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# The Impact of COVID-19 on Breast Cancer Treatment: A Systematic Review

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ABSTRACT

**Background**: During the COVID-19 pandemic, health resources were stretched, access was impacted by lockdowns and there were concerns about exposure to the virus during visits to hospitals. The purpose of this study was to examine how breast cancer treatments (presentation, surgery, radiotherapy, chemotherapy and/or endocrine therapy) changed or were adapted during the early phase of the pandemic.

**Methods**: A systematic review was conducted using PRISMA guidance. Eligible studies presented original data reporting changes to early breast cancer treatment by comparing 'pandemic' treatment to a 'pre-pandemic' cohort or to 'ideal' treatment of individual cases. Data were extracted into evidence tables and narrative synthesis was used to analyze results.

**Results**: Fifteen studies with paired design were eligible. These reported outcomes for 6,353 people treated for early breast cancer (January 2020–June 2021). All studies reported some change to treatment due to the pandemic. The nature of reported changes was inconsistent. Changes included: more advanced tumours at presentation compared to pre-pandemic, an increase in breast conserving surgery; an increase in simple mastectomy (without breast reconstruction); a trend towards increased wait times, delays to start of treatment, shorter post-operative hospital stay and hypofractionation or omission of radiotherapy. Centres used more or less neoadjuvant chemotherapy or endocrine therapy.

**Conclusion**: In the early stage of the pandemic, fewer early-stage breast cancer cases were treated at many centres. Treatment for breast cancer was impacted and various local solutions were developed. These included less complicated breast surgery, increased use of neoadjuvant therapy, and changes to radiotherapy regimens. Surgery was frequently delayed and breast reconstruction was often unavailable. These results have implications for breast cancer services during the pandemic recovery as a 'catch-up' increase in cancer diagnoses is expected. Women may wish to access breast reconstruction, unavailable due to COVID-19. The impact of changes to treatment on long-term quality of life should be evaluated.



## INTRODUCTION

COVID-19 has had a huge impact worldwide. The first COVID-19 infection was reported in Wuhan, China in December 2019[1], and the World Health Organization (WHO) declared a pandemic in March 2020.[2] By mid-2022, over 536 million confirmed cases and more than 6.3 million deaths were reported globally.[3] This has had a huge impact on the management of resources towards the care of COVID-19 patients. In addition to this, government enactments of stay-at-home orders had a direct effect on the care of chronic disease and cancer patients.

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Before the pandemic, nearly two and a half million women around the world were diagnosed with breast cancer each year.[4] The pandemic has potentially had an effect on breast cancer diagnosis and treatment for these millions of women due to changes in health-seeking behavior and reduced availability of screening and treatment services.[5] Understanding the changes that occurred due to the pandemic is essential as women may be at risk of poor cancer outcomes due to suboptimal treatment.[6] Reviewing the experience in cancer treatment centers may also assist in planning for future variants, pandemics or other major disruptions to health care.

This study has systematically reviewed the published literature and explored changes to breast cancer treatments (surgery, radiotherapy, chemotherapy and endocrine therapy) during the COVID-19 pandemic by comparing 'pandemic' treatment to 'pre-pandemic' or 'ideal' treatment.

This review was registered on PROSPERO (Study ID CRD42021279655)[7] and it was performed using PRISMA methodology.[8]

## METHODS

*Eligibility criteria*

Studies were eligible if they reported the management of breast cancer during the early phase of the COVID-19 pandemic (January 2020–June 2021) and used a paired design, which included a comparison group (either a non-COVID time period or an individual patient comparison to 'usual' or 'ideal' treatment that would have been delivered during a non-COVID period). Studies reporting surgery, chemotherapy, radiotherapy and/or primary endocrine therapy were eligible. A change to treatment was defined as a delay, replacement of one treatment with another, change in the sequencing of treatment modalities or omission of one or more standard treatment options.

Additional eligibility criteria were: original studies, published in full in English in the peer-reviewed literature. Exclusion criteria were abstract-only publications, letters, review articles and studies reporting treatment during the pandemic that did not include a comparison group.

A search of EBSCO (including CINAHL, MEDLINE and Psych INFO), PubMed and Cochrane Library was performed using the search terms:

("Breast Cancer" OR "Breast neoplasm") AND (Surgery OR Chemotherapy OR Radiotherapy OR Treatment OR Management) AND (Pandemic OR COVID OR "COVID-19" OR coronavirus OR "SARS COV-2")

*Selection process*

Following removal of duplicates, titles and abstracts were screened for eligibility by both authors. Full-text papers were retrieved and re-screened by both authors.

Data were extracted by one author (MSB) and checked by the other (MEB). Data were collected on study characteristics (study setting, design, population, comparison group, number of participants), COVID setting (country, associated COVID protocols/ health order, COVID prevalence in study group) and cancer treatment outcomes (presentation, change or delay to treatment types). Data were extracted into a spreadsheet. Data were analyzed by grouping studies according to outcomes of interest and treatment type and comparing the results. Results were presented in narrative form.

*Risk of bias assessment*

The Newcastle-Ottawa Quality Assessment Form for Cohort Studies was used to assess the risk of bias. It measures the quality of nonrandomized studies based on three criteria: selection of the study groups; comparability of the groups; and the ascertainment of either the exposure or outcome of interest. It produces a score for each criterion with a total maximum score of 7.[9] Risk of bias was independently assessed by each author and consensus was reached after discussing discordant results.

