



The impact of the COVID-19 pandemic on clinical staging, pathological staging and surgical management of breast cancer patients

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ABSTRACT

Background: This study analyzes the impact of the first six lockdown months during the COVID-19 pandemic on breast cancer (BC) patients at a regional cancer center in western Poland (Greater Poland region).

Materials and methods: Patient age, clinical stage, pathological stage, surgical management, and use of neoadjuvant therapy (NT) for patients diagnosed with BC during the pandemic (March–August 2020, $n = 290$) were compared with pre-COVID-19 data (March–August 2019, $n = 405$).

Results: There were statistically significant differences in the average age (58.2 pre-COVID-19 vs. 55.9 during COVID-19, $p = 0.014$), clinical stage ($p = 0.017$) with a stage shift (stage I being dominant pre-pandemic, stage II during the pandemic). Additionally, when comparing the 2019 and 2020 groups, there were statistically significant differences in clinically node-positive cases (27% vs. 37%, $p = 0.007$), pathologically node-positive cases (26% vs. 34%, $p = 0.014$), and NT use (27% vs. 43%, $p = 0.001$). Moreover, there was a notable increase in the prevalence of mastectomies from 44% to 53% ($p = 0.017$) and axillary lymph node dissections from 27% to 33% ($p = 0.029$).

Conclusions: The first six months of the COVID-19 pandemic had a discernible impact on BC patients in the Greater Poland region. Changes in patient age, clinical stage, pathological stage, and treatment approach were observed during this period. These findings underscore the importance of further research and adaptations in healthcare delivery to address the evolving needs of BC patients during times of crisis.

Key words: breast cancer; COVID-19; neoadjuvant chemotherapy

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Introduction

Impact of the COVID-19 pandemic on cancer patients

The COVID-19 pandemic had a significant impact on cancer patients worldwide, leading to a decrease in cancer diagnoses during the initial stages of the pandemic [1, 2]. This decline in the number of cancer cases diagnosed was particularly notable for cancers that are commonly screened for in the population, such as breast cancer (BC), colorectal cancer, and cervical cancer. However, as the initial severe restrictions of the pandemic eased, there was a gradual increase in cancer diagnoses [3–6]. A similar trend was observed for cancer screening programs, wherein the participation rates collapsed during the early stages of the pandemic but began to rise in the second half of 2020 [7, 8].

Impact of the COVID-19 pandemic on BC

In 2020 BC was the most frequently diagnosed cancer among women worldwide, surpassing colorectal and lung cancer [9]. Disruptions in nationwide BC screening programs resulted in a significant impact of the pandemic on BC patients [10]. Several studies consistently demonstrated a decline in the number of BC cases diagnosed in 2020 compared with 2019 [6, 11, 12]. Nevertheless, the impact of the pandemic on BC clinical stage (cTNM), pathological stage (pTNM), and treatment type is not entirely clear, as various studies have shown divergent findings. Some studies revealed no significant differences in BC staging between 2019 and 2020 [13, 14]. Conversely, other studies showed an opposite trend, with a higher proportion of more advanced BC cases in 2020 [15, 16].

Interesting results were observed in a multicentric study from Italy comparing BC patients who underwent surgery in the early phase of the pandemic (from March to May 2020) with the same period in 2019. This study found no significant differences in clinical staging of BC, including no significant change in clinical indications for sentinel lymph node biopsy (SLNB). However, pathological staging revealed a statistically significant increase in the number of lymph node positive BC cases in March-May 2020, which, in turn, leads to a significant rise in the number of axillary lymph node dissections (ALND) [17].

Impact of the COVID-19 pandemic on BC patients at the Greater Poland Cancer Centre (GPCC)

The GPCC, located in Poznań, Poland, serves as a prominent tertiary referral center for oncology. Notably, GPCC plays a critical role in providing surgical treatment of BC in the region, accounting for 54.1% of all BC surgeries conducted in the Greater Poland region between 2019 and 2021 [18]. Moreover, the center offers comprehensive BC diagnostics, radiotherapy, and clinical oncology services.

A study analyzing the clinical staging of BC cases at GPCC from 2019 to 2021 revealed an expected decline in the number of BC cases in 2020, but no statistically significant differences in clinical staging when compared with 2019. However, in 2021, a noteworthy statistically significant increase in more advanced BC cases was identified, particularly a rise in stage III BC cases [19].

