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Impact of the COVID-19 Pandemic on Brain Metastases in Breast Cancer Patients

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ABSTRACT

Objectives: *To evaluate the impact of the COVID-19 pandemic on the diagnosis and treatment delays of brain metastases secondary to breast cancer, and to compare patient demographics, disease characteristics and outcomes before and during the pandemic.*

Materials and methods: *A retrospective study was conducted on 100 patients who were surgically treated for brain metastases in the Neurosurgery Clinic of "Prof. Dr. Nicolae Oblu" Clinical Emergency Hospital, Iasi, Romania. Patients were divided into two groups: pre-pandemic (2018–2020, n=57) and pandemic (2020–2022, n=43). Clinicopathological data, including demographics, metastasis localization, number and duration, were collected and analyzed.*

Results: *The pandemic period saw a shift towards younger patients, with 51% younger than 55 years compared to an average age of 57.9 years before the pandemic. Metastases were mostly located in the parietal lobe (61%). Despite a balanced rural-urban patient distribution, diagnostic delays were observed, with an average metastasis duration of 17 months. Patients from rural areas and older subjects showed tendencies towards later diagnosis. The number of metastases varied, with nearly half presenting a single lesion.*

Conclusions: *COVID-19 pandemic-related disruptions in healthcare services led to delayed diagnosis and treatment of brain metastases, particularly impacting older and rural patients. These findings underscore the need for improved healthcare resilience and equitable access to oncological care to minimize delays and optimize outcomes during public health emergencies.*

Keywords: brain metastases, breast cancer, COVID-19 pandemic, diagnosis delay, healthcare.

INTRODUCTION

Delays in cancer treatment can have significant implications for patient survival and quality of life. One of the most worrying effects of delay is the increased risk of mortality and recurrence (1). Studies have shown that prompt initial diagnosis and treatment are crucial to improve patient prognosis (2). When treatments are delayed, cancer has time to progress, which can make interventions more complex and less effective (3). This situation underlines

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the importance of early interventions and careful monitoring of disease progression (4).

In addition to the biological risks, delays can also have a considerable financial impact on patients. This can translate into additional long-term costs if the disease progresses and requires more intensive and costly treatments (5). Patients may not only face the financial burden of treatments (6), but also the economic losses caused by the inability to work or to continue their daily activities (7). Thus, the effect of delay is not only medical, but also socio-economic, affecting the daily lives of patients and their families (8).

The context of the COVID-19 pandemic has amplified these challenges, putting health systems around the world under pressure (9). Many institutions have had to postpone elective cancer surgery (10) and reduce the use of systemic treatments (11), while medical resources have been re-allocated to cope with the health emergency (12). These measures have raised concerns about the long-term consequences of delays for cancer patients (13). Although it is clear that treatment delays have had negative effects on outcomes (14), the absence of data makes it difficult to determine the actual effect of these delays on survival and disease progression (15).

In retrospective, the pandemic has been a moment of reflection for the medical community. It is essential that health systems re-evaluate how they manage their resources and develop strategies to minimize delays in essential treatments. This requires not only better coordination between health professionals, but also a patient-centered focus that allows treatments to continue even in times of crisis.

In this context, our study focuses on the impact of COVID-19 in the field of neuro-oncology, emphasizing the potential delays in the diagnosis of brain metastases, which often manifest acutely, generating new or progressing neurologic deficits. These clinical situations require prompt diagnosis and treatment to prevent further deterioration of the patient's condition.

MATERIAL AND METHODS

We performed a retrospective study on patients who received surgical treatment in the Neurosurgery Clinic of "Prof. Dr. Nicolae Oblu" Clinical Emergency Hospital of Iasi, Romania, between 2020 and 2022, and compared them with data from the pre-pandemic period 2018-2020.

The study analyzed 100 patients diagnosed with brain metastases originating from breast cancer (57 patients in the pre-COVID group and the remaining 43 ones in the COVID group). Clinicopathological data were collected from electronic medical records and included demographic information, morphological characteristics of brain metastases (localization, cytopathological features).

Cytopathologic examination was performed on intraoperative smears using small samples obtained during surgery. We placed a small sample (1-2 mm3) of the biopsy specimen on one edge of a clean and dry labelled slide and crushed it with the edge of another clean and dry labelled slide with sufficient pressure to spread the biopsy tissue in a thin film on both slides. Both slides were then immediately stained with 1% toluidine blue. In all cases, the cytologic diagnosis was brain metastasis.

RESULTS

Data analysis provided a detailed insight into the characteristics of the brain metastatic patients included in the study, revealing valuable information on both the demographic profile and disease course.

