

# Covid-19 Pandemic Impact on Breast Cancer Detection-The Major Effects Over an Early Diagnosis

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**ABSTRACT:** The COVID-19 pandemic has disrupted medical care systems, by decreasing patient addressability to outpatient care. The main objective of this study was to compare the patient's addressability to breast imaging techniques for diagnosis, and follow-up in the Clinical Emergency County Hospital of Craiova, Romania. We selected the mammographies performed over a period of 4 years (2018-2021) in our clinic. We divided the patients into four groups, one for each year (2018, 2019, 2020, 2021). Furtherly, we merged the data into two groups, one group for the pre-pandemic years (2018 and 2019) and one for the pandemic years (2020 and 2021). In our clinic, the number of mammographies plummeted to 0 during the month of April 2020 due to the lockdown and closure of non-urgent outpatient services in hospitals treating COVID-19 patients, and slowly crept to 11 in the month of May and peaked to 160 in July (for the rest of the year). There was a huge difference regarding the patient's addressability to mammography immediately after the lockdown, with a 95.2% less addressability compared to the pre-pandemic period (May 2020 compared to May 2018). As an overall, by comparing both pre-pandemic years included in the study with the pandemic years, we obtained an addressability reduced with 37.3% suggesting the possible future delays in diagnosing breast tumors.

**KEYWORDS:** Mammography, COVID-19, advanced breast cancer, anxiety, screening.

## Introduction

The Coronavirus disease 2019 (COVID-19) pandemic has disrupted all aspects of life, but has disproportionately affected patients with cancer, both directly, severely increasing mortality, and indirectly, by decreasing patient addressability and changes in therapeutic plans [1-8].

Regrettably, given that Romania is one of the few European countries that has not implemented a national screening program, breast cancer is routinely discovered in more advanced stages, and has an increased mortality compared with the European Union average [9].

The COVID-19 pandemic has severely impaired breast cancer management, due to the severe restrictions implemented, by postponing outpatient breast imaging investigations, which determined delays in early diagnosis and treatments [10,11].

Breast cancer, as any other type of cancers, needs an early detection to properly apply treatment plans in order to improve the quality of life, disease-free interval (DFI) and overall survival rates. Due to the unexpected mortality and morbidity rates, the COVID-19 pandemic

has had an important impact on all outpatient medical services, severely affecting the screening programs and greatly reducing addressability to medical care [12].

It is a well-known fact that the most common cause of death from cancer in women worldwide is represented by breast cancer [13,14].

According to literature, an early detection and a well-established therapeutic plan suited for every case in particular (surgical procedures, radiation, cytotoxic chemotherapies and molecularly targeted agents), is considered to improve the survival and the quality of life for breast cancer patients [15,16].

## Material and Methods

The main objective of this study was to compare the patient's addressability to breast imaging techniques for diagnosis, and follow-up in the Clinical Emergency County Hospital of Craiova, Romania.

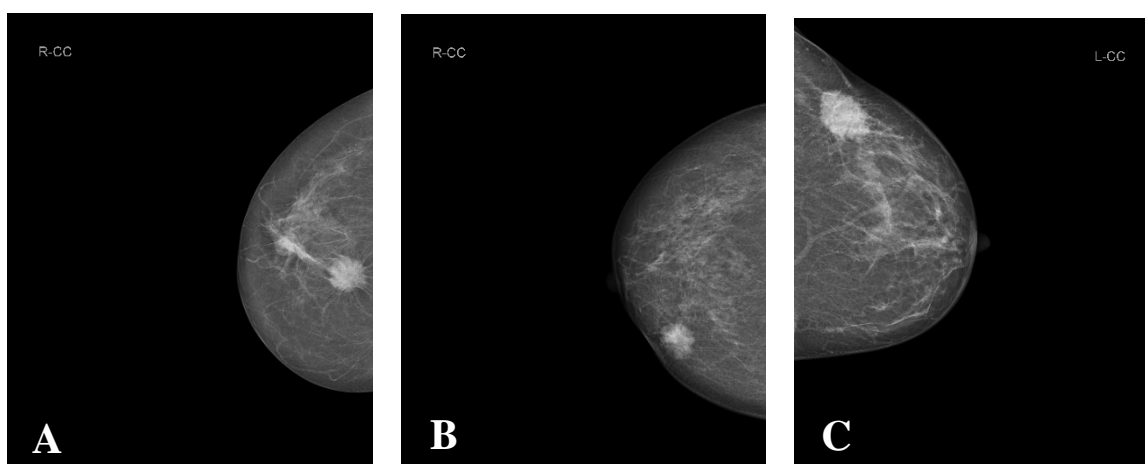
The current study received approval from the local Ethics Committee. The patients included in the report freely stated their written approval regarding the use of medical data for research purposes.

