Surgical Resection of Brain Metastases from Breast Cancer in the Modern Era: Clinical Outcome and Prognostic Factors

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Abstract. *Background: Incidence of brain metastases (BM) from breast cancer (BC) is increasing. However, prognostic evaluation and treatment strategies are still a matter of debate. Aim: To describe the clinical outcome of BM from BC treated by neurosurgical resection and to identify the actual prognostic factors in this specific population. Patients and Methods: We retrospectively reviewed all patients (n=49) with BM from BC treated at our institutions by surgical resection, between December 2001 and July 2011. Patient, tumor and treatment characteristics were recorded. Results: Median cerebral progression-free survival (CPFS) was 11.3 months (95% Confidence Interval (CI)=6.0-16.6 months) and median overall survival (OS) was 19.4 months (95% CI=16.1-22.7 months). By multivariate analyses, altered Mini Mental Status (MMS) (CPFS: p=0.012, OS: p=0.009), multiple systemic metastases (CPFS: p=0.020, OS: p<0.001) and absence of post-operative chemotherapy (CPFS: p=0.013, OS: p=0.006) had independent adverse prognostic values. Hormonal receptors, Human epidermal growth factor-2 (HER2) and molecular subtype were not significantly correlated to survival. Conclusion: Surgical resection is an effective treatment in selected patients with BM from BC. MMS, number of systemic metastases and the use of postoperative systemic treatment are associated with better outcome.*

Breast cancer (BC) is the most common cancer type in women, with approximately 1.3 million cases worldwide, and an estimated 465,000 BC-related deaths, most of them related to distant relapses (1). Thus, metastatic breast cancer (MBC) is still considered as an incurable disease, but continuous progress in systemic therapy is likely to improve overall survival (OS) (2). In addition, MBC may display diverse clinical outcomes. Gene expression profiling studies have revealed that such a clinical heterogeneity may rely upon the existence of distinct BC subtypes, with important prognostic role (3) and which can be approximated in a routine setting using Human epidermal growth factor-2 (HER2), estrogen receptor (ER), and progesterone receptor (PR) status (4).

BC is the second most common cause of brain metastases (BM), with 10-15% of patients experiencing metastasis to the brain (5). In the context of more sensitive and accurate diagnostic methods, as well as the above-mentioned improvement in survival, both incidence and prevalence of BM from BC are thought to be increasing (6). The optimal management of BM from BC is still under debate. Available therapeutic strategies include whole-brain radiation therapy (WBRT), stereotactic surgery (SRS) and/or surgical resection (SR). In addition, systemic treatment may have significant antitumor activity (7). In patients with single- or oligo-metastatic BM and good performance status, a multi-modal approach based on SR followed by WBRT was demonstrated to be superior to WBRT alone in term of OS (8) and to SR alone (9,10) in terms of brain control. Most of the studies evaluating post-SR survival and associated prognostic factors have included multiple primary tumor types, and only limited and relatively old data which specifically focus on BM from BC are available (11, 12).

Several BM-specific prognostic classifications have been built to better-select among available therapeutic strategies. The seminal recursive partitioning analysis (RPA) and graded prognostic assessment (GPA) were based on age, Karnofsky performance status (KPS), extracranial disease and the number of BM (13) but were not primary tumor-specific.

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Recently, GPA was refined with diagnosis-specific prognostic indices according to the primary, including BC, and a specific breast-GPA was proposed, based on KPS, age and molecular subtype (14). Other BC-specific prognostic scoring systems have also been recently proposed based on the same elements and systemic treatment, interval from primary BC diagnosis and lymphopenia (15-19). However, most of these scoring systems were built on cohorts of BM from BC predominantly treated with WBRT, on a large but relatively old period of time and their performance on patients subjected to modern surgical treatments, as well as other therapeutic procedures have not been adequately evaluated.

The aim of this retrospective study was to describe the clinical outcome of BM from BC treated by SR and to identify the actual prognostic factors in this specific population, including the actual molecular status of BM. An additional objective was to test the relevancy of established BC-specific prognostic classification systems.

