European Journal of Surgical Oncology 51 (2025) 109643

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Clinico-pathological features predicting indication to mastectomy in breast cancer patients achieving complete response after neoadjuvant therapy: A retrospective analysis of the EUSOMA database

Giuseppe Catanuto [a], Damiano Gentile [b], Federica Martorana [a,c,*], Mariano Tomatis [d], Antonio Ponti [d,e], Lorenza Marotti [d], Cynthia Aristei [f,g], Maria Joao Cardoso [h,i], Kwok Leung Cheung [j,k], Giuseppe Curigliano [l,m], Jakob De Vries [n], Andreas Karakatsanis [o,p], Donatella Santini [q], Francesco Sardanelli [r], Peter Van Dam [s], Isabel T. Rubio [t], andEUSOMA Working Group

[a] *Humanitas-Istituto Clinico Catanese Misterbianco, Catania, Italy*
[b] *Breast Unit, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy*
[c] *Department of Clinical and Experimental Medicine, University of Catania, Italy*
[d] *European Society of Breast Cancer Specialists (EUSOMA), Florence, Italy*
[e] *CPO Piemonte, Turin, Italy*
[f] *Radiation Oncology Section, Department of Medicine and Surgery, University of Perugia, Italy*
[g] *Perugia General Hospital Sant'Andrea delle Fratte Perugia, Italy*
[h] *Breast Unit, Champalimaud Clinical Center/Champalimaud Foundation, Portugal*
[i] *Lisbon University Faculty of Medicine, Lisbon, Portugal*
[j] *Nottingham Breast Cancer Research Centre, University of Nottingham, United Kingdom*
[k] *School of Medicine, University of Nottingham, United Kingdom*
[l] *Division of New Drugs and Early Drug Development for Innovative Therapies, European Institute of Oncology, IRCCS, Milan, Italy*
[m] *Department of Oncology and Hemato-Oncology, University of Milano, Italy*
[n] *University Medical Center Groningen, the Netherlands*
[o] *Department for Surgical Sciences, Uppsala University, Uppsala, Sweden*
[p] *Section for Breast Surgery, Department of Surgery, Uppsala University Hospital, Uppsala, Sweden*
[q] *Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy*
[r] *Lega Italiana per la Lotta contro i Tumori (LILT), Milano, Monza Brianza, Italy*
[s] *Multidisciplinary Oncologic Center, Antwerp University Hospital, Edegem, Belgium*
[t] *Breast Surgical Oncology, Clinica Universidad de Navarra, Cancer Center Universidad de Navarra, Madrid, Spain*

ARTICLE INFO

Keywords:
Breast cancer
Breast conserving surgery
Mastectomy
Neoadjuvant therapy
Pathological complete response

ABSTRACT

Aims: We investigated factors related to the type of surgery, i.e. mastectomy *versus* breast conserving surgery (BCS), in breast cancer (BC) patients with complete pathologic response in the breast (ypT0) after neoadjuvant therapy (NAT).

Methods: A retrospective analysis from the EUSOMA database was performed using data from 55 certified centers across 14 European countries, including ypT0 BC patients (i.e., neither invasive nor in situ residuals), treated between 2017 and 2022. Variables analyzed included year of surgery, age, number and distribution of tumor focality, extent, clinical and pathological stages, and biologic subtype. Logistic regression was used to identify predictors of surgical choice. The Kaplan-Meier method was used for comparison of local recurrence-free survival (LRFS) between surgical groups.

Results: Of 1416 BC patients included, 67.5 % underwent BCS and 32.5 % mastectomy. At multivariable analysis, factors increasing the likelihood of mastectomy included: more recent year of surgery [odds ratio (OR) 2.61, 95 % confidence interval (95%CI): 1.51–4.51,$p = 0.001$], younger age (OR: 0.96, 95%CI: 0.95–0.97,$p < 0.001$), multifocality (OR: 2.20, 95%CI: 1.61–3.00,$p < 0.001$) and multicentricity (OR: 12.66, 95%CI: 6.82–23.49,$p < 0.001$), advanced clinical tumor stage (OR: 14.54, 95%CI: 5.80–36.47,$p < 0.001$), and baseline axillary nodal

* Corresponding author. Department of Clinical and Experimental Medicine, University of Catania, Via Santa Sofia, 89 – 95123, Catania, Italy.
E-mail address: federica.martorana@unict.it (F. Martorana).

https://doi.org/10.1016/j.ejso.2025.109643
Received 2 December 2024; Received in revised form 14 January 2025; Accepted 24 January 2025
Available online 25 January 2025

involvement (OR: 1.56, 95%CI: 1.12–2.17,p = 0.009). Comparison between groups did not show a significant difference in LRFS (p = 0.389).
Conclusion: Many BC patients undergo mastectomy despite achieving complete response of primary tumor after NAT. Patients-related and tumor-related features, as well as having surgery in more recent years, seems to influence this choice. Our findings suggest the need for an optimized decision-making to spare unnecessary mastectomies.

1. Introduction

Surgical de-escalation is one of the expected benefits of neoadjuvant therapy (NAT) in patients with non-metastatic breast cancer (BC), as demonstrated in early studies exploring this treatment strategy [1,2].

Over the last three decades, improved knowledge of BC biology and the advent of highly effective targeted therapies, significantly increased tumor response following NAT [3–5]. Additionally, the extent of response to preoperative therapies is strongly prognostic and is used to determine post-neoadjuvant treatment strategies [6,7]. For these reasons, NAT has been increasingly used in non-metastatic BC patients, based not only on baseline tumor extent but also on its biology [7].

