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Original Research Article

CORRELATION OF MENINGIOMA SURFACE FACTOR WITH WHO GRADE OF MENINGIOMA

Vishesh Guglani[1], Vivek Yadav[2], Amit Dagar[3], K B Shankar[4], Charanjeet Ahluwalia[5], Rupi Jamwal[6]

[1]*Mch Resident, Department of Neurosurgery, VMMC and Safdarjung Hospital, New Delhi, India.*
[2]*Associate Professor, Department of Neurosurgery, VMMC and Safdarjung Hospital, New Delhi, India.*
[3]*Associate Professor, Department of Neurosurgery, VMMC and Safdarjung Hospital, New Delhi, India.*
[4]*HOD and Professor, Department of Neurosurgery, VMMC and Safdarjung Hospital, New Delhi, India.*
[5]*Professor, Department of Pathology, VMMC and Safdarjung Hospital, New Delhi, India.*
[6]*Professor, Department of Radiology, VMMC and Safdarjung Hospital, New Delhi, India.*

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Corresponding Author:
Dr. Vivek Yadav
Associate Professor, Department of Neurosurgery, VMMC and Safdarjang Hospital, New Delhi, India.
Email: vivekmamc99@gmail.com

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ABSTRACT

Background: Assess the correlation of meningioma surface factor on pre-operative imaging with WHO grade of meningioma. **Objective:** Atypical and anaplastic meningiomas account for 20% of all meningiomas. An irregular shape of meningioma has been associated with higher grade histology. However, this subjective allocation does not allow quantification of comparisons. An objective parameter, like surface factor could substantially influence the aggressiveness towards a more aggressive resection strategy.
Materials and Methods: A prospective study on meningioma was concluded at the Department of Neurosurgery, Vardhman Mahavir Medical College and Safdarjung Hospital from May 2022 to May 2024. A demographic and tumor volumetric assessment in terms of age, gender, WHO grade and volumetric parameters like volume, surface area and surface factor was assessed. A comparison of the volumetric parameters like volume, surface area and surface factor were also done as per the grade of the meningioma.
Result: A total of 76 patients were included in the study, 90.79% had a WHO grade I, 6.58% a WHO grade II, and 2.63% a WHO grade III meningioma. Calculation of SF demonstrated a significant difference in SFs between WHO grade I (0.79±0.03) and WHO grade II/III (0.70±0.02) meningioma ($p<0.0001$). Multivariate analysis identified SF as an independent prognostic factor for WHO grade. (95% CI 0.279-5.247).
Conclusion: SF is a mathematical model to objectively quantify the irregularities in the shape of meningioma based on pre-operative MRI. This study revealed significant differences between the SFs of WHO grade I and grade II/III meningiomas and demonstrated that SF is an independent prognostic factor for WHO grade.
Keywords: Surface factor, WHO Grade, surface irregularity

INTRODUCTION

Meningiomas are among the most common intracranial tumors. Meningiomas are the most prevalent primary brain tumors accounting for approximately 1/3rd of all primary CNS tumors in adult patients.[1] Meningiomas account for 37.6% of all primary CNS tumors and 53.3% of total benign CNS tumors.[2]

After resection, meningiomas are graded histo-pathologically according to the WHO classification, with 80.6% reported as WHO grade I, 17.6% as WHO grade II, and 1.7% as WHO grade III. High grade meningiomas have been shown to have a high recurrence rate. In grade 3, the recurrence rate ranges from 50 to 94%. Grades I and II have recurrence rates of 7–25% and 29–52%, respectively.

Pre-operative MRI features like tumor volume, perilesional edema, and others have been previously correlated with WHO grading, and response and survival outcomes. An irregular tumor shape has consistently been associated with WHO grade II–III histology. As reported in these publications, the tumor shape was divided into arbitrary chosen categories, e.g., round, irregular, or mushroom shaped. However, these classifications are subjective and do not allow generalization of the results or quantification and comparison of the irregularity. [3-5] Therefore, a reliable objective parameter characterizing this histology could be beneficial.

Surface factor is one of the novel approaches in assessment and management of the meningiomas via objectively characterizing the shape irregularities. The SF is a mathematical model that has been developed to replace the current subjective assessment of meningioma form with a quantitative as well as objective measurement. Promising outcomes have been observed in the very limited trials that have evaluated the effect of SF in meningiomas. [6,7]

Thus, the aim of this study was to quantify meningioma shape irregularities on pre-operative MRI using surface factor and corelate it with WHO grade on histopathology.

MATERIAL AND METHODS

A prospective study was conducted in the Department of Neurosurgery, Vardhman Mahavir Medical College and Safdarjung Hospital from May 2022 to May 2024. 76 patients who were diagnosed with meningiomas were included in the study. An assessment of the severity of meningiomas, based on the WHO grading system was done. An evaluation of the meningioma volume, surface area and surface factor were also assessed and corelated with the WHO severity grade.