Patients and Methods

We conducted a retrospective analysis using the medical records of 49 patients with histologically-confirmed BC with BM and treated with initial SR at the Paoli-Calmettes Insitut and Timone Hospital (Marseille, France), between December 2001 to July 2011. The indications for SR were as follows: accessible solitary or limited number of brain lesions; establishment of diagnosis in patients with uncertain primary; molecular characterization (ER, PR and HER2) of metastatic relapse; symptomatic, accessible BM. BM were diagnosed by brain magnetic resonance imaging (MRI), with pathological confirmation after surgery. Patients with leptomeningeal disease were not included. Following SR of BM, postoperative treatment modalities could include WBRT (WBRT, 30 Gy in 10 fractions), stereotactic radiosurgery (SRS) and/or systemic treatments such as chemotherapy, endocrine therapy and/or targeted therapies. Complete clinical examination including neurological examination and brain MRI was performed every three months. Response and progression were evaluated by revised RECIST 1.1 criteria (20).

Expression status of ER, PR and HER2 in primary BC were obtained from medical records, whereas it was centrally reviewed on BM tissue. Staining was performed using primary antibodies to ER, PR and HER2 (all Ventana, Tucson, Arizona, USA). For the evaluation of ER and PR expression, all cases with ≥10% stained cancer nuclei were classified as positive. Fluorescence *in situ* hybridization (FISH) was used for all HER2 2+ tumors using the Path-Vysion HER2 DNA Probe Kit (Abbott Molecular, Des Plaines, Illinois, USA). HER2-positive staining was defined as immunohistochemistry 3+ or, in the case of 2+, FISH positivity. Molecular tumor subtypes were approximated as follows: basal-like, HER2/ER/PR-negative; Luminal A, HER2- negative/ER- or PR-positive; Luminal B, HER2-positive/ER- or PR-positive; and HER2, HER2-positive, ER- and PR- negative.

The following data were analyzed: age, KPS and Mini Mental Status (MMS) at the time of diagnosis of BM, topography and number of BM, ER, PR and HER2 status on primary BC and on BM, BM molecular tumor subtype, extracranial metastases and systemic disease status, postoperative treatment modalities, interval between initial diagnosis of primary BC and diagnosis of BM, interval between initial diagnosis and first metastatic relapse, interval between the first diagnosis of metastastic relapse and diagnosis of BM. Using these parameters, RPA score as well as BC-specific scores of Sperduto *et al*. (14), Niwinska *et al*. (21) and Nieder *et al*., (15) were applied. Other breast-specific prognostic scores from Claude *et al*., (19) and Le Scodan *et al*., (18) were not evaluated, since they incorporate the degree of lymphopenia, which was not available in the medical records. Scores according to Park *et al*., (17) and Ahn *et al*., (16) were not evaluated since they incorporate postoperative chemotherapy use, and thus could not be considered as tools helping in the therapeutic decision. Written informed consent was obtained from patients in accordance with institutional guidelines. This protocol was approved by our Institutional Review Board and complies with the principles laid of the Declaration of Helsinki.

Categorical variables were summarized as frequencies and corresponding percentages and continuous variables as median and range. OS was measured from the date of cerebral surgery to death from any cause, with censoring at the date of the last contact. Cerebral progression-free survival (C-PFS) was measured from the date of SR to cerebral progression or death, with censoring at the date of last documented disease evaluation. Follow-up was measured from the date of cerebral surgery to the date of last contact. Time-to-event end-points (OS and C-PFS) were estimated using Kaplan Meier method and compared using log-rank test. Multivariate analyses and hazard ratio estimation were performed with the Cox proportionnal hazards models. All analyses were carried out with a bilateral alpha type-1 error of 5%. The analyses were performed with the statistical software SPSS® version 17.

Results

Patient, tumor and treatment characteristics (Table I). Between December 2001 and July 2011, 49 consecutive patients with newly-diagnosed (n=39) or recurrent (n=10) BM from BC were treated by SR. The median age was 54 (range=28-75) years. There were 48 women and one man. Eight patients (17.4%) presented with inflammatory breast cancer. The median number of previous chemotherapy lines was two (range=0-4). The molecular status of primary BC was as follows: basal-like in 11 (25.6%), luminal-A in 13 (30.2%), HER2 in 12 (27.9%) and luminal-B in seven (16.3%) cases.

