

Outcome of surgical and radiation therapy treatment of grade II meningiomas: A single institution experience

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Objective To evaluate local control and survival rates with two different treatment modalities: surgery alone and surgery plus adjuvant radiation therapy (RT).

Methods Cases of 104 patients diagnosed with grade II meningiomas between 2004 and 2014 were retrospectively reviewed. Of those, 68 patients had complete medical records. For inclusion in this study, we required a follow-up period of more than 2 years. Age at diagnosis, initial tumor size, tumor location, extent of resection and adjuvant RT were categorized to identify possible parameters that may have affected the outcome of this disease.

Result Thirty-seven patients (54%) received surgery alone while 31 patients (46%) received adjuvant RT. The 2-year and 5-year rates of local control (LC) were 94% and 87%, respectively. No correlation was found between other parameters and recurrence of tumors. Patients in our study who received adjuvant RT had significant lower overall survival rate ($p=0.044$). The 2-year overall survival (OS) was 99% and 5-year OS was 93%.

Conclusion Tumor control and survival were found to be excellent in this retrospective study. Adjuvant RT did not influence local control, but was statistically associated with lower survival rates. Further prospective study should be performed to clarify the management of grade II meningiomas. **Chiang Mai Medical Journal 2018;57(3):135-41.**

Keywords: WHO grade II meningiomas, outcome, adjuvant radiation therapy

Introduction

Meningiomas are the most common primary intracranial neoplasms in adults, accounting for approximately 34% of all central nervous system (CNS) tumors (1). The World Health Organization (WHO) grading system classifies meningiomas into three categories: grades I, II, and III (2). While most meningiomas are benign (WHO grade I), and are associated with slow growth and a low rate of recurrence

after surgery, WHO grade II and III meningiomas appear to often have higher recurrence rates leading subsequently to more debilitating signs and symptoms. The optimal management of these groups of grade II and III meningiomas needs to be clarified. Although surgery is considered a mandatory modality for all meningiomas, adjuvant radiation therapy (RT) is still controversial for WHO grade II tumors

(3-5). Retrospective study has reported 5-year recurrence rates of 41% after gross total resection (GTR) (6), but the benefits of adjuvant RT remain unclear. Radiotherapy has been shown to significantly lower the risk of tumor recurrence for subtotally resected WHO grade II meningiomas (3,7). However, to date, no large randomized clinical trials have been conducted which clearly identify the benefits of adjuvant RT in this subtype of meningiomas.

In the Chiang Mai University Hospital, management of grade II meningiomas is discussed among the neurosurgeon, neuropathologist and radiation oncologist for each patient. The result has been that varying treatment modalities: biopsy alone, radical surgery and surgery combined with adjuvant RT.

Objectives

The primary objective of this study was to evaluate the local recurrence rate after surgery with and without RT. The secondary objectives were to identify possible factors which may impact on the risk of recurrence and to report overall survival rate of our patients.

Method

Patient populations

We retrospectively reviewed a total of 104 patients who were diagnosed with grade II meningiomas who were treated at our institution between 2004 and 2014. The diagnosis of each patient was confirmed by the neuropathologist after surgical resection. Of the patients diagnosed, 68 had complete medical records including a follow-up period of more than 2 years.

This study was approved by the Research Ethics committee, Faculty of Medicine, Chiang Mai University.

Parameters assessed

Patients were divided into groups based on age at diagnosis: <30 year, 30-50 year and > 50 year. Initial tumor size was categorized as <2 cm, 2-5 cm and >5 cm. Tumor location was divided into five categories. 1) cerebral convexity, 2) falx cerebri, 3) sphenoid wing, 4) cavernous sinus, and 5) other. The pathological subtypes of WHO gr II meningiomas were classified as atypical, chordoid and clear cell variant of meningiomas. The degree of surgical resection was determined following Simpson's Grading system (8). In this study, GTR refers to Simpson grade I-III, subtotal resection

(STR) is equivalent to Simpson grade IV, while biopsy is Simpson grade V.

Statistical analysis

Characteristics of patients are presented as number and percentages. The Fisher exact test was used to compare distribution of variables. The overall survival and local recurrence control rates were calculated using the Kaplan Meier method, and the log rank test was performed for significance testing of factors predicted to potentially affect the prognosis. All reported P values are 2 sided and P values < 0.05 are considered statistically significant. All analyses were performed using STATA software version 10.1 (Stata Corp, College Station, TX).

