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Original Article

Analysis of Prognostic Factors in Malignancies of Gynecological Origin with Brain Metastases

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ABSTRACT

Objective: We aimed to evaluate the demographic and clinical characteristics of patients diagnosed with brain metastases of gynecological origin and to analyze the factors affecting prognosis after the diagnosis of brain metastases.

Material and Methods: Forty-eight patients with brain metastases who were followed for gynecological cancer in Başkent University's Department of Gynecological Oncology between 2008 and 2021 were evaluated retrospectively. Demographic, clinical, and pathological characteristics of the patients and the distribution of treatments according to gynecological cancers since the time of primary diagnosis were noted. Median survival times after the diagnosis of brain metastasis were evaluated statistically. Prognostic factors affecting the process of brain metastasis and survival after diagnosis were statistically analyzed.

Results: The median survival time after the diagnosis of brain metastasis was 8 months. It was 12 months in cases of ovarian cancer, 4 months for endometrial cancer, 8 months for cervical cancer, 3 months for vulvar cancer, and 4 months for uterine sarcomas. In univariate analysis, lesion number, localization, extracranial metastasis status, and treatment method were found to be associated with survival after brain metastasis, while lesion localization and treatment method were independent variables affecting prognosis in multivariate analysis.

Conclusion: Patients with the best prognosis after brain metastasis were treated with combined therapy. However, stereotactic brain radiotherapy alone had a better prognosis compared to patients who received whole brain radiotherapy alone.

Keywords: Gynecologic malignancy, Brain metastasis, Prognostic Factor, Radiotherapy

ÖZET

Amaç: Jinekolojik kökenli beyin metastazı tanısı alan hastaların demografik ve klinik özelliklerini değerlendirmeyi ve beyin metastazı tanısından sonra prognozu etkileyen faktörleri incelemeyi amaçladık.

Materyal ve Metod: Başkent Üniversitesi Jinekolojik Onkoloji Anabilim Dalı'nda 2008-2021 yılları arasında jinekolojik kanser nedeniyle takip edilen ve beyin metastazı tanısı alan 48 hasta retrospektif olarak değerlendirildi. Hastaların demografik, klinik ve patolojik özellikleri ile ilk tanı anından itibaren uygulanan tedavilerin jinekolojik kanserlere göre dağılımı tespit edildi. Beyin metastazı teşhisi konulduktan sonra medyan sağkalım süreleri istatistiksel olarak değerlendirildi. Tanı sonrası beyin metastazı sonrası sağkalımı etkileyen prognostik faktörler istatistiksel olarak analiz edildi.

Bulgular: Beyin metastazı teşhisi konulduktan sonra medyan sağkalım süresi 8 aydı. Over kanserinde 12 ay, endometrial kanserde 4 ay, rahim ağzı kanserinde 8 ay, vulva kanserinde 3 ay, rahim sarkomlarında 4 aydı. Univaryant analizde lezyon sayısı, lokalizasyonu, ekstrakraniyal metastaz durumu ve tedavi yöntemi beyin metastazı sonrası sağkalım ile ilişkili bulunurken, multivaryant analizde lezyon lokalizasyonu ve tedavi yöntemi prognozu etkileyen bağımsız değişkenler olarak bulundu.

Sonuç: Beyin metastazından sonra prognozun en iyi kombine tedavi sonrasında elde edildiği görüldü. Bununla birlikte, tek başına stereotaktik beyin radyoterapisi, tek başına tüm beyin radyoterapisi alan hastalara kıyasla daha iyi bir prognoza sahipti.

Anahtar kelimeler: Jinekolojik malignite, Beyin metastazı, Prognostik faktör, Radyoterapi

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Introduction

Brain metastasis (BM) is an important condition associated with serious morbidity and mortality in cancer patients (1). While it is more common in cases of breast cancer, lung cancer, and malignant melanoma, it is rarely seen in gynecological cancers (2). It was reported to occur at rates of 0.3% to 12% in cases of ovarian cancer, 0.2% to 2% in endometrial cancer, and 0.2% to 2.1% in cervical cancer (3-7). There is not enough knowledge about the incidence of BM in cases of vulvar cancer or uterine sarcoma (8, 9).

