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Review

EAONO position statement on Vestibular Schwannoma: Imaging Assessment Question: How should growth of Vestibular Schwannoma be defined?

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The relevance of defining the growth of vestibular schwannoma (VS) is that any significant VS growth may impact treatment strategy. A conservative treatment strategy is often proposed as a primary treatment option in the management of VS. Several authors have demonstrated that a significant proportion of VSs do not grow, and those that do, usually grow slowly. Surgical and/or radiosurgical treatment options may be offered to the patient according to the VS growth. Therefore, defining the VS growth is a determinant in managing treatment strategies. A comprehensive literature search was performed to examine the definition of tumor growth for VS. The literature review was conducted using PubMed and Embase databases dated back to 20 years (1995–2015) and was updated until February 2015. VS growth should be measured on contrast-enhanced T1-weighted images. Although there the overall quality of the present studies is low, all highlight a significant VS growth of >2 mm, and/or 1.2 cm3, and/or 20% change in volume, and/or the square of the product of the 2 orthogonal diameters. We suggest that VS growth should instead change management strategies when a 3-mm increase in diameter on two consecutive MRI scans are performed 1 year apart.

KEYWORDS: Vestibular Schwannoma, growth rate, natural history, imaging assessment

MATERIALS and METHODS

As part of the Vestibular Schwannoma Project conducted by the European Academy of Otology & Neuro-Otology (EAONO), a comprehensive literature search was conducted to examine the definition of tumor growth for vestibular schwannoma (VS).

The literature review was conducted on the databases Pubmed and Embase dated back to 20 years (1995-2015) and was updated until February 2015.

A PubMed search using the key words "Natural history,""vestibular schwannoma,""acoustic neuroma," and "tumor growth" alone and in combination was performed: This query identified 680 papers in the last 20 years, between 1995 and 2015.

Search syntax

Inclusion and exclusion criteria

a) Article titles and abstracts were screened according to the following criteria:
b) Clinical articles reporting original data, thereby excluding reviews and case reports
c) Data only from adult patients

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d) Series using conservative management; microsurgery, radiosurgery, or fractioned stereotactic radiotherapy; and single and/or combined treatment for solitary VS
e) More than 50 patients included
f) Quantitative assessment of VS growth as one of the primary study end-points
g) Mean follow-up of at least 3 years
h) Studies in which the reported data included patients with neurofibromatosis type 2; if these data could not be separately identified from the reported data for patients with VS, the articles were excluded.

After the initial search, 763 articles were obtained, but 721 did not meet one or more of the inclusion criteria and hence were discarded. The remaining 41 articles were reviewed for methodology and scored using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [1].

RESULTS

The question: How should growth of VS be defined?

INTRODUCTION

The relevance of defining the growth of VS is that any significant VS growth may impact the treatment strategy. A conservative treatment strategy is often proposed as a primary treatment option in the management of VS. Several authors have demonstrated that a significant proportion of VS do not grow, and those that do, usually grow slowly. Surgical and/or radiosurgical treatment options may be offered to the patient according to VS growth. Therefore, the definition of VS growth is a determinant in managing treatment strategies.

Evidence

The reviewed articles selected to find an answer how should VS growth be defined comprised 2 meta-analysis, 6 cohort studies, and 33 case series. The mean number of patients included for the clinical series was 215 (50-2500).

Literature review

AUTHOR	YEAR	STUDY DESIGN	n	METHOD	VS GROWTH RATE mm/year	VS GROWTH CHANGING STRATEGY mm/year	GRADE Quality of evidence	GRADE Strength of recommendation
Jethanamest et al. [2]	2015	Case series	94	2	1	1.14	Low	Weak
Hougaard et al. [3]	2014	Case series	72	2	1-2	3	Moderate	Weak 1
Jeltema et al. [4]	2014	Case series	55	4			Very low	Weak
Tang et al. [5]	2014	Case series	88	2,3,4	91.4 mm for 1D, 7 mm2 for 2D, and 133.3 mm 3 for 3D		Low	Weak
Niu et al. [6]	2014	Case series	58	4	20%		Low	Weak
Nikopoulos et al. [7]	2013	Meta-analysis			1-2	2-4	Moderate	Weak
González-Orús Álvarez-Morujo et al. [8]	2013	Case series	73	2	2	2	Low	Weak
Stangerup and Caye-Thomasen [9]	2012	Case series prospective	2500	1	3	3	Moderate	Weak 2
Varughese et al. [10]	2012	Case series prospective	178	4	1	5.22 years VDT	Low	Weak
Moffat et al. [11]	2012	Case series	381	2	2		Low	Weak
Kim et al. [12]	2012	Case series	60	4	20%		Low	Weak
Breivik et al. [13]	2012	Case series	193	1	>2	>2	Moderate	Weak
Sughrue et al. [14]	2011	Case series prospective	59	2	2.5	2.5	Low	Weak 3
Eljamel et al. [15]	2011	Case series	53	1,3	2		Very Low	Weak
Varughese et al. [16]	2010	Case series	139	3			Low	Weak
Agrawal et al. [17]	2010	Case series	180	1,4	1		Moderate	Weak
Suryanarayanan et al. [18]	2010	Case series	286		1.1 (range 0 to 15/y)		Low	Weak
Whitehouse, et al. [19]	2010	Case series	88	2	1.24 (range -4,7 to 14 mm/y)		Low	Weak
Bakkouri et al. [20]	2009	Case series	325	1	1-2	3	Low	Weak
Artz et al. [21]	2009	Case series	234	2			Low	Weak
Van de Landergerg et al. [22] remark 5	2008	Case series	68	4	19.7 % volume change		Moderate	Weak

