

COVID-19 and Breast Cancer Prognosis: A Comparative Analysis of Disease-Free Survival Rates in Taiwan

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Purpose: This study evaluates the effect of pandemic-related diagnostic and treatment delays on 3-year disease-free survival (DFS) in Taiwanese breast cancer patients.

Material and Methods: This single-institution study analyzed breast cancer patients across three distinct periods: non-COVID-19 in 2017, pre-COVID-19 in 2019, and during the COVID-19 pandemic in 2020, to investigate the impact of the COVID-19 pandemic on DFS rates and recurrence rates. DFS was defined as the interval from surgery to the occurrence of breast cancer recurrence or death, whereas overall survival (OS) was defined as the interval from surgery to death from any cause. Follow-up protocol included regular clinical examinations and annual imaging, with a minimum follow-up of 36 months unless an event occurred earlier.

Results: The demographics of breast cancer patients changed from 2017 to 2020, with an average age increasing from 54.6 to 58.6 years. While overall survival (OS) did not vary significantly across the cohorts, DFS differed significantly, with the 2020 cohort experiencing a significant decline in DFS compared to 2017 ($p = 0.027$). Recurrence rates also increased, from 3.1% in 2017 to 7.6% in 2020.

Conclusion: The COVID-19 pandemic had a negative impact on the DFS of breast cancer patients, with the 2020 cohort experiencing a significantly shorter DFS time compared to the 2017 cohort.

Keywords: breast cancer, COVID-19, disease-free survival, overall survival, recurrence rates, Taiwan

Introduction

The COVID-19 pandemic disrupted healthcare systems worldwide, echoing patterns from historical epidemics such as the Plague of Athens, the Antonine Plague, and the Black Death, with similar themes of reduced access to preventive services and lasting effects on disease detection and treatment.¹ Screening suspensions delayed breast cancer detection and treatment initiation, underscoring the long-term effects that pandemics can have on early disease detection and management.² These disruptions may impact disease-free survival (DFS)—a critical early predictor of overall survival that enables timely assessment of treatment efficacy before mortality data becomes available.³

Taiwan's universal coverage and early containment measures sustained low COVID-19 case numbers, demonstrating healthcare resilience during the crisis.^{4,5} However, the pandemic subsequently necessitated major adaptations to clinical practice, with screening and diagnostic mammography rates declining by 51%–80%, reductions in chemotherapy delivery, and a sharp rise in COVID-19 cases during 2022–2023 due to emerging variants and slow vaccination progress.⁶ These modifications potentially affected timely detection of recurrence, with any delay in treatment significantly increasing the risk of tumors progressing from curable early stages to incurable advanced stages, resulting in reduced survival rates and altered DFS metrics.⁷ By elucidating the effects of COVID-19 on breast cancer prognosis, this research seeks to contribute valuable insights for future clinical practices and public health policies.⁸

Taiwan provides a distinctive research setting due to its robust health insurance system and successful COVID-19 containment strategies.⁴ However, Taiwan has experienced a significant increase in breast cancer incidence over the past few decades, with the rate reaching 128.2 per 100,000 population in 2016.⁹ The 5-year survival rate for female breast cancer patients in Taiwan from 2018 to 2022 was 89%.¹⁰ The outcome of breast cancer related to the pandemic is less understood. This study compares pre-pandemic and pandemic-era breast cancer DFS rates to assess COVID-19's long-term impact after three years, addressing a significant research gap as little evidence exists regarding pandemic effects on cancer survival beyond short-term outcomes. By examining potential pandemic-related changes in recurrence rates, patient demographics, mammography utilization patterns, and stage distribution, this research aims to identify vulnerabilities in cancer care and inform targeted strategies to maintain treatment efficacy during public health crises.