BM was the first and only metastatic site for 15 patients (30.6%). Only one patient had BM synchronously at the primary BC diagnosis. Fifteen patients had three or more BMs, 16 patients (32.6%) were asymptomatic, MMS was normal for 42 patients (85.7%) and the median KPS was 80 (50-90). Median intervals from diagnosis of primary BC to diagnosis of the first metastasis and to BM diagnosis were 34 (range=0-214) months and 43 (range=0-214) months, respectively.

Centrally-reviewed pathological analysis of resected metastatic disease showed that 19 patients (41.3%) had HER2-positive and 21 patients (43.6%) had ER- and/or PR-

Table I. *Patient, tumor and treatment characteristics*.

Characteristic	Data	%
Patient-related	49	
Age (range)	54 years (28-75)	
Gender (men/women)	1/48	
Median KPS	80 (50-90)	
≥80	34	69
<80	15	31
Primary BC-related		
Stage		
M 0	43	87.8
M 1	5	10.2
NA	1	2
Histology		
ER- and/or PgR-positive	24	50
HER2-positive	19	44.2
NA	6	5.8
Inflammatory breast cancer	8	17.4
Menopausal	19	43.2
Number of previous chemotherapy lines		
0	3	6.1
1	22	44.9
2	14	28.6
≥3	10	20.4
BM-related		
Interval of primary to BM diagnosis	43 (0-214) months	
Interval of primary to first metastases diagnosis	34 (0-214) months	
Number of BMs		
1	24	51.1
2	8	17
≥3	15	31.9
Topography		
Supratentorial	28	57.1
Posterior fossa	10	20.4
Both supra and infratentorial	11	22.4
First BM occurrence		
Yes	39	79.6
No	10	20.4
Absence of symptoms	16	32.7
Normal MMS	42	85.7
BM histology		
HER2 positive	19	41.3
ER- and/or PR-positive	21	43.6
Systemic disease		
Stable or responsive	29	59.2
Progressive	20	40.8
Systemic sites of metastasis		
0	12	24.5
1	15	30.6
≥2	22	44.9
Post-SR treatment		
WBRT	41	83.7
SRS	11	22.4
Chemotherapy	39	79.6
Hormonal therapy	13	61.9
Anti-HER2 therapy	16	72.7

KPS, Karnofsky performance status; ER, estrogen receptor; PR, progesterone receptor; BM, brain metastases; MMS, mini mental status; WBRT, whole-brain radiation therapy; SRS, stereotactic surgery.

positive BM. Molecular subtypes were luminal-A in 15 (32.6%), HER2 in 13 (28.3%), basal-like in 12 (26.1%), and luminal-B in 6 (13%). Median intervals between diagnosis of first metastasis and diagnosis of BM were 0 months in those with basal-like disease, 6.9 months in luminal-A, 8.0 months in HER2 and 8.5 months in luminal-B, respectively. Thus, the majority of first metastatic events for patients with basal-like disease were cerebral (n=9).

After surgery, 41 patients (83.7%) underwent WBRT, 11 (22.4%) underwent SRS and 39 (79.6%) were given systemic treatment. Among HER2-positive cases (n=19), 14 (73.7%) received an anti-HER2 therapy after BM SR and among ER- and/or PR-positive cases (n=21), 9 (42.9%) received hormonal therapy after BM SR.

Patient outcome. At the time of the last contact, 37 patients (73.5%) had experienced cerebral progression and the median follow-up duration for patients without cerebral progression was 25.6 (range, 3.9-63.0) months. The median C-PFS was 11.3 (95% CI=5.9-16.7) months.

Twenty-eight patients (57.1%) were dead at the time of the last contact and the median duration of follow-up for surviving patients was 25.6 (range=3.9-63.0) months. Median OS was 19.4 (95% CI=16.1-22.7) months. The two-year OS rate was 26.5%.

Prognostic factors. By univariate analysis (Table II), patients with abnormal MMS (p=0.007), short interval between primary BC and BM diagnoses (p=0.049) and multiple sites of systemic metastases (p=0.017) had significantly worse C-PFS. Patients with multiple previous chemotherapy lines (p=0.037), abnormal MMS (p=0.006), and multiple systemic sites of metastasis (p<0.001) had poor OS. Thus, the median OS for patients with normal or abnormal MMS were 20.1 (95% CI=18.1-22.1) months and 3.8 (95% CI=0.2-7.5) months respectively, whereas the one for patients with and without multiple sites of systemic metastasis were 14.1 (95% CI=9.9-18.4) months and 49.0 (95% CI=20.0-78.1) months respectively (Figure 1).