Literature review (Continued)

AUTHOR	YEAR	STUDY DESIGN	n	METHOD	VS GROWTH RATE mm/year	VS GROWTH CHANGING STRATEGY mm/year	GRADE Quality of evidence	GRADE Strength of recommendation
Ferri et al. [23]	2008	Cohort study	123	2	1.2		Low	Weak
Stangerup et al. [24]	2006	Case series prospective	552	2	2	2	Moderate	Weak
Battaglia et al. [25]	2006	Case series	111	3	0.7±1.4		Low	Weak
Yoshimoto [26]	2005	Meta-analysis	1340		1.2		Moderate	Weak
Flint, et al. [27]	2005	Case series	100		2.7		Low	Weak
Hearwadjer et al. [28]	2005	Case series	50	4	109 mm3/y		Low	Weak
Bozorg Grayeli et al. [29]	2005	Case series	111	2	1.1±0.21		Low	Weak
Raut et al. [30]	2004	Case series prospective	72	3 remark 4	1	3.1	Low	Weak
Quaranta et al. [31]	2003	Case series	122		1.09 (range -6.32 to 10 mm/y)		Low	Weak
Tanaka et al. [32] remark 6	2002	Case series	52	1			Very low	Weak
Nutik et al. [33]	2001	Case series	75	1	3.1±2.8		Low	Weak
Hoistad et al. [34]	2001	Case series	102	2	2.17		Low	Weak
Rosenberg [35]	2000	Case series	80	3	0.91		Low	Weak
Mirz et al. [36]	2000	Cohort study	64		2;3		Low	Weak
Walsh et al. [37]	2000	Case series	72	3	1.16 (range - 0.75 to 9.65/y)		Low	Weak
Shin et al. [38]	2000	Case series	87	3	1.52 (range - 13 to 18 mm/y)		Low	Weak
Tschudi et al. [39]	2000	Case series	74		2.2 mean first year 2.7		Low	Weak
Fucci et al. [40]	1999	Case series	119	2	1.2±3.1		Low	Weak
Deen et al. [41]	1996	Case series	68	3	0.72	3	Low	Weak
Wiet et al. [42]	1995	Case series	53	2	4.2		Very Low	Weak

1 Extrameatal diameter
2 Largest tumor diameter including intracanalicular portio
3 Two-dimensional data,i.e., larger diameter according to AAO-HNS guidelines 1995
4 Volumetric measurements using three-dimensional reconstruction
VS: vestibular schwannoma; VDT volume doubling time; AAO-HNS American Academy of Otolaryngology-Head and Neck Surgery

- *Volume measurements estimated by the slice area method. Tumor areas were measured in each slice of gadolinium-enhanced magnetic resonance imaging (MRI) scans throughout the entire tumor. Each slide volume was estimated by multiplying the slice area by the slice interval, and the tumor volume was calculated by summarizing all slices.
- $Volume measurement: (A × B × C)/2 A: anteroposterior diameter; B: medial-to-lateral diameter; C: vertical diameter. Growth in the first year was a strong predictor of future growth and a VS volume >1.2 cm3 at presentation was also a predictor of future growth.
- Remark 1: The best way to measure VS needs further investigation; measurements ought to be standardized and clearly defined, and the current growth criterion ≥1-2 mm needs to be redefined. We suggest that VS growth should instead be defined as a 3-mm linear increase in d1 on two consecutive MRI scans one year apart.
- Remark 2: The present criterion for growth of a purely intrameatal tumor was the growth to an extrameatal extension tumor.
- Remark 3: 2.5 mm/year is a clear indication for treatment of patients who wish to maintain hearing.
- Remark 4: The A-P measurement was calculated parallel to the posterior surface of the petrous bone and the M-L measurement was calculated perpendicular to it. The size of the tumor was calculated as the square root of the product of these two diameters according to the 1995 guidelines of the AAO-HNS.
- Remark 5: Contrast-enhanced T1-weighted volume measurements showed better interobserver agreement and reliability compared to the two-dimensional measurements for the assessment of VS growth. Small intracanalicular VS form an exception. When evaluating VS growth, the VS baseline characteristics should be considered, because standard deviation (%) strongly depends on VS size. The 1- or 2-mm difference commonly used to define the growth of VS in consecutive scans in two-dimensional measurements lies within the measurement error and should not direct clinical practice.
- Remark 6: The maximum diameter of the CPA portion is the simplest method, and it is appropriate to represent the tumor volume in unselected tumors. The maximum diameter or axis diameter with the internal auditory canal portion are better when only small tumors (<0.5 cm3), i.e., tumors with the maximum CPA≤1 cm.
- Remark 7: Measurements performed on the post-contrast axial T1 images included maximum axial diameter, maximum axial area, total tumor volume, and enhancement pattern. An excellent correlation was found between the planar and volumetric methods.

