Prognostic Factors and Their Impact on Survival in Patients with De Novo Metastatic Breast Cancer

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ABSTRACT

This study aimed to investigate the prognostic factors affecting overall survival (OS) in patients with de novo metastatic breast cancer (dnMBC). Additionally, the importance of local treatments on survival was evaluated. The data of 106 patients with dnMBC were analyzed. Primary breast surgery was performed in 15 patients (14%), while first-line systemic therapy constituted the initial treatment modality for 91 patients (86%). Local treatments were administered to 48 patients (45%), of which 63% underwent breast surgery alone and 37% underwent both breast surgery and radiotherapy. In univariate analysis, patient performance status, extent of metastasis, response of primary breast tumors and metastatic lesions to first-line systemic therapy, administration of local treatments, and the use of breast radiotherapy and surgery were identified as prognostic factors ($p< 0.050$). In multivariate analysis, being in the triple-negative subgroup (HR: 5.06, 95% CI: 2.46–10.43, $p< 0.001$), having polymetastatic disease (HR: 1.19, 95% CI: 1.15–3.17, $p= 0.013$), partial response of metastatic lesions to first-line systemic therapy (HR: 2.25, 95% CI: 1.84–4.29, $p= 0.014$), and non-response to first-line systemic therapy (HR: 2.67, 95% CI: 1.56–4.59, $p< 0.001$) were identified as independent poor prognostic factors. The median OS was 34 months, with 2-year OS at 58% and 5-year OS at 19%. The most significant prognostic factors for dnMBC in this study were molecular subtyping, extent of metastasis, and response of metastatic lesions to first-line systemic therapy. Although local treatments targeting the breast influenced prognosis, their impact was not as strong as the aforementioned variables.

Keywords: De novo metastatic breast cancer, Radiotherapy, Prognostic factors, Overall survival

INTRODUCTION

The occurrence of metastasis before, at the time of, or within three months after the diagnosis of primary breast cancer is defined as de novo metastatic breast cancer (dnMBC).[1] Although dnMBC encompasses the spectrum of breast cancer subtypes, it is considered to have a more aggressive biology.[1-5] dnMBC accounts for 5-15% of all breast cancer cases.[6-7]

Historically, the treatment of dnMBC has been considered a therapeutic challenge, with standard treatment often limited to systemic chemotherapy.[5] In recent years, longer survival durations, particularly in oligometastatic patients with good responses to systemic therapy, have raised the possibility that local treatments (e.g., breast surgery, radiotherapy) may contribute to survival in these patients. Indeed, some studies have demonstrated a survival benefit.[8,9] However, other studies have not supported these findings.[10-12] At this point, appropriate patient selection and identification of prognostic factors become critical.

Identifying prognostic factors and understanding their impact on overall survival (OS) are essential for determining treatment strategies. Due to the heterogeneous nature of dnMBC patients, each case requires individualized treatment management. Based on previous studies, factors such as patient age, performance status, molecular subtype of the disease, tumor burden, response to systemic therapies, and the efficacy of administered treatments appear to be crucial considerations in managing these patients.[9,12-14] However, strong prognostic factors are still needed to establish guidelines for managing dnMBC patients.

This study aimed to investigate the prognostic factors affecting OS in dnMBC patients. Additionally, the importance of local treatments on survival was evaluated.

MATERIALS AND METHODS

In this study, data from 106 dnMBC patients treated at the Oncology Center of Cumhuriyet University Faculty of Medicine between January 2010 and December 2020 were retrospectively analyzed. Ethical approval for the study was granted by the Ethics Committee of Sivas Cumhuriyet University Faculty of Medicine (Date: 17.10.2024, No: 2024-10/25). This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the local ethical committee (Sivas Cumhuriyet University Ethical Committee). Written informed consent could not be obtained due to the retrospective nature and anonymous data.

Patient Selection

Female patients aged 18 years or older with histologically confirmed dnMBC were included in the study. Distant metastases detected at the time of presentation or within three months of diagnosis were defined as dnMBC.[1] Patients with non-metastatic breast cancer, bilateral breast cancer, dual primary cancers, early or locally advanced breast cancer at diagnosis that developed metastases more than three months after diagnosis, or those with incomplete demographic or clinical data were excluded from the study.

