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CLINICAL STUDY

Analysis of patterns of failure and appraisal of postoperative radiation field for grade II–III meningioma

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Abstract

Purpose To analyze patterns of failure according to treatment modalities and evaluate the adequacy of an institution's current volume of postoperative radiotherapy (PORT) for World Health Organization (WHO) grade II or III meningiomas.

Patients and methods Data of 98 patients treated by either surgery and PORT (PORT group, n = 53) or surgery alone (surgery group, n = 45) between March 2000 and December 2013 were reviewed. Clinical target volume of PORT was delineated as a 1.5–2-cm expansion from the tumor bed. Local failure (LF) was defined as recurrence within a 2-cm margin from the tumor bed. Failures other than LF were defined as out-field failure (OFF). Median total dose of PORT was 59.4 (range 45.0–69.0) Gy.

Results The PORT group had larger proportions of grade III meningiomas (18/53, 34.0%) than the surgery group (8/46, 15.6%) ($p = 0.037$). After a median 73.4-month follow-up, 29 patients experienced LF and 5 developed OFF. The actuarial 5-year local control (LC) rates were 86.7% and 59.3% in the PORT and surgery groups, respectively ($p = 0.002$). PORT was a significant factor of LC in the univariate ($p = 0.003$, hazard ratio [HR] 3.449, 95% confidence interval [CI] 1.516–7.846) and multivariate analyses ($p < 0.001$, HR 5.486, 95% CI 2.178–13.820).

Conclusions Despite the larger proportion of grade III meningiomas in the PORT group, PORT reduced LF in patients with WHO grade II or III meningiomas compared with the surgery group. The current PORT field seems reasonable because LF was the dominant pattern of failure in patients treated by surgery alone.

Keywords Meningioma · Adjuvant radiotherapy · Local control

Introduction

Meningiomas are common intracranial neoplasms accounting for one-third of primary brain and central nervous system tumors [1]. Currently, despite the wide acceptance of the World Health Organization (WHO) grading criteria, universally accepted treatment consensus for each grade is

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not yet achieved [2]. According to the WHO criteria, about 80–90% of meningiomas are grade I and can be managed by observation in selected cases or by surgery or radiosurgery alone, when treatment is indicated [3, 4]. Treatment for grade II or III meningiomas is rather complicated because these meningiomas have relatively high recurrence rates after surgery alone [5, 6]. Improved patients' outcomes have been reported with a combination of surgery and postoperative radiation; however, controversial issues persist [7–9].

Although many studies analyzed postoperative radiotherapy (PORT) outcomes in grade II or III meningiomas, evaluation of the PORT field is limited. This study aimed to compare pattern of failures in grade II or III meningiomas according to treatment modalities and identify the optimal PORT field.

Patients and methods

Patients

From March 2000 to December 2013, 127 patients underwent surgery for WHO grade II or III intracranial meningioma in Severance hospital, Yonsei University Health System. Of 127 patients, 18 with no registered images in the electronic database, 10 who received radiation in other institutions, and 1 who expired owing to surgical complication were excluded. Overall, 98 patients' medical records and follow-up brain magnetic resonance (MR) images were reviewed retrospectively. Forty-one patients were diagnosed before the publication of 2007 WHO classification system. However, all pathological diagnosis for patients included in this study were confirmed retrospectively based upon the 2007 WHO classification system.

Treatment

Indications for surgical intervention were large tumors not eligible for radiosurgery or tumors with peritumoral edema or adjacent to anterior optic pathway. In all cases, tumor mass and the dura of origin were resected as much as possible unless such surgical intervention could cause serious complications.

All patients underwent preoperative and postoperative brain MRI within 48 hours. The decision for administering PORT was mainly determined at the neurosurgeon's discretion. To make time for the brain tissue to replace and recover, PORT was delayed for about 1 or 2 months. Each patient underwent brain MR imaging (MRI) before PORT to visualize sequential changes in brain tissue and adjacent structures.

