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PUBLICAÇÃO OFICIAL DA **SBC**

REVISTA DA SOCIEDADE BRASILEIRA DE
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Sociedade
Brasileira de
Cancerologia

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EDITORIAL

REVISTA DA SOCIEDADE BRASILEIRA DE CANCEROLOGIA



Caro leitor,

É notória a velocidade com que o conhecimento oncológico preventivo, diagnóstico e terapêutico consolida-se, renova-se e aprimora-se a cada dia, em todos os seus cenários e capítulos.

Diante desta miríade de conhecimento diariamente produzida, garantir informação técnica de altíssima qualidade e forte evidência científica, sobretudo no cenário atual de desinformação, charlatanismo e deturpação da Medicina, é uma missão desafiadora, mas gratificante.

A Revista da Sociedade Brasileira de Cancerologia, com seus colaboradores, parceiros e conceituado conselho editorial, tem a honra de iniciar mais um ano este compromisso em difundir os importantes avanços em pesquisa, prevenção, rastreamento, diagnóstico e tratamento oncológico, com rigor crítico, técnico e ético.

Autores e coautores do país e além das fronteiras são convidados a compor este time em 2024, produzindo e publicando conhecimentos capazes de transformar a realidade daquele que é o motivo da nossa profissão: o paciente oncológico.

Boa leitura!

Cleydson Santos

Oncologista Clínico e Coordenador do Serviço de Oncologia do Hospital Mater Dei Salvador

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Sociedade
Brasileira de
Cancerologia



**PUBLICAÇÃO OFICIAL DA
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DE CANCEROLOGIA, COM
A PARTICIPAÇÃO DA
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Breast Cancer – Reflections about screening and early detection

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1 - INTRODUCTION

The Brazilian population and health managers have been facing an increase in the number of cancer cases due not only to the rapid aging of the population, but also to lifestyle changes and an increase in environmental exposure and occupational risk that results in a bigger risk in the development of the disease¹.

In Brazil, excluding non-melanoma skin tumors, breast cancer is the one with the highest incidence in all regions, with higher rates in the South and Southeast. It is also the main cause in death in Brazilian women per cancer, with 17,825 deaths from the disease per year, which is equivalent to a risk of 16.47 deaths/100,000 women. Only in the north region the deaths from breast cancer are supplanted by cervical cancer².

The movement October Pink is, without doubt, the more successful campaign linking one symbolic color to the work in awareness from the population about prevention and early diagnosis of a neoplastic disease, with the development of actions in Brazil and around the world in the area of comprehensive care for breast disease.

Despite of countless initiatives carried out in our country at the scope of the Brazilian Unified Public Health System (SUS) and from the Supplementary Health Care system, yet we live together with worrying mortality rates and many inequities.

Data generated by the National Cancer Institute (INCA) makes it possible to define priorities in actions and investments. We evolve in decades at the biological knowledge of this heterogeneous disease. We progress in the diagnosis, at the molecular classification, local treatment, systemic treatment and supportive care, with a great impact on the management of the disease and great potential for reducing mortality.

The economic repercussion generated by this neoplasm is also immense. The costs direct and indirect in all line in care require planning strategic shared between state and society civil organized, optimizing resources to obtain more promising results.

This article expresses the personal opinion of the authors. We briefly focus on some aspects that we consider important, to contribute to the reflection of the actors involved in tackling the issue. An invitation to synergism, union and reconstruction.

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2 - OCTOBER PINK

The October Pink movement is celebrated throughout the world. This color symbolizes the fight against Breast Cancer and encourages the participation of the population, companies and entities at the coping of the illness.

The history of the movement dates back to the last decade of the 20th century. After several American states began to develop actions isolated drawing attention to breast cancer, particularly encouraging mammography, the pink ribbon was launched by the "Susan G. Komen for The Cure" Foundation and distributed during a traditional race realized in New York (USA). In this period, the American Congress approved the adoption of October as national breast cancer prevention month.

In Brazil, the first impactful initiative related to the October Pink was the lighting of "Constitutionalist Soldier Mausoleum", Ibirapuera obelisk, occurred in 21st October, 2002. From 2008, miscellaneous entities related to breast cancer spread the initiative with lighting several monuments and buildings in their cities, including The Statue of Christ Redeemer in Rio de Janeiro in January, that was for the first turn lit up in Pink in October of that year.

Since 2010, INCA participate of this movement, opening space for debates, propagating information to the population and professionals, as well as promoting actions in set with medical entities - Brazilian society of Mastology, Cancerology and Clinical oncology (SBM, SBC, SBOC), among others. Such initiatives aim to stimulate awareness of the problem, prevention, incentive the coping and the reduction of prejudices, in addition to seeking confluences in opinions for fight untruths, unfortunately common and of easy propagation in ours times.

The undeniable success of this movement brings us the need of a deep reflection about its impacts. There is a standard seasonal pattern during October in searching Internet terms such as "breast cancer" and "mammography", suggesting strong relationship causal with the October Pink campaign³, requiring the responsibility for disseminating correct information.

One concern, is the danger in oversizing the benefits of screening isolated⁴. Campaigns as October pink targeted exclusively for young women can induce the realization in screening outside from the target population with practice of different periodicities of those recommended by the Ministry of Health. (MS)

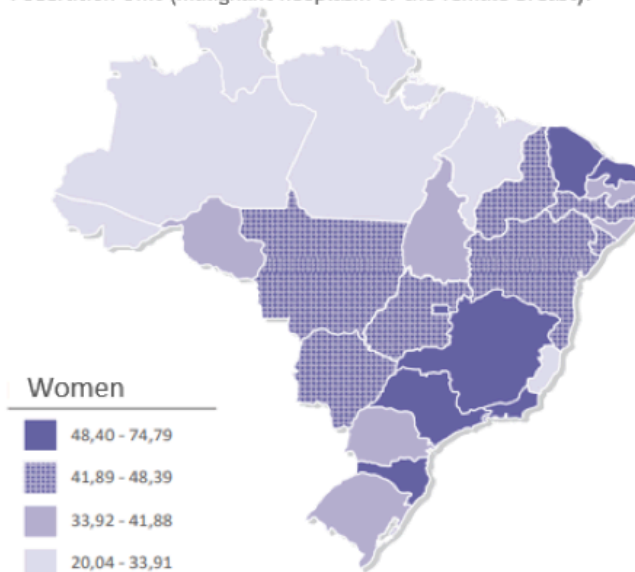
We need promote the interlocution between epidemiologists, managers and care professionals, converging interests and concerns for ramp up clear information based in scientific evidence advisors to the professionals in health and the general population.

3 - EPIDEMIOLOGY

Cancer is one of the main problems in public health in the world, corresponding, in most of the countries, as the first or the second cause of premature death. In countries with a high level of human development (IDH), as U.S, which screening, early detection and treatment are organized, there was progressive reduction at mortality rates for the disease⁶. At Brazil, however, that rate has increased or at the maximum kept stable, highlighting the urgent need for greater effectiveness in controlling the disease.

There is a significant improvement in availability and quality of information on cancer incidence and mortality in our country. The cancer incidence estimates presented by INCA show the growth of the disease in Brazil. In 2018, we evaluate 600,000 new cases per year. In 2021, 625,000 new cases and now in 2023, 704,000 new cases are estimated for the next three years².

Figure 1: Spatial representation of adjusted incidence rates per 100 thousand women, estimated for the year 2023, according to Federation Unit (malignant neoplasm of the female breast).



Source: Estimate | 2023 - Cancer Incidence in Brazil.

REGION	ESTIMATED RISK
SOUTH EAST	84,46/100.000
SOUTH	71,44/100.000
MIDWEST	57,28/100.000
NORTHEAST	52,20/100.000
NORTH	24,99/100.000

Mortality is also quite high: there were 17,825 deaths per breast feminine cancer in Brazil, equivalent 16.47/deaths/ 100,000 women, according to INCA data from 2020⁵.

4 - RISK FACTORS

Primary prevention of a malignant neoplasm includes the knowledge of risk factors associated and searching the best measures for reduction or elimination of its deleterious action. Cancer is a complex and multifactorial disease. The most important risk factor for its incidence is age above in 50 years. Others factors are associated with hormonal or reproductive conditions – nulliparity, pregnancy late, smaller time in breast-feeding; conditions behavioral – obesity, alcoholism, sedentary lifestyle; occupational – work night shift and exposure to radiation, in addition to hereditary factors – 10% of the cases, in syndromes increasingly well-defined genetics⁶.

O newly released “Code Latin American and Caribbean against cancer” for the International Agency for Research on Cancer (IARC) and the Pan American Health Organization (PAHO) recommends actions to prevent the illness. A list includes healthy weight maintenance, regular physical activity, food balanced avoiding consumption of ultra-processed foods, sugary drinks, sausages preferring house cooking foods. It also highlights breastfeeding for as long as possible as form in to bring impacts significant at incidence from the disease⁷.

5 - SCREENING

Mammography screening is the strategy more implemented at the world for early detection of breast cancer, and consists at periodic realization of exam in women without signals or symptoms of the illness. Mammography tracking is a public politics since 2004⁸.

The World Health Organization (WHO) emphasizes the necessity of actions in systematic communication, planning, monitoring, and the assessment of the impact of tracking. The strategy ranges from identifying and inviting women from the target population considering their range age, continuing to diagnostics investigation and further care with patients with abnormal exams and treatment.

