Surgical Neurology International

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Original Article

Benefits and limitations of diameter measurement in the conservative management of meningiomas

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Received: 30 August 11 Accepted: 26 September 11 Published: 14 November 11

This article may be cited as:
Oya S, Sade B, Lee JH. Benefits and limitations of diameter measurement in the conservative management of meningiomas. Surg Neurol Int 2011;2:158.
Available FREE in open access from: http://www.surgicalneurologyint.com/text.asp?2011/2/1/158/89857

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Abstract

Background: Meningiomas are the most common benign brain tumors that are frequently followed-up by neurologists, general practitioners, and neurosurgeons. Some recent studies advocate the accurate volumetric method (VM) over measuring the linear maximum diameter although its clinical significance still remains unknown. The aim of this study is to directly compare the linear method (LM) and VM to delineate the characteristics of both measurements.

Methods: Between 2003 and 2010, growth analysis using magnetic resonance imaging DICOM files was performed for 189 meningiomas in 161 patients at the Cleveland Clinic. In LM, a minimum increase of 2 mm in maximum diameter was defined as tumor growth. The absolute volume growth (VG, in cm^3) was calculated for each tumor.

Results: Linear growth (LG) was seen in 71 tumors (37.6%) within the median follow-up of 2.0 years. These tumors with LG showed a mean VG of 2.80 cm^3. Some large LG-positive tumors can be larger than estimated from LG. In addition, the skull base location was correlated to greater VG. On the other hand, 118 tumors without LG demonstrated the minimal actual volume increase, i.e., mean VG of 0.16 cm^3. Although a small subset of these LG-negative tumors might have slightly high VG when they were large, the location of tumor had no correlation to VG.

Conclusions: Our data demonstrated some important precautions in measuring the tumor growth. We believe that it is mandatory in the conservative management of meningiomas to correctly understand benefits and potential limitations of different measurement methods utilized.

Key Words: Conservative management, diameter, growth, meningioma, volumetry

Access this article online

Website: www.surgicalneurologyint.com

DOI: 10.4103/2152-7806.89857

Quick Response Code:

INTRODUCTION

Meningiomas are the most common intracranial benign tumors, accounting for 13-26% of all primary intracranial tumors.[8] Asymptomatic meningiomas are being detected more frequently due to the increased use of brain imaging studies such as computed tomography and magnetic resonance imaging (MRI) for various nasal sinus and neurological disorders as well as head trauma. As many newly diagnosed meningiomas do not require immediate therapeutic intervention at the time of diagnosis, the growth of meningiomas during the observation period

should be carefully monitored to decide the appropriate therapeutic approach and its timing when tumors show significant progression. In the literature, there is no standard method established in optimally studying the natural history of brain tumors in general and in meningiomas in particular. To assess the tumor growth, previous natural history studies of meningiomas have adopted the prolate ellipse formula,[6,7,18] largest linear method (LM),[2,5,13,14,20] and volumetry.[1,3,11,12,21] The measurement of the maximum diameter is obviously simple and commonly used in clinical settings, although some recent studies emphasized the importance of volumetry in the follow-up of meningioma.[3,11] Since there has been no study of direct comparison of LM and volumetric method (VM), the clinical significance of the volumetry still remains unknown. In this study, we conducted an accurate comparison between the LM and the VM in evaluating the growth of meningiomas to determine the optimal follow-up strategy for conservatively treated meningiomas.

MATERIALS AND METHODS

Between February 2003 and August 2010, 330 patients harboring 371 meningiomas were treated conservatively and followed by the senior author at the Cleveland Clinic. The radiographic diagnosis of meningioma was made based on MRI. Patients with an established diagnosis of meningiomas made prior to 2003 who were conservatively managed were included in the study population provided that all radiographic (initial and subsequent) studies were available. A complete radiological follow-up by means of MRI DICOM files was available for 189 tumors in 161 patients. These tumors were subjected to the current investigation of comparison between the LM and the VM. Although slice thickness of MRI ranged from 1 to 7 mm, 85% of the data were obtained from 4-mm- to 6-mm-thick MRI slices in this study. Patients with neurofibromatosis or with a history of radiation to the brain were eliminated from this study.

