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Original Research Article

Residual cancer burden (RCB) profiling of post neoadjuvant therapy breast cancer resections in a tertiary cancer care hospital

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Abstract

Background: Neoadjuvant therapy (NAT) has become a standard of care for locally advanced breast cancers. It is also considered for tumours which are large (> 2cm). This shift in treatment paradigm has brought major benefits in care for breast cancer patients in terms of long term prognosis. To calculate the response after NAT, MD Anderson has developed a scoring system which has shown a great concordance between RCB class & prognosis. This study aims to categorise breast cancer patients in different RCB groups based on their score. It also aims to correlate each score group with clinicopathological features & to profile RCB scoring amongst different molecular subtypes in Indian scenario.
Materials and Methods: This was a 5 year retrospective study carried out in the department of Surgical Pathology in a tertiary cancer care hospital.
Grossing of resection specimens & microscopic examination were done according to CAP protocol & included residual tumour size, histological grade, lymphovascular space invasion, nodal metastasis with size of metastatic focus, fibrosis, calcification, histiocytes and necrosis.
Results: The highest number of pathological complete response was seen in the Her 2 enriched subtype (46.15%) followed by Luminal B Her2 positive subtype (34.48%), then TNBC subtype (31.08%). LA subtype had the lowest response rate (11.11%).
Conclusions: Different molecular subtypes of Breast carcinoma show different grades of response to NAT. The highest frequency of pathologic complete response (PCR) was seen in the Her 2 neu enriched subtype, followed by the Luminal BH subtype.

Keywords: Molecular subtypes, Residual cancer burden, Neoadjuvant therapy, Breast carcinoma, Pathologic complete response (PCR).

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1. Introduction

NAT (Neoadjuvant Therapy) is now the international standard of care for locally advanced breast carcinomas and is increasingly being given even in early stages with T size > 2cm. The specific drugs in NAT are decided on the molecular subtype of breast carcinoma, which is determined by a core needle biopsy and IHC test. The molecular subtypes are Luminal A, Luminal B, Her2 enriched and Triple negative Breast Carcinomas.[1,2]

Since the advent of NAT it has been mostly used for high risk triple negative breast carcinomas (TNBC) & HER2+neu enriched cancers, however it is now being given to many hormone receptor (HR) positive & HER 2 negative patients.[3,4]

NAT comprises of neoadjuvant chemotherapy (NACT) & targeted therapy for Her 2 positive breast cancers. Neoadjuvant hormonal therapy (NAHT) is also a form of NAT which is indicated in patients who are not eligible for the standard cytotoxic chemotherapy.

NAT can shrink the tumour size, making it more amenable to surgical resection. This approach may facilitate breast-conserving surgery (lumpectomy) instead of mastectomy, which can have significant cosmetic and psychological benefits for the patient. (Tumour downsizing).[1,3,5]

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Advantages of NAT can be summarized as below:

Evaluation of treatment response: NAT provides an opportunity to assess the sensitivity of the tumour to chemotherapy. Pathological examination of the resected tumour specimen after NAT can help determine the extent of tumour response. This information can guide further treatment decisions, such as the need for additional chemotherapy, targeted therapy, or radiation therapy postoperatively.[1,5,6]

Tailored treatment approach: Response to NAT can provide valuable information about the tumour's biology and sensitivity to specific chemotherapeutic agents. This information can help personalize subsequent treatment strategies, such as selecting the most effective adjuvant chemotherapy regimen or incorporating targeted therapies based on the tumour's molecular characteristics.[7-9]

Clinical trial enrolment: NACT offers an opportunity for patients to participate in clinical trials evaluating novel chemotherapy regimens, targeted therapies, or experimental treatment approaches. Clinical trials conducted in the neoadjuvant setting can accelerate the development of new treatment strategies and improve patient outcomes.[4,8,9]

The Neoadjuvant therapy protocol for an individual patient is decided on many factors, e.g. Age, clinical TNM stage, performance score, receptor status, menopausal status, affordability / cost of individual drugs.

