Chemotherapy for Breast Cancer in the State of Rio de Janeiro during the COVID-19 Pandemic: Time Series Analysis

Quimioterapia para Câncer de Mama no Estado do Rio de Janeiro durante a Pandemia da Covid-19: Análise de Séries Temporais
Quimioterapia para el Cáncer de Mama en el Estado de Río de Janeiro durante a la Pandemia de Covid-19: Análisis de Series de Tiempo

Natalia Farias Santos¹; Claudia Garcia Serpa Osorio-de-Castro²; Mario Jorge Sobreira-da-Silva³

ABSTRACT

Introduction: Cancer is one of the main causes of death in Brazil and worldwide. For each year of the triennium 2023-2025, 483,000 new cases are estimated for the country, except non-melanoma skin cancer, breast cancer being the most incident in women with 74,000 new cases. After the declaration of the COVID-19 pandemic by the World Health Organization, several Brazilian states determined restrictive measures to reduce the contamination and cancer diagnosis reference centers were impacted. **Objective:** To analyze the number of approved breast cancer chemotherapy procedures before and during the COVID-19 pandemic in SUS-affiliated cancer-care facilities in the State of Rio de Janeiro, Brazil. **Method:** Descriptive design, with time series and ecological analyses using publicly available data of chemotherapy procedures authorized by SUS between March 2018 and February 2021. **Results:** A total of 394,926 procedures were identified, an increase of 47% with a rising linear trend (R²=0,5203) during the period. Increases in hormonal receptor-positive cancer (46%) and in HER-2 positive carcinoma (900%) were observed. The patients travelled smaller distances for chemotherapy procedures. **Conclusion:** Results point out a possible effective response by the cancer care network and strengthening of the regionalization during the first pandemic year.
Key words: antineoplastic agents; breast neoplasms; COVID-19; oncology services, hospital.

RESUMO

Introdução: O câncer é uma das principais causas de morte no Brasil e no mundo. Estimam-se 483 mil novos casos no país, para cada ano do triênio 2023-2025, excetuando-se o câncer de pele não melanoma, sendo o câncer de mama o mais incidente em mulheres, com 74 mil novos casos. Após a declaração da pandemia da covid-19 pela Organização Mundial da Saúde, vários Estados brasileiros estabeleceram medidas restritivas, visando à redução da contaminação, e os centros de referência em diagnóstico do câncer foram impactados. **Objetivo:** Analisar séries temporais das quantidades de procedimentos aprovados de quimioterapia para câncer de mama antes e durante a pandemia da covid-19 nos estabelecimentos habilitados para alta complexidade em oncologia no Estado do Rio de Janeiro. **Método:** Estudo descritivo com análises de séries temporais e ecológica, usando dados públicos de procedimentos de quimioterapia autorizados pelo Sistema Único de Saúde entre março de 2018 e fevereiro de 2021. **Resultados:** Foram identificados 394.926 procedimentos, representando um aumento de 47% com tendência linear crescente (R²=0,5203) no período. Verificou-se um aumento de procedimentos para câncer de mama receptor hormonal positivo (46%) e carcinoma de mama HER-2 positivo (900%). **Conclusão:** Observou-se um aumento nos procedimentos de quimioterapia, assim como uma diminuição do deslocamento de tratamento dos grandes centros. Os resultados apontam para uma possível resposta efetiva da rede de atendimento e fortalecimento da regionalização durante o primeiro ano da pandemia.
Palavras-chave: antineoplásicos; neoplasias da mama; COVID-19; serviço hospitalar de oncologia.

RESUMEN

Introducción: El cáncer es una de las principales causas de muerte en el Brasil y en el mundo. Se estiman 483 000 nuevos casos en el país, para cada año del trienio 2023-2025, excluyendo el cáncer de piel no melanoma, siendo el cáncer de mama el más incidente en mujeres, con 74 000 nuevos casos. Luego de la declaración de la pandemia de covid-19 por la Organización Mundial de la Salud, varios Estados del Brasil establecieron medidas restrictivas con el objetivo de reducir la contaminación y los centros de referencia para el diagnóstico del cáncer fueron impactados. **Objetivo:** Analizar series de tiempo de las cantidades de procedimientos de quimioterapia aprobados para el cáncer de mama, antes y durante la pandemia de covid-19, en los establecimientos calificados para la alta complejidad en oncología en el Estado de Rio de Janeiro, Brasil. **Método:** Diseño descriptivo con análisis de series de tiempo y ecológico, utilizando datos públicos de procedimientos de quimioterapia aprobados por el Sistema Único de Salud entre marzo de 2018 y febrero de 2021. **Resultados:** Fueran identificados 394 926 procedimientos, representando un aumento de 47% con una tendencia lineal creciente (R²=0,5203) en el periodo. Fueron observados aumentos de procedimientos para cáncer de mama receptor hormonal positivo (46%) y carcinoma de mama HER-2 positivo (900%). **Conclusión:** Los resultados apuntan hacia una posible respuesta efectiva de la red de atención y fortalecimiento de la regionalización durante el primer año pandémico. **Palabras clave:** antineoplásicos; neoplasias de la mama; COVID-19; servicio de oncología en hospital.