The mean VS growth was calculated according to the maximal diameter in the CPA, maximal total diameter, mean of 2 measurements and volume changes in 7, 14, 7, and 8 studies, respectively. Once the VS reaches 2 cm in intracranial diameter, it is likely to continue growing.

The mean VS growth was 1.75±0.83 mm/year but ranged from −13–+18 mm/year. In 3 studies reporting volume change measurements, 20% of volume change was considered to be significant growth. A minimum of 2 mm/year of VS growth was considered to be significant for changing management strategies. When considering VS

growth that changed management strategies, values retained were 3 mm, 2.5, and 2 mm of VS growth per year in 4, 1, and 2 articles, respectively.

Although there is an overall low quality of the present studies, all highlight a significant VS growth >2 mm, and/or, 1.2 cm^3, and/or 20% change in volume, and/or the square of the product of the 2 orthogonal diameters.

Following the GRADE system, 29 articles were considered to have a "low" level of evidence for being observational studies. Furthermore, 4 observational studies were down-graded to "very low" evidence for possible confounding factors. Finally, the 2 meta-analysis and 6 good quality observational studies were graded as "moderate" evidence.

CONCLUSION

VS growth should be measured on contrast-enhanced T1 weighted images.

Although there is an overall low quality of the present studies, all highlight a significant VS growth >2 mm, and/or 1.2 cm^3, and/or 20% change in volume, and/or the square of the product of the 2 orthogonal diameters. We suggest that VS growth should instead change management strategies when there is a 3-mm increase in the diameter on two consecutive MRI scans 1 year apart.

Remarks

Most of the available evidence for VS growth comes from retrospective case series. The follow-up period in these series is quite heterogeneous. The VS growth rate should be assessed by VS growth per year in further prospective designed studies.

Position EAONO

- There is no high-quality evidence of the definition of VS growth. Future studies should try to overcome the present limitations in the study design to provide VS growth rate per year.
- Nevertheless, the consistency of results across different studies allows for a "moderate" recommendation to consider a significant VS growth of >2 mm, and/or 1.2 cm^3, 20% volume, with VS growth rate >3 mm/year as a sign of evolution requiring a change in the treatment strategy.
- The optimal method of measuring VS volumes continues to be debated.
- In literature, the most common method used clinically is to measure the maximum diameter of the tumor, sometimes excluding the dimensions of the intracanalicular component but often including the intracanalicular component.
- The mean growth rate for all tumors, when growing, varies between 1 and 2 mm/year (1.75±0.83 mm/year) and between 2 and 4 mm/year for only those that grow.
- There are various patterns of growth, and a tumor that grows may stop growing and vice versa. Nevertheless, the first years of observation may give a good estimate of the pattern of growth. Some cases can exhibit significant regression or exceptional growth.
- Clinicians should seek to instigate national tumor registries in their countries and a common data set to facilitate international cooperation.
- The 2-mm cut-off should be recommended to avoid the effect of MRI slice thickness and partial volume effects. Tumor shrinkage was defined as tumor-size reduction in any plane by at least 2 mm.
- VS growth rate >3 mm/year should be considered a sign of evolution requiring a change in the treatment strategy.

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Editor's Note:

The EAONO Project on guidelines of Otology and Neurotology was initiated by Franco Trabalzini and the Working Groups began working in 2011. Since then a considerable work has been issued to produce the first Consensus Documents.

The working Group on Vestibular Schwannoma have esteemed members from dedicated centers all over Europe. I wish to express my thanks to the working group leaders Miguel Aristegui and Jacques Magnan for their great effort as well as to all the other active members of the group.

Miguel Aristegui, Shakeel Saeed, Simon Lloyd, Per-Caye Thomasen and Jacques Magnan's comments for this "Consensus Document" have been very much appreciated.

This study is very much respected by the Editorial of the Journal in this regard.

Prof. Dr. O. Nuri Ozgirgin
Editor in Chief

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