## RESULTS

The initial search identified 485 abstracts. After screening, 15 full-text studies met our eligibility criteria[10-24] (Figure 1: PRISMA flowchart). These studies reported outcomes for 6,353 people treated for early breast cancer from January 2020 to June 2021.

*Study characteristics*

Study characteristics are shown in Table 1. There were eight studies from Europe,[10,12-14,19,21,23,24] five from North America,[11,15-17,22] and two from Asia.[18,20] Eleven studies compared treatment during the COVID period to a similar non-COVID period.[10,11,13-15,17,19-21,23,24] There were four,[12,16,18,21] prospective and 11 retrospective studies.[10,11,13-15,17,19,20,22-24] Four compared the actual treatment of individual patients during the COVID to the 'usual' or 'ideal' treatment that would usually have been delivered in a non-COVID period.[12,16,18,22]

For treatment modalities, 14 studies included data for surgery[10-16,18-24], ten for neoadjuvant chemotherapy,[10,12-16,18,21,23,24] four for adjuvant chemotherapy,[12,18,22,24] nine for neoadjuvant endocrine therapy,[10,12,13,15,16,18,21,22,24] seven for adjuvant radiation therapy,[10,12,15,17,18,22,24] and four studies included data on a 'no treatment' group.[12,13,16,18]

The studies were all conducted in settings that were negatively affected by the COVID-19 pandemic. Specifically, 10 studies were under lockdown

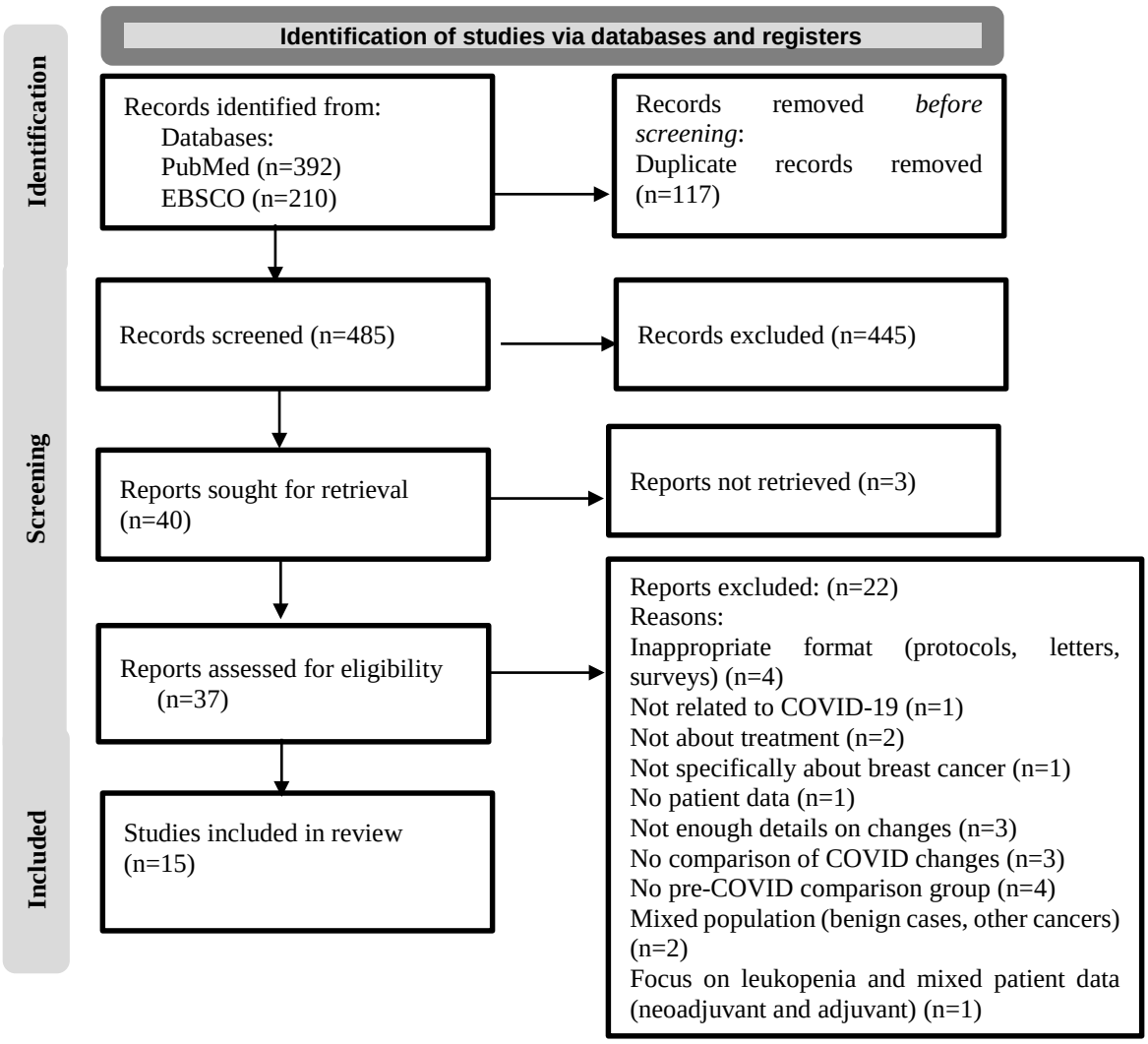


**Figure 1.** PRISMA Flowchart

conditions, which included stay-at-home orders.[10,12,14,16-18,21-24] Five studies were conducted at times when services were affected by challenges to the hospital or health system due to COVID-19 infection in the community.[11,13,15,19,20]