Patient Selection

During the study period, patients with convexity, parafalcine and tentorial meningioma without skull base contact were included. Eligible patients were those aged ≥18 years and all histologically verified meningiomas. Skull base contact, prior meningioma treatment (e.g. Radiation, Embolization), previous neurosurgical procedure in proximity to the meningioma, large superficial cysts, Meningioma en plaque, and recurrent meningiomas were exclusion criteria.

Surface Factor

Surface factor is one of the novel approaches in assessing and managing the meningiomas via objectively characterizing the shape irregularities. The SF is a mathematical model that has been developed to replace the current subjective assessment of meningioma form with a quantitative and objective measurement. [6,7] The surface factor driven strategy, is predicated on the idea that a regularly formed tumor has less area on its surface than a formless tumor of the same volume. A sphere is the shape with the least surface area that can be created for a given volume, hence a factor was created using its surface area as a reference. Thus, the surface area of the sphere with the identical volume as the tumor was divided by the surface area of the tumor to determine the surface factor (SF). Thus, the range of the resultant SF's value is > 0 to 1.

First, the volumetric analysis was performed to determine the volume (semiautomated segmentation) and the surface area of the tumor, by using 3D Slicer (version 4.10.2; https://www.slicer.org). Second, individual tumor volume was used to calculate the surface area of a sphere with a volume identical to that of the tumor. Third, the surface factor was calculated using the formula

SF = SA sphere/SA tumor,

Where SA sphere is the surface area of a sphere with the same volume as the tumor and SA tumor is the surface area of the tumor.

The resulting value of the SF ranges from > 0 to 1, with the value 1 showing a hypothetical tumor with a spherical shape. The higher the degree of irregularity, the lower the calculated SF.

Sample Size Calculation

The association between SF and WHO grade was explored by comparing the mean of SF between patients with WHO grade I and II-III lesions.

The sample size for the study was based on the study which reported the mean outcome measure in the two subgroups as follows.[6]:

Parameter	
Group 1: Mean ± SD	Group 2: Mean ± SD
0.851 ± 0.066	0.788 ± 0.089

The sample size required in each arm of the study was calculated according to the formula.

Sample size (n) =	1 + $\frac{2(z\alpha + z1\text{-}\beta)2\ \sigma 2}{\Delta 2}$

Where:

Σ (pooled SD) = 0.08

Δ (difference of means) = 0.06

Type i error (α) = 5%, zα (value of standard normal distribution for α = 5%) = 1.96

Type ii error (β) = 20%, power (1 – β) = 80%, z1-β = 0.842

Based on the formula given above, using the mentioned values, the sample size required is.

$$\text{Sample size (N)} = 1 + \frac{2(1.96 + 0.842)^2\, 0.08^2}{0.06^2} = 25.29 \approx 26$$

Thus, a minimum of 26 patients are required in each subgroup. Since approximately 39.6% of patients were expected to have WHO grade II-III lesions, the final sample size required was 26/0.396 ≈ **71 (at least 71 patients)**

Stastical Analysis

Data was coded and recorded in MS Excel spreadsheet program. Statistical Package for Social Sciences (SPSS) version 21.0 was used for data analysis. Descriptive statistics were elaborated as means/standard deviations and medians/IQRs for continuous variables, and frequencies as well as percentages for categorical variables. Data was presented in a graphical manner wherever appropriate for data visualization using histograms/ box-and-whisker plots/ column charts for continuous data and bar charts/pie charts for categorical data. Group comparisons for continuously distributed data were made using independent sample 't' test, when comparing two groups, and One-Way ANOVA, when comparing more than two groups. Post-Hoc pairwise analysis was performed using Tukey's HSD test in case of One-Way ANOVA to control for alpha inflation. If data was found to be non-normally distributed, appropriate non-parametric tests in the form of Wilcoxon Test/ Kruskal Wallis test was to be used for these comparisons. Chi-squared test was used for group comparisons for categorical data. In case the expected frequency in the contingency tables were found to be <5 for >25% of the cells, Fisher's Exact test was used. Linear correlation between two continuous variables was explored using Pearson's correlation (if the data was normally distributed) and Spearman's correlation (for non-normally distributed data). Statistical significance was considered at $p < 0.05$.

RESULTS

Patient characteristics

There was a female preponderance in the study (60.53%). The median age of patients was 47 years, with a range of 32-72 years. Most of the meningioma patients in the study had grade I severity (90.79%), with 5 patients having grade II severity (6.58%). 2 patients had grade III severity of meningioma (2.63%). Meningiomas were mainly on the convexity (51, 67.11%) followed by parafalcine (23, 30.26%). 2 tentorial meningiomas were also seen. The average volume and surface area were 30.66±3.71 cm^3 and 61.08±7.40 cm^2, respectively. [Table 1]

Differences between grade I and grade II/III

The average age of the patients with grade II/III meningiomas was significantly higher compared to the grade I meningiomas (p<0.0001). The proportion of females was significantly higher in grade II/III meningiomas compared to the grade I meningiomas, however it was not statistically significant (p=0.0259). No prominent location-related difference between the two groups, was observed, based on severity. Grade II/III meningiomas had a significantly higher volume and surface area, compared to grade I meningiomas (p<0.0001). [Table 2]

Surface Factor

The median surface factor was 0.79 with a range of 0.66-0.85. Grade II/III meningiomas had significantly lower surface factor compared to the grade I meningiomas (0.70 vs 0.79); p<0.0001.