The present study included a total of 100 patients diagnosed with brain metastases, of whom 57 were treated before the pandemic and 43 during the COVID-19 pandemic. This split allowed comparison of possible differences in the approach and outcomes between the two distinct periods.

In terms of background, almost half of patients were from rural areas (55%) and the remaining ones from urban areas (45%). This relatively balanced distribution may suggest similar access to health care services or, at least, recognition of the need for specialized treatment regardless of the place of residence. However, it is also important to analyze whether differences in access to health care between rural and urban areas had any influence on patients' diagnosis and treatment.

Patients' educational level reveals a diversified profile: 62% of them had a high school education, while a considerable percentage of 36% had a higher education (20% undergraduate and

16% postgraduate), with 4% of subjects having only primary education. This aspect of educational attainment may be important in understanding how patients perceive and manage their own illness, as well as their ability to access information and actively participate in treatment decisions.

By age group, the average age of patients was 57.9 years (most of them in the sixth and seventh decades of life) in the pre-pandemic period, while 51% of cases were younger than 55 years in the post-pandemic period.

The number of metastases ranged from 1 to 5, the mean value was close to the median value (1.97 *vs*. 2) and the Skewness test result was 0.975, suggesting that significance tests for continuous variables can be applied. Most frequently, only one metastasis was identified in 47% of cases, but in 28% of patients in this study group the number of metastases was three or more (Figure 1).

The duration of metastasis ranged from 0 to 60 months, the mean value was relatively close to the median value (17.03 *vs*. 14 months) and the Skewness test result was 0.949, suggesting that significance tests for continuous variables can be applied (Table 1, Figure 2).

Depending on the location of metastasis, the parietal lobe (61%) was more frequently involved. Of the 61 cases with parietal lobe localization, 59% were over 55 years of age (p=0.013), 54.1% from rural areas (p=0.169) and 54.1% had a single metastasis (p=0.001).

The duration of metastasis was shorter in patients younger than 55 years (16.0 *vs* 18.10 months; p=0.387). Only in 17.9% of patients, older age correlated with longer duration of metastasis (r = 0.179; p=0.075) (Figure 3).

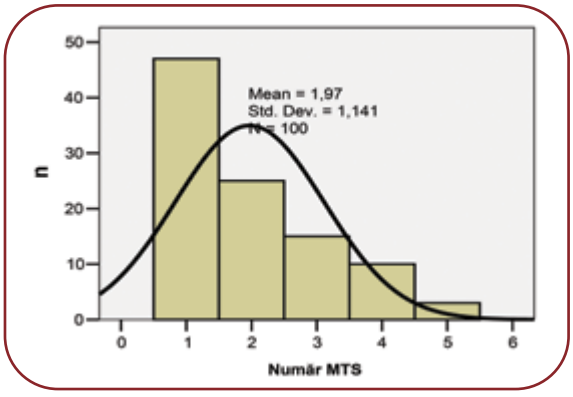

FIGURE 1. Histogram of the number of metastases

TABLE 1. Descriptive statistical indicators of metastasis duration

N		**100**
Mean		17,03
Median		14,00
Standard deviation		12,08
Variance		70,93
Skewness test		0,949
Standard error of Skewness test		0,241
Minimum		0
Maximum		60
Percentila	25	8
	50	14
	75	24

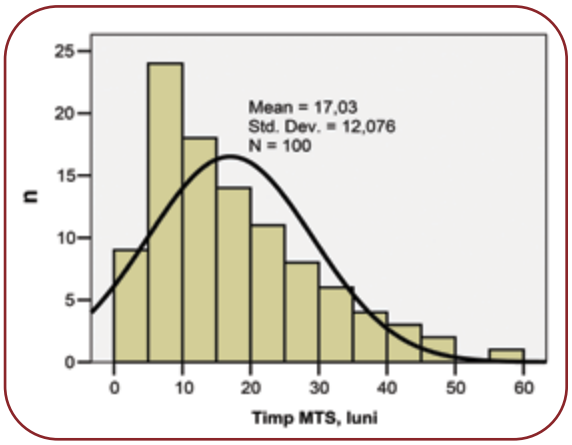

FIGURE 2. Histogram of metastatic duration

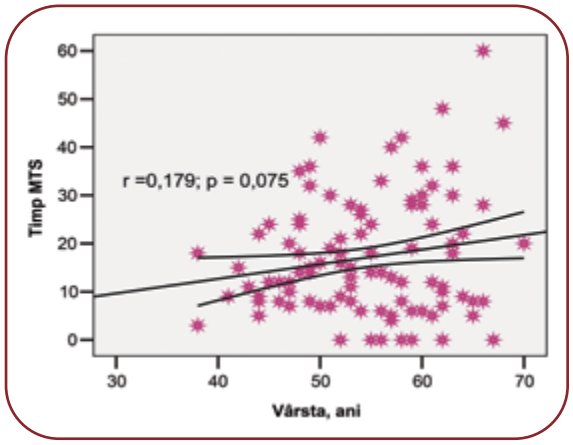

FIGURE 3. Correlation of age with duration of metastasis

Taken together, the above-described data contribute to a complex profile of patients with brain metastases, including demographic, time and educational factors. They may be useful both for assessing the specific support needs of these patients and for identifying possible dif-

ferences in care and access to treatment, especially in the context of the additional challenges posed by the COVID-19 pandemic.

