

Original article

## Comparison of Survival Outcomes between Modified Radical Mastectomy and Breast Conserving Surgery in Libyan Women with Early Breast Cancer

Doaa Ahmed<sup>1\*</sup>, Rodaba Bitrou<sup>2</sup>, Najat Alrumerayh<sup>2</sup>, Enas Ramih<sup>3</sup>, Mohamed Emhemed<sup>2</sup>, Abdalla Juwid<sup>1</sup>, Abdussalam Sahoub<sup>1</sup>, Abdsalam Rabie<sup>1</sup>, Monsef Algouti<sup>1</sup>, Mussa Alragig<sup>1</sup>, Rabia Awaad<sup>1</sup>, Mohamed Elfagieh<sup>4</sup>, Eramah Ermiah<sup>5</sup>

<sup>1</sup>Department of Surgical Oncology, National Cancer Institute, Misurata, Libya

<sup>2</sup>Internal Medicine, Faculty of Medicine, Zawia University, Zawia, Libya

<sup>3</sup>Family and Internal Medicine, Faculty of Medicine, Zawia University, Zawia, Libya

<sup>4</sup>Faculty of Medicine, Alrazi University, Misurata, Libya

<sup>5</sup>Medical Research Unit, National Cancer Institute, Misurata, Libya, and Faculty of Medicine, Zawia University, Zawia, Libya

\* Correspondence Email. [do3anaelie@gmail.com](mailto:do3anaelie@gmail.com)

### Abstract

The early stage of breast cancer requires modified radical mastectomy (MRM) or breast conserving surgery (BCS). However, there are disagreements regarding the outcome of these two types of therapies in terms of patient outcomes. This study aimed to assess the overall survival and disease-free survival in Libyan women with early stages of breast cancer who underwent MRM and those treated by BCS. A total of 225 women with breast cancer (stage I and II) treated at the National Cancer Institute, Misurata, Libya, were retrospectively evaluated. 168 patients (74.7%) underwent MRM, and 57 patients (25.3%) received BCS. The associations between survival outcomes and different surgical modalities (MRM vs. BCS) were analyzed using the Kaplan-Meier method and the log-rank test. At a median follow-up of 72 months (range, 24-150 months), the 5-year overall survival (OS) rates in the BCS group were 98.2 % and 88.7% in the MRM group ( $P=0.012$ ), and the corresponding 5-year disease-free survival (DFS) -Meier method, log-rank test were 98.2 and 82.1%, respectively ( $P=0.073$ ). Libyan women with early-stage breast cancer: MRM was applied in 74.7% of patients, and only 25.3% of patients underwent BCS. Patients who underwent MRM were associated with poorer prognosis ( $P=0.012$ ) and an increased rate of recurrence. At a median follow-up of 72 months (range, 24-150 months), the 5-year overall survival (OS) rates in the BCS group were 98.2 % and 88.7% in the MRM group ( $P=0.012$ ), and the corresponding 5-year disease-free survival (DFS) rates were 98.2 and 82.1%, ( $P=0.073$ ) respectively. Libyan women with early-stage breast cancer: MRM was applied in 74.7% of patients, and only 25.3% of patients underwent BCS. Patients who underwent MRM were associated with poorer prognosis ( $P=0.012$ ) and an increased rate of recurrence.

**Keywords.** Breast Cancer, Breast Conserving Surgery, Modified Radical Mastectomy, Prognosis

### Introduction

Breast cancer (BC) is thought to be the most common and the most fatal female cancer in the world, accounting for 30% of cancer cases in women [1]. Although there is improvement in the clinical outcome and patients' prognosis with advances in therapy strategies. Recently, the incidence and severity of this type of cancer have continued to increase. This points to an urgent need for finding new therapies to identify patient prognosis and improve treatment strategies [2]. With the development of diagnostic imaging, biopsy technology, and women's health awareness, the early diagnosis rate of BC has been greatly improved [3]. Early diagnosis and thorough treatment of BC remain the cornerstone of BC control.