Of note, as the use of NAT increased, the rates of conversion from a pre-planned mastectomy to breast conserving surgery (BCS) decreased [8,9]. Consistently, two published meta-analyses of randomized clinical trials showed that achieving a partial or even complete response of primary BC after NAT has not translated to a respective increase of BCS [10,11].

While several reasons have been proposed to explain the decreasing trend toward conversion to BCS in patients responding to NAT, no definitive explanations exist [12]. Concerns about potentially higher rates of local recurrence in patients receiving BCS after NAT have been raised by an Early Breast Cancer Trialists' Collaborative Group meta-analysis [13]. However, these results have not been confirmed by several subsequent evidences, showing comparable recurrence outcomes in patients treated with NAT regardless of surgery type [14–16].

We conducted a retrospective analysis on a large cohort from the EUSOMA registry, aiming at identifying clinical and pathological features associated with mastectomy in BC patients with complete response of primary tumor (ypT0) and without evidence of in situ carcinoma after NAT. In the same cohort, we compared local-recurrence rates between patients undergoing BCS and those receiving mastectomy.

2. Materials and methods

EUSOMA database is a central data warehouse of prospectively collected information, including pseudonymized individual patient records on primary breast cancer from European breast Centre that undergo the voluntary EUSOMA certification process and agreed to participate in benchmarking and research activities. No personal identifiers exist in the entire database.

For this analysis, data were analyzed for the period 2017–2022 and included 55 Breast Centers in 14 European countries (Austria = 1, Belgium = 9, Croatia = 1, Cyprus = 1, France = 1, Germany = 2, Greece = 1, Italy = 27, Poland = 1, Portugal = 3, Spain = 1, Sweden = 1, Switzerland = 4, The Netherlands = 2).

Eligible patients were female with a diagnosis of non-metastatic BC treated with NAT between 2017 and 2022, with no residual invasive or in situ cancer in the breast at definitive surgery, regardless of pathological nodal status (ypT0 population). Patients with known germline pathogenic variants in *BRCA1/2* genes (*gBRCA1/2*) were excluded.

The following variables were registered: surgery year, surgery type (BCS or mastectomy), age, focality (single, multifocal, multicentric), tumor extent (in millimetres, mm), clinical stage of primary (cT), TNM stage (according to AJCC staging system, 7th edition), histology (no special type, lobular, other), clinical nodal status (cN), pathological nodal status (ypN), immunophenotype of disease [luminal A-like, luminal B-like, hormone receptor positive (HR+)/HER2 positive (HER2+), HER2+, triple negative], Ki67 proliferation index, adjuvant radiotherapy.

The study population was divided in two groups according to the type of surgery received (BCS or mastectomy), and descriptive statistics were reported accordingly.

Median and interquartile ranges (IQR) were used for continuous variables, while percentages were used for categorical variables. Univariable logistic regression for type of surgery was performed including all the aforementioned variables. Variables showing a significant correlation were then included in a multivariable analysis model.

Local recurrence rates (i.e. breast cancer relapse in ipsilateral mammary gland after BCS or in chest wall after mastectomy, including recurrence on surgical scar) in the two subgroups were reported, and local recurrence free-survival (LRFS) was evaluated using the log-rank test, illustrating outcomes by the Kaplan-Meier method. Statistical significance level was set at < 0.05.

All the analyses were performed using R software version 4.3.2.

3. Results

3.1. Patient population

Between 2017 and 2022, 10775 women with non-metastatic BC were treated with NAT in 55 EUSOMA-certified Breast Centers across 14 European countries. Of these, 3058 (28.4 %) achieved ypT0. After exclusion of *gBRCA1/2* mutated patients (n = 865) and of those with incomplete data (n = 777), 1416 (13.1 %) were included in the analysis (Fig. 1A). Among them, 956 (67.5 %) underwent BCS, while 460 (32.5 %) were treated with mastectomy after NAT (Fig. 1B).

Median age in the whole cohort was 54 years (IQR: 46–62). Most patients had a unifocal primary (n = 1096, 77.4 %), with a median size of 23 mm (IQR: 17–33 mm), corresponding to cT2 disease in 802 (56.6 %) patients. Baseline axillary nodal involvement (cN+) was present in 687 (48.5 %) patients. Most patients had stage II disease (n = 915, 64.6 %), while 210 (14.8 %) had stage III disease. Hormone receptor positive/HER2+ was the most prevalent subtype (n = 464, 32.8 %), followed by HER2+ (n = 381, 26.9 %), and triple negative BC (n = 357, 25.2 %). The median Ki67 proliferation index was 50 % (IQR: 30–70 %). The majority of patients had no pathological nodal involvement after NAT (ypN0, n = 1304, 92.1 %), regardless of baseline nodal status. Most of women treated with BCS received adjuvant radiotherapy (n = 841, 95.5 %), while 181 patients (45.6 %) had radiotherapy after mastectomy. Descriptive statistics are summarized in Table 1.

3.2. Univariable and multivariable analyses

Univariable analysis showed several factors associated with the likelihood of undergoing mastectomy.

