



# Impact of COVID-19 on the curative treatment of prostate cancer: a national cross-sectional study

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## ABSTRACT

**Background:** COVID-19 pandemic affected access to cancer treatment worldwide. However, there is a lack of data about the impact in developing countries. The objective was to evaluate COVID-19 impact on curative prostate cancer (Pca) treatment in Brazil.

**Materials and methods:** With data extracted from the Brazilian Ministry of Health database, the Non-COVID and COVID periods were analyzed to compare the absolute number of radical prostatectomy (RP) and radiotherapy (RT) executed in the country and regions.

**Results:** With data from 50,169 Pca patients (Non-COVID = 28,106 cases and COVID = 22,063) treated with RP or RT in Brazil, a significant decline in patients receiving RT or RP (-6.043 cases;  $p = 0.0001$ ) was detected. Both treatment procedures (RT or RP) were reduced in all five Brazilian regions comparing the Non-COVID and COVID periods. Overall, there was a reduction on RP and RT procedures in 92% (24/25) and 76% (19/25) of the evaluated states, respectively. Comparing the variation of RT and RP per state between COVID and Non-COVID period, there is a significant difference (-18.6% vs. -29%,  $p = 0.03$ ) with a higher negative impact on the RP group. The RT and RP variation had no significant relationship with the incidence of COVID cases in the states. Limitations include the non-evaluation of treatment combinations, the impact of hypofractionated radiotherapy, and other factors influencing the treatment choice.

**Conclusions:** During the COVID-19 pandemic, the curative treatment with RP and RT of Pca was abruptly limited and affected. However, the number of RP was more impacted than RT during the COVID period.

**Keywords:** COVID-19; prostate cancer; radical prostatectomy; radiotherapy

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## Introduction

Until November 2021, Brazil registered about 22 million COVID 19 cases with more than 600.000 related deaths (Supplementary File — Fig.

S1) [1]. The COVID-19 pandemic has profoundly impacted Brazilian society, causing unprecedented economic, healthcare access and infrastructure disruptions. The COVID-19 pandemic has also contributed and led to interruptions in health-

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care delivery. For oncology, the main reason for care delivery disruption was related to transforming hospitals and cancer center activities to ensure greater access and care for patients diagnosed with COVID-19. Like many other countries, several hospitals canceled elective surgeries to ensure that intensive care units were available for COVID-19 patients. Consequently, reductions in access to surgeries, radiotherapy, and chemotherapy have been reported for many solid tumors during the pandemic [2–5].

In Brazil, prostate cancer (Pca) is the most common malignancy among men, excluding non-melanoma skin cancer [6]. Radiotherapy (RT) and radical prostatectomy (RP) are the primary curative treatment alternatives in patients with localized disease [7–9]. The choice between RP or RT considers patients and tumor factors such as age, life expectancy, comorbidities, clinical stage, and toxicity profile [7–9]. However, access and availability to radiotherapy or surgery have emerged as a relevant factor when choosing oncological treatments in several countries [10–13].

For more than two decades, Brazil has passed through a severe undersupply of linear accelerator (LINAC) machines [14–16]. LINAC shortage can negatively impact oncological outcomes, imbalances between treatment options and, ultimately, considerable damages to patients and the health system [16–18]. Despite this, the impact of the availability of LINACs on the treatment of prostate cancer has been a neglected aspect in previous studies.

After the Brazilian COVID -19 lockdown, there have been speculations that many prostate cancer patients were treated with RT instead of surgery during the pandemic due to lack of access and operating rooms. However, the existence of a LINAC shortage has raised questions about the capacity of the Brazilian radiotherapy network to accommodate the increased flow of patients adequately. Thus, currently, the real impact of COVID-19 on the management of prostate cancer in Brazil remains unknown.

Therefore, the primary objective is to evaluate the impact of the COVID 19 pandemic on the curative treatment of prostate cancer (radical prostatectomy and radiotherapy) in a country with one of the highest numbers of COVID 19 cases worldwide.

## Materials and methods

This cross-sectional study collected data from the publicly available national database from the Brazilian Ministry of Health [19]. The database is a public domain which provides information about oncology treatment executed and paid for by the Brazilian government all over the country. Data were collected for patients treated with RP or RT from August 2020 to March 2021 during the pandemic period (hereinafter referred to as the COVID period) and from August 2019 to March 2020 as a Non-COVID pandemic (hereinafter referred to as the Non-COVID period). Data collection included diagnosis, the burden of disease, treatment modality, and patient city of origin. Furthermore, to perform our analysis, these data were grouped considering the 27 Brazilian states and five regions where patients were treated.

