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Development of graded prognostic assessment for breast Cancer brain metastasis incorporating extracranial metastatic features: a retrospective analysis of 284 patients

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Abstract

Background Breast cancer brain metastasis (BCBM) is associated with poor survival outcomes and reduced quality of life. The Graded Prognostic Assessment (GPA) score model serves as a well-established tool for predicting the prognosis of BCBM. Notably, the presence of extracranial metastasis (ECM) is considered as a significant prognostic factor in the breast GPA model. This study aims to further refine other features of ECM to enhance the prognostic prediction for BCBM.

Methods This study included all inpatients diagnosed with BCBM at the Cancer Hospital, Chinese Academy of Medical Sciences, from January 2010 to July 2021. Baseline characteristics of patients were compared based on features of ECM, including the presence, number, location, and control status of metastases. Overall survival (OS) were compared using the Kaplan–Meier method with log-rank tests. Cox regression analyses were conducted to identify significant prognostic factors. The aforementioned ECM features were incorporated into the original Breast-GPA model to enhance its prognostic accuracy. The concordance index (C-index) and restricted mean survival time (RMST) were utilized to evaluate and compare the predictive accuracy of the updated and original survival models.

Results 284 patients with BCBM were included in the study. Kaplan–Meier survival curves suggested that patients without ECM when diagnosed with BCBM showed better survival ($p=0.007$). In the subgroups with ECM, more than 3 organs involved, both bone and visceral metastasis and progressive ECM portended dismal OS ($p=0.003$, 0.001 and <0.001). Multivariate analysis demonstrated that molecular subtype, presence of ECM, and number of brain metastasis significantly influenced OS after BCBM. By modifying the current GPA model to include more precise characteristics of ECM, the predictive accuracy was further enhanced as indicated by the C-index and RMST curve.

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Conclusions More ECM sites, both bone and visceral invasion and uncontrolled ECM were dismal prognostic factors for survival outcomes of BCBM patients. A new Breast-GPA model with better predictive effect was constructed.

Keywords Breast cancer, Brain metastasis, Extracranial metastasis, GPA model, Prognosis

Introduction

Breast cancer is the second frequent malignant tumors of suffering from brain metastasis, although the incidence was always thought to be underestimated [1]. Upon diagnosis, breast cancer brain metastasis (BCBM) portends poor survival outcomes and the blood brain barrier also poses a significant clinical quandary, given limited penetration of many chemotherapies and lack of information regarding their central nervous system efficacy [2, 3]. With further research, more and more therapeutic methods had been developed and utilized in the clinical practice, including surgery, stereotactic radiosurgery (SRS), whole-brain radiation therapy (WBRT), chemotherapy, targeted therapy and immunotherapy [4]. The advanced treatment strategies and prolonged life expectancy emphasized the significance of predicting prognosis to optimize physicians' choice, patients' decision and palliative treatment.

Apart from the features of brain lesions, extracranial metastasis (ECM) was also related to the occurrence risk and long-term survival for BCBM. The National Comprehensive Cancer Network guideline recommended brain magnetic resonance imaging scan for the patients with recurrent or metastatic breast cancer if suspicious symptoms of central nervous system occur [5]. A study based on the Surveillance, Epidemiology, and End Results database concluded that when using bone metastasis as a reference, lung metastasis increased the risk of brain metastasis in patients with triple negative breast cancer [6]. Other retrospective study also demonstrated the predictive value of ECM pattern, which was included in their newly established risk model for BCBM [7].

As for the predictive value of ECM for overall survival (OS) after BCBM, numerous studies have explored [8–13] and the most authoritative was the Graded Prognostic Assessment (GPA) tool. The Breast-GPA tool only included the age of diagnosis, Karnofsky performance score (KPS) and molecular subtype for survival predication in 2012 [14]. With gradual update, the modified GPA incorporated the number of brain lesions in 2015 [15], and the 2020 updated version included the presence of ECM [16]. Regarding ECM, there are many other characteristics, such as the number of ECM organs, the specific location of ECM and whether extracranial diseases are controlled or progressive. All these features were also confirmed to be closely related with the long-term mortality of BCBM patients in other analysis [13, 17–19].

In light of the aforementioned factors, we set up the database of BCBM patients treated in our institution, intending to clarify the impact of the presence, quantity, site and control status of ECM on the prognostic outcomes to optimize the GPA model.