Broadly speaking, the Luminal A group is given the AC (Adriamycin + Cyclophosphomide) protocol - 3 weekly for four cycles. Paclitaxel/ Docitaxel may be added in some patients.[3]

The Luminal B Her2 neu negative and the TNBC group is given the AC protocol. Some patients may be given FEC /FAC protocol (5-FU + Etoposide/ Adriamycin + Cyclophosphamide) for 6 cycles.[3,10]

Herceptin or Herceptin and Pertuzumab is added to the above protocol for the Luminal B Her2neu positive and the Her2 neu enriched groups.[3,10]

Only NAHT is given to selected patients, and consists of GnRH + CDK 4/6 inhibitors + Tamoxifen / Letrozole as per the menopausal status.[3,9-11]

Pathologic response to NAT can be assessed by several scoring systems like Miller-Payne, RCB, Sataloff, Chevallier etc. Out of all the methods available to assess response to NAT, The MD Anderson Residual Disease Burden Calculator offers the most objective method to assess the tissue response. Changes after NAT in resection specimens can be examined by gross & microscopic examination, by documenting primary tumour (size and cellularity) and nodal metastases (number and size) along with morphological changes like necrosis, inflammatory exudates, calcification and fibrosis.[4,7,12]

The residual cancer burden index has been found to be tightly associated with both event-free and distant disease–free survival.[12,13]

According to Globocan data 2020, in India, breast carcinomas accounts for 13.5% (178361) of all cancer cases and 10.6% (90408) of all deaths with a cumulative risk of 2.81. NAT has become a standard treatment approach for selected breast carcinoma patients in India. The pathological response to NAT is a significant factor in the prognosis of breast cancer patients.[2,5,6]

In the present study, we aim to categorize patients according to the RCB score groups, and correlate the different RCB groups with clinico-pathological features as well as molecular subtypes.

2. Materials and Methods

This was an observational retrospective study conducted at a tertiary cancer care institute from the January 2019 to December 2023.

NAT included Neoadjuvant Chemotherapy (NACT) as well as Neoadjuvant hormonal therapy (NAHT).

Preoperative evaluation included a Core Needle Biopsy for documentation of the diagnosis of Carcinoma as well as Immunohistochemical testing for molecular sub typing.

Total—262 surgically excised Post NAT Breast carcinoma cases were studied.

Hormone receptor markers namely estrogen receptor (ER), progesterone receptor (PR) along with human epidermal growth factor receptor 2 (HER2) & Ki 67% were assessed in all of the cases. The IHC was performed on Roche Ventana benchmark XT machine and appropriate protocols were used. The clones used were ER (Roche SP1, Rabbit Monoclonal, RTU), PR (Roche 1E2, Rabbit monoclonal, RTU), Pathway anti-Her2/neu, Roche 4B5, Rabbit Monoclonal, RTU), Confirm anti Ki67 (Roche 30-9, Rabbit Monoclonal, RTU).

Cases with equivocal Her2 status were sent for molecular confirmation by fluorescent in situ hybridization (FISH) from associated Accredited Laboratory.

Each case was sub typed into one of the following groups:

Luminal A (ER +, PR +, Her2neu-, Ki67<20%)
Luminal B (ER +, PR +/-, Her2neu-, Ki67 >20%)
Luminal BH (ER +, PR +/-, Her2neu +, Ki67 >20%)
Her2neu enriched (ER -, PR -, Her2neu +)
TNBC (ER -, PR -, Her2neu -)

Every patient was given NAT depending on the age, performance status, menopausal status, clinical TNM stage, molecular subtype, affordability/cost of individual drugs.

After the requisite NAT, breast resection surgery was performed.

Each resection specimen received in the pathology laboratory was subjected to gross dissection according to the CAP protocol. The entire tumour bed was sampled as a grid and microscopic examination was done on the sampled tissues. The histopathology reporting followed the CAP guidelines[14] and also incorporated the parameters for the RCB (Residual cancer burden) calculator provided on the website www.mdanderson. org/breast cancer_RCB.

d1 and **d2**-- bidimensional diameters of primary tumour bed in mm

dprim- d1 x d2 in sq mm

finv -- proportion of primary tumour area containing invasive carcinoma = 1-(%CIS/100) x %CA/100 (**CA** is carcinoma, **CIS** is in situ carcinoma)

LN -- number of positive lymph nodes

dmet -- diameter of largest nodal mets (mm)

(RCB index = 1.4 (finv x dprim) raised to 0.17 + 4 (1-0.75 raised to LN) x dmet) raised to 0.17)