Contrast-enhanced computed tomography (CT) was performed for PORT planning. In our institution, regardless of WHO grade, target volumes were defined as (1) gross tumor volume (GTV), defined as residual gross tumor after surgery, and (2) clinical target volume (CTV), categorized into two groups. (2a) CTV1 was delineated as postoperative tumor bed plus 1.5–2 cm margin along meninges and 0.5–1 cm margin to the brain parenchyma. Adjacent bone structure was included within the 5-mm width of CTV; however, peritumoral edema was not included. (2b) CTV2 for cone-down boost in three-dimensional conformal radiotherapy (3D-CRT) or simultaneous integrated boost in intensity-modulated radiotherapy (IMRT) was defined as a 5-mm margin around the tumor bed. Planning target volume (PTV) was each CTV plus 3-mm margin.

Thirty-three patients treated before October 2011 received PORT with 3D-CRT, and another 21 received IMRT. For 3D-CRT population, the median dose of 50.4 (range 36.0–64.0) Gy with a median fractional dose of 1.8 (range 1.8–2.0) Gy was prescribed to PTV1, while 25 patients received cone-down boost with a median dose of 9.0 (range 5.4–15.0) Gy. For IMRT population, a median dose of 54.0 (range 50.4–59.4), 60.0 (range 60.0–66.0), and 66.0 (range 63.0–69.0) Gy were prescribed to PTV1, PTV2, and GTV, respectively. Fractional dose for each target volume was 2.1–2.2 Gy for GTV if the remaining tumor was radiographically identifiable after surgery, 1.8 Gy for PTV1, and 2.0 Gy for PTV2.

Analysis methods for recurrence

Every patient was followed-up with brain MRI. Brain MRI of each patient with recurrence was transferred to MIM software version 6.4.6 (MIM Software, Inc., Cleveland, OH, USA). To determine the adequacy of current PORT field described above, the shortest distance to recurrent mass from tumor bed margin in brain MRI was measured by three experienced radiation oncologists. If the shortest distance from tumor bed to recurrent tumor mass was shorter than 2 cm, this case was defined as local failure (LF). Failures other than LF are defined as outfield-failure (OFF). Figure 1 illustrates the methods of recurrence analysis.

Statistics

Primary endpoint was local control (LC) rate, defined as controlled disease without LF as described above. Secondary endpoints included outfield control (OC) rate (defined equivalent to LC), progression-free survival (PFS), and overall survival (OS). LC, OC, PFS, and OS were calculated from the date of surgery in both the PORT and surgery groups. Progression events, including LF and OFF were regarded as positive if only radiographic evidence of recurrence or progression was available, while national health insurance data was also used to establish

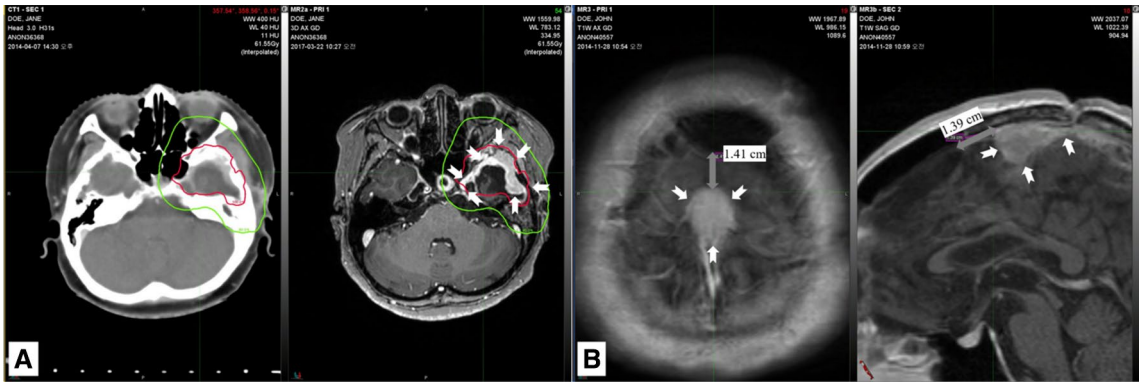

Fig. 1 Illustrations of local failures in both groups. White arrows indicate recurrent mass in each patient. **a** PORT group: PORT planning CT is on the left and MRI taken at recurrence on the right. Inner and outer circles show isodose line of prescribed dose and 90% isodose line of the prescribed dose, respectively. This case indicates failure at surgical margin. **b** Surgery group: the distance from surgical bed to recurrent mass was measured manually in all planes of brain MRI. Numbers inside the box describe the distance between tumor bed and recurrent mass. *PORT* postoperative radiotherapy, *CT* computed tomography, *MRI* magnetic resonance imaging

survival outcomes. Each survival curve was generated by Kaplan–Meier method. *P* values < 0.05 were considered significant, and all statistical analyses were performed using IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY, USA).