¹,³Instituto Nacional de Câncer (INCA), Coordenação de Ensino (Coens). Rio de Janeiro (RJ), Brazil. E-mails: sfariasnatalia@gmail.com; mario.silva@inca.gov.br. Orcid iD: https://orcid.org/0000-0001-8258-1846; Orcid iD: https://orcid.org/0000-0002-0477-8595
²Escola Nacional de Saúde Pública Sérgio Arouca (Ensp), Departamento de Políticas de Medicamentos e Assistência Farmacêutica. Rio de Janeiro (RJ), Brazil. E-mail: claudiaosorio.soc@gmail.com. Orcid iD: https://orcid.org/0000-0003-4875-7216
Corresponding author: Mario Jorge Sobreira da Silva. Rua Marquês de Pombal, 125 – Centro. Rio de Janeiro (RJ), Brazil. CEP 20230-240. E-mail: mjsobreira@yahoo.com.br

INTRODUCTION

Cancer is one of the leading causes of death in Brazil and worldwide. The number of cases is expected to increase as the population grows, ages, and adopts a lifestyle that favors the development of the disease[1].

According to estimates by the National Cancer Institute (INCA)[2], for each year of the 2023-2025 triennium, there will be 483,000 new cases of cancer in the country, excluding non-melanoma skin cancer. Among women, breast cancer remains the most frequent, accounting for 30.1% of cases[2]. The delay in diagnosis has been highlighted as a negative prognostic factor and is related to the difficulty of access to health services and the deficit in the training of professionals working in cancer care[3], among other factors.

In 2020, with the COVID-19 pandemic, there was a need for changes in the organization of the provision of cancer care, from diagnosis to treatment schemes[4]. These measures were taken by health professionals and managers in several countries[5] and, since then, it has been necessary to monitor the results and effects of these strategies on cancer outcomes at the population level. A real possibility to be investigated, given the demands imposed by the pandemic, would be the reduction of chemotherapy procedures offered by the Breast Cancer Care Network. This potential decrease would have great relevance for the outcomes of the disease and for the implications on future care.

This study aimed to analyze the time series of the number of approved chemotherapy procedures for breast cancer before and after the onset of the COVID-19 pandemic in establishments qualified for high complexity in oncology in the State of Rio de Janeiro.

METHOD

This was a descriptive study with a two-pronged approach: the time series analysis, and the ecological analysis, in order to identify trends among the number of records of chemotherapy procedures. Resources were limited to the State of Rio de Janeiro, comprising the two-year pre-pandemic period of SARS-CoV-2, from March 2018 to February 2020, and the first pandemic year in Brazil, considering the period from March 2020 to February 2021.

The population selected for the study was that of female patients undergoing chemotherapy in the State of Rio de Janeiro according to the tenth International Statistical Classification of Diseases and Related Health Problems (ICD-10)[6] of type C50, referring to breast cancer and its subtypes.

The public and open access database was used, made available in the Outpatient Information System of the Unified Health System (SIA/SUS)[7]. Within the data modality, the files of the Authorizations for High Complexity Procedures (APAC) of Chemotherapy, available on the portal of the SUS Informatics Department (DATASUS), were selected for analysis.

The data files for each of the 36 months under study were extracted in a compressed format, resulting in 36 data files containing the APAC records. The data were decompressed and converted from the compressed format (.dbc) to the data base file (.dbf) and later to the comma-separated value format (.csv), through the Tabwinprogram, available for download on the DATASUS portal. The files in the (.csv) version were viewed by the Microsoft Excel 2016 program.

The source bank had 25,275,264 observations, containing all the information on the chemotherapy procedure for female breast cancer conducted in the State. Within this database, 17 descriptive variables were selected (Chart 1) applied to the data of each of the 36 months under analysis.

The data were aggregated into year I (from March 2018 to February 2019), year II (from March 2019 to February 2020) and year III (March 2020 to February 2021) for the purpose of comparing the totals. The numbers of records for each of the months under study were analyzed. In addition, the difference test between the monthly values per year (Pearson's chi-square) was performed, accepting 95% confidence (WINPEPI version 11.65, ABA COMPARE2, module F2)[8].

The time series were constructed based on the temporal variation in the number of procedures during the study period. The linear trend of each distribution was calculated. For this, the least squares method was used. Linear regression was chosen after testing for the best fit for the data. The fit quality test was applied and the R-square (R^2) was used as a statistical measure to identify whether the model was properly adjusted. The data were compared between the different periods in order to verify changes in trend as a function of time.

Procedure records were analyzed for: patient characteristics (age and race/color), place of occurrence (establishment), type of procedure, type of APAC (initial, unique or continuity), Region of origin and treatment, and outcome (discharge, closure, permanence, transfer, or death). Descriptive statistics were performed using measures of central tendency.

To analyze the municipalities of origin and treatment, data were aggregated according to the Health Regions (Ilha Grande Bay, Baixada Litorânea, Centro-Sul, Médio Paraíba, Metropolitana I, Metropolitana II, Northwest, North and Serrana) and later grouped by Health

Chart 1. Variables used to prepare the set of APAC spreadsheets

Variable	Description
AP_MVM	Indicates the processing/movement date
AP_CODUNI	Indicates the code of the establishment in the CNES
AP_AUTORIZ	Indicates the APAC number
AP_PRIPAL	Indicates the code of the main APAC procedure
AP_UFMUN	Indicates the code of the UF + code of the municipality of the establishment
AP_TPUPS	Indicates the type of establishment
AP_CNPJCPF	Indicates the CNPJ of the performing establishment
AP_CNSPCN	Indicates the patient's CNS number
AP_NUIDADE	Indicates age number
AP_RACACOR	Indicates the patient's race/color
AP_MUNPCN	Indicates the code of the State + code of the municipality of residence of the patient
AP_TPAPAC	Indicates whether APAC is initial (1), continuity (2), or single (3)
AP_OBITO	Indicates the occurrence of death
AP_ENCERR	Indicates the occurrence of closure
AP_PERMAN	Indicates continuation of treatment
AP_ALTA	Indicates discharge
AP_TRANSF	Indicates transfer

Captions: CNES = National Registry of Health Establishments; APAC = Authorizations of High Complexity Procedures; UF = Federation Unit; CNPJ = National Registry of Legal Entities; CNS = National Health Card.