For this study, we selected the mammographies performed over a period of 4 years (2018-2021) in our clinic. The images were acquired using a Siemens Mammomat digital mammography device.

All the patients included in the study were women aged between 30 and 85 years old. We only performed mammographies on patients under 40 years old who had a family history of breast cancer, clinical breast changes and/or ultrasound (US) or magnetic resonance imaging (MRI) aspects suggestive for malignant pathology.

We divided the patients into four groups, one for each year (2018, 2019, 2020, 2021). Furtherly, we merged the data into two groups, one group for the pre-pandemic years (2018 and 2019) and one for the pandemic years (2020 and 2021).

In order to obtain histopathological diagnosis, US-guided breast biopsies were performed on the patients with suspect breast lesions included in BI-RADS 4 and 5 categories-regarding the shape (irregular), margins (obscured, indistinct, spiculated), or density±the presence of suspicious calcifications on mammograms (Figure 1 A-C) [17].



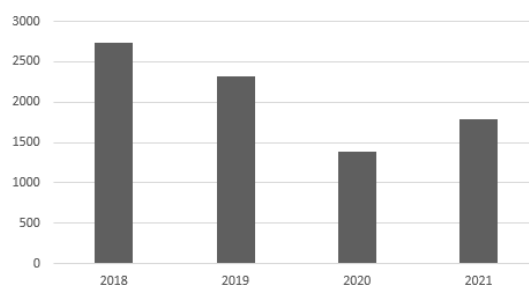
**Figure 1. (A-C) Mammographic images representing breast tumors. (A, B. Spiculated right-breast masses, C. Left-breast mass with discrete adjacent skin retraction).**

We compared the percentage of mammographies which necessitated US-guided breast biopsies in the pre-pandemic years with the pandemic years.

Statistical analyses and graphical representations were performed with Microsoft Excel and GraphPad Prism software.

**Results**

We performed a total of 8228 mammographies over 4 years (2018-2021), distributed thusly-2739 in 2018 and 2319 in 2019 (for a total of 5058 in the pre-pandemic years) and 1387 in 2020 and 1783 in 2021 (for a total of 3170 in the pandemic years) (Figure 2).



**Figure 2. Total number of mammographies-distribution per year.**

In 2018, 186 US-guided breast biopsies were performed, 146 in 2019, 95 in 2020 and 133 in 2021.

We evaluated our data with a Shapiro-Wilk test and found that the population is normally distributed ( $p>0.05$ ) (Table 1, Figure 3).

**Table 1. Shapiro-Wilk test.**

	2018	2019	2020	2021	Pre-pandemic	Pandemic
W	0.95698	0.91200	0.93839	0.93282	0.93499	0.94206
p	0.7399	0.2263	0.4775	0.4110	0.4360	0.5252

Table 2. Two-tailed test-p values.

p-values	2019	2020	2021
2018	0.085	0.0001	0.0001
2019		0.0030	0.0109
2020			0.123