Year of surgery was a significant factor; patients treated in 2022 had higher odds of receiving a mastectomy [odds ratio (OR): 2.04, 95 % confidence interval (95%CI): 1.25–3.32, p = 0.004] compared to the reference year 2017. Age inversely correlated with the choice of mastectomy; for each additional year, the odds slightly decreased (OR: 0.97, 95%CI: 0.96–0.98, $p < 0.001$). Focality also played a role; multicentric tumors were markedly more likely to lead to mastectomy (OR: 13.89, 95%CI: 7.70–25.06, $p < 0.001$) than unifocal tumors. Larger tumor

extent at diagnosis increased the odds of mastectomy (increase per mm OR: 1.02, 95%CI: 1.01–1.03, $p < 0.001$). Patients with stage III disease were significantly more likely to have mastectomy than those with stage I disease (OR: 3.92, 95%CI: 2.68–5.72, $p < 0.001$). Clinically, cT3 (OR: 2.97, 95%CI: 1.95–4.53, $p < 0.001$) and cT4 (OR: 12.16, 95%CI: 6.25–23.67, $p < 0.001$) BC had significantly higher odds of resulting in mastectomy than cT1 BC. Patients with cN + disease before NAT were almost twice as likely to undergo mastectomy compared to those without nodal involvement (OR: 1.96, 95%CI: 1.57–2.46, $p < 0.001$).

Subsequently, multivariable logistic regression analysis was conducted to determine the independent predictors of mastectomy. Surgery year remained a significant predictor, with patients treated in 2022 showing a significantly increased likelihood of undergoing mastectomy compared to those treated in 2017 (OR: 2.61, 95%CI: 1.51–4.51, $p = 0.001$). Age was inversely associated with the probability of mastectomy; for each one-year increase in age, the odds of mastectomy decreased (OR: 0.96, 95%CI: 0.95–0.97, $p < 0.001$). Additionally, tumor focality was a critical determinant for mastectomy; multifocal disease was associated with an increased likelihood of mastectomy (OR: 2.20, 95%CI: 1.61–3.00, $p < 0.001$), and this association was even stronger for multicentric disease (OR: 12.66, 95%CI: 6.82–23.49, $p < 0.001$). Clinical tumor stage prior to NAT played a significant role; with the odds substantially higher for cT3 (OR: 3.02, 95%CI: 1.54–5.91, $p = 0.001$) and cT4 tumors (OR: 14.54, 95%CI: 5.80–36.47, $p < 0.001$). Moreover, the presence of cN + disease before therapy also predicted the choice of mastectomy over BCS (OR: 1.56, 95%CI: 1.12–2.17, $p = 0.009$). Univariable and multivariable analyses are summarized in Table 2.

3.3. Outcomes

The LRFS of BC patients who achieved ypT0 post-NAT was analyzed. Overall, data for 264 cases (18.6 %) were missing, leaving a cohort of 1152 patients with a median follow up of 21.4 months. Among patients with available data, 785 underwent BCS, while 367 received a mastectomy. The incidence of local recurrence was low, with 6 (0.8 %) events occurring in the BCS group and 4 (1.0 %) events in the mastectomy group. Comparison between groups did not show a significant difference in LRFS between the two surgical modalities ($p = 0.389$). Kaplan-Meier curves are depicted in Fig. 2.

4. Conclusions

Over the past decades, NAT has increasingly being used for the treatment of non-metastatic BC patients, with increasing rates of pCR [3–5]. However, a concomitant increase in BCS has not been observed [8,9]. In the NeoALTTO trial, a doubling in pCR rates with dual HER2 blockade did not translate in a proportional increase in BCS. In this study, negative estrogen receptor status, multicentricity and the presence of a palpable mass before surgery were significantly associated with a lower likelihood of BCS [17]. A recent meta-analysis of 36 randomized trials including 12311 patients, showed a BCS rate of 57 % among patients achieving pCR. According to this analysis, baseline axillary nodal involvement and HER2 positivity were negatively associated with BCS [11].

To further investigate factors contributing to the choice of performing a mastectomy in patients with complete response after NAT, we performed a large retrospective study from EUSOMA registry.

According to our analysis, compared to 2017, there was an increasing trend toward mastectomy in the time-span going from 2020 (OR 1.60) to 2022 (OR 2.04). The SARS-CoV-2 (COVID-19) pandemic could have played a role in determining this trend. A retrospective report from the EUSOMA database investigating adherence to EUSOMA quality indicator during the first COVID-19 wave (March–June 2020) does, however, not support this hypothesis [18]. Other reports from the United States suggest higher rates of mastectomies during 2020, correlated with COVID-19 outbreak [19,20]. Whether this relationship between surgical choices and COVID-19 exists, a decreasing trend in the use of mastectomies should be expected in the following years, and further studies are needed to prove it.

Younger age at diagnosis predicted higher chance of being treated with mastectomy in our population. In a reported large cohort including 3536 BC women aged 20–49 years, treated between 1992 and 2011, the proportion of patients who underwent BCS slightly increased over time (from 33.0 % in 1996 to 40.1 % in 2011). However, the overall mastectomy rate (63.5 %) was high, and surgical trends in very young women (20–39 years old) remained unchanged between 1996 and 2011

