit the numerical analysis. On the other hand, studies that analyzed the delay in biopsies and radical surgeries in European countries concluded that there was no association between those and an unfavorable prognosis for the patient^{20,21}. Nonetheless, a similar study conducted in England²² realized that the proven deficit of prostate cancer diagnosis led many men to discover their illness in a much more advanced stage, with metastases.

As observed, the pandemic negatively impacted the care of oncological patients in the whole world; however, it can be noticed that the effect was not the same in the whole of Brazil, not even in every country. Thus, it's important that every health facility seek to understand the impact of COVID-19 on their patients and devise a plan of action to minimize the possible harm.

CONCLUSION

Given the results, it is possible to infer that in spite of the SARS-CoV-2 pandemic having reduced the number of consultations in the studied hospitals, specially in 2020, fortunately it did not worsen the course of the neoplasm in the studied patients, since they continued the proposed

treatments and, even those who contracted COVID-19, did not develop complications or died.

Due to inconsistencies in the records regarding first appointment dates and diagnosis confirmation, it was not possible to create a comparison between 2019, 2020 and 2021 to identify if, due to the pandemic, there was a decrease in the amount of diagnosis.

Finally, it is worth noting that follow-up and maintaining the care of these men was crucial to prevent the disease from advancing to worse stages, reinforcing the idea that, even in situations of world health calamity, the cancer patient should not be neglected.

CONTRIBUTIONS

All the authors have substantially contributed to the study design, acquisition, analysis and interpretation of the data, wording, and critical review. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

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Table 5. Comparison of pandemic impact in the two hospitals in 2019, 2020 and 2021

Pandemic impact	Original p	Corrected p (Bonferroni)	Odds ratio	CI 95%*
2019 vs. 2020	<0.001	0.0001	0.0429	0, 0.28
2019 vs. 2021	0.269	0.809	0.2192	**
2020 vs. 2021	0.001	0.003	5.1053	1.79, 17.9

Captions: (*) = confidence interval.

(**) Calculated just for significant factors.

Note: The impact was considered if, due to the pandemic, appointments and treatments were postponed or canceled and if patients contracted or died from COVID-19.



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