Results

Patients and treatment characteristics

Patient and treatment characteristics according to the treatment groups and their comparisons are summarized in Table 1. Median age of patients at diagnosis was 53.1 (range 12.2–79.3) years. Median period between surgery and PORT was 1.5 (range 0.5–6.2) months. Fifty-three (54%) patients received PORT, while forty-five were initially treated by surgery alone. The PORT group had higher number of grade III patients (18/53, 34.0%) than the surgery group (7/45, 15.6%) ($p = 0.037$). Patients in the surgery group were significantly more likely to receive gamma knife radiosurgery (GKS) than those in the PORT group ($p = 0.027$). Eight patients in the PORT group (8/53, 15.1%) received GKS after PORT, while seventeen patients in the surgery group (17/45, 37.8%) received GKS after surgery. Only two patients in the PORT group received GKS twice or more, while seven in the surgery group did. Median period between surgery and first GKS was 89.7 (range 10.1–199.9) and 43.4 (range 1.4–178.4) months in the PORT and surgery groups, respectively. No significant difference between the two groups was observed in other characteristics.

Local control rate and survival analysis

By median imaging follow-up time of 73.4 (range 10.0–209.8) months, 33 patients experienced treatment failures. Median time to treatment failure from diagnosis in these patients was 24.0 (range 1.4–169.1) months; with 24.0 (range 1.4–169.1) and 23.3 (range 4.0–79.3) months in grade II and III, respectively. Twenty-nine LF and five OFF were noted while one grade III patient in the PORT group developed both local and outfield failure with spinal cord seeding. In the PORT group (n = 53), there were 8 LF, 4 OFF, and 11 deaths. In the surgery group (n = 45), 21 LF, 1 OFF, and 9 deaths were noted. In terms of WHO grade, among 73 WHO grade II patients, gross total resection (GTR) alone resulted in 6 LF (6/24, 25.0%) and 1 OFF (1/24, 4.2%), while GTR with RT led to 3 LF (3/20, 15.0%) and 1 OFF (1/20, 5.0%). WHO grade II patients with subtotal resection (STR) alone had 10 LF (10/14, 71.4%) without OFF, while STR with RT showed 1 LF (1/15, 6.7%) and 2 OFF (2/15, 13.3%). Among WHO grade III patients, GTR alone had 4 LF (4/6, 66.7%) without OFF, GTR with RT resulted in 3 LF (3/14, 21.4%) without OFF, STR alone had 1 LF (1/1, 100.0%) without OFF, and STR with RT led to 1 local failure (1/4, 25.0%) and 1 OFF (1/4, 25.0%). Numbers of events according to the histologic grade, surgical extent, and use of PORT are summarized in Supplementary Fig. S1.

The actuarial 3-, 5-, and 10-year LC were 93.9%, 86.7%, and 71.4%, respectively, in the PORT group and 65.2%, 59.3%, and 51.0%, respectively, in the surgery group ($p = 0.002$). Four OFF developed in the PORT group, with 5- and 10-year outfield control rates of 93.5% and 89.8%; and one OFF was found in the surgery group at 10 years after surgery ($p = 0.153$). By median imaging follow-up

Table 1 Patient and treatment characteristics with comparison between two treatment groups