Objectives of the study

We aimed to perform a comprehensive analysis of the effects of the early stages of the COVID-19 pandemic on BC patients' clinical and pathological characteristics and management in GPCC. Specifically, we compared clinical and pathological staging of BC. Furthermore, this study explored the potential impact of the pandemic on BC treatment choice at GPCC, including a comparison of breast-conserving therapy (BCT) versus mastectomy, and SNLB versus ALND, and the utilization of neoadjuvant therapy (NT).

Materials and methods

Study material and design

This is a single-center, retrospective cohort study analyzing female BC patients surgically treated at GPCC, Poznań, Poland. We included all incident BC cases [International Classification of Diseases, Tenth Revision (ICD-10) codes C50 and D05] diagnosed either between 1st of March 2019 and 31st of August 2019 (unexposed to COVID-19 pandemic) or between 1st of March 2020 and 31st of August 2020 (exposed to COVID-19 pandemic). The date of cancer diagnosis was established according to the European Network of Cancer Registries recommendations on coding the incidence date [20].

Patients with bilateral BC were treated as two independent cases.

Data on clinical staging was obtained from the Greater Poland Cancer Registry. Information on pathological staging, use of NT, and type of surgical procedure performed [breast-conserving therapy (BCT) / mastectomy; sentinel lymph node biopsy (SLNB) / axillary lymph node dissection (ALND)] was extracted from the GPCC hospital information system. Patients who initially underwent SLNB but were later converted to ALND due to pathologically positive nodes were included in the ALND group. To ensure data completeness (especially regarding surgical procedures following NT, which may be performed several months after the diagnosis date) our hospital record search involved a 12-month period starting from the date of cancer diagnosis. The enrollment of cases into the exposed or unexposed groups was solely based on the date of cancer diagnosis to accurately reflect the possible impact of the pandemic.

Statistical analysis

In this study, we performed several statistical analyses to investigate the impact of the COVID-19 pandemic on various aspects of BC patients' characteristics and management.

To analyze the age at diagnosis, we calculated the mean and standard deviation (SD) of patient age for both the exposed and unexposed groups. The Shapiro-Wilk test confirmed that the age distribution followed a normal distribution. We then compared the mean ages between the two groups using the Wilcoxon rank sum test with continuity correction.

For categorical variables, we used Pearson's chi-squared tests to assess the association between different factors and the year of diagnosis. Specifically, we examined the association between clinical tumor stage (cT), clinical node stage (cN), clinical stage, pathological invasiveness ($pT \geq 1$), pathological tumor stage (pT), pathological node-positive status ($pN > 0$), pathological node stage (pN), and lymph node procedure type with the year of diagnosis. Additionally, Pearson's chi-squared tests with Yates' continuity correction were conducted to investigate the association between clinical invasiveness ($cT \geq 1$), clinical node-positive status ($cN > 0$), clinical M stage (cM), use of neoadjuvant therapy (NT), and surgery type with the year of diagnosis.

All statistical analyses were performed using R Studio software, version 2023.06.0+421.

Compliance with ethical standards

Ethical review and approval were waived by the Ethics Committee of the Poznań University of Medical Sciences as our study was not classified as a medical experiment.

Results

Patient demographics

During the study period, a total of 695 BC cases were diagnosed, with 405 cases (58%) occurring in March–August 2019, and 290 cases (42%) in March–August 2020 (Tab. 1). The number of BC cases diagnosed in March–August 2020 fell by 28% compared with the same period in the previous year. The mean age at diagnosis was 58.2 years (SD

Table 1. Patient demographics, clinical stage (cTNM), pathological stage (pTNM), and treatment type — female breast cancer patients, Greater Poland, 2019–2020

		Overall		March–August 2019		March–August 2020		p-value
Cases, n		695		405		290		
Age at diagnosis, mean (SD)		57.2	(11.9)	58.2	(11.6)	55.9	(12.1)	0.014*
cT	Tis	58	8%	31	8%	27	9%	0.027**
	1	293	42%	191	47%	102	35%	
	2	251	36%	137	34%	114	39%	
	3	55	8%	26	6%	29	10%	
	4	38	5%	20	5%	18	6%	
Clinically invasive	Yes ($T \geq 1$)	637	92%	374	92%	263	91%	0.523***



Table 1. Patient demographics, clinical stage (cTNM), pathological stage (pTNM), and treatment type — female breast cancer patients, Greater Poland, 2019–2020