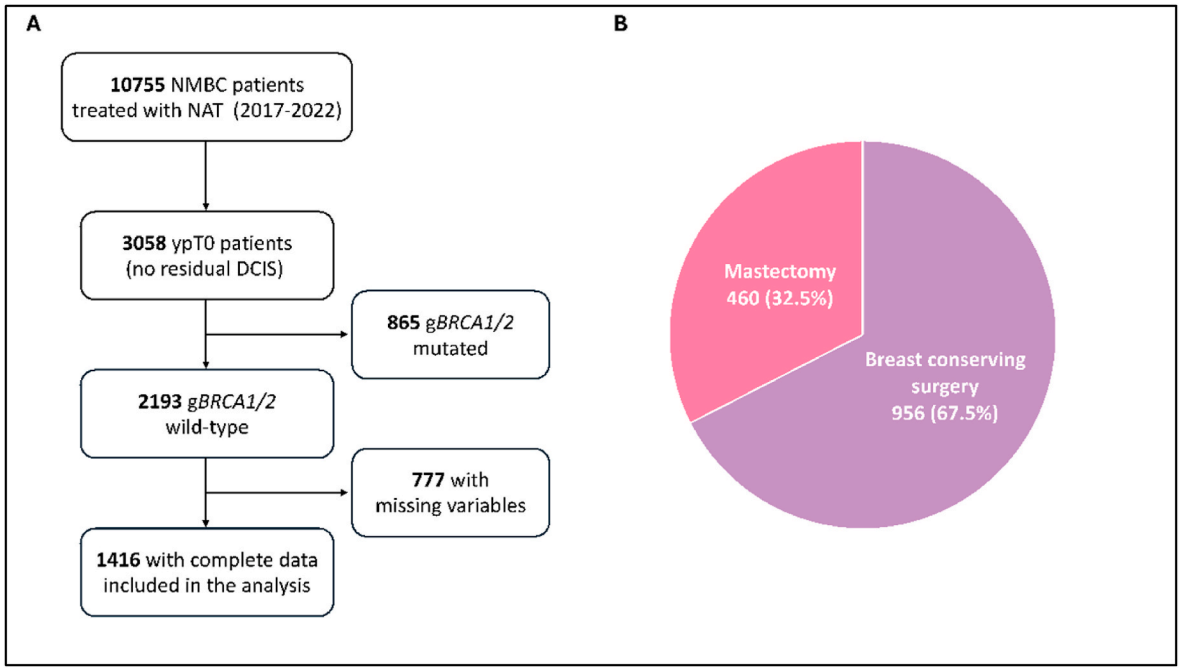

Fig. 1. A–B. Population's disposition
DICS ductal in situ carcinoma; NAT neoadjuvant therapy; NMBC non metastatic breast cancer.

Table 1
Population's characteristics.

Variables		Total	BCS	Mastectomy
		1416 (100 %)	956 (67.5 %)	460 (32.5 %)
Surgery year, n (%)	**2017**	156	118 (75.6)	38 (24.4)
	2018	238	165 (69.3)	73 (30.7)
	2019	277	193 (69.7)	84 (30.3)
	2020	285	188 (66.0)	97 (34.0)
	2021	306	199 (65.0)	107 (35.0)
	2022	154	93 (40.4)	61 (39.6)
Age in years, median (IQR)		54 (46–62)	56 (48–64)	52 (43–59)
Focality, n (%)	**Single**	1096	809 (73.8)	287 (26.2)
	Multifocal	237	133 (56.1)	104 (43.9)
	Multicentric	83	14 (26.9)	69 (83.1)
Extension in mm, median (IQR)		23 (17–33)	22 (17–30)	25 (18.38)
cT, n (%)	**cT1**	435	324 (74.5)	111 (25.5)
	cT2	802	562 (70.1)	240 (29.9)
	cT3	117	58 (49.6)	59 (50.4)
	cT4	62	12 (19.4)	50 (80.6)
cN, n (%)	**cN0**	729	544 (74.6)	185 (25.4)
	cN+	687	412 (60.0)	275 (40.0)
Stage, n (%)	**I**	291	216 (74.2)	75 (25.8)
	II	915	651 (71.9)	264 (28.9)
	III	210	89 (42.4)	121 (57.6)
Histotype, n (%)	**NST**	1313	891 (68.9)	422 (32.1)
	Lobular	31	20 (64.5)	11 (35.5)
	Other	55	36 (65.5)	19 (34.5)
Ki67 %, median (IQR)		50 (30–70)	50 (30–70)	45 (30–70)
Intrinsic variant, n (%)	**Luminal A-like**	19	10 (52.6)	9 (47.4)
	Luminal B-like	181	129 (71.3)	52 (28.7)
	HR+/ HER2+	464	321 (69.2)	143 (30.8)
	HER2+	381	239 (62.7)	142 (37.3)
	Triple Negative	357	251 (70.3)	106 (29.7)
Adjuvant radiotherapy, n (%)		1022	841 (95.5)	181 (45.6)

Table legend: HR + hormone receptor positive; IQR interquartile range; NST no special type.

[21]. Other evidence shows young women are increasingly choosing mastectomy, even without a known hereditary predisposition to the disease [22]. Historically, younger women are considered more likely to develop aggressive BC, to present with advanced stage of disease and to have poorer survival compared to older women [23–25]. These unfavourable features may push towards a more aggressive surgical approach. However, a retrospective analysis including 23810 women under 40 years of age with stage I-II BC, treated between 1988 and 2016, showed that BCS was associated with improved BC-specific and overall survival compared to mastectomy [26]. Overall, young age should not be a contraindication for BCS *per se* [22].