Patient and treatment characteristics	All patients (%)	PORT group (%)	Surgery group (%)	*p* value
Median age at diagnosis (range)	53.1 (12.2–79.3)	53.7 (12.2–73.8)	53.1 (12.2–79.3)	0.950
Gender				0.960
Male	46 (46.9)	25 (47.2)	21 (46.7)	
Female	52 (53.1)	28 (54.3)	24 (53.3)	
Karnofsky Performance Scale				0.451
50	1 (1.0)	1 (1.9)	0 (0.0)	
60	5 (5.1)	4 (7.5)	1 (2.2)	
70	44 (44.9)	23 (43.4)	21 (46.7)	
80	46 (46.9)	23 (43.4)	23 (51.1)	
90	2 (2.0)	2 (3.8)	0 (0.0)	
WHO grade				0.037
II	73 (74.5)	35 (66.0)	38 (84.4)	
III	25 (25.5)	18 (34.0)	7 (15.6)	
Location				0.439
Skull base	17 (17.3)	12 (22.6)	5 (11.1)	
Falx	8 (8.2)	5 (9.4)	3 (6.7)	
Parasagittal	28 (28.6)	12 (22.6)	16 (35.6)	
Convexity	35 (35.7)	17 (32.1)	18 (40.0)	
Periventricular	4 (4.1)	3 (5.7)	1 (2.2)	
Cerebellopontine angle	6 (6.1)	4 (7.5)	2 (4.4)	
Resection status				0.794
Total (Simpson grade I–III)	64 (65.3)	34 (64.2)	30 (66.7)	
Subtotal (Simpson grade IV)	34 (34.7)	19 (35.8)	15 (33.3)	
Number of GKS after surgery				0.027
None	73 (74.5)	45 (84.9)	28 (62.2)	
1	16 (16.3)	6 (11.3)	10 (22.2)	
≥ 2	9 (9.2)	2 (3.8)	7 (15.6)	

WHO World Health Organization, *GKS* Gamma knife surgery

time of 73.4 months and median follow-up time of 88.2 (range 10.0–213.3) months, 3-, 5-, and 10-year PFS were 88.4%, 73.5%, and 53.0%, respectively, in the PORT group and 63.5%, 54.9%, and 47.2%, respectively, in the surgery group ($p = 0.047$); the 3-, 5-, and 10-year OS rates were 92.5%, 84.1%, and 74.0%, respectively, in the PORT group and 93.3%, 86.5%, and 81.2%, respectively, in the surgery group ($p = 0.553$). LC and survival outcomes for all patients are summarized in Fig. 2.

The WHO grade II meningioma patients' 3- and 5-year LC for the PORT (96.9% and 90.4%) and surgery (70.3% and 66.6%) groups ($p = 0.018$) were reported. Two groups showed no statistically significant differences in OC, PFS, and OS.

The 3- and 5-year LC for WHO grade III patients were 87.8% and 80.5%, respectively, for the PORT group and 26.8% and 0.0%, respectively, for the surgery group ($p = 0.001$). Only 1 patient developed OFF 5 years after PORT, whereas no patient experienced OFF after surgery alone ($p = 0.655$). Three- and 5-year PFS rates were 73.7% and 67.5%, respectively, in the PORT group and 18.8% and 0.0%, respectively, in the surgery group ($p = 0.002$). Their respective OS rates were 83.3% and 72.2% in the PORT group and 71.4% and 42.9% in the surgery group ($p = 0.181$).

Further analysis on LC rates for WHO grade II and III patients according to surgical extent and usage of PORT was done. Results are displayed in Fig. 3. In both grades, STR alone resulted in significantly worse LC compared with other subgroups. Respective *p* values when STR was compared with GTR + PORT, STR + PORT, or GTR alone were 0.003, 0.002, and 0.003 in grade II; patients and 0.029, 0.046, and 0.128 in grade III patients. These results suggest the efficacy of PORT in both grades of meningioma patients, specifically grade III patients, and grade II patients with STR.

Recurrence pattern analysis and factors related to local control

The range of the distance from tumor bed to recurrent mass was 0.0–0.8 cm in the PORT group and 0.0–1.4 cm in the surgery group. In the surgery group, 14 patients showed recurrence at tumor bed, 4 had recurrence within 0.5 cm

