



# Risk of Breast Conservation in Triple Negative Breast Cancer: Is It A Myth?????

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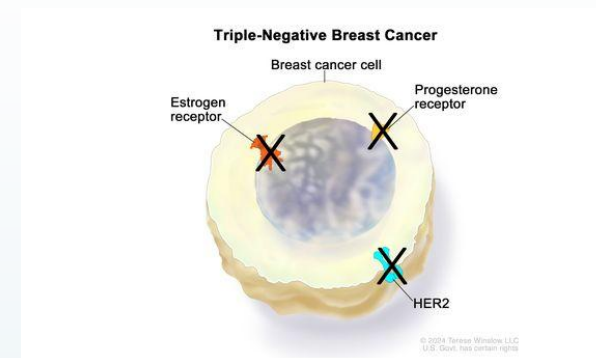
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# What is a triple negative cancer!!

- ER, PR, HER 2 negative cancer
- Signifies poorly differentiated nature
- Hence more aggressive
- 10-15% of the breast cancer
- More common in Asians and Africans as compared to the Caucasian population
- More common in younger women under the age of 40 years
- Often associated with BRCA 1 mutation



# Poor Prognosis.....

- Generally more aggressive
- Early stage TNBC is 4 times likely to cause distant mets as compared to HR +ve HER2 Negative cancers
- About 5% present with de-novo metastasis
- More risk of local recurrence
- Even in the localized disease, 25% have distant relapse

## 5-year relative survival rates for triple-negative breast cancer

SEER Stage	5-year Relative Survival Rate
Localized	91%
Regional	66%
Distant	12%
All stages combined	77%

# Good news.....

- ▶ Newer treatments like PD-L1 inhibitor have shown promising anti-tumour activity (KEYNOTE 173- Pembrolizumab + NACT)
- ▶ I-SPY phase 2 trial showed more PCR when NACT was given with Pembrolizumab
- ▶ PARP inhibitors have also shown promising results in adjuvant setting in TNBCs associated with BRCA mutations. (OlympiAD, EMBRACA Trials)
- ▶ However PARP inhibitors in neo-adjuvant setting haven't shown to be of benefit with PCR, EFS or OS (PARTNER Trial)

# Management.....Upfront surgery

- Early stage breast cancer (Stage 1 disease)
- Tumor is small
- Clinically node negative
- A large retrospective study involving stage 1 TNBC has shown OS advantage with Surgery followed by Adjuvant Chemotherapy (*Huang et al*).

# Management – Stage 2 and stage 3 disease

- NACT followed by surgery
- To downgrade an unresectable tumour
- Inflammatory breast cancer
- To facilitate BCS
- To facilitate axillary surgery
- NACT offers significant OS and DFS benefit, in presence of PCR (*Biswas et al*)

# Surgical management

- Breast conserving surgery- for smaller tumours/ downgraded tumours, PCR
- Mastectomy- for larger tumours, multifocal disease, inflammatory breast cancer, patient choice.
- Several RCTs stated that BCS had no advantage in Overall Survival over mastectomy (Litière S *et al*, Veronesi *et al*)



# Mastectomy or BCS????

- There is a higher risk of LRR after NACT where there is no PCR (9.5%) as against PCR (4.5%).
- We see a higher rate of mastectomy in TNBC.
- Majority of these are not needed .
- There is a fear of higher chance of recurrence after the BCS.
- Both, the surgeons and the patients wish for mastectomy.
- Is that a myth????????????

Breast-conserving surgery is not associated with increased local recurrence in patients with early-stage node-negative triple-negative breast cancer treated with neoadjuvant chemotherapy

- David Krug et al- [The Breast Volume 74](#), April 2024, 103701
- Meta analysis
- 2632 patients with early TNBC from the German Breast Group meta-database
- Patients with cT1-2 cN0 and ypN0, available surgery and follow-up data were enrolled- a total of 1074
- End points- Loco regional recurrence, disease free survival and overall survival
- Univariate and multivariate Fine-Gray analysis and [Cox regression](#) models.

