Original Article

Intracranial meningiomas: Prognostic factors and treatment outcome in patients undergoing postoperative radiation therapy

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Abstract

Background: Meningioma constitutes 20% of the intracranial neoplasms. Followed by surgery as the primary treatment for most patients, radiotherapy becomes indicated in high-grade tumors with incomplete surgical removal. We evaluated the prognostic factors and overall outcome in meningioma patients who underwent radiotherapy.

Materials and Methods: In this retrospective analysis, data from all patients with documented diagnosis of meningioma who referred to the Omid and Ghaem Oncology Centers (Mashhad, Iran) from 2002 to 2013 were included. We calculated the overall survival rates using the Kaplan–Meier method and compared the survival curves between groups by the log-rank test.

Results: Eighty-three patients with a median age of 50 years (ranging: 16–84) were included. Grade I, II, and III meningiomas were seen in 40 (48%), 31 (37%), and 12 (15%) patients, respectively. Radiation therapy was indicated due to tumor recurrence, incomplete excision, or tumor grade in 32, 8, and 43 patients, respectively. Tumor grade had a significant effect on the overall survival with a 3-year overall survival of 76.7%, 43.5%, and 13.3% in Grade I, II, and III, respectively ($P < 0.001$). Gender, age, and tumor location were not correlated with the overall survival. Moreover, patients with Grade II and III who underwent total resection had a significantly higher overall survival than those with subtotal resection or biopsy alone (5-year survival rates of 82% vs. 17.1%, respectively; $P = 0.008$).

Conclusion: Tumor grade was the most important prognostic factor in meningioma patients undergoing radiation therapy. In patients with Grade II and III tumors, the extent of surgical resection is significantly correlated with the overall survival.

Key Words: Meningioma, prognostic factors, radiotherapy, survival, treatment outcome

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INTRODUCTION

Brain tumors are the most important intracranial space occupying lesions, of which meningiomas (comprising 20% of all intracranial tumors) followed by gliomas are the most abundant pathologies. Over 90% of meningiomas are intracranial, while the remaining occur in the spinal cord.[1-3] Meningiomas are 2–3 times more prevalent in women compared to men.[3,4] Surgery

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is considered the main treatment for all meningioma types. In addition, the prognosis largely depends on factors such as tumor grade and the extent of surgical removal. In Grade I meningiomas (the benign type) that constitutes 70–85% of all types, 80% of patients were treated with surgery, resulting in a 10-year progression-free survival. Radiation therapy is indicated in the treatment of Grade II (atypical) and III (malignant) meningiomas, as well as in the recurrent and inoperable tumors or in those with incomplete surgical removal.[5] Most of the available data on meningioma outcome are focused on surgery. There is a paucity of research on treatment outcome and patients' survival as well as demographic and clinicopathological variables and prognostic factors in patients receiving radiation therapy. This study evaluated the treatment results and analyzed the prognostic factors affected the survival in meningioma patients who underwent treatment in our radiotherapy-oncology centers in Mashhad, Iran.

MATERIALS AND METHODS

In this retrospective study, the demographic and treatment-specific data of all meningioma patients (as confirmed by pathology and reviewed in 10%), who underwent radiation therapy in Omid and Ghaem Oncology Centers in Mashhad over the last 11 years (2002–2013) were reviewed. Patients were treated with either two-dimensional radiotherapy using cobalt-60 in the earlier cases or three-dimensional conformal radiotherapy with a 6-MV linear accelerator in the last ones. The same technique and radiation dose were used in all patients. Demographic data, tumor location, clinical symptoms at presentation, the extent of the surgery, and pathology report details were extracted from the patient records. In cases of lost follow-ups and incomplete records, patients were contacted and interviewed over the phone. Where data were not reachable, patients were excluded from the analysis. Overall survival was defined as the duration between the date of initial diagnosis and death due to any cause or the date of the last follow-up. Progression-free survival was calculated as the duration from the date of initial diagnosis until the date of recurrence or disease progression. All retrieved and consolidated data were then statistically analyzed. Kaplan–Meier method was applied to calculate the survival rates. In addition, the log-rank test was applied to compare the survival curves between groups. *P*- values less than 0.05 were considered statistically significant.