Surgery is the primary choice of treatment for patients with early BC, and modified radical mastectomy (MRM) is one of the most commonly performed surgeries. However, breast aesthetics are greatly affected by MRM [4]. Breasts are an important secondary sexual characteristic of women whose quality of life is seriously deteriorated after mastectomy. With advances in breast surgery, breast-conserving surgery (BCS) has become a new therapeutic option for patients with early BC, which preserves the breast and ensures effective resection of the tumour, thus meeting the needs of patients [5].

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Anyhow, surgical options for cancer patients include MRM and BCS. Over the decades, numerous studies have been published in this context to compare patient outcomes between two surgical procedures [6-9]. They have shown that BCS followed by radiotherapy has equivalent disease-free survival (DFS) and overall survival (OS) as compared with MRM [6]. Social, emotional, and physical adjustment after BCS is significantly better than MRM, and the postoperative morbidity and return to normal function are also better for the BCS group [7]. Patients undergo of BCS were associated with fewer surgical site complications and desirable cosmetic outcomes than the MRM group [8]. In the USA, more than 50% of women with early-stage breast cancer undergo BCS [9]. The study aims to assess and compare the outcomes of modified radical surgery versus breast conserving surgery in Libyan patients with early breast cancer

## Methods

### *Study design and patients*

A retrospective cohort study between January 2008 and December 2017, out of all surgically treated patients at the National Cancer Institute, Misurata, Libya, all patients with stage I and II breast cancer were included in the study (225 patients).

### *The inclusion criteria*

1. Hisopathologically diagnosed with breast cancer, stage I and II.
2. Received therapy at the National Cancer Institute, Misurata, Libya, in the Surgery and Oncology Departments between January 2008 and December 2017.
3. Complete data and follow-up.

Treatment included surgical resection of the tumor (either Modified Radical Mastectomy or Breast Conserving Therapy) and/or chemotherapy and/or radiotherapy and/or hormone treatment.

### *The exclusion criteria*

- 1- Triple-negative breast cancer received neoadjuvant chemotherapy.
- 2- Bilateral breast cancer.

### *Data collection*

Demographic and clinicopathological data included patient age, place of residence, occupation, comorbidity, family history, menopausal status, side of breast cancer, TNM staging, lympho-vascular invasion, histology type, histology grade, hormone status (estrogen and progesterone receptors), Human Epidermal Growth Factor Receptor 2 (HER2) status, type of treatment, and follow-up data. These data were extracted from the patients' medical records and are shown in (Table 1 and 2). The mean age of the patients was 46.7 years (range, 21-78 years), (Figure 1). TNM staging of breast cancer was evaluated according to the American Joint Committee on Cancer (AJCC), TNM staging (7th ed) [10].

### *Treatment and follow-up*

The included patients were treated either with modified radical mastectomy (MRM) or breast conserving surgery (BCS). Out of 225 patients included, 168 patients underwent MRM (the first group), and 57 patients underwent BCS (the second group) (Figure 2). Regional lymph node dissection (Level I and II axillary dissection) was done in both approaches.

In the National Cancer Institute in Misurata, the following guidelines were established: adjuvant combined chemotherapy based on the FAC protocol (5-fluorouracil, Adriamycin, and cyclophosphamide) for 6 cycles every 3 weeks or 4AC (Adriamycin and cyclophosphamide) plus Taxol protocol was given to all patients with node-positive or high-risk node-negative tumors. All HER2-positive patients received adjuvant trastuzumab therapy for 1 year. Adjuvant hormonal therapy was given for all hormone-dependent breast cancer patients using tamoxifen or aromatase inhibitors with or without goserelin according to menopausal status. Adjuvant radiotherapy was given to all BCS group (n=57) and to 136 patients treated with MRM. The indications for Post MRM radiotherapy included large tumor size and/or 1-3 positive lymph nodes with adverse pathology or age less than 40 years (Table 3).