On November 1<sup>st</sup>, 2021, we extracted the data on RP and RT from the Brazilian Public Health Database (Datusus/Tabnet) for the two periods previously specified [19]. The RP data came from the hospital production area, and was obtained with the specific codes 0409030031, 0409030023, 0416010121, and 0416010130. The RT information came from the ambulatory production area and was extracted with the code 0304010456. The same database sources and methods were previously used to evaluate the covid impact on general surgical procedures, cardiovascular diseases, and oral health [20–23].

All the data were downloaded as .csv files and compiled in a master Microsoft excel database. Other treatments, like chemotherapy and anti-hormone therapy, were not evaluated because they are frequently used to treat metastatic disease. The use of treatment combinations, including hormone therapy, radiotherapy and surgery, were not evaluated because of the database limitation to separate or merge data from patients receiving such treatment combinations. Data about total COVID cases and deaths were also collected from the National Official Database [1].

The number of procedures (RP or RT) by states and regions were summarized for the COVID and NON-COVID periods using mean and 95% confidence interval (95%CI) for continuous variables and proportions for categorical variables. A map was created to describe the number of

COVID cases per state. The number of procedures between two periods was compared with the Chi-square test for categorical variables. Linear regression using the Pearson test was conducted to assess the relationship between the number of COVID cases and the percentage of variation in RP and RT between the time frame periods. All analyses were conducted using SPSS (version 23.0) software (SPSS Inc, Chicago, IL) and Graph Prism. A significance level of 0.05 was used for all the analyses.

## Results

In total, considering both periods and all included regions, we identified data of 50,169 prostate cancer treatments, either RP or RT (Non-COVID = 28,106 cases and COVID = 22,063). Comparing the number of treatments (RP + RT) between COVID and Non-COVID, a significant reduction of 6,043 cases in the NON-COVID group ( $-22\%$ ,  $p = 0.0001$ ) was observed between the periods.

The patients' origin was 4,005 cities in the Non-COVID period and 3,624 cities in the COVID time. Moreover, these data were grouped considering the five Brazilian regions and the 27 states. The reduction in the treatment procedures was seen in all Brazilian regions, as described in Figure 1A. The Brazilian regions with a more profound reduction in the absolute number of Pca treated cases were Southeast (2,404 cases,  $-18\%$ ), South (1,072,  $-23\%$ ), and Northeast (1,770,  $-24\%$ ) (Fig. 1A). Comparing COVID vs NON-COVID periods by treatment modality, RP had a more significant reduction of the number of cases (4,371 cases,  $-29\%$ ) between the two periods nationally ( $p = 0.0001$ ), with Southeast (1,778,  $-26\%$ ), Northeast (1,338,  $-31\%$ ), and South (787,  $-35\%$ ) regions reporting the most significant reduction in the RP cases (Fig. 1B). The RT also had a significant reduction in the number of cases (1,672 cases,  $-13\%$ ), with a greater reduction in the Southeast (626 cases,  $-10\%$ ), Northeast (382,  $-13\%$ ) and South (285,  $212\%$ ) regions (Fig. 1C).

In the Non-COVID period, 28,106 patients were treated with RP (14,993) or RT (13,113). RP was significantly more utilized nationally compared to RT (+1,880 cases,  $14\%$  difference) (Fig. 1D). Considering the Brazilian regions, RP was more employed in the Northeast (+1,638 cases,  $57\%$  difference),

Southeast (+281 cases,  $4\%$  difference) and Midwest (+224 cases,  $36\%$  difference) regions (Fig. 2D), with RT being slightly more used in the North (+83 cases and  $13\%$  difference) and South (+180 cases  $7\%$  difference) regions.