In cases of gynecological cancer with BM, the prognosis is very poor and survival is unfortunately still expressed in months. The median survival time after BM was reported as 6 months in cases of gynecological cancer in general and as 10.1, 7.5, and 5 months in ovarian, endometrial, and cervical cancers according to gynecological origin, respectively (3, 10).

In recent years, it has been reported that the survival rates of patients with BM have increased with developments in surgical techniques and radiotherapy technology. Whole brain radiotherapy (WBRT) has been used for many years to treat BM and it is applied as irradiation to the whole brain. Stereotactic brain radiotherapy (SBRT), on the other hand, involves the application of a high-dose gamma knife beam specifically to the lesion. Its use is becoming more common due to the high efficacy of the treatment and fewer side effects (11, 12).

It has been reported that patients with younger ages, high performance status, and no extracranial metastases have better prognosis after the diagnosis of BM (13). The morphological features of the tumor are thought to be important factors in determining both the prognosis and the appropriate treatment (14).

The current study aimed to evaluate the demographic and clinical characteristics of patients diagnosed with BM of gynecological origin and to analyze the factors affecting prognosis after the diagnosis of BM.

Material and Methods

A retrospective analysis of the data of patients followed in Başkent University's Gynecological Oncology Department between January 2008 and December 2021 was performed. Patients with clinical suspicion of BM underwent surgical confirmation with imaging modalities as appropriate for each case **(Figure 1)**. The inclusion criteria of the study included pathological diagnosis of primary gynecological malignancies, diagnosis of BM by computed tomography and/or magnetic resonance imaging, and no prior BM. Exclusion criteria were a history of malignancy other than gynecological cancer and the presence of neuromuscular disease unrelated to central nervous system disease and/or BM. The follow-up data and treatment information of patients who received part of their treatment in another center due to gynecological malignancy and/or BM were included in the study after their eligibility for the

