



# Timing of Breast Cancer Surgery after Neoadjuvant Chemotherapy in COVID-19 Asymptomatic Patient: Case Report and Review of Literature

Cristina La Tessa<sup>1\*</sup>, Valentina Galluzzo<sup>1</sup>, Andrea Zarabini<sup>2</sup>, Grazia Sorbo<sup>1</sup>, Riccardo Ferrarini<sup>1</sup> and Maria Cristina Cucchi<sup>1</sup>

<sup>1</sup>Division of Breast Surgery, Bellaria Hospital, Italy

<sup>2</sup>Department of Plastic Surgery, Bellaria Hospital, Italy

## Abstract

COVID-19 pandemic overwhelmed our health care system. The need to preserve resources forced us to rethink therapeutic strategies and postpone all not priority surgeries. This situation is particularly critical for cancer patients. Different organizations developed recommendations set to guide the decision making of multidisciplinary team in breast cancer treatment strategy and most of them suggest postponing surgery procedures and shifting care to neoadjuvant chemotherapy and endocrinotherapy. However, this strategy has caused a backlog of breast cancer patients subjected to neoadjuvant chemotherapy and requiring surgery. A novel strategy is required to manage the percentage of these cases that are found COVID-19 infected. In this study, we report the clinical course and management of a young woman who completed cancer neoadjuvant chemotherapy, was then confirmed asymptomatic COVID-19 infection positive and underwent nipple-skin-sparing mastectomy with sentinel node biopsy and reconstruction with tissue expander.

## Introduction

The emergency due to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) associated diseases (COVID-19) has hard testing the global health care system. In order to preserve health care resources to manage potential surplus COVID-19 cases, several jurisdictions have started to reprioritize medical and surgical procedures and delay all non-essential ones [1,2]. This policy is especially challenging for cancer patients for whom the risk of COVID-19 exposure has to be balanced with the disease progression. In these cases, strategies should be developed to minimize treatment interruption, especially for patients treated with curative intent, as it is for most of breast cancer types. One of the keys for finding a successful approach is to identify the cases requiring more urgent care and those that instead can delay the treatment once the pandemic will be contained. Advances in breast cancer diagnosis and cures provide several alternatives to surgery that allow gaining time and postponing the procedures until the end of the emergency. Different organizations develop recommendations set to guide the decision making of multidisciplinary team in breast cancer treatment strategy and most of them suggest postponing surgery procedures and shifting care to neoadjuvant chemotherapy and endocrinotherapy [3-8]. According to these guidelines, breast cancer patients were stratified in priority classification for surgical oncology in three groups (high, medium, low). Patients completing neoadjuvant therapy belong to the medium group and, in these cases; surgery should not be delayed beyond 6 to 8 weeks to avoid a potential negative impact on the overall outcome [3-9]. Surgery procedures must be postponed in patients with symptomatic COVID-19 disease but the strategy for asymptomatic patients positive to nasopharyngeal swab and who have completed neoadjuvant chemotherapy is not clear. In this study we report the clinical course and management of a young woman who completed cancer neoadjuvant chemotherapy, was then confirmed asymptomatic COVID-19 infection positive and underwent nipple-skin-sparing mastectomy with sentinel node biopsy and reconstruction with tissue expander.

## Case Presentation

The patient was a 39-year-old woman with a diagnosis of invasive ductal ER+HER2+ breast cancer cT2N1. She was referred to mammogram, ultrasound, MRI, biopsy and clinical examination. Staging exams were negatives. She was a no-smoker, with a negative personal or family history, BMI: 21.8. She underwent Neoadjuvant Chemotherapy (NAC) with administration of epirubicin-

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### \*Correspondence:

Cristina La Tessa, Division of Breast Surgery, AUSL di Bologna, Bellaria Hospital, Via Altura 3, 40139 Bologna, Italy,

E-mail: [cristina.latessa@ausl.bologna.it](mailto:cristina.latessa@ausl.bologna.it)

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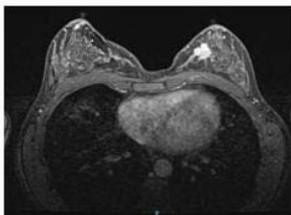


Figure 1: Baseline MRI.