The use of chemotherapy tended to be significantly associated with a more favourable outcome for C-PFS (p=0.077) and OS (p=0.100). Of note, the use or absence of anti-HER2 therapies in HER2-positive cases were associated with a median OS of 20.6 (95% CI=18.5-22.7) months and 13.8 (95% CI=10.8-16.8) months respectively (p=0.16) but presented no impact on C-PFS. Importantly, neither topography, number nor presence of clinical symptoms of BM were significantly associated with survival. Neither primary or BM hormonal receptors nor HER2 status significantly impacted survival, similarly to molecular subtypes (Table II). Thus, the median OS was 19.0 (95% CI=11.2-26.9) months in ER- and in PR-positive BM and 19.4 (95% CI=13.9-25.0) months in ER- and PR-negative

Table II. *Univariate and multivariate analyses*.

	PFS			OS		
Parameters	Univariate	Multivariate	HR	Univariate	Multivariate	HR
Number of previous lines of systemic treatment (≤1 *vs*. >1)	0.119			0.039	0.454	
Age (less *vs*. more than median age)	0.121			0.153		
Number of BM (unique *vs*. multiple)	0.680			0.853		
Topography (supratentorial *vs*. infratentorial *vs*. both)	0.386			0.068	0.402	
Symptoms (absent *vs*. present)	0.220			0.655		
MMS (normal *vs*. abnormal)	0.007	0.002	0.220 (0.086-0.561)	0.006	0.017	0.189 (0.048-0.472)
ER/PR (BM) (positive *vs*. negative)	0.580			0.965		
HER2 (BM) (positive *vs*. negative)	0.851			0.666		
Molecular subtype (BM) (luminal A, luminal B, HER2, basal-like)	0.616			0.946		
Number of systemic sites of metastasis (1 *vs*. >1)	0.017	0.007	2.750 (1.316-5.745)	<0.001	0.004	6.015 (1.748-20.694)
Systemic therapeutic response on BM diagnosis (yes *vs*. no)	0.755			0.165		
KPS (<80 *vs*. ≥ 80, median KPS)	0.193			0.086	0.996	
Post-operative WBRT (yes *vs*. no)	0.162			0.921		
Post-operative chemotherapy (yes *vs*. no)	0.077	0.016	0.311 (0.120-0.807)	0.100	<0.001	0.018 (0.003-0.115)
Hormonotherapy[#] (yes *vs*. no)	0.107			0.227		
Interval between primary BC and BM diagnosis (<43 *vs*. ≥43 months, median)	0.049	0.021	2.325 (1.133-4.769)	0.143		
Interval between primary BC and first metastases diagnosis (< 37.5 *vs*. ≥37.5 months)	0.132			0.099	0.107	
HER2 therapy*	0.810					
BM diagnosis (newly diagnosed *vs*. recurrent disease)	0.320			0.920		
Surgical resection (complete *vs*. partial)	0.417			0.972		
Number of resected MC (1 vs. 2 vs. ≥3)	0.687			0.933		

PFS, Progression-free survival; OS, overall survival; HR, hazard ratio; BM, brain metastases; MMS, Mini Mental Status; ER, estrogen receptor; PR, progesteron receptor; KPS, Karnofsky performance status; WBRT, whole-brain radiation therapy; BC, breast cancer; MC, metastatic cancer. [#]Hormonal therapy was only analyzed for the subgroup of ER- and/or PR-positive patients; *anti-HER2 therapy was only analyzed for the subgroup of HER2-positive cases.

BM (p=0.895), 20.6 (95% CI=12.8-28.5) months in HER2-positive and 17.1 (95% CI=9.3-24.9) months in HER2-negative cases (p=0.666). When BM were grouped by molecular subtype, the median OS was 14.1 (95% CI=16.3-31.3) months for luminal A, 20.6 (95% CI=17.3-21.9) months for luminal B, 23.8 (95% CI=9.0-19.3) months for HER2 and 20.1 (95% CI=9.8-30.4) months for basal-like tumors (p=946, Figure 2).

By multivariate analysis, independent prognostic predictors for poor C-PFS and poor OS were abnormal MMS (p=0.002 and p=0.017), multiple systemic metastases (p=0.007 and p=0.004) and absence of postoperative chemotherapy (p=0.016 and p<0.001). The interval between primary BC and BM diagnoses remained relevant for C-PFS (p=0.021) (Table II).