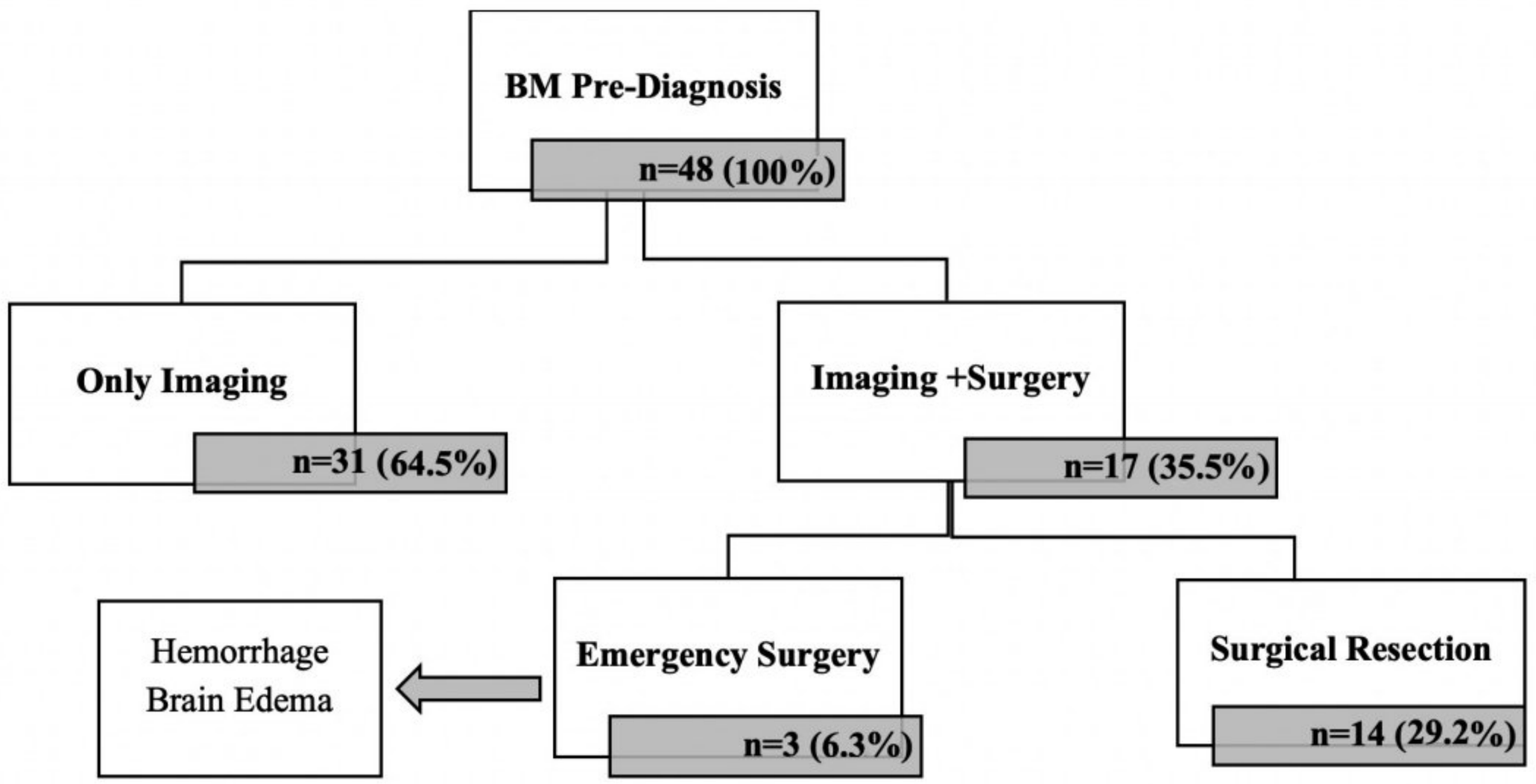

Figure 1: Distribution of brain metastasis diagnosis methods according to patients

study was confirmed. From the time of diagnosis of the primary malignancy, all treatments applied for the patients were determined by the gynecological oncology board.

BMs were detected in 48 patients followed for gynecological malignancies. Stage, tumor grade, and initial treatments applied were noted according to the origin of the gynecological malignancy. The origin and grade of the tumors were determined by pathologists experienced in gynecological cancers and subsequently re-evaluated and revised by a different pathologist according to the 2020 classification of the World Health Organization (WHO). The current International Federation of Gynecology and Obstetrics (FIGO) classification was used for staging. Initial treatments for gynecological malignancies included neoadjuvant chemotherapy, chemotherapy and radiotherapy, surgery (primary staging or primary cytoreduction) followed by chemotherapy, and surgery followed by chemotherapy and radiotherapy. The age, Karnofsky performance status (KPS) score, diagnostic method, extracranial metastasis status, morphological features of the lesion, and treatment modality of the patients diagnosed with BM were specified. The number of lesions was evaluated as single or multiple (≥2). Lesion localization was evaluated as supratentorial (brain parenchyma tissue), infratentorial (cerebellum, brain stem), or both infratentorial and supratentorial, and lesion sizes were recorded as <3 cm or ≥3 cm. Treatment modalities for BM were evaluated in 4 main groups that included patients who underwent palliative treatment, surgery, radiotherapy (WBRT/SBRT), and combined treatment (postsurgical radiotherapy).

IBM SPSS Statistics 23.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Data were reported as medians and ranges for continuous variables, while binary variables were reported as numbers and percentages. Chi-square tests, ANOVA, and t-tests were used as appropriate for comparisons between variables. Kaplan-Meier and log-rank tests were used to analyze survival. Factors affecting survival were evaluated with multivariate Cox regression analysis ($p<0.05$). Hazard ratios (HRs) were stated at 95% confidence intervals (95% CIs).