Materials and Methods

Patients

This retrospective study, conducted at Kaohsiung Veterans General Hospital, was approved by the Institutional Review Board, which waived the requirement for informed consent due to the retrospective nature of the study. This study initially identified a total of 1186 patients (mean age $\pm$ SD: 56.3 $\pm$ 11.6 years) who underwent breast biopsies with concordant histopathological results and complete medical records during the January to July periods of 2017, 2019, and 2020. This study included female breast cancer patients diagnosed through biopsy during the study periods who had concordant histopathological results, complete medical records, and sufficient follow-up data for survival analysis. Patients were excluded if they had incomplete medical records, missing clinical data, or findings. Patients were categorized into three groups based on the year of diagnosis: the Non-COVID-19 group included 136 patients diagnosed in 2017; the Pre-COVID-19 group included 115 patients diagnosed between January 21 and July 31, 2019; and the During COVID-19 group included 111 patients diagnosed during the same period in 2020. During the DFS analysis, patients diagnosed with Stage IV breast cancer and receiving ongoing regular treatment were excluded due to the inapplicability of a disease-free status, leading to the elimination of 20 patients from this segment of the study.

To evaluate the potential impact of treatment delays caused by the pandemic and to provide historical context, the study additionally included a control cohort of 136 women diagnosed with breast cancer through biopsy in 2017, prior to the pandemic. Including 115 patients from 2019 and 111 from 2020, the total study population across the three time periods amounted to 362 patients.

Study Design

This study conducted a survival analysis of 362 patients diagnosed with breast cancer across three distinct periods: non-COVID-19 in 2017 (n=136), pre-COVID-19 in 2019 (n=115), and during the COVID-19 pandemic in 2020 (n=111), as delineated in [Table 1](#). The division of patients into the 2017, 2019, and 2020 cohorts was based on the year of diagnosis according to the American Joint Committee on Cancer (AJCC) 7th edition staging system. An important facet of the research involved categorizing patients who underwent ultrasound-guided biopsies according to the timing of the procedure: prior to the pandemic in 2017, before the onset of the COVID-19 pandemic in 2019, and during the pandemic in 2020. This allowed the researchers to investigate the overall and disease-free survival rates over a three-year period, providing a baseline for comparison against the cohorts impacted by the pandemic.¹¹ Additionally, the adopted technique for these procedures was ultrasound-guided core needle biopsy (CNB), deployed specifically to assess ultrasound-detectable breast lesions.

Subsequent to receiving a malignant diagnosis from their biopsies, patients were followed for a period of three years. The purpose of follow-up was to track vital status and detect any recurrence, with DFS defined as the time from surgery to either the first documented breast cancer recurrence or breast cancer-related death, and OS defined as the time to death from any cause. This longitudinal analysis enabled the exploration of the COVID-19 pandemic's potential impact on OS and DFS rates among these patients.

**Table I** Clinical Characteristics of Enrolled Women of Breast Cancer During Three Time Periods

Clinical Characteristics	Non-COVID-19 in 2017 (n=136)	Pre-COVID-19 in 2019 (n=115)	During COVID-19 in 2020 (n=111)	P [†] (2020 vs 2019)	P ^{††} (2020 vs 2017)
Mean age±SD (years)	54.6±11.1	56.2±11.1	58.6±12.7	0.143	0.009**
Vital status, n(%)				0.775	0.510
Dead	3 (2.2)	5 (4.3)	4 (3.6)		
Alive	133 (97.8)	110 (95.7)	107 (96.4)		
Age Group				0.150	0.066
≥60 years old	48 (35.3)	43 (37.4)	52 (46.8)		
<60 years old	88 (64.7)	72 (62.6)	59 (53.2)		
Mammography Type				0.934	<0.001***
Screening	12 (8.8)	46 (40.0)	45 (40.5)		
Diagnostic	124 (91.2)	69 (60.0)	66 (59.5)		
Stage AJCC 7th				0.0059	0.184
0	25 (18.4)	34 (29.6)	19 (17.1)		
I	39 (28.7)	49 (42.6)	45 (40.5)		
II	47 (34.5)	15 (13.0)	25 (22.5)		
III	19 (14.0)	9 (7.8)	16 (14.4)		
IV	6 (4.4)	8 (7.0)	6 (5.4)		
3-year OS rate (95% CI)	97.7 (95.2–100.0)	94.6 (90.0–99.2)	95.1 (90.3–99.9)	0.775	0.510

Notes: Numbers in parentheses are the percentage. [†]P for comparison of 2019 vs 2020. ^{††}P for comparison of three time periods. **P < 0.01, ***P < 0.001.