Methods

Enrolled cohort

We conducted a retrospective cohort study enrolling patients diagnosed with BCBM at the Cancer Hospital, Chinese Academy of Medical Sciences (CHCAMS) from January 1st, 2010, to July 1st, 2021. BCBM was diagnosed either at the initial diagnosis of breast cancer or during follow-up after treatment. The study was approved by the Ethics Committee of CHCAMS (the ethical approval number: NCC4835) and adhered to the Helsinki Declaration. We excluded cases with duplicate registration, inadequate neuroimaging or pathological evidence of brain metastasis, and patients with other primary malignancies or contralateral breast cancer. All BCBM patients who did not meet these exclusion criteria were included in the study. The last follow-up was on July 1st, 2023.

Data collection

We documented detailed clinicopathological data for all participants, including age at first diagnosis, menopausal status, KPS or Eastern Cooperative Oncology Group (ECOG) performance status, pathological grade, TNM stage, hormone receptor (HR) status, and human epidermal growth factor receptor 2 (HER2) status. Treatment history for primary breast cancer, including neoadjuvant therapy, surgical interventions, and adjuvant chemotherapy or radiotherapy, were recorded. Disease-free survival was calculated as the duration from the date of radical surgery to the occurrence of any disease progression, including local recurrence, distant metastasis, the development of new tumors, or death due to the tumor.

For BCBM, we extracted data encompassing ECM characteristics, diagnostic mode (symptomatic diagnosis or occasional findings in imaging), brain lesion features (including number, location and maximum diameter), and administered therapy (including local and systemic therapy). In detailing ECM, we noted the presence (present or absent), number of involved organs (0, 1–3, or ≥4), location (bone-only, visceral-only, or both bone and visceral), and control status (controlled or uncontrolled) of the metastases. These ECM features were then analyzed across different subgroups. OS after brain metastasis was determined from the time of BCBM diagnosis to either the occurrence of breast cancer-related death or the date of the last follow-up, whichever occurred first.

Statistical analysis

The baseline characteristics across different subgroups were compared using the chi-square test or Fisher's exact test for categorical variables and the t-test or Mann-Whitney U test for continuous variables, as appropriate. Survival outcomes were analyzed using the Kaplan-Meier method, and differences between groups were assessed using the log-rank test. A Cox proportional hazards model was employed for multivariate analysis, including all clinicopathological features with a univariate p-value < 0.1. To compare the prognostic performance of the original and updated Breast-GPA models, both the restricted mean survival time (RMST) at a fixed time point of 24 months and the concordance index (C-index) were employed. The RMST is a measure of the average survival time of different score groups within a specified time period. A two-tailed p-value < 0.05 was considered statistically significant. All analyses were performed using SPSS version 26.0 (SPSS Inc, Chicago, IL, USA) and the "ggplot", "survminer", "survival", "survRM2" packages of R software (version 4.2.3; http://www.r-project.org).

Results

Baseline characteristics

Totally, 284 patients diagnosed with BCBM were included in this study. In analyzing baseline characteristics of BCBM patients with or without ECM, we observed that those diagnosed with one or more extracranial lesions prior to brain metastasis had a higher incidence of M1 stage at initial breast cancer diagnosis (16% vs. 4%, $p=0.040$), underwent more radical mastectomies for their primary tumors (71% vs. 58%, $p=0.044$), and were more frequently detected through occasional imaging screenings (58% vs. 29%, $p<0.001$) (Supplementary Table 1). Additionally, patients with ECM tended to have a higher number of brain lesions (69% vs. 46%, $p=0.003$), which reduced the likelihood of undergoing neurosurgical interventions (11% vs. 27%, $p=0.003$).

Further analysis of the specific number of extracerebral organs showed similar baseline comparisons (Supplementary Table 2). Notably, patients with involvement of more than 4 organs were less likely to have HER2-positive disease ($p=0.044$) and thus rarely received anti-HER2 targeted therapy ($p=0.024$). Regarding the baseline comparison between patients with controlled versus uncontrolled extracranial disease, differences were observed in the surgical intervention of primary tumors and brain metastases ($p=0.041$ and <0.001, respectively), disease-free survival ($p=0.001$), and the diagnostic mode for BCBM ($p<0.001$) (Supplementary Table 3).

Survival outcomes

The study compared the long-term survival of BCBM patients across subgroups, differentiated by factors like the presence, number, location and control status of ECM. Patients without ECM showed a significantly longer median OS of 46 months, compared to 22 months in those with ECM ($p=0.007$, Fig. 1A). Furthermore, an increase in the number of affected extracranial organs correlated with poorer prognosis. Specifically, patients with more than four affected extracranial organs had a median OS of 18 months, considerably lower than 22 months for those with 1–3 metastatic sites and 46 months for patients without ECM ($p=0.003$, Fig. 1B). Analyzing the ECM locations, significant differences in OS were observed between patients with bone-only, visceral-only, and both bone and visceral metastases ($p=0.001$, Fig. 1C). As for the control status of ECM, patients with controlled ECM showed a clear trend in favorable OS compared to those with uncontrolled ECM ($p<0.001$, Fig. 1D).