Data Collection

Clinicopathological data, including age at diagnosis, menopausal status, performance status, disease stage, pathological characteristics, treatments, and vital status, were obtained from medical records and pathology reports.

Patients who had been amenorrheic for more than one year before their breast cancer diagnosis were classified as postmenopausal. Performance status was assessed based on the ECOG (Eastern Cooperative Oncology Group) scoring system. All patients were staged according to the 8th Edition of the American Joint Committee on Cancer (AJCC) staging manual at the time of diagnosis (15).

Hormone receptor (HR) and human epidermal growth factor receptor 2 (HER2) status were determined by immunohistochemical (IHC) staining. Patients were considered HR-positive if 1–100% of their cells showed estrogen receptor (ER) or progesterone receptor (PR) expression. HER2 status was assessed using IHC or in situ hybridization (ISH) testing. Those with IHC 3+ were classified as HER2-positive, while IHC 2+ cases were confirmed using ISH (16). Patients were classified into three molecular subtypes:

i. HR+/HER2-

ii. HR±/HER2+

iii. Triple-negative

Metastases were confirmed using relevant clinical, imaging, and/or pathological verification. Patients with 1–4 metastatic lesions were classified as oligometastatic, while those with ≥5 lesions were classified as polymetastatic.[6] Metastases were also categorized into three groups: bone, solid (liver, lung, parenchymal brain metastases, etc.), or both.

OS was defined as the time from dnMBC diagnosis to the date of death or the last follow-up.[1]

Treatment

Patients were evaluated by a multidisciplinary tumor board.

In accordance with standard treatment approaches for dnMBC, HR+/HER2- patients with visceral crisis received hormonotherapy and systemic

chemotherapy (e.g., paclitaxel, gemcitabine). HR+/HER2- patients without visceral crisis were treated with hormonotherapy and CDK4/6 inhibitors. All HER2-positive patients received anti-HER2 therapy (trastuzumab, pertuzumab, taxane). Patients with the triple-negative dnMBC subtype were treated with systemic chemotherapy (platinum-based chemotherapy combinations).

Breast surgery was performed in the Surgical Oncology Department. Depending on the patient's and/or oncologic surgeon's choice, mastectomy or breast-conserving surgery was performed. Breast surgery was carried out either before or after first-line systemic therapy (1st line ST).

Breast radiotherapy (RT) was planned for oligometastatic patients and/or those responding well to 1st line ST. RT was applied to the whole breast or chest wall (50 Gy in 25 fractions over five weeks). Patients who underwent breast-conserving surgery received a boost dose of 10 Gy to the tumor bed in five fractions. Regional nodal irradiation was performed in the presence of lymph node positivity or other risk factors. Intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) techniques were used for all patients during RT planning.

Statistical Analysis

Statistical analyses were performed using SPSS Version 23 (IBM Corp., Armonk, New York, USA). Descriptive statistics (frequency, median, minimum, maximum, etc.) were used to present patients' demographic, clinical, and pathological characteristics. Survival analyses were conducted using the Kaplan-Meier method. Prognostic factors were identified through univariate and multivariate Cox regression analyses. P values <0.05 were considered statistically significant.

RESULTS

The median age of the patients was 57 years (range: 18-83), with the majority being postmenopausal (n= 72, 68%). Among the 106 patients, 94 (89%) had invasive ductal carcinoma, while the remaining 12 (11%) had other histopathological types. Primary breast surgery was performed in 15 patients (14%), while first-line systemic therapy (1st line ST), including chemotherapy and/or hormonotherapy, was the initial treatment modality for 91 patients (86%). Local treatments were planned based on the response to therapy. Local treatments were administered at a median of 8 months (range: 5–24 months) after diagnosis. Among all patients, 48 (45%) underwent local treatments (breast surgery and/or RT). Of these, 30 patients (63%) underwent breast surgery alone, while 18 (37%) received both breast surgery and RT. Breast surgery was performed before 1st line ST in 15 patients (34%) and after 1st line ST in 29 patients (66%). No patients received RT alone as a local treatment. Table 1 presents the demographic, clinical, pathological characteristics, treatments, and 1st line ST responses of the patients.