*Risk of bias*

Assessment using the Newcastle-Ottawa Quality Assessment Form for Cohort Studies[9] indicated a very low risk of bias across the studies (Table 1). Thirteen studies received the maximum scores of 4, 2, and 1 for the three individual components (total score of 7, indicating low risk of bias).[10-19,22-24] Two studies received scores of 4, 1 and 1 (total score of 6).[20,21] Both studies scoring 6 lost a point under the Outcome/Exposure domain due to not reporting follow-up data on the cohort. This was not considered to be a significant bias for this review, which is focused on initial treatment of breast cancer rather than longer-term outcomes.

*Number of Breast Cancer Cases during COVID-19 Period*

Table 2 shows the characteristics of cancer presentations. Six studies reported a significant decrease in the number of cases treated during COVID-19 period.[10,13,15,17,20,23] The difference ranged from a 19–33% decrease in cases compared to non-COVID-19 period.[13,15] Three studies reported an increase in the number of cases: one reported a non-significant increase,[11] and two others reported a 7% and 18% increase.[19,24] One of these studies attributed the increase to receiving cancer patients from designated COVID hospitals in the region,[19] while the other study attributed the increase to the exclusion of non-oncological breast surgery cases (mostly breast reconstruction), which were more common in the pre-COVID control group.[24] The remaining 5 studies did not report on the difference in the number of cases during COVID-19 period.[12,16,18,21,22]

**Table 1.** Studies reporting changes to breast cancer treatment during the early phase wave of the COVID-19 pandemic, compared to pre-pandemic or 'ideal/usual' management (grouped by study methodology and ordered alphabetically)

| First Author (Journal, year) | Country | Dates of study (Duration) | Study setting | Study design | Study population | Number in study, COVID period (number in comparison period) (control) | Treatments examined | | | | | | | Risk of bias score** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Surgery | Chemo (Neoadj) | Chemo (Adj) | Endocrine (Neoadj) | Endocrine (Adjuvant) | Radiation (Adjuvant) | No treatment | Selection/ Comparability/ Outcome (Total score) |
| Studies comparing a COVID-period cohort to a pre-COVID cohort | | | | | | | | | | | | | | |
| Acea-Nebril (Breast J, 2020) | Spain | Mar-May 2020 (10 weeks) | Single centre (Specialist breast unit, COVID-free hospital) | Cohort (retrospective) | All patients diagnosed and treated | 93 (131) | x | x | | x | | | | 4/2/1 (7) |
| Cadili (BCRT, 2020) | Canada | Mar-Apr 2020 (6 weeks) | Specialist breast cancer centre | Cohort (retrospective) | All breast surgery patients | 162 (66) | x | | | | | | | 4/2/1 (7) |
| Eijkelboom (J Hematol Oncol, 2021) ( | Netherlands | Jan-Apr 2020 (16 weeks) | National cancer registry | Cohort (retrospective) | All new early bc diagnoses | 4769 (5761) | x | x | | x | | | x | 4/2/1 (7) |
| Fancellu (Multidisciplinary Digital Publishing Institute, 2020) | Italy(Sassari) | Mar-Apr 2020 (9 weeks) | Single centre (General Surgery unit) | Cohort (retrospective) | All breast surgery patients | 42(41) | x | x | | | | | | 4/2/1 (7) |
| Hawrot (JCO Onc Pract, 2021) | USA (PA) | Jan-May 2020 (19 weeks) | Multicentre (6 breast units) | Cohort (retrospective) | All new early bc diagnoses | 164 (202) | x | x | | x | | x | | 4/2/1 (7) |
| Koch (Adv Rad Onc, 2020) | Canada | Mar-Apr 2020 (9 weeks) | Single centre (Specialist | Cohort (retrospective) | All new breast radiotherapy starts | 118 (160) | | | | | | x | | 4/2/1 (7) |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | breast unit) | | | | | | | | | | | |
| Montagna (EJSO, 2020) | Italy (Milan) | Mar-Apr 2020 (9 weeks) | Single centre (Specialist breast unit) | Cohort (retrospective) | All patients diagnosed and treated | 562 (526) | x | | | | | | | 4/2/1 (7) |
| Ngaserin (Breast J, 2020) | Singapore | Jan-Apr 2020 (17 weeks) | Single centre (Specialist breast unit) | Cohort (retrospective) | All new early bc diagnoses | 41 (56) | x | | | | | | | 4/1/1 (6) |
| Romics (The Breast, 2020) | Scotland | Mar-May 2020 (8 weeks) | Multicentre (3 NHS health boards) | Cohort (prospective) | All breast surgery patients | 179 (1415) | x | x | | x | | | | 4/1/1 (6) |
| Vanni (2020)* (Anticancer Research, 2020) | Italy (Rome) | Mar-May 2020 (11 weeks) | Multicentre (4 breast units) | Cohort (retrospective) | All breast surgery patients | 203 (172) | x | x | x | x | | | | 4/2/1 (7) |
| Vanni (2021)* (Anticancer Research, 2021) | Italy (Rome) | Feb 2020-Feb 2021 (52 weeks) | Single centre (Specialist breast unit) | Cohort (retrospective) | All new early bc diagnoses | 182 (263) | x | x | | | x | | | 4/2/1 (7) |
| Studies comparing treatment during the COVID-period to 'ideal/usual' pre-COVID treatment | | | | | | | | | | | | | | |
| Dave (BJC, 2021) | United Kingdom | Mar-May 2020 (2 months) | Multicentre/National (64 breast units) | Cohort (prospective) | All new cancer cases in MDT | 3776 | x | x | x | x | x | x | | 4/2/1 (7) |
| Kennard (Ann Surg Onc, 2021) | USA (PA) | Mar-Jun 2020 (15 weeks) | Multicentre (4 breast units) | Cohort (prospective) | All new early bc diagnoses | 73 | x | x | | x | | x | | 4/2/1 (7) |
| Lee (Frontiers in Surgery, 2020) | South Korea | Feb-Apr 2020 (9 weeks) | Single centre (Specialist breast unit) | Cohort (prospective) | All breast surgery patients | 62 | x | x | x | x | x | x | | 4/2/1 (7) |
| Satish (JCO Onc Pract, 2021) | USA (NY) | Feb-Apr 2020 (13 weeks) | Single centre (Specialist breast unit) | Cohort (retrospective) | All medical oncology patients for chemo/infusion therapy | 350 | x | | x | x | x | | | 4/2/1 (7) |