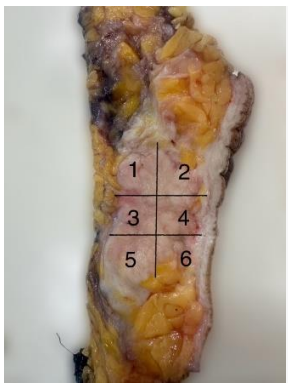

Figure 1: Gross appearance of post NAT mastectomy specimen with residual carcinoma. (The whole residual tumor is sampled in a grid pattern, the sections are labelled as 1, 2, 3,…… etc. and submitted for microscopic examination)

Figure 1 depicts tumour grid for grossing of tumour bed in post NACT MRM. The figure shows a transverse slice of Post NACT MRM specimen with a viable tumour. Whole tumour bed is sampled with appropriate numbering to asses exact percentage of treatment response on microscopy.

The residual cancer burden (RCB) calculator, an online tool available at the website (www.mdanderson.org/breastcancer_RCB) was used to compute the index score for each case.

Then the cases were classified into four groups according to the pathologic response:

Pathologic complete response (PCR) –Score 0 –No carcinoma in breast or lymph node.

RCB-I: Score >0-1.36 (minimal burden): Partial response

RCB-II: Score 1.36–3.26 (moderate burden): Partial response

RCB-III: Score >3.26 (extensive burden): Chemo resistant

The RCB index and class were correlated with clinical and pathological parameters e.g. Age, grade of tumour, tumour type and molecular subtype.

Formal written informed consent was not required as this was an observational study and all data was obtained from Institutional records.

All procedures performed in the current study were approved by IRB (Reference number- NCIEC Reg.No.: ECR/1130/Inst/MH/2018/RR-21, Dated 21-Oct-2021) in accordance with the 1964 Helsinki declaration and its later amendments.

3. Results

A total of 262 cases were identified, who received either NACT or NAHT from the period of 2019 to 2023.

Table 1 shows distribution of patients across RCB classes according to gender, age group, Ki 67 expression and Grade of IDC.

Age: The patients' age ranged between 25 to 82 years.

Sex: Only 2 patients were males, rest were females.

Grade and type: Out 262 breast carcinomas, 249 were invasive duct carcinoma Grade 3. Out of all grade 3 carcinomas, 3 were metaplastic, 1 of invasive papillary & 1 had medullary features.

11 were IDC Grade 2 duct carcinomas.

2 were IDC Grade 1 of which 1 was tubular carcinoma & other was an invasive papillary carcinoma.

Majority of cases were females and grade III. Notably, RCB III has the highest percentage among females aged 61 and above, and those with Ki 67 expression greater than 20%.

Out of 262 cases, 15 cases did not have molecular subtyping and so were excluded from following analysis (n=247).

Among these, 242 patients received NACT while remaining 5 cases were given NAHT. **Table 2** shows the molecular subtype distribution.

Table 1: Distribution of patients across RCB classes according to gender, age group, Ki 67 expression and Grade of IDC

		PCR	%	RCB I	%	RCB II	%	RCB III	%	Total	P
Gender/RCB class	F	79	30.38	28	10.77	58	22.31	95	36.54	260	NA
	M	0	0.00	1	50.00	1	50.00	0	0.00	2	
Age Group/RCB class	20 to 40	13	34.21	7	18.42	7	18.42	11	28.95	38	0.1782
	40 to 60	53	33.33	12	7.55	36	22.64	58	36.48	159	
	61 & above	13	20.00	10	15.38	16	24.62	26	40.00	65	
Ki 67/RCB Class	<=20%	7	21.88	2	6.25	10	31.25	13	40.63	32	0.4958
	>20%	67	32.06	25	11.96	41	19.62	75	35.89	209	
Grade	IDC I	0	0	1	100	0	0	0	0	1	0.08792
	IDC II	0	0	0	0	6	50	6	50	12	
	IDC III	69	30.80	27	12.05	47	20.98	81	36.16	224	

Table 2: Shows the molecular subtype distribution

Molecular Subtype	Number of cases
Luminal A	18
Luminal B	87
Luminal BH	29
Her2neu enriched	39
TNBC	74
Total cases	247

Table 3: Distribution of patients across RCB classes concerning different treatments, NACT and NAHT

Treatment/RCB	PCR	RCB I	RCB II	RCB III	Grand Total	p Value
NACT	74	28	53	87	242	NA
%	30.58	11.57	21.90	35.95	100.00	
NAHT			1	4	5	
%	0.00	0.00	20.00	80.00	100.00	
Grand Total	74	28	54	91	247	

In **Table 3**, the distribution of patients across RCB classes concerning different treatments, such as Neoadjuvant Chemotherapy (NACT) and Neoadjuvant Hormone Therapy (NAHT), illustrates varying responses to treatment modalities.

