Clinical–pathological patterns and prognosis of young women with breast cancer brain metastases: a single-center retrospective study

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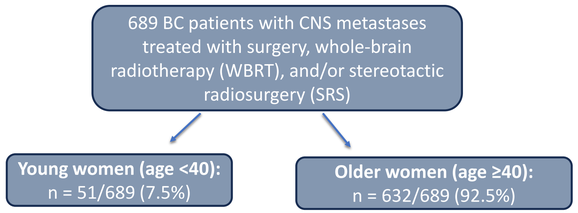
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Background

- Although most patients diagnosed with breast cancer (BC) present with early-stage disease, a high proportion ultimately develop metastatic recurrences outside and/or within the central nervous system (CNS)[1].
- The incidence of CNS metastases among patients with metastatic BC is increasing, largely because they are living longer due to more effective systemic therapies[2].
- Some literature suggests that young women (age <40) have more aggressive disease biology and higher risk of relapse and death than older women[3,4,5].
- However, the clinical-pathological features, treatment patterns and outcomes of young women with CNS metastases are not well characterized.

Methods

- Retrospective cohort study of patients with metastatic BC who were treated at the Sunnybrook Odette Cancer Centre between 2008 - 2018 for CNS metastases using local therapy.



- Patient characteristics and treatment patterns were described with medians and interquartile ranges for continuous variables and percentages for categorical variables.
- Categorical variables were compared between young patients (<40 years of age) and older patients (≥ 40 years of age) using Chi-square tests and continuous variables using Wilcoxon rank-sum tests.
- Univariable and multivariable Cox proportional hazards models were also completed.

Patient characteristics

- Median time between metastatic BC diagnosis and CNS metastases was 8 months for both younger and older patients (p=0.38).
- 75.5% of young women vs. 66.4% of older women had ductal tumor histology (p = 0.36).
- No significant differences in BC subtype were observed among women <40 years vs. ≥ 40 years of age (p = 0.30).
- While there was no significant difference in the sites of metastatic disease involvement in the bone, liver, lung or lymph nodes, **young women were significantly more likely to develop leptomeningeal metastatic disease (LMD) than older women (39.6% vs. 22.3%, p = 0.004).**
- We did not identify any baseline clinical and/or pathological variables, nor treatment variables that were associated with the development of LMD (Table 1).

Table 1. Factors associated with LMD development among young women < 40 years of age

	LMD present n=21	LMD absent n=32	p-value*
BC subtype, n (%)			0.18
HR+HER2-	7 (33.3%)	8 (25%)	
HER2+	7 (33.3%)	13 (40.6%)	
TNBC	7 (33.3%)	6 (18.8%)	
Unknown	0 (0%)	5 (15.6%)	
Histology, n (%)			0.08
Lobular	2 (9.5%)	1 (3.1%)	
Ductal	18 (85.7%)	22 (68.8%)	
Unknown	1 (4.8%)	9 (28.1%)	
First line local therapy, n (%)			0.32
SRS only	4 (19%)	9 (28.1%)	
WBRT only	12 (57.1%)	19 (59.4%)	
Surgery-based	3 (14.3%)	4 (12.5%)	
No Treatment	2 (9.5%)	0 (0%)	
Re-treated for CNS metastases, n (%)			0.95
Yes	9 (42.9%)	14 (43.8%)	
No	12 (57.1%)	18 (56.2%)	

Abbreviations: MBC, metastatic breast cancer; BCBM, breast cancer brain metastasis; HR+, hormone receptor positive; TNBC, triple negative breast cancer; SRS, stereotactic radiosurgery; WBRT, whole brain radiotherapy.

a p-values from Chi-square to test the hypothesis of no association.

Results

- Median CNS-specific progression-free survival (PFS) for the overall population was 13 months (95% CI 10-15 months). There was no significant difference in median CNS-specific PFS between women <40 and ≥40 years of age.
- In total, 179 patients (26%) were re-treated with radiation therapy due to CNS progression; patients age <40 years were more likely to be re-treated than their older counterparts (43.4% vs. 24.5%, p=0.003).