**Table 1.** The association between surgical treatment approaches (MRM vs. BCS) with socio-demographic and genetic variables in breast cancer (n=225).

Variables		Number of patients	MRM group (percent)	BCS group (percent)	p value
Age	< 50 years	138	71.7	28.3	0.199
	≥ 50 years	97	79.3	20.7	
Menopausal status	Pre-menopausal	136	70.6	29.4	0.078
	Post-menopausal	89	80.9	19.1	
Place of residence	Urban	185	73.0	27.0	0.236
	Rural	40	82.5	17.5	
Occupation	Housewife	194	75.3	24.7	0.615
	Employed	31	71.0	29.0	
Marital status	Married	195	75.4	24.6	0.534
	Single	30	70.0	30.0	
Comorbidity	Yes	53	79.2	20.8	0.373
	No	172	73.3	26.7	
Family history	Positive	18	66.7	33.3	0.429
	Negative	207	75.4	24.6	

MRM: Modified Radical Mastectomy, BCS: Breast Conservative Surgery.

**Table 2.** The association between surgical treatment approaches (MRM vs. BCS) with clinicopathological variables in breast cancer (n=225).

Variables		Number of patients	MRM group (n=168)	BCS group (n=57)	p value
Site	Right	104	76.0	24.0	0.679
	Left	121	73.6	26.4	
Histological type	IDC	200	73.5	26.5	0.235
	Other types	25	84.0	16.0	
Tumor size	T1 (≤2cm)	21	76.2	23.8	0.865
	T2 (2-5cm)	204	74.5	25.5	
Nodal status	N0	97	67.2	32.8	0.003
	N1	128	84.5	15.5	
TNM staging	Stage I	17	76.5	23.5	0.858
	Stage II	208	74.5	25.5	
Histological grade	Grade 1	16	68.8	31.3	0.795
	Grade 2	136	74.3	25.7	
	Grade 3	73	76.7	23.3	
Estrogen receptor status	Positive	160	76.3	23.7	0.396
	Negative	65	70.8	29.2	
Progesterone receptor status	Positive	148	72.3	27.7	0.252
	Negative	77	79.2	20.8	
HER2 status	Positive	65	73.8	26.2	0.857
	Negative	160	75.0	25.0	
Lympho-vascular invasion	Positive	32	75.0	25.0	0.957
	Negative	164	75.0	25.0	
	Unknown	29	72.4	27.6	

MRM: Modified Radical Mastectomy, BCS: Breast Conservative Surgery. HER2: Human Epidermal Growth Factor Receptor 2

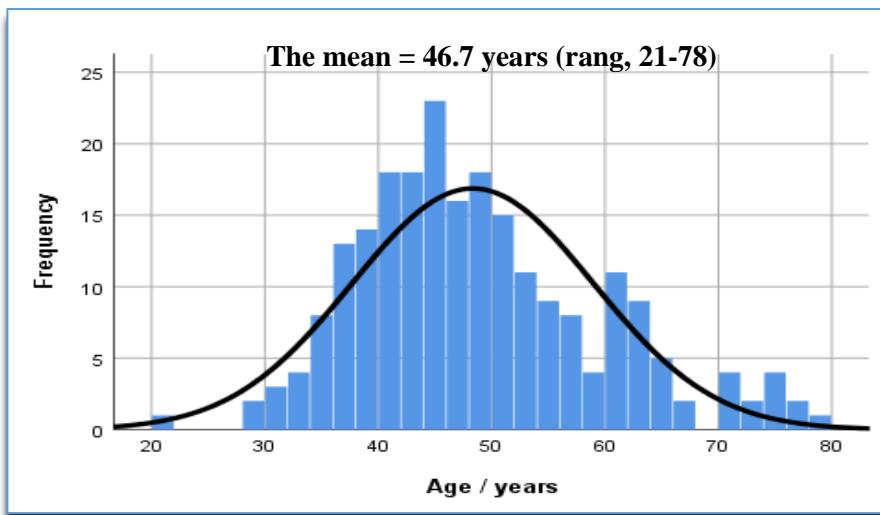


Figure 1. Age distribution of 225 patients with breast cancer in Libya (2007-2018).

