"Wait-and-See" Strategies for Newly Diagnosed Intracranial Meningiomas Based on the Risk of Future Observation Failure

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■ OBJECTIVE: **To analyze factors affecting observation failure (Ob-F) of untreated intracranial meningiomas (IMs) and to develop a "wait-and-see" strategy for newly diagnosed IMs based on risk.**

■ METHODS: **Factors affecting Ob-F (i.e., development of neurologic symptoms, significant growth, loss of opportunity to do radiosurgery, and tumor invasion into the adjacent sinus) were examined using a multivariate Cox proportional hazard model. The utility of the Asan Intracranial Meningiomas Scoring System (AIMSS) for screening out patients at risk for Ob-F was also analyzed. The "wait-and-see" strategy was based on the growth rate affecting the 5-year observation success (Ob-S) rate.**

■ RESULTS: **Over 46.9 months, 77 of 232 patients (33.2%) experienced Ob-F. Larger tumors, preexisting neurologic symptoms, absence of calcification, and isointense/hyperintense signal were predictors of Ob-F. An AIMSS score of 4 for tumors <2.5 cm in diameter ($P = 0.0002$) and a score of 6 for tumors ≥2.5 to <4.0 cm in diameter screened out tumors at risk for Ob-F ($P = 0.0023$). Initial growth rates of ≥20%/year for tumors <2.5 cm ($P < 0.0001$) and ≥1 cm^3/year for tumors ≥2.5 to <4.0 cm ($P = 0.0019$) were predictive of 5-year Ob-S rate; however, tumors ≥4 cm tended to experience Ob-F, regardless of score group or growth rate.**

■ CONCLUSIONS: **The AIMSS is helpful for screening out IMs at risk for Ob-F at the time of diagnosis. The initial growth rate after follow-up predicts the risk of future Ob-F in small- to medium- sized IMs.**

INTRODUCTION

Intracranial meningiomas (IMs) are the most common brain tumor, accounting for approximately 35% of primary brain tumors.[1-3] Most IMs are benign and slow-growing, and incidental findings have increased due to advances in neuroimaging tools and growing interest in health.[4] Large tumors causing neurologic symptoms should undoubtedly be treated, but a definite requirement to treat benign tumors is uncertain in numerous cases. Tumor size and location, the presence of neurologic symptoms, and the age and general condition of the patient vary greatly among cases. Therefore, the need for treatment, along with the related risks, should be carefully considered when making the decision to treat or observe.

Observing tumors, or a "wait-and-see" approach, is a common strategy for management of newly diagnosed IMs, especially in older patients with small tumors without neurologic symptoms. These patients usually undergo serial imaging follow-up until they become symptomatic or their tumors are considered large enough to treat. However, this method of management is not always safe, because the tumors can increase in size before the next follow-up, and patients could miss an opportunity for stereotactic radiosurgery in the case of a small tumor. Moreover, delaying treatment until neurologic symptoms become overt, or after the tumor is significantly enlarged, can make the surgery challenging.[5] In older

Key words
- Meningioma
- Natural history
- Prognosis
- Risk assessment

Abbreviations and Acronyms
AGR: Absolute growth rate
AIMSS: Asan Intracranial Meningiomas Scoring System
IM: Intracranial meningioma
MRI: Magnetic resonance imaging
NSFS: Neurologic symptom—free survival
Ob-F: Observation failure
Ob-S: Observation success
RGR: Relative growth rate
SI: Signal intensity

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Table 1. Demographic Data for the Ob-S and Ob-F Groups After Continuous Observation of Untreated Intracranial Meningiomas