Baseline multifocality and multicentricity significantly predicted the choice of mastectomy, despite the presence of ypT0. Despite data about post-NAT imaging are missing in our study, it is possible to speculate that this result is potentially influenced by the complexity of radiological tumor assessment after NAT. Challenges in radiological evaluation may be related to heterogeneity of biologic subtypes, diversity in patterns of response and absence of direct indicators of response to NAT [27]. Consensus suggests that magnetic resonance imaging (MRI) should be the standard of care for preoperative evaluation of primary tumor after NAT, even though evidence are not completely consistent and conclusive [28–30]. Additionally, MRI may overestimate the extent of residual disease in the breast, making surgical planning not straightforward and influencing decisions toward a more radical surgery. Recent perspectives take into account the different MRI performances according the tumor subtype or biologic profile, with higher reliability in triple negative cancers [31–33], and also include artificial intelligence deep learning approaches [34,35]. The choice of radical surgery in women with baseline multifocal or multicentric BC can also be influenced by concern of recurrence. Indeed, evidence suggests that multifocal and multicentric diseases are associated with higher risk of local recurrence and poorer survival [36]. On the other hand, a large retrospective series and a pooled analysis of three prospective clinical trials demostrated that patients with multifocal/multicentric disease at diagnosis have no significant difference in LRFS and overall survival, compared to patients with unicentric disease [37,38].

In our analysis, patients with more advanced tumor stage at baseline (cT3-T4 and cN + disease) were more frequently treated with mastectomy. As for multifocal/multicentric disease, the preference for a more radical surgery in patients with more advanced disease may partially be explained by the fear of locoregional recurrences. However, a meta-analysis by the Early BC Trialists' Collaborative Group (EBCTCG) indicated that the proportional increase in local recurrences did not vary

Table 2
Univariate and multivariate logistic regression analysis.

Variables		UNIVARIATE			MULTIVARIATE		
		OR	95 % CI	p-value	OR	95 % CI	p-value
Surgery year	**2017**	ref.			ref.		
	2018	1.37	0.87-2.17	0.174	1.44	0.86-2.39	0.163
	2019	1.35	0.86-2.11	0.186	1.40	0.85-2.30	0.186
	2020	**1.60**	**1.03-2,49**	**0.036**	**1.75**	**1.07-2.86**	**0.026**
	2021	**1.67**	**1.08-2.58**	**0.021**	**1.91**	**1.18-3.10**	**0.009**
	2022	**2.04**	**1.25-3.32**	**0.004**	**2.61**	**1.51-4.51**	**0.001**
Age		**0.97**	**0.96-0.98**	**<0.001**	**0.96**	**0.95-0.97**	**<0,001**
Focality	**Single**	ref.			ref.		
	Multifocal	**2.20**	**1.65-2.95**	**<0.001**	**2.20**	**1.61-3.00**	**<0,001**
	Multicentric	**13.89**	**7.70-25.06**	**<0.001**	**12.66**	**6.82-23.49**	**<0,001**
Stage	**I**	ref.			ref.		
	II	1.17	0.87-1.58	0.309	**0.50**	**0.28-0.91**	**0.023**
	III	**3.92**	**2.68-5.72**	**<0.001**	0.73	0.32-1.67	0.458
Clinical Tumor Stage	**cT1**	ref.			ref.		
	cT2	1.25	0.96-1.62	0.101	**1.81**	**1.14-2.88**	**0.012**
	cT3	**2.97**	**1.95-4.54**	**<0.001**	**3.02**	**1.54-5.91**	**0.001**
	cT4	**12.16**	**6.25-23.67**	**<0.001**	**14.54**	**5.80-36.47**	**<0.001**
Clinical Nodal Stage	**cN0**	ref.			ref.		
	cN+	**1.96**	**1.57-2.46**	**<0.001**	**1.56**	**1.12-2.17**	**0.008**

Table legend: OR odds ratio; CI confidence interval.

