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Predictive Value of Tumor Size on The Incidence of Peritumoral Edema on Pre-Surgery Head Mri of Meningioma Patients

Rahmawati Dianing Pangestu[1], Arif Faisal[2], Bambang Purwanto Utomo[2], Hesti Gunarti[2], Wigati Dhamiyati[2]

[1]Departement of Radiology Faculty of Medicine, Public Health and Nursing Universitas Gadjah Mada, Yogyakarta
*Correspondence: dyantata@gmail.com

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Abstract

Background: Peritumoral brain edema (PTBE) of meningioma causes morbidity, poor clinical outcomes and complicates surgery. Tumor size correlates with the incidence of PTBE. However, the threshold value for tumor size that cause PTBE in meningioma has not been widely studied.
Objective: To determine the threshold value for meningioma size that can predict the incidence of peritumoral edema in general and based on specific intracranial locations on pre-operative head MRI.
Methods: This is a cross sectional study on patients with intracranial meningioma who had undergone head MRI imaging at Dr.Sardjito Hospital in the period of 2018-2022 retrospectively. An analysis was carried out to find the threshold value for meningioma size and the prevalence ratio to predict the incidence of PTBE.
Results: The cut-off volume for intracranial meningioma was >44 cm3 with RP of 3.61 (p=0.01) in general. Simultaneously, large tumor volume (≥44 cm3) has the strongest correlation to the incidence of peritumoral edema (p=0.01). The cut-off volume for meningioma in supratentorial non-skull base was >22 cm3 with RP of 2.54, while in supratentorial skull base was >54 cm3 with RP of 23.33 (p=0.01). The cut off volume for meningioma in infratentorial region was >19.75 cm3 with RP 3.0 (p=0.52).
Conclusion: The cut-off value for intracranial meningioma volume to predict the incidence of peritumoral edema is 44 cm3. There are differences in the cut-off values of meningioma volume and prevalence ratios based on specific intracranial locations to predict the incidence of PTBE in meningioma.

Keywords: Meningioma, peritumoral edema, tumor volume

1. INTRODUCTION

Meningioma is the most common primary central nervous system (CNS) tumor, accounting for 38.3% of all tumors with an incidence rate of 8.81 per 100,000 people/year. The incidence of peritumoral brain edema (PTBE) in intracranial meningiomas is 38%-67% of cases. The production of peritumoral edema will result in mass effect on the surrounding tissue causing significant morbidity as well as poor clinical outcomes. Meningiomas with PTBE are significantly more symptomatic than meningiomas without PTBE including cognitive deficits, paralysis and seizures. In addition, perifocal edema may complicate the surgical resection procedure, which is the main therapeutic option for meningioma and is associated with prognostic meningima. Peritumoral edema will also increase the risk of post-surgical complications including postoperative intracranial hematoma, intracranial hypertension, use of blood transfusions, and increased length of hospital stay (1,2,3).

Several studies have shown that peritumoral edema can be caused by vascular and non-vascular factors. In cases where surgery or radiotherapy is not performed, tumor size may be an important factor that compromises the integrity of the tumor parenchyma boundary with the brain and causes peritumoral edema (4,5,6).

Previous research at Dr. Sardjito Hospital by Pangestu (2023) stated that there was a correlation between tumor size and the incidence of peritumoral edema on pre-operative head MRI of meningioma patients. The study also stated that the incidence of peritumoral edema correlated with tumor location and margin (7). However, this study has not shown the threshold value of tumor size that can cause peritumoral edema in patients with meningioma. Therefore, this study aims to determine the threshold or cut off value of meningioma tumor size that can predict the incidence of peritumoral edema both in general and based on specific intracranial locations on preoperative head MRI of meningioma patients.

2. MATERIALS AND METHODS

This study was an observational analytic study with a cross sectional design to test the predictive value of tumor size on the incidence of peritumoral edema on MRI examination of intracranial meningioma patients at Dr. Sardjito Hospital and data collection was carried out retrospectively using secondary data in the form of MRI image results of meningioma tumor volume size and peritumoral edema.

The study subjects were 88 patients with meningioma in the period 2018-2022 with the method of convinience non-random sampling. Inclusion criteria included intracranial meningioma, patients had undergone MRI examination of the head with a minimum sequence of T1W, T2W, FLAIR, and T1W post-contrast and data stored and accessible from the MRI aircraft reading room and or Picture Archiving and Communication System (PACS) at the Radiology Installation of Dr. Sardjito Hospital Yogyakarta and had complete medical record data.