According to the guidelines for early detection of breast cancer published in 2015 by INCA, mammographic screening should be offered to women aged 50 to 69, once every two years, considering that this is the range age and frequency observed as a favorable balance between risks and benefits of this strategy⁹. This recommendation was ratified in 2022 in the National Commission for the Incorporation of Technologies of SUS (CONITEC) which evaluated the enlarge-

ment of use of mammography for tracking breast cancer in asymptomatic women, with habitual risk, outside the recommended age range. After extensive evaluation, it was concluded that, although some meta-analyses demonstrated potential reduction in 15 to 20% mortality rate per breast cancer in women with less in 50 years submitting tracking mammography, this strategy cannot be recommended below this range age to the total populational. Several factors were considered in this decision, such like the possible increase in unnecessary procedures such as images, biopsies and surgeries; anxiety related to breast cancer; discomfort at the time of screening and exposure to low-level radiation dose. For the range age above 69 years, it was considered also no benefit in this indication. However, there are few studies in this age group of worse quality¹⁹.

6 - CONSIDERATIONS

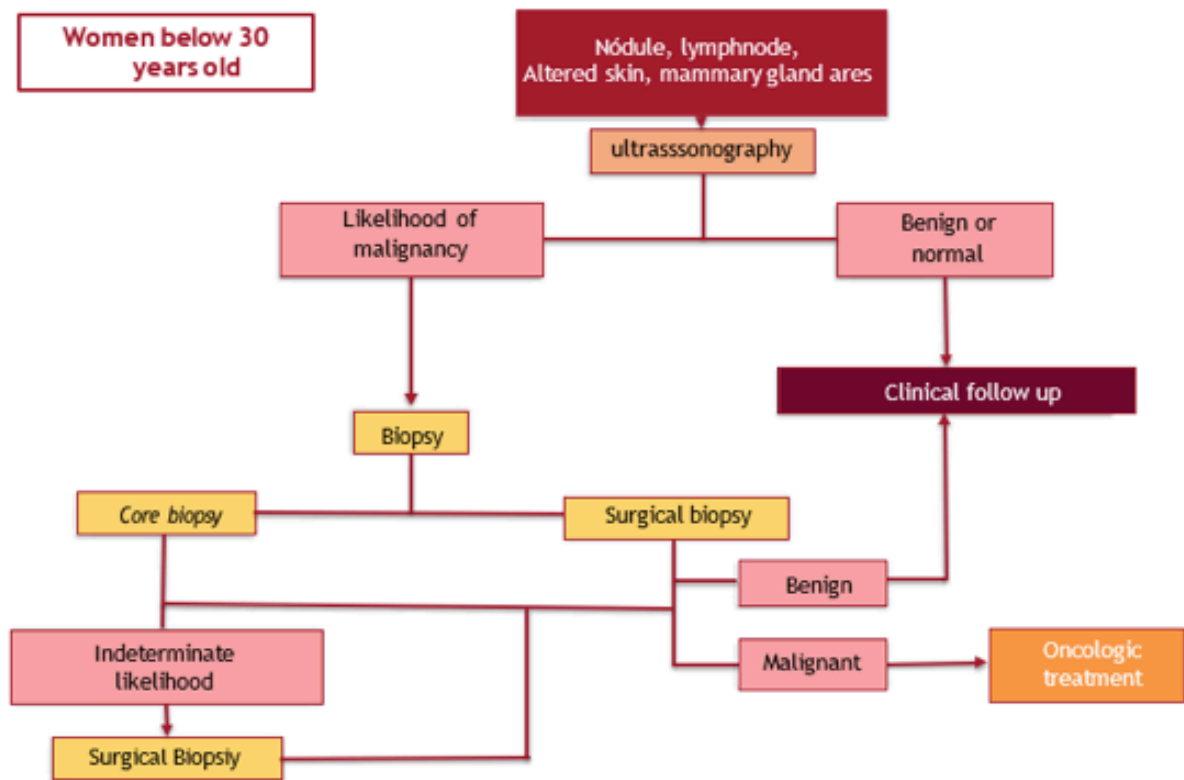
The age range and frequency of exams recommended by INCA and MS guidelines in breast cancer screening is still a controversial subject¹¹. We follow recommending screening in age range from 50 to 69 years, biennial. We recognize that there is evidence of an increase in the number cases in breast cancer in young women and that what in others countries age range target starts to the 40 years. Study in cohort published shows effectiveness of early tracking, mainly from 45 to 50 years¹². Nonetheless, in Brazil, the screening rate is below the recommended considering the range age current adopted. Enlarging it before achieving a better organization of system and a resolution of the existing difficulties can be harmful. Furthermore, tracking in young women demand the incorporation of technology not totally available, such as digital mammography and tomosynthesis. Another difficulty is the need to complement the screening with breast ultrasonography, indicated in BI RADS 0 and 3 results on mammography, which can represent 7% of women tracked in the range of 50 to 69 years, and with potential significant increase of this percentage in younger women, in function of the bigger density of breasts.

The realization of a biopsy per needle thick or surgery, as well as the anatomy pathological exam is another big challenge to be faced. Today is fully necessary in all cases to perform immunohistochemistry and the classification of tumors in molecular bases as that defines all treatment strategy. The biggest impacts at decrease in mortality for breast cancer comes from the association of tracking and treatment of the disease in initial stage. Efforts exaggerated in trying to expand mammography coverage without improving the treatment quality cannot modify our current situation¹³.

Increasing the range from 69 to 74 years can be consistent between INCA and the recent recommendation of the 'Latin American and Caribbean Code against Cancer', at the which INCA had important contribution. This document indicates the realization of clinical examination of breasts in women above 40 years and biennial mammography at age range from 50 to 74 years old. A uniformity in conduct at the continent must be an objective to be achieved⁷.

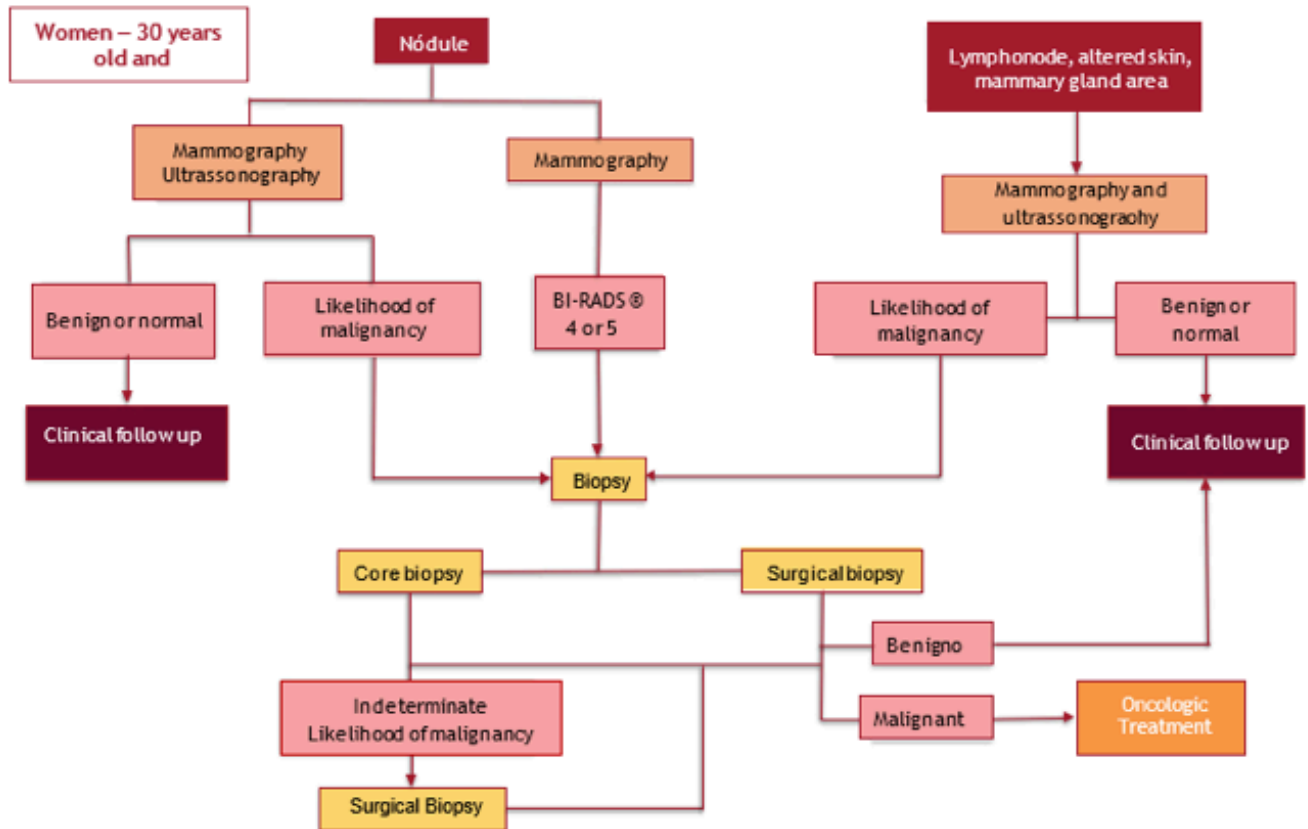
We reaffirm to the recommendations of INCA. Figures 2, 3 and 4.

Figure 2 - Flowchart Proceedings - Investigation Breast Cancer - Women below 30 years old.



Source: Technical parameters for breast cancer early detection / Instituto Nacional de Câncer. - Rio de Janeiro : INCA, 2022.

Figure 3 - Investigation Breast Cancer - Symtomatic Women above 30 years old.