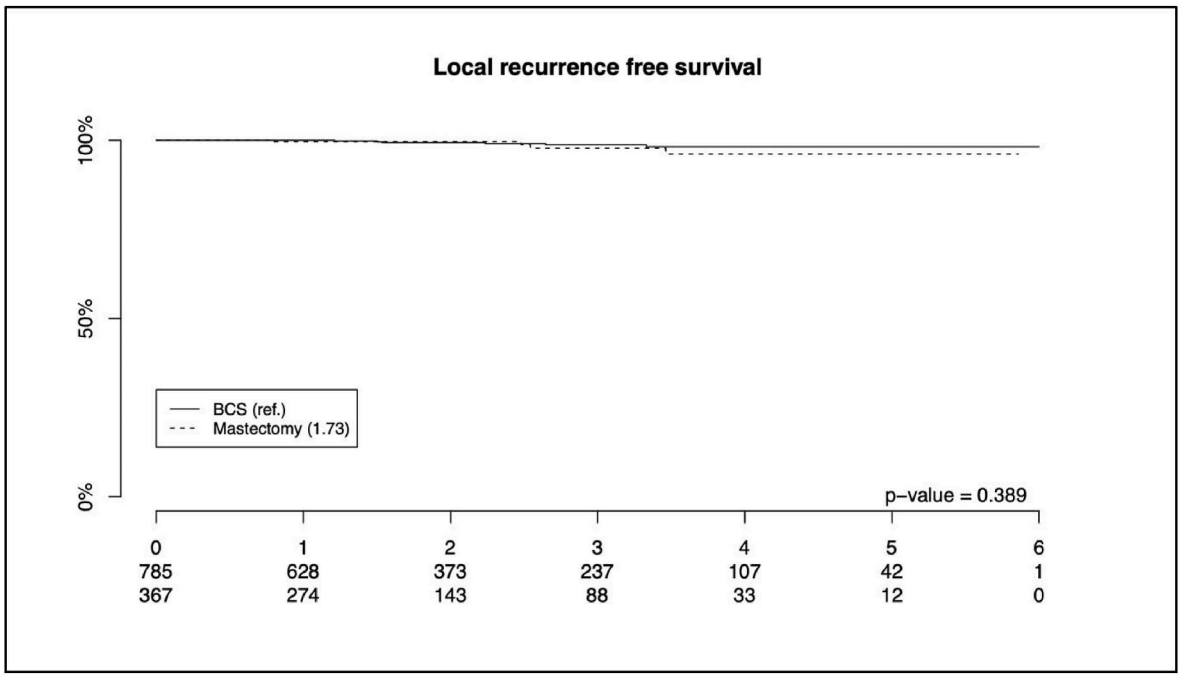

Fig. 2. Local recurrence free survival
BCS breast conserving surgery.

significantly with tumor size or nodal status [13].

In a correlative analysis of the I-SPY2 trial including 1462 BC patients treated between 2010 and 2021, no association emerged between type of surgery (BCS versus mastectomy) and LRFS. This result was maintained even in patients with cT3-T4 tumors undergoing BCS compared to those with cT1-T2 disease undergoing the same surgical treatment [39]. Hence, more advanced stage at diagnosis (cT3-T4 or cN+) should not preclude breast conservation, particularly in cases responding to NAT, since favourable oncological outcomes can be achieved with BCS following NAT even in this subgroup of patients [40]. Similarly, a German retrospective cohort study included 1074 patients with early-stage triple-negative BC who received BCS (n = 916) or mastectomy (n = 158) after NAT. With a median follow-up of 64 months, the type of surgery did not show a significant association with locoregional recurrence rate, while the lack of pCR represented the main risk factor for having a local relapse [41].

Hence, the results of our survival analysis are in line with pre-existing literature, even though the short follow-up and the scarce number of local recurrence events in our cohort must be taken into account.

Our study presents some limitations, mainly stemming from its retrospective nature, that makes our findings merely hypothesis generating. As stated above, data about post-NAT assessment were not available, making impossible to drive any conclusion about the role of radiological findings for surgical planning. Due to our study's design, we were not able to delve into patients' preferences and values, which are key element for surgical choices. The subjective apprehensions of patients, including concerns over adjuvant radiotherapy or anxiety regarding the possibility of local recurrences, could have affected surgical decisions in some cases. Still, existing literature suggests that receiving a mastectomy does not translate into increased "peace of mind" in women with BC [42]. Additionally, we could not investigate issues related to skills and confidence in more advanced oncoplastic techniques for breast conservation, that may have influenced the surgical choice toward mastectomy. Lastly, in order to comply with General Data Protection Regulation (GDPR), we could not analyze country by country data to show geographical variability. However, as part of the EUSOMA consortium, all the participating centers are expected to adhere to specific standards, eventually pursuing an uniform clinical conduct. Hence, the lack of a subgroup analysis according to the location does not substantially mines the internal validity of our work.

In conclusion, EUSOMA data shows that many BC patients undergo mastectomy despite achieving complete response of primary tumor after NAT. Surgical decision-making for BC patients after NAT is a complex issue, and the choice between mastectomy and BCS is influenced by patient and tumor characteristics, including year of treatment, age, baseline dimension, focality and disease stage. Even though response to NAT is a major determinant of favourable outcomes, it is frequently disregarded for surgical decision-making. Our findings support the need for a more balanced, individualized and multidisciplinary approach in surgical planning, to align oncological safety and breast preservation in the treatment of BC.

CRediT authorship contribution statement

Giuseppe Catanuto: Conceptualization, Methodology, Writing – original draft. **Damiano Gentile:** Conceptualization, Methodology, Writing – original draft. **Federica Martorana:** Conceptualization, Methodology, Writing – original draft. **Mariano Tomatis:** Methodology, Formal analysis, Investigation, Writing – review & editing. **Antonio Ponti:** Methodology, Formal analysis, Investigation, Writing – review & editing. **Lorenza Marotti:** Writing – review & editing, Data curation. **Cynthia Aristei:** Writing – review & editing. **Maria Joao Cardoso:** Writing – review & editing. **Kwok Leung Cheung:** Writing – review & editing. **Giuseppe Curigliano:** Writing – review & editing. **Jakob De Vries:** Writing – review & editing. **Andreas Karakatsanis:** Writing – review & editing. **Donatella Santini:** Writing – review & editing. **Francesco Sardanelli:** Writing – review & editing. **Peter Van Dam:** Writing – review & editing. **Isabel T. Rubio:** Conceptualization, Writing – review & editing.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: **FM:** Grant for presentations: Lilly, Gilead, Pfizer, Travel grant: Lilly, Gilead, Pfizer.**KFL**: Unrelated advisory funding from Pfizer**LF**: Advisory Board AstraZeneca**AK**: Advisory Board/Consultation: Akira Medical Sciences, Resitu AB; Honoraria: Kubtec, Pfizer, Astra Zeneca, Endomag (all to the institute of the author); Travel Expenses: Elsevier, GBCC, UEMS, ESSO, Endomag. All outside the scope of the present work.

Acknowledgment

Andreas Karakatsanis is Deputy Editor-In-Chief of the *European Journal of Surgical Oncology*.

Isabel T. Rubio is a Guest Editor of the *European Journal of Surgical Oncology*.