Prognostic Factors

In univariate analysis, the following were identified as poor prognostic factors: ECOG performance status ≥ 2 (HR: 1.96, 95% CI: 1.96–3.47, p= 0.019), triple-negative disease (HR: 4.24, 95% CI: 2.10-8.56, p< 0.001), polymetastatic disease (HR: 2.29, 95% CI: 1.45-3.61, p< 0.001), partial response of the primary tumor to 1st line ST (HR: 1.99, 95% CI: 1.19–3.33, p= 0.008), lack of response of the primary tumor to 1st line ST (HR: 3.25, 95% CI: 1.66–6.34, p= 0.001), partial response of metastatic lesions to 1st line ST (HR: 2.40, 95% CI: 1.31-4.39, p< 0.001), and lack of response of metastatic lesions to 1st line ST (HR: 3.46, 95% CI: 2.07-5.79, p< 0.001). Local treatments (HR: 0.64, 95% CI: 0.42-0.99, p= 0.047), breast RT (HR: 0.47, 95% CI: 0.25-0.87, p= 0.017), and breast surgery (HR: 0.64, 95% CI: 0.42-0.99, p= 0.047) were identified as favorable prognostic factors.

In multivariate analysis, the following were identified as independent poor prognostic factors:

The triple-negative molecular subtype (HR: 5.06, 95% CI: 2.46-10.43, p< 0.001),

polymetastatic disease (HR: 1.19, 95% CI: 1.15-3.17, p= 0.013),

partial response of metastatic lesions to 1st line ST (HR: 2.25, 95% CI: 1.84-4.29, p= 0.014), and lack of response of metastatic lesions to 1st line ST (HR: 2.67, 95% CI: 1.56-4.59, p< 0.001).

Table 1. Demographic, clinical, and pathological characteristics of patients, treatments, and treatment response

	Number of patients n= 106	%
Menopausal status		
Premenopausal	37	32
Postmenopausal	72	68
ECOG		
ECOG 0	26	24
ECOG 1	45	43
ECOG ≥2	35	33
Molecular subtypes		
HR+/HER2-	47	44
HR ±/HER2+	47	44
Triple-negative	12	12
Grade		
Grade I	22	21
Grade II	54	51
Grade III	30	28
CEA		
Normal	33	35
High	62	65
CA 15.3		
Normal	55	57
High	41	43
Extent of metastasis		
Oligometastatic	40	38
Polymetastatic	66	62
Type of metastasis		
Bone	33	31
Solid	26	25
Both	47	44
Primary tumor response* (n=101)		
Full	30	30
Partial	54	53
No response	17	17
Metastatic lesion response* (n=101)		
Full	41	41
Partial	21	21
No response	39	38
Local treatment (surgery/RT)		
None	58	55
Present	48	45
Type of local treatment		
Surgery	30	63
Surgery+RT	18	37
Breast radiotherapy		
None	88	83
Present	18	17
Breast surgery		
None	58	55
Present	48	45
Timing of surgery		
Before 1st line ST	15	34
After 1st line ST	29	66
Type of surgery		
Mastectomy	36	82
Breast-conserving surgery	8	18

*ECOG PS: Eastern Cooperative Oncology Group performance status. CEA: Carcinoembryonic antigen (normal <5.2 ng/mL, high ≥5.2 ng/mL). CA 15.3: Cancer antigen 15-3 (normal <25 U/mL, high ≥25 U/mL). *Response to first-line systemic therapy (ST).*

Table 2 presents the univariate and multivariate analysis results of the prognostic factors affecting OS.

Overall Survival

The median follow-up duration was 34 months (range: 1-122 months). The 2-year and 5-year OS rates for all patients were 63% and 26%, respectively, with a median survival of 34 months. Table 3 presents the 2-year, 5-year, and median survival outcomes of the patients. As shown in the table, ECOG performance status (p= 0.054), molecular subtyping (p< 0.001), extent of metastasis (p< 0.001), site of metastasis (p= 0.047), response of the primary tumor to 1st line ST (p= 0.001), response of metastatic lesions to 1st line ST (p< 0.001), local treatments (p= 0.043), breast RT (p= 0.014), and breast surgery (p= 0.043) were statistically significant for survival.

Figures 1, 2, and 3 show the OS curves based on molecular subtypes, extent of metastasis, and response of metastatic lesions to 1st line ST.

