

Neoadjuvant Therapy in Nonmetastatic Breast Cancer in Kurdistan, Iraq

Karez Sarbast Namiq, MBChB¹ and Luqman Rahman Sulaiman, MD, MSc, PhD¹

PURPOSE The core management of nonmetastatic breast cancer includes surgical tumor removal by either breast-conserving surgery (BCS) or mastectomy. The use of neoadjuvant chemotherapy (NACT) has shown the potential to downstage locally advanced breast cancer (LABC) and reduce the extent of breast or axillary surgery. This study aimed to assess the treatment approach for nonmetastatic breast cancer in the Kurdistan region of Iraq and to compare its alignment with the current international recommendations for cancer treatment.

METHODS We retrospectively reviewed the records of 1,000 patients with prespecified eligible inclusion criteria who underwent either BCS or mastectomy for nonmetastatic invasive breast cancer at oncology centers in the Kurdistan region of Iraq between the period 2016 and 2021.

RESULTS Of 1,000 patients (median age, 47 years [range, 22-85 years]), 60.2% underwent mastectomy and 39.8% underwent BCS. The proportion of patients treated with NACT has increased over time, with 8.3% of patients receiving neoadjuvant treatment in 2016 compared with 14.2% in 2021. Similarly, BCS increased from 36.3% in 2016 to 43.7% in 2021. Most patients who underwent BCS had early breast cancer with low nodal involvement burden.

CONCLUSION The increasing trends of BCS practice in LABC along with the increased use of NACT in the Kurdistan region in recent years comply with international guidelines. Our large multicenter, real-life series emphasizes the need to implement and discuss more conservative surgical approaches, enhanced with the broader use of NACT, through education and information programs for health providers and patients, in the context of multidisciplinary team discussions, to deliver high-quality, patient-centric breast cancer care.

JCO Global Oncol 9:e2200276. © 2023 by American Society of Clinical Oncology

Licensed under the Creative Commons Attribution 4.0 License 

INTRODUCTION

Breast cancer is one of the most common cancers worldwide and the most commonly diagnosed malignancy in women, internationally.¹ The International Agency for Research on Cancer states that breast cancer represents one in four cancer types diagnosed in women, with an estimated 2,261,419 (24.5%) new breast cancer cases diagnosed in 2020.² Cancer is the main cause of death in Eastern Mediterranean Region countries, including Iraq.³ In 2020, breast cancer accounted for 22.2% of all recently detected cancers, 37.9% of female malignancies, and 15.3% of cancer-related deaths among Iraqi female patients,⁴ similar in incidence to Syria, the United Arab Emirates, and Jordan.²

Locally advanced breast cancer (LABC) is a heterogeneous group of breast tumors with a locoregional spread that may be operable (stages IIB and IIIA) or potentially inoperable (stages IIIB and IIIC) without any clinicoradiologic evidence of metastasis.⁵ The lack of breast

health care education in developing countries leads to the advanced stages of breast cancer. In Iraq and our region, a majority of population is diagnosed at a later stage.⁶⁻⁸

Breast cancer management involves a multidisciplinary approach. Pretherapeutic staging is based on a multitude of triple assessments of palpable breast lumps, including clinical examinations, imaging, and laboratory techniques.^{9,10} Histologic diagnosis and pathologic evaluation of essential markers, such as hormone receptors (HRs) and human epidermal growth factor receptor 2 (HER2), are critical for breast cancer treatment.^{9,11}

For women with LABC, multimodal treatments aim to optimize locoregional disease control and eradicate occult systemic metastases. Neoadjuvant therapy was first introduced in the 1970s.¹² Neoadjuvant chemotherapy (NACT) is defined as the administration of chemotherapy before definitive surgery, which is now widely used for patients with early- and locally

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on February 10, 2023 and published at ascopubs.org/journal/go on May 22, 2023; DOI <https://doi.org/10.1200/GO.22.00276>

CONTEXT

Key Objective

To examine clinical trends in breast cancer care in the Kurdistan Region of Iraq.

To review the local stage distribution and treatment methods for patients with nonmetastatic breast cancer.

To identify shifts in the therapeutic paradigm and assess adherence to international guidelines.

Knowledge Generated

This study, comprising a large series of 1,000 patients, provides a comprehensive assessment of breast cancer care in the Kurdistan Region of Iraq. The study reveals a gradual but significant shift in the therapeutic paradigm toward conservative breast surgery due to increased usage of neoadjuvant therapy. However, the majority of patients continue to undergo radical surgery, even when they could be candidates for breast-conserving surgery. The study also highlights the lack of adherence to international guidelines with respect to neoadjuvant therapy and the absence of multidisciplinary discussion in treatment decision making.

Relevance

This study sheds light on the current state of breast cancer care in the Kurdistan Region of Iraq and provides important insights for healthcare professionals and policymakers in the region. The findings underscore the need for greater adherence to international guidelines, including the implementation of neoadjuvant therapy and multidisciplinary discussion in treatment decision making. The study highlights the potential for conservative breast surgery to be more widely adopted, leading to improved patient outcomes and quality of life. Finally, this study highlights the need for continued research in this area to further optimize breast cancer care in the Kurdistan Region of Iraq.

advanced-stage breast cancer.¹³ NACT is usually followed by locoregional management and has been successfully used in clinical practice to minimize the extent of breast surgery, downstaging, and shrinking tumor size.^{11,14,15} Another benefit of NACT is the opportunity to de-escalate axillary nodal surgery.¹⁶

Neoadjuvant treatment is becoming the standard approach in many institutes and is usually offered to younger patients, clinically large tumor sizes, and node-positive, multifocal, and multicentric breast cancer. In addition, patients with triple-negative or HER2-positive breast cancer are usually recommended to be treated with NACT.¹⁷

For eight decades, radical mastectomy has been the only option for breast cancer surgery.¹⁸ In 1969, the term quadrantectomy was approved by the World Health Organization.¹⁹ Subsequently, breast-conserving surgery (BCS) plus adjuvant radiation therapy has been proven to be equivalent to mastectomy.²⁰ Since then, the standard surgical procedures for breast cancer management have included either BCS or mastectomy with axillary dissection.²¹

The LABC management is complex²² and requires all appropriate specialties in a multidisciplinary team (MDT), including radiologists; pathologists; surgical, medical, and radiation oncologists; gynecologists; oncology psychologists; social workers; nursing teams; nutritionists; and palliative care specialists.²³ Once a patient has been identified for NACT, a multimodal radiologic assessment before and during NACT is essential to assess tumor response.²³ Pre-therapy radiologic marker clips can be placed in the breast and any biopsy-proven positive nodes to help the surgeon to locate the tumor during the surgery and have less extensive axillary lymph node dissection (ALND).²⁴

Unlike most cancer treatment programs worldwide that prioritize BCS in the early cancer stages, mastectomy is widely embraced over BCS in our region, regardless of the breast cancer stage at the time of diagnosis.²⁵ Globally, studies have provided an elaborate comparison of BCS and mastectomy to encourage patients with breast cancer to consider BCS in breast cancer management as an equally beneficial treatment option while considering mastectomy in advanced stages of the disease.^{26,27}

The aim of our study was to assess the treatment approaches in patients with nonmetastatic breast cancer with regard to the administration of NACT and its effects on surgical practice in the Kurdistan region of Iraq and compare it with the current international guidelines. Because most patients with advanced breast cancer are still treated outside the MDT, our work intends to report the status of breast cancer treatment in the Kurdistan region of Iraq and advocates for an evidence-informed and MDT approach to deliver individualized, patient-centric shared treatment decision making.