Macroregions, in force in the State of Rio de Janeiro until February 2021, which are: Macroregion I (Centro-Sul, Médio Paraíba and Ilha Grande Bay), II (Metropolitanas I and II, Serrana) and III (Northwest, North and Baixada Litorânea). From this aggregation, the filters related to each health macro-region of the place of origin and destination were applied, and it was possible to identify whether the patients underwent treatment in the same macro-region or if they required travelling for care.

RESULTS

The total number of chemotherapy procedures for breast cancer in the State of Rio de Janeiro in the analyzed period was 394,926, with 118,059 in year I, 132,329 in year II and 144,538 in year III. By comparing the monthly values in each year, the annual differences between years I and II, II and III and between I and III were statistically significant (p <0.001).

When analyzing the evolution of the time series, an increasing trend of procedures (R^2 =0.5203) was identified, with 8,825 registered in March 2018 and 12,997 in February 2021 (Figure 1), representing an increase of 47%. No outliers were observed between the monthly measurements.

The comparative analysis showed that there was an upward trend in the number of chemotherapy procedures in all years, corresponding to approximately 23% in the first year, 26% in the second and 24% in the third.

The median age of patients treated in the period was 60 years (min. 22; max. 99) and the mean ages, calculated for years I, II and III, were 61 (standard deviation – SD+13), 61 (SD+12) and 61 (SD+12) years, respectively. There was no variation in the median or in the distribution of the mean age during the period.

An increase in the number of procedures was identified in self-declared white and non-white patients in the analyzed periods, which formed 50.1% of the total. However, the absence of race/color information was observed in 10.6% of the records.

In terms of care facilities, the procedures (39%) were mostly performed in two establishments, INCA and Hospital Mário Kröeff. However, hospitals based outside the capital of Rio de Janeiro showed an increase in the number of chemotherapies performed in the pandemic period (year III), with emphasis on the Darcy Vargas Regional Hospital in Rio Bonito and the Santa Izabel Hospital in Cabo Frio (Figure 2).

Some hospitals located in the capital of Rio de Janeiro, however, had reduced attendance in the pandemic period. Among these, we highlight the Gaffree and Guinle University Hospital, the Pedro Ernesto University Hospital, the Federal Hospital for State Employees, Bonsucesso General Hospital and the Clementino Fraga Filho University Hospital, which had an increase in production in year II and a reduction in year III.

There was a greater increase in the production of chemotherapy in general hospitals (24.5% between years I and III), when compared to specialized hospitals (9.5% in the same period).

In general, an increasing number of procedures were observed, regardless of type (Figure 3).

The largest number of chemotherapy procedures performed in the period, 46% of the total, was for the treatment of hormone therapy-positive receptor breast cancer (stage III) and hormone therapy-positive receptor without axillary lymph node involvement (stage II). Although the largest number is concentrated in hormone therapy procedures, those of multi-chemotherapy and chemotherapy with double anti-HER-2 of HER-2 positive breast carcinoma (1st line) were those that showed the
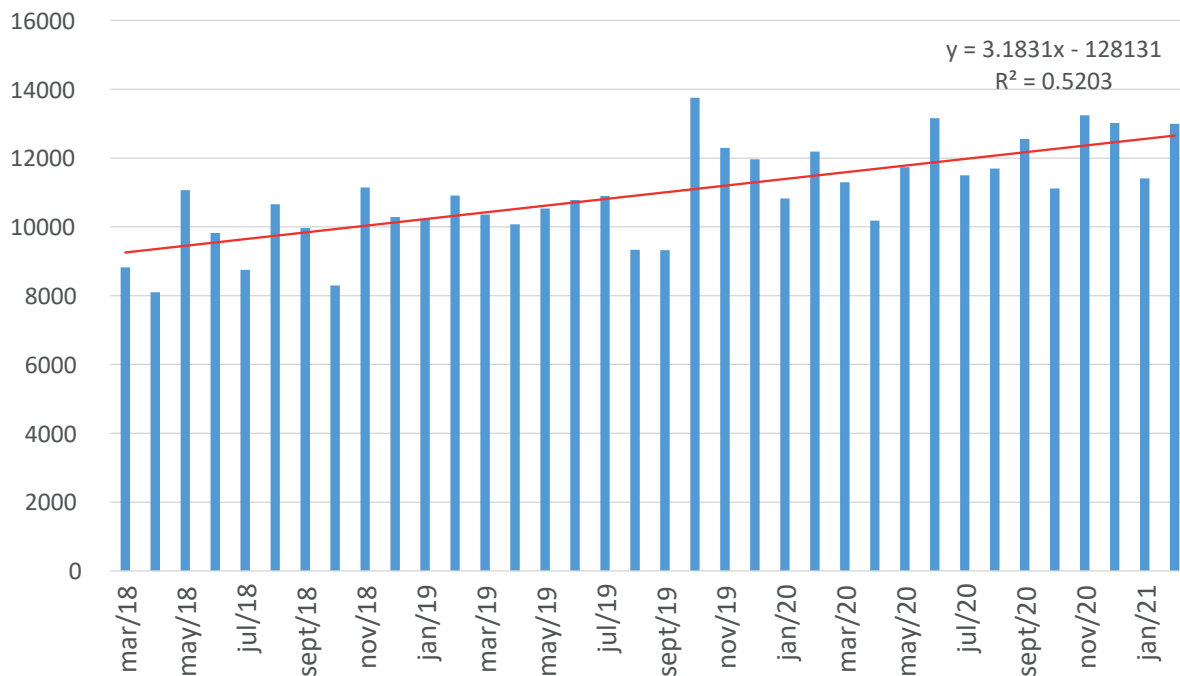
$$y = 3.1831x - 128131$$
$$R^2 = 0.5203$$