Results

The median follow-up time of the patients was 37.5 (1-161) months. According to cancer type, the follow-up duration was 42 (1-161) months for ovarian cancer, 28 (5-115) months for endometrial cancer, 25 (5-93) months for cervical cancer, 49.5 (37-62) months for vulvar cancer, and 35 (5-116) months for sarcoma. Twenty-seven (56.3%) patients had ovarian cancer, 8 (16.8%) had endometrial cancer, 7 (14.6%) had cervical cancer, 2 (4.2%) had vulvar cancer, and 4 (8.4%) had sarcoma. The demographic and clinical characteristics of patients diagnosed with BM are provided in **Table 1** according to the diagnosis of the primary malignancy

Table 1 • Demographic and Clinical Characteristics

	Gynecologic Cancer n=48 (100%)	Ovary n=27 (56.3%)	Endometrium n=8 (16.8%)	Cervix n=7 (14.6%)
Follow-up period after BM diagnosis (months)	20.5 (1-147)	27 (1-147)	12.5 (1-111)	14 (2-85)
Median Age at Diagnosis of BM	59.5 (29-81.5)	56 (27-80)	64 (53-70)	55 (47-67)
Stage				
I	3 (6.3%)	-	1 (12,5%)	1 (14.2%)
II	6 (12.6%)	1 (3.8%)	1 (12,5%)	3 (43.2%)
III	33 (74.3%)	22 (81.4%)	4 (50%)	2 (28.4%)
IV	8 (16.8%)	4 (14.8%)	2 (25%)	1 (14.2%)
Grade				
Low	-	-	-	-
Modarate	6 (14,3%)	-	2 (25%)	3 (50%)
High	36 (85,75)	27 (100%)	6 (%75)	3 (50%)

Devam ediyor

Table 1 • Demographic and Clinical Characteristics (Devamı)

	Gynecologic Cancer n=48 (100%)	Ovary n=27 (56.3%)	Endometrium n=8 (16.8%)	Cervix n=7 (14.6%)
Initial Treatment				
Neodjuvant Chemotherapy	3 (6.3%)	1 (3.8%)	1 (12.5%)	1 (14.3%)
Chemotherapy + Radiotherapy	2 (4.2%)	-	-	1 (14.3%)
Surgery + Chemotherapy	35 (79%)	26 (96.2%)	6 (75%)	1 (14.3%)
Surgery + Chemotherapy + Radiotherapy	5 (10,5%)	-	1 (12.5%)	4 (57.1%)
KPS Score				
≤ 30	28 (58.3%)	14 (51.9%)	6 (75%)	4 (57.1%)
> 30	20(41.7%)	12(48.1%)	2 (25%)	3 (42.9%)
Extracranial Metastases				
Absent	14 (29.2%)	11 (68.7%)	1 (6.25%)	2 (13.5%)
Present	34 (70.85%)	16 (50.5%)	7 (21.8%)	5 (15.6%)

BM: Brain Metastasis; KPS: Karnofsky Performans Scale

as ovarian, endometrial, or cervical cancer. The median time between cancer diagnosis and BM was 20.5 months. According to the gynecological origin, it was 27 (1-147), 12.5 (1-111), and 14 (2-85) months for ovarian, endometrial, and cervical cancers, respectively. The median age at the time of diagnosis of BM was 59.5 (29-81.5) years. For ovarian, endometrial, and cervical cancers it was 56 (27-80), 64 (53-70), and 55 (47-67) years, respectively. Forty-two (73.2%) cases were stage III-IV and 6 (16.8%) cases were stage I-II, while 36 (85.7%) patients had grade 3 tumors and 6 (14.3%) had grade 2 tumors. The initial treatment for the primary malignancy was surgery followed by chemotherapy for 35 (79%) patients, chemotherapy and radiotherapy for 5 (10.5%), chemotherapy and radiotherapy for 2 (4.2%), and neoadjuvant chemotherapy for 3 (6.3%).

At the time of BM diagnosis, the KPS score of 28 (58.3%) patients was ≤30 and 20 (41.7%) patients had KPS scores of >30. The diagnosis of BM was made by imaging after clinical preliminary diagnosis for 31 (61.5%) patients, while both imaging and surgical biopsy were performed for 17 (30.5%) patients. Thirty-four (70.8%) patients had extracranial metastases and 14 (29.2%) patients had isolated BMs, and 28 (58.7%) patients had multiple BM lesions and 20 (41.3%) had a single lesion. Tumor size was <3 cm in 24 (50%) cases and ≥3 cm in 24 (50%) cases. Tumors were present in 22 (45.8%) cases in a supratentorial location, in 7 (14.6%) cases in an infratentorial location, and in 19 (39.6%) cases in both locations **(Table 2).**

Considering the treatments for BM, 11(22.9%) patients underwent palliative treatment and 1 (2.1%) patient underwent surgical resection alone. There were 23 (48%) patients in the radiotherapy-only group, and 17 (35.5%) of those patients received WBRT while 6 (12.5%) underwent SBRT. Combined therapy was applied for 13 (27 %) patients, and after surgical resection, 9 (18.7%) patients received WBRT while 4 (8.3%) patients received SBRT.