METHODS

Patient Selection

This retrospective cohort study was based on data obtained from the medical records of female patients with breast cancer treated in oncology centers located in the Kurdistan region of Iraq. These centers include Nanakali Hospital for Blood Diseases and Cancer (Erbil), Rizgary Hospital (Erbil), Hiwa Hospital (Sulaymaniyah), and Azadi Teaching Hospital (Duhok).

This study included 1,000 patients with breast cancer diagnosed with primary, previously untreated, noninflammatory breast cancer (American Joint Committee on Cancer [AJCC] stage groups I, II, IIIA, and IIIC disease at

diagnosis⁵) from the abovementioned oncology centers between January 2016 and December 2021.

Male patients with breast cancer with evidence of metastatic disease at presentation, locally recurrent disease, skin invasion, or T4 disease and those lacking clinical and/or histopathologic data were excluded. Patients with rare histologic subtypes (phyllodes tumor, breast sarcoma, and primary lymphoma of the breast) were also excluded.

Patients with conditions that would contraindicate radiation therapy, such as connective tissue disorders and a history of radiotherapy in the breast area, were excluded from this study.

The following clinicopathologic information was obtained and reviewed from the patient’s medical records:

1. Age at diagnosis, body surface area, and menopausal status.
2. Breast cancer molecular subtypes according to the 2013 St Gallen consensus.²⁸
3. Tumor histology, grade, and tumor node metastasis staging were based on the AJCC Cancer Staging Manual, Eighth Edition.⁵

4. Local and systemic therapies, use of neoadjuvant systemic therapy, and chemotherapy with or without targeted therapy. Adjuvant systemic therapy, chemotherapy, targeted therapy, radiotherapy, and endocrine therapy.
5. Surgical approaches, that is, mastectomy or breast conservation surgery.
6. ALND or sentinel lymph node biopsy (SLNB).

Confidentiality and Ethical Approval

All the identifying variables of the participants were removed. This study was approved by the Ethics Committee of the Ministry of Higher Education and Scientific Research, Hawler Medical University (approval No. 2/1466; May 17, 2021). Written informed consent was obtained from the participating hospitals to access patients’ medical records. This was a low-risk investigation, and data were only collected as anonymized and presented as grouped; therefore, consent from a single patient was not requested on the basis of the local ethical policies on the medical research matter and conditions of the Ministry of Health approval.

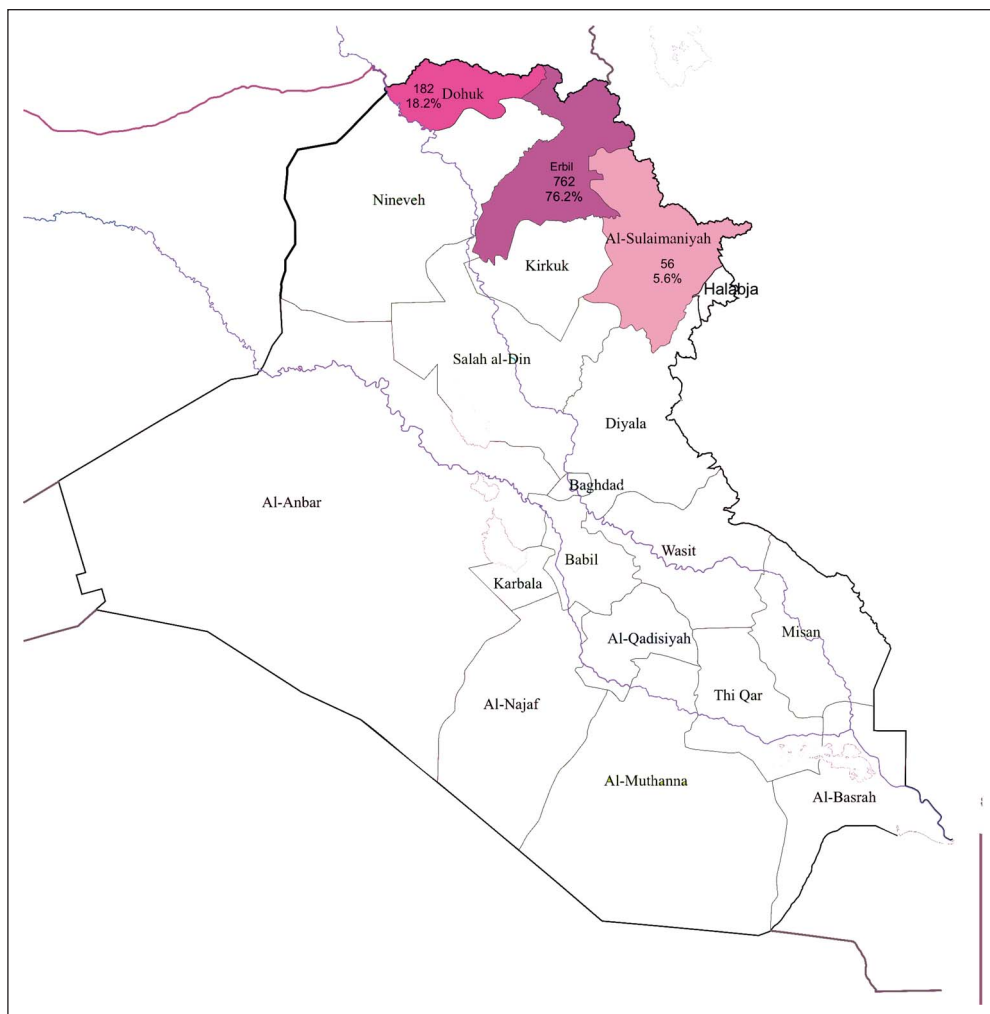


FIG 1. Iraq map showing the 18 Iraqi provinces including Erbil, Dohuk, and Sulaymaniyah, where the patients included in our study were diagnosed and treated from 2016 to 2021.