*likely overlap in patient populations in the two Vanni studies;

**Quality/risk of bias score Newcastle-Ottawa Quality Assessment for Cohort Studies

nr=not reported; na=not applicable; BCS=breast conservation surgery; BR=breast reconstruction; ET=endocrine therapy; WLE=wide local excision; SLNB=sentinel lymph node biopsy; ALND=axillary lymph node dissection; *likely overlap in patient populations in the two Vanni studies

*Patient and tumour characteristics*

Most studies reported no difference in the age of the cohort during the COVID period (Table 2).[10,11,14,15,20,23,24] Two studies reported a younger COVID cohort compared to non-COVID cohort and.[12,17] Two studies reported that older patients are more likely to delay surgery or have a change to their treatment.[18,22]

Six studies reported a higher proportion of invasive cancers (compared to DCIS cases) and a higher proportion of more advanced tumour stage in the COVID cohort.[15,19-21,23,24] Three studies reported that the group with higher tumour stage were less likely to experience delays of changes to their treatment.[16,18,22] Two studies reported no difference in tumour characteristics between the COVID and control group.[13,14]

*Changes to treatment modalities*

*Surgery*

Changes to surgical treatment are shown in Table 3. Several aspects of surgical treatment were changed during the COVID-19 period. For surgical procedure, six studies reported no difference to the type of breast surgery during the COVID-19 period.[10,11,13,16,20,24] This included comparisons between breast conserving surgery (BCS), mastectomy, breast reconstruction (BR). Three studies reported an increase in cases and proportion of surgical cases undergoing BCS.[18,21,23] The same studies also reported a decrease in mastectomy with BR. One study reported a decrease in the proportion of BCS and BR with an increase in simple mastectomy (without reconstruction).[14] One study reported a decrease in prophylactic surgery and increase in nipple-sparing mastectomy.[19]

Some of the studies also reported data on axillary surgery during the COVID-19 period. These include data on axillary lymph node dissection (ALND) and sentinel lymph node biopsy (SLNB). Four studies reported an increase in ALND proportion, along with a decrease in SLNB. Three studies reported no differences in the proportion or number of ALND and SLNB procedures.

Most of the studies reported whether changes to waiting time for surgery/treatment occurred. Five studies reported no difference in the wait time during the COVID-19 period.[10,11,14,15,20] Six studies reported an increased wait time during the COVID-19 period.[12,13,16,18,21,22,24] The additional wait time for surgery (delay) ranged from 8 to 47 days. No study reported a shorter wait time for treatment during the COVID-19 period. One study grouped surgical delay into cases that were directly related to service issues, where delay was unavoidable, and cases where patients elected to delay their surgery to avoid exposure to the virus and/or additional stress on the system.[18] It is unclear in the remaining studies how much of the reported delay may have been due to 'system' issues versus patient choice.

Five studies reported a shorter hospital stay after surgery.[10,11,14,19,24] Some studies showed an increase in proportion of same day discharges,[11,19] others show a 0.7 to 1-day decrease in hospital stay during the COVID-19 period.[10,14] One study reported no difference in hospital stay duration.[24]

Some of the studies also noted additional data relating to changes in surgery during the COVID-19 period. One study reported an increase in regional anaesthesia (relative to general anaesthesia), and another study reported a decrease in the use of regional anaesthesia. One study reported an increase in telehealth usage for surgical follow-up during the COVID-19 period. Two studies reported no difference in re-operation rate, readmission and surgical complications.

*Chemotherapy*

Three studies reported no change in the use of neo-adjuvant chemotherapy (NACT) during the COVID-19 period. Three studies reported a decrease in the use of NACT; one specified the decrease was in Stage I and II patients. Another study noted the substitution of NACT with endocrine therapy instead. Two studies reported an increase in the use of NACT during the COVID-19 period.

Three studies reported using primary systemic therapy (PST, data for NACT and NAET reported together). One had an increase in its use,[22] and two others reported no changes.[10,16]

Three studies reported a decrease in or omission of adjuvant chemotherapy (CT), while one reported no significant difference in CT cases during the COVID-19 period.