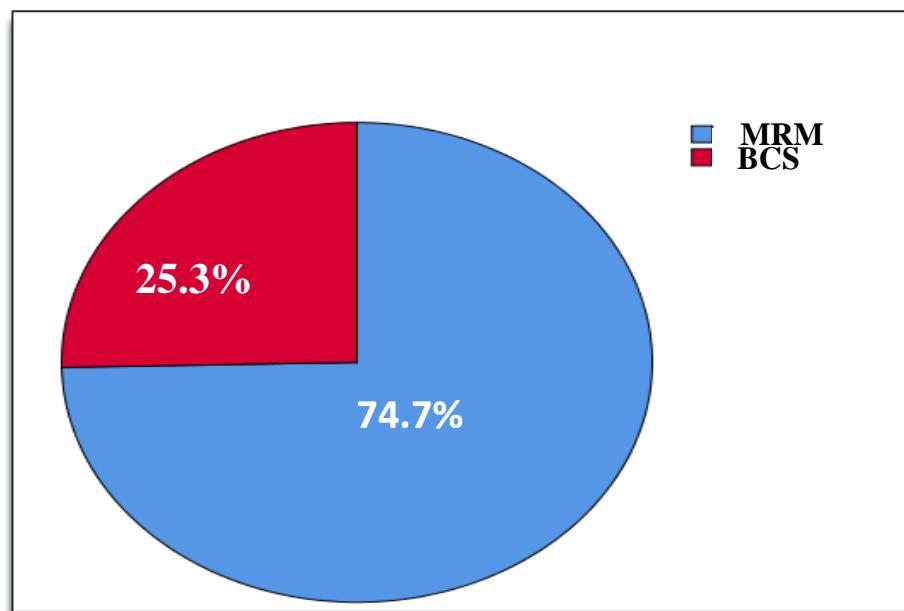


Figure 2. Surgical treatment approach (MRM vs. BCS) in Libyan patients with breast cancer (n=225).

MRM: Modified Radical Mastectomy, BCS: Breast Conservative Surgery.

Table 3. Adjuvant therapy of the studied groups, MRM and BCS (N=225).

Category		Number of patients	MRM group (percent)	BCS group (percent)	p value
Adjuvant chemotherapy	Yes	210	75.2	24.8	0.473
	No	15	66.7	33.3	
Radiotherapy	Yes	193	70.5	29.5	<0.0001
	No	32	100.0	0.0	
Hormonal therapy	Yes	170	74.1	25.9	0.738
	No	55	76.4	23.6	
Anti HER2 therapy	Yes	65	73.8	26.2	0.857
	No	160	75.0	25.0	

MRM: Modified Radical Mastectomy, BCS: Breast Conservative Surgery.

Follow-up of patients was carried out every 3 months during the first 2 years, every 6 months from year 2 to year 5, and annually thereafter. Follow-up included a clinical examination at every visit, plain chest X-ray, pelvic-abdominal ultrasound, and mammography once a year, complete blood cell counts and tumor markers twice a year; other image examinations were performed when needed.

Disease recurrence (local and distant) was confirmed by a clinical examination, laboratory results, biopsy, and imaging (CT, MRI, or PET) performed when clinical symptoms suggestive of disease recurrence were present. Patients' outcomes were considered as follows: overall survival, duration between the date of pathological diagnosis and the date of death and/or to date of the end of the follow-up period; disease-free survival, duration between the date of pathological diagnosis to the date of diagnosis of recurrence (local and/or distant) or death. Patients were followed up until death or to the end of the observation period (until December 2023). The median follow-up duration was 72 months (range, 24-150 months). At the end of the follow-up period, 35 patients (15.6%) had disease recurrence, and 20 patients (8.9%) had died of breast cancer.