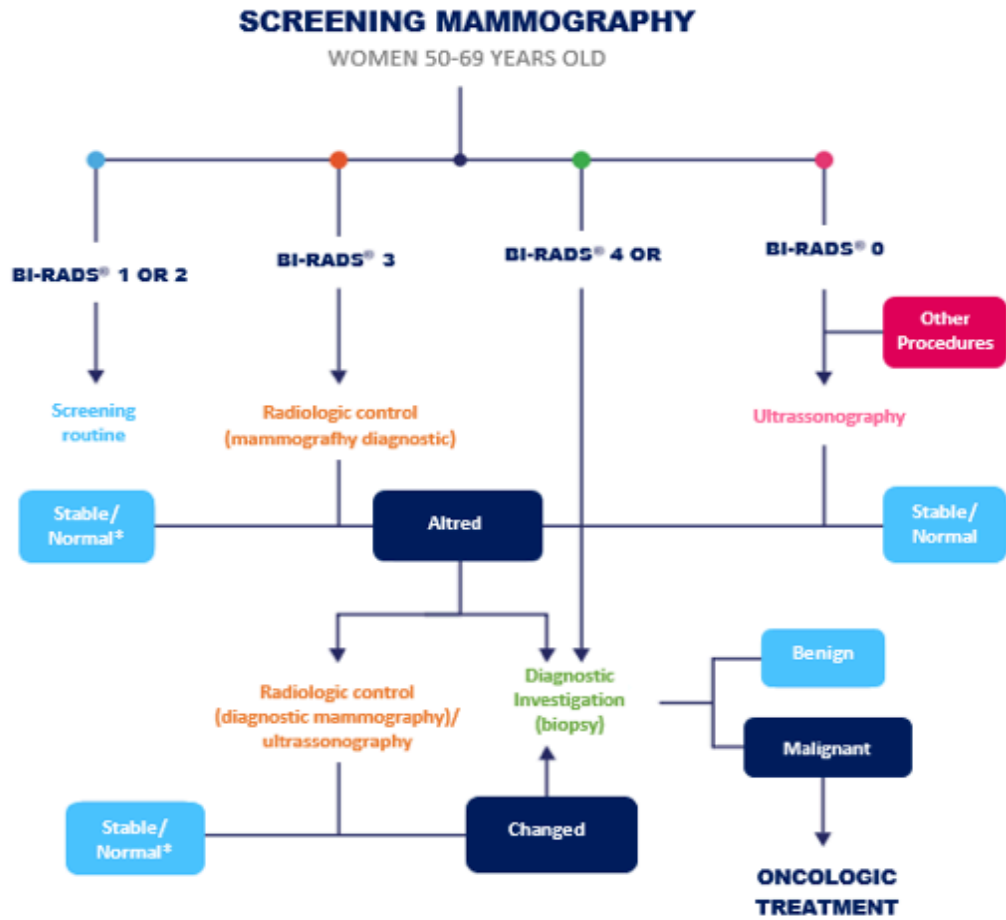
Source: Technical parameters for breast cancer early detection / Instituto Nacional de Câncer. - Rio de Janeiro : INCA, 2022.

CONCLUSION

Breast cancer is the main in incidence among women. We improve our possibilities in early detection instituting treatment based at molecular profile with greater chance in success¹⁴. We need unity, joining the knowledge of the health professionals with the efforts of society civil organized, building consensus and informing the population with clarity, allowing managers a rational use of the resources.

Without interlocution we may waste resources and not modifying the hard reality we live today. INCA reaffirms his position in technical execution, but it's ever open to the dialogue with constructive intention.

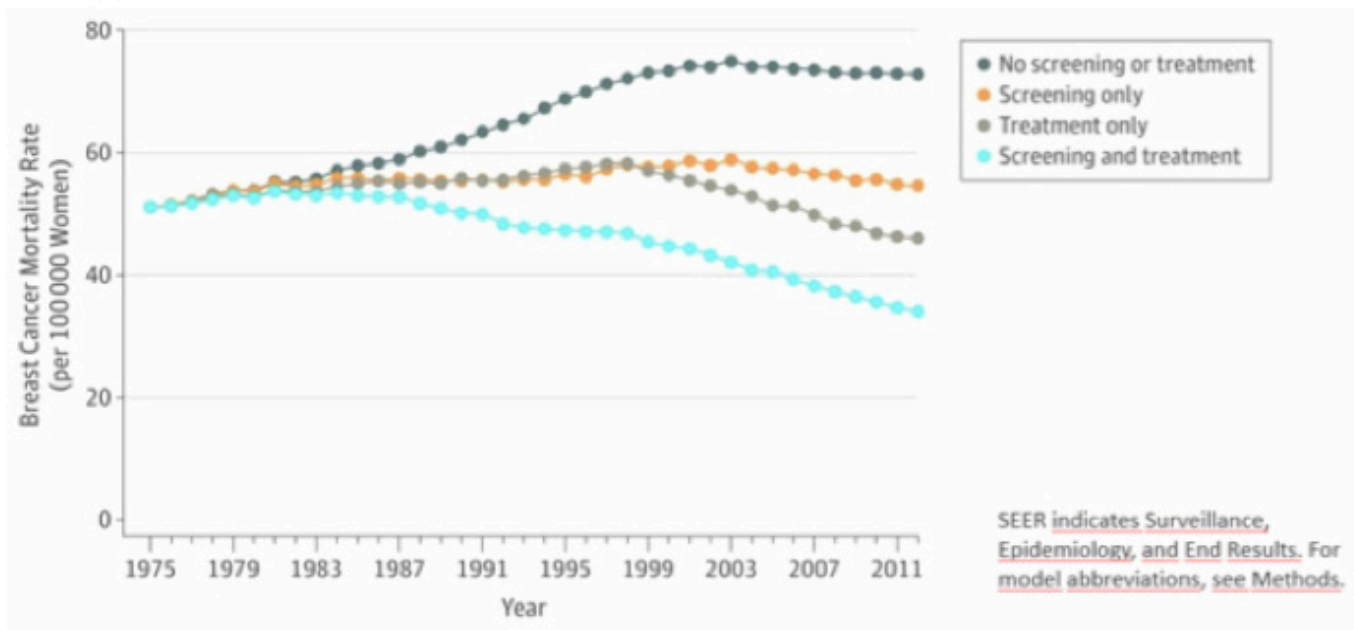
Figure 4 - Flowchart Proceedings - Breast Cancer Screening and diagnostic investigation.



SOURCE: Technical parameters for breast cancer screening. / Instituto Nacional de Câncer José Alencar Gomes da Silva. - Rio de Janeiro: INCA, 2021.

Note: Draft based on Breast Cancer Guidelines (age range, periodicity)⁴ and Atlas BI-RADS⁵.

Figure 5. Impact from the mortality Preview, associated to the Tracking, treatment.



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Time between the diagnosis and treatment of esophagus cancer: comparative study in between 2018-2019 and 2020-2021 in Brazil

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ABSTRACT

INTRODUCTION: Esophagus cancer is the fifth most frequent tumor in the gastrointestinal tract, responsible for 358 thousand deaths per year (1). Because most of the patients are asymptomatic, clinical suspicion is usually low. As it is a rapidly progressive cancer, it needs a fast intervention. This is guaranteed by the law n° 127232/2012, in which an oncologic patient must start treatment at least 60 days after diagnosis. This research aims to analyze if this right was guaranteed in Brazil between 2018 and 2021, considering the COVID-19 pandemic period. **OBJECTIVES:** To establish a comparison in the time between the diagnosis and the treatment of esophagus cancer in Brazil, during the biennia 2018-2019 and 2020-2021, considering the impact of COVID-19 pandemic. **METHODS:** This research is an ecologic study with secondary data, about the consequences of the pandemic in the time to start the treatment of malignant esophagus neoplasm in Brazil, between 2020-2021 and 2018 and 2019. The data was obtained from the "PAINEL – oncologia do Departamento de Informática do Sistema Único de Saúde (DATASUS)", considering the variables' time to start the treatment and year of treatment. The data was analyzed and categorized utilizing the program Microsoft Excel (2019). **RESULTS:** Between 2018 and 2021 there were 19186 patients diagnosed and treated, the number of treated people in at least 60 days after the diagnosis being 9713 (50,62%), while the ones in which the beginning in less than 60 days was 9473 (49,37%), a difference of 240 (2,5%). There was a non-linear increase in the number of patients treated in more than 60 days, with a decay of 0,98% in 2020 and, right after, an increase of 2,18% in 2021. However, from 2019, the cases with more than 60 days to treat stand out in relation to the less than 60 days. Still, it was observed a discreet increase of 328 cases (6,46%) with less than 60 days to treat in the whole period. **CONCLUSION:** This study showed that the treatment in more than 60 days after the diagnosis of esophagus cancer has increased quantitatively in a non linear form, while the treatment in less than 60 days increased discreetly in percentage value. Considering these findings, it is suggested that treatment made in more than 60 days has increased during the COVID-19 pandemic, evidencing a possible delay in the start of the treatment in Brazil during this period.

Keywords: Esophagus cancer, comparative study, Brazil, cancer, esophagus, diagnosis, treatment.

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INTRODUCTION

Esophagus cancer is the fifth most frequent tumor in the gastrointestinal tract, responsible for 358 thousand deaths per year¹. Esophageal neoplasia is among the 10 most common in Brazil, according to data from the National Cancer Institute (INCA). In 2000 it was the 6th deadliest type of cancer, leading to approximately 5,000 deaths³. The potential risk factors one might possess for being diagnosed with esophageal adenocarcinoma, according to the results of these studies, are white race, male sex, gastroesophageal reflux disease (GERD), cigarette smoking (or a history of smoking), and obesity⁶. Because most of the patients are asymptomatics, clinical suspicion is usually low and, as it is a rapidly progressive cancer, it needs a fast intervention, but because the symptoms usually come late we have worse prognostics. Over the last few centuries there have been advancements in the visualization and removal of these lesions, but with no real overall impact on survival rates². The treatment is required to be urgent and the Brazil government has the obligation to give it to the patients in need, this is guaranteed by the law nº 127232/2012, in which an oncologic patient must start treatment at least 60 days after diagnosis. This research aims to analyze if this right was guaranteed in Brazil between 2018 and 2021, considering the difficulties of the healthcare system during the COVID-19 pandemic period.