Abbreviations: AJCC, American Joint Committee on Cancer; BI-RADS, Breast Imaging-Reporting and Data System; SD, Standard deviation; CI, confidence interval; OS, Overall survival.

Statistical Analysis

Continuous variables were summarized using means and standard deviations (SD). The characteristics of the study population within groups were examined using the chi-square test for categorical variables and independent *t*-test or ANOVA for continuous variables. The Kaplan-Meier (K-M) method was used to compare DFS and OS between the year groups, using log-rank or Breslow tests for tied events. All statistical analyses were performed using IBM SPSS version 22 (IBM Corp., Armonk, NY, USA). A value of *p* < 0.05 was considered statistically significant.

To analyze DFS, two complementary statistical approaches were used. The first method assessed survival rates at a fixed timepoint, providing a straightforward comparison of outcomes. The second method analyzed survival curves over the entire follow-up period, taking into account the timing of recurrence events and censored cases. These two approaches offer different but complementary perspectives—one focusing on outcome at a specific time, the other capturing the temporal distribution of events. Both were used to ensure a comprehensive and robust evaluation of DFS differences.

Result

Characteristics

The mean ages for the 2017, 2019, and 2020 cohorts were 54.6±11.1, 56.2±11.1, and 58.6±12.7 years, respectively. A shift was observed in the patient population aged 60 years and above, increasing from 35.3% in 2017 to 46.8% in 2020. Concurrently, the utilization of screening mammography significantly rose from 8.8% in 2017 to 40.5% by 2020, whereas diagnostic mammography declined from 91.2% in 2017 to 59.5% by 2020. In terms of cancer stages, the prevalence of Stage I cancer was higher in 2019 and 2020 (42.6% and 40.5%), whereas Stage II cancer was most common in 2017 (34.5%).

Age Difference

Significant differences were found in the average age across the three cohorts (*p* = 0.028), with a significant difference between the 2017 and 2020 cohorts (Bonferroni *p* = 0.009), indicating a trend of increasing average age from 2017 to 2020 (Table 1).

OS Analysis

The 3-year OS rates of the 2017, 2019, and 2020 cohorts were 97.7%, 94.6%, and 95.1%, respectively. In the comparison of OS across the three patient cohorts from 2017, 2019, and 2020, the K-M curve showed no significant difference ($p = 0.369$) either among these cohorts as distinct groups or between any two specific cohorts ($p > 0.05$) (Figure 1).

DFS Analysis

Table 2 shows the clinical characteristics of breast cancer patients included in the DFS analysis. The 2020 cohort had the highest mean age (58.7 ± 12.9 years) and a correspondingly shorter mean DFS time (21.4 ± 12.8 months) compared to the other two patient cohorts. Recurrence rates for the cohorts from 2017, 2019, and 2020 were 3.1%, 2.8%, and 7.6%, respectively. Moreover, there was a shift in the age distribution; during the COVID-19 period in 2020, patients aged ≥ 60 years accounted for 48.6%. The implementation of screening mammography escalated from 9.2% in 2017 to 42.1% in 2019 and 41.9% in 2020 ($p < 0.001$). Additionally, there was a significant variation in the distribution of cancer stages ($p < 0.001$). Stage I was predominantly seen in 2019 pre-COVID-19 (45.8%), while Stage II was more common in 2017 non-COVID-19 (36.2%), and Stage III was more common in 2020 during COVID-19 (15.2%).