Figure 1. CNS-specific PFS and overall survival by age group

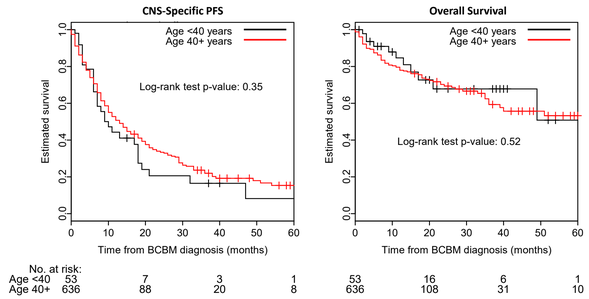


Table 2. Variables associated with CNS-specific PFS

	Univariable models N=689, HR, (95% CI), P	p-value*	Multivariable model, N=689, HR, (95% CI), P	p-value**
Age group				
≥ 40 years	1		1	
< 40 years	1.19 (0.83, 1.72)	0.34	1.11 (0.77, 1.61)	0.57
BC subtype				
HR+HER2-	1		1	
HER2+	0.63 (0.48, 0.83)	0.001	0.7 (0.53, 0.92)	0.01
TNBC	1.33 (1, 1.79)	0.05	1.46 (1.09, 1.96)	0.01
Unknown	0.43 (0.26, 0.71)	0.001	0.48 (0.29, 0.81)	0.006
First line local therapy				
SRS only***	1		1	
WBRT only	2.09 (1.55, 2.81)	<0.001	1.81 (1.34, 2.45) 4	<0.001
Surgery based	1.04 (0.7, 1.56)	0.84	0.89 (0.59, 1.34)	0.59
No Treatment	1.58 (0.78, 3.19)	0.20	1.52 (0.75, 3.08)	0.24
LMD status				
Absent	1		1	
Present	1.58 (1.24, 2.01)	<0.001	1.42 (1.11,1.82)	0.006

* p-values from separate univariable Cox regression models, ** p-values from a multivariable Cox regression model, *** Includes the one patient who was treated with SRS+WBRT.

Results

Table 3. Variables associated with overall survival (OS)

	Univariable models N=689, HR, (95% CI), P	p-value*	Multivariable model N=689 , HR, (95% CI), P	p-value**
Age group				
≥ 40 years	1		1	
< 40 years	0.82 (0.44, 1.52)	0.52	0.81 (0.43, 1.51)	0.51
BC subtype				
HR+HER2-	1		1	
HER2+	0.41 (0.26, 0.64)	<0.001	0.49 (0.31, 0.77)	0.002
TNBC	1.06 (0.68, 1.63)	0.81	1.27 (0.82, 1.98)	0.29
Unknown	0.2 (0.07, 0.56)	0.002	0.24 (0.09, 0.67)	0.006
First line local therapy				
SRS only***	1		1	
WBRT only	3.42 (2.01, 5.85)	<0.001	2.79 (1.62, 4.8)	<0.001
Surgery based	0.9 (0.4, 2.05)	0.81	0.72 (0.32, 1.65)	0.44
No Treatment	2.86 (1.05, 7.83)	0.04	2.66 (0.97, 7.3)	0.057
LMD status				
Absent	1		1	
Present	1.73 (1.19, 2.51)	0.004	1.43 (0.98, 2.09)	0.065

p-values from separate univariable Cox regression models, ** p-values from a multivariable Cox regression model, *** Includes the one patient who was treated with SRS+WBRT

Discussion/Conclusions

In our study of women with metastatic BC and CNS metastases, women who were <40 years of age were more likely to develop LMD than women ≥40 years of age. Although young women were also more likely to be re-treated for progression of CNS metastases, their CNS-specific PFS and OS were not inferior that of patients ≥ 40 years-of-age.

- Limitations of our study include its retrospective nature, a small sample size of patients <40 years of age, the fact that some patients had missing clinical and pathological data, and lack of tissue-based analyses.

References

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