JUSTIFICATION

During the COVID-19 pandemic, the healthcare system in Brazil was severely affected by this disease, not only that but most patients got scared of going to hospitals, leading to less amounts of diagnosis and treatment of other infirmities. That is why it is important to know if the law nº 127232/2012, in which an oncologic patient must start treatment at least 60 days after diagnosis, was followed correctly during that period of time. Since esophagus cancer is one of the most frequent and fatal tumors, these fragilized patients need to have their rights realized.

OBJECTIVES

To establish a comparison in the time between the diagnosis and the treatment of esophagus cancer in Brazil, during the biennia 2018-2019 and 2020-2021, considering the impact of COVID-19 pandemic.

METHODS

This research is an ecologic study with secondary data, about the consequences of the pandemic in the time to start the treatment of malignant esophagus neoplasm in Brazil, between 2020-2021 and 2018 and 2019. The data was obtained from the "PAINEL – oncologia do Departamento de Informática do Sistema Único de Saúde (DATASUS)", considering the variables time to start the treatment and year of treatment.

This research is using public data made available on the DATASUS platform without individual identification. Due to this fact, in accordance with Law No. 12,527/201, which regulates the constitutional right of citizens to access public information, and Resolution CNS No. 510, 2016, Article 2, VI, it is exempt from submission to the Ethics Research Committee (CEP/Conep) due to the characteristics of the data.

In this modeling process, percentages for each year were calculated in correlation with the sum of the total for the period 2018, 2019, 2020, and 2021. This allows for a quantitative analysis of how each year relates to the whole and between the two subtopics of more or less than 60 days.

RESULTS

Between 2018 and 2021 there were 19186 patients diagnosed and treated, the number of treated people in at least 60 days after the diagnosis being 9713 (50,62%), while the ones in which the beginning in less than 60 days was 9473 (49,37%), a difference of 240 (2,5%). There was a non-linear increase in the number of patients treated in more than 60 days, with a decay of 0,98% in 2020 and, right after, an increase of 2,18% in 2021. However, from 2019, the

cases with more than 60 days to treat stand out in relation to the less than 60 days. Still, it was observed a discreet increase of 328 cases (6,46%) with less than 60 days to treat in the whole period.

plasia it is mandatory a multidisciplinary team with 3 fronts: surgical, chemotherapy and radiotherapy, with the need of those 3 because there will be no efficacy if isolated. During the COVID-19 pandemic

Table 1. Rate for the time to the beginning of the esophagus malignant neoplasm treatment in Brazil from 2019-2022. "Datusus: tempo até o início do tratamento oncológico - painel- oncologia"

	2018	2019	2020	2021	Total
Time (n%)					
< 60 days	2130 (22,48%)	2299 (24,26%)	2586 (27,29%)	2458 (28,94%)	9473
> 60 days	1771 (18,23%)	2640 (27,18%)	2545 (26,20%)	2757 (28,38%)	9713

DISCUSSION

Esophageal cancer can be seen as one of the most important from a medical point of view, due to its high fatality rate and the frequency with which it occurs throughout the world.⁷ and this cancer is one of the 10 most common in Brazil.³

The two most common types of esophagus neoplasia are the squamous cell carcinoma and the adenocarcinoma, which correspond to more than 90% of this neoplasia. According to INCA the early diagnosis of this disease generally leads to a better chance of cure, since there is no tracking, because it generally has slow and progressive symptoms, leading to the unconscious adaptation of the patient before he/she looks for a doctor. And this is a country with a good part of its population matching the common affected group of this cancer.

Besides, the diagnosis by itself is late, since the principal symptoms only start to appear when the organ is already compromised.³ With that in mind, it becomes even more necessary to begin that patient treatment, because in this case, time is the esophagus.

Most of its inhabitants cannot afford a correct treatment, so they recur to the "Sistema Único de Saúde" (SUS) that is financed by the government along with some private enterprises. To treat esophageal neo-

plasia it is mandatory a multidisciplinary team with 3 fronts: surgical, chemotherapy and radiotherapy, with the need of those 3 because there will be no efficacy if isolated. During the COVID-19 pandemic the SUS was overloaded with patients suffering from sars cov-2, and it was not able to take an actual response for those who had other conditions, such as esophagus cancer.

The results of this study shows that the treatment in less than 60 days for oncologic patients provided by law was not correctly followed, evidencing that patients with esophageal neoplasia could have been treated in an appropriate way if there was no pandemic. Unfortunately this disease has a very bad prognosis, and that is why it has to be treated since its diagnosis, so that the patients can have a better quality of life.

CONCLUSION

This study showed that the treatment in more than 60 days after the diagnosis of esophagus cancer has increased quantitatively in a non linear form, while the treatment in less than 60 days increased discreetly in percentage value. Considering these findings, it is suggested that treatment made in more than 60 days has increased during the COVID-19 pandemic, evidencing a possible delay in the start of the treatment in Brazil during this period showing that the law nº 127232/2012 was violated.

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Malign neoplasia of encephalon on Piauí-Brazil: incidence in hospitalizations and deaths

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ABSTRACT

Introduction: Encephalon malignant neoplasms represent about 2% of all malignant tumors worldwide, mainly in the brain. They are classified in primary forms, originating from encephalic tissue, arranged in benign and malignant, and in secondary forms (metastatic representation). **Objective:** Evaluate the incidence of hospitalizations and deaths by encephalon malignant neoplasms in Piauí-Brazil per year of notification, age, sex and race, between January 2014 and March 2023. **Method:** This is a transversal, retrospective and quantitative study. The data was collected on the Hospital Information System (SIH/SUS) and the variables selected were: sex, age, and autodeclared race. The Excel software was used to table and evaluate the data. **Results:** It was evaluated the total of 1935 hospitalizations and 179 deaths by encephalon malignant neoplasm, being the apex of cases in 2021 (258) and 2022 (32), respectively. In relation to age, the most affected were 50 to 59 year-olds, with 295 hospitalizations (15,25%) and 37 deaths (26,67%). On hospitalizations by the pathology, there was a predominance of males with 995 cases (51,42%), on deaths there was no specific sex predominance. The race that most predominated was the mixed race, with 1584 hospitalizations (81,86%) and 143 (79,89%) deaths. **Conclusion:** The epidemiological evaluation evidenced that the most affected by hospitalizations and deaths were the mixed race people from ages 50 to 59, with a predominance of male hospitalization. This research is important to group and improve resources to reduce the incidence of deaths.

Keywords: neoplasia; encephalon; hospitalizations; death.

INTRODUCTION

Malignant encephalon neoplasms are a global health concern, accounting for approximately 2% of all malignant tumors worldwide. These tumors primarily originate in the brain and have a significant impact on the patients' quality of life¹.

Despite advances in neuroimaging, molecular biology, and genetics enabling earlier diagnosis and more targeted treatment, Central Nervous System (CNS) neoplasms remain one of the leading causes of death in developed countries. The origin of these tumors is widely debated, with environmental and behavioral factors being as relevant as genetic factors².

Brain tumors are subdivided into primary and secondary forms. Primary forms originate from brain tissue and can be grouped into benign and malignant categories. Secondary forms, on the other hand, represent metastatic tumors originating from other parts of the body³.

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They can be classified by age of onset, histological type, or the site of presentation on the brain. This diversity adds to the complexity of diagnosis and treatment. Symptoms vary widely and depend on the tumor classification, and understanding them is crucial for early diagnosis and effective treatment⁴.

This study aimed to assess the incidence of hospitalizations and deaths from malignant brain neoplasms in the state of Piauí, Brazil, by year of notification, age group, gender, and race/ethnicity, between January 2014 and March 2023.

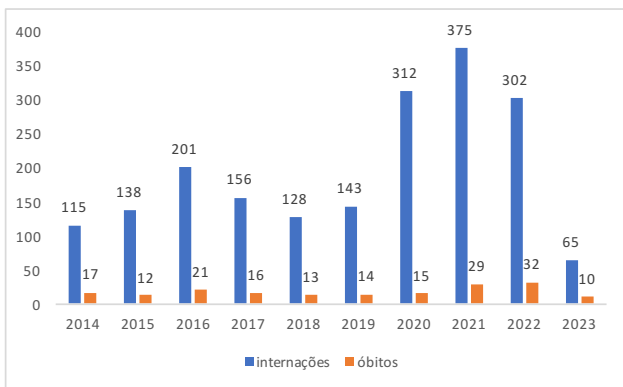
METHOD

This is a cross-sectional, retrospective, and quantitative study. Data was collected from the Hospital Information System (SIH/SUS) of DataSUS⁵, pertaining to hospitalizations and deaths due to malignant brain neoplasms. The selected variables included processing year, gender, age, and self-declared race. Ethical committee review was not required as publicly available data were used. The Excel program was used for data tabulation, analysis, and the production of graphs.

RESULTS

A total of 1935 hospitalizations were analyzed, with the highest numbers in 2021 (375 cases), 2020 (312 cases), and 2022 (302 cases). Regarding mortality, there were 32 deaths in 2022, followed by 29 deaths in 2021 and 21 deaths in 2016, as shown in **Graph 1**.