A significant difference in DFS was observed across the three time periods ($p = 0.040$), indicating that the length of time patients remained free from disease after treatment differed significantly between these years (Figure 2). When comparing DFS rates between any two specific cohorts, there was a significant decline for the 2020 cohort compared to the 2017 cohort ($p = 0.027$) based on the Kaplan-Meier survival curve analysis. This p-value differs from the 3-year endpoint rate (Table 2, $p = 0.116$), as Kaplan-Meier analysis considers all recurrence events over time. Furthermore, no significant differences in DFS were observed between the 2019 and 2020 cohorts ($p = 0.065$) and the 2017 and 2019 cohorts ($p = 0.910$).

Recurrence

As presented in Table 3, the 2017 and 2019 cohorts noted recurrences in 4 and 3 patients, respectively, whereas the 2020 cohort recorded death or recurrence in 9 patients. The mean ages of patients who experienced recurrence were 53.8 (± 10.2), 55.7 (± 12.5), and 58.6 (± 13.3) for the 2017, 2019, and 2020 cohorts, respectively. Additionally, Table 3 indicates

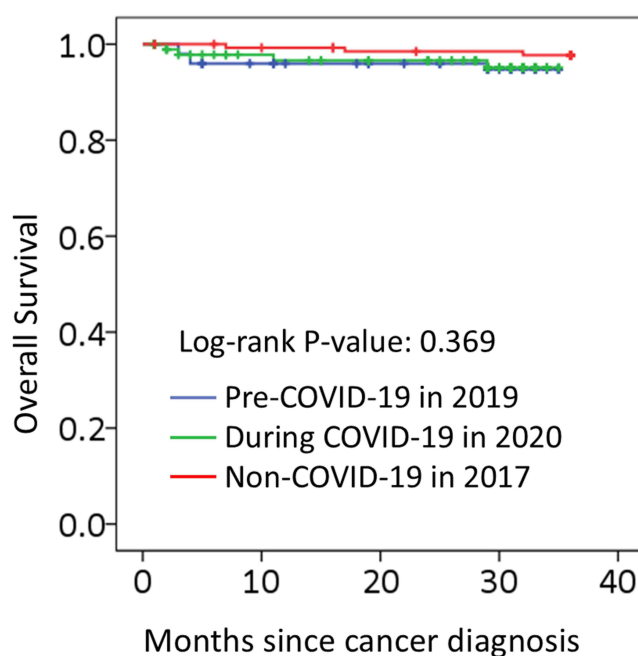


Figure 1 Comparison of overall survival (OS) through the Kaplan-Meier (K-M) survival curves for the 2017, 2019, and 2020 breast cancer patient cohorts. The y-axis shows the percentage of patients who are still alive at a specific point in time, while the x-axis shows the number of months since diagnosis.

Table 2 Clinical Characteristics of Breast Cancer Patients Included for Disease Free Survival Analysis During Non-COVID-19 in 2017, Pre-COVID-19 in 2019, and During COVID-19 in 2020

Clinical Characteristics	Non-COVID-19 in 2017 (n=130)	Pre-COVID-19 in 2019 (n=107)	During COVID-19 in 2020 (n=105)	P [†] (2020 vs 2019)	P ^{††} (2020 vs 2017)
Mean age± SD (years)	54.3±10.9	55.5±10.8	58.7±12.9	0.310	0.159
DFS time (months)	34.5±5.8	25.9±11.1	21.4±12.8	0.15	< 0.001***
Status, n(%)				0.114	0.116
Recurrence	4 (3.1)	3 (2.8)	8 (7.6)		
No recurrence	126 (96.9)	104 (97.2)	97 (92.4)		
Age Group				0.074	0.022*
≥60 years old	44 (33.8)	39 (36.4)	51 (48.6)		
< 60 years old	86 (66.2)	68 (63.6)	54 (51.4)		
Mammography Type				0.982	< 0.001***
Screening	12 (9.2)	45 (42.1)	44 (41.9)		
Diagnostic	118 (90.8)	62 (57.9)	61 (58.1)		
Stage AJCC 7th				0.031*	0.131
0	25 (19.2)	34 (31.8)	19 (18.1)		
I	39 (30.0)	49 (45.8)	45 (42.9)		
II	47 (36.2)	15 (14.0)	25 (23.8)		
III	19 (14.6)	9 (8.4)	16 (15.2)		
3-year DFS rate	96.8 (93.7–99.9)	96.5 (92.5–100.0)	89.4 (82.4–96.4)	0.114	0.116