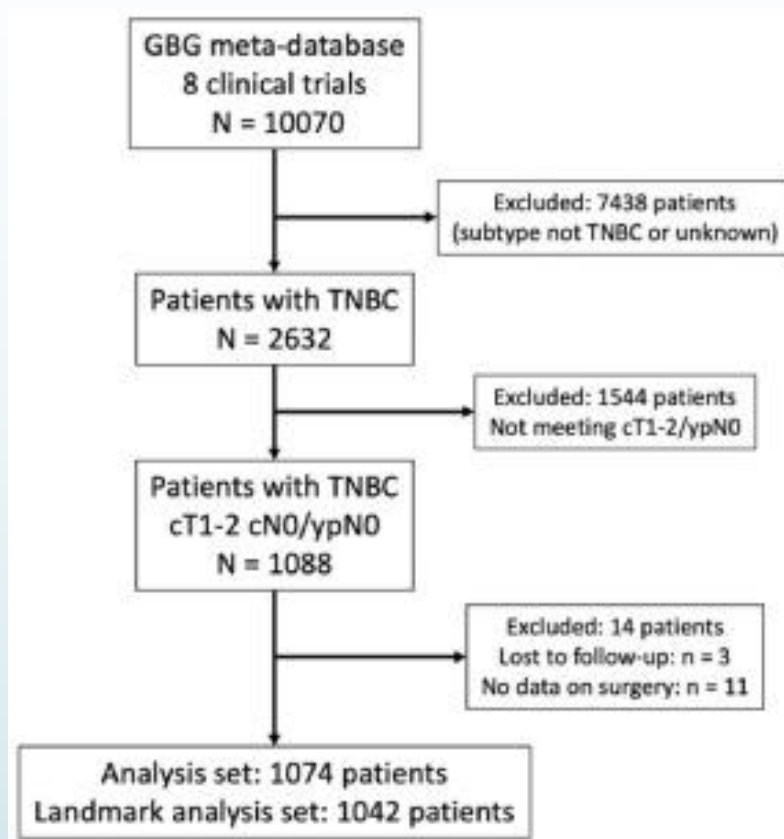


Table 1. Patient characteristics.

BCS = Breast-conserving surgery; ILC = [invasive lobular carcinoma](#); M = mastectomy; mt = mutated; NST = no special type.

Parameter	Category	BCS (N = 916)	Mastectomy (N = 158)	Total (N = 1074)	P-value (BCS vs. M)
		N (%)	N (%)	N (%)	Empty Cell
Age, years	≤50	549 (59.9)	115 (72.8)	664 (61.8)	0.002
	>50	367 (40.1)	43 (27.2)	410 (38.2)	
cT	cT1	278 (30.3)	49 (31.0)	327 (30.4)	0.852
	cT2	638 (69.7)	109 (69.0)	747 (69.6)	
Grading	G1-2	218 (24.1)	42 (26.9)	260 (24.6)	0.481
	G3	685 (75.9)	114 (73.1)	799 (75.4)	
	missing	13	2	15	
Histological	NST	773 (84.4)	138 (87.3)	911 (84.8)	0.629
type	ILC	13 (1.4)	2 (1.3)	15 (1.4)	
	other	130 (14.2)	18 (11.4)	148 (13.8)	
ypT	ypT0/is	512 (60.0)	80 (55.2)	592 (59.3)	<0.001
	ypT1/2	341 (39.9)	60 (41.4)	401 (40.1)	
	ypT3/4	1 (0.1)	5 (3.4)	6 (0.6)	
	missing	62	13	75	
BRCA1 or BRCA2 mt	no	404 (86.1)	60 (60.6)	464 (81.7)	<0.001
	yes	65 (13.9)	39 (39.4)	104 (18.3)	
	missing	447	59	506	
BRCA1 mt	no	416 (88.7)	62 (62.6)	478 (84.2)	<0.001
	yes	53 (11.3)	37 (37.4)	90 (15.8)	
	missing	447	59	506	
BRCA2 mt	no	457 (97.4)	97 (98.0)	554 (97.5)	1.000
	yes	12 (2.6)	2 (2.0)	14 (2.5)	
	missing	447	59	506	