References

[1] Fisher B, Bryant J, Wolmark N, Mamounas E, Brown A, Fisher ER, et al. Effect of preoperative chemotherapy on the outcome of women with operable breast cancer. J Clin Oncol 1998;16:2672–85.
[2] van Nes JG, Putter H, Julien JP, Tubiana-Hulin M, van de Vijver M, Bogaerts J, et al. Preoperative chemotherapy is safe in early breast cancer, even after 10 years of follow-up; clinical and translational results from the EORTC trial 10902. Breast Cancer Res Treat 2009;115:101–13.
[3] Gianni L, Eiermann W, Semiglazov V, Lluch A, Tjulandin S, Zambetti M, et al. Neoadjuvant and adjuvant trastuzumab in patients with HER2-positive locally advanced breast cancer (NOAH): follow-up of a randomised controlled superiority trial with a parallel HER2-negative cohort. Lancet Oncol 2014;15:640–7.
[4] Gianni L, Pienkowski T, Im YH, Roman L, Tseng LM, Liu MC, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. Lancet Oncol 2012;13:25–32.
[5] Schmid P, Cortes J, Pusztai L, McArthur H, Kummel S, Bergh J, et al. Pembrolizumab for early triple-negative breast cancer. N Engl J Med 2020;382:810–21.
[6] Yau C, Osdoit M, van der Noordaa M, Shad S, Wei J, de Croze D, et al. Residual cancer burden after neoadjuvant chemotherapy and long-term survival outcomes in breast cancer: a multicentre pooled analysis of 5161 patients. Lancet Oncol 2022;23:149–60.
[7] Loibl S, Andre F, Bachelot T, Barrios CH, Bergh J, Burstein HJ, et al. Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol 2024;35:159–82.
[8] Golshan M, Cirrincione CT, Sikov WM, Berry DA, Jasinski S, Weisberg TF, et al. Impact of neoadjuvant chemotherapy in stage II-III triple negative breast cancer on eligibility for breast-conserving surgery and breast conservation rates: surgical results from CALGB 40603 (Alliance). Ann Surg 2015;262:434–9. discussion 8-9.
[9] Golshan M, Loibl S, Wong SM, Houber JB, O'Shaughnessy J, Rugo HS, et al. Breast conservation after neoadjuvant chemotherapy for triple-negative breast cancer: surgical results from the BrighTNess randomized clinical trial. JAMA Surg 2020;155:e195410.
[10] Karakatsanis A, Tasoulis MK, Warnberg F, Nilsson G, MacNeill F. Meta-analysis of neoadjuvant therapy and its impact in facilitating breast conservation in operable breast cancer. Br J Surg 2018;105:469–81.
[11] Criscitiello C, Golshan M, Barry WT, Viale G, Wong S, Santangelo M, et al. Impact of neoadjuvant chemotherapy and pathological complete response on eligibility for breast-conserving surgery in patients with early breast cancer: a meta-analysis. Eur J Cancer 2018;97:1–6.
[12] Pfob A, Dubsky P. The underused potential of breast conserving therapy after neoadjuvant system treatment - causes and solutions. Breast 2023;67:110–5.
[13] Early Breast Cancer Trialists' Collaborative G. Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. Lancet Oncol 2018;19:27–39.
[14] Symmans WF, Yau C, Chen YY, Balassanian R, Klein ME, Pusztai L, et al. Assessment of residual cancer burden and event-free survival in neoadjuvant treatment for high-risk breast cancer: an analysis of data from the I-SPY2 randomized clinical trial. JAMA Oncol 2021;7:1654–63.
[15] He X, Ji J, Qdaisat A, Esteva FJ, Yeung SJ. Long-term overall survival of patients who undergo breast-conserving therapy or mastectomy for early operable HER2-Positive breast cancer after preoperative systemic therapy: an observational cohort study. Lancet Reg Health Am 2024;32:100712.
[16] Gentile D, Martorana F, Karakatsanis A, Caruso F, Caruso M, Castiglione G, et al. Predictors of mastectomy in breast cancer patients with complete remission of primary tumor after neoadjuvant therapy: a retrospective study. Eur J Surg Oncol 2024;50:108732.
[17] Criscitiello C, Azim Jr HA, Agbor-tarh D, de Azambuja E, Piccart M, Baselga J, et al. Factors associated with surgical management following neoadjuvant therapy in patients with primary HER2-positive breast cancer: results from the NeoALTTO phase III trial. Ann Oncol 2013;24:1980–5.
[18] van Dam P, Tomatis M, Ponti A, Marotti L, Aristei C, Biganzoli L, et al. The impact of the SARS-COV-2 pandemic on the quality of breast cancer care in EUSOMA-certified breast centres. Eur J Cancer 2022;177:72–9.
[19] Roskam JS, Uretsky M, Fornari M, Chappuis CA, Bolourani S, Soliman SS, et al. The effects of the COVID-19 pandemic on mastectomy outcomes for breast cancer. Clin Breast Cancer 2023;23:431–5.
[20] Rubenstein RN, Stern CS, Plotsker EL, Haglich K, Tadros AB, Mehrara BJ, et al. Effects of COVID-19 on mastectomy and breast reconstruction rates: a national surgical sample. J Surg Oncol 2022;126:205–13.