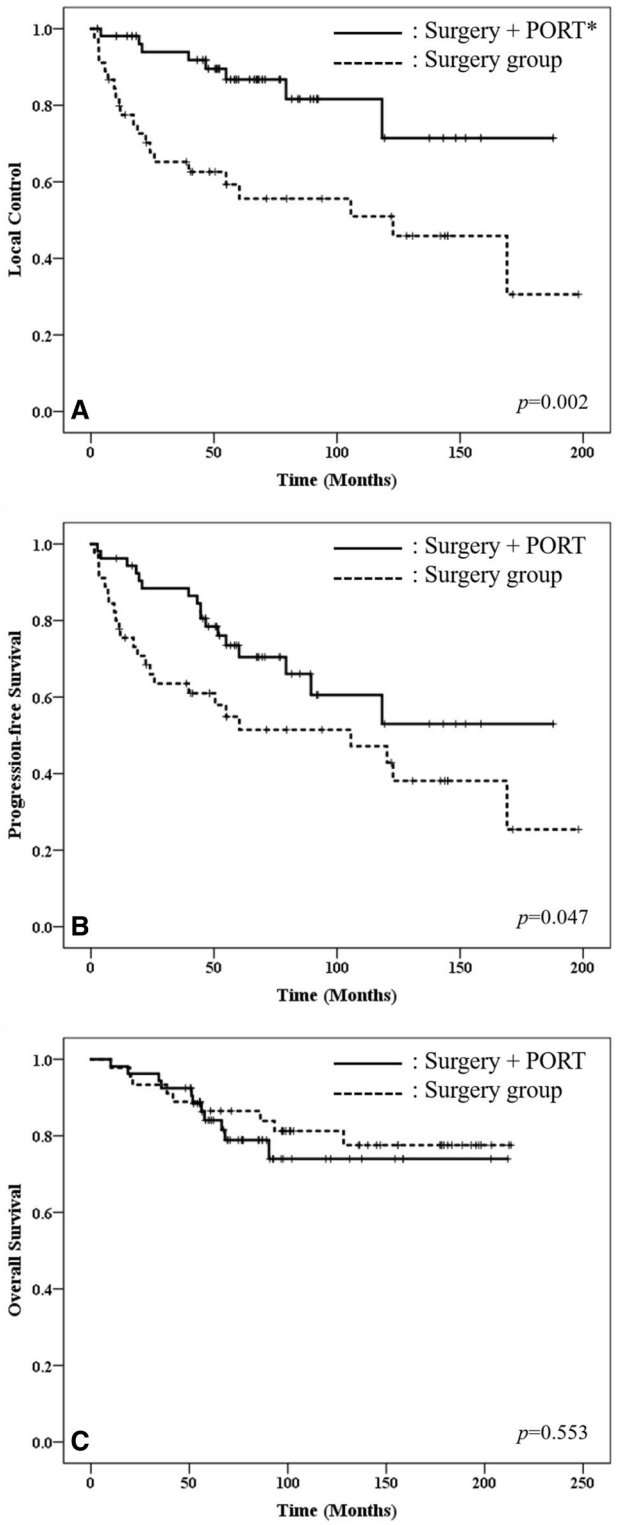

Fig. 2 Kaplan–Meier curves with *p* values determined by log-rank test based on treatment groups. Correlation between treatment groups and **a** local control, **b** progression-free survival, and **c** overall survival. *Postoperative radiotherapy

expansion from tumor bed margin, and 3 developed recurrences at 0.8, 1.0, and 1.4 cm away from tumor bed margin. Supplementary Table S2 shows the total profile of the shortest distance between tumor bed margin and recurrent mass in LF cases.

Considering their well-known significance in prognosis and treatment failure, WHO grade, and surgical extent were included in multivariate analysis, although these factors were not significantly related to LC in univariate analysis ($p = 0.330$, 0.251). Treatment group was a significant factor associated with LC in both univariate ($p = 0.003$, hazard ratio [HR] 3.449, 95% CI 1.516–7.846) and multivariate analyses ($p < 0.001$, HR 5.486, 95% CI 2.178–13.820). Age of patients separated by a value of 50 showed statistical significance in univariate analysis ($p = 0.036$, HR 2.633, 95% CI 1.063–6.522) and borderline significance in multivariate analysis ($p = 0.064$, HR 2.377, 95% CI 0.952–5.936). WHO grade and surgical extent were significant in multivariate analysis ($p = 0.012$, HR 3.207, 95% CI 1.299–7.919, $p = 0.030$, HR 2.337, 95% CI 1.083–5.040). Table 2 displayed the results of analysis of clinical factors related to LC.