Linear growth (LG) was assessed by measuring the maximum linear diameter of the tumor in any direction on at least two contours of axial, coronal, and sagittal images. Positive LG (LG+) was determined as a minimum increase of 2 mm in the maximum diameter. Volumetric growth (VG) was evaluated by ImageJ Version 1.43 (downloaded from http://rsbweb.nih.gov/ij/). The contour of the tumor in each slice image was traced using freehand tools, and the actual area was measured. The tumor volume was calculated by multiplying each tumor area by the number of slices evaluated. All measurements were performed by a single investigator (S.O.) to prevent any interobserver errors. Absolute VG (cm^3) was calculated as a growth indicator. To investigate the influences of tumor location on the results of growth assessment, tumors arising from the olfactory groove, sphenoid wing, parasellar regions, cavernous sinus, petrosal and clival regions, and foramen magnum were defined as skull base.

The nonparametric Spearman's correlation coefficient method was performed to assess the statistical significance of the correlation between the LG and the VG. A *t* test was used for comparison of the means. JMP Version 7.0.2 (SAS Institute, Cary, NC, USA) was used for the analysis. A *P* value less than 0.05 was considered significant.

RESULTS

Patient population and tumor locations

The mean age of the patients at the initial diagnosis was 59.1 years (range 31–92 years) with a median follow-up period of 2.0 years (mean 2.9 years, range 0.3–16.8 years). Thirty-three patients were men (20.5%) and 128 were women (79.5%). The mean initial tumor diameter and volume were 20.4 mm (range 3–65 mm) and 3.40 cm^3 (range 0.04–43.48 cm^3), respectively. Tumor locations and percentages of the tumor are shown in Table 1. Convexity meningiomas were the most common (22.8%) site of the tumor origin. Almost all locations that are frequently encountered are included in this study.

Comparison of tumor growth assessment: LM versus VM

LG was observed in 71 tumors (37.6%). Figure 1 shows correlation between the LG and the VG. The colored area represents the 95% prediction interval. There is

Table 1: Location of the meningiomas

Location	Number of patients (%)	Skull base?
Convexity	43 (22.8)	Non-skull base
Petrosal Petrous Clival Petroclival/petrotentorial	28 (14.8)	Skull base
Parasellar Anterior/posterior clinoid Tuberculum sellae Planum sphenoidale	27 (14.3)	Skull base
Parasagittal	23 (12.2)	Non-skull base
Falx	17 (9.0)	Non-skull base
Cavernous sinus	11 (4.5)	Skull base
Sphenoid	9 (5.8)	Skull base
Tentorial	8 (4.2)	Non-skull base
Foramen magnum	7 (3.7)	Skull base
Olfactory groove	6 (3.2)	Skull base
Others	10 (5.3)	Non-skull base
Total	189	

a moderate correlation between the LG and the VG (Spearman's correlation coefficient = 0.64; $P < 0.0001$). All seven tumors that did not fall into the 95% prediction interval range were medium to large at the beginning of follow-up (range 28–65 mm), consisting of two nonskull base meningiomas and five skull base meningiomas [Table 2]. Seventy-one tumors with LG showed a mean VG of 2.80 cm^3 (range 0.04–18.10 cm^3). In contrast, 118 tumors without LG demonstrated the minimal actual volume increase, i.e., a mean VG of 0.16 cm^3 (range 0.87–2.20 cm^3).

We next examined the influences of tumor location on the growth evaluation. Analysis of 71 tumors with LG demonstrated that 36 skull base tumors had a significantly higher VG than did 35 non-skull base tumors (mean 3.71 cm^3 vs. 1.86 cm^3, $P = 0.043$; Figure 2) although there was no significant difference in LG between skull base and non-skull base tumors (mean 5.3 mm vs. 5.0 mm; $P = 0.71$).

We then studied the actual volumetric increase in 118 LG-negative tumors. When we grouped the tumors without LG into 53 skull base tumors and 65 non-skull base tumors, we did not find any correlation between the tumor location and the VG [Figure 3] (mean VG; skull base 0.16 cm^3 vs. non-skull base 0.15 cm^3, $P = 0.87$). There was no significant difference in LG between skull base and non-skull base tumors (mean 0.19 mm vs. 0.15 mm, $P = 0.62$). Finally, among these LG-negative tumors, we selected tumors that showed at least one high