To further elucidate the prognostic factors influencing OS of BCBM patients, we performed a Cox regression analysis (Table 1). We included all clinicopathological features with univariate p-value lower than 0.1 in the multivariate study. These features included the age at breast cancer diagnosis, HR status, HER2 status, the presence, number, and status of ECM, the number and size of BM, surgical intervention for BM and endocrine and targeted therapy post-BCBM. Notably, the HR and HER2 status, presence of ECM, number of BM and targeted therapy after BM were identified as independent prognostic factors for BCBM in the multivariate analysis, with respective p-values of 0.009, 0.002, 0.038,0.001 and 0.012.

New Breast-GPA model construction

According to the previous updated Breast-GPA scoring model (Table 2), all the enrolled patients were divided into four distinct subgroups. Significant differences were observed between different scoring subgroups ($p=0.004$, Fig. 2A). It was evident that higher GPA scores were associated with more favorable OS in patients. Considering the number and control status of ECM were independent prognostic factors in the multivariate Cox analysis, we constructed a new Breast-GPA scoring model by incorporating these factors (Table 3). The new Breast-GPA model focused not only the presence, but also the quantity and control status of ECM. Cases with 3 or less controlled ECM were scored with 0.5, while those with more than 3 or progressive ECM were marked with 0. Survival outcomes were further measured by the new Breast-GPA model. In this model, the median OS of subgroups with a score of 3.5-4.0, 2.5-3.0, 1.5-2.0 and 0–1.0 were 41 months, 29 months, 18 months and 11 months, respectively ($p<0.001$, Fig. 2B). The C-index for the original Breast-GPA model was 0.582, whereas the C-index for the new Breast-GPA model was 0.616. The estimated 24-RMST for each score group in the two models were