Figure 1. Linear trend of records of breast cancer chemotherapy procedures in the State of Rio de Janeiro between March 2018 and January 2021 (N=394,926)
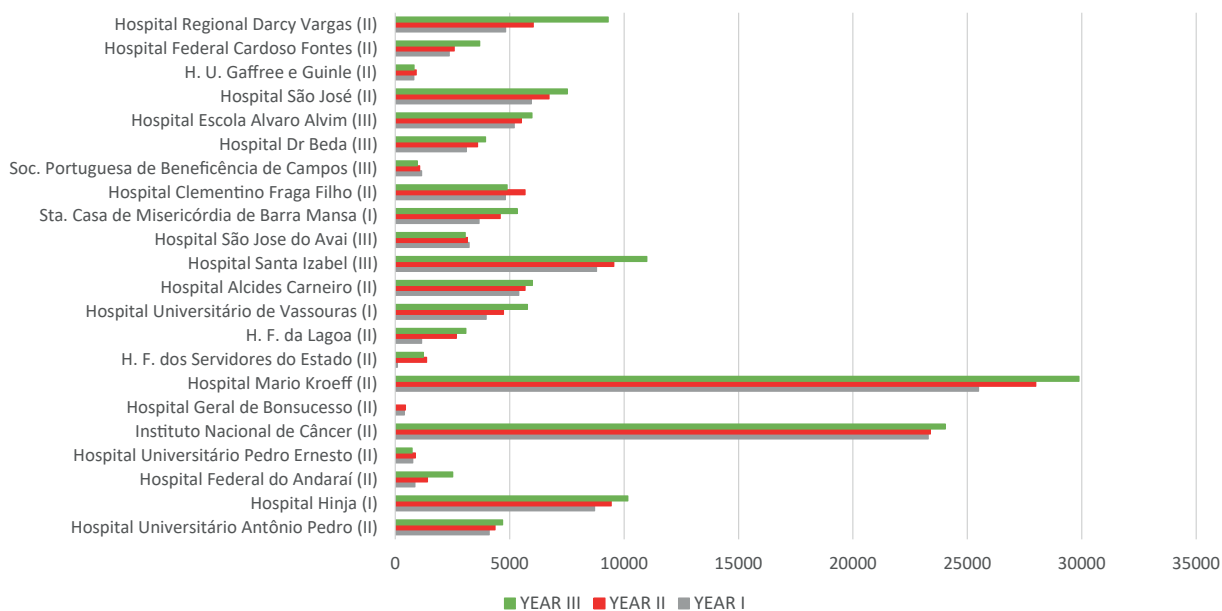
Figure 2. Comparative analysis of years I, II and III. Breast cancer procedures registered in SIA/SUS in the State of Rio de Janeiro considering health facility and their respective health macro-regions (I, II or III), 2019-2021 (N=394,926)

Captions: (a) Macro-region I; (b) Macro-region II; (c) Macro-region III.

highest growth in the period, representing, respectively, 533% and 100% for year II and 1,300% and 900% for year III. Also noteworthy are the procedures of polychemotherapy and monochemotherapy of HER-2 positive breast carcinoma in stages I, II and III (adjuvant), which showed relevant increases for both years II and III.