*Radiotherapy*

Six studies reported data for radiotherapy.[12,15,17,18,22,23] In one study, fewer women commenced treatment in the study period,[17] and in another there was an increase (in a study that had more BCS cases during the pandemic).[23] Another study reported changes to treatment regimens, with an increase in recommendations for omission or hypofractionation (15 fractions reduced to five).[12]

*Endocrine therapy*

Studies reported increased use of neoadjuvant endocrine therapy. Four studies reported increased use of neoadjuvant endocrine therapy (NAET)[12,13,15,16]. These include a general increase in the use of NAET to postpone non-urgent surgery and as a replacement for neo-adjuvant chemotherapy. One study reported no significant difference in the use of NAET during the COVID-19 period,[23] and the remaining studies did not report outcomes for NAET.

**Table 2.** Characteristics of breast cancer cases during the COVID-19 pandemic, compared to pre-pandemic or 'ideal/usual' management (ordered alphabetically)

| First Author | New cancer cases (n) overall | | Age (mean or median) | | Tumour characteristics | | |
|---|---|---|---|---|---|---|---|
| | COVID period (comparison period), p-value | Interpretation (COVID compared to comparison) | COVID period (comparison period), p-value | Interpretation (COVID compared to comparison) | Characteristics reported | Significance | Interpretation (COVID compared to comparison) |
| Acea-Nebril | 93 (131), p nr | Decrease (29% fewer cases in covid period) | 58(57), p=0.48 | No difference | nr | nr | nr |
| Cadili | 162 (99), p=0.53 | Increase (not significant) | 57(60), p=0.24 | No difference | nr | nr | nr |
| Dave | nr | nr | 60(56), p<0.01 | Younger cohort during COVID (signficant) | nr | nr | nr |
| Eijkelboom | 4769 (5761), p nr | Decrease 33.5% (weeks 9-17) | nr | nr | Proportion DCIS, IDC , ILC at presentation | p>0.05 | no significant difference |
| Fancellu | 42(41), p nr | No difference | 62(61), p=0.62 | No difference | Proportion DCIS, IDC , ILC at presentation | p values all >0.05 | no significant difference |
| Hawrot | 164(202), p nr | Decrease 19% | mean nr; p=0.62 | No difference | Proportion of DCIS vs invasive; and IDC, ILC, mixed invasive | p=0.062 | More invasive tumours treated during COVID (significant); no significant difference in histology features for invasive cancer |
| Kennard | nr | nr | nr | nr | Proportion of DCIS, triple neg or HER2 pos cases experiencing change in treatment | p<0.001 | HER2 pos and triple neg on core less likely to have change to treatment (significant) |
| Koch | 118 (160), p<0.01 | Decrease 26% (significant) | mean nr; p<0.01 | Younger cohort during COVID (signficant) | nr | nr | nr |
| Lee | nr | nr | 58(55), p<0.01 | Older patients more likely to delay surgery | Proportion of DCIS vs invasive; and IDC, ILC, mucinous; multifocality; and | p=0.78 for histological type, multifocality p=0.02, clinical n stage p=0.049; | no sig difference in invasion, histological type, significant diff multifocal and clinical node positive= less likely to delay |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | TNM stage experiencing delay | path tumour and n stage not significant | |
| Montagna | 562(526), p nr | Increase 7% (patients came from other hospitals) | nr | nr | Proportion of DCIS vs invasive at presentation | p=0.05 | More invasive tumours treated during COVID (significant) |
| Ngaserin | 41(56), p=0.49 | Decrease 27% (not significant) | mean nr; p=0.36 | No difference | Proportion of histo grade, TNM stage at presentation | Grade p=0.84, T stage p=0.03 | Higher T stage (tumour size) in covid group (significant); tumour features otherwise no different |
| Romics | 179(nr) | nr | 54 | nr | Proportion of histo grade, TNM stage; ER;HER2 status at presentation | Grade p=0.11, T stage p<0.01; ER p<0.01; HER3 p<0.01; node status p=0.80 | Higher T stage (tumour size) in covid group; more ER neg; grade and HER2 not sig different |
| Satish | nr | nr | 58(56), p<0.01 | Older patients more likely to have delay or change | Proportion of stage, receptor status experiencing delay | Stage OR, 0.38; Receptor p=0.50 | Stage II or III (OR, 0.38) less likely to have a delay; receptor status no difference |
| Vanni (2020)* | 203(172), p nr | Increase 18% | 62(61), p=0.20 | No difference | Proportion of SLNB positivity, TNM stage, Grade, lesion diameter, histo type at presentation | SN positivity p=0.04; N stage p=0.03, Grading p=0.03 | Higher SN positivity, N stage and grade in COVID group; no difference in histologial type, ER/PR or HER2 status |
| Vanni (2021)* | 182(263), p nr | Decrease 30% | 63(61), p=0.21 | No difference | Proportion of SLNB positivity, TNM stage, Grade, lesion diameter, histo type at presentation | SLNB positive p=0.04; p=0.01 for N stage, Grade p=0.07, diameter p<0.01, pathology (ductal,lobular) p=0.74 | Higher N stage, larger tumour sizes in COVID group |

*likely overlap in patient populations in the two Vanni studies
nr=not reported; DCIS=ductal carcinoma in situ; IDC=invasive ductal carcinoma; ILC=invasive lobular carcinoma; SLNB=sentinel lymph node biopsy

## DISCUSSION

This systematic review evaluated the impact of COVID-19 on breast cancer treatment. Fifteen studies with a paired design were identified and these were all of high quality (low risk of bias) despite the challenges of conducting research during the pandemic.