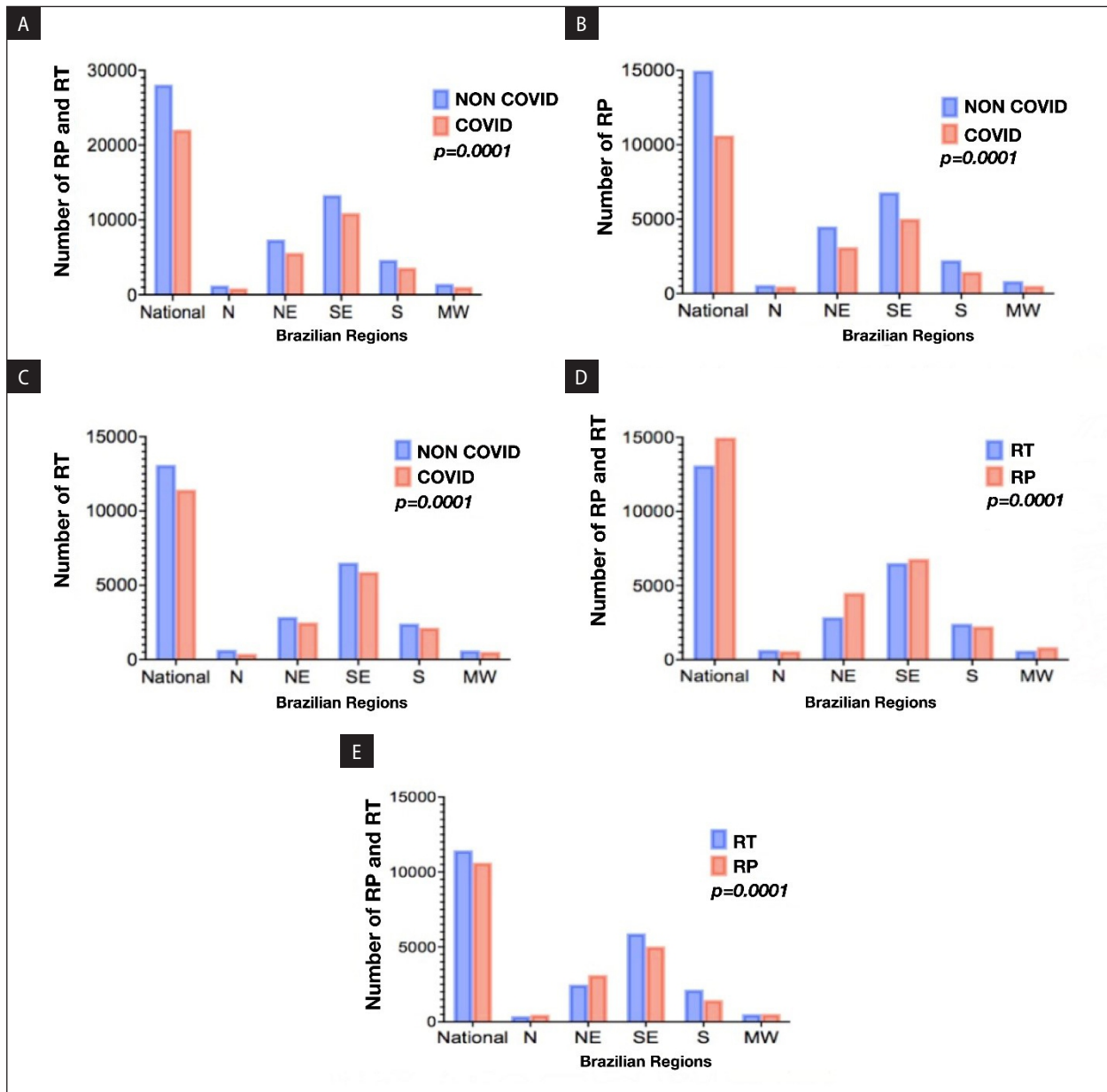
In the COVID period, 10,622 prostate cancer patients were treated with RP and 11,441 with RT, resulting in a significant difference in favor of RT (+819 cases,  $7\%$  difference) (Fig. 1E). In two regions, Southeast (+871 cases,  $15\%$  difference) and South (+682 cases,  $32\%$  difference), RT was more frequently used. In contrast, RP was slightly more utilized in the Northeast (+632 cases,  $25\%$  difference), North (+92 cases,  $24\%$  difference), and MW (+10 cases,  $2\%$  difference).

When analyzing the variation between the procedures per state and considering the COVID and Non-COVID periods, RT had an overall mean negative variation of  $-18.6\%$  [95% confidence interval (CI) from  $+4$  to  $-68\%$ ], with six states reporting a positive variation (mean =  $15.6\%$ , 95% CI:  $4$ – $24\%$ ), as shown in Figure 2A, and 19 states reporting a negative variation (mean =  $-29\%$ , 95% CI:  $12$ – $68\%$ ). RP had an overall mean negative variation of  $-29\%$  (95% CI from  $0$  to  $-62\%$ ), with one state reporting a positive variation, and 24 states, a negative variation (mean  $-35\%$ , 95% CI:  $18$ – $63\%$ ) (Fig. 2B). Data from Sergipe and Roraima states were excluded from our per state analysis due to inconsistency or missing information.