Result

From 2004 to 2014, a total of the 68 patients who had undergone surgical resection and who had complete medical records at Chiang Mai University Hospital were included in the statistical analysis. Patient characteristics are shown in Table 1. Among the patients, 37 received surgery alone while 31 also had adjuvant RT. The indicated parameters were balanced in both arms. Most of the patients were middle-aged females. The tumors were typically located at the cerebral convexity (47%). An atypical meningioma variant was the most common subtype in our study, found in 61 of 68 patients (90%). Thirty-seven patients (54%) had a large initial tumor size; more than 5 cm. Surgical procedures included GTR for 40 patients, STR for 27 patients and biopsy alone for 1 patient. In the surgery only group, 5 patients (14%) had a recurrence of the disease, while there were 3 patients (10%) with a recurrence in the surgery plus adjuvant RT group. Those patients with a recurrent tumor received further surgery, radiation therapy or chemotherapy. In this study, none of the parameters studied were found to be associated with local recurrence (Table 2). In the survival analysis, receipt of adjuvant RT was the only parameter that was significantly associated with lower overall survival (Table 3). The Kaplan-Meier method showed 94% local control at 2 years (95%CI: 85% to 98%) and 87% at 5 years (95%CI: 75% to 93%) (Figure 1). Two-year and 5-year overall survival rates were 99% and 93%, respectively (Figure 2).

Table 1. Patient characteristics

Variables		No radiation (n=37)	Radiation (n=31)	p-value*
Sex	Male	8	8	0.777
	Female	29	23	
Age (years)	<30	1	1	0.903
	30-50	19	17	
	>50	17	13	
Location of tumor	Cerebral convexity	22	10	0.086
	Falx cerebri	2	8	
	Sphenoid wing	4	5	
	Cavernous sinus	6	6	
	Other	3	2	
Pathology	Atypical	31	30	0.165
	Chordoid	4	0	
	Clear cell	2	1	
Tumor size	<2 cm	0	2	0.503
	2-5 cm	10	8	
	>5 cm	20	17	
	N/A	7	4	
Extent of resection	Gross total resection	25	15	0.169
	Subtotal resection	12	15	
	Biopsy	0	1	

*;p-value by Fisher exact test

Table 2. Association between local recurrence and selected factors

Variables		No recurrence (n=60)	Recurrence (n=8)	*p-value	#p-value
Sex	Male	12 (75%)	4 (25%)	0.081	0.055
	Female	48 (92%)	4 (8%)		
Age (years)	<30	1 (50%)	1 (50%)	0.258	0.078
	30-50	3 (92%)	3 (8%)		
	>50	26 (87%)	4 (13%)		
Location of tumor	Cerebral convexity	29 (91%)	3 (9%)	0.833	0.809
	Falx cerebri	8 (80%)	2 (20%)		
	Sphenoid wing	8 (89%)	1 (11%)		
	Cavernous sinus	10 (83%)	2 (17%)		
	Other	5 (100%)	0 (0%)		
Pathology	Atypical	53 (87%)	8 (13%)	> 0.999	0.593
	Chordoid	4 (100%)	0 (0%)		
	Clear cell	3 (100%)	0 (0%)		
Tumor size	< 2 cm	2 (100%)	0 (0%)	0.112	0.182
	2-5 cm	18 (100%)	0 (0%)		
	> 5 cm	30 (81%)	7 (19%)		
	N/A	10 (91%)	1 (9%)		
Extent of resection	Gross total resection	37 (92%)	3 (8%)	0.340	0.249
	Subtotal resection	22 (82%)	5 (18%)		
	Biopsy	1 (100%)	0 (0%)		
Radiotherapy	No	32 (86%)	5 (14%)	0.719	0.704
	Yes	28 (90%)	3 (10%)		