Performance of established prognostic scores. The ability of RPA, as well as other previously reported BC-specific prognostic classifications, to predict OS in this populationing was evaluated. For each scoring system, the re-partition of patients into different prognostic classes is shown in Table III. The number of patient per class ranged from 1 to 48 and most of them were found in low- or intermediate-risk classes. Of note, in the Niwinska score (which relies exclusively upon KPS), 48 out of 49 patients were in the same intermediate class. Univariate analysis of the prognostic impact of each score on OS is reported in Table III. While RPA reached a prognostic value of borderline significance (p=0.057), other scores were not significantly associated with OS (Figure 3).

Discussion

In this retrospective study of BM from BCs treated by SR, to our knowledge the first reported in the past 15 years, we have observed impressive median C-PFS and OS of 11.3 and 19.4 months, respectively. Independent prognostic factors for survival in this population were MMS, the number of

Table III. *Analyses of prognostic scoring systems of brain metastases from breast cancer.*

Scoring system	Class	Median OS (months)	95% CI	*p*-Value
RPA	I (n=8)	55	0-114.5	0.057
	II (n=35)	19.4	17.7-21.2	
	III (n=6)	10.8	0-23.0	
Nieder (15)	1 (n=18)	23.8	11.7-35.9	0.109
	2 (n=22)	19	0-47.1	
	3 (n=5)	7.6	6.1-9.1	
	4 (n=3)	17.1	0-40.6	
Niwinska (24)	2 (n=48)	19.4	15.7-23.2	0.852
	3 (n=1)	20.1	-	
Sperduto (14)	3.5-4 (n=7)	55.1	-	0.299
	2.5-3 (n=24)	19.9	17.4-22.4	
	1.5-2 (n=15)	15.3	11.9-18.7	
	0-1.0 (n=3)	10.8	2.9-18.8	

OS, Overall survival; CI, confidence interval.

systemic sites of metastasis and the use of postoperative chemotherapy. Interestingly, hormonal receptor, HER2 and molecular subtype status of BM, as well as previously reported BC-specific prognostic classification systems, were not significantly associated with survival.

An improved survival for patients with BM treated with SR and WBRT over those treated with WBRT-alone has been shown in randomized studies (8). However, specific data on BM from BC patients treated with SR are scarce and ancient. In 1997, Wronski *et al*., reported a series of 70 patients and recorded a median OS of 13.9 months (11). With a median OS of nearly 20 months, our results confirm that patients with BM from BC treated with SR may experience very significant cerebral control and survival. In similar populations of BM from BC with a minority of SR-treated patients, recently reported median OS ranged from seven months (22) to 13.8 months (14). Thus, our study reinforces the need to systematically consider SR within the context of a multidisciplinary therapeutic management. A striking difference between the two studies was the impact of hormonal receptor status, with negative status being associated with a significantly worse survival in the US study, which was not found in the current study. Another difference was the availability of anti-HER2 treatments in the present study, which was unlikely in the US cohort due to its different time period. Of note, accumulating data (23), but also the results of the present study, support a survival benefit for patients with HER2-positive disease receiving anti-HER2 treatments. In multivariate analysis, adjuvant WBRT was significantly associated with survival in the US cohort. In our series, post-operative WBRT did not impact either C-PFS or OS. This may be explained by the fact that almost all patients were given some sort of postoperative radiation (WBRT or SRS), including 41 out of 49 patients who actually received post-operative WBRT. In addition, only an advantage in local control but no OS benefit was proven in randomized trials evaluating SR alone versus SR followed by WBRT (10).