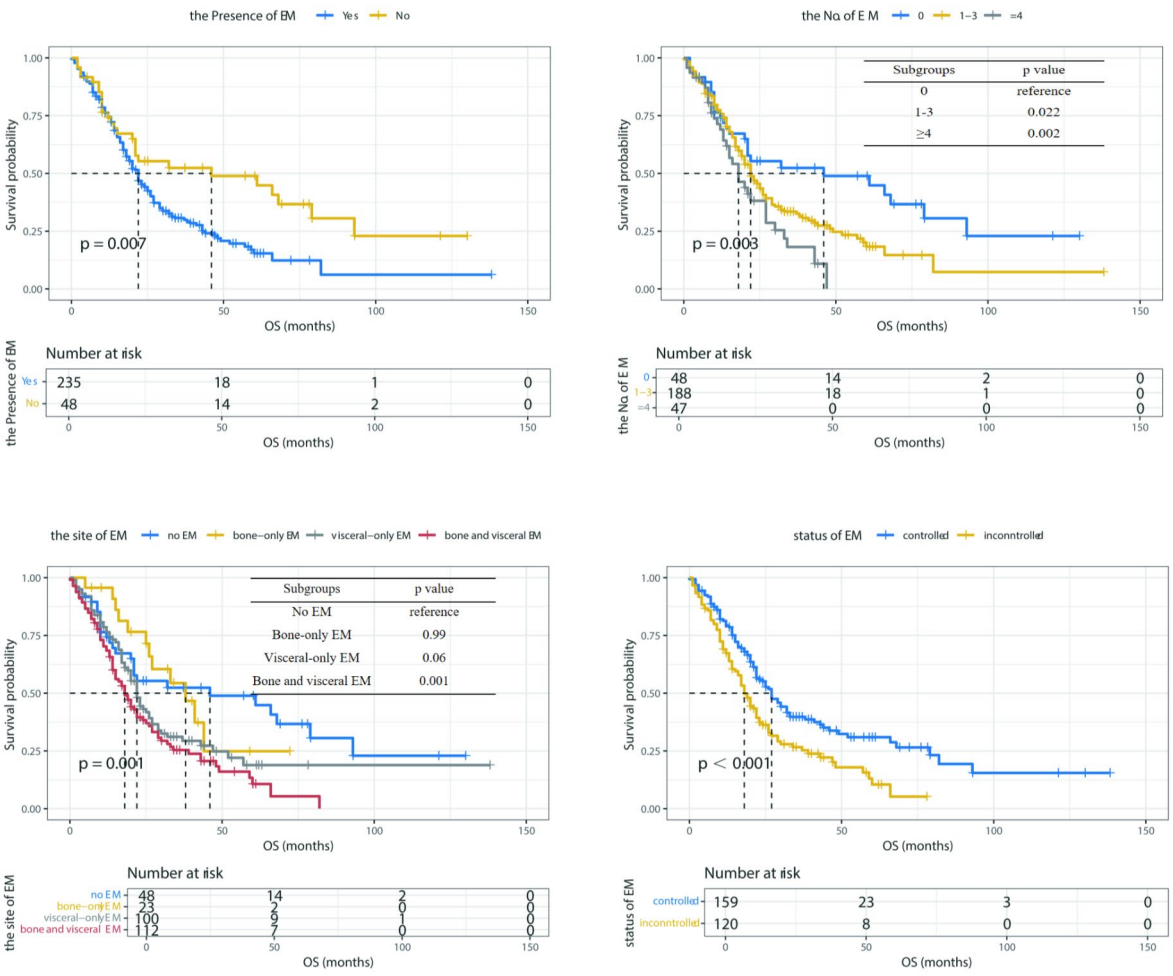

Fig. 1 Kaplan-Meier curves for OS of BCBM patients based on ECM characteristics
Note: The subfigures were categorized by (**A**) the presence of ECM, (**B**) the number of involved ECM organs, (**C**) the location of ECM, and (**D**) the control status of ECM
Abbreviations: ECM: extracranial metastasis; OS: overall survival; BCBM: breast cancer brain metastasis

shown in the Supplementary Table 4. The RMST curve indicated that the new model had improved accuracy since the RMST values generally increased with higher Breast-GPA scores (Fig. 3).

Discussion

With the number of multi-disciplinary and patient-tailored therapeutic strategies increases exponentially, BCBM is not regarded as uncurable disease. Among a great number of treatment regimens, it is crucial to select the optimal therapeutic strategies in appropriate time. Therefore, there is an urgent requirement for prognostic models to guide clinical practice.

The gradually updated Breast-GPA prognosis model validated that the presence of ECM had impact on the prognosis of BCBM patients. According to this standard model, patients in our institution with higher GPA scores were confirmed with longer survival period. The Kaplan-Meier survival curves of different GPA score groups clustered into separate lines when classified into four groups (GPA 0–1.0, 1.5-2.0, 2.5-3.0 and 3.5-4.0), of which the median survival time were 16months, 18months, 32 months and 46 months respectively. It could be found that the life expectancy of patients in our constitution was comparatively longer than the GPA model [16], of which the OS after brain metastasis were 6months, 13 months, 24 months and 36 months in the corresponding GPA layers. This tendency could be explained by the improved therapeutic methods and sufficient supportive treatments for patients in the advanced stage, indicating that a new prognostic model is warranted in the current clinical practice.

Numerous previous studies have posited that many characteristics of ECM had impact on the prognosis

Table 1 Univariate and multivariate analysis of variables correlated with OS after brain metastasis

Variables	Univariate Analysis		Multivariate Analysis	
	Hazard Ratio (95% CI)	*p*-value	Hazard Ratio (95% CI)	*p*-value
Age, years		**0.066**		0.116
<40	Reference		Reference	
40–59	1.33 (0.95–1.86)	0.099	1.20 (0.80–1.79)	0.394
60–79	1.79 (1.01–2.98)	0.025	1.86 (1.03–3.37)	0.041
Menopausal Status		0.280		
Premenopausal	Reference			
Postmenopausal	1.17 (0.88–1.56)	0.280		
Performance Status		0.175		
KPS 80–100 / ECOG 0–1	Reference			
KPS ≤ 70 / ECOG 2–3	1.30 (0.90–1.89)	0.164		
Unknown	0.86 (0.60–1.23)	0.393		
Grade		0.138		
Grade I-II	Reference			
Grade III	1.43 (0.96–2.01)	0.053		
Unknown	1.08 (0.78–1.50)	0.670		
T Stage		0.542		
Tis/T0-2	Reference			
T3-T4	0.78 (0.49–1.23)	0.281		
Unknown	0.92 (0.66–1.28)	0.627		
N Stage		0.762		
N0-N1	Reference			
N2-N3	0.94 (0.69–1.30)	0.722		
Unknown	0.86 (0.58–1.28)	0.466		
M Stage		0.815		
M0	Reference			
M1	1.05 (0.70–1.58)	0.815		
TNM Stage		0.741		
Stage 0-II	Reference			
Stage III-IV	0.94 (0.68–1.28)	0.676		
Unknown	0.85 (0.57–1.28)	0.443		
HR Status		**0.058**		**0.009**
Positive	Reference		Reference	
Negative	1.33 (0.99–1.78)	0.058	1.86 (1.16–2.97)	0.009
HER2 Status		**0.035**		**0.002**
Positive	Reference		Reference	
Negative	1.37 (1.02–1.84)	0.035	1.77 (1.22–2.57)	0.002
Neoadjuvant Therapy		0.259		
No	Reference			
Yes	0.81 (0.57–1.16)	0.259		
Surgery		0.108		
No	Reference			
Yes-Radical Mastectomy	0.61 (0.37–1.01)	0.053		
Yes-Conserving Surgery	0.56 (0.32–0.98)	0.042		
Adjuvant Chemotherapy		0.126		
No	Reference			
Yes	0.98 (0.63–1.52)	0.932		
Without Surgery	1.66 (0.89–3.11)	0.112		
Adjuvant Radiotherapy		0.116		
No	Reference			
Yes	0.94 (0.69–1.28)	0.695		
Without Surgery	1.59 (0.54–2.65)	0.075		
Presence of ECM		**0.008**		**0.038**