Variable	All	Ob-S Group	Ob-F Group	*P* Value
Total, number (%)	232	155 (66.8)	77 (33.2)	
Age (years), mean ± SD	60.3 ± 10.2	59.0 ± 10.0	63.0 ± 10.2	0.004
Male sex, number (%)	40 (17.2)	18 (11.6)	22 (28.6)	0.003
Presenting symptoms				
Neurologic deficit, number (%)	32 (13.8)	9 (5.8)	23 (29.9)	0.000
Initial tumor size (cm^3), mean ± SD	11.5 ± 19.3	5.6 ± 10.0	23.8 ± 27.6	0.000
>8.18 (≈sphere 2.5 cm diameter)	73 (31.5)	24 (15.5)	49 (63.6)	0.000
Location, number (%)				
Eloquent	133 (57.3)	80 (51.6)	53 (68.8)	0.016
Infratentorial	35 (15.1)	25 (16.1)	10 (13.0)	0.566
Skull base	54 (23.3)	34 (21.9)	20 (26.0)	0.512
Calcification, number (%)	91 (5*) (40.1)	73 (4*) (48.3)	18 (1*) (23.7)	0.000
Edema, number (%)	46 (19.8)	17 (11.0)	29 (37.7)	0.000
Arachnoid plane, number (%)	96 (6*) (41.4)	73 (5*) (47.1)	23 (1*) (29.9)	0.016
T2-weighted MRI, number (%)				
Hyperintense	30 (13.3)	17 (11.3)	13 (17.1)	0.299
Isointense	150 (66.4)	93 (62.0)	57 (75.0)	0.054
Hypointense	46 (20.4)	40 (26.7)	6 (7.9)	0.001
Absolute growth rate (cm^3/year), mean ± SD	2.2 ± 4.6	0.3 ± 0.4	5.9 ± 5.8	0.000
Relative growth rate (%/year), mean ± SD	20.4 ± 38.7	6.9 ± 13.5	46.8 ± 55.5	0.000
Tumor doubling time (year), mean ± SD	18.0 ± 35.3	23.2 ± 39.2	7.4 ± 22.7	0.000
Follow-up duration (months), median (range)	47 (6–151)	49 (18–151)	44 (8–131)	0.154

Ob-S, observation success; Ob-F, observation failure; SD, standard deviation; MRI, magnetic resonance imaging.
*Number of patients with missing data for each variable.

patients (>70 years), delaying surgery increases the risk of perioperative morbidity.[5,6] Therefore, if we could preselect patients who may require treatment in a few years, we could devise appropriate treatment strategies in a more timely and safe fashion. Conversely, unnecessary treatment of patients with little chance of observation failure (Ob-F) could be avoided, thereby reducing medical expenses and the burden of treatment-related complications.

There are no systematic guidelines (e.g., dealing with such issues as which tumors should be treated immediately and the optimal interval for follow-up imaging for tumors according to risk) for the management of newly diagnosed IMs. Several authors have studied the natural history of IMs, and large tumors,[7-10] absence of calcification,[2,4,5,7,9-11] peritumoral edema,[2,9,10] and isointense/hyperintense signal intensity (SI) on T2-weighted magnetic resonance imaging (MRI)[4,5,7,9,10,12] have been identified as factors associated with tumor growth. Based on the integration of influences of these risk factors, we designed the Asan Intracranial Meningiomas Scoring System (AIMSS) to predict the risk of rapid growth of untreated IMs in the previous study.[10] However, the AIMSS was developed to screen out IMs at high risk for rapid growth (≥2 cm^3/year) that necessitate early intervention, and does not account for the general growth potential of common IMs. Even slow-growing tumors can enlarge over time and eventually cause neurologic symptoms. Thus, the aim of this study was to examine the risk factors affecting Ob-F of untreated IMs and to develop an evidence-based "wait-and-see" strategy based on the risk of Ob-F for newly diagnosed IMs.

METHODS

Patients

Between January 1997 and July 2013, 232 consecutive patients (40 males, 192 females; mean age, 60 years) who underwent "wait-and-see" management (i.e., observation) for presumed IMs as part of an imaging study conducted by the senior author (J.H.K.) at Asan Medical Center were enrolled in the study. The inclusion and exclusion criteria were as described previously.[10] Serial neuroimaging studies were first performed at 6 months or 1 year after diagnosis, and then at 1 year or every other year until the patient dropped out. All patients were followed for at least 2