Notes: Numbers in parentheses are the percentage. [†]P for comparison of 2019 vs 2020. ^{††}P for comparison of 2017 vs 2020. *P < 0.05, ***P < 0.001.

Abbreviations: AJCC, American Joint Committee on Cancer; BI-RADS, Breast Imaging-Reporting and Data System; SD, Standard deviation; CI, confidence interval; DFS, Disease free survival.

that among the 16 patients who experienced a recurrence of breast cancer, 14 were diagnosed with invasive ductal carcinoma (IDC), while the remaining 2 had different diagnoses, namely invasive lobular carcinoma (ILC) and metaplastic carcinoma.

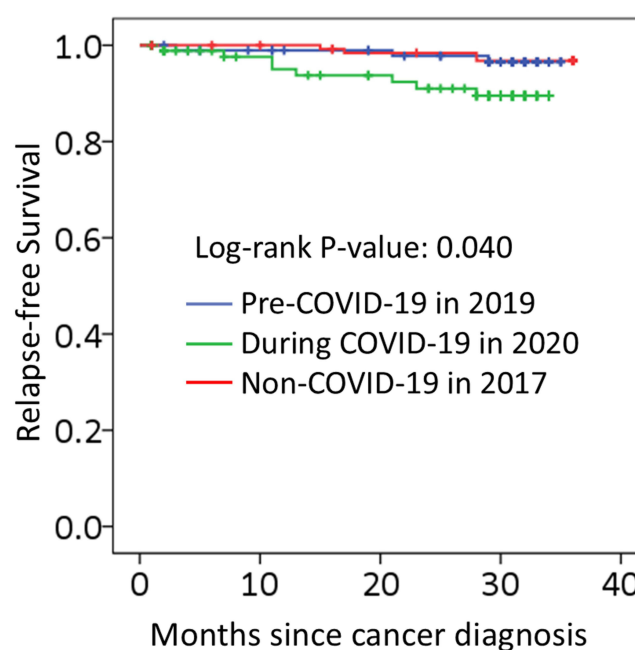


Figure 2 Comparison of disease-free survival (DFS) through the Kaplan-Meier (K-M) survival curves for the 2017, 2019, and 2020 breast cancer patient cohorts. The y-axis shows the percentage of patients who are disease-free at a specific point in time, while the x-axis shows the number of months since diagnosis.

Table 3 Clinical Characteristics of Breast Cancer Patients with Death or Recurrence During Non-COVID-19 in 2017, Pre-COVID-19 in 2019, and During COVID-19 in 2020

Clinical Characteristics	Non-COVID-19 in 2017	Pre-COVID-19 in 2019	During COVID-19 in 2020
Death or recurrence (n)	4	3	9
Mean age $\pm$ SD (years)	53.8 $\pm$ 10.2	55.7 $\pm$ 12.5	58.6 $\pm$ 13.8
Mean time to event $\pm$ SD (months)	22.0 $\pm$ 7.0	17.7 $\pm$ 13.3	14.5 $\pm$ 8.8
Patients aged over 60 years old	50.0%	33.3%	33.3%
Pathological stage			
Stage 0	0.0%	0%	0%
Stage I	25.0%	0%	11.1%
Stage II	25.0%	33.3%	33.3%
Stage III	50.0%	66.7%	55.6%
Treatment received			
Radiotherapy treatment	0.0%	66.7%	55.6%
Chemotherapy treatment	100.0%	100.0%	66.7%
Tumor type			
Pathology type I (IDC)	75.0%	100.0%	88.9%
Pathology type II (other types)	25.0%	0%	11.1%

Abbreviations: IDC, Invasive Ductal Carcinoma; SD, Standard deviation.