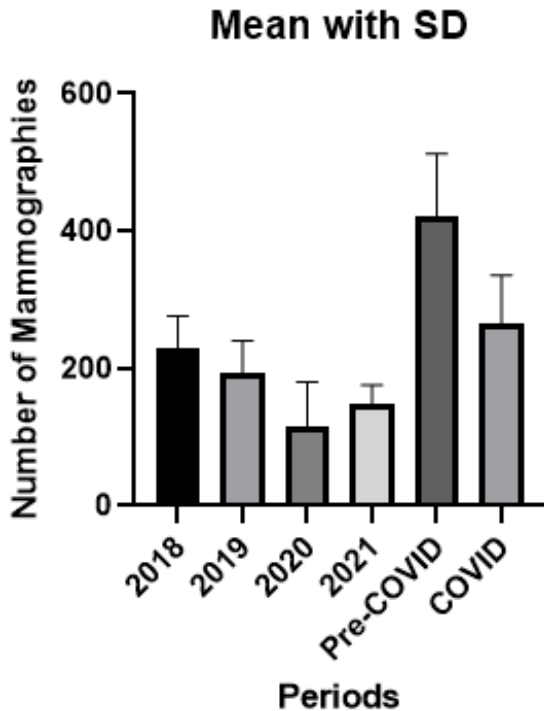


Figure 3. Mean number of mammographies/month with standard deviation.

After this, we performed an analysis of variance (ANOVA) test and deduced that the groups are statistically different ( $p < 0.01$ ,  $SS = 88145.33$ ,  $F = 12.49535$ ,  $F_{crit} = 2.816466$ ).

We proceeded in comparing the pre-pandemic years (2018 and 2019) and the pandemic years (2020 and 2021) between each other using a two-tailed test.

We found no statistical differences between 2018 and 2019, no statistical differences between 2020 and 2021 ( $p > 0.05$ ), but there was a statistical difference between pre-pandemic and pandemic years ( $p < 0.01$ ) (Table 2).

We performed another statistical analysis (Welch's t-test) for the pre-pandemic and pandemic periods (Figure 4).

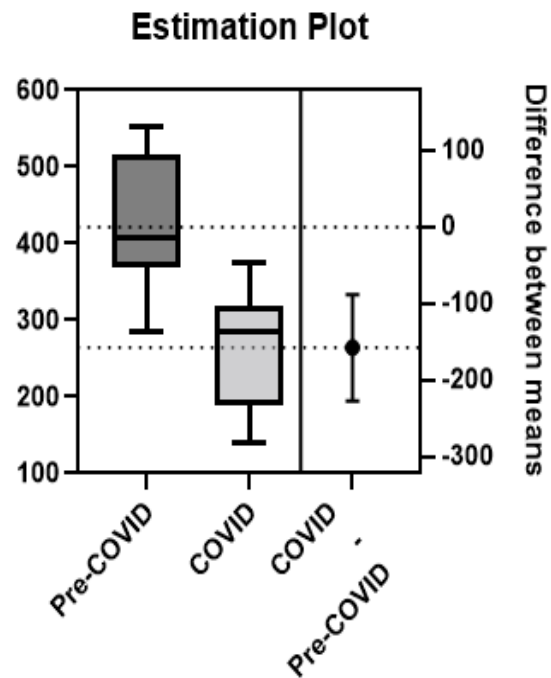


Figure 4. Welch's t-test.

Despite the remarkably lower number of patients seeking medical advice during the pandemic period, an increased number of clinically advanced cancers was observed, especially in 2021 (nipple retraction, breast changes in size and shape, nipple discharge, lumps or nodes felt on or inside of the breast or axilla) (Figure 5 A-C, Figure 6 A-C).