Treatment for recurrence

Among 33 patients who experienced treatment failure, 22 patients underwent GKS as an initial treatment for recurrence, 6 patients underwent salvage operation, 4 patients received conservative care, and 1 patient was lost to follow-up after recurrence had been confirmed. Among 22 patients with GKS, 6 patients required additional salvage surgery and successive PORT due to recurrence after GKS. Three patients out of 6 patients who received salvage surgery as an initial treatment for recurrence received PORT after salvage surgery, and 3 patients underwent GKS due to recurrence during their follow-up after salvage surgery. Eighteen patients were alive after recurrence or progression; their median survival periods after progression was 56.1 (range 3.5–146.5) months.

For the PORT group, in 8 patients comprising 5 WHO grade II patients and 3 WHO grade III patients, with a median follow-up of 36.0 months (range 24.4–83.5) from the first GKS to the last follow-up, GKS after PORT was performed safely without radiation-related adverse effects or radiation necrosis. Among those 8 patients, 5 patients experienced recurrence after GKS while other 3 patients did not. Among those 5 patients, 2 patients underwent a second surgery with secondary PORT, 2 patients underwent additional GKS, and 1 patient was observed without further treatment.

In the surgery group, after a median follow-up of 82.3 months (range 5.6–187.6) from the first GKS to the last follow-up, 17 patients comprising 13 WHO grade II patients and 4 WHO grade III patients underwent GKS. Seven patients were followed-up with stable disease, while

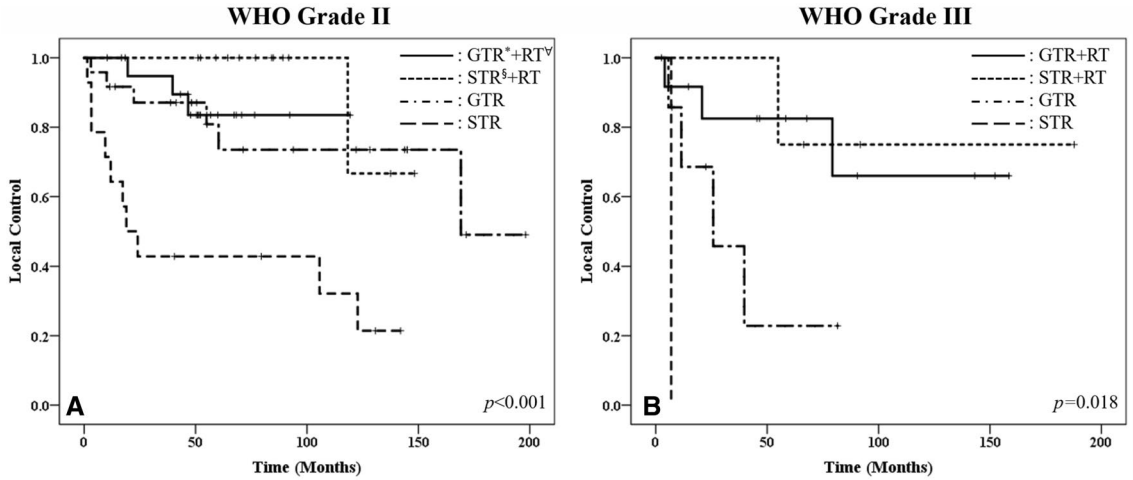

Fig. 3 Comparison of actuarial local control rate according to treatment groups combined with surgical extent in WHO grade II and III meningioma patients. STR alone resulted in significantly worse LC than other treatment modalities in **a** WHO grade II and **b** WHO grade III patients. *WHO* World Health Organization, *STR* subtotal resection, *LC* local control, *Gross total resection, ∀Radiotherapy, §Subtotal resection

Table 2 Univariate and multivariate Cox proportional hazards associations between clinical factors and local control

Variable	Univariate analysis		Multivariate analysis	
	95% CI	*p* value	95% CI	*p* value
Sex	0.277–1.207	0.144		
Age < 50 vs Age ≥ 50	1.063–6.522	0.036	0.952–5.936	0.064
KPS < 80 vs KPS ≥ 80	0.857–3.879	0.119		
WHO grade (grade II vs. grade III)	0.673–3.249	0.330	1.299–7.919	0.012
Surgical extent (Simpson 1–3 vs. subtotal)	0.738–3.205	0.251	1.083–5.040	0.030
PORT group vs. surgery group	1.516–7.846	0.003	2.178–13.820	< 0.001
Skull base vs. non-skull base	0.482–4.009	0.543		

CI confidence interval, *KPS* Karnofsky Performance Scale, *WHO* World Health Organization, *PORT* post-operative radiotherapy

the other 10 patients experienced progression of disease. Among 10 patients who experienced recurrence or progression after the first GKS, 4 received more GKS, 3 patients underwent additional GKS and a second operation with PORT, 1 patient underwent a second operation with PORT, and 2 patients did not receive further treatment due to poor general condition.