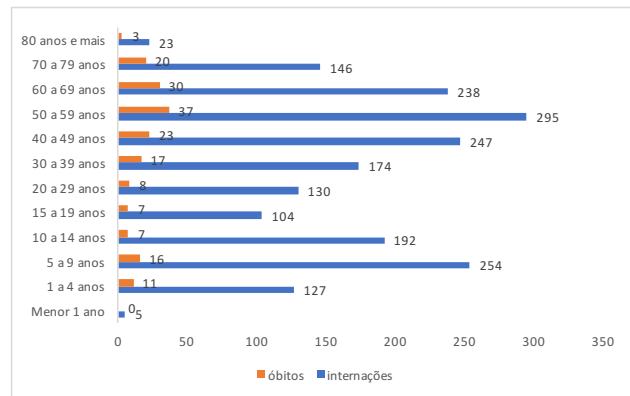
Graph 1: Number of hospitalizations and deaths due to malignant brain neoplasms by year of processing in Piauí, from January 2014 to March 2023.



SOURCE: Datasus. Teresina-PI, 2023.

Regarding age groups, the highest number of hospitalizations was in the 50-59 age group with 295 hospitalizations (15.25%), followed by the 5-9 age group with 254 hospitalizations (13.12%). As for deaths, the 50-59 age group also had the highest mortality, with 37 deaths, followed by the 60-69 age group with 30 deaths. These data are graphically represented in **Graph 2**.

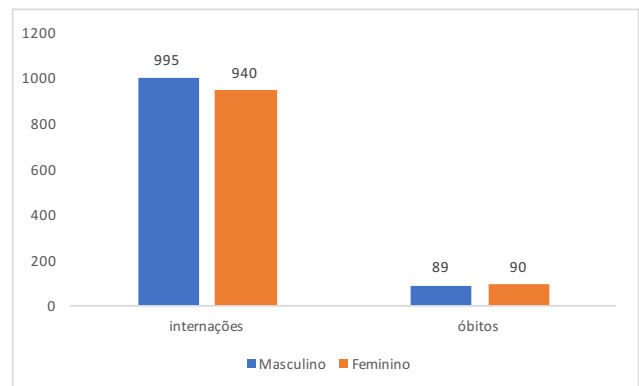
Graph 2: Number of hospitalizations and deaths due to malignant brain neoplasms by age group in Piauí, from January 2014 to March 2023.



SOURCE: Datasus. Teresina-PI, 2023.

As shown in **Graph 3**, in hospitalizations for this condition, there was a slight predominance of males with 995 cases (51.42%) compared to females with 940 cases (48.58%). In terms of deaths, there was no significant gender predominance, with females having 90 cases and males having 89 cases.

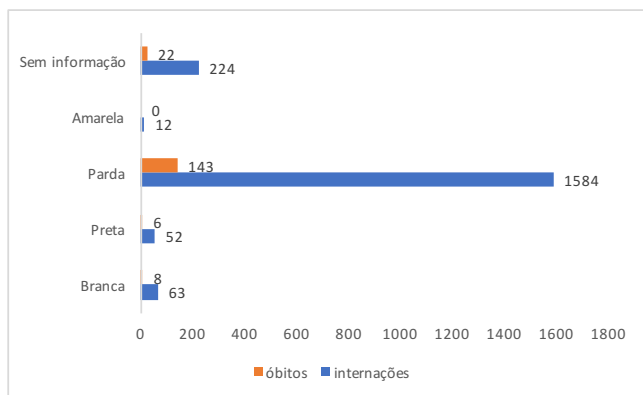
Graph 3: Number of hospitalizations and deaths due to malignant brain neoplasms by gender in Piauí, from January 2014 to March 2023.



SOURCE: Datasus. Teresina-PI, 2023.

The prevalent race/ethnicity was mixed with 1584 hospitalizations (81.86%) and 143 deaths (79.89%), as shown in **Graph 4**.

Graph 4: Number of hospitalizations and deaths due to malignant brain neoplasms by race/ethnicity in Piauí, from January 2014 to March 2023.



SOURCE: Datasus. Teresina-PI, 2023.

DISCUSSION

During the period under analysis, the region presented a total of 1935 hospitalizations and 179 deaths caused by malignant brain neoplasms. It is noteworthy that there was a substantial increase in cases in 2021 and 2022, indicating a clear upward trend in the incidence of the disease. Malignant brain neoplasms are a significant public health issue. In Brazil, between 2002 and 2004, there were 405415 deaths from neoplasms, with central nervous system tumors representing a considerable portion of these deaths⁶.

It's worth noting that the age group of 50 to 59 years had the highest number of hospitalizations, indicating a possible predominance of this condition in that age group. However, it's crucial to emphasize that additional investigations are needed to confirm this assumption, as these tumors can occur at any age, gender, and race⁷.

Regarding gender, the data reveals a slight male predominance in hospitalizations, while in deaths, this

disparity is not significant, suggesting that gender may not be a determining factor in mortality from malignant brain neoplasms. Each year, the longevity of the Brazilian population has been increasing, which could be associated with a reduction in the mortality rate. According to the IBGE News Agency, the projection is that life expectancy in 2030 will be approximately 73 years⁸.

In terms of race/ethnicity, it is observed that the mixed population was the most affected, indicating a possible higher incidence in this group. However, it's of utmost importance to consider the influence of other socioeconomic and health factors that may be contributing to these results⁹.

These results provide valuable information about the incidence of malignant brain neoplasms in the Piauí region, Brazil. However, it is crucial to conduct further in-depth research to understand the underlying factors behind these trends and, thus, develop effective strategies for the prevention and treatment of this condition.

CONCLUSION

From the study, it can be concluded that the age group with the highest number of hospitalizations and deaths due to malignant brain neoplasms was 50 to 59, the most prevalent race was the mixed one, and there was a slight male predominance in hospitalizations for the condition. Therefore, it is necessary to implement public policies for the early diagnosis of malignant brain neoplasms by conducting preventive campaigns, especially targeting the population highlighted in the study.

Furthermore, the study noted a significant increase in cases of malignant brain neoplasms in the years 2021 and 2022, indicating a trend of the condition worsening and potentially becoming a considerable public health issue. Hence, it is necessary to encourage symptomatic patients to seek medical care and allocate resources to improve patient diagnosis and prognosis, ultimately reducing the incidence of deaths from this disease.

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Prostate cancer mortality: temporal trend in Brazil.

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ABSTRACT

Prostate cancer (CaP) is the second most common malignant tumor among men in Brazil and represents a significant factor in mortality when diagnosed late. Studies on mortality are relevant sources for understanding the epidemiological profile and measuring the importance of PCa as a public health problem. The objective was to describe the distribution and temporal trends of the mortality rate in different age groups (30 to 80 years or more) in Brazil between the years 2011 - 2020. The research has a quantitative and analytical character, through the collection of mortality data in the Mortality Information System (SIM) of the Ministry of Health (SIM/MS/DATASUS). The mortality rate due to malignant prostate neoplasia was calculated annually, considering age range, and then arranged in simple dispersion data. According to the analyses, it was observed that the incidence of prostate cancer was 95.17% in individuals over 60 years of age, highlighting the age group of 80 years or more in which it was 44%. Furthermore, the mortality rate prevailed in white ethnic groups, with low education and married people. Among the years analyzed, the period with the peak in mortality was in 2017, representing 29.25%. Furthermore, a linear decline in PCa mortality rates was evidenced in all age groups between 2011 and 2020. However, there was a higher prevalence of deaths from the sixth decade of life onwards, with emphasis on the population over 80 years. And, it was possible to observe a lower number of deaths among individuals aged 30 to 59 years.

Keywords: Prostate cancer. Time trend. Mortality.

INTRODUCTION

Prostate cancer (CaP) is the second most common malignant tumor among men in Brazil and represents a significant factor in mortality when diagnosed late. Tumor growth is insidious, therefore, screening tests are necessary to identify the disease early and favor the prognosis¹.

The increase in its incidence over the years is attributed to the increase in the population's life expectancy and advances in diagnostic procedures². The disease mainly affects people over the age of 65. According to the National Cancer Institute (INCA), CaP is predominant in all Brazilian states, accounting for 72 thousand new cases, as an estimate, per year over the next 30 years, second only to cancer of non-melanoma skin, in which approximately 74 thousand new cases are expected to occur in Brazil during the three-year period between 2023 - 2025³. This corresponds to an estimated risk of 67.86 new cases per 100,000 men, according to INCA estimates⁴.

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Early detection impacts treatment success and prognosis. Currently, this screening is carried out annually with a digital rectal exam and the Prostate Specific Antigen (PSA) value, with changes being signs of PCa. The Brazilian Society of Urology (SBU) recommends that all men begin clinical screening, even without complaints, from the age of 50 or from the age of 45, if there are risk factors such as a family history of the disease or black race ⁵.

The Gleason system, named after pathologist Donald Gleason, is a key part of prostate cancer risk classification according to the D'Amico scheme. This system assesses the degree of differentiation of prostate cancer cells, based on microscopic analysis of biopsy samples. The Gleason score ranges from 2 to 10 and is determined by the appearance of the cancer cells, with higher levels indicating less differentiated and more aggressive cells. In conjunction with other factors such as tumor stage and PSA levels, the Gleason score is used in the D'Amico risk classification to help guide treatment decisions in patients with prostate cancer. ⁶ Prostate cancer staging is based on histopathological analysis of the prostate and is classified as low, intermediate and high risk. Low-risk patients have T1-T2a, Gleason 6 (ISUP 1) and PSA less than 10, not requiring additional imaging tests. On the other hand, those with intermediate risk have T2b or Gleason staging 7 (ISUP 2 and 3) or PSA between 10 and 20, and undergo imaging tests such as CT or MRI, along with a bone scan to screen for metastases. High-risk patients, in turn, have T2c or Gleason greater than 7 (ISUP 4 and 5) or PSA greater than 20, requiring the same tests to be carried out to screen for metastases ⁷.