		Overall		March–August 2019		March–August 2020		p-value
cN	0	481	69%	297	73%	184	63%	0.037**
	1	169	24%	87	21%	82	28%	
	2	32	5%	14	3%	18	6%	
	3	13	2%	7	2%	6	2%	
Clinical node-positive	Yes (N ≥ 1)	214	31%	108	27%	106	37%	0.007***
cM	0	688	99%	402	99%	286	99%	0.656***
	1	7	1%	3	1%	4	1%	
Clinical stage	0	58	8%	31	8%	27	9%	0.017**
	IA	251	36%	168	41%	83	29%	
	IB	0	0%	0	0%	0	0%	
	IIA	186	27%	109	27%	77	27%	
	IIB	103	15%	50	12%	53	18%	
	IIIA	45	6%	20	5%	25	9%	
	IIIB	34	5%	18	4%	16	6%	
	IIIC	11	2%	6	1%	5	2%	
pT	0	44	6%	20	5%	24	8%	0.174**
	Tis	67	10%	35	9%	32	11%	
	1	362	52%	224	55%	138	48%	
	2	179	26%	105	26%	74	26%	
	3	23	3%	15	4%	8	3%	
	4	10	1%	4	1%	6	2%	
	x	10	1%	2	0%	8	3%	
Pathologically invasive	pT ≥ 1	584	85%	350	87%	234	83%	0.005**
pN	0	479	69%	295	73%	184	63%	0.071**
	1	141	20%	78	19%	63	22%	
	2	32	5%	15	4%	17	6%	
	3	22	3%	9	2%	13	4%	
	x	21	3%	8	2%	13	4%	
Pathological node-positive	pN ≥ 1	195	29%	102	26%	93	34%	0.014**
pM	X	695	100%	405	100%	290	100%	N/A
Neoadjuvant therapy	Yes	232	33%	108	27%	124	43%	<0.001***
	No	463	67%	297	73%	166	57%	
Surgery type	BCT ¹	362	52%	227	56%	135	47%	0.017***
	Mastectomy	333	48%	178	44%	155	53%	
Lymph node procedure type	SLNB ²	471	68%	289	71%	182	63%	0.029**
	ALND ³	206	30%	109	27%	97	33%	
	None	18	3%	7	2%	11	4%	

*Wilcoxon rank sum test with continuity correction; **Pearson's Chi-squared test; ***Pearson's Chi-squared test with Yates' continuity correction; N/A — at least one entry of "x" must be positive to calculate p; BCT — breast conserving therapy; SLNB — sentinel lymph node biopsy; ALND — axillary lymph node dissection; SD — standard deviation

11.6) in the 2019 group, and 55.9 (SD 12.1) years in the 2020 group ($p = 0.014$).

Clinical staging

In 2020, when compared to 2019, there was a slight increase in the proportion of BC in situ cases (from 8% to 9%), and a corresponding decrease in the fraction of clinically invasive BC (92% to 91%, $p = 0.523$; Tab. 1), although this difference was not statistically significant. However, significant disparities in clinical staging were observed between patients diagnosed in 2019 and 2020 ($p = 0.017$). Before the pandemic, stage I was the most frequently diagnosed (41%) followed by stage II (39%), while during the pandemic, stage II became the most commonly diagnosed (45%), followed by stage I (29%).

A more detailed analysis of clinical staging revealed notable differences in cT, denoting clinical tumor staging ($p = 0.027$). In comparison with the pre-pandemic period, there was a decrease in the proportion of cT1 cases (from 47% to 35%) during the pandemic, accompanied with an increase in cT2 (from 34% to 39%), cT3 (from 6% to 10%), and cT4 (from 5% to 6%) cases. Additionally, a significant increase in the fraction of clinically node-positive BC cases was observed during the pandemic (27% pre-COVID-19 vs. 37% during COVID-19, $p = 0.007$).

Furthermore, changes in the distribution of cN during the pandemic, when compared with the pre-pandemic period, were also significant ($p = 0.037$). There was a decrease in the fraction of cN0 cases (from 73% to 63%), along with an increase in the proportion of cN1 (from 21% to 28%) and cN2 (from 3% to 6%) cases. No differences were observed in the fraction of cN3 cases, which remained at 2% in both groups. Lastly, no significant differences were observed in the percentage of patients with distant metastases (cM), which remained at 1% in both the pre-pandemic and pandemic groups ($p = 0.523$).