Of all patients who received NACT, best response, i.e. pCR is seen in 30.58% cases(n-74), RCB I was observed in 11.57% cases(n-28), RCB II in 21.90% (n -53) cases while 35.95% cases(n- 87) had no response, RCB III.

Amongst the 5 patients who received NAHT, 1 patient had RCB II & 4 patients had RCB III. None of them showed pCR. However, the number is too less to come to any conclusion.

Based on the results of the chi-square test for independence, there is a significant association between molecular subtype and RCB class in breast cancer patients ($p < 0.05$).

Residual cancer burden: The highest chemotherapy response was seen in the Her 2 enriched subtype i.e. 46.15% (n-39) followed by 34.48% in Luminal B Her2 positive subtype (n-29), then in TNBC subtype 31.08% (n-74). LA subtype had the lowest response rate 11.11% (n-18). **Table 4** shows the correlation between molecular subtypes & RCB.

4. Discussion

Neoadjuvant therapy is increasingly being preferred for high risk TNBC & HER2 enriched subtypes & is also indicated for some select Hormone receptor positive (HR+), HER2-negative cases. For evaluating treatment response to NACT, pathological assessment of breast tissue and metastatic lymph nodes after surgery is the Gold standard. A large number of studies have proven that cases who achieve a pathological complete response (pCR) have improved long term outcome & lower probability of recurrence & death. The Food and Drug Administration (FDA) suggested pCR as a surrogate endpoint for accelerated appraisal of new drugs for NACT in patients with BC.[7,16]

Table 4: Correlation between molecular subtypes & RCB

Molecular type/RCB	PCR	RCB I	RCB II	RCB III	Grand Total	p Value
Her2-neu enriched	18	6	9	6	39	P<0.05
%	46.15	15.38	23.08	15.38	100.00	
Luminal A	2		7	9	18	
%	11.11	0.00	38.89	50.00	100.00	
Luminal B	21	8	18	35	82	
%	25.61	9.76	21.95	42.68	100.00	
Luminal BH	10	3	6	10	29	
%	34.48	10.34	20.69	34.48	100.00	
Triple negative	23	11	13	27	74	
%	31.08	14.86	17.57	36.49	100.00	
Grand Total	74	28	53	87	242	

LA- Luminal A, LB-Luminal B, LBH- Luminal B Her2neu positive, Her 2- Her 2neu enriched, TNBC (ER, PR, Her2 -ve)