TABLE 1. Patient and Tumor Characteristics

Clinicopathologic and Treatment Parameters	Year of Diagnosis						Total
	2016	2017	2018	2019	2020	2021	
All patients	157 (100)	117 (100)	150 (100)	175 (100)	204 (100)	197 (100)	1,000 (100)
Age at breast cancer diagnosis (age categories), years							
<40	36 (22.9)	26 (22.2)	36 (24)	37 (21.1)	44 (21.6)	37 (18.8)	216 (21.6)
40-49	59 (37.6)	50 (42.7)	46 (30.7)	68 (38.9)	70 (34.3)	65 (33)	358 (35.8)
50-59	34 (21.7)	18 (15.4)	40 (26.7)	39 (22.3)	53 (26)	56 (28.4)	240 (24)
60-69	23 (14.6)	19 (16.2)	23 (15.3)	25 (14.3)	28 (13.7)	26 (13.2)	144 (14.4)
70-79	5 (3.2)	4 (3.4)	5 (3.3)	6 (3.4)	8 (3.9)	13 (6.6)	41 (4.1)
≥80	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.5)	0 (0)	1 (0.1)
Menopausal status							
Premenopausal	99 (63.1)	79 (67.5)	90 (60)	114 (65.1)	119 (58.3)	117 (59.4)	618 (61.8)
Postmenopausal	58 (36.9)	38 (32.5)	60 (40)	61 (34.9)	85 (41.7)	80 (40.6)	382 (38.2)
FNAC/biopsy							
FNAC	15 (9.6)	17 (14.5)	9 (6)	14 (8)	14 (6.9)	11 (5.6)	80 (8)
Biopsy	142 (90.4)	100 (85.5)	141 (94)	161 (92)	190 (93.1)	186 (94.4)	920 (92)
Tumor histology, invasive cancers only							
IDC	148 (94.3)	101 (86.3)	135 (90)	147 (84)	181 (88.7)	178 (90.4)	890 (89)
ILC	6 (3.8)	8 (6.8)	11 (7.3)	17 (9.7)	11 (5.4)	13 (6.6)	66 (6.6)
IDC and ILC	2 (1.3)	7 (6)	3 (2)	8 (4.6)	9 (4.4)	4 (2)	33 (3.3)
Mixed	1 (0.6)	1 (0.9)	1 (0.7)	3 (1.7)	3 (1.5)	2 (1)	11 (1.1)
AJCC stage group at diagnosis							
IA	16 (10.2)	10 (8.5)	17 (11.3)	24 (13.7)	28 (13.7)	31 (15.7)	126 (12.6)
IB	0 (0)	1 (0.9)	2 (1.3)	0 (0)	0 (0)	0 (0)	3 (0.3)
IIA	47 (29.9)	34 (29.1)	46 (30.7)	42 (24)	63 (30.9)	60 (30.5)	292 (29.2)
IIB	35 (22.3)	26 (22.2)	46 (30.7)	54 (30.9)	66 (32.4)	44 (22.3)	271 (27.1)
IIIA	38 (24.2)	35 (29.9)	27 (18)	32 (18.3)	31 (15.2)	36 (18.3)	199 (19.9)
IIIC	21 (13.4)	11 (9.4)	12 (8)	23 (13.1)	16 (7.8)	26 (13.2)	109 (10.9)
Hormone receptor status							
Negative	18 (11.5)	12 (10.3)	13 (8.7)	18 (10.3)	30 (14.7)	36 (18.3)	127 (12.7)
Positive	139 (88.5)	105 (89.7)	137 (91.3)	157 (89.7)	174 (85.3)	161 (81.7)	873 (87.3)
HER2 status							
Positive	36 (22.9)	26 (22.2)	31 (20.7)	37 (21.1)	44 (21.6)	34 (17.3)	208 (20.8)
Negative	112 (71.3)	79 (67.5)	105 (70)	123 (70.3)	136 (66.7)	139 (70.6)	694 (69.4)
Positive by FISH/CISH	5 (3.2)	2 (1.7)	5 (3.3)	5 (2.9)	3 (1.5)	6 (3)	26 (2.6)
Negative by FISH/CISH	4 (2.5)	10 (8.5)	9 (6)	10 (5.7)	21 (10.3)	18 (9.1)	72 (7.2)
Ki67 expression							
≤14	78 (49.7)	58 (49.6)	60 (40)	81 (46.3)	106 (52)	94 (47.7)	477 (47.7)
>14	79 (50.3)	59 (50.4)	90 (60)	94 (53.7)	98 (48)	103 (52.3)	523 (52.3)
Molecular subtype							
Luminal A	64 (40.8)	50 (42.7)	49 (32.7)	64 (36.6)	87 (42.6)	72 (36.5)	386 (38.6)
Luminal B	49 (31.2)	32 (27.4)	60 (40)	64 (36.6)	58 (28.4)	63 (32)	326 (32.6)
HER2-enriched	37 (23.6)	27 (23.1)	33 (22)	38 (21.7)	43 (21.1)	38 (19.3)	216 (21.6)
Triple-negative	7 (4.5)	8 (6.8)	8 (5.3)	9 (5.1)	16 (7.8)	24 (12.2)	72 (7.2)

(Continued on following page)

TABLE 1. Patient and Tumor Characteristics (Continued)

Clinicopathologic and Treatment Parameters	Year of Diagnosis						Total
	2016	2017	2018	2019	2020	2021	
Breast surgery							
Mastectomy	100 (63.7)	73 (62.4)	90 (60)	105 (60)	123 (60.3)	111 (56.3)	602 (60.2)
BCS	57 (36.3)	44 (37.6)	60 (40)	70 (40)	81 (39.7)	86 (43.7)	398 (39.8)
Treatment							
Adjuvant	144 (91.7)	103 (88)	134 (89.3)	157 (89.7)	180 (88.2)	169 (85.8)	887 (88.7)
Neoadjuvant	13 (8.3)	14 (12)	16 (10.7)	18 (10.3)	24 (11.8)	28 (14.2)	113 (11.3)
Treatment options							
No therapy	0 (0)	0 (0)	1 (0.7)	1 (0.6)	0 (0)	2 (1)	4 (0.4)
Hormonal therapy	14 (8.9)	8 (6.8)	11 (7.4)	19 (10.9)	36 (17.6)	20 (10.2)	108 (10.8)
Chemotherapy	15 (9.6)	12 (10.3)	17 (11.4)	18 (10.3)	30 (14.7)	34 (17.3)	126 (12.6)
Chemotherapy > hormonal therapy	128 (81.5)	97 (82.9)	120 (80.5)	137 (78.3)	138 (67.6)	141 (71.6)	761 (76.2)

NOTE. Data are No. (%).

Abbreviations: AJCC, American Joint Committee on Cancer; BCS, breast-conserving surgery; CISH, chromogenic in situ hybridization; FISH, fluorescence in situ hybridization; FNAC, fine-needle aspiration cytology; HER2, human epidermal growth factor receptor 2; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

Statistical Analysis

The results were analyzed using the Statistical Package for Social Sciences (SPSS v26). Differences in patient age at breast cancer diagnosis, stage, lymph node status, and tumor characteristics were assessed using the chi-square test after categorical subdivision. A *P* value <.05 was regarded as statistically significant.

RESULTS

Patient and Tumor Characteristics

In the present study, after excluding missing data, 1,000 female patients from Erbil, Duhok, and Sulaymaniyah (Fig 1) who met the inclusion criteria in the specified period (2016-2021) were recruited.

The patient characteristics are summarized in Table 1. The median age at diagnosis was 47 years (range, 22-85 years). Patient age was categorized into groups <40 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, and ≥80 years. Most patients (35.8%) were age 40-49 years, one patient was

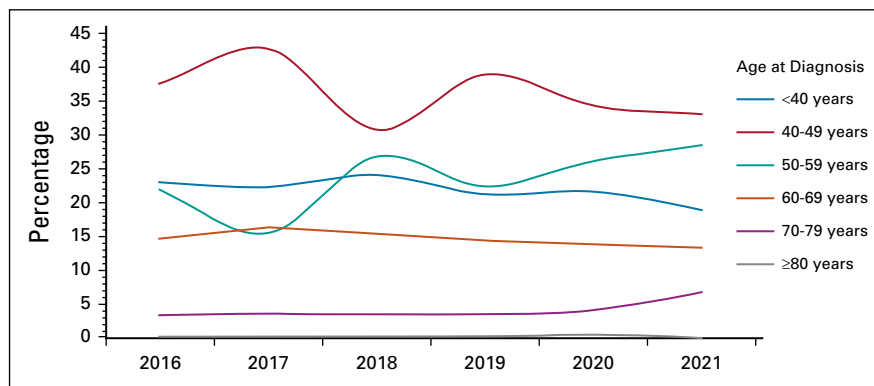
older than 80 years, and approximately one fourth (22%) of the patients were younger than 40 years (Fig 2).