DISCUSSION

This study enhances the understanding of the impact of the COVID-19 pandemic on brain metastases secondary to breast cancer. The results show significant differences between the pre-pandemic and post-pandemic periods, reflecting changes in patient profiles.

The distribution of patients according to their area of residence was relatively balanced: 55% from rural areas and 45% from urban areas. This observation may suggest a relatively uniform accessibility to oncological neurosurgery services, but should be interpreted with caution. International studies show that patients from rural areas often face delays in accessing specialized services, mainly due to the distance from treatment centers, limited resources and poor medical education (16).

The educational level of patients included in our study is an important indicator of their ability to understand the complexity of the disease and to actively participate in the decision-making process. Thus, 36% of patients had higher education and 62% secondary education. Only four percent had primary education, which makes it all the more important to provide clear communication tailored to each patient's level of understanding. Recent studies confirm once again that a high level of education is associated with delayed diagnosis and poorer oncological outcomes (17).

An interesting aspect is that, during the pandemic period, 51% of patients were younger than 55 years compared to the average of 57.9 years in the pre-pandemic period. This change may have multiple explanations: delays in older patients seeking medical care due to fear of exposure to COVID-19, prioritization of other conditions, or a more pronounced disruption in the triage system for oncological cases among the elderly.

A study published in the *Journal of Cancer Policy* in 2023 supported that advanced age was a risk factor for delays in oncological treatments during the COVID-19 period, due to voluntary self-isolation or imposed restrictions (18). These observations are consistent with the age distribution recorded in our study and raise important questions regarding equity of access to treatment in times of public health crisis.

This significant decrease in average age is not a mere statistical accident, but reflects a series of profound disruptions in both access to medical services and patient behavior (19).

Among the contributing factors to this change was the older patients' fear of exposing themselves to the risk of infection, which led them to postpone medical consultations or avoid screening investigations (20). In addition, the redirection of medical resources toward the management of COVID-19 cases led to delays in cancer diagnosis and treatment, which especially affected older patients who generally rely more heavily on public health services (21). Studies show that delays in diagnosis have significantly increased the risk of advanced-stage disease, with serious implications for survival rates (22).

On the other hand, the decrease in average age of oncology patients may also be a sign of the increasing incidence of cancer among young adults, a phenomenon observed in recent years and potentially amplified by factors such as chronic stress, sedentary lifestyles, or poor diet (23). However, it is important to emphasize that this trend does not necessarily indicate a real increase in the number of cases among younger individuals, but rather a decrease in detection among the elderly due to barriers in accessing medical services (24).

These observations compel us to reflect on how health systems can be better prepared for future crises. It is essential to develop strategies that protect vulnerable populations, ensure the continuity of screening programs and promote awareness of the importance of early diagnosis, regardless of the social or medical context (25). The pandemic has shown us that health equity is not a luxury, but a vital necessity (26-27).

Brain metastases ranged from 1 to 5, with an average of 1.97 and a median of 2. A single metastasis was the most commonly identified (47%), but 28% of patients presented with three or more metastases. The age of the metastases, defined as the time between the onset of neurological symptoms and the histopathological diagnosis, ranged from 0 to 60 months, with an average of 17.03 months.

These parameters suggest that a significant portion of patients experienced a slow and undiagnosed or undetected progression over an

extended period. Recent studies confirm that delays in the diagnosis of brain metastases can lead to worsening symptoms and reduced chances for surgical intervention or effective management (28-32).

According to an article published in *The Lancet Oncology* (2021), a delay of four weeks in cancer treatment increased mortality by 6–8%, which was directly correlated with the type of treatment and tumor location (33). In the case of brain metastases, where symptoms can be acute and disabling, every week of delay may result in irreversible loss of neurological function.

The majority of brain metastases in our study were located in the parietal lobe (61%), which was in accordance with observations from other recent studies that indicated a predilection of breast cancer metastases for well-vascularized brain regions such as the cerebellum and parietal lobe (34).