Among the three independent OS and C-PFS prognostic factors identified in our series, the number of extracranial sites of metastasis has been already identified in other studies evaluating various therapeutic approaches in BM from BC (15, 24). However, the median OS of patients with more than one systemic site of metastasis was far from being irrelevant (14 months), still justifying consideration of SR in this population. To our knowledge, our study is the first to report a prognostic value for abnormal MMS in BM, whereas this parameter was incorporated in the RPA score specifically dedicated to primary cerebral tumors (25). In the present cohort, abnormal MMS was observed in seven out of 49 patients and was likely to reflect either a high brain tumor burden or location near critical cerebral structures, which could be associated with infra-optimal SR and subsequent poor clinical outcome. MMS evaluation may be an easy-to-use and robust prognostic parameter to identify very poor-prognosis BM from patients with BC, in which surgery may be not necessary. An independent prognostic value of post-operative chemotherapy was found in this population. Recent studies of BM from BC have also documented a similarly favourable impact for postoperative systemic treatment (17, 21, 23, 24), but the present study is the first to document it in a series of patients specifically treated with SR. The role of systemic therapy in BM from BC has been largely controversial during the last 20 years. However, if approximately 50% of patients with BM from BC will die from brain progression of the disease, the remaining 50% will die from extracranial progression (8), at least justifying the need for systemic treatment. Thus, our data strongly support the administration or continuation of systemic treatment in BM from BC treated with SR. This may be particularly true in HER2-positive BC. Indeed, even though the small sample size of our population did not allow for statistical significance to be reached, the administration of anti-HER2 treatments tended to be associated with favourable OS in HER2-positive cases. This prognostic factor was also identified in several series of BM from BC (17, 26), all including a minority of SR-treated patients. Since trastuzumab is considered to have little or no penetration through the blood-brain barrier, it is likely that its impact on survival relies upon control of extracranial disease. Consistent with this hypothesis, anti-HER2 treatments did not significantly affect C-PFS. However, lapatinib, a small molecule supposed to better-penetrate the blood-brain barrier, was recently demonstrated to have significant antitumor activity at the CNS level (27) and could also impact local control.