Pathological staging

A statistically significant reduction in the percentage of pathologically invasive BC cases ($pT \geq 1$) was observed during the pandemic (87% pre-COVID-19 vs. 83% during COVID-19, $p = 0.005$; Tab. 1). However, no statistically significant disparities were ob-

served for pT distribution. In both groups, the pT1 category was the most frequent (55% pre-COVID-19 vs. 48% during COVID-19), followed by pT2 (26% in both groups) ($p = 0.174$).

Notably, there was a statistically significant increase in the percentage of pathological node-positive cases ($pN \geq 1$) during the pandemic (26% pre-COVID-19 vs. 34% during COVID-19, $p = 0.014$). However, the differences in pN distribution were non-significant ($p = 0.071$).

Management

A significant increase in the use of NT was observed during the COVID-19 pandemic ($p < 0.001$). Prior to the pandemic, 27% of patients received NT, whereas during the pandemic, the percentage of patients treated with NT rose to 43%.

Furthermore, notable differences were observed in terms of surgical management, both in breast surgery and lymph node procedures. Before the pandemic, the majority of patients with BC underwent BCT (56%) while 44% underwent mastectomy. During the pandemic, there was a shift in surgical approach, with a higher proportion of patients receiving mastectomy (BCT 47%, mastectomy 53%; $p = 0.017$). Additionally, the percentage of ALND performed also differed significantly (27% pre-COVID-19 vs. 33% during COVID-19; $p = 0.029$).

Discussion

Patient demographics

The reduction in the average age of patients diagnosed with BC during the pandemic can be partly explained by an over 90% drop in BC screening participation rates in Poland (screening age in Poland 50–69) during the initial stages of the pandemic [21], or by the reported avoidance of medical care among older adults during the pandemic [22, 23]. This finding aligns with a recent study conducted at the GPCC, which demonstrated a reduction in BC cases in the screening age group in 2020, but showed no significant differences in the average age at diagnosis in 2020 compared to 2019 [19]. The difference in findings may be attributed to our study's distinct methodology, which focused more closely on the initial six months of the pandemic-related restrictions in Poland, as opposed to the entire calendar year.

It is essential to acknowledge that the average age at diagnosis and the notable reduction in the number of incident BC cases in March–August 2020 (a drop of 28% compared to the previous year) do not fully represent the true BC incidence gap in the Greater Poland region. Our study specifically examines cases surgically treated at the GPCC and, therefore, it does not encompass the entire BC population of the region. This exclusion encompasses patients treated without surgery at the GPCC or those treated surgically in other hospitals.

Clinical staging of BC and use of NT

We observed a significant increase in clinically advanced BC cases during the pandemic, closely related with the increased use of NT. For instance, prior to the pandemic, 27% of BC cases were clinically node positive, and 27% of cases received NT. However, during the pandemic, these figures rose to 37% of BC cases being clinically node positive, and 43% receiving NT. Considering the additional increase in the percentage of cT3–4 cases during the pandemic (from 11% to 16%), it appears that the rise in NT at the GPCC during the pandemic resulted mainly from clinical indications rather than other pandemic-related factors.

The data on the use of NT at the GPCC are similar to findings presented in a study from Mayo Clinic Rochester, USA, which analyzed the same time periods. In their study, during March–August 2019 (pre-COVID-19), 29% of patients received NT, and during March–August 2020 (during COVID-19), 39% of patients received NT. However, in the American study, the rise in NT was not driven by an increase in clinically advanced BC cases but rather by the increased use of neoadjuvant endocrine therapy in early-stage hormone receptor-positive disease, as an alternative to surgical management [13].

Thanks to COVID-19 preventative policies implemented at the GPCC, which included regular testing and dividing on-site staff into separate teams with minimal contact, the first wave of the pandemic did not cause significant disruptions in the functioning of the hospital [24]. It is worth noting that, unlike data from Italy and the USA [13, 17] this study demonstrates a statistically significant rise in clinically advanced BC cases during the first wave of the pandemic, which aligns with reports from the UK or South Korea [25, 26].

Surgical management and pathological staging

Before the pandemic, the majority of breast surgeries at the GPCC were BCT procedures (56%). However, patients diagnosed with BC during the initial stages of the pandemic were more likely to undergo mastectomy (mastectomy 53% vs. BCT 47%). This shift in surgery type aligns with different cT categories (cT2–4 45% pre-COVID-19 vs. 56% during COVID-19). Additionally, it is possible that the pandemic changed the way patients perceive certain cancer treatments [27]. Some patients may have opted for mastectomy instead of BCT to reduce the number of hospital visits during the pandemic, particularly due to radiotherapy or chemotherapy procedures linked with BCT.