Table 1 (continued)

Variables	Univariate Analysis		Multivariate Analysis	
	Hazard Ratio (95% CI)	***p*-value**	**Hazard Ratio (95% CI)**	***p*-value**
Absent	Reference		Reference	
Present	1.77 (1.16–2.71)	0.008	1.84 (1.03–3.27)	0.038
Number of ECM		**0.004**		0.110
Without ECM	Reference		Reference	
1–3 sites	1.67 (1.08–2.57)	0.020	1.83 (1.02–3.26)	0.042
≥4 sites	2.41 (1.43–4.07)	0.001	1.96 (0.99–3.90)	0.055
Status of ECM		**0.004**		0.088
Controlled	Reference		Reference	
Uncontrolled	1.67 (1.18–2.37)	0.004	1.36 (0.96–1.94)	0.088
Diagnostic Mode		0.739		
Symptomatic Diagnosis	Reference			
Occasional in Imaging	1.05 (0.79–1.40)	0.739		
Number of BM		**<0.001**		**0.001**
1	Reference		Reference	
≥2	1.97 (1.40–2.75)	<0.001	1.89 (1.28–2.79)	0.001
Maximum of BM Diameter		**0.052**		0.070
<3 cm	Reference		Reference	
≥3 cm	0.82 (0.54–1.25)	0.350	1.14 (0.70–1.86)	0.600
Unknown	1.32 (0.97–1.80)	0.079	1.53 (1.06–2.19)	0.022
Radiotherapy for BM		0.106		
No Radiotherapy	Reference			
SRS alone	0.79 (0.52–1.22)	0.286		
WBRT alone	1.26 (0.86–1.83)	0.238		
SRS plus WBRT	0.96 (0.56–1.66)	0.888		
Surgical Intervention for BM		**0.001**		0.065
No	Reference		Reference	
Yes	0.46 (0.28–0.74)	0.001	0.57 (0.31–1.04)	0.065
Chemotherapy after BM		0.475		
No	Reference			
Yes	0.87 (0.60–1.27)	0.475		
Endocrine Therapy after BM		**0.038**		0.051
ET for HR + tumors	Reference		Reference	
no ET for HR + tumors	1.46 (0.97–2.19)	0.071	1.57 (1.00-2.49)	0.051
HR- tumors	1.71 (1.13–2.59)	0.011	/	
Targeted Therapy after BM		**0.004**		**0.012**
TT for HER2 + tumors	Reference		Reference	
no TT for HER2 + tumors	2.00 (1.26–3.19)	0.003	2.00 (1.16–3.42)	0.012
HER2- tumors	1.57 (1.13–2.19)	0.008	/	

Note: P-values lower than 0.1 in the univariate analysis and 0.05 in the multivariate analysis were marked in bold. Due to an overlap in the definitions between the potential prognostic factors "presence of ECM" and "number of ECM", they were not incorporated simultaneously in the multivariate analysis. Instead, the "number of ECM" was included in the final multivariate model in place of the "presence of ECM"