The extent of the impact of the pandemic varied across studies. Most studies reported stable numbers or fewer cases of breast cancer presenting for treatment during the pandemic. A decrease is unsurprising given the lockdowns and restrictions in access to health care, including screening and diagnostic services. However, many studies reported an increase in the proportion of later stage cancers, suggesting that the 'missing' cancers (predicted but not diagnosed) are likely to be early cancers that would have been detected by screening during this period. One hypothesis could be that mortality from breast cancer will not be impacted by the pandemic if these early-stage cancers are identified in the early months of COVID recovery (while delayed but still early-stage). The increase in case numbers was seen in one study appeared to be due to restructuring of local health services for dedicated COVID-19 treatment hospitals rather than a true increase in case numbers in the health jurisdiction.[19] Therefore, the numbers in individual hospitals may not always reflect the total number of cases in a health district or state/province and population-level data is required to examine the true incidence of breast cancer during 2020 and 2021.

There was a general trend towards increased wait time for treatment or increased delays during the COVID-19 pandemic.[12,13,16,18,21,22,24] There was also a trend towards reduced hospital stay duration and increased number of same-day discharges.[10,11,14,19] This is likely to represent an aim to minimise the amount of time that patients were in hospital to reduce the risk of cancer patients contracting COVID-19 and to minimise the burden of non-COVID cases in the hospital. Services demonstrated an ability to adapt to the local conditions by performing more breast conservation surgery or using more neoadjuvant chemotherapy and endocrine therapy in response to the challenges of admitting patients to hospital for surgery. In some studies, delay to surgical treatment was intentional and even chosen by patients in consultation with their doctors. In one study, women who were older, with ER-positive early-stage breast cancer were more likely to take up the option of delayed surgery combined with neoadjuvant endocrine therapy.[12]

Most of the studies reviewed in this paper reported on surgical therapy. Other treatment modalities were less frequently reported. While most studies reported no change in the type of surgical procedure performed, some reported an increase in breast conserving surgery (including a study that reported an increase in oncoplastic procedures).[21] The explanation for this is unclear. It may reflect an attempt to conserve the breast in women who may have otherwise undergone mastectomy, to minimise hospital stay and avoid breast reconstruction surgery, which was suspended by many centres during the pandemic. The increase in the proportion of breast conservation procedures may also be related to the fact that neoadjuvant chemotherapy or neoadjuvant chemotherapy was used to delay surgery in some cases, resulting in tumour shrinkage. However, the increase in breast conservation could be expected to result in an increasing proportion of women requiring breast radiotherapy. Only six studies discussed the impact of COVID on breast radiotherapy and these generally indicated a trend towards hypofractionation and partial breast irradiation protocols rather than an increase in radiotherapy case numbers overall. An increase in axillary lymph node dissection with a decrease in sentinel lymph node biopsy was observed in some studies.[10,21,23,24] This may imply more advanced stage of cancer in surgical patients, and it is difficult to reconcile with the increase in breast conservation.

It was rare for centres to continue performing breast reconstruction during the pandemic.[19] While some patients with more extensive in-breast disease may have been treated with extended oncoplastic conservation procedures,[20] others may have been forced to accept simple mastectomy without reconstruction.[16,18,24] This is consistent with other cohort studies during the pandemic that indicated breast reconstruction was unavailable in many places.[10,12,14,18,25] Lack of access to immediate breast reconstruction may be one of the long-term negative quality-of-life impacts of cancer during the pandemic. Long-term follow-up of these cases is needed to investigate the number of women who access delayed reconstruction procedures and the impact of waiting for reconstruction or not having the option at all.

This study has some limitations. The included studies are heterogenous in the method they used to report changes in treatment due to COVID-19, so pooling the results was not possible. Publication bias was not assessed, and this may have had an impact on the studies that were available for inclusion.

## CONCLUSION

The 15 studies included in this review demonstrated a significant impact of COVID-19 on breast cancer treatment. The changes to treatment were not consistent across the studies. This reflects

**Table 3a.** Changes in surgical management of breast cancer during the COVID-19 pandemic compared to pre-pandemic or 'ideal/usual' management (changes to breast and axillary surgery)