A majority of patients (61.9%) were premenopausal at the time of diagnosis, whereas the remaining (38.1%) were postmenopausal. For patients with BMI data available for analysis (652 patients in total), more than half of them (54.8%) had a mean BMI of 30.4 kg/m².

Tru-cut biopsy was the most common method of pathologic diagnosis performed in 92% of the patients, which is of particular importance in the setting of NACT, whereas fine-needle aspiration cytology alone was used for cancer diagnosis in only 80 patients. Invasive ductal carcinoma was the most prominent histopathologic subtype, accounting for approximately 89% of all cases. The remaining histology represented a small percentage of invasive lobular carcinoma (6.6%) and mixed histology (4.4%).

HR (estrogen receptor [ER] and/or progesterone receptor [PR]) positivity was demonstrated in 87.3% of the patients (Table 1). Furthermore, HER2-overexpressing tumors (3+ by

FIG 2. Age group distribution during 2016-2021.



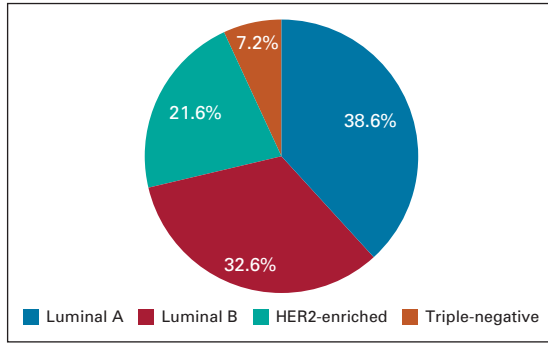


FIG 3. Immunohistochemical breast cancer subtype. HER2, human epidermal growth factor receptor 2.

immunohistochemistry or amplified by in situ hybridization) were observed in 23.4% of patients. The molecular subtype categorization was as follows: luminal A (HR-positive, HER2-negative, and Ki-67 $\leq 14\%$) and luminal B (HR-positive, HER2-negative, and Ki-67 $> 14\%$) were the most common molecular subtypes reported in 38.6% and 32.6% of cases, respectively, whereas approximately 22% had HER2-enriched disease. Triple-negative breast cancer (TNBC; HR-negative, HER2-negative) was the least common cancer and was reported in only 7.2% of the study population (Fig 3). Ki67 was high (> 14) in 52.3% and low (≤ 14) in 47.7% (Table 1).

Among the total cases included in this study, approximately 13% had stage I disease (12.6% stage IA, 0.3% stage IB), 563 (56.3%) were diagnosed with stage II disease (29.2% stage IIA, 27.1% stage IIB), and 308 (30.8%) had stage III disease (19.9% stage IIIA, 10.9% stage IIIC; Fig 4). Both stages IIA and B were associated with higher ER- and PR-positive luminal A tumors (10.4% and 10.8%, respectively; Fig 5).

Overall, 887 (88.7%) patients were administered adjuvant treatment and 113 (11.3%) patients received NACT (Fig 6). The use of adjuvant chemotherapy has decreased over time, particularly in women with HR-positive breast cancers. In total, 78.8% of patients received radiotherapy.

Patient Characteristics and Definitive Surgery Information

In this study, female patients with breast cancer were classified into two groups: patients who underwent BCS followed by adjuvant radiotherapy and those who were elected for mastectomy. We evaluated both groups with regard to patient and disease characteristics, including age, BMI, tumor differentiation, pathologic type, molecular subtype, and site and location of the primary tumor within the breast; no significant differences were identified. Approximately 60% of patients underwent mastectomy, whereas the remaining (approximately 40%) patients underwent BCS (Table 2).

In this study, 51.6% of the women had tumors in the left breast. The primary tumor sites within the breast varied, with the highest frequency in the upper outer quadrant observed in 75.6% of the cases and the lowest frequency in the lower inner quadrant at 4.2% (Fig 7).

All the patients in this study underwent axillary lymph node staging. This was performed by either ALND or SLNB. In total, 94% of the patients underwent ALND upfront or after a positive SLNB and approximately 60% of the patients underwent mastectomy, compared with 34% of the patients who underwent BCS. Thirty-four patients with SLN-positive tumors underwent complete ALND. SLNB, without complete dissection, was performed in 64 patients.

Characteristics of the Patient With Locally Advanced Breast Cancer

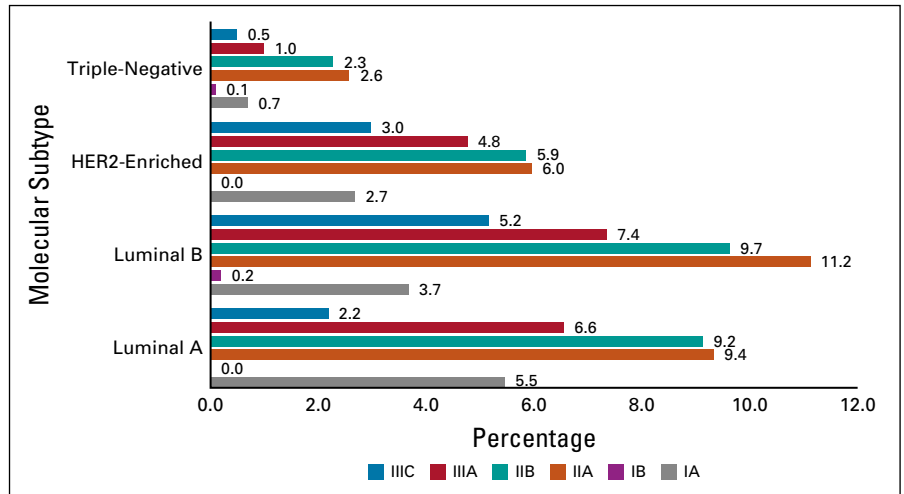
This study included 113 patients treated with NACT followed by breast surgery (Fig 8). T1 tumors accounted for 6%, T2 for 72%, and T3 for 22%. Regarding the clinical lymph node status, 13.2% were N0, 53.1% were N1, 21.2% were N2, and 12.3% were N3. Among the patients in the BCS group, a larger proportion (67.3%) were premenopausal, whereas 41.9% were postmenopausal in the mastectomy group.

Most patients with LABC were treated with primary surgery followed by adjuvant chemotherapy (83.5%), and the rest with NACT, among whom only 31 (27.4%) had undergone

FIG 4. AJCC stage group at diagnosis. AJCC, American Joint Committee on Cancer; N, node; N1mi, micrometastasis of ≥ 2 mm to 1 axillary node; T, tumor.

	T1	T2	T3	Total
N0	Stage IA: 12.6%	Stage IIA: 23.6%	Stage IIB: 1.9%	38.1%
N1mi	Stage IB: 0.3%	Stage IIB: 24.7%	Stage IIIA: 2.9%	33.6%
N1	Stage IIA: 5.7%			
N2	Stage IIIA: 2.3%	Stage IIIA: 11.1%	Stage IIIA: 3.9%	17.3%
N3	Stage IIIC: 0.7%	Stage IIIC: 7.6%	Stage IIIC: 2.7%	11.0%
Total	21.6%	67.0%	11.4%	100.0%

FIG 5. Distribution of molecular subtypes according to the stage of the disease. HER2, human epidermal growth factor receptor 2.