### **Statistical analysis**

Continuous variables were calculated using SPSS 26.0 for Windows (IBM Corp.). Frequency tables were analyzed using the Chi-square ( $\chi^2$ ) test to evaluate the power of association between categorical variables. Kaplan-Meier curves were constructed for survival rate analysis, and differences between curves were analyzed using the log-rank test.  $P<0.05$  was considered to indicate a statistically significant difference. -Meier curves were constructed for survival rate analysis, and differences between curves were -rank test.

## **Results**

### ***Patients' characteristics of the two studied groups:***

Out of 225 patients, 168 patients (74.7%) had MRM and 57 (25.3%) had BCS (Figure 2). The association between the two studied groups (MRM vs. BCS) with socio-demographic, genetic, and clinical-pathological variables is represented in (Tables 1 and 2). The mean age of patients in the MRM group was insignificantly different from the mean age of patients in the BCS group (49 vs. 46,  $p = 0.199$ , respectively).

Comparison of menopausal status between two groups, 80.9% of patients in the post-menopausal age underwent MRM, while 29.4% of patients in the pre-menopausal were undergone BCS. This difference was not statistically significant ( $p = 0.078$ ). There were no statistically significant differences in other socio-demographic and genetic variables such as place of residence, occupation, marital status, co-morbidity, and family history of breast cancer (Table 1).

Regarding the clinicopathological variables between the two groups. This study observed that the rate of patients with positive lymph nodes was significantly higher in MRM compared to BCS (84.5% vs 15.5%, respectively). This difference between the two groups was statistically significant ( $p = 0.003$ ) (Table 2). Anyhow, there were no statistically significant differences with histological type, size of tumor, stage, histological grade, lympho-vascular invasion, and receptor status (ER, PR, and HER2) ( $p>0.05$ ).

### ***Patient outcome***

The median follow-up was 72 months (maximum 155 months). At the cut-off date for this analysis, 35 patients (15.6%) had disease recurrence, and 20 patients (8.9%) had died of breast cancer. This study observed that 35 patients (16.5%) showed post-operative recurrence in both studied groups. The frequency of local and distant recurrence after MRM was higher than BCS; no statistically significant difference was found ( $p=0.096$ ) (Table 4). Regarding the overall survival between the two groups. This study observed that the overall survival rate was lower for the MRM group (88.7%) than the BCS group (98.2%) with statistical significance ( $p= 0.012$ ) (Table 5). In addition, Kaplan Meier survival curves for both MRM and BCS groups showed that shorter survival was associated with patients who received MRM (Figure 3). Regarding the DFS assessment between the two studied group was done using the log-rank test and Kaplan-Meier curve (Figure 4). The result showed that there was no significant difference between the two groups ( $P = 0.073$ ). (Figure 3). Overall survival curves between different surgical modalities (MRM vs. BCS. Kaplan-Meier survival analysis shows a significant statistical difference in 5-year survival between the MRM and BCS groups.

Table 4. Prevalence of recurrence of the studied groups.

Type of recurrence	Number of patients	MRM (percent)	BCS (percent)	p value
No recurrence	190	72.6	27.4	0.096
Local	11	72.7	27.3	
Distant	20	95.0	5.0	
Local and distant	4	75.0	25.0	

Table 5. Univariate survival according to analysis of surgical treatment approaches (MRM vs. BCS) in Libyan patients with breast cancer (n= 225).