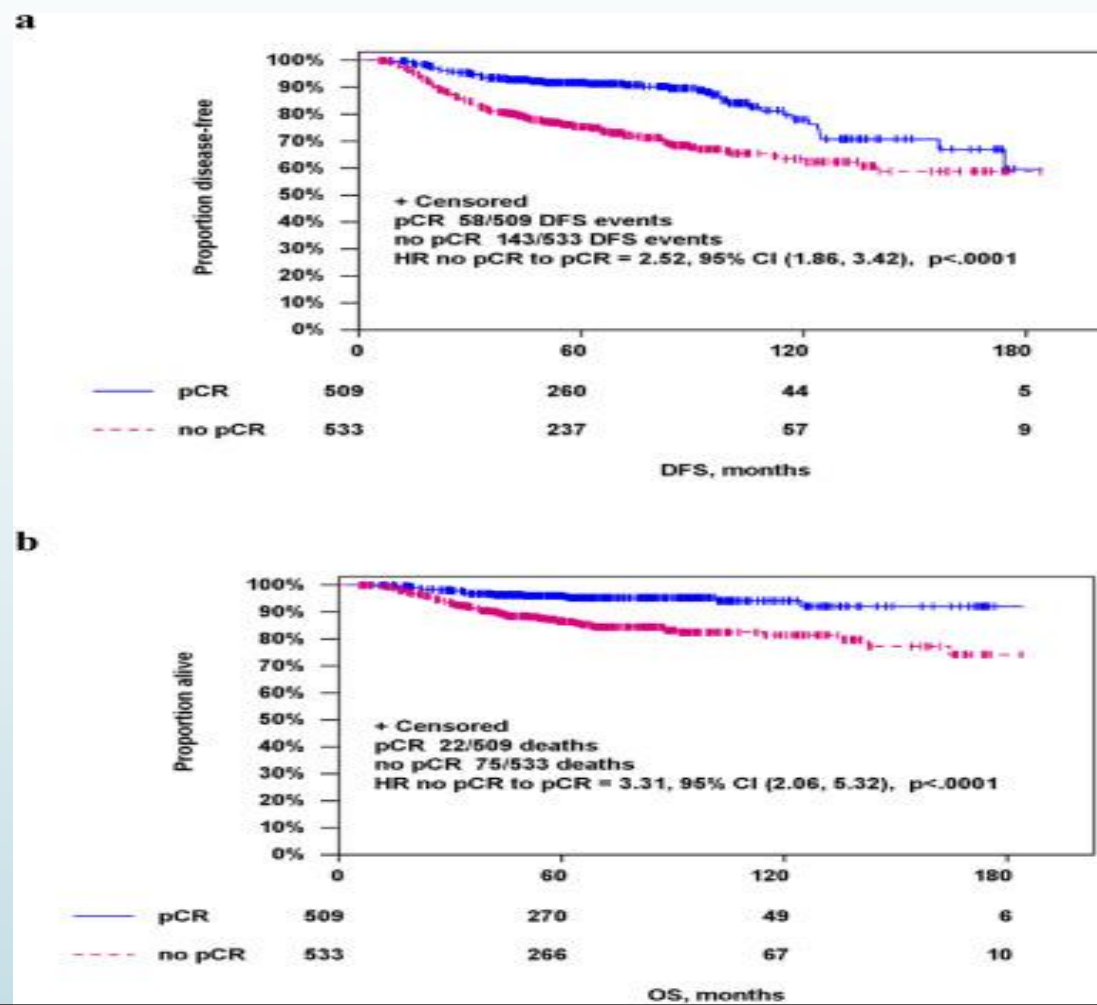
# Patterns of recurrence

Event	N	N in %
Locoregional	94	8.8
Distant	77	7.2
Secondary malignancy	21	2.0
Death	16	1.5