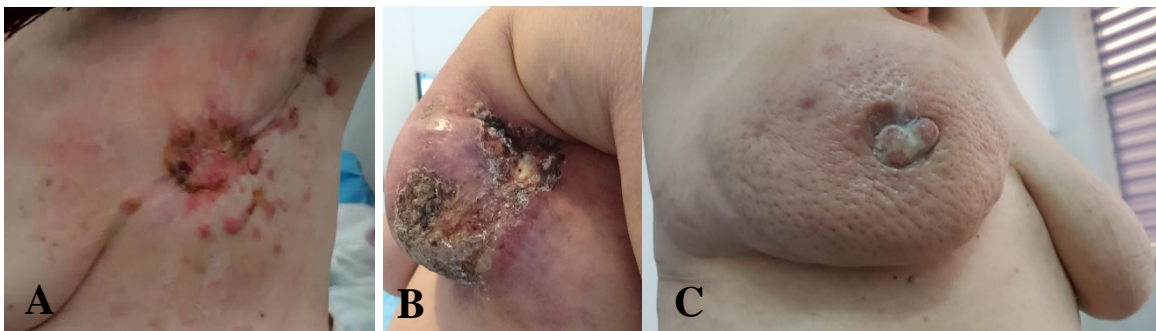
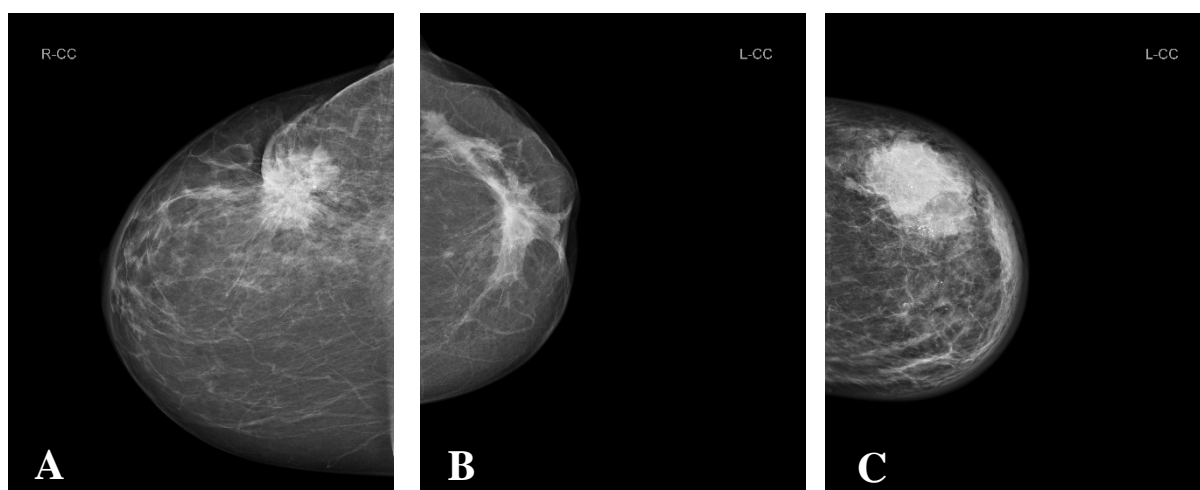


Figure 5. (A-C) Clinical aspects of neglected, advanced breast tumors suggesting important skin and nipple retraction, breast changes in shape and size, skin changes, suspicious nipple discharge.



**Figure 6. (A-C) Mammographic images representing advanced breast tumors (A. Spiculated right-breast mass associated with skin retraction, B. Left-breast spiculated mass, with important skin and nipple retraction C. Left-breast enlarged mass with suspicious calcifications and skin thickening).**

We compared the percentage of mammographies which required an US-guided breast biopsy, following the discovery of suspect lesions.

We discovered a statistically significant ( $p < 0.05$ ) increase in the number of biopsies performed in 2021 (7.46%) compared to 2018 and 2019 (6.79% and 6.29%).

## Discussion

Breast cancer, as the most common type of cancer among women, implies both primary and secondary prevention.

Eliminating the causes mainly responsible for this pathology and enhancing the population immune system is considered to be responsible for primary prevention.

The secondary prevention targets to slow down the development of breast cancer from early stages, by diagnosing before full symptoms arise, to screening specific groups at higher risk [18].

The objective is an early detection of cancers in order to reduce the mortality in this pathology.

The imaging techniques used in evaluating breast tissue are represented by mammography (as a screening program supplemented in selected cases with US, MRI, or digital breast tomosynthesis) [19], breast-US and MRI [20].

Nowadays, a serial screening using mammography is considered to be most accurate and effective in decreasing mortality with the help of early tumor detection.

Unfortunately, mainly due to economics, there are still countries who have not

implemented a screening programme based on mammography detection.

Self-breast examination and US are used as mainly tools to lesion detection, implying lower costs [21].

Although digital mammography is still considered to be the gold standard in breast-cancer early detection, imaging techniques such as US and contrast-enhanced breast MRI can be used in diagnosing breast lesion, staging and also follow-up [22].