		Survival analysis			p-value
		Median time (months)	Mean time (months)	Survival rate (present)	
Overall survival					
All patients	72.00	76.98	91.1		
	74.50	78.35	88.7		0.012
	67.00	71.17	98.2		
Disease-free survival					
All patients	66.00	70.87	84.4		
	66.50	71.17	82.1		0.073
	65.00	69.98	98.2		

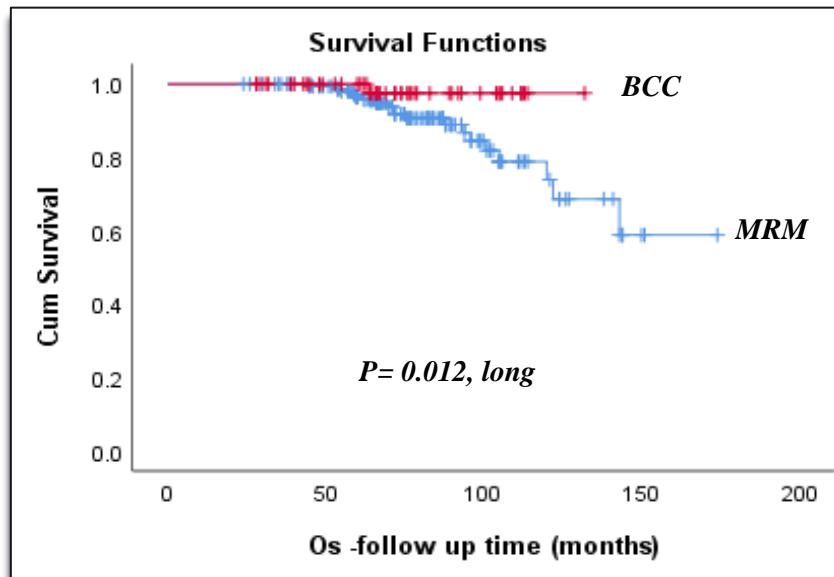
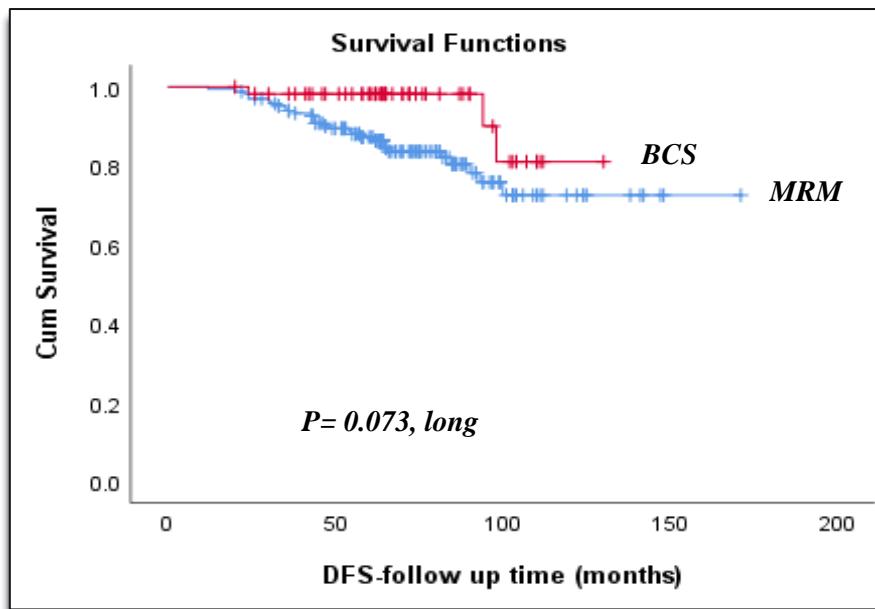


Figure 3. Overall survival curves between different surgical modalities (MRM vs. BCS). MRM: Modified Radical Mastectomy, BCS: Breast Conservative Surgery.



**Figure 4. Disease-free survival curves between different surgical modalities (MRM vs. BCS).**  
 MRM: Modified Radical Mastectomy, BCS: Breast Conservative Surgery.