With respect to the records of municipalities of origin and treatment, it was possible to note that Macroregion II, both for the records of origin and for treatment, showed, from year I to year II, an increase of 18% and 13% and, from year II to year III, an increase of 9% and 8%, respectively.
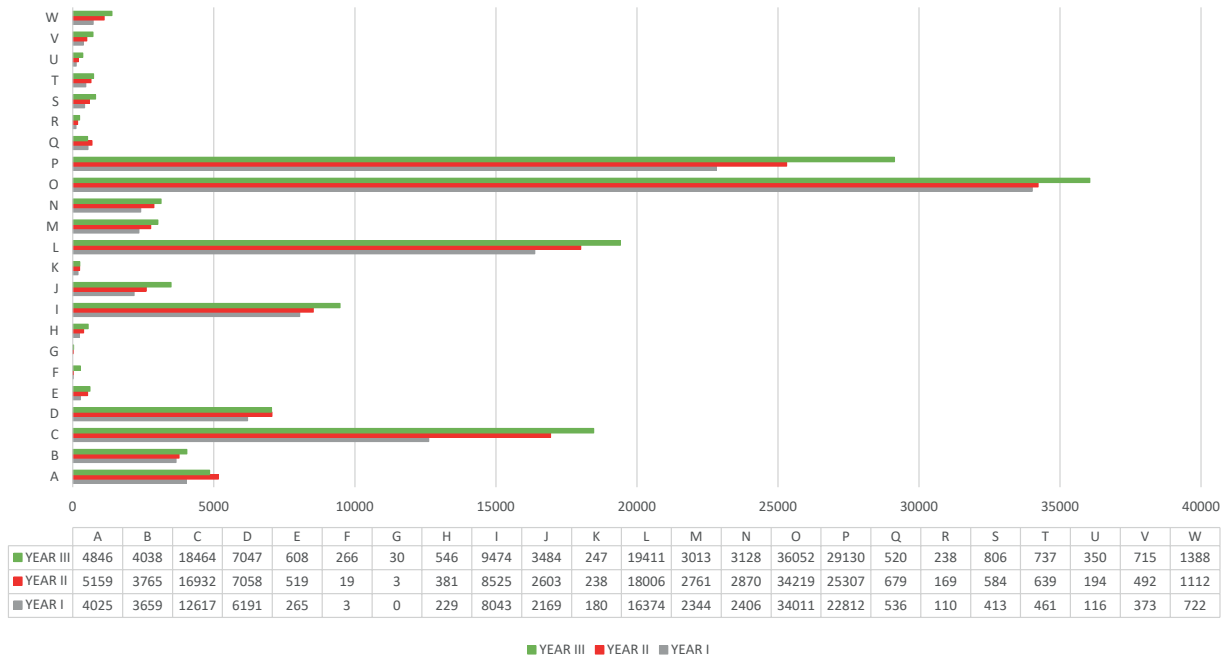
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W
YEAR III	4846	4038	18464	7047	608	266	30	546	9474	3484	247	19411	3013	3128	36052	29130	520	238	806	737	350	715	1388
YEAR II	5159	3765	16932	7058	519	19	3	381	8525	2603	238	18006	2761	2870	34219	25307	679	169	584	639	194	492	1112
YEAR I	4025	3659	12617	6191	265	3	0	229	8043	2169	180	16374	2344	2406	34011	22812	536	110	413	461	116	373	722

■ YEAR III ■ YEAR II ■ YEAR I

Figure 3. Comparative analysis of years I, II and III. Breast cancer procedures registered in the SIA/SUS database in the State of Rio de Janeiro, 2019-2021 (N=394,926)

Acronyms: A = treatment of breast carcinoma by chemotherapy (1st line); B = treatment of breast carcinoma by chemotherapy (2nd line); C = treatment of breast cancer by hormone therapy exclusively for postmenopausal women (2nd line); D = treatment of positive receptor breast cancer by hormone therapy (1st line); E = polychemotherapy of HER-2 positive breast carcinoma (1st line); F = polychemotherapy with double anti-HER-2 positive breast carcinoma (1st line); G = chemotherapy with double anti-HER-2 positive breast carcinoma HER-2-positive breast (1st line); H = HER-2-positive breast carcinoma monochemotherapy (1st line); I = stage III chemotherapy breast cancer treatment (1st line); J = stage III HER-2-positive breast carcinoma polychemotherapy (previous); K = stage III breast carcinoma hormone therapy (previous); L = stage I clinical/pathological hormone therapy positive receptor breast cancer treatment; M = stage III clinicopathological chemotherapy breast cancer treatment); N = receptor-negative breast cancer without axillary lymph node involvement by stage II chemotherapy; O = treatment of receptor-positive breast cancer by stage III hormone therapy; P = treatment of receptor-positive breast cancer without axillary lymph node involvement by hormone therapy (stage II); Q = treatment of breast carcinoma by stage I clinicopathological chemotherapy; R = polychemotherapy of HER-2 positive breast carcinoma in stage I (adjuvant); S = polychemotherapy of HER-2 positive breast carcinoma in stage II (adjuvant); T = polychemotherapy of HER-2 positive breast carcinoma in stage III (adjuvant); U = monochemotherapy of HER-2 positive breast carcinoma in stage I (adjuvant); V = monochemotherapy of HER-2 positive breast carcinoma in stage II (adjuvant); W = monochemotherapy of HER-2 positive breast carcinoma in stage III (adjuvant).

In Figure 4, when selecting patients who underwent treatment in the same Macro region as that of origin, it was possible to notice the linear trend of increase for Macro regions I and III, with R² equal to 0.9908 and 0.8446, respectively. However, for Macro region II, despite the upward trend (R²=0.3481), there was a monthly variation in the number of records.

For death records, 1% and 16% increases were observed for year II and year III respectively. For the closure records, there was an increase of 8% for year II and a reduction of 17% for year III. As for discharge records, a reduction of 28% for year II and 12% for year III. For continuation of treatment records, there was an increase of 13% between years I and II, and 10% between years II and III. As for the transfer records, there was only one occurrence for each of the years under analysis.

DISCUSSION

The data pointed to a growing yearly trend of chemotherapy procedures for breast cancer in the period,

and it was not possible to observe a negative direct effect of the COVID-19 pandemic. Some studies have demonstrated the impact caused by the pandemic on cancer treatment, showing a reduction[9] or increase[10] in the number of patients receiving systemic intravenous treatment and the start of new treatments.

The characteristics of the patients showed that the age records did not change in the median or in the means, indicating that the increase in records continued to follow the pattern of the most affected age group, 50 years and above[11]. The absence of race/color information in 10.6% of the database did not allow us to verify whether the distribution of procedures follows the composition of the population, but the existing data did not show differences in the distribution for self-declared white and non-white patients. However, it should be noted that studies have shown an increase in the number of cases[12] and mortality[13] due to breast cancer in black women when compared to white women, pointing to disparities in access to oncology care[14,15].