Univariate and multivariate analysis

Univariate analysis showed that increasing age, female sex, higher volume and higher surface area were positively corelated with the severity of meningiomas, and surface factor was negatively corelated with the severity of meningiomas. Multivariate analysis showed that gender, volume, surface area and surface factor were independent predictors of high grade meningiomas, with statistically significant findings. [Table 3,4]

Table 1: Patient Characteristics

Parameter	Values
Total no. of patients	**76(100)**
Sex Females Males	 46 (60.53%) 30 (39.47%)
Age; years	47 (39-48.25)
Location Convexity Parafalcine Tentorial	 51 (67.11%) 23 (30.26%) 2 (2.63%)
Histology; WHO grade I II III	 69 (90.79%) 5 (6.58%) 2 (2.63%)

Table 2: Difference between Grade I and Grade II/III

Parameter	WHO I	WHO II/III	p value
Patients	69 (90.79%)	7 (9.21%)	
Sex Female Male	 39 (56.52%) 30 (43.48%)	 7 (100%) 0 (0.00%)	0.0259
Age; years	47.26±10.46	66.29±3.77	<0.0001
Location Covexity Parafalcine Tentorial	 46 (67.63%) 22 (31.88%) 1 (1.44%)	 5 (71.42%) 1 (14.29%) 1 (14.29%)	 0.8388 0.3376 0.0441

Volume; cm³	29.51±0.76	41.97±1.00	<0.0001
Surface Area; cm²	58.85±2.39	83.00±1.25	<0.0001

Table 3: Univariate analysis for the WHO grade severity

Severity Predictors	Rho	95% CI	p-value
Age	0.45	0.24 to 0.61	<0.0001
Sex (Males)	-0.26	-0.46 to -0.027	0.0249
Location (Parafalcine/ tentorial)	-0.029	-0.26 to 0.20	0.8016
Volume	0.5	0.31 to 0.66	<0.0001
Surface Area	0.5	0.31 to 0.66	<0.0001
Surface Factor	-0.49	-0.65 to -0.30	<0.0001

Table 4: Multivariate analysis – Predictors of WHO severity

Predictors	Unstd B	SE	Std B	t	Sig.	95% Lower	95% Upper
(Constant)	-4.696	1.268		-3.702	0	-7.226	-2.167
Age	-0.003	0.002	-0.089	-1.744	0.086	-0.007	0
Sex	-0.075	0.036	-0.092	-2.09	0.04	-0.146	-0.003
Volume	0.052	0.024	0.487	2.203	0.031	0.005	0.1
Surface Area	0.037	0.016	0.678	2.297	0.025	0.005	0.068
Surface Factor	2.763	1.245	0.257	2.218	0.03	0.279	5.247

DISCUSSION

Meningiomas of grade I histology are benign, and the most common subtype; those of grade II are of intermediately aggressive behavior and typically have histologic atypia; and those of grade III, which exhibit anaplastic histology, are of malignant aggressive behavior. The site, grade, and symptomatology of the tumor have a significant impact on management.[9] Most of the meningioma patients in the study had grade I severity (90.79%), with 5 patients having grade II severity (6.58%). 2 patients had grade III severity of meningioma (2.63%).

Irregular meningioma shape has been shown to corelate with WHO grade II/III histology. [3-5] The tumor shape has previously been assessed using various subjective methods. Surface factor provides an objective and a mathematical method to assess the meningioma shape. Surface factor relies on the conclusion that a regularly shape tumor has a small surface area compared to an irregularly shaped tumor. Surface area of a sphere is the smallest for a given volume, so surface area of a sphere is used as a reference to calculate the surface factor.

Calculation of surface factor showed a significant difference between grade I and grade II/III meningioma (0.79 vs 0.70, $p<0.0001$). On multivariate analysis, surface factor was found to be an independent predictor of the severity of meningioma.

Major increase in the daily usage of surface factor can be expected with the increasing use of artificial intelligence in medical diagnostics. Automated volumetric analysis and calculation of surface factor, based on artificial intelligence would make the usage of this mathematical model more practical and user friendly.

CONCLUSION

The study was able to conclude that SF or surface factor, could be an important parameter to preoperatively assess the grade of meningioma. SF corelated with the grade of meningioma lesion in our study, and was significantly corelated with the meningioma grade both on univariate and multivariate analysis. This study contributes to the pool of a handful of studies exploring the utility of this parameter. Larger studies with multicentric study designs and heterogeneous patient populations, comprising of more patients with grade II/III disease would be needed, to further validate the findings of this study.

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