BCS compared with 82 (72.6%) who had undergone mastectomy (Fig 8).

Most patients who underwent BCS had operable LABC (cT2N1, 36.9%). The corresponding proportion of those who underwent mastectomy was 24%; 81 patients who received NACT underwent axillary dissection in the mastectomy group, and 29 patients who received NACT underwent axillary dissection in the BCS group.

A total of 68 patients received taxane- and anthracycline-based chemotherapy courses, whereas 45 patients with HER2-enriched cancer received chemotherapy plus target therapies, of whom eight patients received dual blockade anti-HER2 therapy; of them, six patients achieved pathologic complete response (pCR). The overall pCR rate in

patients who received NACT was 29.2%. By contrast, 70.8% of the patients had a partial response on the basis of clinical criteria (tumor shrinkage, as reported by clinicians in the medical records).

In total, 62% of the breast surgeries were performed by general surgeons, and 38% by breast surgeons. Approximately 48% of patients who received NACT underwent BCS performed by a breast surgeon (Table 2).

DISCUSSION

Breast cancer is the most common cancer among women worldwide and in Iraq.²⁹ It is currently diagnosed and treated at an early stage in most developed countries.³⁰ There are still great disparities in clinicopathologic profiles,

FIG 6. Local and systemic therapy patterns according to the stage of the disease.

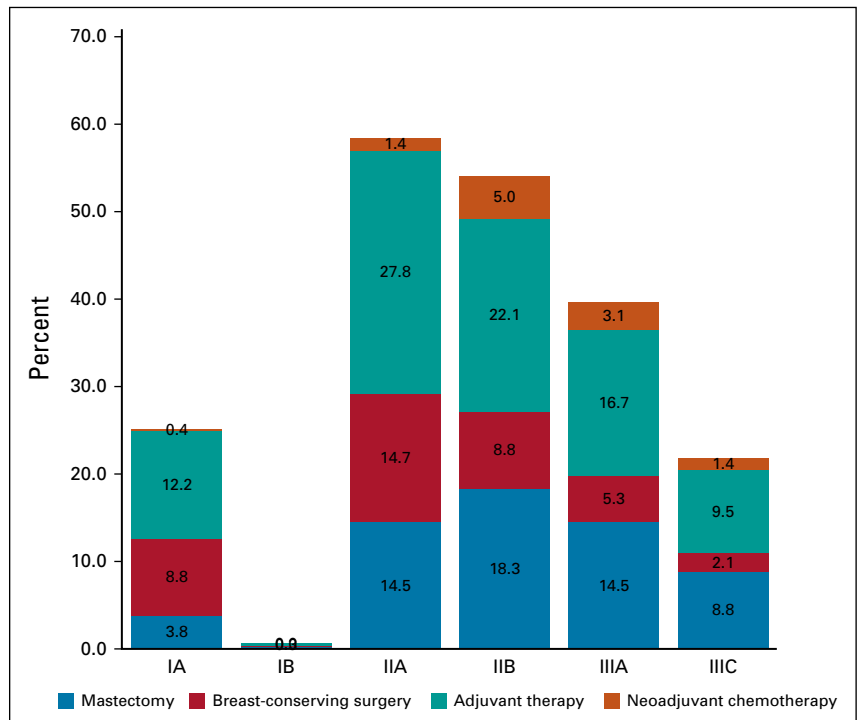


TABLE 2. Clinicopathologic Features According to the Surgical Method

Characteristic	Surgery Type		
	Surgical Procedure, No. (%)		
	Mastectomy 602 (100)	Breast-Conserving Surgery 398 (100)	Total, No. (%) 1,000 (100)
Site			
Right	283 (47.1)	186 (46.7)	469 (46.9)
Left	307 (51.1)	209 (52.5)	516 (51.7)
Bilateral	11 (1.8)	3 (0.8)	14 (1.4)
Menopausal status			
Premenopausal	350 (58.1)	268 (67.3)	618 (61.8)
Postmenopausal	252 (41.9)	130 (32.7)	382 (38.2)
Axillary procedure			
ALND	571 (57.2)	330 (33.)	901 (90.2)
SLNB	11 (1.1)	53 (5.3)	64 (6.4)
ALND + SLNB	19 (1.9)	15 (1.5)	34 (3.4)
Bloom and Richardson grade ^a			
1	21 (3.5)	40 (10.1)	61 (6.1)
2	392 (65.2)	229 (57.5)	621 (62.2)
3	188 (31.3)	129 (32.4)	317 (31.7)
Morphology			
IDC	525 (87.4)	364 (91.5)	889 (89.0)
ILC	46 (7.7)	20 (5.0)	66 (6.6)
IDC and ILC	22 (3.7)	11 (2.8)	33 (3.3)
Mixed	8 (1.3)	3 (0.8)	11 (1.1)
Tumor stage			
T1	82 (13.6)	134 (33.7)	216 (21.6)
T2	427 (71.0)	243 (61.1)	670 (67.1)
T3	92 (15.3)	21 (5.3)	113 (11.3)
Nodal stage			
N0	171 (28.5)	210 (52.8)	381 (38.1)
N1	219 (36.4)	116 (29.1)	335 (33.5)
N2	122 (20.3)	51 (12.8)	173 (17.3)
N3	89 (14.8)	21 (5.3)	110 (11.0)
Tumor focality			
Unifocal	508 (84.5)	380 (95.5)	889 (88.9)
Multifocal	93 (15.5)	18 (4.5)	111 (11.1)
Stage at diagnosis			
IA	38 (6.3)	88 (22.1)	126 (12.6)
IB	2 (0.3)	1 (0.3)	3 (0.3)
IIA	145 (24.1)	147 (36.9)	292 (29.2)
IIB	183 (30.4)	88 (22.1)	271 (27.1)
IIIA	145 (24.1)	53 (13.3)	198 (19.8)
IIIC	88 (8.8)	21 (2.1)	109 (10.9)
ER status			
Positive	515 (85.7)	347 (87.2)	862 (86.3)
Negative	86 (14.3)	51 (12.8)	137 (13.7)

(Continued on following page)

TABLE 2. Clinicopathologic Features According to the Surgical Method (Continued)

Characteristic	Surgery Type		
	Surgical Procedure, No. (%)		Total, No. (%)
	Mastectomy	Breast-Conserving Surgery	
	602 (100)	398 (100)	1,000 (100)
PR status			
Positive	504 (83.9)	338 (84.9)	842 (84.3)
Negative	97 (16.1)	60 (15.1)	157 (15.7)
HER2 status			
Positive	140 (23.3)	68 (17.1)	208 (20.8)
Negative	410 (68.2)	283 (71.1)	693 (69.4)
Positive by FISH/CISH	12 (2.0)	14 (3.5)	26 (2.6)
Negative by FISH/CISH	39 (6.5)	33 (8.3)	72 (7.2)
Molecular subtype			
Luminal A	226 (37.5)	160 (40.2)	386 (38.6)
Luminal B	194 (32.2)	132 (33.2)	326 (32.6)
HER2-enriched	138 (22.9)	78 (19.6)	216 (21.6)
Triple-negative	44 (7.3)	28 (7.0)	72 (7.2)
Treatment			
Adjuvant	520 (86.4)	367 (92.2)	887 (88.7)
Neoadjuvant	82 (13.6)	31 (7.8)	113 (11.3)
Surgeon			
Breast surgeon	215 (35.7)	165 (41.5)	379 (38)
General surgeon	387 (64.3)	233 (58.5)	620 (62)

Abbreviations: ALND, axillary lymph node dissection; CISH, chromogenic in situ hybridization; ER, estrogen receptor; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; N, node; PR, progesterone receptor; SLNB, sentinel lymph node biopsy; T, tumor.