Abbreviations: CI: confidence interval; KPS: Karnofsky performance status; ECOG: Eastern Cooperative Oncology Group; HR: hormone receptor; HER2: human epidermal growth factor receptor 2; ECM: extracranial metastasis; BM: brain metastasis; SRS: stereotactic radiosurgery; WBRT: whole-brain radiotherapy; ET: endocrine therapy; TT: targeted therapy

of BCBM patients. Some researches revealed the large quantity of ECM organs as dismal prognosis factors [17–20]. Others explored the impact of exact ECM sites on long-term survival. The results suggested that the presence of lung [18, 20] or liver metastasis [20] exhibited a propensity for limited life expectancy and were incorporated to establish prognostic models. Besides, the control status of extracranial lesions was also proven to be influential for the prognosis of BCBM patients [21, 22]. Considering the definition of quantity and location of extracranial metastases overlap each other, for example "both visceral and bone metastasis" portends larger number of ECM, these two aspects could not be included in the prognostic model simultaneously. We ultimately took the quantity and control status of ECM into consideration to renew the current Breast-GPA model [16], namely

Table 2 The definition of original Breast-GPA model

Factor	0	0.5	1	1.5	2
KPS	≤60	70–80	90–100	NA	NA
Age	≥60	<60	NA	NA	NA
Number of BM	≥2	1	NA	NA	NA
ECM	Present	Absent	NA	NA	NA
Subtype	Basal	Luminal A	NA	HER2 or Luminal B	NA

Note: The tumor subtypes were categorized into four distinct groups including basal-like subtype (triple-negative), luminal A subtype (ER/PR-positive and HER2-negative), HER2 subtype (ER/PR-negative and HER2-positive), and luminal B subtype (triple-positive)

Abbreviations: GPA: the Graded Prognostic Assessment; KPS: Karnofsky performance status; NA: not applicable; BM: brain metastasis; ECM: extracranial metastasis; ER: estrogen receptor; PR: pro gesterone receptor; HER2: human epidermal growth factor receptor 2

new Breast-GPA scoring model. The newly established GPA model no longer determined the survival outcomes of BCBM patients based on the presence or absence of extracranial metastases. Instead, patients with less than 3 stable ECM organs were marked with 0.5 points for GPA score, equivalent to those without ECM. This modification maintained the overall scoring structure of the Breast-GPA model. The discrepancy of survival curves in four GPA groups were much more conspicuous. Survival outcomes were further assessed using both the C-index and RMST at 24 months. The C-index for the updated Breast-GPA model was higher, and the differences in RMST across each scoring group were more obvious, as demonstrated by the RMST curve. These findings indicate that the updated model offers improved predictive accuracy compared to the original model. Depending on these results, clinical therapeutics for BCBM patients with limited number of controlled ECM were supposed to be relatively optimistic. For these patients, the clinical practice should focus more on the intracranial lesions, such as the craniocerebral operations, SRS and WBRT. In contrast, the population with multiple progressive visceral metastases were predicted with dismal prognosis, who require more aggressive systematic treatments and close surveillance after initial diagnosis of BCBM.

Except for the features of ECM, other characteristics were also verified to be independent prognostic factors for BCBM patients, including HR and HER2 status, the number of brain metastasis and targeted therapy after BCBM. The negative impact of HR and HER2 negativity

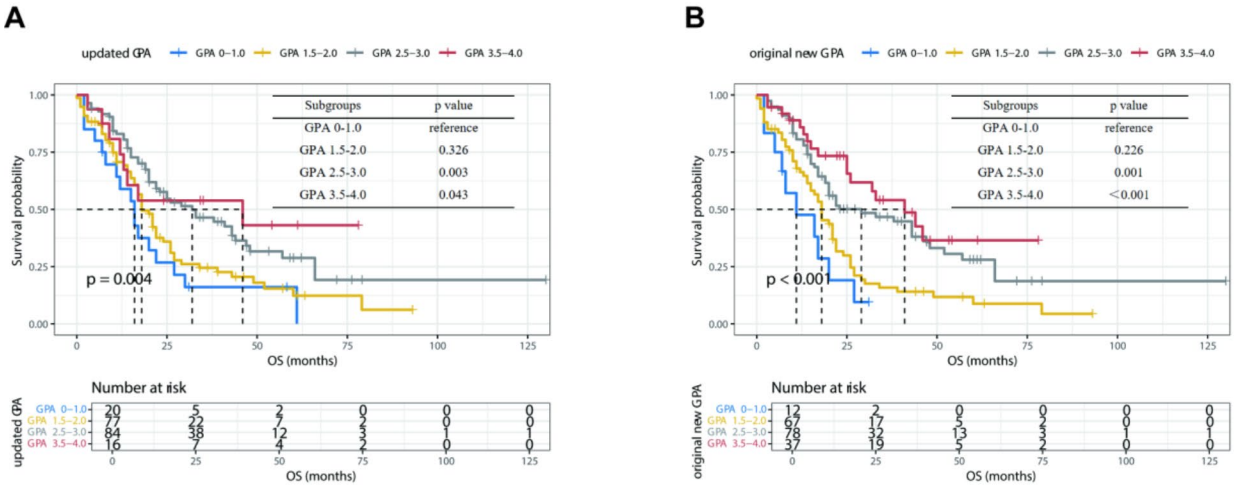

Fig. 2 Kaplan-Meier curves for OS of BCBM patients by Breast-GPA models

Note: The subfigures were categorized by (**A**) the original Breast-GPA model, and (**B**) the new Breast-GPA model.

