ASSESMENT OF PROGNOSTIC VALUE OF METASTATIC FREE INTERVAL AS OVERALL SURVIVAL SURROGATE IN METASTATIC BREAST CANCER FEMALE PATIENTS

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INTRODUCTION

Various surrogate endpoints for overall survival (OS) have been recently used by FDA for drug approval in miscellaneous cancer types. This aims to facilitate the establishment of clinical trials, propose beneficial treatment options after shorter duration of assessment and provides new clinical prognostic tools. Metastasis Free Survival (MFS) has been proven to be a Strong Surrogate for Overall Survival in Localized Prostate Cancer. However, this surrogacy has not been studied in breast cancer or any other solid tumor.

AIM OF THE WORK

To determine the prognostic value of metastasis free interval (MFI) to be a surrogate for overall survival after metastasis in female patients with metastatic breast cancer and To compare MFI among the Breast cancer subtypes in metastatic breast cancer female patients.

PATIENTS AND METHODS

Patients:

This retrospective study included 332 breast cancer female patients whose data was retrieved from the archives of medical research institute from December 2009 to December 2019. All included patients had an initial diagnosis of stage 1–3 breast cancer and all have developed subsequent distant metastasis.

Methods:

Data was retrieved in a retrospective approach from December 2009 to 2019 to identify patients with initial diagnosis of stage I-III breast cancer who developed subsequent distant metastasis. Metastatic free Survival was measured from the date of diagnosis of initial breast cancer to the date of first evidence of distant metastases confirmed by imaging or histologic evidence. Metastasis-Free interval (MFI) is categorized into three categories (short: <3years, intermediate: 3-5 years, long: >5years). We aimed to evaluate the surrogacy correlation between MFI and OS in breast cancer patients, the relationship between MFI and clinicopathological tumor characteristics and to compare MFI in breast cancer subtypes.

RESULTS

Table 1: Correlation between MFI time and OS time (n=332)

	MFI time	
	r	p
Total sample	0.855*	<0.001*
Short MFI<3y	0.429*	<0.001*
Intermediate MFI 3-5y	0.067	0.566
Long MFI >5y	0.694*	<0.001*

r: Pearson coefficient *: Statistically significant at $p \leq 0.05$

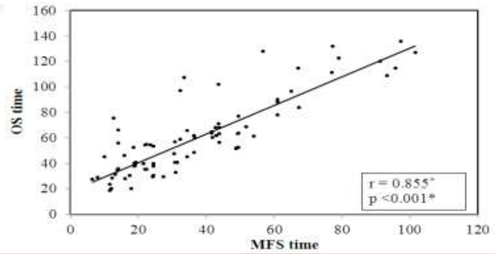

Figure 1: Correlation between MFI time and OS time in the study population (n=332)

Table 2: Relation between MFI and Tumor subtype (n=332)

Subtype	N	MFI time			H	p
		Min. – Max.	Mean ± SD.	Median		
ER+ve, PR+ve HER2 –ve	197	6.43– 101.50	42.57 ± 25.17	41.60	41.358*	<0.001*
ER+ve, PR+ve HER2 +ve	54	13.20– 67.37	35.43± 13.95	34.37		
ER-ve, PR–ve HER2 +ve	20	12.0 – 101.50	24.25 ± 19.10	19.15		
TNBC	61	13.97 – 101.5	23.97 ± 13.26	19.20		

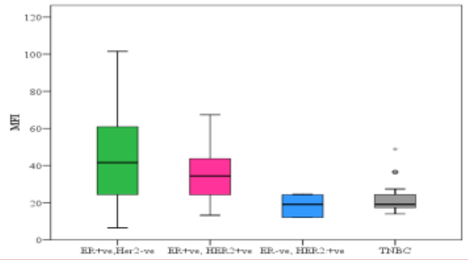

Figure 2: Relation between MFI time and BC subtype

Table 3: Multivariate analysis Logistic COX regression for MFI time

	Sig.	HR	95% CI	
			LL	UL
Age	0.001*	0.091	.021	0.389
Tumor size (pT)	<0.001*	10.749	3.014	38.340
LNs (pLN)	0.045*	6.194	1.045	36.714
Subtype	<0.001*	0.061	0.013	0.289
Chemotherapy	0.315	3.255	0.326	32.515
Duration of adjuvant endocrine treatment (years)	0.134	0.418	0.133	1.308
ECE	0.222	1.978	0.661	5.919
Targeted therapy	0.019*	0.166	0.037	0.743

HR: Hazard ratio
C.I: Confidence interval
LL: Lower limit
UL: Upper Limit
*: Statistically significant at $p \leq 0.05$

CONCLUSION

MFI is strongly correlated to OS in breast cancer in addition to its relation to the tumor clinicopathological characteristics, which provides the potential validity of its usage as a surrogate endpoint for OS in clinical trials assessing novel adjuvant therapies in treatment paradigm and an additional clinical prognostic tool for metastatic breast cancer female patients.