Seven establishments showed a reduction in the number of APAC records, all general hospitals, which
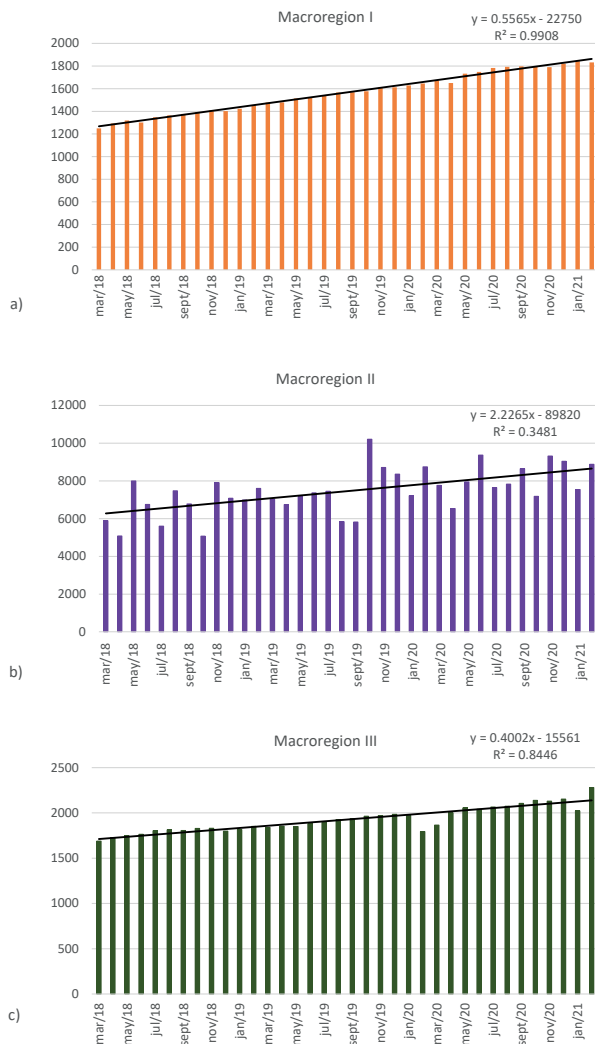
Figure 4. Month-by-month analysis of variation in the number of procedures originating from the same treatment. Macroregions in the State of Rio de Janeiro, 2019-2021 (N=394,926). A) Macroregion I; B) Macroregion II; C) Macroregion III

seems to be related to the emergence of the need to provide hospital beds for COVID-19, requested through a joint action by the Federal Public Prosecutor's Office and the Federal Public Defender's Office[16].

The highest number of chemotherapies performed in the period, 46% of the total, involved hormone therapy, which remains the most frequently performed systemic treatment in women with breast cancer. About 75% of identified tumors are responsive to endocrine therapy, according to the literature[17].

A decrease in patients with early-stage (I and II) breast cancer was detected for systemic therapy during the pandemic in Brazil[18]. However, this study observed an increase in the number of chemotherapies in patients with early-stage HER-2 positive breast cancer, indicating an adjuvant procedure – after surgical treatment. Due to the aggressiveness of this tumor subtype, which requires

priority interventions, surgery should not be postponed, and chemotherapy treatment needs to be done first[19], explaining the high number of procedures.

Procedures with double anti-HER-2 blockade also had a percentage increase above 100%, when compared to previous years, which can be explained by the inclusion of the biological agent pertuzumab in SUS. Although its association with trastuzumab was recommended for incorporation by the National Commission for the Incorporation of Technologies (Conitec), in December 2017 20, and its inclusion in the SUS list of procedures approved in July 2018 21, only in December 2020 was the agent made available to authorized SUS facilities[22,23].

The increase in procedures outside the capital of Rio de Janeiro and the performance of chemotherapy in the same Macroregion of residence during the pandemic period reflect important aspects of the regionalization of oncology care in the State as proposed by Ordinance nº. 1.559/2008[24]. The favoring of access to treatment in one's own Macroregion of residence may be related, especially after the beginning of the pandemic, to the circulation restrictions established by the risk of contamination posed by SARS-CoV-2[25]. It should be noted, however, that, in August 2021, a new agreement was made with the Bipartite Intermanagerial Commission of the State of Rio de Janeiro (CIB-RJ)[26] reducing the number of health macro-regions to only one, including all municipalities[26]. Such a change may promote longer itineraries and increased travel distances, potentially leading to inequities in access and continuity of treatment for breast cancer, and requires monitoring.

The pandemic situation seems to have strengthened the regionalization of chemotherapy treatment for breast cancer in the State of Rio de Janeiro, which can be demonstrated by the better fit of the model in Macroregions I and III. Despite the lower R2 in Macroregion II, it is noteworthy that this is where most of the procedures occurred in the period.

There was a sharp increase in the number of deaths in year III. Jardim et al.[27] identified that, in 2020, there was an excess of deaths from cancer and cardiovascular diseases as comorbidities, indicating that COVID-19 had an important impact among patients who had these underlying conditions. Costa et al.[28], when analyzing data from 322,817 Brazilian patients who were affected by SARS-CoV-2 in 2020, pointed out that those who had a cancer diagnosis had greater disease severity and mortality compared to the others.

During the pandemic, treatment decisions were expected to be postponed, given the risk of cancer patients being exposed to COVID-19[29]. However, in year III, there was a decrease in numbers of closure and discharge

outcomes, and an increase in the record of continuity of treatment, apparently pointing to the clinical decision to prioritize treatment even with the risks of worse prognoses[30].