Comparing the variation of RT and RP per state between the COVID and Non-COVID period, a significant difference ( $-18.6\%$  vs.  $-29\%$ ,  $p = 0.03$ ) was observed (Supplementary File — Fig. S2). Finally, evaluating the relationship between the COVID-19 cases across the states and the % variation of RP and RT procedures, no association was observed ( $p = 0.598$  and  $p = 0.562$ ) (Supplementary File — Fig. 3A and 3B).

## Discussion

The present study shows that curative Pca treatments experienced an important reduction in Brazil when comparing a COVID versus a Non-COVID period. RP and RT procedures underwent a reduction in all BR regions, with 92% (23/25 states) suffering RP shortage and 76% (19/25 states) experiencing RT shortage. Despite the significant efforts made by the national lead-

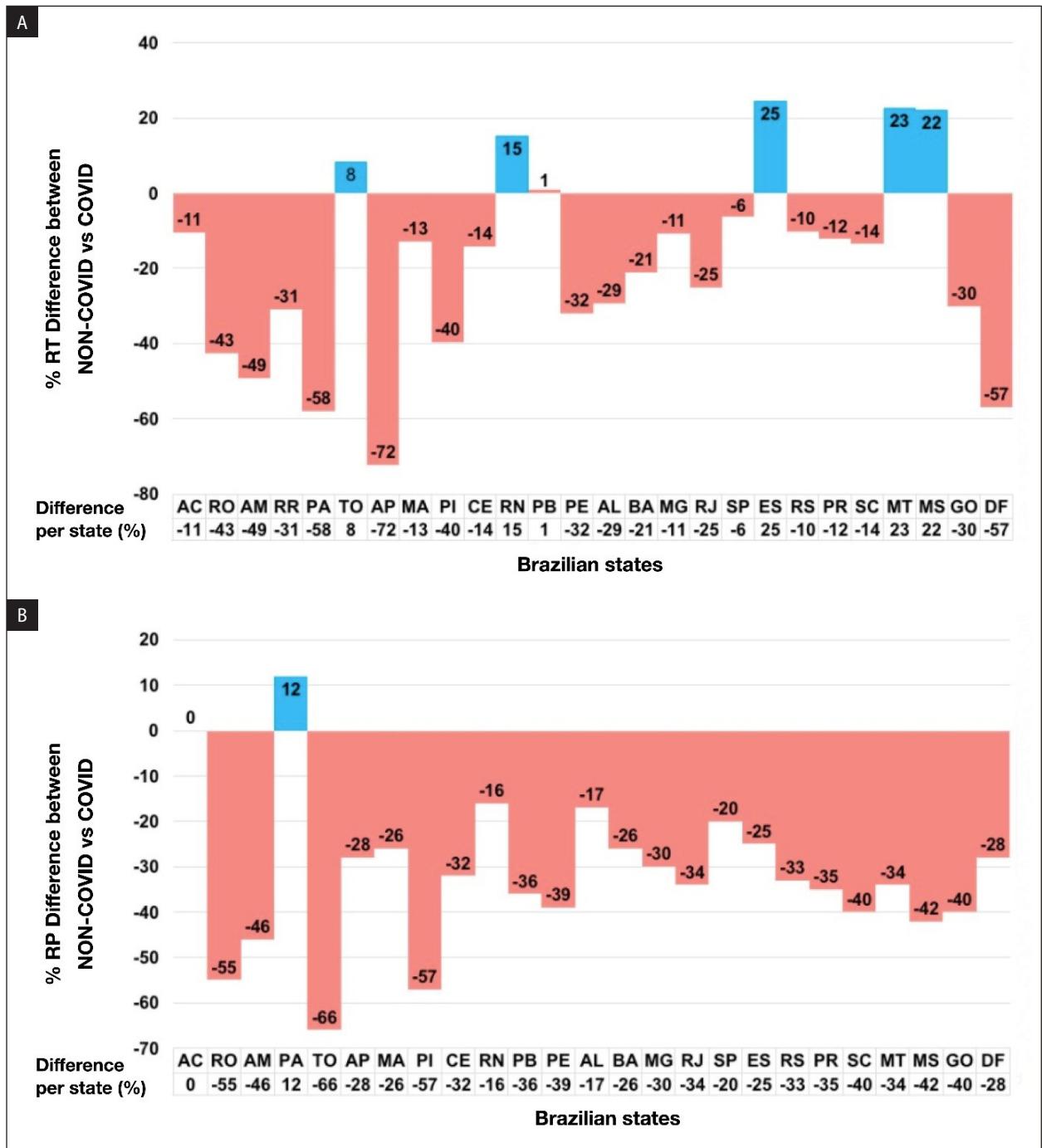


**Figure 1.** A. Number of radical prostatectomy (RP) and RP cases, nationally and per regions comparing the Non-COVID vs. COVID periods; B. Number of radical prostatectomy, nationally and per regions comparing the Non-COVID vs. COVID periods; C. Number of radiotherapy, nationally and per regions comparing the Non-COVID vs. COVID periods; D. Number of radical prostatectomy vs radiotherapy, nationally and per regions during the Non-COVID period; E. Number of radical prostatectomy vs. radiotherapy, nationally and per regions during the COVID period

ership, during the pandemic and the COVID period, approximately 6000 patients, as we assessed, did not receive curative treatment compared to the same time period in a NON-COVID scenario. This means that in one and two years, about 9,000 and 18,000 curative Pca did not receive radical treatment.

On our analysis, the reduction in RP and RT procedures did not have any relationship with the num-

ber of COVID cases in the states, and it might reflect the national policy of prioritizing COVID care and access to complex care. Although RT was also affected, the impact was lower compared to RP. In our view, this difference can be explained by two main reasons. First, RT was used as a substitute treatment for surgery in patients who had no access to the operating room. Second, outpatient procedures, such as prostate biopsy, were allowed



**Figure 2.** A. Radiotherapy difference per state comparing the Non-COVID vs. COVID periods (%); B. Radical prostatectomy difference per state comparing the Non-COVID vs. COVID periods

in some states with a reduced number of COVID cases or a slow kinetic of the outbreak, maintaining patients with the diagnosis being referred to RT during the pandemic.

Some regions presented a complete inversion in the curative treatment numbers for Pca comparing both periods. For example, in the Non-COVID period, RP was significantly more employed in