[21] Sinnadurai S, Kwong A, Hartman M, Tan EY, Bhoo-Pathy NT, Dahlui M, et al. Breast-conserving surgery versus mastectomy in young women with breast cancer in Asian settings. BJS Open 2019;3:48–55.
[22] Rosenberg SM, Dominici LS, Gelber S, Poorvu PD, Ruddy KJ, Wong JS, et al. Association of breast cancer surgery with quality of life and psychosocial well-being in young breast cancer survivors. JAMA Surg 2020;155:1035–42.
[23] Azim Jr HA, Partridge AH. Biology of breast cancer in young women. Breast Cancer Res 2014;16:427.
[24] Assi HA, Khoury KE, Dbouk H, Khalil LE, Mouhieddine TH, El Saghir NS. Epidemiology and prognosis of breast cancer in young women. J Thorac Dis 2013;5(Suppl 1):S2–8.
[25] Keegan TH, DeRouen MC, Press DJ, Kurian AW, Clarke CA. Occurrence of breast cancer subtypes in adolescent and young adult women. Breast Cancer Res 2012;14:R55.
[26] Sun ZH, Chen C, Kuang XW, Song JL, Sun SR, Wang WX. Breast surgery for young women with early-stage breast cancer: mastectomy or breast-conserving therapy? Medicine (Baltimore) 2021;100:e25880.
[27] Tinterri C, Fernandes B, Zambelli A, Sagona A, Barbieri E, Di Maria Grimaldi S, et al. The impact of different patterns of residual disease on long-term oncological outcomes in breast cancer patients treated with neo-adjuvant chemotherapy. Cancers (Basel) 2024;16.
[28] Marinovich ML, Houssami N, Macaskill P, Sardanelli F, Irwig L, Mamounas EP, et al. Meta-analysis of magnetic resonance imaging in detecting residual breast cancer after neoadjuvant therapy. J Natl Cancer Inst 2013;105:321–33.
[29] Rauch GM, Adrada BE, Kuerer HM, van la Parra RF, Leung JW, Yang WT. Multimodality imaging for evaluating response to neoadjuvant chemotherapy in breast cancer. AJR Am J Roentgenol 2017;208:290–9.
[30] Fowler AM, Mankoff DA, Joe BN. Imaging neoadjuvant therapy response in breast cancer. Radiology 2017;285:358–75.
[31] Wang M, Du S, Gao S, Zhao R, Liu S, Jiang W, et al. MRI-based tumor shrinkage patterns after early neoadjuvant therapy in breast cancer: correlation with molecular subtypes and pathological response after therapy. Breast Cancer Res 2024;26:26.
[32] Shi Z, Huang X, Cheng Z, Xu Z, Lin H, Liu C, et al. MRI-Based quantification of intratumoral heterogeneity for predicting treatment response to neoadjuvant chemotherapy in breast cancer. Radiology 2023;308:e222830.
[33] Kuzmova M, Cullinane C, Rutherford C, McCartan D, Rothwell J, Evoy D, et al. The accuracy of MRI in detecting pathological complete response following neoadjuvant chemotherapy in different breast cancer subtypes. Surg Oncol 2023;51:102011.
[34] Zhou Z, Adrada BE, Candelaria RP, Elshafeey NA, Boge M, Mohamed RM, et al. Prediction of pathologic complete response to neoadjuvant systemic therapy in triple negative breast cancer using deep learning on multiparametric MRI. Sci Rep 2023;13:1171.
[35] Dietzel M, Trimboli RM, Zanardo M, Schultz-Wendtland R, Uder M, Clauser P, et al. The potential of predictive and prognostic breast MRI (P2-bMRI). Eur Radiol Exp 2022;6:42.
[36] Vera-Badillo FE, Napoleone M, Ocana A, Templeton AJ, Seruga B, Al-Mubarak M, et al. Effect of multifocality and multicentricity on outcome in early stage breast cancer: a systematic review and meta-analysis. Breast Cancer Res Treat 2014;146:235–44.
[37] Oh JL, Dryden MJ, Woodward WA, Yu TK, Tereffe W, Strom EA, et al. Locoregional control of clinically diagnosed multifocal or multicentric breast cancer after neoadjuvant chemotherapy and locoregional therapy. J Clin Oncol 2006;24:4971–5.
[38] Ataseven B, Lederer B, Blohmer JU, Denkert C, Gerber B, Heil J, et al. Impact of multifocal or multicentric disease on surgery and locoregional, distant and overall survival of 6,134 breast cancer patients treated with neoadjuvant chemotherapy. Ann Surg Oncol 2015;22:1118–27.
[39] Mukhtar RA, Chau H, Woriax H, Piltin M, Ahrendt G, Tchou J, et al. Breast conservation surgery and mastectomy have similar locoregional recurrence after neoadjuvant chemotherapy: results from 1462 patients on the prospective, randomized I-SPY2 trial. Ann Surg 2023;278:320–7.
[40] Tinterri C, Barbieri E, Sagona A, Bottini A, Canavese G, Gentile D. De-escalation surgery in cT3-4 breast cancer patients after neoadjuvant therapy: predictors of breast conservation and comparison of long-term oncological outcomes with mastectomy. Cancers (Basel) 2024;16.
[41] Krug D, Vladimirova V, Untch M, Kuhn T, Schneeweiss A, Denkert C, et al. 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. Breast 2024;74:103701.
[42] Hamid SA, Bakkila B, Schultz KS, Grimshaw AA, Gunderson CG, Godfrey EL, et al. "Peace of mind" after mastectomy: a scoping review. Ann Surg Oncol 2024;31:5168–79.