The median survival time after BM was 8 months. It was 12 months for patients with ovarian cancer, 4 months for endometrial cancer, 8 months for cervical cancer, 3 months for vulvar cancer, and 4 months for sarcoma (p=0.41) **(Figure 2).**

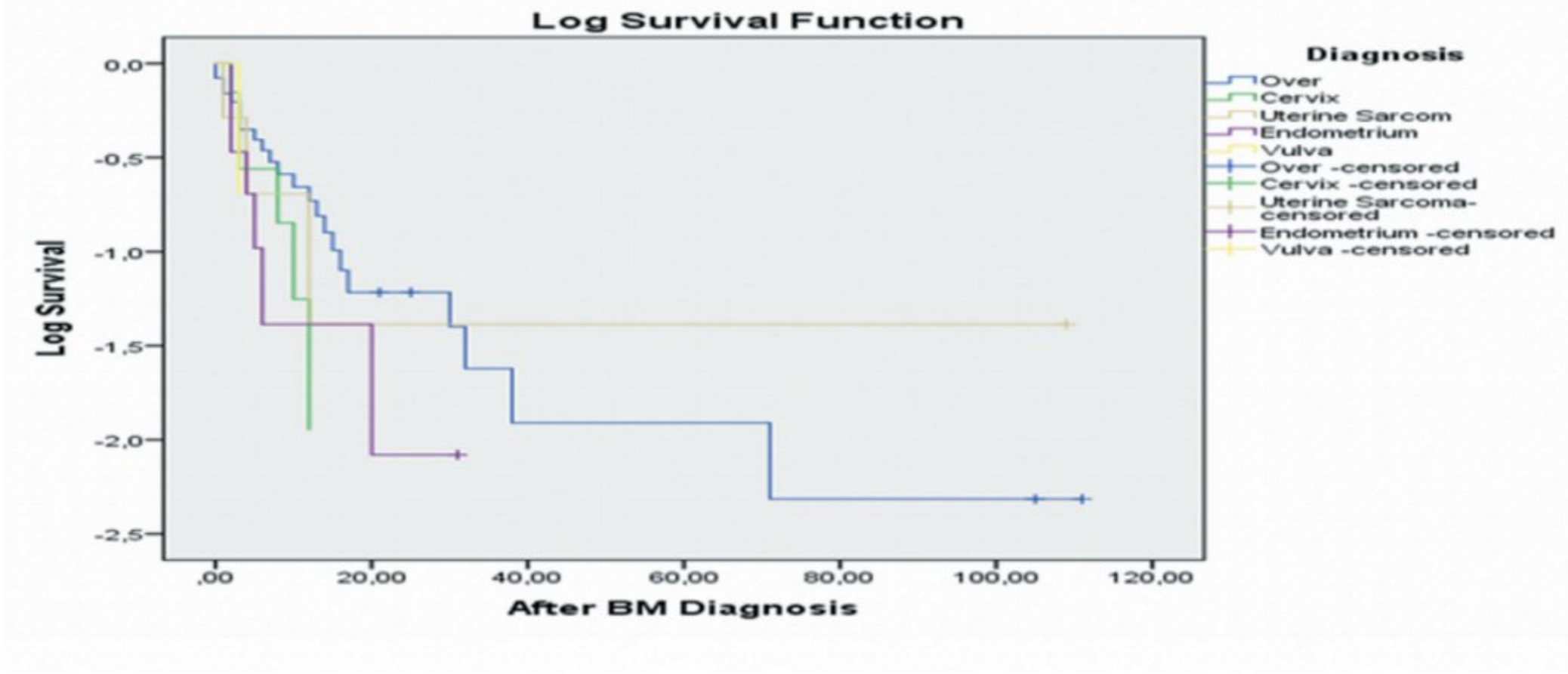

Figure 2: Median survival times after brain metastasis (months)