Abbreviations: GPA: the Graded Prognostic Assessment; OS: overall survival; BCBM: breast cancer brain metastasis.

Table 3 The definition of new Breast-GPA model

Factor	0	0.5	1	1.5	2
KPS	≤60	70–80	90–100	NA	NA
Age	≥60	<60	NA	NA	NA
Number of BM	≥2	1	NA	NA	NA
ECM	>3 or progressive	≤3 and stable	NA	NA	NA
Subtype	Basal	Luminal A	NA	HER2 or Luminal B	NA

Note: The tumor subtypes were categorized into four distinct groups including basal-like subtype (triple-negative), luminal A subtype (ER/PR-positive and HER2-negative), HER2 subtype (ER/PR-negative and HER2-positive), and luminal B subtype (triple-positive)

Abbreviations: GPA: the Graded Prognostic Assessment; KPS: Karnofsky performance status; NA, not applicable; BM: brain metastasis; ECM: extracranial metastasis; ER: estrogen receptor; PR: progesterone receptor; HER2: human epidermal growth factor receptor 2

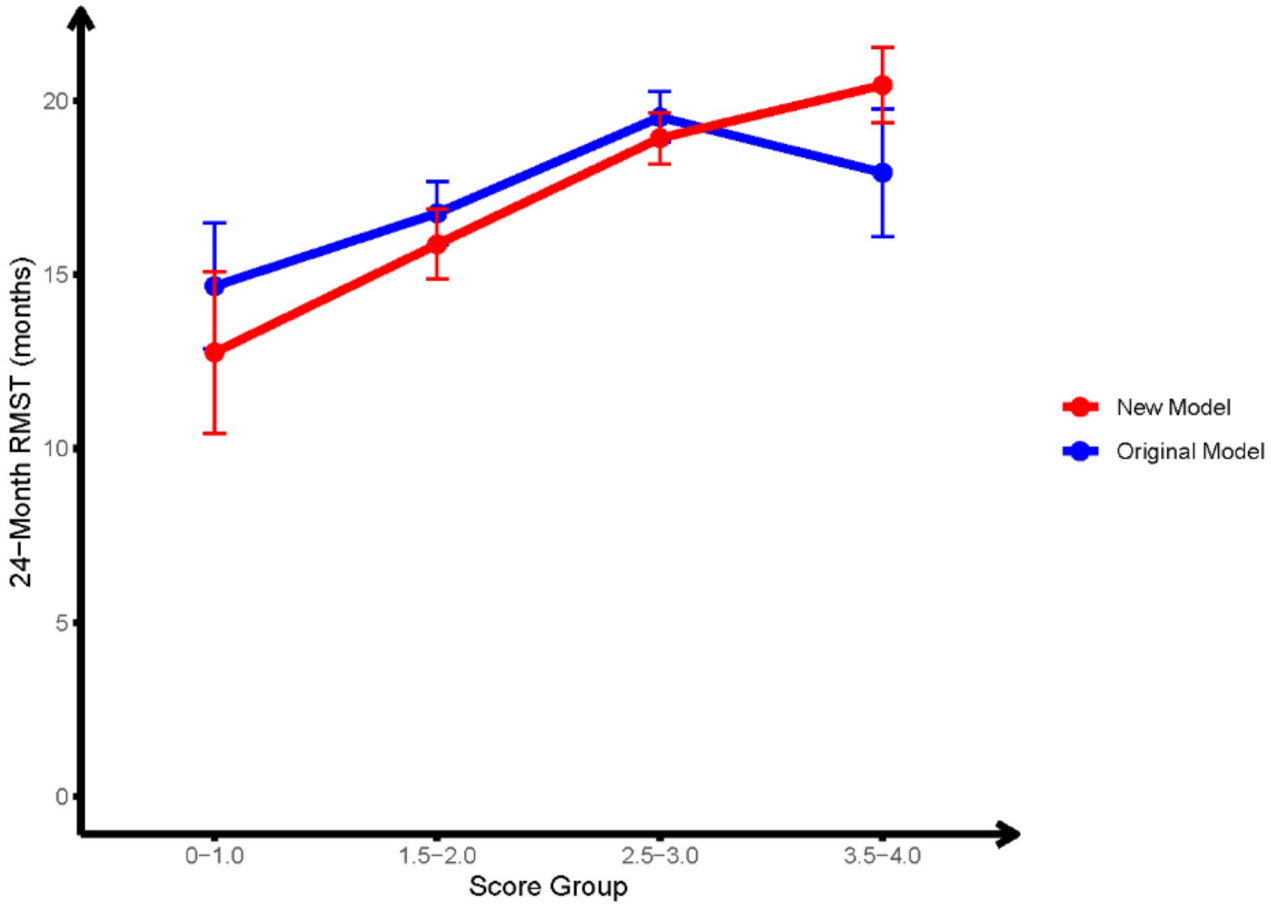

Fig. 3 Comparison of 24-Month RMST between original and new breast-GPA Models
Note: Plot of RMST curves for the original Breast-GPA model (blue), and the new Breast-GPA model (red). The error bars indicate the standard error associated with each RMST value
Abbreviations: RMST: restricted mean survival time; GPA: Graded Prognostic Assessment; BCBM: breast cancer brain metastasis

on BCBM patients was validated in the Breast-GPA model [16], which was in concordance with other studies [23–25]. As for the quantity of brain metastasis, limited number of brain lesions was also associated with the feasibility of neurosurgical interventions and local radiotherapy, leading to prolonged OS. Moreover, patients with HER2-positive tumors who received targeted therapy after BCBM revealed much better prognosis than those without anti-HER2 treatment. These findings suggested that the HER2 targeted drugs were highly effective for BCBM patients. Of note, both tyrosine kinase inhibitor [26, 27] and antibody-drug conjugate [28, 29] were validated efficacious for BCBM patients despite the existence of blood brain barrier. TNM staging did not show significant prognostic value in the univariate or multivariate analyses. This may be due to the advanced disease stage of the patient cohort, where brain metastasis has a more dominant impact on prognosis than the primary tumor's stage.

Undeniably, there exist several limitations. Firstly, this study is based on the population of one single institution and implemented retrospectively, which has some intrinsic deficiency. In details, the confounding, selection and information bias cannot be avoided utterly in the research process. Secondly, the progressive or stable status of extracranial disease was evaluated subjectively, restricted by the deficiency of official definition. Notably, three co-authors finished the assessment separately and discussed the inconsistent opinions. Plenty of other studies have also suggested