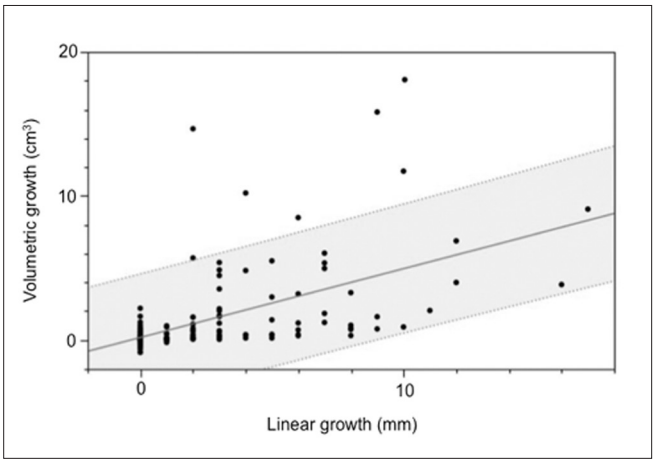

Figure 1: Scatter plot with regression line and 95% prediction intervals

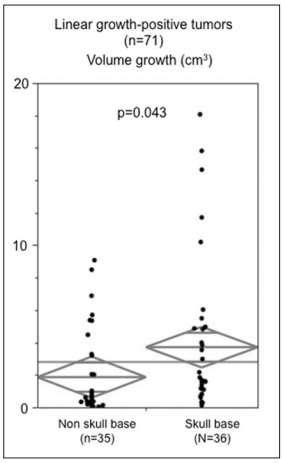

Figure 2: Ninety-five percent confidence interval mean diamond plots for tumors with linear diameter growth. Mid-bars in diamonds represent the mean. The horizontal line represents a grand mean. Heights of diamonds mean 95% confidence interval, and the width of the diamonds are proportional to the sample size of each group. Points are replaced in a shifted manner to avoid overlap. The mean volume growth of skull base meningiomas was significantly greater than that of non-skull base meningiomas

Table 2: Characteristics of seven tumors outside of 95% prediction interval range in the correlation

Tumor	Location	Skull base?	Initial size (mm)	LG (mm)	Absolute volume growth (cm^3)
1	Petrous	Skull base	28	4	9.36
2	Sphenoid wing	Skull base	35	9	13.77
3	Anterior clinoid	Skull base	35	10	18.10
4	Olfactory groove	Skull base	40	10	9.27
5	Parasagittal	Non-skull base	48	6	8.49
6	Parasagittal	Non-skull base	58	2	5.70
7	Petrous	Skull base	65	2	8.71

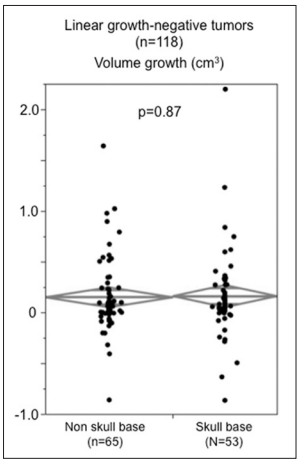

Figure 3: Ninety-five percent confidence interval mean diamond plots for tumors showing no linear maximum diameter growth. There was no significant difference in the mean volume growth between skull base and non-skull base meningiomas

growth potential, namely, VG greater than 1.0 cm^3 to evaluate the potential risk of missing these 'outliers'. As summarized in Table 3, four tumors showing higher VG had large initial diameters (range 23–42 mm).

DISCUSSION

The use of volumetric analysis has been advocated especially for the evaluation of the results of radiotherapy for intracranial benign tumors.[4,9,10,17,19] To evaluate the tumor response after radiosurgery, the accurate volumetric quantification is mandatory because the tumor growth means the treatment failure in most cases, indicating the high potential of cell proliferation and the necessity of surgical intervention to prevent tumor progression. On the other hand, most neurosurgeons, neurologists, and primary care physicians are frequently measuring the maximum tumor diameter in the conservative management of meningiomas on the outpatient basis. Volumetric analysis can be complicated and rather time-consuming to perform routinely in clinical settings. As a consequence, LM has been commonly adopted in spite of the importance of accurately quantifying tumor volume by VM.