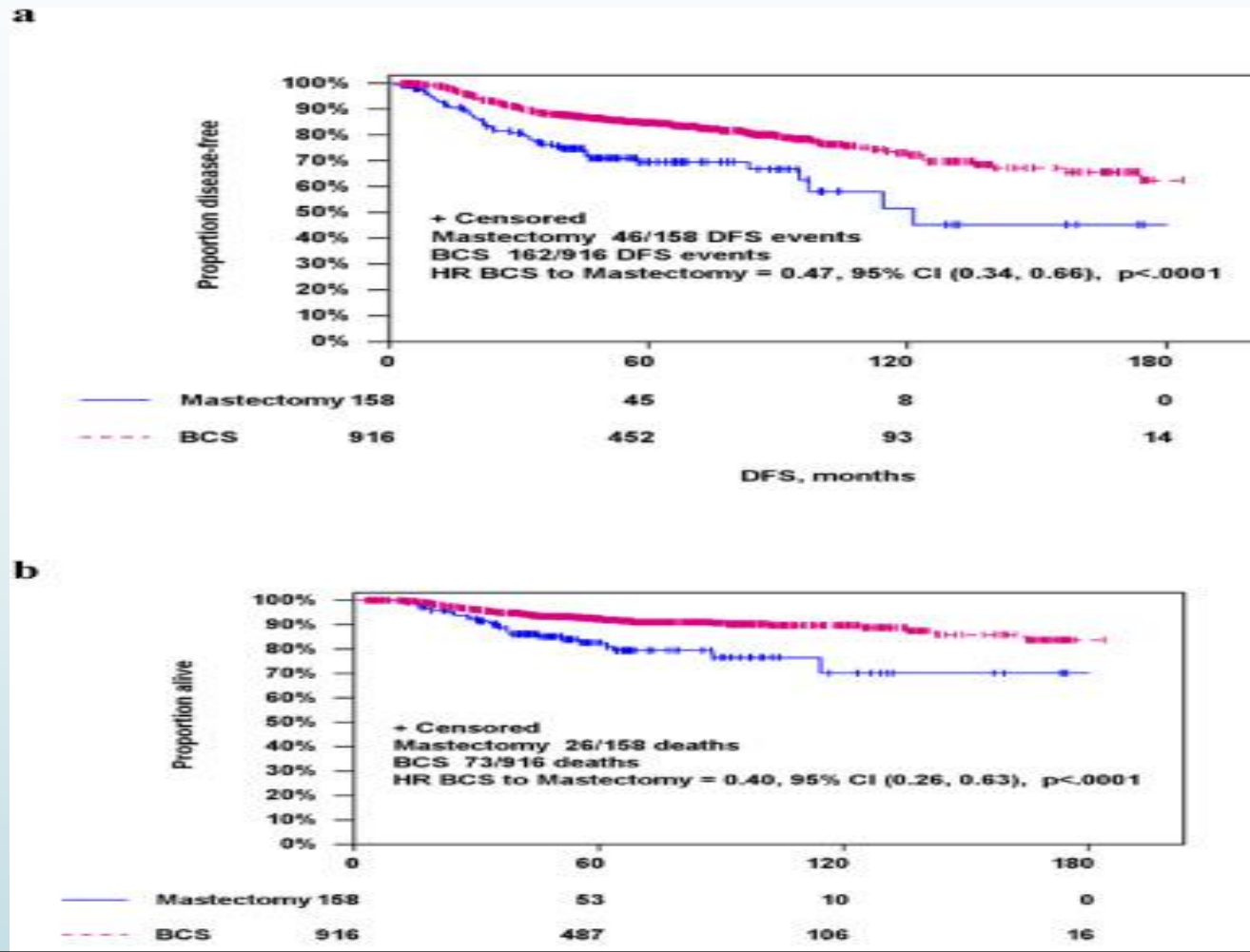
# Locoregional recurrence rates (LRR) and results of multivariate Cox-regression analysis.

Parameter	Category	5-year LRR (%)	Hazard ratio (95%CI)	P-value
Surgery type	BCS	6.71 (5.11–8.60)	1.213 (0.673–2.187)	0.5209
	mastectomy	12.31 (7.17–18.93)		
Age	≤50	7.59 (5.60–9.97)	1.090 (0.709–1.675)	0.6949
	>50	7.25 (4.85–10.27)		
cT	cT1	6.66 (4.14–9.98)	1.088 (0.622–1.902)	0.7676
	cT2	7.74 (5.85–9.97)		
ypT (3 groups)	ypT0/is	4.88 (3.24–7.01)	not included	n. a.
	ypT1	8.64 (5.68–12.36)		
	ypT2/3	13.34 (6.99–21.75)		
pCR (landmark)	no pCR	10.11 (7.57–13.06)	2.223 (1.381–3.578)	0.0010
	pCR	3.57 (2.12–5.61)		

DFS was significantly better in patients that underwent BCS (HR 0.47 [95%-CI 0.34–0.66];  $p < 0.001$ ) while it was significantly impaired in patients with residual disease in the breast (HR 2.52 [95%-CI 1.86–3.42];  $p < 0.001$ ). This was confirmed using multivariate Cox-regression analysis



# Multivariate Cox-regression analysis for disease free survival (DFS) and overall survival (OS).





## Conclusion- of the .....

- BCS following neoadjuvant chemotherapy was not associated with an increased risk of LRR in patients with early stage TNBC.
- Use of BCS was associated with superior DFS and OS compared to mastectomy. Treatment response was the major determinant of favorable outcome.
- TNBC-subtype should not be used as an argument to withhold BCS followed by adjuvant RT in eligible patients.