## Discussion

Many studies observed that BCS plus adjuvant radiotherapy can produce equivalent OS and DFS for early-stage breast cancer patients [11-13]. In addition, some other studies have observed that BCS was associated with better survival than MRM [14- 16]. In the present study, we investigated the impact of the surgical procedures (BCT vs. MRM) on prognosis (OS and DFS) in Libyan patients with early stage of breast cancer.

225 patients who underwent surgery for breast cancer at the National Cancer Institute, Misurata, Libya, were retrospectively investigated. We observed that 74.7 % (168 patients) received MRM with a mean age of 49 and 25.3% (57 patients) had BCS with a mean age (46). This is in line with a study in Africa that reported 70% of women with early-stage breast cancer underwent MRM, and only 28% received BCS [17]. However, these results are inconsistent with a study in the United States, which reported that among women with early-stage breast cancer, 60% underwent BCS [18]. This study observed that the rate of patients with positive lymph nodes was significantly higher in the MRM group than in BCS ( $p = 0.003$ ). This is in line with other studies. El-Maghawry et al. [19] showed that MRM patients were significantly associated with lymph node involvement.

In this cohort, the median follow-up duration was 72 months (range, 24-150 months) and at the end of follow up period, 35 patients (15.6%) had disease recurrence and 20 patients (8.9%) had died of breast cancer. The incidence of Local and distant recurrence was higher in the MRM group than in the BCS group, but this difference was not statistically significant ( $p<0.05$ ). This finding was consistent with other studies [20]. The results of our study observed that 5-year OS and DFS rates in the BCS group were better than the MRM group. This observation is in line with other studies. Houshyari et al [21] reported that 5-year OS and DFS in the BCS group were better than in the MRM group ( $P = 0.041$  and  $P< 0.001$ , respectively).

Despite a higher rate of recurrence, overall survival is equivalent in patients who have undergone BCS or MRM [22,23]. Further analysis showed that the BCS plus radiotherapy had comparable survival outcomes with the MRM plus radiotherapy [13]. As reported in early randomized controlled studies, BCS followed by radiotherapy is at least equivalent to MRM [24]. Recent population-based retrospective studies [25- 28] reported that BCS plus radiotherapy is even superior to mastectomy [29]. The survival benefit of BCS over MRM observed in our study and others appears to be related to the combination of BCS and adjuvant RT. In developed countries, BCS has been performed in clinical practice for more than 25 years. In Libya, there are lower rates of BCS in comparison to Western countries, which might relate to some factors, such as socioeconomic factors and concern over the increased risk of local recurrence. Moreover, Libyan breast cancer patients often present with advanced stage, dominant premenopausal status, have early disease recurrence, and are associated with high mortality [30].

This analysis has some limitations. Given that this was a single institution retrospective analysis, only a single source of previously documented data was available for assessment. Further prospective studies are required to emphasize these analysis findings, alongside the constant collection of clinical data, for more comprehensive and precise results in the future.

## Conclusion

Considering the aspects evaluated in this study, we can conclude that OS and DFS rates in the BCS group were better than the MRM group. The recurrence rate in the MRM group was more than that of the BCS group. These findings need further validation.

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### ***Availability of data and materials***

The data sets used and/ or analyzed in the current study are available from the corresponding author upon request.

### ***Authors' contributions***

DA conceived the present study, drafted the manuscript, and wrote the text. RB, NA, ER, ME, AJ, AS, AR, MA, MA and ME analyzed the data and performed the data interpretation and analysis, writing and proofreading, and discussions. EE performed the statistical analysis. prepared the figures and tables, reviewed the study, interpreted the data, and helped write and proofread the manuscript.

### ***Ethical approval***

The cohort study was done under research ethics approval by the ethical committee at the National Cancer Institute, Misurata. Written informed consent was obtained from all patients for surgical treatment, pathologic examinations, and investigations performed according to the institutional guidelines of the National Cancer Institute, Misurata, Libya.

### ***Competing interests***

The authors declare that they have no competing interests.

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