In fact, there was a general increase in the number of APAC records for chemotherapy procedures for breast cancer in the State of Rio de Janeiro, although the expected result was some loss in the number of procedures during the pandemic, given the need to reallocate human and material resources. However, the results should be analyzed with caution since there is some evidence that there was an increase in national expenses with chemotherapy, especially for stages III and IV, in the pandemic period[31].

It should be noted that the increase in the number of procedures cannot be directly attributed to the increase in the number of breast cancer cases in the period. There are estimates of incidence, but no historical data; the best estimator would be the burden of disease, but this analysis was related to the procedures which effectively resulted in treatment, and reimbursed in the period. In addition, in the period, there was no information available on an increase in service capacityof pre-qualified cancer-care facilities.

It is important to point out that this study presented limitations inherent to the data source itself, such as possible failures in completion and missing data. Another issue was the the study setting, the State of Rio de Janeiro, where the main cancer treatment center in the country is located. However, in an analysis involving national data, Ribeiro et.al. 10 identified that, for all types of cancer, there was an increase of 3.2% in chemotherapy procedures in 2020, which indicates an absence of impact of the COVID-19 pandemic for this type of procedure.

CONCLUSION

The results point to an apparently effective response of the cancer-care network even in the face of restrictive measures to control the pandemic and the growth in the number of COVID-19 cases in the state. There was an increase in the number of APAC records for procedures with codes referring to chemotherapy in initial and first-line stages, as well as an increase in the number of treatment records in the health macro-regions themselves, showing an apparent strengthening of regionalization.

CONTRIBUTIONS

All authors contributed substantially to the design and/or planning of the study; in the analysis and/or interpretation of the data; in the writing and/or critical review; and approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

FUNDING SOURCES

None.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49. doi: https://doi.org/10.3322/caac.21660

2. Santos MO, Lima FCS, Martins LFL, et al. Estimativa de incidência de câncer no Brasil, 2023-2025. Rev Bras Cancerol. 2023;69(1):e-213700. doi: https://doi.org/10.32635/2176-9745.RBC.2023v69n1.3700

3. Medeiros GC, Teodozio CGC, Fabro EAN, et al. Fatores associados ao atraso entre o diagnóstico e o início do tratamento de câncer de mama: um estado do coorte com 204.130 casos no Brasil. Rev Bras Cancerol. 2020;66(3):e-09979. doi: https://doi.org/10.32635/2176-9745.RBC.2020v66n3.979

4. Marques NP, Silveira DMM, Marques NCT, et al. Cancer diagnosis in Brazil in the Covid-19 era. Semin Oncol. 2021;48(2):156-9. doi: https://doi.org/10.1053/j.seminoncol.2020.12.002

5. Richards M, Anderson M, Carter P, et al. The impact of the Covid-19 pandemic on cancer care. Nat Cancer. 2020;1(6):565-7. doi: https://doi.org/10.1038/s43018-020-0074-y

6. Organização Mundial da Saúde. CID-10: Classificação Estatística Internacional de Doenças e problemas relacionados à saúde. São Paulo: Edusp; 2008.

7. SIA/SUS: Sistema de Informações Ambulatoriais do SUS [Internet]. Brasília (DF): DATASUS. [data desconhecida] – [acesso 2023 ago 11]. Disponível em: http://sia.datasus.gov.br/principal/index.php

8. Abramson JH. WINPEPI updated: computer programs for epidemiologists, and their teaching potential. Epidemiol Perspect Innov. 2011;(8):1-9. doi: https://doi.org/10.1186/1742-5573-8-1

9. Araujo SEA, Leal A, Centrone AFY, et al. Impact of Covid-19 pandemic on care of oncological patients: experience of a cancer center in a Latin American pandemic epicenter. Einstein (São Paulo). 2020;19:eAO6282. doi: https://doi.org/10.31744/einstein_journal/2021AO6282

10. Ribeiro CM, Correia, FM, Migowski, A. Efeitos de curto prazo da pandemia de Covid-19 na realização de procedimentos de rastreamento, investigação diagnóstica e tratamento do câncer no Brasil: estudo descritivo, 2019-

2020. Epidemiol Serv Saúde. 2022;31(1):e2021405. doi: https://doi.org/10.1590/S1679-49742022000100010

11. Medeiros GC, Thuler LCS, Bergmann A. Determinants of delay from cancer diagnosis to treatment initiation in a cohort of Brazilian women with breast cancer. Health Soc Care Community. 2021;29(6):1769-78. doi: https://doi.org/10.1111/hsc.13284

12. Yedjou CG, Sims JN, Miele L, et al. Health and racial disparity in breast cancer. Adv Exp Med Biol. 2019;(1152):31-49. doi: https://doi.org/10.1007/978-3-030-20301-6_3

13. Marcelino AC, Gozzi B, Cardoso-Filho C, et al. Race disparities in mortality by breast cancer from 2000 to 2017 in São Paulo, Brazil: a population-based retrospective study. BMC Cancer. 2021;21:998. doi: https://doi.org/10.1186/s12885-021-08735-2

14. Beltrán Ponce SE, Thomas CR, Diaz DA. Social determinants of health, workforce diversity, and financial toxicity: a review of disparities in cancer care. Curr Probl Cancer. 2022;46(5):100893. doi: https://doi.org/10.1016/j.currproblcancer.2022.100893

15. Guerra MR, Silva GA, Nogueira MC, et al. Sobrevida por câncer de mama e iniquidade em saúde. Cad Saúde Pública. 2015;(31):1673-84. doi: https://doi.org/10.1590/0102-311X00145214