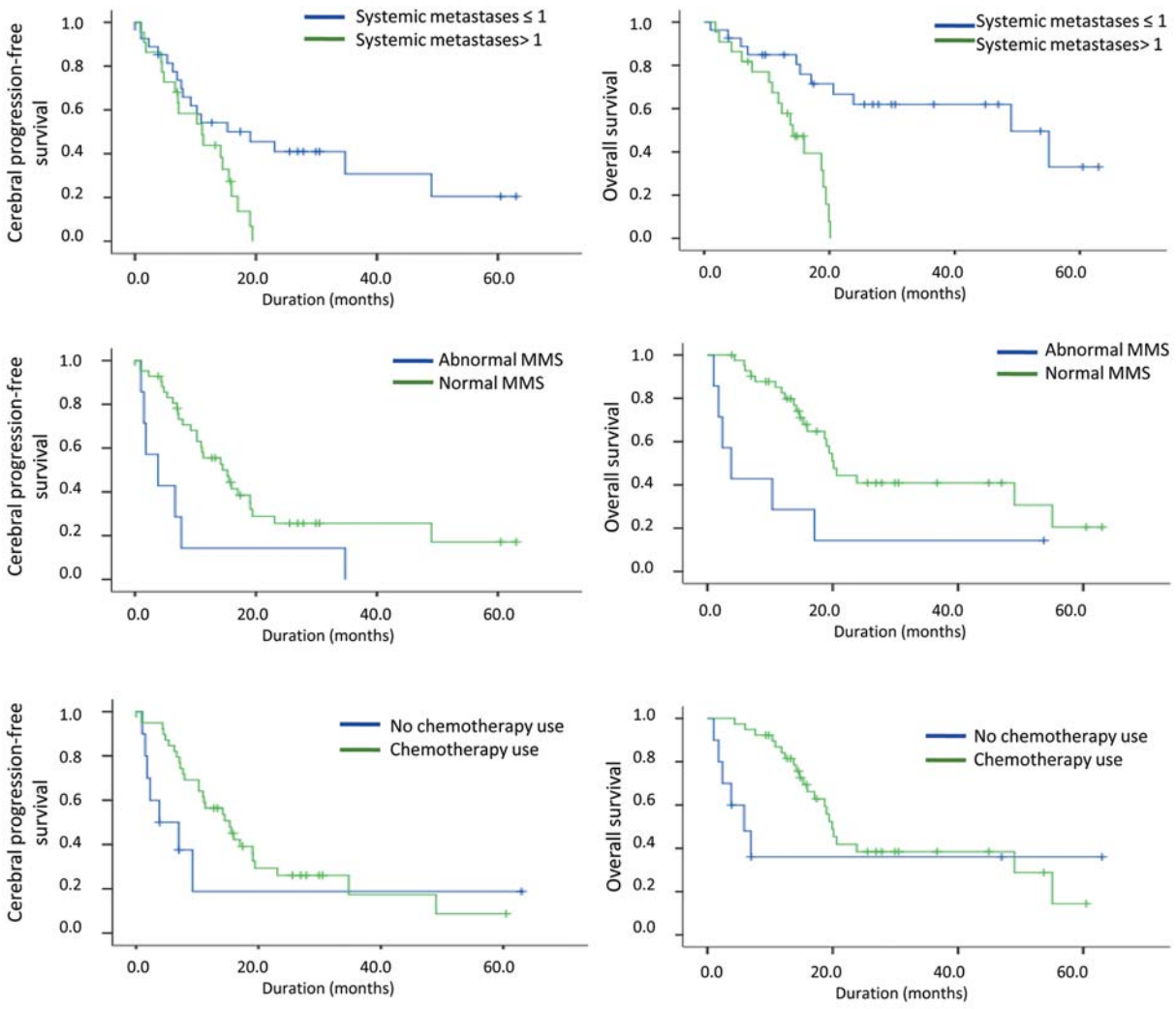

Figure 1. *Cerebral progression-free survival and overall survival according to the chemotherapy use, Mini Mental Status (MMS) and number of sites of systemic metastasis.*

In contrast with most of the recent reports (14, 17, 23), no prognostic impact was detected for molecular subtypes. Although the small sample size of the current series limits its power to detect significant differences, there could be other explanations. Firstly, this study is the only one to have evaluated ER, PR and HER in BM from BC, and discordances between the molecular status of metastases and primary tumors have been repeatedly documented in BC. Secondly, it is conceivable that patients indicated for SR could represent a distinct subset of BC disease, with similar behavior, and possibly biology, across molecular subtypes. This is particularly consistent with recent data describing molecular heterogeneity within molecular subtypes themselves (28). Thirdly, the impact of systemic treatment, particularly on HER2 tumors, may also have complicated the evaluation of the prognostic value of molecular subtypes.

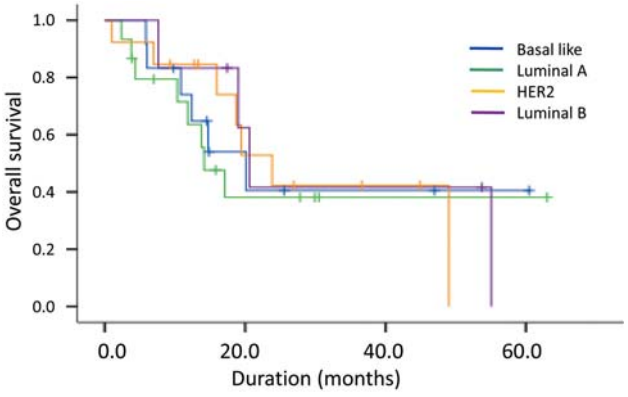

Figure 2. *Cerebral-progression-free survival and overall survival according to the cerebral molecular subtypes: basal-like, luminal A, luminal B and HER2.*