Some recent volumetric studies on the natural history of meningioma depicted the accurate growth patterns of meningiomas, revealing what tumor characteristics are associated with higher growth rate.[1,3,11,12,21] Volumetric analysis, however, also contains several limitations that may contribute to the variations of results. Different slice positions at each examination may account for some potential errors in delineating the tumor's exact size and contour. There is also significant institutional variation in MR protocols and slice thickness captured. In addition, tumor contours may be difficult to delineate due to unclear tumor borders in some tumors. Tumors abutting the orbit (in the absence of fat-saturated sequences), those adjacent to enhanced large arteries or cortical veins, or those causing bony erosion or hyperostosis make it difficult to determine the exact tumor boundaries on MRI. These factors may produce wider intra- and interobserver variability in VM than in LM. Snell *et al*. also reported that fewer than five slices delineating lesions resulted in unacceptably larger errors in the volumetric analysis on intracranial tumors.[16] Therefore, small meningiomas may not be adequately evaluated on VM. Some patients are not eligible for MRI because of medical conditions such as pacemakers. Despite these issues, little has been discussed regarding the optimal measurement method in the conservative management of meningiomas based on a direct comparison between the LM and the VM.

Table 3: Characteristics of four LG-negative tumors that showed volume growth greater than 1.0 cm^3

Tumor number	Initial size (mm)	Diameter growth (mm)	Absolute volume growth (cm^3)	Tumor location	Skull base?
1	42	0	2.19	Clinoid	Skull base
2	33	0	1.63	Convexity	Non-skull base
3	32	0	1.23	Sphenoid	Skull base
4	23	0	1.02	Parasagittal	Non-skull base

Some methodological limitations are present in this study. Patients' MR images were obtained not only at our institution but also at multiple regional imaging centers. Therefore, the imaging protocol was not identical in this study. In addition, the single investigator performed the volumetry in our study, which is not always possible in a real clinical setting. However, we believe that measuring by multiple investigators would cause a wider margin of errors and decrease the consistency of volumetric analysis in this type of study. Therefore, we chose this method to eliminate the influence due to interobserver bias. This method was also adopted in another previous volumetric study.[3]

Some previous studies mentioned that LM is unsuitable for skull base tumors because they tend to have more complicated shapes.[3,11] This common belief, however, has never been tested so far. Our direct comparison based on a large sample size demonstrated that the differences of tumor location would not have any influence for tumors if their size increase was smaller than 2 mm. However, our data also indicated that when large skull base tumors demonstrate LG of 2 mm or larger, it should be kept in mind that they might have larger increase in volume than estimated from a linear change.

Recent volumetric studies in the literature all revealed a higher incidence of tumor growth utilizing the VM. Previous publications on natural history of meningiomas reported tumor progression detected by LM in 22–37% during the mean follow-up of 21–93.6 months.[5,13,14,20] Nakamura *et al*.[11] performed volumetric growth measurements on 41 conservatively treated meningiomas and found that all the tumors showed some volumetric growth with a mean follow-up of 43 months. Hashiba *et al*.[3] reported that 44 of 70 tumors (62.9%) increased in volume by more than 15% with a mean follow-up of 39.3 months.

The similar tendency was confirmed in our study based on 189 tumors. To define the significant VG in our study, we randomly chose 20 tumors and conducted the volumetry three times to calculate the mean and standard deviation, which revealed that the average percentage of the standard deviation to the mean was 4.1%. If the volume increase greater than 8.2% is determined as a

significant VG as reported in the previous literature,[3] 67.2% of tumors demonstrated VG in our study. The fact that the incidence of growth detected by volumetry is much higher than that of growth detected by LM raises the question whether this discrepancy between the LM and the VM has any clinical significance to be addressed. Based on our data, a small subset of large tumors had relatively small but actual VG despite the absence of maximum diameter change. Although we could not draw any definitive conclusion regarding the safety of continuing observation for LG-negative tumors without evaluating the treatment outcome, the volumetry appears to be detecting small growths of those tumors and show higher sensitivity.

Therapeutic decision making for conservatively treated meningiomas requires careful integration of the patient characteristics such as age, symptoms, and comorbidities as well as the tumor characteristics such as size and location.[15] However, radiological confirmation of significant growth remains an important factor in deciding whether to institute a therapeutic intervention following the initial observation period. It seems that the LM, albeit sounding rather simple, is a safe and effective way to evaluate the growth in most intracranial meningioma if we properly understand its limitations.

CONCLUSIONS

We described the limitations of simply applying the maximum linear diameter method in the evaluation of conservative management of intracranial meningiomas. If a linear progression was smaller than 2 mm, the volume increase was minimal in most of meningiomas regardless of the location of tumor. However, large tumors might have relatively small but actual volume growth even without LG. On the other hand, large skull base tumors with a diametric increase of 2 mm or larger could have a greater VG than estimated from LG. Although measuring the maximum linear diameter is simple and overall a safe method, it is important to understand its advantages, validity, and potential limitations to optimize patient management during observation.