^aDefined using the modified Bloom-Richardson system. Patients with lower grades have a better prognosis.

stage at presentation, and treatment approaches for patients with breast cancer in developing countries.^{31,32}

In the current study, LABC constituted approximately 58% of the new breast cancer cases in the Kurdistan region of Iraq, which is in agreement with other studies from developing countries.³³ Previously published studies from Iraq conducted in 2016 and 2018 reported an incidence of advanced breast cancer stages at diagnosis of 47% and 67%, respectively.^{34,35} A recently published local study reported (46%) advanced-stage disease at presentation.³⁶ This delayed presentation could be explained by various factors such as lack of education, poor awareness of cancer, lack of population screening programs, cultural barriers, and poor socioeconomic status.^{37,38}

This study investigated the treatment approach in patients with LABC and found that 56% of women, most of whom (84%) underwent surgery first and 16% received neoadjuvant therapy. Most patients who received NACT underwent mastectomy, 82 (72.6%), rather than BCS, 31 (27.4%). Unfortunately, modified radical mastectomy

remains the standard surgical approach in Iraq and other Arab countries.^{34,39-41}

Trends in the use of BCS in our study have increased from 36.3% in 2016 to 43.7% in 2021. Many studies have reported that NACT reduces mastectomy rates. In the BrighTNess randomized clinical trial, more than 50% of the patients became BCS-eligible after NACT.⁴² In New York, 69% became BCS candidates between 2013 and 2019 at the Memorial Sloan Kettering Cancer Center.⁴³ The BCS rate increased from 40.4% to 62.6% in a prospective study conducted in Seoul, Korea, between 2014 and 2015.⁴⁴ In the Netherlands, BCS increased from 43% to 57% between 2011 and 2016.⁴⁵

In this study, 113 patients with breast cancer were treated with NACT. The proportion of patients treated with NACT has increased over time, from 13 (8.3%) in 2016 to 28 (14.2%) in 2021, in line with international trends.⁴⁶ Currently, systemic treatment is customized according to each breast cancer subtype and has moved toward NACT rather than adjuvant chemotherapy.⁴⁷ The highest use of NACT was in HER2-enriched and TNBC in approximately 44% of

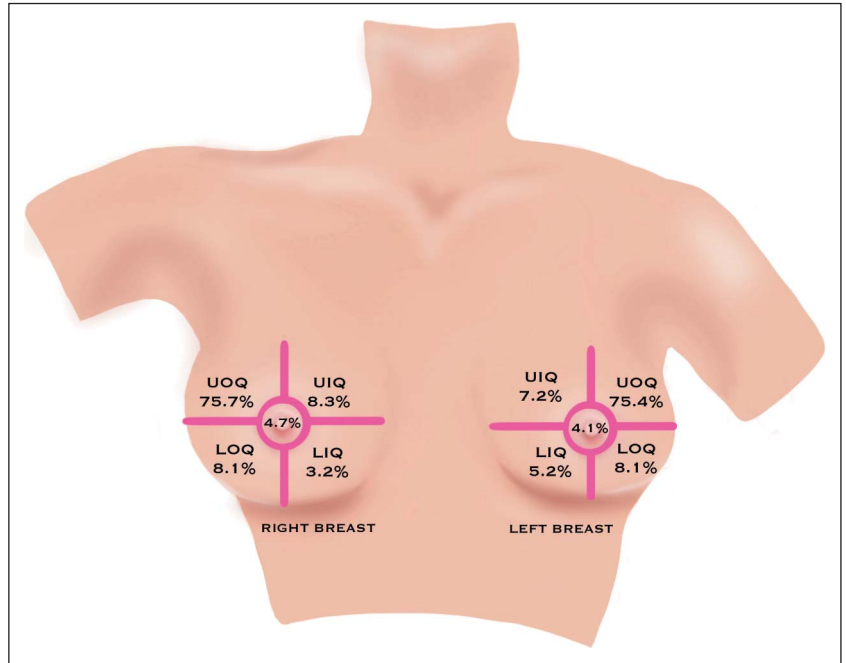


FIG 7. Site of primary tumor. LIQ, lower inner quadrant; LOQ, lower outer quadrant; UIQ, upper inner quadrant; UOQ, upper outer quadrant.

the patients, whereas luminal types constituted 55.7% of the patients. The Ki-67 proliferation index was >14 in 73.4% of the patients.

Response to NACT was evaluated clinically, radiologically, and pathologically. Preoperative clinical and radiologic response evaluations were also performed. Although computed tomography and magnetic resonance imaging are best for evaluating the response to NACT owing to cost considerations, the response was measured clinically by physical examination and radiologically by ultrasonography. The pathologic response was assessed by measuring the tumor and lymph node sizes after NACT using the RECIST guidelines (version 1.1).⁴⁸

The prognostic value of pCR after NACT depends on the molecular subtype of breast cancer⁴⁹; TNBC and HER2-enriched patients have higher pCR rates than luminal breast cancer.⁵⁰ Thirty-three (29.2%) patients achieved

pCR, 9 (7.9%) had luminal breast cancer, 21 (18.6%) had HER2 overexpression tumors, and 3 (2.7%) had TNBC.^{51,52}

Studies have shown an increase in the BCS rate after neoadjuvant treatment and because of the gradual expansion of treatment options to less toxic-targeted therapies.¹⁴ The conversion rate from mastectomy to BCS was more than 50% after NACT plus dual-target therapy in the Asian population.⁵³ In our data, of 45 patients who received NACT plus target therapies, eight patients received dual blockade anti-HER2 therapy and six patients achieved pCR and then were treated with BCS.

Currently, the use of neoadjuvant therapy is associated with a lower need for extensive axillary lymph node treatment, especially for those who achieve axillary lymph node downstaging.⁵⁴ Although all the patients included in our study underwent axillary surgery, the majority of them had ALND (94%) and only a minority had SLNB (6%),

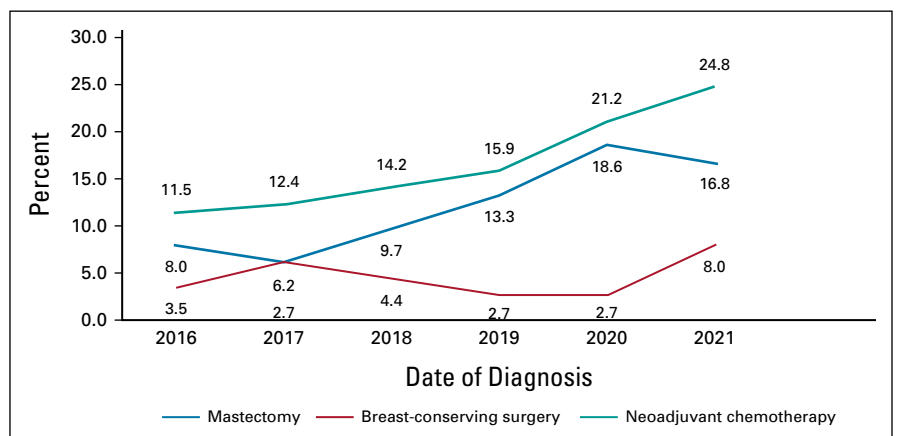


FIG 8. Correlation between neoadjuvant chemotherapy use and the breast surgery type during the period 2016-2021.