Treatment

Twenty-three (27.7%) and 56 (67.51%) patients underwent complete and partial surgical resection of their tumors, respectively. Meanwhile, 4 patients (4.8%) were assigned to biopsy only. Table 1 outlines the indications for administered radiotherapy in studied patients. They received a median radiation dose of 55 Gy (range: 48–60). Seventy-eight patients (94%) were able to complete their course of radiotherapy, whereas in 5 cases (6%), the treatment was discontinued due to disease complications and patients' inappropriate clinical status.

RESULTS

The current investigation included 83 cases of meningioma. The median age of the patients was 50 years (range: 16–84) with a female to male ratio of 1.5. With regard to the tumor location, 64 cases (77.1%) presented in brain convexities and 19 cases (22.9%) in other brain regions including 5 cases in the sphenoidal wing, 3 in orbits, 4 in the cerebellopontine angle, 1 in the cavernous sinus, and 6 in the base of the skull. Among all, 40 patients (48.2%) had Grade I, 31 (37.3%) Grade II, and 12 (14.5%) Grade III meningiomas. Of the 43 patients with Grade II and III meningioma, 41 (95.3%) were found to have convexity meningiomas. The convexity meningioma presentation in Grade II and III tumors was significantly higher than the proportion recorded for patients with Grade I tumor (23 cases, 57.5%).

Treatment outcome

Due to the lacking follow-up data, 4 patients were excluded from survival curve analysis. The remaining 79 patients had a median follow-up of 35 (4–110) months since their initial radiotherapy session. By the end of the follow-up period, 50 patients (63.3%) survived. 34 cases experienced treatment failure (relapsed) and 29 (36.7%) patients deceased where 2 deaths were considered unrelated to tumor. Tumor recurrence was defined as any new clinical or imaging finding that could be attributed to disease progression. The 3- and 5-year overall survival rates were 66.2 ± 5.8% and 51.4 ± 7%, and the 3- and 5-year progression-free survival rates were 54.9 ± 6.1% and 49.4 ± 6.6%, respectively [Figures 1 and 2]. The relation between the clinicopathological variables and survival indicated that those with low-grade meningioma had a more extended overall and progression-free survival as compared to high-grade ($P < 0.001$). Although

Table 1: The proportion of patients underwent radiotherapy based on indications

Radiotherapy indication	*n* (%)
Incomplete tumor resection	32 (38.6)
Tumor recurrence	8 (9.6)
Grade II and III	43 (51.8)

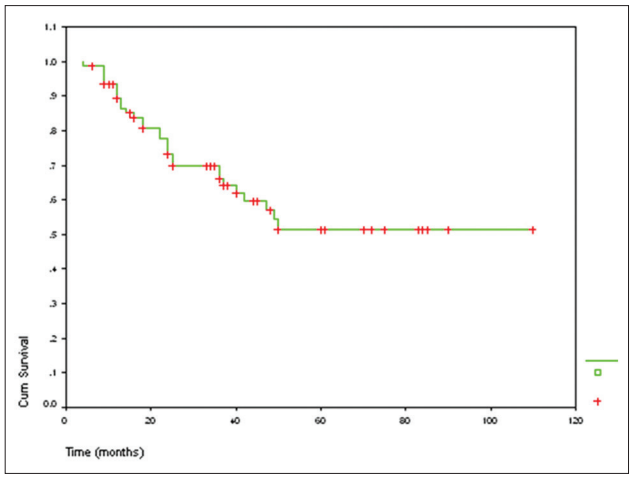

Figure 1: Kaplan–Meier graph demonstrating the overall survival

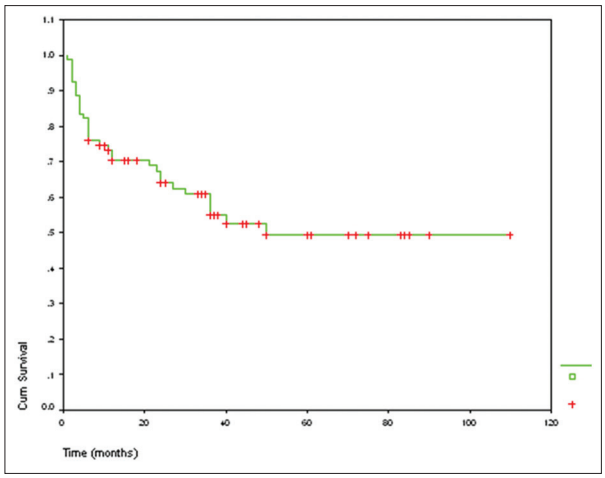

Figure 2: Kaplan–Meier graph demonstrating the progression-free survival

female patients and those who aged <50 years demonstrated a relatively higher survival rates than males and >50 years old patients, such difference was not found to be statistically significant. Moreover, variables such as the tumor location and the radiotherapy dose were not affected the survival outcome significantly [Table 2]. Among 19 patients with Grade II and III meningiomas, the 3-year survival was significantly higher in those who underwent complete or near-complete tumor resection, compared to those with incomplete resection (82 ± 9.5% vs. 17.1 ± 8.5%, $P = 0.008$).