DISCUSSION

In this study, the 2-year and 5-year OS rates in dnMBC patients were found to be 63% and 26%, respectively, with a median OS of 34 months. The most significant independent prognostic factors in these patients were determined to be molecular subtypes, the extent of metastasis, and the response of metastatic lesions to 1st line ST. Although local treatments (breast surgery and RT) partially influenced the prognosis of these patients, this finding was not supported in multivariate analysis.

The OS duration in dnMBC patients is approximately 2-3 years, and recent advancements in treatments have led to slight improvements in survival outcomes.[13,15,17-18] Andre et al. demonstrated that the mean survival time of dnMBC patients increased from 23 months in 1987-1993 to 29 months in 1994-2000.[17] Similarly, den Brok et al. reported a median OS of 29 months for dnMBC patients between 2001 and 2009.[18] In the study by Zhang et al. (2008–2017), the median OS of dnMBC patients was 34 months, with 3-year and 5-year OS rates

Table 2. Prognostic factors affecting overall survival in patients

Variables	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	p	HR	95% CI	p
Menopausal status						
Premenopausal	RF					
Postmenopausal	1.15	0.74-1.80	0.518			
ECOG						
ECOG 0	RF			RF		
ECOG 1	1.42	0.81-2.47	0.211	2.02	0.75-5.44	0.160
ECOG ≥2	1.96	1.96-3.47	0.019	1.39	0.68-2.84	0.354
Molecular subtypes						
HR+/HER2-	RF			RF		
HR ±/HER2+	0.82	0.52-1.29	0.401	0.78	0.49-1.26	0.780
Triple-negative	4.24	2.10-8.56	< 0.001	5.06	2.46-10.43	<0.001
Grade						
Grade I	RF					
Grade II	0.61	0.36-1.04	0.074			
Grade III	0.86	0.48-1.55	0.635			
CEA						
Normal	RF					
High	1.51	0.96-2.36	0.069			
CA 15.3						
Normal	RF					
High	1.40	0.90-2.19	0.127			
Extent of metastasis						
Oligometastatic	RF			RF		
Polymetastatic	2.29	1.45-3.61	<0.001	1.191	1.15-3.17	0.013
Site of metastasis						
Bone	RF					
Solid	0.71	0.39-1.29	0.269			
Both	1.37	0.85-2.22	0.187			
Primary tumor response*						
Full	RF					
Partial	1.99	1.19-3.33	0.008	0.81	0.26-2.43	0.690
No response	3.25	1.66-6.34	0.001	1.13	0.48-2.53	0.799
Metastatic lesion response*						
Full	RF			RF		
Partial	2.40	1.31-4.39	0.004	2.25	1.84-4.29	0.014
No response	3.46	2.07-5.79	<0.001	2.67	1.56-4.59	<0.001
Local treatment (surgery/RT)						
None	RF			RF		
Present	0.64	0.42-0.99	0.047	0.76	0.43-1.35	0.356
Type of local treatment						
Surgery	RF					
Surgery+RT	0.55	0.27-1.112	0.103			
Breast radiotherapy						
No	RF			RF		
Yes	0.47	0.25-0.87	0.017	0.57	0.25-1.29	0.181
Breast surgery						
No	RF			RF		
Yes	0.64	0.42-0.99	0.047	0.65	0.37-1.12	0.123
Type of surgery						
Mastectomy	RF					
Breast-conserving	1.49	0.64-3.46	0.347			
Timing of surgery						
Before 1st line ST	RF					
After 1st line ST	0.60	0.28-1.28	0.188			

*ECOG PS: Eastern Cooperative Oncology Group performance status. CEA: Carcinoembryonic antigen (normal <5.2 ng/mL, high ≥5.2 ng/mL). CA 15.3: Cancer antigen 15-3 (normal <25 U/mL, high ≥25 U/mL). *Response to first-line systemic therapy (ST).*