Morphology of NAT response

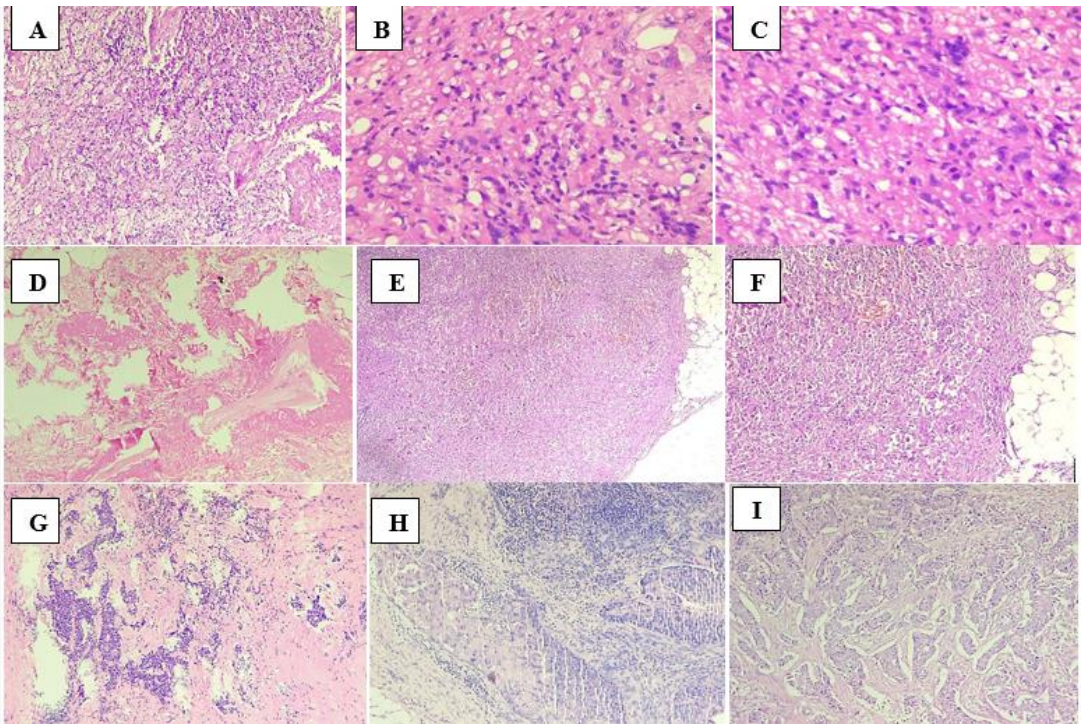

Figure 2: Variable microscopic appearance of different grades of RCB. **A, B & C)** Show complete pathologic response in form of fibro-histiocytic response in A (4X), B (40X), giant cells C (40X) & necrosis D (10X). **E** (10X) & **F** (10X) show viable metastatic tumour in lymph nodes. G, H, & I show residual viable tumours amongst different grades of RCB, RCB I (**G**), RCB II (**H**), RCB III (**I**), all 10X magnification. Slides were stained with H & E stain

Correlation between good response (pCR) & long-term outcome is strongest for TNBC, somewhat less for HER2+, and least for ER+. On the contrary triple negative cancers with a residual disease carry a high probability of recurrence.[7,10]

By definition, pCR is complete disappearance of all invasive breast carcinoma cells and axillary lymph nodes (ypT0/ypN0), and is determined pathologically in the resected tissue after NAT.[1,8,12]

While patients with pCR exhibit an excellent prognosis, a wide clinical heterogeneity remains within those patients failing to reach complete response, and the identification of patients with residual disease at a high risk of relapse is a substantial challenge. Hence, the subdivision of the BC population into several prognostic groups could help improving the prediction of survival benefits.[6,13]

To evaluate the pathological response after NACT, numerous grading systems have been followed till now, like AJCC(y), B-18, Miller-Payne, MPNI etc.[5,12]

Out of all these grading systems, RCB index has shown the consistent association with long term prognosis in patients treated with NACT.[6,12,17]

Residual cancer burden (RCB) index has been developed in 2007 by Symmans and colleagues from the M.D. Anderson Cancer Centre (MDACC) & it combines pathological findings in the primary tumour bed and the regional lymph nodes to calculate a continuous index. In a cohort of 241 BC patients who completed NAC, they found that with each unit increase of RCB index, the relapse risk almost doubles in post NACT patients. And this finding was significantly associated with the risk of disease recurrence.[12] Despite having 6 variables in RCB calculation, RCB index was found to be highly reproducible.[6,12,13]

A study done by Anne-sophie Amy et al after observing 717 patients found that RCB index was significantly associated with RFS. The RCB-0 patients displayed similar prognosis when compared to the RCB-I group, while patients from the RCB-II and RCB-III classes were at increased risk of relapse.[13]

They also stated that the prognostic impact of RCB index was significant for TNBC and HER2-positive cancers; but not for luminal cancers. RCB II tumours had intermediate prognosis. Lastly, prognosis of RCB-III patients was poor (8-years RFS: 52.7%) particularly in the TNBC subgroup, where the median RFS was 12.7 months.[13,17] Another study done by Peintinger et al also found the reproducible long term prognostic significance of RCB.[18]

In short RCB index is a reliable prognostic score. RCB accurately identifies patients at a high risk of recurrence, those showing RCB-III with TNBC or HER2-positive, who must be offered second-line adjuvant therapies.[7,13]

RCB score shows a prominent association with different molecular subtypes of breast cancers.