Very similar results for surgery type were observed in the same time period in Mayo Clinic Rochester, USA, where the percentage of BCT was 55% pre-COVID-19 and dropped to 48% during the pandemic in March–August 2020 [13]. The decrease in BCT procedures during the pandemic was also observed in Scotland and the Netherlands [28, 29].

The increased number of ALND from 27% to 33% during the COVID-19 is not surprising, considering the marked rise in clinically node-positive cases during the pandemic (from 27% to 37%), which was later confirmed by an increase in the percentage of pathologically node-positive cases (from 26% to 34%). However, the increase in ALND is not as prominent as the increase in cN1–3 categories, most likely due to the intensified use of NT during the COVID-19 period, which led to the downstaging of pN and allowed for more SLNB. Similarly, the reduction in the percentage of pathologically invasive cancers during the pandemic, as well as the lack of statistically significant differences in pT staging, may also result, at least partially, from the increased use of NT that led to the downstaging of pT. The increased use of NT during the pandemic is also a likely explanation for the rise in pT0 categories and the statistically significant drop in the percentage of pathologically invasive BC cases during the pandemic.

Strengths and limitations of the study

The BC Unit, as well as the GPCC, remained fully operational during the pandemic, enabling

the collection of reliable data on BC patients. This allowed for a valid comparison. The methodology of this study, in which hospital record entries were reviewed up to 12 months from the date of cancer diagnosis, provides insight into pathological staging and surgical management in patients who underwent prolonged NT or had temporary contraindications for surgery.

However, it is important to acknowledge certain limitations. This study focuses solely on patients surgically treated at the GPCC, excluding many patients with metastatic BC (stage IV) who do not receive surgical treatment. Therefore, this paper does not reliably represent the impact of the pandemic on stage IV BC patients. Additionally, being a single-center study, this research may not accurately reflect the general impact of the pandemic on BC patients in Poland as a whole.

Suggestions for further research

Although this study demonstrated a rise in NT during the pandemic, we did not differentiate between neoadjuvant endocrine therapy and neoadjuvant chemotherapy, as both types of NT have the same pathological staging of γ TNM. Further research is required to examine what proportion of patients at the GPCC received neoadjuvant endocrine therapy as an alternative to surgical management during the pandemic.

There are inconsistent reports in literature on the impact of the COVID-19 pandemic on BC clinical stage, with our study showing a marked impact of the pandemic on both cT and cN categories. Further research is needed to investigate potential causes for the reported differences. Identifying factors that lead to a rise in clinically advanced BC cases is essential to mitigate increased cancer morbidity and mortality during future pandemics.

Aside from changes in surgical and systemic management, significant alterations in radiation therapy for BC have been observed during the pandemic, with international guidelines released on this topic in May 2020 [30]. In the UK, during the initial months of the pandemic, a sharp rise in the use of ultra-hypofractionated breast radiotherapy was observed (as a percentage of all courses) [31]. Further research is required to examine the impact of the pandemic on breast radiation therapy at the GPCC.

Conclusions

This study highlights a multifaceted impact of the COVID-19 pandemic on the clinical and pathological characteristics of BC patients treated surgically at the GPCC. During the pandemic, there was a significant reduction in average patient age, along with significant differences observed in both cT and cN categories, as well as BC clinical stage. Notably, a stage shift was observed, with stage II being most frequently diagnosed during the pandemic, as opposed to stage I before the pandemic. Additionally, there was a significant rise in the percentage of pathologically node-positive cases.

Moreover, patients diagnosed with BC during the pandemic were more likely to receive invasive surgical treatment at the GPCC, as evidenced by a significant rise in the percentage of mastectomies and ALND procedures. Furthermore, a significant rise in NT was also observed during the pandemic, primarily driven by an increase in clinically advanced BC cases. The lack of significant differences in pT categories may result from the downstaging effect of NT, which was more widely used during the pandemic.

Conflicts of interest

The authors declare no conflicts of interest.

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Ethical permission

Ethical review and approval were waived by the Ethics Committee of the Poznań University of Medical Sciences as our study was not classified as a medical experiment.

Author contributions

P.R.; M.T. — writing, original draft preparation; I.M. — statistical software and analysis, data curation, review for critical intellectual content; W.K. — review for critical intellectual content.

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