# Outcomes after breast-conserving surgery or mastectomy in patients with triple-negative breast cancer: meta-analysis

- A meta-analysis was performed to evaluate locoregional recurrence (LRR), distant metastasis (DM), and overall survival (OS) rates in patients with TNBC who had breast-conserving surgery versus mastectomy.
- Estimates were pooled in random-effects analysis. The effect of study-level co-variables was assessed by univariable meta-regression.
- *Fancellu et al, British Journal of Surgery, Volume 108, Issue 7, July 2021, Pages 760–768*

# Results

- Fourteen studies, including 19 819 patients operated for TNBC met the inclusion criteria.
- 9828 patients (49.6 per cent) underwent BCS and 9991 (50.4 per cent) had a mastectomy.
- Patients with smaller tumours were more likely to be selected for BCS (pooled odds ratio (OR) for T1 tumours 1.95, 95 per cent c.i. 1.64 to 2.32;  $P < 0.001$ ).
- The pooled OR for LRR was 0.64 (0.48 to 0.85;  $P = 0.002$ ), indicating a statistically significantly lower odds of LRR among women who had BCS relative to mastectomy.
- The pooled OR for DM was 0.70 (0.53 to 0.94;  $P = 0.02$ ), indicating a lower odds of DM among women who had BCS; however, this difference diminished with increasing study-level age and follow-up time.
- A pooled hazard ratio of 0.78 (0.69 to 0.89;  $P < 0.001$ ) showed a significantly lower hazard for all-cause mortality among women undergoing BCS versus mastectomy.

# Does Breast-Conserving Surgery with Radiotherapy have a Better Survival than Mastectomy? A Meta-Analysis of More than 1,500,000 Patients.

- De la Cruz Ku, G., Karamchandani, M., Chambergo-Michilot, D. *et al.*
- *Ann Surg Oncol* **29**, 6163–6188 (2022). <https://doi.org/10.1245/s10434-022-12133-8>
- Meta-analysis

# Methodology

- Evidence was searched up to 31 October 2021 in : PubMed, Scopus, and EMBASE. No limit on the search by publication date or language.
- any trial or cohort studies that compared BCS and mastectomy in patients with breast cancer with American Joint Committee on Cancer (AJCC) stages I–III.
- Case reports, case series, reviews, letters to the editor, congress or conference abstracts, editorials, interviews, comments, and newspaper articles were excluded.
- Studies that included male sex, stage 0, distant metastasis at diagnosis, bilateral synchronous cancer, neoadjuvant radiation, or chemotherapy in more than 5% of the studied population, oncoplastic surgery, and articles without available hazard ratio (HR) or incomplete data were excluded.

# Analysis

- **Selection:** 18,997 publications. After removing duplicates and screening phase, 86 articles selected for full-text screening. Finally, 24 cohort studies and 6 RCTs were included in this systematic review.

# Results

- This meta-analysis, which included a total of 30 studies including 1.8 million women, found that women with early breast cancer who underwent BCS had better OS compared with those who underwent mastectomy. This survival benefit was noted to be higher in studies with less than 10 years of follow-up.
- Compared with mastectomy, BCS was associated with improved OS (RR 0.64, 95% CI 0.55–0.74). When performing the stratified analysis by study type, it was found that the association was intensified in cohorts (RR 0.57, 95% CI 0.49–0.67), but it became nonsignificant in the trial subgroup (RR 1.03, 95% CI 0.96–1.10).
- In general, studies with retrospective cohorts included more recently published large database comparison studies that, while not prospective in design, had much larger sample sizes than the prospective trial studies.
- Additionally, we found that the association became more intensified with the subgroup of studies with a follow-up of less than 10 years (RR 0.54, 95% CI 0.46–0.64); however, this was not significant in those with a follow-up of 10 years or more (RR 0.91, 95% CI 0.76–1.10).
- Upon performing additional analysis without the studies with high influence in the heterogeneity of the analysis, we obtained similar results with benefit of BCS over mastectomy in overall survival.
- Regarding the DFS, only 11 studies reported this outcome. A total of 37,486 and 21,419 patients underwent BCS and mastectomy, respectively. We found that there was no difference between BCS and mastectomy (RR 0.86, 95% CI 0.60–1.22).

# For those still not convinced.....

- More recent studies looking at large databases have demonstrated that BCT has better outcomes in OS compared with mastectomy. For example, Almahariq *et al* reported that OS for BCS was 97.2% compared with 93.7% for mastectomy at 5 years in patients younger than 50 years.
- Similarly, Chen *et al* reported 93.2% and 58.6%, for BCS and mastectomy at 5 years, respectively.



# .....No more a myth

- ▶ Looking at the studies and especially meta-analyses, BCS with radiotherapy is a safe option, with comparable OS and DFS with mastectomy in case of TNBC
- ▶ In some instances, its shown to have a better OS.

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Thank you!!