The incidence of prostate cancer has increased significantly over the years, becoming one of the most common neoplasms among the male population ⁴. In this context, the current study seeks to describe the distribution and temporal trends of the PCa mortality rate in different age groups (30 to 80 years or more) in Brazil between the years 2011 - 2020, in order to support future public policies and more effective promotion, prevention and treatment strategies for the disease, in addition to guiding, raising awareness and educating the male population about the importance of preventive exams and early diagnosis. Furthermore, investigating the evolution of the PCa mortality rate in different age groups is necessary in order to identify possible variations and trends.

METHODS

This ecological study aims to describe the distribution and temporal trends of the prostate cancer mortality rate in different age groups in Brazil between 2011 and 2020, in addition to identifying the

prevalence of the PCa mortality rate in people over 30 years old, using collection of mortality data in the Mortality Information System (SIM) of the Ministry of Health (SIM/MS/DATASUS).

Population estimates, classified by sex and age group (>30 years), were obtained from the Brazilian Institute of Geography and Statistics (IBGE) and used to calculate prostate cancer (CaP) mortality coefficients. The ICD-10: C61 category was selected from the available options, and age groups under 30 years old were excluded, obtaining the desired variables one at a time until the completion of the data collection used in this study. The information was obtained by selecting the DATASUS website, followed by the choice of "TABNET" and "Vital Statistics". Then, the option "Mortality - since 1996 according to ICD-10" and "General Mortality" were selected, selecting the option "Brazil by region and Federation unit", directed to the electronic address: <http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sim/cnv/obt10uf.def>. In which, the selected study location was Brazil, divided by Region/Federation Unit".

The mortality coefficient for malignant prostate neoplasia was calculated in each year investigated, considering the age group, where the mortality coefficient was defined as the ratio between the number of deaths and the population at risk, multiplied by 100,000 inhabitants to improve data visualization. It is noteworthy that the mortality coefficient refers to the relationship between the total number of deaths in a given region and the population exposed to the risk of death, unlike the lethality rate, which relates the number of deaths to the number of people affected by the disease. in question.

The inclusion and exclusion criteria were established to begin data collection using SIM/MS/DATASUS data, as seen in **table 1**.

Chart 1. Identification of inclusion and exclusion criteria.

Criteria	
Inclusion	Exclusion
<ul style="list-style-type: none"> - ICD61; - Age group (30 years or more); - Color/Race (white, brown, black, yellow and indigenous); - Education (none, 1-3 years, 4-7 years, 8-11 years, 12 years and more, 1-8 years and 9-11 years); - Marital status (single, married, widowed, legally separated and others). 	<ul style="list-style-type: none"> - Age group <30 years old; - Metastases; - Another CID.

Source : written by the author.

This study follows national research ethics standards and, as it uses only public domain data, does not require approval from the ethics and research committee, regulated by the Guidelines and Standards for Research on Human Beings, in accordance with Resolution No. 466/12 of the National Health Council/Ministry of Health.

The data obtained was compiled and analyzed by GraphPad 8 – Prism. A descriptive analysis of temporal trends was carried out using simple dispersion data. Considering mortality trends that may be different in each age group.

RESULTS

Of the deaths that occurred in Brazil between 2011 and 2020 related to prostate cancer, 95% occurred in individuals over 60 years of age, with 44% of these cases occurring in people aged 80 or over. The majority of deaths were of individuals of white color/race, representing 51% of the total, followed by individuals of brown color/race, with 34% and to a lesser extent in indigenous people. In relation to education, 27% of records had between 1 and 3 years of education and 19% of deaths occurred in individuals who did not have the ability to understand and produce texts in accordance with social practices involving reading and writing, which are based on language, as they do not have education. The lowest proportion was in individuals with 12 years or more of education, represented by 6%. The majority of deceased individuals (54%) were married, totaling 79,277 records and, to a lesser extent, they had another marital status (3%), as shown in **Table 1**.

Table 1. Epidemiological data on deaths from prostate cancer in Brazil, between 2011 – 2020, in people over 30 years of age, in Brazil.

	N	%
Age Range		
80 years and over	64,034	43.71
70 to 79 years old	50,165	34.24
60 to 69 years old	25,222	17.22
50 to 59 years old	6,177	4.22
40 to 49 years old	756	0.52
30 to 39 years old	129	0.09
Age ignored	11	0.01
Color/Race		
White	75,290	51.39
brown	49,795	33.99
Black	14,659	10.01
Yellow	917	0.63
Indigenous	236	0.16
Ignored	5,597	3.82
Education		
1 to 3 years	40,129	27.39
None	28,527	19.47
4 to 7 years	26,527	18.11
8 to 11 years old	15,598	10.65
12 years and over	8,335	5.69
Ignored	27,378	18.69
Marital status		
Married	79,227	54.08
Widower	28,428	19.41
Single	16,586	11.32
Legally separated	8,216	5.61
Other	4,518	3.08
Ignored	9,465	6.46

In 2011, the prostate cancer mortality rate per 100,000 inhabitants was approximately 29, in 2017 reaching its maximum peak of approximately 29 and reaching approximately 28 in the last year (2020). The values referring to the annual mortality rate are shown in **figure 1**.

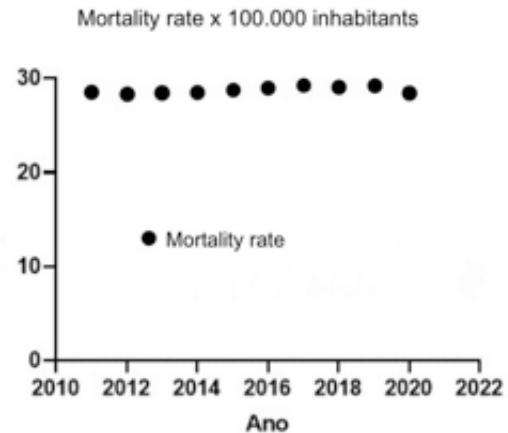


Figure 1. Prostate cancer mortality rate, by year, per 100,000 in habitants among men over 30 years old, between 2011 – 2020, in Brazil.

Source: written by the author, 2023.

Table 2. Prostate cancer mortality rate, per year, among men over 30 years old, between 2011 – 2020, in Brazil.

Year	Number of deaths	Population at Risk	Mortality Rate x 100,000 Inhabitants
2011	13,117	45,995,986	28.5177
2012	13,342	47,195,152	28.2699
2013	13,760	48,408,565	28.4247
2014	14,154	49,607,268	28.5321
2015	14,473	50,414,358	28.7081
2016	14,910	51,494,614	28.9545
2017	15,377	52,567,080	29.2521
2018	15,562	53,628,677	29.0181
2019	15,972	54,672,862	29.2138
2020	15,827	55,696,224	28.4166

Source: written by the author, 2023.

Variations were found in prostate cancer mortality rates per 100,000 inhabitants, in different periods. Variations were found in prostate cancer mortality rates per 100,000 inhabitants, in different periods and in the different age groups analyzed in this study. In the younger age group (men aged 30 to 39), rates varied approximately from 0.07 (2011) to 0.11 (2015), decreasing to 0.08 in 2020. On the other hand, in the younger age group more advanced (more than 80 years old), rates started at 536 (2011) and decreased to 426 in 2020. There was an increase of rates that start from the age of 60, with a value of 41.10 (2011) and 35.56 in 2020 observed in this age group. The analyzes indicated a possible increase in mortality rates over 60 years of age and plausible stability in younger age groups.

The collected data was analyzed using **Figure 2**, which displays dispersion points along with their respective linear trend lines. These analyzes make it possible to identify possible patterns of behavior in the mortality rate in relation to the age of individuals, making it possible to understand the relationship between time and number of individuals. It can be seen in figure 2 that the graphic elements of the age groups of 30 – 39, 40 – 49 and 50 – 59 years are overlapping, as they are close to the x axis, due to their results and the size of the graph.

Table 3. Prostate cancer mortality rate, per 100,000 inhabitants, per year, by age group, among men over 30 years old, between 2011-2020, in Brazil.

	30 to 39 years old	40 to 49 years old	50 to 59 years old	60 to 69 years old	70 to 79 years old	80 years or more
2011	0.0716	0.5852	6.1643	41.1072	173.7894	536.4607
2012	0.1081	0.6017	6.1868	40.5945	172.1766	517.9439
2013	0.0435	0.6257	6.3329	40.0159	167.6800	523.7561
2014	0.1035	0.6716	5.9712	38.8470	169.2200	516.0981
2015	0.1114	0.6246	6.0420	37.3764	155.4219	457.9166
2016	0.0855	0.5165	6.0023	39.5571	148.5854	457.9553
2017	0.0725	0.5605	6.0247	39.7229	149.0325	447.8062
2018	0.0659	0.4701	5.8056	37.7286	148.2538	433.6334
2019	0.0476	0.5334	5.8016	38.6451	142.8626	428.9269
2020	0.0829	0.5512	5.5873	35.5639	131.2904	425.8609

Source: written by the author, 2023

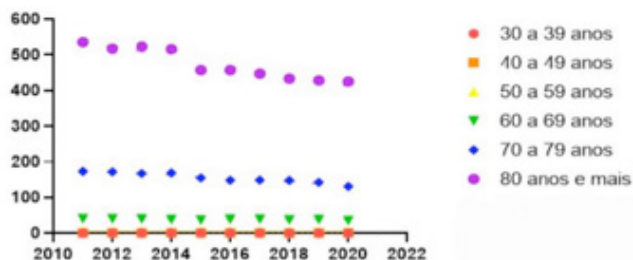


Figure 2. Prostate cancer mortality rate, per 100,000 inhabitants, per year, by age group, among men over 30 years old, between 2011-2020, in Brazil.