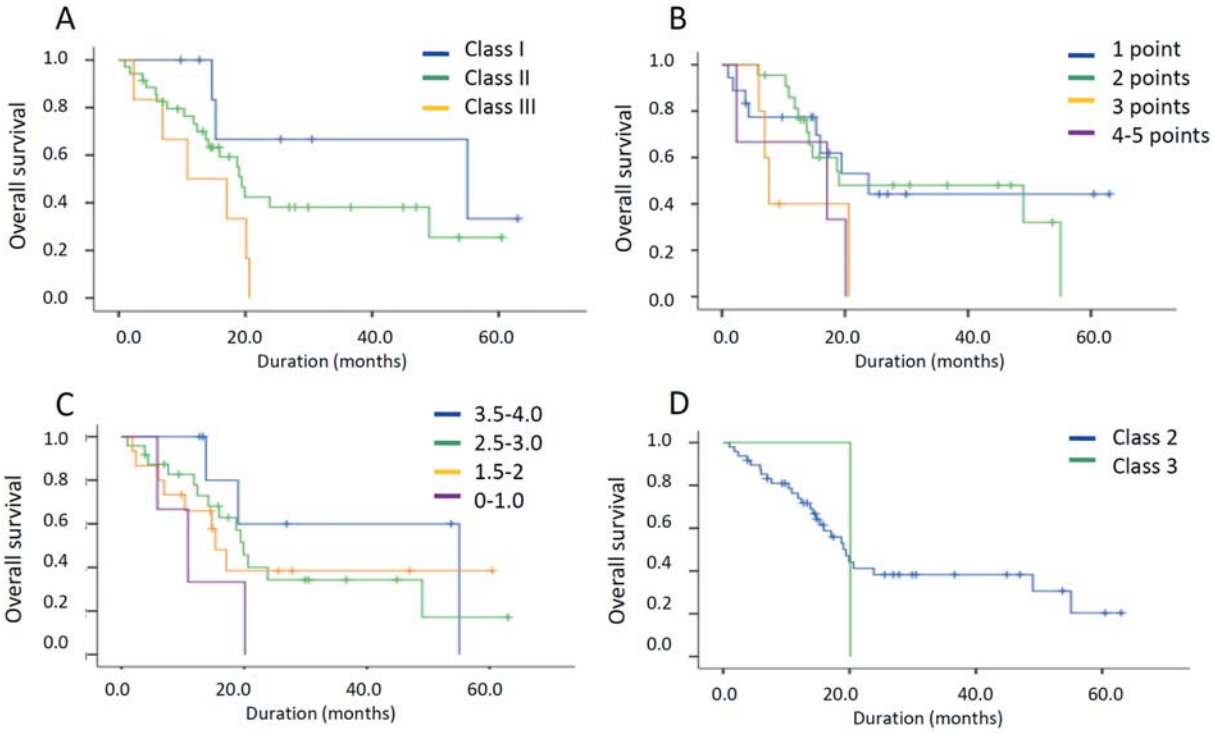

Figure 3. *Overall survival according to recursive partitioning analyses (**RPA**) (A), Nieder (15) (B), Sperduto (14) (C) and Niwinska (24) (D) scoring systems.*

Finally, the variable time occurrence of BM according to the molecular subtype could have limited their prognostic impact, since OS was calculated from the date of BM diagnosis. Thus, in our series, BM were diagnosed synchronously with metastatic disease in 75% of basal-like tumors, whereas they occurred after a median interval of 6.9 to 8.5 months in other subtypes. Interestingly, a recent study from Niwinska *et al*., (24) also failed to identity a prognostic impact for molecular subtypes. Thus, we believe that there is no reason for precluding aggressive neurosurgical procedures in SR-accessible BM from BC, in any particular molecular subtype.

Another important parameter lacking prognostic value by multivariate analysis in this series was KPS, which has been described as one of the major prognostic parameters in series of BM from BC (14, 15, 17, 19, 21). Again, this may be due to the limited power of the present study. Nevertheless, it is also obvious that BM can lead to significant neurological deficits *via* compression of brain tissue and perifocal edema, which can strongly alter KPS. These alterations may be at least partly reversed by surgery (29), which can contribute to the lack of prognostic value identified for KPS in the present series.

To our knowledge, this study is the first to evaluate the prognostic performances of RPA, as well as most recent BC-specific scoring systems of BM, in a series of SR-treated patients. Although RPA reached borderline significance, none of the BC-specific prognostic classifications was significantly associated with survival in this context. The limited sample size may have led to a lack of statistical power, and thus unbalanced re-partitioning of patients into favourable prognostic classes could explain these results. In addition, these scores were determined based on BM populations composed with a minority of surgically-treated BM (14, 15, 24). Moreover, some of the criteria used in these scores, such as KPS or molecular subtypes appeared to be not relevant for our surgical population, explaining their overall non-significance. Accordingly, we believe that none of the tested systems should be used in routine practice to dictate therapeutic management in patients with SR-accessible BM from BC.

Conclusion

Surgery is an effective treatment in oligometastatic brain disease of patients with BC whatever the hormonal receptor, HER2 or molecular subtype status of BM. MMS, presence of systemic metastases and use of post-operative systemic treatment are associated with better OS in this population whereas conventional established scoring systems are not significantly correlated to outcome. Therefore, in the

therapeutic management of BM from BC, surgical opportunity should be systematically and carefully evaluated by the multidisciplinary team. Further investigations are needed to validate specific prognostic factors in this population, allowing for selection of the most appropriate therapeutic approach in this setting.

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