the status of extracranial disease, instead of their presence, was an independent prognostic factor for BCBM patients [22, 30, 31]. Thirdly, the quantity of enrolled patients was relatively small, resulting in the difficulty to achieve baseline matching between groups. Lastly, the lack of external validation limits the generalizability of our findings. In spite of these limitations, our study represents a pioneering effort in analyzing the impact of overall aspects of ECM on the prognosis

of BCBM patients, considering a large proportion of clinical trials excluded the patients with brain metastasis.

In summary, many characteristics of the ECM displayed remarkable influence on the prognosis of patients with BCBM. More extracranial sites, both bone and visceral intrusion and progressive lesions indicated dismal survival outcomes. When expanded the presence of extracranial disease to their exact number and control status, the GPA model became more accurate. Other pathological and clinical characteristics were also regarded as independent predictions for long-term survival after BCBM but interfered with some inherent features and remains a subject of debate. To shed more light on this issue, more large scale prospective clinical researches are supposed to be implemented.

Conclusions

When diagnosed with BCBM, the limited number and stable status of ECM organs portends better life expectancy. These clinical features could be utilized to expand and optimize the Breast-GPA model.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-024-12983-3.

Supplementary Material 1

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Author contributions

Yan Wang: Conceptualization, Data curation, Formal analysis, Validation, Visualization, Writing - original draft. Hangcheng Xu: Conceptualization, Data curation, Formal analysis, Validation, Visualization, Writing - review & editing. Qiang Sa: Data curation, Formal analysis, Visualization, Writing - original draft. Li Li: Conceptualization, Data curation, Validation. Yiqun Han, Yun Wu and Yiran Zhou: Data curation, Validation. Binghe Xu and Jiayu Wang: Conceptualization, Funding acquisition, Methodology, Supervision, Writing - review & editing.All authors reviewed the manuscript.

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Data availability

The data presented in this study are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Cancer Hospital, Chinese Academy of Medical Sciences (CHCAMS) and adhered to the Helsinki Declaration. The study is retrospective cohort study and only clinical information of patients will be collected without interfering with patients' treatment plans or posing physiological risks to patients. Informed consent was obtained from all patients prior to being included.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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