Table 2 • Morphological Features of BM Lesion

	Gynecologic Cancer (n=48, %100)	Ovary (n=27, 56.3%)	Endometrium (n=8, 16.8%)	Cervix (n=7, 14,6%)
Number of BM				
Single	20 (41.7%)	11 (55%)	3 (15%)	4 (20%)
Multiple	28 (58.3%)	16 (57.1%)	5 (17.8%)	3 (10.7%)
Location of BM				
Supratentorial	22 (45.8%)	10 (20.8%)	6 (12.5%)	3 (6.25%)
Infratentorial	7 (14.6%)	5 (10.4%)	-	1 (2.1%)
Supratentorial + Infratentorial	19 (39.6%)	12 (25.0%)	2 (4.2%)	3 (6.2%)
Maximum Diameter of BM				
< 3 cm	24 (50%)	17 (53.0%)	5 (62.5%)	3 (42.8%)
≥ 3cm	24 (50%)	10 (37.0%)	3 (37.5%)	4 (57.2%)
Treatment Modality				
Paliative	11 (22.9%)	6 (12.5%)	2 (4.2%)	2 (4.2%)
Surgical Resection	1 (2,1%)	–	1 (2.1%)	–
WBRT	17 (35.5%)	9 (18.7%)	2 (4,2%)	4 (83.0%)
SBRT	6 (12.5%)	4 (8.3%)	1 (2,1%)	–
Surgical Resection + WBRT	9 (18.7%)	6 (12.5%)	1 (2.1%)	1 (2.1%)
Surgical Resection + SBRT	4 (8.3%)	2 (4.2%)	1 (2.1%)	–

BM: Brain Metastasis; WBRT: Whole Brain Treatment; SBRT: Stereotactic Brain Radiotherapy

Table 3 • Univariate and Multivariate Analysis of Prognostic Factors in Patients with BM*

	Univariate Analysis			Multivariate Analysis		
Initial	**HR**	**CI 95%**	**p values**	**HR**	**CI 95%**	**p values**
Number of BM	3.26	0.31-8.92	0.02	2.13	0.38-13.09	0.41
Location of BM	0.43	0.02-0.67	0.01	0.22	0.06-0.78	0.02
Extracranial Metastases	2.85	0.34-11.82	0.01	2.20	0.57-8.48	0.25
Treatment Modality	7.45	1.37-8.54	0.001	3.71	1.44-9.57	0.007

BM; brain metastases

The effects of prognostic factors in gynecological cancers after the diagnosis of BM are summarized in **Table 3**. In univariate analysis, extracranial metastasis status (p=0.01), tumor localization (p=0.01), tumor number (p=0.02), and treatment type (p=0.00) affected prognosis. In addition, lesion localization (p=0.007; HR: 0.22; 95% CI: 0.06-0.78) and treatment modality (p=0.02; HR: 3.71; 95% CI: 1.44-9.57) were independent factors affecting survival after BM diagnosis in multivariate regression analysis.

Discussion

In the present study, we found that the incidence of BM among patients with gynecological malignancies was 0.6%. According to cancer type, the rates were 0.85%, 0.31%, 0.39%, 1.1%, and 1% for ovarian, endometrial, cervical, vulvar, and uterine sarcoma, respectively. In multivariate analysis, patients with supratentorial tumors and combined therapy had a better prognosis after the diagnosis of BM.

In an Italian multicentric study (MITO-19) of patients with ovarian cancer, the median survival time after BM was 12 months (15). In the review of endometrial cancer patients performed by Ucella et al., the median survival after the development of BM was reported as 5 months (16). Curo et al. reported survival of 2.3 months in their study of cervical cancer patients (17). These survival outcomes for ovarian and endometrial cancer are similar to our findings, but we have reported longer survival times for patients with cervical cancer. The survival times of patients with vulvar cancer and uterine sarcoma have also been presented here, but more studies are needed to draw appropriate comparisons (9, 18, 19).