Table 3. Overall survival outcomes of patients

	2-year survival (%)	5-year survival (%)	Median survival (months)	p value
ECOG				
ECOG 0	73	34	40	
ECOG 1	69	24	35	0.054
ECOG ≥2	46	17	18	
Molecular subtypes				
HR+/HER2-	66	32	36	<0.001
HR ±/HER2+	70	28	40	
Triple-negative	8	-	12	
Extent of metastasis				
Oligometastatic	80	45	44	<0.001
Polymetastatic	52	14	30	
Type of metastasis				
Bone	70	36	40	0.047
Solid	69	35	40	
Both	53	15	31	
Primary tumor response*				
Full	87	47	52	
Partial	57	22	30	0.001
No response	53	6	31	
Metastatic lesion response*				
Full	83	51	66	
Partial	76	10	36	<0.001
No response	41	8	18	
Local treatment (surgery/RT)				
None	55	19	32	0.043
Present	71	30	36	
Type of local treatment				
Surgery	60	20	34	0.095
Surgery+RT	83	56	72	
Breast radiotherapy				
None	58	21	33	0.014
Present	83	56	72	
Breast surgery				
None	55	19	32	0.043
Present	71	33	36	
Timing of surgery				
Before 1st ST	66	28	35	0.180
After 1st ST	73	40	40	

*ECOG PS: Eastern Cooperative Oncology Group performance status. CEA: Carcinoembryonic antigen (normal <5.2 ng/mL, high ≥5.2 ng/mL). CA 15.3: Cancer antigen 15-3 (normal <25 U/mL, high ≥25 U/mL). *Response to first-line systemic therapy (ST).*

of 46% and 25.7%, respectively.[13] Our study's survival outcomes were found to be quite similar to those reported by Zhang et al. Our study included dnMBC patients treated between 2008 and 2020, with a median OS of 34 months and 2-year and 5-year OS rates of 63% and 26%, respectively. According to the aforementioned reports, the average survival time of dnMBC patients has increased in recent years due to the introduction of new drugs and advances in treatment approaches.

Molecular characteristics, such as ER, PR, HER2, and Ki-67 percentages, significantly influence survival in breast cancer patients, leading to the classification of molecular subtypes. Molecular subtyping is not only prognostic but also guides breast cancer treatment. In a study utilizing a national database, Press et al. found that triple-negative patients had twice the risk of death compared to HR+/HER2- patients. In HER2-positive patients, better outcomes were observed compared to triple-

