Project Title

Predicting the pathological complete response (pCR) in breast cancer patients who have undergone neoadjuvant chemotherapy

Project Lead and Members

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Organisation(s) Involved

Tan Tock Seng Hospital, Onkolyze Pte Ltd, Radlink

Healthcare Family Group(s) Involved in this Project

Medical, Allied Health

Applicable Specialty or Discipline

General Surgery, Diagnostic Radiology

Project Period

Start date: 01 Jan 2019

Completed date: 30 Jun 2023

Aims

To explore the potential of minimally invasive biopsies as a decision- making tool to decide regarding breast cancer surgery, in patients who have proven pCR on biopsy.

The primary objectives of this study are to:

a) Determine how well a pre-operative biopsy of the original breast tumour site after completion of neoadjuvant chemotherapy predicts for pCR

b) Determine how well contrast enhanced mammogram (CESM) changes pre and post neoadjuvant chemotherapy predict for pCR
c) Evaluate the above together with other pre-operatively available clinicopathological and radiological parameters as predictors of pCR

Background

Up to a third of patients who receive neoadjuvant chemotherapy achieve pCR, which is associated with improved disease- free recurrence and overall survival. This increases to 40-75% with Human Epidermal Growth Factor Receptor (HER)2 positive and triple negative subtypes. This improvement in pCR rate is largely attributed to an increasing number of early breast cancer women who are keen to go through neoadjuvant chemotherapy for breast conservation and increasing use of targeted therapy in patients who are HER2-Positive.There is currently no reliable means of predicting pCR and surgery is always recommended following neoadjuvant chemotherapy to document the pathological response. Pathological complete response is defined as there being no viable tumour in the breast or the ipsilateral axillary nodes at surgery. Some have adopted a less stringent definition, where the presence of ductal carcinoma in situ but not invasive carcinoma is also defined as pCR.

Methods

The experimental design workflow involves:

1. Identification of eligible patients scheduled for neoadjuvant chemotherapy who fit the inclusion criteria
2. CESM (Pre- chemotherapy) Will be performed for the research if it was previously not done as part of their standard clinical workup
3. Insertion of Ultrasound- visible clip, if this had not been previously inserted at the time of the biopsy
4. Neoadjuvant chemotherapy. Regimen will be according to oncologist’s discretion.
5. CESM (Post chemotherapy) to assess tumour response

6. On the day or surgery, patients will undergo vacuum assisted biopsy of the clipped breast tumour under GA, just prior to the planned surgery. This will be performed with a 11 gauge needle, with 8 to 10 cores being taken. Surgery will involve either a wide excision of the breast tumour or a mastectomy, as discussed with patients prior to surgery
7. Histology correlation and analysis:.
   i. Correlation of biopsy specimen and surgical specimen:
   ii. CESM correlation with pCR
   iii. Correlation with the rest of the pre-op parameters
   iv. Development of software model to predict for pCR

Results

Recruitment was much affected by the COVID outbreak and the subsequent lockdowns and re-deployment of manpower.

In total 51 number of patients were recruited and 38 patients completed the study (i.e had surgery done). 13 number of patients did not complete the pre and post CESM assessments were planned; either because of contraindications that arose or because patients did not wish to proceed with the scans.

Pathological complete response (pCR) occurred in 38 patients.

The mammotome biopsy had shown no residual tumour in 20 patients: of these, 13 patients were confirmed to have pCR and 7 patients had residual disease. On the other hand, the mammotome biopsy had shown residual disease in 18 patients: of these 16 patients were confirmed with residual disease and 2 patients had no residual disease seen in the surgical specimen. Mammotome biopsy of the clipped tumour had a PPV of 65%.

All post-CESM assessments showed a decrease in contrast enhancement. There was no clear correlation between the loss of enhancement and pathological response. We felt that this could be because the current subjective manner of assessing contrast enhancement failed to pick up subtle changes. We are exploring this further.

Work on this grant formed the preliminary results of a NMRC IRG grant proposal which was not awarded.

The work on CESM is part of the preliminary results of a currently ongoing NTF funded study to develop an objective means of CESM contrast enhancement measurement.

We will analyse the results further and publish our work. We will also be reviewing the data to determine how CESM and mammotome can be incorporated into our current clinical workflow.

This study demonstrates that post-treatment mammotome can be used in certain patients to predict the pathological response.

Lessons Learnt

The uptake for neoadjuvant treatment is not high. Many patients still prefer to have surgery done first. Since it has to do with patient's perception of the importance of the treatment modalities, there is little that we can do to change this.

Patient recruitment was also affected by the suspension of research activities during COVID. Even outside of the lockdown periods, patients were less keen to participate in what they felt to be 'extra' procedures. New cases were also being diverted away from our unit so there were less potential candidates to recruit.

Conclusion

The project gives an initial insight to the post-treatment methods of assessment of non-surgical evaluation of pathological response. Further work needs to be done in the following areas: 1) correlation of the site of the clip in relation to the residual disease foci, 2) a better means of assessing the degree of contrast enhancement

Project Category

Care & Process Redesign

Quality Improvement, Clinical Practice Improvement

Keywords

Predictive Model, Mammography, Chemotherapy

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