Combined treatment had the best prognosis among the treatment groups. In the group of patients receiving radiotherapy alone, better survival outcomes were obtained with SBRT. Moreover, patients treated for BM had a better prognosis than untreated patients. Mahmoud-Ahmed et al. reported that the median survival time of patients who received radiotherapy after surgery was 15 months and the median survival of patients who received only radiotherapy was 2.4 months (20). In another study, Gressel et al. reported that the median survival time of patients who received radiotherapy after surgery was 10.5 months, while it was 4 months for patients who received radiotherapy alone (14). Recent studies have shown that better results can be obtained with SBRT treatment compared to WBRT because SBRT has fewer side effects and can be used more effectively for the lesion (21, 22). Meixner et al. reported that patients who received only SBRT had a median survival time of 10.7 months and had better prognosis than patients who received WBRT (23).

Patients with no extracranial metastases, supratentorial localization, and a single lesion may have much better survival with optimal treatment. However, the correlation with lesion size was not found to be statistically significant. In previous reports, it was underlined that the number of lesions and extracranial metastases are the two most important prognostic factors (12, 23). In this study, although it was found to be significant in univariate analysis, its statistical significance could not be shown in multivariate analysis.

The reported incidence of BM in cases of gynecological cancers is similar across studies conducted in the last 50 years and remains lower than 1% (24). At present, routine screening is not recommended due to the rarity of BM among patients with gynecological cancers (25). These recommendations may change with early predictions of the diagnosis of BM and the development of treatment methods (26).

Due to the general rarity of BM in cases of cancers of gynecological origin, the low number of cases included in the present study, and the fact that this was a single-center study, the frequency of BM in this patient population may not have been fully expressed. Additionally, the retrospective nature of the study may have caused misrepresentation in patient selection.

In most studies performed to date, survival outcomes after BM were found to be very poor. We suggest that the extracranial metastasis status and morphological characteristics of the lesion (lesion location, number of lesions, and size of lesions) should be considered in the selection of the most appropriate treatment method. We recommend combined therapy as the best approach in suitable cases. The more effective use of SBRT applications rather than WBRT may increase survival times, but more studies are needed in this regard.