| First Author | Comparison group | Number of surgical cases in COVID period (vs pre-covid period) | Significance (p-value) | Change to type of BREAST surgery | Significance (p-value) | Further information | Change to type of AXILLARY surgery | Significance (p-value) |
|---|---|---|---|---|---|---|---|---|
| Studies comparing a COVID-period cohort to a pre-COVID cohort | | | | | | | | |
| Acea-Nebril | Patients from same dates in 2019 | Decrease in number but not proportion of cases having up-front surgery during COVID (72 vs 102) | nr | No difference in proportion undergoing BCS, oncoplastic procedure, mastectomy, immed BR; delayed BR | p=0.73 | na | Increase in ALND overall and proportion going straight to ALND rather than SNB first during COVID period | p=0.05 |
| Cadili | Patients from same dates in 2019 | Increase (non-sig) in numbers in up-front surgery during covid (162 vs 99) | p=0.53 | No difference in proportion undergoing BCS, mastectomy, BR | p=0.18 to 0.34 | na | No difference in proportion undergoing SLNB, ALND or no axillary surgery | nr |
| Eijkelboom | Patients from same dates in 2018-19 | Decrease in numbers of surgery patients in COVID (1778 vs 2542, calculated from data) | nr | No difference in proportion undergoing mastectomy or IBR; Decrease in stage I cases undergoing BCS in last month of study (55 vs 70%) | p< 0.05 (for last month BCS stage I) p> 0.05 all others | Reduction in proportion of BCS in one time period; no corresponding increase in mastectomy but increase in chemo and ET noted. | nr | nr |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Fancellu | Patients from same dates in 2019 | No difference (42 vs 41) | nr | Reduction in BCS (n=32 v, 29) Increase in simple mastectomy (9 vs 1), stopped BR during covid (0 vs 12) | p<0.001 for BCS/m/m+ibr overall | Proportion and number of BCS cases decreased | No difference in proportion undergoing SLNB (78 vs 76%) | p=0.84 |
| Hawrot | Patients from same dates in 2018 | nr | nr | nr | nr | nr | nr | nr |
| Koch | Patients from same dates in 2019 | nr | nr | nr | nr | nr | nr | nr |
| Montagna | Patients from same dates in 2019 | nr | nr | Decrease in prophylactic surgery; increase in nipple sparing mastectomy + BR with implant (152 vs 130) | p<0.01 for prophylactic mx; no p value for NSM/IBR | less patients underwent prophylactic breast surgery, more patients underwent nipple-sparing mastectomy + BR with implant during COVID | nr | nr |
| Ngaserin | Patients from same dates in 2019 | Decrease in number (23 vs 44) and proportion (56 vs 79%) patients undergoing upfront surgery; correlates with more having NACT | p=0.04 | No difference in proportion undergoing BCS, simple mastectomy, nipple sparing mastectomy, BR | p=0.244 for all treatment except reconstruction; p=0.350 for recon | Non sig trend to less simple mastectomy (45 vs 58%); more nipple sparing mastectomy (15 vs 9%) more BCS (25 vs 23%) | nr | nr |

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|---|---|---|---|---|---|---|---|---|
| Romics | Registry data Jan-Dec 2015 same region | nr | nr | Increase in proportion undergoing oncoplastic procedures (14 vs 4%), and simple mastectomy (38 vs 27%); decrease in WLE (48 vs 61%) and IBR (0 vs 8%) | p<0.01 | Higher oncoplastic and BCS rate to avoid mastectomy because IBR not available during COVID | Borderline increase in ALND and reduction in SLNB and axillary sampling | p=0.05 |
| Vanni (2020)* | Patients from same dates in 2019 | Increase (18%) in cases during COVID period (203 vs 172) | nr | No differnce in propotion of BCS vs mastectomy | mastectomy p=0.36, BCS p=0.65 | Non sig trend to more mastectomy (31 vs 26%) | Increase in ALND (29% vs 20%) and decrease in SLNB (86% vs 88%) during COVID period | SLNB p=0.04 ALND p=0.04 |
| Vanni (2021)* | Patients from same dates in 2019 | Decrease (30%) in procedures during COVID period (182 vs 263) | nr | Increase in proportion of BCS cases (64 vs 58%); decrease in mastectomy rate (20 vs 30%); BR not reported | p=0.002 | More conservative surgery in COVID period; BR nr | Increase in ALND (27% vs 21%) and no change in SLNB (81% vs 85%) during COVID period | SLNB p=0.24 ALND p=0.04 |
| Studies comparing treatment during the COVID-period to 'ideal/usual' pre-COVID treatment | | | | | | | | |
| Dave | Compared 'standard' vs 'COVID-altered' management in study group | nr | nr | Proportion with a change to usual (pre-COVID) care: | nr | Bridging ET group 82% postmen; 96% strongly ER pos; 85% | Changes to treatment: 13/3776 positive SNB would normally | nr |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Bridging ET 25%; not offered IBR 8%; simple Mx when BCS was possible 1% | | preop node neg | have had ALND but didn't; 122/3776 standard lympho omitted, blue dye only | |
| Kennard | Compared 'standard' vs 'COVID-altered' management in study group | nr | nr | No difference in BCS, unilateral simple mastectomy, bilateral mastectomy, BR | p=0.427 | Non sig trend to more BCS and unilat simple mastectomy; less bilateral mx and less reconstruction | nr | nr |
| Lee | Patients grouped into 'delayed due to COVID' and 'non-delayed' groups (patient choice to delay) | nr | nr | Increase in proportion of BCS cases (81 vs 65%) and less mastectomy (19 vs 34%); and less BR (7 vs 25%) in those electing to delay surgery | p=0.04 for BCS vs mastectomy, p =0.10 for BR yes/no | Patients with more 'serious' cancers requiring mastectomy less likely to delay treatment | No difference in rates of SLNB, ALND or no surgery in delay vs no delay groups | p=0.19 |
| Satish | Compared 'standard' vs 'COVID-altered' management in study group | nr | nr | nr | nr | nr | nr | nr |