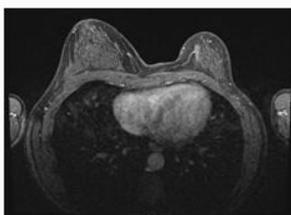


Figure 2: Post-NAC MRI.

cyclophosphamide for 4 cycles followed by paclitaxel-trastuzumab weekly for 12 cycles; she also received monthly administration of LHRH agonist. At the end of the therapy she presented a persistent neutropenia so she received a reduced dose during last two cycles. After NAC, the exams (ultrasound, MRI (Figure 1), clinical examination) show a relevant downstaging passing to a cT1N0 disease but surgery was delayed because of the COVID-19 pandemic spread. When we decided to proceed with preoperative exams, she reported a 1-day history of fever about 20 days earlier without other symptoms. Physical exam and chest X-ray was unremarkable; laboratory results were all in range except for a slight neutropenia. The rapid nucleic acid amplification test on nasopharyngeal swab was positive. Thus she started a 5-day course of oral hydroxyclozoquine (400 mg twice a day on day 1, then 400 mg daily) according to infectious indications, and spent two weeks in quarantine. Then she was tested twice to control swabs, which both resulted negative, so she was certified as cured and cleared for surgery. Preoperative nasopharyngeal swab, performed 24 h before surgery according to our standard protocol, showed a new positivity. She was completely asymptomatic and clinical, laboratory, radiological and physical exams were all negatives. To avoid decreasing NAC effects, we decided to not delay surgery any further. Despite of chemotherapy downstaging the multidisciplinary team decided to proceed with a mastectomy because of the unfavorable breast volume/cancer ratio and the tumor fragmentation shown at MRI (Figure 2). She received a nipple-skin-sparing mastectomy with sentinel node biopsy and reconstruction with tissue expander in a COVID-19 dedicated surgical unit. The sentinel node detection was performed with dual tracers (radioisotope and blue dye combination) according to the standard protocol. The postoperative course was regular. Patient was a febrile and totally asymptomatic; laboratory and clinical exams were in range. She was discharged on day 2 with prophylactic antibiotic therapy and programmed controls and quarantined. The anatomopathologic reports from the specimen showed a multifocal tumour with a partial response to NAC (residual tumour <10% according to Pinder 2007) but a nodal complete response with sign of node downstaging due to therapy (ypT1pN0).

## Discussion

Covid-19 pandemic overwhelmed our health care system and the need to preserve resources forced us to rethink therapeutic strategies

and postpone all not priority surgery [1,2]. The sudden disruption of routine medical procedures was particularly critical for cancer patients for whom outcomes are dramatically dependent on timely and high-quality multidisciplinary actions. These patients are more susceptible to infections because of several factors including frequent hospital visits and immunosuppressive state caused by the malignancy and treatments [10,11]. Moreover, recent data suggested that SARS-Cov-2 had often a worse outcome in these patients. Recommendations for prioritization, treatment, and triage of patients with breast cancer during the COVID-19 pandemic have been recently published [3-7]. Most of the recommendations stratify cancer patients in different levels of priority, suggesting postponing surgery in the majority of cases and employing different type of primary systemic therapy (chemotherapy, anti HER2 therapy, endocrine therapy) as short-term countermeasures until the pandemic ends. However, once the COVID-19 emergency is over (or at least contained), we will have a backlog of breast cancer patients to be treated and we have to plan for now the surge case and an effective strategy to manage all of it. Ideally, patients that underwent neoadjuvant chemotherapy/HER2 therapy should receive surgery not later than 4 to 6 weeks after treatment completion because it was observed that a period of >8 weeks may be associated with adverse effects on DFS and OS. Literature indicate that patients who underwent chemotherapy or surgery in the month before diagnosis with COVID-19 had a numerically higher risk (three out of four) of clinically severe events than those who did not receiving it. However, most of COVID-19 patients had a mild course or were asymptomatic and will not develop the disease [12]. The standard preoperative protocol recommends a rapid nucleic acid amplification testing on nasopharyngeal swab before surgery. We know that around 30% of swabs from clinically symptomatic patients give a false negative [13,14] so, ideally, we miss COVID-19-infected cases that undergo surgery without any complication. The nasopharyngeal swab can remain positive a long time after infection and furthermore recent evidences suggest that a potential false-positive rate could exist among the asymptomatic infected individuals [15]. These findings suggest that a percentage of surgeries that are currently delayed could be instead safely. This approach could be very important especially in cancer surgery as delays can have a major impact on long-term survival and patient morbidity. In addition, we must also consider patient psychological well-being needs and anxiety-provoking by delays of treatment. The patient reported in this study was totally asymptomatic except for 1-day-fever occurred more than a month prior the procedure. She received COVID-19 therapeutic protocol and both the recovery and surgery were performed in a COVID-19 dedicated unit care in order to monitor potential complications and treat them immediately.

## Conclusions

The COVID-19 emergency has caused a backlog of breast cancer patients subjected to neoadjuvant chemotherapy and requiring surgery. As a certain percentage of these cases might be found COVID-19 infected, we must develop a strategy to face this scenario. In our experience, positivity to nasopharyngeal swab in a totally asymptomatic patient is not a mandatory contraindication to surgery. Each case should be discussed within the multidisciplinary team to identify the most beneficial approach for the patient's care. In case the team decides to proceed with surgery, it is mandatory to perform it in a COVID-19 dedicated unit in order to best protect patients and operators. Although we require a large-scale epidemiological investigation to strengthen the validity of the

proposed strategy, we believe that our experience will help other teams to define the direction of care in similar cases.

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