Source: written by the author, 2023.

DISCUSSION

It is observed that the number of deaths is higher in white men aged 80 or over, with the highest mortality rate among those who have 1 to 3 years of education. Furthermore, the majority of victims are married men. In 2017, the death rate reached 29.3, the highest peak during the years observed. The mortality rate was consistently higher in individuals aged 80 and over in every year, especially in 2011, with significant increases starting at age 60. No significant results were found related to death from prostate cancer in individuals under 69 years of age.

In general terms, the articles used as a research basis pointed out that prostate cancer mortality in Brazil has demonstrated a trend of stability or reduction in recent years. However, this trend may vary depending on the age group examined. In particular, among the youngest, there is a propensity for stability, in contrast to the more advanced age groups, from the sixth decade of life onwards. These results emphasize the importance of carrying out preventive screenings and ongoing monitoring, especially in older men, to enable early detection and effective treatment of prostate cancer.

There was a reduction in the death rate from prostate cancer in all age groups. However, the incidence of prostate cancer remains high among men aged 70 and over, with a mortality rate 14 times higher than that of men under 60. This suggests that the reduction in mortality can be attributed to early diagnosis and improved treatment.

The current study confirms the findings of Luizaga et al. In 2020 and by Brito and Weller in 2022, highlighting that the majority of deaths occur among men aged 70-79 and 80 years or older compared to other age groups. This provision was attributed to the lack of access to treatments and the aging of the population, as well as the consequences of socioeconomic inequalities in Brazil, highlighting the importance of public policies that address socioeconomic inequalities and promote equitable access to health services throughout the country, especially in relation to CaP. The need for actions that promote awareness about the disease among low- income and low-education populations is highlighted. It was pointed out that patients' quality of life is also an important indicator to be considered and that adequate and individualized treatment can contribute in this aspect.

In this context, analyzes suggest that mortality related to prostate cancer in Brazil is decreasing, although this trend varies according to age, race and level of education. Therefore, carrying out early diagnoses, followed by personalized and appropriate treatments, can lead to a reduction in the mortality rate, resulting in a better quality of life for patients and fewer deaths .

CONCLUSION

The study evaluated prostate cancer mortality rates in Brazil between 2011 and 2020, finding that the mortality rate is higher in men aged 80 or over and the majority of victims are white men with less education. . The analysis showed a downward trend in prostate cancer mortality in Brazil in recent years, but with a significant increase from the age of 60 onwards, with stabilization in the population aged 30 – 59 years. The importance of public policies that

address socioeconomic inequalities and promote equitable access to health services throughout the country is highlighted, especially in relation to prostate cancer, in addition to raising male awareness about the importance of promotion, prevention and early diagnosis of the disease .

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RELATO DE CASO | CASE REPORT

“Under the Shoulders of Giants” - Bilateral Elastofibroma Dorsi: A case report of a rare benign pseudotumor.

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SUMMARY

Elastofibroma dorsi is a rare type of slow-growing benign pseudotumour with a higher prevalence in women over the age of fifty, and knowledge about its physiopathology is still in its early stages. The tumour typically affects predominantly one side but can, however, occur bilaterally. Surgical intervention is usually curative when performed with adequate margins. Due to its rarity, few cases are reported in the current literature. This study presents a case of symptomatic bilateral Elastofibroma dorsi in a 64-year-old female patient.

Key Words - Thoracic Surgery; Surgical Oncology; Tumors.

INTRODUCTION

Elastofibroma dorsi constitutes a rare type of soft tissue pseudotumour of mesenchymal origin, characterized by slow growth and an eminently benign appearance. Due to its rarity, there are few studies on this tumour in the current literature, most of which are case reports and case series.

Its anatomical location, although potentially variable, is classically observed in the lower pole of the scapula, deep below the fibres of the serratus anterior muscle. The physiopathology of elastofibromas is still poorly understood. Some recent histological and immunohistochemical studies suggest the degradation of elastin and the presence of local microtraumas as potential central agents in the pathogenesis of these tumours.

Predominantly unilateral, especially on the right side, these pseudotumours can, however, occur bilaterally, being more than 5 times more prevalent in women, particularly in elderly individuals between the ages of 65 to 70.

This work aims to present a case report of bilateral elastofibroma dorsi in a 64-year-old female patient treated at the Thoracic Surgery outpatient service at Hospital das Clínicas - UFPE, describing clinical, radiological, and pathological findings, as well as therapeutic conduct and postoperative evolution. Thus, it is hoped that this report contributes to illustrating one of the less prevalent presentations of this rare type of pseudotumor.

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CASE REPORT

M.J.S.O., 64, female, referred due to suspicion of the presence of tumours in subscapular regions. The patient has reported the presence of tumours and burning sensations in the scapular regions for the past two years. Regarding comorbidities, she had a history of smoking over thirty years ago and also high blood pressure. She had not lost weight. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) of the chest were performed, showing masses with partially defined contours, signal intensity similar to muscle, and areas of interspersed fat, measuring 8.0 x 7.5 x 2.9 cm on the right and 6.3 x 5.2 x 1.9 cm on the left (**Figure 1**). The lesions were located in the subscapular regions, with no bone changes or signs of fracture. Resection was recommended and performed in two stages.

The patient did not have follow-up during the COVID-19 pandemic, returning to the hospital approximately two years after the initial procedure, when the resection of the second lesion was planned. An ultrasound was requested, demonstrating the persistence of the left subscapular tumour, measuring 3.9cm. A thoracotomy was performed on the left hemithorax, also with complete resection. Postoperatively, a vacuum drain was used once again, and a moderate seroma requiring relief puncture was observed. Fluid analysis ruled out infection. After a week she returned for reassessment with a clean wound and there was no fever, or signs of sepsis. The pathological examination of the specimen found an irregular, compact, and brownish tissue formation, measuring 8.5 x 7.5 x 4cm, weighing 100.5g, also consistent with a diagnosis of elastofibroma,

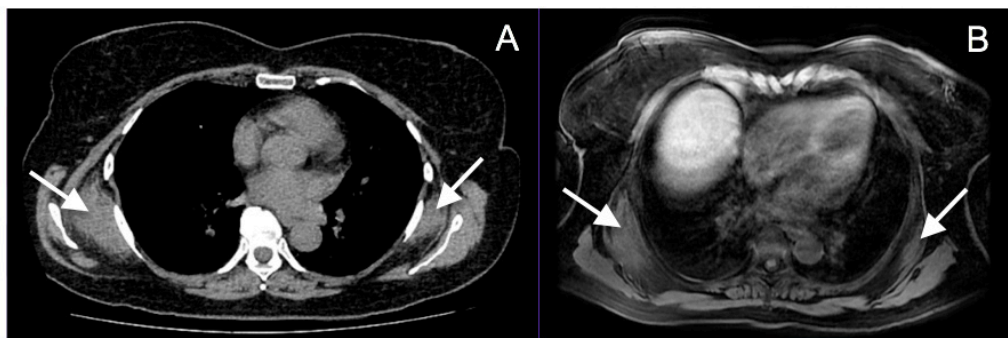


Figure 1 - **Figure A** (Chest CT in axial cut without contrast) and **Figure B** (Chest MRI in axial cut) showing the presence of bilateral tumour masses in subscapular regions (arrows).

Firstly, a thoracotomy of the tumour on the back of the right hemithorax was performed with total resection. Postoperatively, the patient was discharged and was using a vacuum drain. A small seroma developed, but without complications or the need for intervention. She experienced minimal pain in the scapular region, easily managed with simple pain killers, without signs of inflammation, and which showed to be healing well.

The pathological examination revealed a compact whitish-yellow fibroelastic tissue formation, covered by fibroadipose tissue, measuring 8.5 x 8.0 x 5cm, weighing 206.5g, consistent with elastofibroma, without malignancy, and with clear margins.

without signs of malignancy and with clear surgical margins (**Figure 2**).

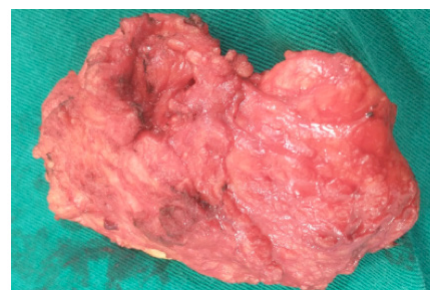


Figure 2 - Surgical specimen representative of the left elastofibroma dorsi, measuring 8.5 x 7.5 x 4cm, weighing 100.5g, without signs of malignancy.

DISCUSSION

The present case is worthy of discussion as it provides a progressive account of the diagnosis, treatment, and postoperative evolution of a bilaterally presenting elastofibroma dorsi. Due to the high risk of developing local postoperative complications, surgical treatment is only indicated for symptomatic cases.

As the patient had reported a burning sensation at the tumour site, tumour resection performed in two stages was recommended for this particular patient. Surgical treatment is often curative, but there may be a risk of recurrence if the tumour is not completely removed with clear margins.

One of the most commonly observed postoperative complications in patients undergoing surgical exci-

sion of elastofibromas, along with hematomas, is the development of seromas, as occurred in this case. It is noteworthy that despite its smaller volume and dimensions, the second tumour on the left led to the formation of a moderate seroma, requiring relief puncture.