16. Ministério Público Federal (BR), Procuradoria da República no Rio de Janeiro [Internet]. Rio de Janeiro: Procuradoria da República no Rio de Janeiro; [data desconhecida]. MPF e DPU querem contratação de pessoal e destinação de mais leitos federais para covid-19; 2020 abr 1 [acesso 2023 ago 10]. Disponível em: https://www.mpf.mp.br/rj/sala-de-imprensa/noticias-rj/mpf-e-dpu-querem-contratacao-de-pessoal-e-destinacao-de-mais-leitos-federais-para-covid-19

17. Awan A, Esfahani K. Endocrine therapy for breast cancer in the primary care setting. Curr Oncol. 2018;25(4):285-91. doi: https://doi.org/10.3747/co.25.4139

18. Duarte MB, Argenton JL, Carvalheira JB. Impact of Covid-19 in cervical and breast cancer screening and systemic treatment in São Paulo, Brazil: an interrupted time series analysis. JCO Glob Oncol. 2022;8:e2100371. doi: https://doi.org/10.1200/GO.21.00371

19. Cavalcante FP, Abdala E, Weissmann L, et al. Impact of Covid-19 disease in early breast cancer management: a summary of the current evidence. JCO Glob Oncol. 2022;8:e2100357. doi: https://doi.org/10.1200/GO.21.00357

20. Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde. Pertuzumabe para o tratamento do câncer de mama HER2-positivo metastático em primeira linha de tratamento associado ao trastuzumabe e docetaxel. Brasília, DF: Conitec; 2017. (Relatório de recomendação, n. 319).

21. Ministério da Saúde (BR). Portaria conjunta nº 19 de 3 de julho de 2018. Aprova as Diretrizes Diagnósticas e Terapêuticas do Carcinoma de Mama. Diário Oficial da União, Brasília, DF. 2018 jul 16; Edição 135; Seção: 1:59

22. Instituto Nacional de Câncer José Alencar Gomes da Silva. Contrato nº 219/2020. Termo de contrato de prestação de serviços que fazem entre si a união, por intermédio do Instituto Nacional de Câncer José Alencar Gomes da Silva – INCA e a empresa Leica do Brasil importação e comércio Ltda [Internet]. Rio de Janeiro: INCA; 2020. [acesso 2023 ago 11]. Disponível em: https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/leica_-_contrato_no_219-2020.pdf

23. Ministério Saúde (BR), Sistema Único de Saúde; Instituto Nacional de Câncer José Alencar Gomes da Silva. Informe SUS-ONCO [Internet]. 2020 [acesso 2023 ago 11];IV(39):1-3. Disponível em: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document/informe-sus-onco-julho-2020_0.pdf

24. Ministério da Saúde (BR). Portaria no. 1559, de 1º de agosto de 2008. Institui a Política Nacional de Regulação do Sistema Único de Saúde – SUS [Internet]. Diário Oficial da União, Brasília, DF. 2008 ago 4. Seção: 1:48. [acesso 2023 ago 11]. Disponível em: https://bvsms.saude.gov.br/bvs/saudelegis/gm/2008/prt1559_01_08_2008.html

25. Aquino EML, Silveira IH, Pescarini JM, et al. Medidas de distanciamento social no controle da pandemia de Covid-19: potenciais impactos e desafios no Brasil. Ciênc saúde coletiva. 2020;25(Suppl 1):2423-46. doi: https://doi.org/10.1590/1413-81232020256.1.10502020

26. Rio de Janeiro, Secretaria de Estado de Saúde, Comissão Intergestores Bipartite. Deliberação CIB-RJ nº 6.475, de 12 de agosto de 2021. Pactua a Macrorregião de saúde do estado do Rio de Janeiro [Internet]. Diário Oficial do Estado do Rio de Janeiro, Rio de Janeiro. 2021 ago 13. Ano XLVII; nº 155:24. [acesso 2023 ago 11]. Disponível em: http://www.ioerj.com.br/portal/modules/conteudoonline/mostra_edicao.php?k=BBBBDC11-5C7PA-4140-A08F-0465A83F095C

27. Jardim BC, Migowski A, Corrêa FM, et al. Covid-19 no Brasil em 2020: impacto nas mortes por câncer e doenças cardiovasculares. Rev Saúde Pública. 2022;56:22. doi: https://doi.org/10.11606/s1518-8787.2022056004040

28. Costa GJ, Azevedo CRAS, Costa Júnior JI, et al. Higher severity and risk of in-hospital mortality for Covid-19 patients with cancer during the year 2020 in Brazil: a countrywide analysis of secondary data. Cancer. 2021;127(22):4240-8. doi: https://doi.org/10.1002/cncr.33832

29. Duarte MBO, Leal F, Argenton JLP, et al. Outcomes of Covid-19 patients under cytotoxic cancer chemotherapy in Brazil. Cancers. 2020;12(12):3490. doi: https://doi.org/10.3390/cancers12123490

30. Mafra da Costa A, Ribeiro AL, Ribeiro AG, et al. Impact of Covid-19 pandemic on cancer-related hospitalizations in

Brazil. Cancer Control. 2021;28:10732748211038736. doi: https://doi.org/10.1177/10732748211038736

31. Hyeda A, Costa ESM, Kowalski SC. The trend and direct costs of screening and chemotherapy treatment of breast cancer in the new coronavirus pandemic: total and interrupted time series study. BMC Health Serv Res. 2022;22(1):1466. doi: https://doi.org/10.1186/s12913-022-08884-5