REFERENCES

1. Firsching RP, Fischer A, Peters R, Thun F, Klug N. Growth rate of incidental meningiomas. J Neurosurg 1990;73:545-7.
2. Go RS, Taylor BV, Kimmel DW. The natural history of asymptomatic meningiomas in Olmsted County, Minnesota. Neurology 1998;51:1718-20.
3. Hashiba T, Hashimoto N, Izumoto S, Suzuki T, Kagawa N, Maruno M, *et al*. Serial volumetric assessment of the natural history and growth pattern of incidentally discovered meningiomas. J Neurosurg 2009;110:675-84.
4. Henzel M, Gross MW, Hamm K, Surber G, Kleinert G, Failing T, *et al*. Significant tumor volume reduction of meningiomas after stereotactic radiotherapy: Results of a prospective multicenter study. Neurosurgery 2006;59:1188-94; discussion 1194.
5. Herscovici Z, Rappaport Z, Sulkes J, Danaila L, Rubin G. Natural history of conservatively treated meningiomas. Neurology 2004;63:1133-4.
6. Kasuya H, Kubo O, Tanaka M, Amano K, Kato K, Hori T. Clinical and radiological features related to the growth potential of meningioma. Neurosurg Rev 2006;29:293-6; discussion 296-7.
7. Kuratsu J, Kochi M, Ushio Y. Incidence and clinical features of asymptomatic meningiomas. J Neurosurg 2000;92:766-70.
8. Louis DN, Scheithauer BW, Budka H, Von Deimling A, Kepes JJ. Meningiomas. Pathology and genetics of tumors of the nervous system: World Health Organization classification of tumors. 2000. p. 176-84.
9. Meijer OW, Weijmans EJ, Knol DL, Slotman BJ, Barkhof F, Vandertop WP, *et al*. Tumor-volume changes after radiosurgery for vestibular schwannoma: Implications for follow-up MR imaging protocol. AJNR Am J Neuroradiol 2008;29:906-10.
10. Mingione V, Yen CP, Vance ML, Steiner M, Sheehan J, Laws ER, *et al*. Gamma surgery in the treatment of nonsecretory pituitary macroadenoma. J Neurosurg 2006;104:876-83.
11. Nakamura M, Roser F, Michel J, Jacobs C, Samii M. The natural history of incidental meningiomas. Neurosurgery 2003;53:62-70; discussion 70-1.
12. Nakasu S, Fukami T, Nakajima M, Watanabe K, Ichikawa M, Matsuda M. Growth pattern changes of meningiomas: Long-term analysis. Neurosurgery 2005;56:946-55; discussion 946-55.
13. Niiro M, Yatsushiro K, Nakamura K, Kawahara Y, Kuratsu J. Natural history of elderly patients with asymptomatic meningiomas. J Neurol Neurosurg Psychiatry 2000;68:25-8.
14. Olivero WC, Lister JR, Elwood PW. The natural history and growth rate of asymptomatic meningiomas: A review of 60 patients. J Neurosurg 1995;83:222-4.
15. Sade B, Lee JH. The novel "CLASS" algorithmic scale for patient selection in meningioma surgery. Meningiomas; 2008. p. 217-21.
16. Snell JW, Sheehan J, Stroila M, Steiner L. Assessment of imaging studies used with radiosurgery: A volumetric algorithm and an estimation of its error. Technical note. J Neurosurg 2006;104:157-62.
17. Van de Langenberg R, de Bondt BJ, Nelemans PJ, Baumert BG, Stokroos RJ. Follow-up assessment of vestibular schwannomas: Volume quantification versus two-dimensional measurements. Neuroradiology 2009;51:517-24.
18. Van Havenbergh T, Carvalho G, Tatagiba M, Plets C, Samii M. Natural history of petroclival meningiomas. Neurosurgery 2003;52:55-62; discussion 62-4.
19. Varma A, Nathoo N, Neyman G, Suh JH, Ross J, Park J, *et al*. Gamma knife radiosurgery for glomus jugulare tumors: Volumetric analysis in 17 patients. Neurosurgery 2006;59:1030-6; discussion 1036.
20. Yano S, Kuratsu J. Indications for surgery in patients with asymptomatic meningiomas based on an extensive experience. J Neurosurg 2006;105:538-43.
21. Yoneoka Y, Fujii Y, Tanaka R. Growth of incidental meningiomas. Acta Neurochir (Wien) 2000;142:507-11.