Every imaging technique has its advantages and disadvantages regarding costs, exposure to radiation and medical centers availability, but there are all complementary imaging techniques which combined with percutaneous needle biopsy, as a minimally invasive method, establish the histopathological report.

As being already known, the pandemic started in China, Wuhan, being quickly followed by the United States and turned into a global pandemic by March 2020.

The reduced number of breast examinations implied many causes such as different periods of lockdown, the reduced number of healthcare workers due to the COVID-19 infections (the imaging technologists, mostly the ones performing mammographies were likely at a higher risk due to the inability to maintain social distancing during examination) and even the fear of possible COVID infections[23].

In our clinic, the number of mammographies plummeted to 0 during the month of April 2020 due to the lockdown and closure of non-urgent outpatient services in hospitals treating COVID-19 patients, and slowly crept

to 11 in the month of May and peaked to 160 in July (for the rest of the year).

The year 2021 saw a slow increase in the addressability of the patients to our clinic, thus the small number of mammographies performed in 2020 and 2021 cannot be wholly explained by the lockdown.

Mammography-related anxiety is an important factor known to play a negative role in patients' addressability to outpatient clinics for these procedures.

The numbers probably stayed low because the COVID-19 pandemic has furtherly increased overall anxiety levels, consequently determining patients to avoid requesting elective medical care.

As compared to the literature, in our clinic there was a huge difference regarding the patient's addressability to mammography immediately after the lockdown, with a 95.2% less addressability compared to the pre-pandemic period (May 2020 compared to May 2018).

As an overall, by comparing both pre-pandemic years included in the study (2018, 2019) with the pandemic years (2020, 2021) we obtained an addressability reduced with 37.3% suggesting the possible future delays in diagnosing breast tumors.

The literature describes the huge impact the pandemic had over breast imaging as a whole, including delayed screening mammography, being described as "the hardest hit" [23].

Because of this situation, breast cancer diagnosis and treatment is delayed, which leads to a worsening the clinical outcome for the patients, and long-term negative effect regarding therapy [24-26].

Some studies from all over the world (Taiwan, Netherlands, United States, India, Canada, Austria, Brazil) suggested that the pandemic effects were considerably important regarding the addressability of the patient to medical care services, despite the number of COVID-19 cases in each region, due to pandemic restrictions and also to the general fear developed during the outcome [26-33].

For example, in Taiwan, despite a COVID-19 low-incidence (20.2 cases per million population), comparing the pre-COVID-19 to COVID-19 period, the total number of breast biopsies decreased by 17%, and the early breast cancer by 30%.

This study established a 51% decrease in early stages breast cancer detection during a period of 7 months of pandemic.

A delay of 3 to 6 months was clearly associated with a worse survival rate, as suggested by a meta-analysis which included 38 studies [26].

A study conducted in the United States suggested that 44% of the patients who took part of a breast cancer survivors survey, delayed their clinical cancer care during the COVID-19 pandemic [26].

A study conducted in Sao Paulo, Brazil found a reduction in the number of mammographies by 35%, between 2020 and 2019 [27].

The delays and the interruptions in cancer screening, including breast screening, definitely lead to an increase in diagnosing advanced stages of disease and an enlarged number of cancer-related deaths, this being considered an important step backwards in the healthcare system all over the world [29-31].

The long-term physical and psychosocial consequences of imaging+histopathological diagnosis delays remain to be established.

Some studies revealed that over one half of the patients with cancer were worried that the delays or cessation of treatment during the pandemic has negatively affected their outcomes [23,34].

At this time there is insufficient data to estimate the end of the outbreak, so the postponement of all oncological treatments until the end of the pandemic is not a realistic possibility for breast cancer patients, as well as for any other pathologies [35-37].

The study may have some potential limitations, which may include other different causes that determined the lowering of numbers of mammographies performed and the fact that the research was conducted in a single medical institution (Clinical Emergency County Hospital of Craiova).

## Conclusion

It is a well-known fact that during the COVID-19 pandemic medical practice was severely disrupted globally.

Based on the results presented in our study, the pandemic has impacted the patients' addressability to mammographies and led to a higher number of cases diagnosed in considerably more advanced stages, compared to those identified before the pandemic.

## Conflict of interests

None to declare.

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