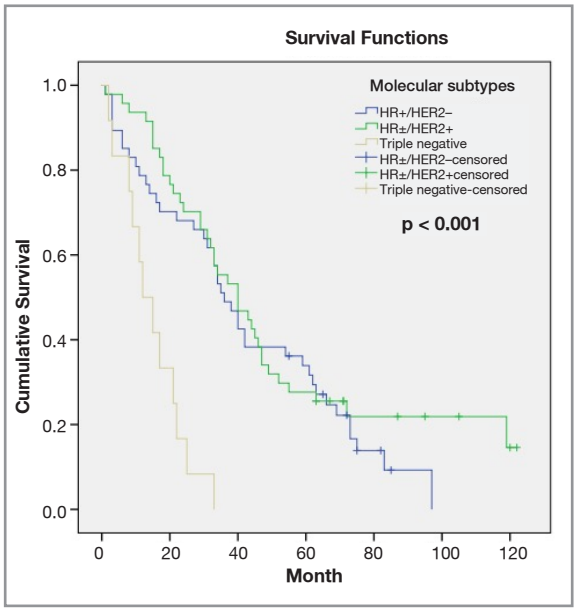

Figure 1. Overall survival curves by molecular subtypes

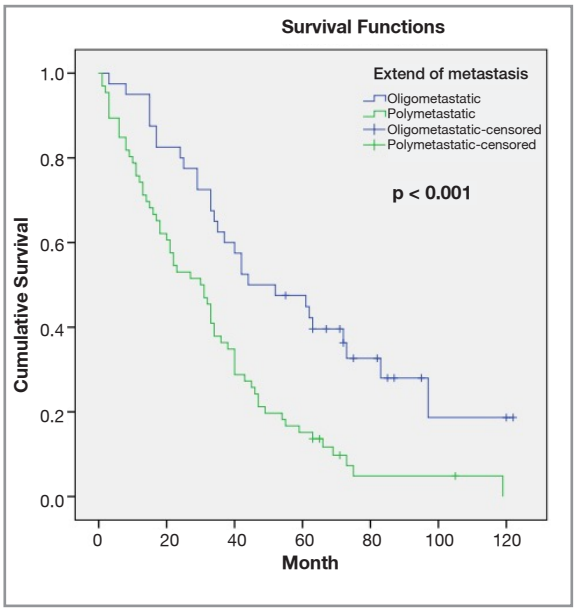

Figure 2. Overall survival curves by extent of metastasis

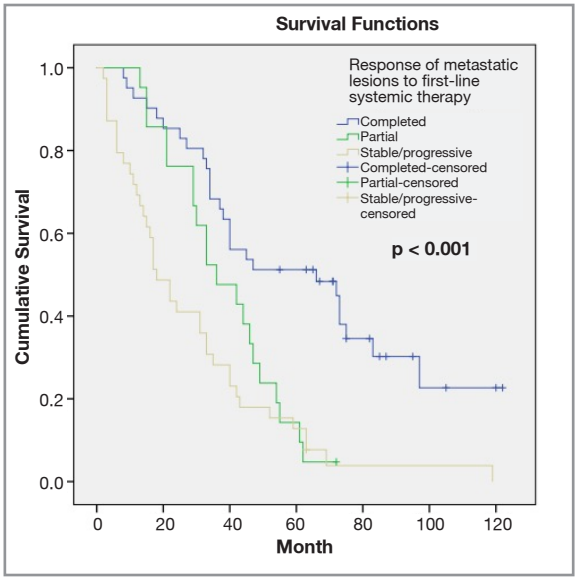

Figure 3. Overall survival curves based on the response of metastatic lesions to first-line systemic therapy

negative patients, attributed to targeted therapies. Additionally, survival outcomes were better in HR+/HER2+ patients compared to HR+/HER2- patients.[14] The study by Zhang et al. also identified statistically significant survival differences among molecular subtypes, with a median OS of 97 months in HR+/HER2– patients, 50 months in HR+/HER2+ patients, and 24 months in triple-negative patients. The 5-year OS rates were reported as 34.7%, 19.8%, and 0%, respectively.[13] In the study by Pons-Tostivint et al., molecular subtyping was identified as an independent prognostic factor, with the triple-negative subtype associated with poor prognosis.[9] Similarly, in our study, molecular subtyping was identified as a prognostic factor in both univariate and multivariate analyses. Triple-negative patients were identified as the group with the worst prognosis, with median and 5-year OS rates of 12 months and 0%, respectively. In comparison, HR+/HER2- patients had median and 5-year OS rates of 36 months and 32%, respectively, and HR±/HER2+ patients had rates of 40 months and 28%.

The extent of metastatic lesions, indicating a higher tumor burden, may lead to treatment resistance and worsen patient prognosis. Several studies have observed better survival in patients with lower tumor burden.[6,9,13,19] This observation has led to the development of the concept of oligometastasis, which is generally defined as having fewer than five metastatic lesions.[6] Soran et al. investigated the contribution of local treatments to survival in 505 dnMBC patients with bone-only metastases and found that the presence of multiple metasta-

ses was an independent poor prognostic factor.[19] In Zhang et al.'s study, oligometastatic patients had a median OS of 41 months, compared to 28 months in polymetastatic patients, with a statistically significant difference.[13] Similarly, Pons-Tostivint et al. identified the extent of metastasis as an independent factor affecting prognosis.[9] In our study, the extent of metastasis was identified as one of the most critical prognostic factors in dnMBC patients. Oligometastatic patients had significantly better survival outcomes compared to polymetastatic patients (median OS: 44 vs. 30 months, respectively).

The site of metastasis may also influence survival outcomes in breast cancer patients. Studies suggest that patients with bone metastases have better survival compared to those with solid organ metastases, such as brain and liver.[20,21] In the study by Wang et al., among dnMBC patients undergoing primary breast surgery, the best OS was observed in those with bone metastases compared to solid organ metastases.[20] Similarly, Press et al. reported worse outcomes in patients with brain and liver metastases compared to those without metastases in these sites.[14] Pons-Tostivint et al. also associated visceral organ involvement with poor prognosis.[9] In our study, patients were categorized into three groups based on the site of metastasis: bone, solid organ, and both. Unlike previous studies, no strong data were obtained in our analysis. Although Kaplan-Meier testing suggested a borderline effect of metastasis site on survival, univariate and multivariate Cox regression analyses did not reveal statistically significant results. This discrepancy is likely due to the small sample size.