Table 2: Treatment outcome according to clinicopathological features

Variables	Total number	Deceased patients	Mean±SEM (%)		Log-rank *P*
			3-year overall survival	5-year overall survival	
Tumor grade					
I	36	5	76.7±7.8	70.8±9.1	<0.001
II	31	15	43.5±10.3	34.8±11.3	
III	12	9	13.3±12	Not reached	
Gender					
Male	31	16	45.9±9.4	40.1±9.8	0.11
Female	48	13	60.8±7.9	55.3±8.9	
Age (years)					
≤50	41	12	63.2±7.9	59.7±8.2	0.16
>50	38	17	50.1±9.1	40.1±9.6	
Tumor location					
Brain convexities	61	28	50.3±7.1	47.1±7.2	0.08
Other regions	18	3	69.9±12.8	59.9±14	

SEM: Standard error of mean

DISCUSSION

The present study suggested the tumor grade as the most important prognostic factor in meningioma outcome. Patients with Grade III had a significantly lower 3-year survival compared to those with Grade I and II. In agreement with the above findings, some investigators including Adeberg *et al*. reported the 5-year survival of 81% and 53% in Grade II and III meningiomas, respectively, after radiotherapy.[6] According to Goldsmith *et al*., the 5-year overall survival of benign and malignant meningioma patients who underwent partial tumor resection were 85% and 58%, respectively.[7] Also, in a report by Zaher *et al*., the 5-year survival of patients with atypical meningioma was 35%.[8] Our study exclusively included all patients who underwent radiotherapy. Those with Grade I tumors who underwent incomplete removal or recurred were assigned to receive radiotherapy. There was a promising outcome in this group, and radiotherapy results in prolonged survival in 30 patients. On the other hand, our survival data in Grade II and III meningioma were less favorable than what reported in some other previous studies.[6] However, it should be noted that other studies (Adeberg *et al*., in particular) employed more advanced radiotherapy techniques such as stereotactic or intensity-modulated radiotherapy.[6] With respect to the correlation between tumor location and survival outcome in meningiomas, study results are contradictory. Based on Pechlivanis *et al*. report in 2011, survival rates in meningioma were not associated with tumor location,[9] whereas Zaher *et al*. reported a more favorable survival outcome in tumors located in the cerebral convexities.[8] One possible reason for this better outcome might be the most accessible location which enables tumor complete resection. Nevertheless, we found a relatively less survival (although not significant) for tumors located in the cerebral convexities. We could justify this finding based on the abundance of Grade II and III meningiomas (rather than Grade I) located in brain convexities (95.3% vs. 57.5%). Earlier investigations on the correlation between age and the survival rate in meningiomas indicated a higher survival rate in

patients younger than 50 years old. This is expected since benign meningiomas typically present in this age group. Meanwhile, according to our findings, although patients younger than 50 years old had a relatively longer survival, no statistically significant correlation between age and survival was noted. Studies show that despite the higher incidence of meningioma among women, gender is not considered as a factor influenced the survival. In line with this, our study demonstrated no association between gender and prognosis. As shown in previous reports, the extent of surgical resection is a critical prognostic factor determining the meningioma treatment outcome. A patient who underwent a complete or near-complete resection demonstrated a more favorable prognosis compared to those with partial resection or biopsy only. Furthermore, the risk of recurrence and progression-free survival is largely dependent on the extent of tumor removal during surgery.[10-14] Our study substantiated that the extent of tumor removal in Grade II and III meningiomas leaves a significant impact on survival.

CONCLUSION

Radiotherapy appears to provide a satisfactory survival outcome in Grade I meningioma patients underwent incomplete tumor removal or recurred. In those with Grade III tumors, long-term survival remains trivial, even after the radiotherapy. In patients with high-grade meningioma, complete surgical resection of the tumor may significantly improve the outcome. Utilizing high-technology radiotherapy equipment and novel techniques may improve the treatment results.

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Conflicts of interest

There are no conflicts of interest.

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