Discussion

This study investigated the impact of the COVID-19 pandemic on breast cancer diagnosis and treatment in Taiwan. While the OS rates among the three cohorts from 2017, 2019, and 2020 were consistent (97.7%, 94.6%, and 95.1%, respectively) with no statistically significant difference, the DFS presented a contrasting pattern (96.8%, 96.5%, and 89.4%). The 2020 cohort demonstrated a lower DFS rate than the previous years, highlighting a potential adverse effect of the pandemic on DFS. The study's results provide valuable insights into the implications of COVID-19 on breast cancer outcomes. Although the 3-year OS rates remained relatively stable, the decline in DFS for patients diagnosed in 2020 raises concerns about the pandemic's impact on healthcare systems and clinical practices. Additionally, the observed demographic changes, shifts in cancer stage distribution, and increased use of screening mammography indicate the multifaceted impacts of the pandemic on health behaviors and disease outcomes. These findings contribute to a broader understanding of how global crises can affect healthcare delivery and patient outcomes, underscoring the need for further investigation and the development of targeted, resilient healthcare strategies to mitigate these effects in future crises.¹

The COVID-19 pandemic has significantly disrupted cancer care, leading to delays in diagnosis and treatment. This disruption could potentially increase the risk of early recurrence of breast cancer, as treatment delays might allow the cancer to progress.⁸ Breast cancer patients with early sentinel-node involvement could potentially avoid axillary dissection without compromising survival, as evidenced by a 5-year disease-free survival rate of 87.8% in the group that did not undergo dissection compared to 84.4% in the group that did.¹² Meanwhile, delays of 3–6 months in treatment from symptom onset are associated with a 12% and 7% lower 5-year survival, respectively. Factors such as the inherent biology of the tumor, the presence of undetected micrometastases at initial treatment, and lymph node involvement can contribute to the recurrence of breast cancer within three years.^{12,13} Furthermore, local recurrence or distant metastasis of cancer, which refers to cancer returning at the original tumor site or spreading to other parts of the body, can occur depending on the tumor type and initial disease stage. Risk factors include tumor size, lymph node involvement, and the status of certain tumor biological characteristics like the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2).¹⁴

The risk of death from breast cancer is highest in the third year after diagnosis and then decreases over time, depending on factors such as the cancer's progression, the effectiveness of treatment, and the patient's overall health.¹⁵ Increasing mortality in the future can be due to factors like late recurrence, development of treatment resistance, and the overall health status of the patient, highlighting the importance of ongoing monitoring and treatment adjustments in cancer management.¹⁴



During the COVID-19 pandemic, mammography examinations in Southern Taiwan saw a significant decrease, with self-requested, screening, and diagnostic exams dropping by 96%, 51%, and 6%, respectively, compared to pre-pandemic levels. Moreover, when new COVID-19 cases exceeded 20 per week, a strong positive correlation was observed between the increase in cases and the decrease in weekly mammography exams.¹⁶ Additionally, the volume of breast biopsies decreased by 17%, and the number of total breast cancers and early breast cancers (stages 0 and 1) decreased by 10% and 38%, respectively, indicating a significant delay in early breast cancer detection despite the country's low COVID-19 incidence.¹⁷ A 3-month COVID-19 lockdown in England could cause an increase in cancer-related deaths and life-years lost due to delayed diagnoses and treatment, with estimates ranging from 181 additional deaths and 3316 life-years lost for a 25% backlog of referrals, up to 542 additional deaths and 9948 life-years lost for a 75% backlog.¹⁸ These figures could rise significantly with further diagnostic delays.¹⁸