Toxicity

Two among fifty-three patients in the PORT group developed asymptomatic radiation necrosis. One patient received 54.0 Gy with 3D-CRT, while another received 60.0 Gy with IMRT. No medical intervention was required and these patients never experienced recurrence of meningioma in serial brain MRI evaluation.

Discussion

Outcomes after RT largely depend upon RT fields. Therefore, consistent target volume definition is necessary in clinical trials investigating the efficacy of RT. However, proper post-operative RT volume for grade II or III meningioma remains unknown. This study mainly aimed to evaluate the adequacy of an institution's PORT field by analyzing patterns of failure after treating grade II or III meningioma. An 8–15-mm margin around the tumor bed in the NRG Oncology RTOG 0539 trial resulted in 3-year LC rate of 95.9% and PFS of 93.8% after a median 3.7-year follow-up [10]. A study from Emory University using median CTV + PTV margin of 0.8 (range 0.3–1.0) cm with IMRT in 46 grade II patients resulted in 3-year LC rate of 74%, after a median 26-month follow-up [11]. In the

recent NRG-BN003 protocol, phase III trial of observation versus irradiation for a gross totally resected grade II meningioma, the CTV margin was 5 mm [12]. In contrast, Adeberg et al. recommended 1–2 cm and 2–3 cm CTV margin for grade II and III meningioma, respectively [13]. In this study, even though the shortest distance from the recurrent tumor to the primary tumor bed was within 1 cm in the majority of cases, the epicenter of the recurrent tumor was likely to be beyond this distance. Moreover, as we observed relatively less frequent LF in irradiated patients, the CTV margin defined in this study is still used in our institution. Only 4 patients (11.4%) who received radiation with grade II meningioma developed local recurrence with 3- and 5-year LC rate of 96.9% and 90.4%, respectively. With improvement in RT technique including IMRT, the adjacent normal brain with no severe treatment-related toxicities could be spared. Only 2 patients developed asymptomatic radiation necrosis, although 1.5–2-cm wider margin was used.

We showed the positive effect of PORT on LC in both grade II and III meningiomas, although PORT did not result in OS benefit. No difference in OS between PORT and surgery alone might be due to indolent progression after local recurrences (especially in grade II meningiomas) and successful salvage treatment. However, as we mentioned above, many salvage treatment modalities were usually employed to control progression of meningioma once treatment failure had developed.

Although adjuvant radiotherapy is recommended for grade III meningiomas because of high recurrence rate after surgery alone, the benefit of PORT in LC remains unknown. Anaplastic meningioma is rare with variable pathologic definition over time and many older retrospective studies included both grade II and III meningiomas together. In a review of 38 patients with 48 malignant meningioma resections, PORT significantly increased the 5-year disease-free survival from 15 to 80% [14]. This study included 11 hemangiopericytomas. From Adeberg's study, the 5-year PFS for 23 patients who received radiation with 1–2-cm margin around tumor bed or gross tumor for primary or recurrent anaplastic meningioma was 13%. In our study of 18 patients with grade III meningioma who received surgery and immediate PORT, the 5-year PFS was 67.5%. The disparity between these two studies might be related to the difference between patients' characteristics, as 40% of patients had progressive disease or biopsy only at the time of receiving RT in the Adeberg's study, while our study comprised patients who received immediate RT after surgery with 77.8% (14/18) GTR rate [13].