References

1. Al-Shamy G, Sawaya R. Management of brain metastases: the indispensable role of surgery. Journal of neuro-oncology. 2009;92:275-82.
2. Nayak L, Lee EQ, Wen PY. Epidemiology of brain metastases. Current oncology reports. 2012;14:48-54.
3. Kato MK, Tanase Y, Uno M, Ishikawa M, Kato T. Brain metastases from uterine cervical and endometrial cancer. Cancers. 2021;13(3):519.
4. Gien LT, Kwon JS, D'Souza DP, Radwan JS, Hammond JA, Sugimoto AK, et al. Brain metastases from endometrial carcinoma: a retrospective study. Gynecologic Oncology. 2004;93(2):524-8.
5. Ogawa K, Yoshii Y, Aoki Y, Nagai Y, Tsuchida Y, Toita T, et al. Treatment and prognosis of brain metastases from gynecological cancers. Neurologia medico-chirurgica. 2008;48(2):57-63.
6. Pakneshan S, Safarpour D, Tavassoli F, Jabbari B. Brain metastasis from ovarian cancer: a systematic review. Journal of neuro-oncology. 2014;119:1-6.
7. Ratner ES, Toy E, O'Malley DM, Mcalpine J, Rutherford TJ, Azodi M, et al. Brain metastases in epithelial ovarian and primary peritoneal carcinoma. International Journal of Gynecologic Cancer. 2009;19(5). :856-9
8. Melone GA, D'Elia A, Brogna C, Salvati M. Uterine leiomyosarcoma metastatic to the brain: case report. Tumori Journal. 2008;94(6):856-60.
9. Yamada S, Yamada SM, Nakaguchi H, Murakami M, Hoya K, Matsuno A. A case of multiple brain metastases of uterine leiomyosarcoma with a literature review. Surgical oncology. 2011;20(4):e127-e31.
10. Borella F, Bertero L, Morrone A, Gambella A, Bovetti M, Cosma S, et al. Brain metastases from ovarian cancer: current evidence in diagnosis, treatment, and prognosis. Cancers. 2020;12(8):2156.
11. Chang EL, Wefel JS, Hess KR, Allen PK, Lang FF, Kornguth DG, et al. Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: a randomised controlled trial. The lancet oncology. 2009;10(11):1037-44.
12. Monaco III E, Kondziolka D, Mongia S, Niranjan A, Flickinger JC, Lunsford LD. Management of brain metastases from ovarian and endometrial carcinoma with stereotactic radiosurgery. Cancer. 2008;113(9):2610-4.
13. Cormio G, Maneo A, Colamaria A, Loverro G, Lissoni A, Selvaggi L. Surgical resection of solitary brain metastasis from ovarian carcinoma: an analysis of 22 cases. Gynecologic oncology. 2003;89(1):116-9.
14. Gressel GM, Lundsberg LS, Altwerger G, Katchi T, Azodi M, Schwartz PE, et al. Factors predictive of improved survival in patients with brain metastases from gynecologic cancer: a single institution retrospective study of 47 cases and review of the literature. International Journal of Gynecologic Cancer. 2015;25(9).
15. Marchetti C, Ferrandina G, Cormio G, Gambino A, Cecere S, Lorusso D, et al. Brain metastases in patients with EOC: Clinico-pathological and prognostic factors. A multicentric retrospective analysis from the MITO group (MITO 19). Gynecologic oncology. 2016;143(3):532-8.
16. Uccella S, Morris JM, Multinu F, Cliby WA, Podratz KC, Gostout BS, et al. Primary brain metastases of endometrial cancer: A report of 18 cases and review of the literature. Gynecologic oncology. 2016;142(1):70-5:141-6.
17. Chura J, Shukla K, Argenta P. Brain metastasis from cervical carcinoma. International Journal of Gynecologic Cancer. 2007;17(1).
18. Dursun P, Ayhan A, Tarhan NC, Coban G, Kuscu E. Cerebellar metastasis in squamous cell vulvar carcinoma. Archives of gynecology and obstetrics. 2009;279:69-71.
19. Jaeger A, Biermann M, Prieske K, Grimm D, Grottke A, Salamon J, et al. Cerebral metastasis in recurrent squamous cell carcinoma of the vulva: case report and review of the literature. Archives of Gynecology and Obstetrics. 2020;301:327-32.
20. Mahmoud-Ahmed AS, Suh JH, Barnett GH, Webster KD, Belinson JL, Kennedy AW. The effect of radiation therapy on brain metastases from endometrial carcinoma: a retrospective study. Gynecologic oncology. 2001;83(2):305-9.

21. Lee Y-K, Park N-H, Kim JW, Song Y-S, Kang S-B, Lee H-P. Gamma-knife radiosurgery as an optimal treatment modality for brain metastases from epithelial ovarian cancer. Gynecologic oncology. 2008;108(3):505-9.
22. Nasioudis D, Persaud A, Taunk NK, Latif NA. Brain metastases from gynecologic malignancies: prevalence and management. American Journal of Clinical Oncology. 2020;43(6):418-21.
23. Meixner E, Eichkorn T, Erdem S, König L, Lang K, Lischalk JW, et al. Stereotactic radiosurgery for brain metastases from pelvic gynecological malignancies: oncologic outcomes, validation of prognostic scores, and dosimetric evaluation. International Journal of Gynecologic Cancer. 2022;32(2):172-180.
24. Deng K, Yang C, Tan Q, Song W, Lu M, Zhao W, et al. Sites of distant metastases and overall survival in ovarian cancer: a study of 1481 patients. Gynecologic oncology. 2018;150(3):460-5.
25. Ewend MG, Morris DE, Carey LA, Ladha AM, Brem S. Guidelines for the initial management of metastatic brain tumors: role of surgery, radiosurgery, and radiation therapy. Journal of the National Comprehensive Cancer Network. 2008;6(5):505-14.
26. Divine LM, Kizer NT, Hagemann AR, Pittman ME, Chen L, Powell MA, et al. Clinicopathologic characteristics and survival of patients with gynecologic malignancies metastatic to the brain. Gynecologic oncology. 2016;142(1):76-82.