The 2019 patient cohort exhibited a lower OS rate compared to the 2017 patient cohort, suggesting an influence by the COVID-19 pandemic on both diagnosis and subsequent cancer treatments.¹⁹ Delays in treatment due to the redirection of healthcare resources, staffing shortages, logistical challenges, and patient fear of infection led to disruptions in radiotherapy and chemotherapy. These delays have serious implications for patient outcomes, further highlighted by Johnson et al's findings that delays in surgery are linked to decreased OS and a systematic review showing a 12% lower 5-year survival rate associated with treatment delays.^{20,21} This emphasizes the importance of timely intervention and illustrates the vulnerabilities in healthcare systems during global crises.

In a study at a cancer center in Brazil during the COVID-19 pandemic, 12.4% of 411 cancer patients analyzed succumbed to COVID-19. Remarkably, mortality was highest among those with lung and hematological cancers, especially patients above 60 years and those undergoing active cancer treatment (OR 2.77, 95% confidence interval (CI) 1.25–6.13).²² The pandemic-induced delays in cancer diagnosis are projected to lead to significant increases in deaths across various cancer types in England within five years, translating to an additional 3291–3621 deaths and 59,204–63,229 total years of life lost.²³ Concurrently, Taiwan, after implementing strict travel restrictions in March 2020, saw a substantial rise in COVID-19 related deaths starting from April-May 2022, surpassing 100 cases weekly from the 18th week.²⁴

The study has some limitations that should be acknowledged. First, it was conducted at a single medical center, which may limit the generalizability of the findings to other populations and settings. Second, the study did not evaluate long-term outcomes beyond five years, which could hinder understanding of the long-term effects and survival rates of the disease. Third, treatment details, including chemotherapy, hormonal therapy, radiotherapy, and home-based care, were not consistently documented. In Taiwan, COVID-19 led to delayed outpatient visits and triage-based clinic access.²⁵ These factors were excluded from multivariate analysis and warrant evaluation in future studies. These limitations should be considered when interpreting the results. However, the significance of the findings highlights future research directions grounded in the observed outcomes, including studies on the long-term effects of COVID-19 on breast cancer prognosis and comparisons with different regions or cancer types during the pandemic.

Conclusion

During the COVID-19 pandemic, breast cancer patients in Taiwan experienced a notable decline in disease-free survival, likely reflecting delays in diagnosis or treatment, even though overall survival remained stable. These findings underscore the importance of maintaining timely cancer care during public health crises, while also acknowledging that limitations in sample size and population differences may affect broader applicability.

Abbreviations

AJCC, American Joint Committee on Cancer; BI-RADS, Breast Imaging-Reporting and Data System; CI, Confidence Interval; CNB, Core Needle Biopsy; COVID-19, Coronavirus Disease 2019; DFS, Disease-Free Survival; ER, Estrogen Receptor; HER2, Human Epidermal Growth Factor Receptor 2; IDC, Invasive Ductal Carcinoma; ILC, Invasive Lobular Carcinoma; K-M, Kaplan–Meier; OR, Odds Ratio; OS, Overall Survival; PR, Progesterone Receptor; SD, Standard Deviation.

Data Sharing Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request. Due to privacy and ethical concerns, individual patient data cannot be made publicly available. Aggregated data may be shared for research purposes following institutional approval and in accordance with relevant data protection regulations. Original research data will be retained for 5 years according to the institutional data retention policy of Kaohsiung Veterans General Hospital.

Ethics Statement

This retrospective study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was granted by the Institutional Review Board of Kaohsiung Veterans General Hospital (IRB No. KSVGH20-CT7-26), which also waived the requirement for informed consent due to the retrospective nature of the investigation. All patient data were de-identified and handled in accordance with institutional privacy policies and ethical guidelines for clinical research.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest in relation to this work.

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