In the present study, the HER2 enriched group showed the highest frequency of pCR i. e RCB-0 followed by LBH subtype. This is slightly different from other studies, where TNBC has shown the highest rate of pCR.[2,4,17]

Her2neu is an epidermal growth factor receptor, which is over expressed in the above two subtypes. The precision and effectiveness of the targeted therapy explains this high response rate. With the addition of new ASCO guidelines for use of Antibody conjugates in Her2 low cases, some cases in other subtypes may also benefit in future.[19]

In our study, the LBH subtype showed a good frequency of PCR. This finding is different than that of other studies. The possible explanation is the co-expression of Her2 neu along with the hormonal receptors makes the tumour cells chemo sensitive and thus shows a good response.

TNBC subtype also exhibited a fairly good rate of PCR. However, the increasing recognition of molecular heterogeneity in TNBC cases may further refine the choice of therapeutic agents and improve the response rate in the residual tumour cells.

Regarding luminal subtypes(ER/PR positive), neoadjuvant chemotherapy achieves a lower rate of pCR in comparison with other subtypes, with a pCR rate of around 10%–24%. Also in ER-positive population, high Ki67 expression increases the probability of a PCR.[10]

In our study, Luminal A subtype group shows the lowest of PCR (11.11%) while luminal B group with a higher Ki 67 index shows a better response (25.61%).

Luminal A & Luminal B (Her2neu negative) subtypes are behaviourally slower growing carcinomas with a low to fair response to NAT. Since pCR rates following NACT are lower in luminal subtypes and a weaker correlation between pCR and long-term outcomes as compared with Her 2 enriched & triple negative breast cancers, NAHT could potentially represent a useful alternative in this patient subset.[11]

On the downside, NAHT comes with a prolonged time to response, low pCR rates, and risk of disease progression while under treatment which has made its use limited in the NAT.[11,19] According to data only 3.0% of newly diagnosed cases of localized and locally advanced, ER-positive patients are being given NAHT.[11]

However as a result of findings published after trial Z1031, NAHT use has been increased in practice. Another study done by Akiko Chiba et al found that NET significantly increased the rates of BCS in patients with hormone receptor positive clinical T2-4c breast cancer.[19]

5. Limitation

RCB index has not been adequately studied in post NAHT cases. In the present study we have tried to assess RCB index in 5 who were given NAHT but conclusions could not be drawn because of low number of cases and it remains a limitation of our study. Further follow up of these cases and recruitment of more cases in future can address this issue.

6. Conclusion

To conclude, neoadjuvant treatment has an impact on the patient, the treating oncologist as well as the pathologist. For the patients, it provides an opportunity for a different treatment regimen when the primary disease is refractory. It also saves them of radical surgeries & prolonged hospital stay. Implementation of NAT has made Pathologists to be considerate of all specific requirements while handling & reporting of Post NAT specimens. In addition to all these benefits, it provides the clinicians with identification of

newer prognostic markers in the ever increasing breast cancer cases.[10,21]

The study gave an insight into clinico-pathological response to NAT and the association of chemo sensitivity with different molecular subtypes of breast cancer patients in our hospital setting.

7. Future Recommendation

A meticulous follow up of all the patients is being done to calculate the disease free survival as well as overall survival at our institute.

8. Ethical Approval

This study was approved by NCIEC with reg. no. ECR/1130/Inst/MH/2018/RR-21.

9. Financial Support and Sponsorship

None.

10. Conflicts of Interest

There are no conflicts of interest.