which further reflects the need for practice change in our region toward less aggressive axillary lymph node staging. The advantage of SLNB is that it reduces the number of lymph nodes removed, limits ALND surgical complications, and does not affect survival as the AMAROS trial confirmed that.⁵⁵

Surgeon preference appears to play a significant role in the selection of patients for neoadjuvant therapy. In total, 62% of breast surgeries were performed by general surgeons and 38% were performed by breast surgeons. Among the total number of patients who received NACT and underwent BCS, 48% of them were treated by a breast surgeon.

In the current study, some factors such as the patient's choice and whether the surgeon discussed the possible surgical approach could not be assessed. In addition, none of these patients were discussed in a proper MDT before treatment. Furthermore, immunohistochemical analysis is not usually performed unless surgery is performed.

This study examines an important aspect of the treatment approach for 1,000 patients with breast cancer who underwent breast surgery, either mastectomy or BCS, and

received either neoadjuvant or adjuvant treatment at oncology centers in the Kurdistan region of Iraq. In this study, an effort was made to collect detailed and accurate data, making our results applicable and useful for understanding breast cancer management in this region. The most important limitation of this study was the retrospective study design with limited data on potentially important factors, such as performance status, detailed comorbidities, patients' wishes, and prior discussion of possible surgical approaches by the surgeon.

In conclusion, our study concluded that temporal trends in the timing of systemic chemotherapy delivery have changed in recent years, with the use of NACT along with BCS in LABC increasing in the Kurdistan region, in line with the international guidelines. However, in our study, mastectomy was more common than BCS. This emphasizes the urgent need to establish functional MDT to determine the best treatment approach for each breast cancer case. In addition, increasing awareness of breast cancer, effective breast cancer screening programs, and early detection are important factors in aiding to move toward BCS.

AFFILIATION

¹Department of Medicine, College of Medicine, Nanakali Hospital for Blood Diseases and Cancer, Hawler Medical University, Erbil, Iraq

CORRESPONDING AUTHOR

Karez Sarbast Namiq, MBChB, Nanakali Hospital for Blood Diseases and Cancer, AzadiQr, Erbil 44001, Iraq; Twitter: @KarezSarbast; e-mail: kareznamiq@gmail.com.

AUTHOR CONTRIBUTIONS

Conception and design: All authors

Administrative support: Luqman Rahman Sulaiman

Provision of study materials or patients: Luqman Rahman Sulaiman

Collection and assembly of data: All authors

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/go/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians ([Open Payments](http://OpenPayments)).

No potential conflicts of interest were reported.

ACKNOWLEDGMENT

All the cancer center coworkers who helped me in the process of data collection gave their valuable time to complete the process within a limited time. This work was made possible by the amazing support that I received from my supervisor, colleagues, family, and friends.

REFERENCES

1. Siegel RL, Miller KD, Jemal A: Cancer statistics, 2020. *CA Cancer J Clin* 70:7-30, 2020
2. Sung H, Ferlay J, Siegel RL, et al: Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 71:209-249, 2021
3. Alwan N: Tumor characteristics of female breast cancer: Pathological review of mastectomy specimens belonging to Iraqi patients. *World J Breast Cancer Res* 1(1):1006, 2018
4. World Health Organization, International Agency for Research on Cancer: Iraq population fact sheet, 2020. <https://gco.iarc.fr/today/data/factsheets/populations/368-iraq-fact-sheets.pdf>
5. Giuliano AE, Edge SB, Hortobagyi GN: Eighth edition of the AJCC cancer staging manual: Breast cancer. *Ann Surg Oncol* 25:1783-1785, 2018
6. Abood RA: Breast cancer in Basra Oncology Center: A clinico-epidemiological analysis. *Asian Pac J Cancer Prev* 19:2943-2946, 2018
7. Hashim HT, Ramadhan MA, Theban KM, et al: Assessment of breast cancer risk among Iraqi women in 2019. *BMC Women's Health* 21:412-419, 2021
8. Mjali A, Jawad SA, Al-Shammari HHJ: Breast cancer in middle Euphrates region of Iraq: Risk factors, presenting symptoms and time to medical help-seeking. *Asian Pac J Cancer Care* 6:243-247, 2021