*; p-value by Fisher exact test, #; p-value by Log rank test

Table 3. Association between overall survival and selected factors

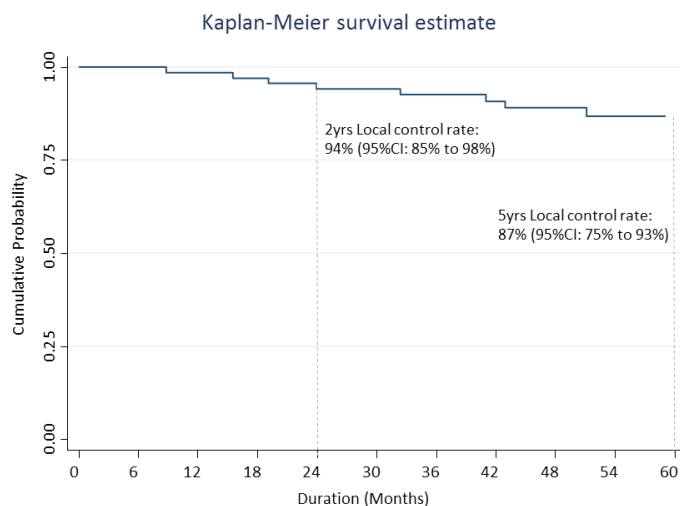
Variables		#p-value
Sex	Male	0.066
	Female	
Age (years)	<30	0.122
	30-50	
	>50	
Location of tumor	Cerebral convexity	0.591
	Falx cerebri	
	Sphenoid wing	
	Cavernous sinus	
	Other	
Pathology	Atypical	0.680
	Chordoid	
	Clear cell	
Tumor size	<2 cm	0.968
	2-5 cm	
	>5 cm	
	N/A	
Extent of resection	Gross total resection	0.959
	Subtotal resection	
	Biopsy	
Radiotherapy	Yes	0.044
	No	

#;p-value by Log rank test

Discussion

In this retrospective study, we found excellent local tumor control and overall survival in WHO grade II meningioma patients. Contrary to several publications which have reported superior outcome using adjuvant radiotherapy (3,6,9-12), our study found worse survival outcomes. Taking this into consideration, the reasonable one possible explanation for the lower survival rates with adjuvant RT in this study may be selection bias on the part of the surgeons who referred more a higher proportion of patients with aggressive tumor characteristics to receive adjuvant radiotherapy. Observation after gross total resection of tumors with no feature of brain invasion was clinically accepted (3,5). However, most supporting data was obtained from retrospectively reviewed. A recent large prospective trial, RTOG 0539, divided WHO grade II meningiomas into intermediate risk (newly diagnosed patients with GTR) and high risk (STR or recurrence of the disease). Both groups received adjuvant RT, 54 Gy for the intermediate risk group and 60 Gy for the high risk group (13). The initial outcomes at 3 years for local failure was 4.1% and overall survival was 96%.

Age at diagnosis was not associated with either local control or survival in our study. This is in agreement with a study from Yang et al (5), which retrospectively reviewed prognostic

**Figure 1.** Two-year and five-year local control rates

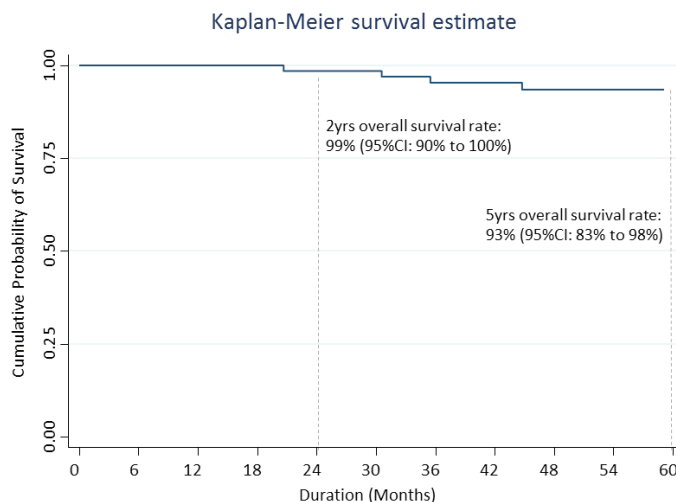


Figure 2. Two-year and five-year overall survival rates

factors in atypical and anaplastic meningiomas, and a study from Adeberg et al(14), which reported long-term outcomes after RT at the University Hospital of Heidelberg. However, many publications have reported worse survival rates after RT in patients aged more than 60 years (9,15-17) while Milosevic et al reported favorable outcomes in patient age less than 40 years (11). Regarding initial tumor size, Detti et al stated that tumors of more than 5 cm were associated with significantly lower disease-free survival rates (9); while no similar correlation was found in our study. Extent of resection is also known to be a prognostic factor. Some retrospective publications have indicated worse tumor control for incompletely resected tumors (5,17), but other data show no association of this factor with local recurrence (9,14,16). Several published papers did not report any impact of tumor location on survival outcome (5,17).