References

1. Mohapatra M, Sarma YS. A study on clinico-pathological assessment of response to neoadjuvant chemotherapy in breast carcinoma. *J Cancer Res Ther*. 2020;16(6):1419–25.
2. Nayak M, Besra K, Samantaray S, Nayak PS. Post neoadjuvant chemotherapy Histopathological evaluation of breast cancer specimens. *Int J Surg Med*. 2023;9(1):20–6.
3. Spring LM, Bar Y, Isakoff SJ. The evolving role of neoadjuvant therapy for operable breast cancer. J Natl Compr Canc Netw. 2022;20(6):723-34.
4. Perubhotla l, Kodandapani S, Murthy SS. Evaluation of Pathological Response in Post-Neoadjuvant Chemotherapy Breast Carcinoma Specimens using Residual Cancer Burden System. *J Clin Diagn Res*. 2021;15(5).
5. Park CK, Jung WH, Koo JS. Pathologic evaluation of breast cancer after neoadjuvant therapy. *J Pathol Transl Med*. 2016;50(3):173-80.
6. Yau C, Osdoit M, van der Noordaa M, Shad S, Wei J, de Croze D, Hamy AS, et al. Steenbruggen TG. Residual cancer burden after neoadjuvant chemotherapy and long-term survival outcomes in breast cancer: a multicentre pooled analysis of 5161 patients. *Lancet Oncol*. 2022;23(1):149-60.
7. Li X, Wang M, Wang M, Yu X, Guo J, Sun T, et al. Predictive and prognostic roles of pathological indicators for patients with breast cancer on neoadjuvant chemotherapy. *J Breast Cancer*. 2019;22(4):497–521.
8. Freitas AJ, Causin RL, Varuzza MB, Filho CMTH, Silva VD, Souza CD, et al. Molecular biomarkers predict pathological complete response of neoadjuvant chemotherapy in breast cancer patients: Review. *Cancers*. 2021;13(21):5477.
9. Zheng C, Liu Y, Bi Z, Qiu P, Qiao G, Bi X, et al. Clinical efficacy and biomarker analysis of neoadjuvant camrelizumab plus chemotherapy for early-stage triple-negative breast cancer: a experimental single-arm phase II clinical trial pilot study. *Int J Surg*. 2024;110(3):1527–36.
10. Colomer R, Saura C, Sánchez-Rovira P, Pascual T, Rubio IT, Burgués O, et al. Neoadjuvant management of early breast cancer: a clinical and investigational position statement. *Oncologist.* 2019;24(5):603–11.
11. Matikas A, Foukakis T, Michalakis I, Georgoulias V. Implementing neoadjuvant endocrine strategies in ER-positive, HER2-negative breast cancer. Expert review of anticancer therapy. *Expert Rev Anticancer Ther*. 2017;17(4):319-26.
12. Symmans WF, Peintinger F, Hatzis C, Rajan R, Kuerer H, Valero V, et al. Measurement of residual breast cancer burden to predict survival after neoadjuvant chemotherapy. *J Clin Oncol*. 2007;25(28):4414–22.
13. Hamy AS, Darrigues L, Laas E, De Croze D, Topciu L, Lam GT, et al. Prognostic value of the Residual Cancer Burden index according to breast cancer subtype: Validation on a cohort of BC patients treated by neoadjuvant chemotherapy. *PloS One*. 2020;15(6):e0234191.
14. Fitzgibbons PL, Connolly JL, Bose S, Chen YY, De Baca ME, Edgerton M, et al. Protocol for the examination of resection specimens from patients with invasive carcinoma of the breast [Internet]. CAP guidelines. 2020;4(1.0). Available from: https://documents.cap.org/protocols/cp-breast-invasive-resection-20-4400.pdf.
15. Diaz-Botero S, Espinosa-Bravo M, Gonçalves VR, Esgueva-Colmenarejo A, Peg V, Perez J, et al. Different prognostic implications of residual disease after neoadjuvant treatment: impact of Ki 67 and site of response. *Ann Surg Oncol.* 2016;23(12):3831–7.
16. Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. *Lancet*. 2014;384(9938):164–72.
17. Symmans WF, Wei C, Gould R, Yu X, Zhang Y, Liu M, et al. Long-term prognostic risk after neoadjuvant chemotherapy associated with residual cancer burden and breast cancer subtype. *J Clin Oncol*. 2017;35(10):1049–60.
18. Peintinger F, Sinn B, Hatzis C, Albarracin C, Downs-Kelly E, Morkowski J, et al. Reproducibility of residual cancer burden for prognostic assessment of breast cancer after neoadjuvant chemotherapy. *Mod Pathol*. 2015;28(7):913–20.
19. Lewis GD, Li G, Guo J, Yu SF, Fields CT, Lee G, et al. The HER2-directed antibody-drug conjugate DHES0815A in advanced and/or metastatic breast cancer: preclinical characterization and phase 1 trial results. *Nat Commun*. 2024;15(1):466.
20. Chiba A, Hoskin TL, Heins CN, Hunt KK, Habermann EB, Boughey JC. Trends in neoadjuvant endocrine therapy use and impact on rates of breast conservation in hormone receptor-positive breast cancer: a national cancer data base study. *Ann Surg Oncol.* 2017;24(2):418–24.
21. Provenzano E, Vallier AL, Champ R, Walland K, Bowden S, Grier A, et al. A central review of histopathology reports after breast cancer neoadjuvant chemotherapy in the neo-tango trial. *Br J Cancer.* 2013;108(4):866–72.

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