9. Ditsch N, Untch M, Kolberg-Liedtke C, et al: AGO recommendations for the diagnosis and treatment of patients with locally advanced and metastatic breast cancer: Update 2020. *Breast Care* 15:294-309, 2020
10. Wong S, Rickard M, Earls P, et al: The International Academy of Cytology Yokohama System for reporting breast fine needle aspiration biopsy cytopathology: A single institutional retrospective study of the application of the system categories and the impact of rapid onsite evaluation. *Acta Cytol* 63:280-291, 2019
11. Puig CA, Hoskin TL, Day CN, et al: National trends in the use of neoadjuvant chemotherapy for hormone receptor-negative breast cancer: A National Cancer Data Base study. *Ann Surg Oncol* 24:1242-1250, 2017
12. Swain SM, Sorace RA, Bagley CS, et al: Neoadjuvant chemotherapy in the combined modality approach of locally advanced nonmetastatic breast cancer. *Cancer Res* 47:3889-3894, 1987
13. Asaoka M, Gandhi S, Ishikawa T, et al: Neoadjuvant chemotherapy for breast cancer: Past, present, and future. *Breast Cancer Basic: Clin Res* 14:1178223420980377, 2020
14. Steenbruggen TG, van Ramshorst MS, Kok M, et al: Neoadjuvant therapy for breast cancer: Established concepts and emerging strategies. *Drugs* 77:1313-1336, 2017
15. Oikawa M: The history, present situation, and future directions of neoadjuvant. *Chin Clin Oncol* 9:29, 2020
16. van der Noordaa MEM, van Duijnhoven FH, Straver ME, et al: Major reduction in axillary lymph node dissections after neoadjuvant systemic therapy for node-positive breast cancer by combining PET/CT and the MARI procedure. *Ann Surg Oncol* 25:1512-1520, 2018
17. Graham PJ, Brar MS, Foster T, et al: Neoadjuvant chemotherapy for breast cancer, is practice changing? A population-based review of current surgical trends. *Ann Surg Oncol* 22:3376-3382, 2015
18. Halsted WS: I. A clinical and histological study of certain adenocarcinomata of the breast: And a brief consideration of the supraclavicular operation and of the results of operations for cancer of the breast from 1889 to 1898 at the Johns Hopkins Hospital. *Ann Surg* 28:557-576, 1898
19. World Health Organization: Meeting of investigators for evaluation of methods of diagnosis and treatment of breast cancer: Final report. Geneva, World Health Organization, 1969
20. Lin J, Lin K-J, Wang Y-F, et al: Association of surgical margins with local recurrence in patients undergoing breast-conserving surgery after neoadjuvant chemotherapy. *BMC Cancer* 20:451, 2020
21. Franceschini G, Martin Sanchez A, Di Leone A, et al: New trends in breast cancer surgery: A therapeutic approach increasingly efficacy and respectful of the patient. *G Chir* 36:145-152, 2015
22. Untch M, Fasching PA, Haidinger R, et al: Advanced Breast Cancer: AGO Recommendations 2022—Focus on ABC6 Consensus, *Geburtshilfe Frauenheilkd* 82:1044-1054, 2022
23. Cardoso F, Kyriakides S, Ohno S, et al: Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 30:1194-1220, 2019
24. Caudle AS, Yang WT, Krishnamurthy S, et al: Improved axillary evaluation following neoadjuvant therapy for patients with node-positive breast cancer using selective evaluation of clipped nodes: Implementation of targeted axillary dissection. *J Clin Oncol* 34:1072-1078, 2016
25. Alassadi M, Alwan N: Treatment follow up in patients diagnosed with breast cancer in Iraq. *Iraqi Postgrad Med J* 19:279-286, 2020
26. Sang Y, Zhou X, Chi W, et al: Surgical options of the breast and clinical outcomes of breast cancer patients after neoadjuvant chemotherapy: A single-center retrospective study. *Front Oncol* 12:984587, 2022
27. Sun Y, Liao M, He L, et al: Comparison of breast-conserving surgery with mastectomy in locally advanced breast cancer after good response to neoadjuvant chemotherapy: A PRISMA-compliant systematic review and meta-analysis. *Medicine (Baltimore)* 96:e8367, 2017
28. Goldhirsch A, Winer EP, Coates AS, et al: Personalizing the treatment of women with early breast cancer: Highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. *Ann Oncol* 24:2206-2223, 2013
29. Republic of Iraq Ministry of Health and Environment Iraqi Cancer Board: Annual Report Iraqi Cancer Registry 2020. Baghdad, Iraq, Republic of Iraq Ministry of Health and Environment, 2021.
30. National Health Service: Cancer Registration Statistics, England 2019, NHS Digital, 2021. <https://digital.nhs.uk/data-and-information/publications/statistical/cancer-registration-statistics/england-2019/content>
31. Unger-Saldaña K: Challenges to the early diagnosis and treatment of breast cancer in developing countries. *World J Clin Oncol* 5:465-477, 2014
32. Balogun OD, Formenti SC: Locally advanced breast cancer—Strategies for developing nations. *Front Oncol* 5:89, 2015
33. Ghoncheh M, Mahdaviyar N, Darvishi E, et al: Epidemiology, incidence and mortality of breast cancer in Asia. *Asian Pac J Cancer Prev* 17:47-52, 2016
34. Alwan NAS: Breast cancer among Iraqi women: Preliminary findings from a regional comparative breast cancer research project. *J Glob Oncol* 2:255-258, 2016
35. Mutar MT, Goyani MS, Had AM, et al: Pattern of presentation of patients with breast cancer in Iraq in 2018: A cross-sectional study. *J Glob Oncol* 5:1-6, 2019
36. Ahmed A, Sheikha A, Abdulla H, et al: Breast cancer in young women: A clinicopathological hospital-based descriptive study from Kurdistan, Iraq. *Middle East J Cancer* 12:137-142, 2021
37. Odongo J, Makumbi T, Kalungi S, et al: Patient delay factors in women presenting with breast cancer in a low income country. *BMC Res Notes* 8:467, 2015
38. Birnbaum JK, Duggan C, Anderson BO, et al: Early detection and treatment strategies for breast cancer in low-income and upper middle-income countries: A modelling study. *Lancet Glob Health* 6:e885-e893, 2018
39. Abdel-Razeq H, Abdel Rahman F, Almasri H, et al: Tumor characteristics and treatment outcomes of older patients with breast cancer in Jordan. *BMC Women's Health* 20:118, 2020
40. Trabulsi NH, Shabkha AA, Ujaimi R, et al: Locally advanced breast cancer: Treatment patterns and predictors of survival in a Saudi tertiary center. *Cureus* 13:e15526, 2021
41. Saadeh S, Abdel-Razeq H: Breast cancer in the Arab world, in Al-Shamsi HO, Abu-Gheida IH, Iqbal F, et al (eds): *Cancer in the Arab World*. Singapore, Springer Singapore, 2022, pp 353-362
42. Golshan M, Loibl S, Wong SM, et al: Breast conservation after neoadjuvant chemotherapy for triple-negative breast cancer: Surgical results from the BrightNESS randomized clinical trial. *JAMA Surg* 155:e195410, 2020
43. Petruolo O, Sevilimedu V, Montagna G, et al: How often does modern neoadjuvant chemotherapy downstage patients to breast-conserving surgery? *Ann Surg Oncol* 28:287-294, 2021
44. Mo H, Kim Y, Rhu J, et al: Actual conversion rate from total mastectomy to breast conservation after neoadjuvant chemotherapy for stages II-III breast cancer patients. *Eur J Cancer* 92:S80, 2018
45. Spronk PER, Volders JH, van den Tol P, et al: Breast conserving therapy after neoadjuvant chemotherapy; data from the Dutch Breast Cancer Audit. *Eur J Surg Oncol* 45:110-117, 2019

46. Patiniott PD, Wong GYM, Lam YH, et al: Neoadjuvant chemotherapy rates for breast cancer in Australia—"Are we there yet?". *Ann Breast Surg* 3, [10.21037/abs.2019.04.01](https://doi.org/10.21037/abs.2019.04.01), 2019
 47. Murphy BL, Day CN, Hoskin TL, et al: Neoadjuvant chemotherapy use in breast cancer is greatest in excellent responders: Triple-negative and HER2+ subtypes. *Ann Surg Oncol* 25:2241-2248, 2018
 48. Eisenhauer EA, Therasse P, Bogaerts J, et al: New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *Eur J Cancer* 45:228-247, 2009
 49. Katayama A, Miligy IM, Shiino S, et al: Predictors of pathological complete response to neoadjuvant treatment and changes to post-neoadjuvant HER2 status in HER2-positive invasive breast cancer. *Mod Pathol* 34:1271-1281, 2021
 50. Al-Tweigeri T, Elshenawy M, Badran A, et al: Impact of pathologic complete response following neoadjuvant chemotherapy \pm trastuzumab in locally advanced breast cancer. *J Oncol* 2021:6639763, 2021
 51. Golshan M, Cirrincione CT, Sikov WM, 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* 262:434-439, 2015
 52. Golshan M, Cirrincione CT, Sikov WM, et al: Impact of neoadjuvant therapy on eligibility for and frequency of breast conservation in stage II-III HER2-positive breast cancer: Surgical results of CALGB 40601 (Alliance). *Breast Cancer Res Treat* 160:297-304, 2016
 53. Chang YK, Co M, Kwong A: Conversion rate from mastectomy to breast conservation after neoadjuvant dual target therapy for HER2-positive breast cancer in the Asian population. *Breast Cancer* 27:456-463, 2020
 54. Pfob A, Heil J: Breast and axillary surgery after neoadjuvant systemic treatment—A review of clinical routine recommendations and the latest clinical research. *Breast* 62:S7-S11, 2022
 55. Donker M, van Tienhoven G, Straver ME, et al: Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): A randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol* 15:1303-1310, 2014
-