Our data show that, in 59% of parietal cases, patients were older than 55 years ($p=0.013$), 54.1% came from rural areas and the same percentage (54.1%) presented with a single metastasis ($p=0.001$). These correlations suggest a possible delay in diagnosis among older patients and those from rural areas, who may have limited access to advanced imaging or interdisciplinary oncological consultations (35).

Although our analysis shows a trend towards a shorter metastasis duration in patients younger than 55 years (16.0 *vs*. 18.1 months), this difference did not reach statistical significance ($p=0.387$). The overall relationship between age and metastasis duration was weak ($r=0.179$; $p=0.075$). However, this observation may have clinical relevance if analyzed in the broader context of patient behavior and medical system accessibility by age (36).

The recent literature supports that younger patients are often diagnosed earlier, as they are more proactive in seeking medical assistance and often benefit from greater vigilance from physicians, which leads to better early detection (37).

The COVID-19 pandemic marked a turning point for health systems worldwide. Studies show that during 2020–2021 there was a significant decline in access to imaging investigations and elective oncological procedures (38). This reduction in access to early diagnosis favored disease presentation in advanced stages, including with brain metastases, which is alarming.

According to an article published in *JAMA Oncology* (2022), screening and oncological investigations dropped by over 30% in the first 12 months of the pandemic, leading to major delays in diagnosis and treatment initiation (39). Data from our study reflect this reality: patients treated during the pandemic were on average younger than those from the pre-pandemic period, but the duration of metastases was similar, suggesting a "silent" progression of the disease in the absence of appropriate medical investigations (40).

This trend is also supported by other research showing that patients diagnosed during the COVID-19 period had a higher rate of presentation with brain or extracranial metastases compared to those diagnosed earlier (41).

These results highlight the need to reassess triage and oncological intervention strategies during crises, as well as the implementation of protocols to ensure the continuity of cancer care, especially for vulnerable patients (42).

CONCLUSION

This study provides a critical insight into the impact of the COVID-19 pandemic on patients diagnosed with brain metastases secondary to breast cancer, with a particular focus on diagnostic delays, demographic shifts and systemic disparities. By comparing cohorts from the pre-pandemic and pandemic periods, we observed both subtle and significant changes in patient characteristics, disease progression and healthcare access.

One of the most notable findings is the shift in age distribution of patients diagnosed during the pandemic. The average age was 57.9 years before the pandemic but dropped to under 55 years old in 51% of cases during the pandemic. This shift likely reflects the compounded barriers faced by older individuals during the pandemic, including fear of virus exposure, self-isolation and reduced access to screening services. It also highlights a troubling trend: vulnerable populations, such as the elderly, may have been unintentionally deprioritized in the context of health system reallocation. Although the duration of metastasis was slightly shorter in younger patients, the difference was not statistically significant, suggesting that delays in detection affected all age groups similarly.

Another key observation is the relatively balanced rural-urban distribution of patients (55% rural, 45% urban), which may superficially suggest equal access to care. However, the international literature and our data imply that patients from rural areas may still experience diagnostic delays due to limited medical infrastructure and less frequent access to advanced imaging and oncological consultation. This disparity is particularly evident in cases of parietal lobe metastases, where older, rural patients were more likely to present with a single lesion, potentially indicating slower detection and progression over time.

Educational background also emerged as a relevant factor, with 36% of patients having higher education and only 4% primary education. This may play a role in healthcare navigation, communication with providers and proactive health-seeking behaviors. Even though education did not directly correlate with metastasis number or duration, its influence on treatment comprehension and patient involvement remains crucial in cancer care.

Statistical analysis revealed that most patients had a limited number of metastases (47% with a single lesion), though a substantial percentage (28%) had three or more. The mean duration between neurological symptom onset and diagnosis was 17.03 months, an alarmingly long interval for a condition that often presents acutely. These delays can significantly impact prognosis, especially in neuro-oncology, where timely intervention is critical to preserving neurological function and quality of life.

The COVID-19 pandemic exacerbated existing gaps in the healthcare system, leading to disruptions in routine screening, delayed diagnoses and postponed treatments. These challenges were reflected in our data, which align with international findings showing increased cancer-related morbidity during the pandemic. As the healthcare community reflects on this crisis, it becomes imperative to design systems that are resilient to such disruptions, ensuring continuity of oncological care, particularly for high-risk and underserved populations.

Ultimately, our findings stress the need for a restructured equitable healthcare model that prioritizes early detection, protects vulnerable groups and guarantees access to essential services in times of stability but also in those of crisis. The pandemic was not just a test of medical capacity but a profound lesson in the importance of preparedness, compassion and patient-centered care. ❑

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