Reported 5-year recurrence rates after complete resection for grade II meningioma are 41.0%-53.6% while respective rate after subtotal removal is higher than 70.0% [7, 15, 16]. However, the efficacy of PORT for grade II meningioma, especially for patients with complete resection, had not been firmly defined because of contradictory results from various studies. While some showed PORT benefit [7, 9, 16], a few others insisted that PORT had no effect on patient outcomes [15, 17]. Most of these studies used retrospective design with small number of patients [11], short follow-up period [7, 16], lack of details provided about target volume definition and RT dose [15, 17], and shortage of precise image follow-up with MRI scan [17]. Two prospective phase II trials assessed role of RT in meningioma. In the NRG Oncology RTOG 0539 trial, intermediate risk (recurrent grade I with any resection extent and grade II with GTR) meningioma patients who received 54 Gy of RT in 30 fractions had excellent 3-year PFS of 93.8%, supporting the use of PORT for these patients [10]. In another recently published results of phase II observation study (EORTC 22042-26042), high-dose radiotherapy with 60 Gy in 6 weeks for patients with grade II and Simpson grade 1–3 resulted in 88.7% of 3-year PFS and 98.1% of 3-year OS [18]. Two prospective randomized clinical trials which could answer the question on efficacy of PORT after gross total resection of intracranial grade II meningioma are underway. NRG-BN003 trial will evaluate PFS after PORT of 59.4 Gy in 33 fractions with CTV defined as 5 mm expansion around tumor bed [12]. ROAM/EORTC-1308 trial is another randomized controlled trial that is also designed to determine the effect of PORT of 60 Gy in 30 fractions on the risk of tumor recurrence [19]. These study results could provide useful information on PORT field in totally resected grade II meningioma. For patients with STR, in our series, PORT markedly decreased local recurrence, but did not affect the OS rate. A recent study using National Cancer Database in the United States, however, observed significantly improved OS with adjuvant RT compared with no adjuvant RT in STR cohort [20].

In the analysis of prognostic factors for LC, histologic grade (II vs. III) and surgical extent were not significant in univariate analysis, but were significant in multivariate analysis. Considering that a larger proportion of grade III patients had received PORT, these findings suggested that the effect of PORT negated the impact of histologic grade and surgical extent on LC. Better LC was achieved in patients aged < 50 years, with statistical significance in univariate analysis and borderline significance in multivariate analysis, which is in line with other studies reporting better outcomes in younger patients [21, 22].

Meningioma is also well-known as a secondary intracranial neoplasm associated with cranial radiation therapy. However, although reports on the occurrence of meningioma as a secondary neoplasm after cranial radiation therapy in childhood are abundant [23, 24], reports on secondary malignancy related to radiation therapy or radiosurgery to meningioma are relatively rare. A case of occurrence of glioblastoma after radiosurgery for meningioma has been

reported [25]. In our study population with a relatively long follow-up period, no such case was observed. Therefore, the risk of induction of secondary malignancy did not seem to be high enough to avoid radiation therapy for meningioma.

Strengths of our study include long imaging follow-up period and detailed review of postoperative images, PORT field, and dose distribution. Another strength is the relatively large number of patients in a single institution where treatment began after 2000, which allowed for homogeneous guidelines for preoperative/postoperative imaging evaluations, surgery, and RT planning with target volume definitions. Also, high-dose radiation around 60 Gy was applied around tumor bed.

This study has some limitations. As increased LC and PFS by PORT did not lead to improvement in OS in this cohort, quality of life, neurocognitive function, and medico-social expenses for salvage treatment should have been compared with the surgery group to provide PORT efficiency results. Still, in this study, the surgery group seemed to require additional salvage treatment compared with the PORT group, as more GKS after surgery were required after surgery alone. Another limitation was the limited number of patients in each group, grade II versus grade III, GTR versus STR, and PORT versus surgery alone, possibly limiting statistical power in analyzing survival outcomes and prognostic factors. Although this study had limitations, it could be a reference in determining proper volume of PORT in grade II–III meningioma by providing the full profile of the distance between tumor bed and recurrent mass.

In conclusion, we confirmed that current PORT target volume in our institution, which defined tumor bed plus generous margin for WHO grade II or III meningioma, was reasonable, showing high LC rate without severe toxicity. Further studies including ongoing prospective studies must be conducted to determine the proper target volume of PORT.

Compliance with ethical standards

Conflict of interest The author(s) disclose no potential conflict of interest.

Research involving human and animal participants This article does not contain any studies with human participants or animals performed by any of the authors.

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