CONCLUSIONS

Elastofibroma dorsi is a rare type of pseudotumor, characterized by its benign nature and slow growth. Although unilateral presentations are most commonly observed, bilateral occurrences can also occur. Surgery, while often curative, is recommended only for symptomatic cases and may lead to complications requiring additional postoperative procedures.

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RELATO DE CASO | CASE REPORT

Challenging expectations: A case of high-grade serous ovarian carcinoma in a young patient with unexpected mutations

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ABSTRACT

Despite the low prevalence, ovarian cancer has high mortality. More common in elderly patients, is mostly diagnosed late, which leads to high recurrence and a low five-years-disease-free-survival. Carcinoma is the most common type, and the high grade serous carcinoma (HGSC) subtype stands out in terms of aggressiveness. Whereas genetic mutations would be responsible for this difference, it was proposed a tumor classification model, which considers the main genetic changes found. Here we describe the genetic associations observed in young patient with HGSC and her clinical outcome.

INTRODUCTION

Ovarian cancer, despite its low prevalence, has a high mortality rate. More frequent in elderly patients, its diagnosis is mostly late, resulting in recurrence in around 70% of cases, with a five-year survival rate of 19.1%^{1,2,3}. Histopathology is classified according to the cell type of origin. Carcinoma is the most common, and the serous subtype, which stands out in terms of aggressiveness, is divided into high grade (HGSC) and low grade (LGSC)⁴. Considering that genetic mutations would be responsible for this differentiation, a classification model for these tumors was proposed that considers the main genomic alterations found⁵. We describe genetic associations observed in a young patient with HGSC and their clinical outcome.

CASE REPORT

This is a 31-year-old patient, born and resident in Belo Horizonte (MG), single, telemarketing operator. She was referred to the Oncology-Gynecology service of the Instituto Mário Penna in Dec/2020 with a history of colic-like abdominal pain that had lasted 10 months, whose initial imaging workup (pelvic-abdominal US) revealed an expansive, multiloculated, borderline solid-cystic lesion poorly defined, measuring approximately 20x18x12 cm, occupying the entire pelvis and extending to the umbilical scar; the cystic stores were anechoic, containing solid papillary projections, in addition to an irregular solid component; showed flow in the solid areas and on the periphery of the cystic stores on Doppler. Before the consultation, the patient used Diane 35® (ethinyl estradiol 0.035 mg + Cyproterone acetate 2 mg), without improvement, progressing with worsening pain and an increase in abdominal volume, in addition to dysuria. In the gynecological-obstetric history, the patient was observed with menarche at 13 years of age, first sexual relation at 18 years of age, nulliparous; never performed cervical-vaginal cytology exams. The patient denied comorbidities, allergies or previous surgeries, and cases of cancer in the family; she reported smoking (10 cigarettes/day) and social alcoholism. The physical examination

demonstrated a free, tense abdomen, without signs of peritoneal irritation, with the presence of ascites and a palpable mass at the level of the umbilical scar; bilateral palpable inguinal lymph node enlargement, mobile, with fibroelastic consistency. Blood tests were requested (CA 19.9: 331.0 U/ml, B-HCG: 9,638.0 mIU/ml, AFP: 1.8 ng/ml, LDH: 164.0 U/l, CEA: 5.9 ng/ml and CA-125: 2,444.1 U/ml), pelvic-abdominal MRI (with a result similar to US, and which did not identify the ovaries) and cervical-vaginal cytology (with a diagnosis of CIN 3). Based on the findings, surgery was proposed and performed, with diagnostic and treatment objectives (hysterectomy + bilateral adnexectomy + omentectomy + implant resection in the vesico-uterine peritoneum). The pathological examination revealed high-grade serous carcinoma of the ovary attached to the uterine body and affecting the ovaries (bilaterally), omentum and vesico-uterine peritoneum (pT3bNX, stage IIIB); the ascitic fluid collected during the operation was positive for neoplastic cells. The DNA of the neoplasia was amplified (Qiaseq Pan-cancer Multimodal Panel™, QIAGEN), and sequenced to analyze the mutations present and their influence on the presentation of the tumor. A pathogenic mutation was found in KRAS, frequently related to LGSC, and none in TP53 (very described in HGSC). Regarding high penetrance genes for hereditary breast and ovarian cancer syndrome, benign mutations were found in BRCA¹ and one variant of uncertain significance and two new ones in BRCA². The patient evolved satisfactorily postoperatively and was referred to Oncology, starting chemotherapy 90 days after the surgical procedure (CDDP + Taxol – 06 cycles, monthly). The first CA-125 after surgery (after 3 months) was 27.5 U/ml; the second, after the first QT cycle, was 19.0 U/ml. The patient tolerated chemotherapy well, presenting to the first post-CT control appointment in good general condition, with an unremarkable physical examination and imaging tests (CT and MRI) showing a complete response. The patient maintains clinical monitoring and imaging tests (CA-125 Mar/2022: 8.4 U/ml), with no signs of disease recurrence.

DISCUSSION

This is a young patient who presented an aggressive form of ovarian cancer, with unexpected mutations for her histological subtype. Ovarian cancer is a common and complex malignancy with poor prognostic outcome. Most women with ovarian cancer are diagnosed with advanced stage disease due to a lack of effective detection strategies in the early stage. Traditional treatment with cytoreductive surgery and platinum-based combination chemotherapy has not significantly improved prognosis and 5-year survival

rates are still extremely poor. Therefore, novel treatment strategies are needed to improve the treatment of ovarian cancer patients. Recent advances of next generation sequencing technologies have both confirmed previously known mutated genes and discovered novel candidate genes in ovarian cancer. Ovarian carcinoma is the most lethal gynecological malignancy and has been classified according to the different epithelia of the reproductive female tract. The tumors are divided into serous, mucinous, endometrioid, clear cell, and transitional cell carcinomas^{4,17}. It has traditionally been thought that ovarian carcinomas are derived from the ovarian surface epithelium and that subsequent metaplasia leads to the development of the various cell types (serous, mucinous, endometrioid, clear cell, and transitional) which constitute the morphological subtypes of ovarian epithelial carcinomas. However, new histopathological, molecular, and genetic studies have recently provided a better model for ovarian carcinogenesis, showing two broad categories, which are designated as type I, where precursor lesions in the ovary have clearly been described, and type II, where such lesions have not been described clearly and tumors may develop *de novo* from the tubal and/or ovarian surface epithelium. Type I tumors include low grade serous, mucinous, endometrioid, clear cell, and transitional cell carcinomas, while type II tumors comprise high grade serous carcinomas, undifferentiated carcinomas, and carcinosarcomas.¹⁷ Each subtype behaves as a distinct disease with differences in clinical presentations, mutations, and responses to treatment such as chemotherapy. It is well-established that EOC develops according to two different carcinogenic pathways⁵. The vast majority of these tumors are high-grade serous tumors that develop according to the type II pathway and present p53 and BRCA mutations. In contrast, low-grade serous tumors are characterized by KRAS, BRAF, PTEN, PIK3CA, CTNNB1, ARID1A, and PPP2R1A mutations and progress according to the type I pathway. According to this dualistic model of epithelial ovarian carcinogenesis high-grade and low-grade serous carcinoma (LGSC) are characterized by different morphologic and molecular features, resulting in distinct clinical outcomes. While HGSC is highly aggressive with rapid development and poor prognosis, LGSC tends to be indolent with better prognosis. At molecular level, somatic TP53 mutations have been reported in more than 90% of HGSC samples⁶. In the other hand, absence of TP53 mutations and the presence of mutation genes involved in RAS/MAPK signaling, such as KRAS, are characteristic of LGSC⁷. In the present study, we report a case of HGSC with a KRAS G12D mutation and no TP53 mutation. Interestingly, G12D is the most common KRAS-activating mutation

occurring in carcinomas and adenocarcinomas, but LGSC is one of the few cancers for which this affirmation is not true⁸. Regarding lacking TP53 mutation, although rare, other HGSC cases have been reported before in larger cohorts and low frequencies⁹. In a recent work, over 1000 tubo-ovarian HGSCs were subjected to targeted NGS, aiming to identify TP53-wildtype cases⁷. Observers blinded to mutation status to avoid potential bias conducted a rigorous molecular and histopathologic review of a mix of TP53-wildtype and TP53-mutated HGSCs. They found evidence supporting the existence of TP53-wildtype HGSCs, a subset of which also harbored driver mutations in KRAS, considered extremely rare in HGSC. These cases were designated as LGSC-like HGSC, a fraction of which likely evolved from a LGSC, according to the authors. KRAS is an oncogene that encodes a protein involved in cell division regulation. Its mutation often causes dysregulated cell proliferation. TP53, in turn, is a tumor suppressor, coding for a protein involved in the cell apoptotic pathway. TP53-mutated cells are

unable to trigger apoptosis as a result of mutated or damaged DNA. Considering that platinum chemotherapy induces DNA damage, we can hypothesize that, in the case reported here, TP53-wildtype contributed to the patient's good response to chemotherapy and long progression free survival (PFS), despite HGSC typical poor prognosis. The usability of genome sequencing has provided exact data of gene mutations in ovarian carcinomas to develop some accurate treatment strategies. In a certain extent biologically targeted therapies and some targeted drug combinations have improved prognosis^{10,11}. Recently, numerous gene mutation studies have offered some potential predictive biomarkers or therapeutics in OC. But few available effective therapies are currently used widely in the clinic. Therefore, the influence of genetic variability on disease progression and response to treatment is highlighted.

KEY WORDS: serous carcinoma - ovary - mutation - genetic tests.

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