the Southeast and South regions. In the COVID, there was a complete inversion, with RT being the most utilized treatment. Our findings are relevant because these two regions are the country's wealthiest regions and have a better RT network and supply compared to the others. Thus, we believe that these factors contributed to RT's ability to absorb the demand of the surgical cases.

Here, we used Pca as a cancer-specific example to demonstrate the alarming reduced rates of cancer treatment care that have occurred in the context of the Brazilian response to the COVID-19 pandemic. It is possible to infer that the same disruption has occurred to other cancer sites, such as the head and neck, cervix, breast, and lung cancer.

The findings of this study are not restricted to Brazil. The global oncology community needs now to focus on ways to improve cancer care disruption. Minimizing further delays to treatment is crucial. A recent meta-analysis detected up to 8% increased chance of death for each 4-week delay for several cancer types (bladder, breast, colon, rectum, lung, cervix, and head and neck) [24]. Thus, our data can be helpful to the Brazilian Government to plan and prepare for the following years to adequately offer an oncological treatment for an excessive demand accumulated from the pandemic years. Besides, these findings can be beneficial for low- and middle-income countries with restricted access to RT treatment due to the lack of LINAC to plan their future policies and action to mitigate the effects of the pandemic in oncological patients.

Lastly, the limitations in the present study need to be acknowledged. First, due to the database limitations, it was impossible to evaluate treatment combinations, like adjuvant or salvage RT after PR, or the integration with androgen deprivation therapy. Second, race, age, and social factors that may influence the treatment decision could not be evaluated. Third, the influence of the adoption of short RT courses (hypofractionation) was not possible to be estimated.

## Conclusion

The COVID 19 pandemic has affected prostate cancer's curative treatment, with a reduction in RP and RT. However, access and number of RP were more affected than RT during the COVID period, with RT access being also impacted nationally. The results observed here are unlikely to be unique to Brazil and challenge all health services to minimize the impact of the COVID pandemic on health services. Therefore, these data can be helpful to plan future actions to attend to an excessive demand accumulated during the pandemic years.

## Conflict of interests

FYM reports previous consulting fee from Elekta and honoraria from Astra Zeneca, both outside the current work. All other authors have no competing interests

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None declared.

## Data availability

Research data are stored and will be shared upon request to the corresponding author.

## Acknowledgements

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