Our study is the first to present clinical outcome of WHO grade II meningioma patients treated at Chiang Mai University Hospital. There were several limitations of this study. First, it was a retrospective review, so it was not possible to control variation in potentially. Second, a second pathologic review of each histologic slide was absent. Third, all patients who received radiotherapy were sent to us based on the decision of an individual neurosurgeon who may have had a selection bias.

Finally, there were only a limited number of recurrent events in this study.

Conclusion

This retrospective study demonstrated excellent tumor control as well as survival rates for WHO gr II meningiomas treated at our institution. Adjuvant RT did not influence local control but was associated with lower survival rates. Further prospective, multicenter studies are necessary to determine optimal management and to identify additional relevant prognostic factors related to outcome of these meningiomas.

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ผลการรักษาโรคเนื้องอกเยื่อหุ้มสมองระดับ 2 ด้วยการผ่าตัดและการฉายรังสีในสถาบัน ที่วิจัยเพียงสถาบันเดียว

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วัตถุประสงค์ เพื่อประเมินอัตราการควบคุมโรคเฉพาะที่ และอัตราการรอดชีวิต ในการรักษาโรคด้วยวิธีที่แตกต่างกันคือการผ่าตัดเพียงอย่างเดียว และการผ่าตัดร่วมกับการฉายรังสี

วิธีการศึกษา เป็นการศึกษาแบบย้อนหลังในผู้ป่วยโรคเนื้องอกเยื่อหุ้มสมองระดับ 2 ที่ได้รับการรักษาตั้งแต่ปี ค.ศ. 2004 ถึงปี ค.ศ.2014 รวบรวมผู้ป่วยได้ทั้งหมด 104 ราย ในจำนวนนี้ มีผู้ป่วย 68 ราย ที่มีการจดบันทึกทางการแพทย์ครบถ้วนและเข้าได้กับเกณฑ์งานวิจัยคือต้องมีการติดตามผู้ป่วยอย่างน้อย 2 ปี ได้มีการศึกษาปัจจัยด้านอายุผู้ป่วย ขนาดก้อนเนื้องอก ตำแหน่ง ลักษณะการผ่าตัด และการได้รับรังสีรักษา ว่ากระทบต่อผลการรักษาในผู้ป่วยกลุ่มนี้หรือไม่

ผลการศึกษา ผู้ป่วยที่ได้รับการผ่าตัดอย่างเดียวมีจำนวน 37 ราย คิดเป็นร้อยละ 54 ผู้ป่วยที่ได้รับการผ่าตัดร่วมกับฉายรังสีมีจำนวน 31 ราย (ร้อยละ 46) อัตราการควบคุมโรคเฉพาะที่ที่ 2 ปีและ 5 ปี คือ ร้อยละ 94 และร้อยละ 87 ตามลำดับ ไม่มีปัจจัยใดที่กระทบต่ออัตราการควบคุมโรคเฉพาะที่ ในขณะที่เดียวกันกลับพบว่า ผู้ป่วยที่ได้รับรังสีรักษาร่วมด้วยมีอัตราการรอดชีวิตน้อยกว่าผู้ป่วยที่ไม่ได้รับรังสีอย่างมีนัยสำคัญทางสถิติ ($p=0.044$) อัตราการรอดชีวิตโดยรวมที่ 2 ปีและ 5 ปี คือ ร้อยละ 99 และร้อยละ 93 ตามลำดับ

สรุปผลการศึกษา ในการศึกษาพบว่าผลการรักษาในสถาบันของเรามีอัตราการควบคุมโรคเฉพาะที่และอัตราการรอดชีวิตที่สูง การฉายรังสีไม่ส่งผลกระทบต่ออัตราการควบคุมโรคแต่ส่งผลต่ออัตราการรอดชีวิตของผู้ป่วย เนื่องจากการศึกษานี้เป็นแบบย้อนหลัง ทางผู้วิจัยเห็นว่าการศึกษาแบบไปข้างหน้าจะช่วยบ่งบอกปัจจัยที่ส่งผลการรักษาได้ รวมถึงสามารถเป็นแนวทางในการรักษาผู้ป่วยเนื้องอกเยื่อหุ้มสมองระดับ 2 ได้ต่อไป **เชียงใหม่ เวชสาร 2561;57(3):135-41.**

คำสำคัญ: เนื้องอกเยื่อหุ้มสมองระดับสอง ผลการรักษา การฉายรังสี