**Table 3b.** Changes in surgical management of breast cancer during the COVID-19 pandemic compared to pre-pandemic or 'ideal/usual' management (changes to waiting time, length of stay and anaesthetic)

| First Author | Comparison group | Delay in surgery or waiting time to treatment (median) | Significance (p-value) | Length of hospital stay (median) | Significance (p-value) | Type of anaesthetic | Significance (p-value) | Other surgical outcomes | Significance (p-value) |
|---|---|---|---|---|---|---|---|---|---|
| Studies comparing a COVID-period cohort to a pre-COVID cohort | | | | | | | | | |
| Acea-Nebril | Patients from same dates in 2019 | No difference in delay from surgery to chemo/radio/adjuvant therapy/ET (45-60 vs 28-60 days) | p=0.34 to 0.72 | Shorter hospital stay during COVID period (0.6 vs 1.3 days) | p<0.001 | nr | nr | No difference in re-operation rate for margins, ALND, mastectomy<br>No difference in complications, readmissions, wait for adjuvant radiotherapy or chemotherapy | p=0.617 (complication)<br>p=0.363 (readmission) |
| Cadili | Patients from same dates in 2019 | No significant difference in waiting times core biopsy to surgery (with consult in between)<br>45 (40) days | p=0.18 | Shorter hospital stay during COVID period (same day discharge 93% vs 68%) | p<0.01 | Increase in regional anaesthesia during COVID period (57% vs 3%) | p<0.01 | nr | nr |
| Eijkelboom | Patients from same dates in 2018-19 | Increase in median time to treatment (22-29 days vs 17 days) | p<0.01 | nr | nr | nr | nr | nr | nr |
| Fancellu | Patients from same dates in 2019 | No difference in wait for surgery (49 vs 46 days) | p=0.38 | Shorter hospital stay during COVID period 2 vs 3 days) | p<0.01 | Decrease in regional anaesthesia during COVID period (2% vs 91%) | p<0.01 | No difference in waiting time for post op consultation, or wait for adjuvant radiotherapy or | p=0.58 to 0.77 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | chemotherapy consultation | |
| Hawrot | Patients from same dates in 2018 | No difference in time to treatment (44 vs 44 days) | p=0.93 | nr | nr | nr | nr | nr | nr |
| Koch | Patients from same dates in 2019 | nr | nr | nr | nr | nr | nr | nr | nr |
| Montagna | Patients from same dates in 2019 | nr | nr | Shorter hospital stay in COVID period (same day discharge 47% vs 53%) | nr | nr | nr | Increase in teleheath, reduction of in-person consultations during COVID period. (Telehealth 63% vs 7%) | nr |
| Ngaserin | Patients from same dates in 2019 | No difference in wait for surgery (49 vs 46 days) | p=0.91 | nr | nr | nr | nr | nr | nr |
| Romics | Registry data Jan-Dec 2015 same region | Surgery delayed in 3.3% (2.8% due to lockdown; 0.5% due to covid infection, no comparison) | nr | Same day discharge 90% (no comparison given) | | nr | nr | Complication rate in COVID period 7.8% (no comparison) | nr |
| Vanni (2020)* | Patients from same dates in 2019 | Longer wait for treatment in COVID period (56 vs 42 days) | p<0.05 | No difference in hospital stay | p=0.436 | nr | nr | No difference in re-operation rate | p=0.51 |
| Vanni (2021)* | Patients from same dates in 2019 | nr | nr | nr | nr | nr | nr | No difference in rate of up-front surgery (16 vs 12%) | p=0.27 |
| Studies comparing treatment during the COVID-period to 'ideal/usual' pre-COVID treatment | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|
| Dave | Compared 'standard' vs 'COVID-altered' management in study group | Median wait 24 days to surgery during COVID (no comparison) | nr | nr | nr | nr | nr | nr | nr |
| Kennard | Compared 'standard' vs 'COVID-altered' management in study group | COVID-altered treatment median wait 53 days to surgery; standard treatment 24 days | p< 0.001 | nr | nr | nr | nr | nr | nr |
| Lee | Patients grouped into 'delayed due to COVID' and 'non-delayed' groups (patient choice to delay) | Median delay to surgery 16 days (no comparison) | nr | nr | nr | nr | nr | nr | nr |
| Satish | Compared 'standard' vs 'COVID-altered' management in study group | 47 days delay in COVID group (no comparison) | nr | nr | nr | nr | nr | nr | nr |

*likely overlap in patient populations in the two Vanni studies
bc=breast cancer; nr=not reported; na=not applicable; BCS=breast conservation surgery; BR=breast reconstruction; ET=endocrine therapy; WLE=wide local excision; SLNB=sentinel lymph node biopsy; ALND=axillary lymph node dissection

the individual solutions that cancer centres found, and these were determined by their local circumstances. Delaying surgery by using more neoadjuvant therapy was seen in six of the 15 studies.[12,15,18,20,21,23] A preference for simpler surgical procedures (breast conservation or simple mastectomy) was seen and most centres were unable to provide immediate breast reconstruction. A higher proportion of later-stage cancers was seen, suggesting that more serious cancers presented for treatment and that early screen-detected cancers were not identified during this period. Ongoing observation of the cohort of women treated during the pandemic, and correlation with population-level incidence and survival data is essential to fully understand the long-term impact of COVID-19 on breast cancer. Lack of access to breast reconstruction may have a lasting negative effect on quality of life and this should also be explored with follow-up studies.

**CONFLICT OF INTEREST**

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**DATA AVAILABILITY**

Data sharing not applicable to this study as no datasets were generated or analyzed during this study.

**ETHICAL CONSIDERATIONS**

This article does not contain any studies with human participants performed by any of the authors.

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