The response of the primary tumor or metastatic lesions to 1st line ST may play a crucial role in determining subsequent treatment strategies and naturally serves as a prognostic factor for patient outcomes. In a prospective multicenter study by King et al. involving 127 dnMBC patients, the role of breast surgery and prognostic factors were evaluated, demonstrating better survival in patients responding to 1st line ST (3-year OS: 78% in responders vs. 39% in non-responders).[12] In our study, the response of primary tumors and metastatic lesions to 1st line ST significantly affected survival outcomes. However, the response of metastatic lesions showed a stronger prognostic impact as an independent prognostic factor. Monitoring treatment responses and optimizing strategies based on these responses may improve survival outcomes. The response of metastatic lesions to 1st line ST, in particular, plays a critical role in determining the overall prognosis of dnMBC patients.

One of the most debated issues in dnMBC patients is the necessity and timing of local treatments. Although numerous studies have been conducted on this subject, the results remain conflicting.[8-10,12,19,22-23] In the prospective study by King et al., it was noted that breast surgery did not affect OS in patients who responded to 1st line ST, regardless of tumor subtype.[12] In a prospective study by Khan et al., dnMBC patients with poor response of the primary tumor to 1st line ST were randomized into two groups: those who received local treatment and those who did not. Despite a 2.5-fold higher risk of local recurrence in patients who did not receive local treatment, no statistical difference was observed in 3-year OS or progression-free survival.[11] In a prospective study by Fitzal et al., dnMBC patients were randomized to systemic therapy following breast surgery or systemic therapy alone. This study demonstrated that breast surgery did not contribute to the survival of dnMBC patients.[10] In the study published by Soran et al. (BOMET MF14-01), local treatments were identified as an independent prognostic factor positively influencing survival in dnMBC patients with bone-only metastases. The researchers observed that breast surgery improved survival in all patient groups except those with triple-negative disease. Additionally, this study showed similar survival outcomes whether breast surgery was performed before or after 1st line ST.[19] In a retrospective study by Jianna et al., breast surgery was found to improve survival outcomes in dnMBC patients (39 vs. 24.6 months). However, unlike the study above, this study found that breast surgery performed after 1st line ST was more beneficial than surgery performed before.[8] In our study, breast surgery was performed before 1st line ST in 34% of patients and after 1st line ST in 66%. Patients who underwent breast surgery had better survival outcomes compared to those who did not (median OS: 36 vs. 32 months). However, this result was not demonstrated in multivariate analysis. Breast surgery performed before or after

1st line ST was not identified as a factor influencing survival.

The necessity of local treatments, the choice of treatment, and the timing of these interventions remain uncertain in dnMBC patients. In the study by Pons-Tostivint et al., the impact of primary RT, surgery, or a combination of both on OS in dnMBC patients was investigated. The study found better OS outcomes in patients who received breast RT or RT combined with surgery compared to those who did not receive local treatment. Additionally, patients who underwent breast RT, surgery, or both had better progression-free survival outcomes compared to those who did not receive local treatment.[9] Reinhorn et al. conducted a meta-analysis of four studies involving 970 dnMBC patients to investigate the contribution of local treatments to survival. All studies included patients who underwent breast surgery, and three studies included patients who received adjuvant breast RT. The meta-analysis concluded that while local treatments did not improve OS, they did improve the time to locoregional progression, and this result was consistent across all molecular subtypes. Similar outcomes were reported for patients with bone-only metastases.[23] In our study, breast RT was performed in patients who responded to 1st line ST. When breast RT was evaluated alone or in combination with breast surgery, it was identified as a factor influencing survival in univariate analysis. However, this result was not supported in multivariate analysis. The conflicting outcomes regarding local treatments in dnMBC patients highlight the importance of appropriate patient selection. Determining which patients should undergo breast surgery, breast RT, or both, as well as the timing of these treatments, remains an area requiring further investigation.

Limitations: The retrospective nature of the study introduces inherent biases and limitations associated with data collection and selection.

Conclusion

In this study, the most significant prognostic factors were identified as molecular subtyping of breast cancer, the extent of metastasis, and the response of metastatic lesions to first-line systemic therapy. Local treatments targeting the breast, including both surgery and radiotherapy (RT), were found to influence the prognosis but did not have as strong an impact as the aforementioned variables.

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