All sample MRI image data were obtained from head MRI examinations using 1.5 Tesla (Achieva 1.5T Philips Medical system, Netherland) and 3 Tesla (Siemens Magnetom Skyra 3T) MRI aircraft with standard coils for head examinations and the minimum protocol performed consisted of pre-contrast T1W, T2W, FLAIR, DWI/ADC sequences and 3D T1W sequences after gadolinium contrast administration of axial, coronal and sagittal cuts, with a slice thickness of 5 mm and a gap of 1 mm. The MRI images were displayed and assessed on 1 PACS computer monitor using the Philips Intelispace Portal program. Post-contrast T1W sequences were assessed for location, tumor margins and tumor volume measurement with a smart segmentation program that produced a region of interest (ROI) in the tumor tissue. Peritumoral edema volume assessment was performed on FLAIR sequences using the edema index. The edema index represents the degree of peritumoural edema compared to tumor volume and is calculated by the formula Edema Index=V.Tumor + Edema/V.Tumor. Edema Index = 1.0 indicates no edema. Assessment of tumor volume, margin, tumor location and edema was performed by 2 assessors, namely radiology specialists.

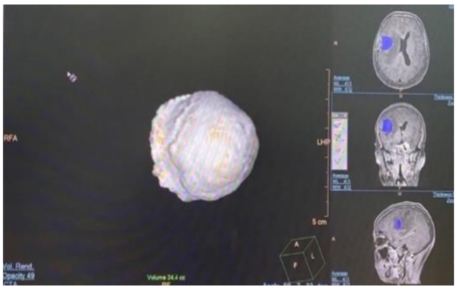

Figure 1. Tumor measurement technique with Smart Segmentation Method using Phillips Intellispace Portal program.

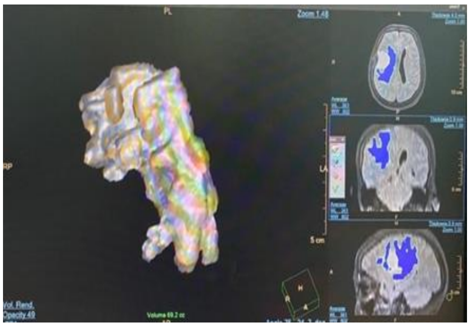

Figure 2. Measurement technique of Peritumoral Edema with Smart Segmentation Method using Phillips Intellispace Portal program

Other variables that were analyzed in this study included age, gender, location, tumor margin and histopathological grade. The researcher divided the tumor location into 3 categories namely supratentorial non basis cranii including parasagittal, falcine, convexity, supratentorial basis cranii including areas in the anterior cranial fossa, media including sphenoid and suprasellar regions and infratentorial location which is a tumor under the tentorium cerebri or posterior fossa.

The interobserver reliability test of the research variables was carried out using the Kappa concordance test. If the Kappa value > 0.6 means a good level of agreement (8).

Determination of the threshold value of tumor size in predicting the incidence of peritumoral edema was performed using Receiver Operating Characteristic (ROC) curves and Youden index and adjusted by calculating sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and likelihood ratio values based on 2x2 tables. Furthermore, the cut off value results were analyzed bivariately with the chi square test and assessed the prevalence ratio (RP) and 95% CI for clinical probability. Multivariate analysis in the form of logistic regression and stratification was performed to assess the association of several variables simultaneously. The statistical significance level of this study was p<0.05.

3. RESULT

The results of the basic characteristics of the research sample data are shown in Table 1.

The results of the reliability test using the Kappa test obtained a Kappa value = 0.824, p = 0.001. This indicates that both assessments have a high suitability (>0.8) (9).

Table 1. Characteristics of Research Subjects

Characteristic	Total	%
Aged		
> 60 years	14	15,91
51 – 60 years	19	21,59
41 – 50 years	42	47,73
31 – 40 years	10	11,36
< 30 years	3	3,41
Gender		
Male	5	5,68
Female	83	94,32
Tumor Location		
Supratentorial non-basis cranii	38	43,18
Supratentorial basis cranii	40	45,45
Infratentorial	10	11,36
Tumor Margin		
Ireguler	32	36,36
Reguler	56	63,64
Histopatology		
Grade 3	4	4,55
Grade 2	10	11,36
Grade 1	74	84,09
Peritumoral Edema		
Yes	44	50,00
No	44	50,00

The results of determining the cut off point value of tumor volume size in general and based on specific intracranial locations are shown in the ROC curve and table below. The results of bivariate analysis and prevalence ratio values and 95% CI based on each volume cut off point by Chi Square test are also shown in the table below.

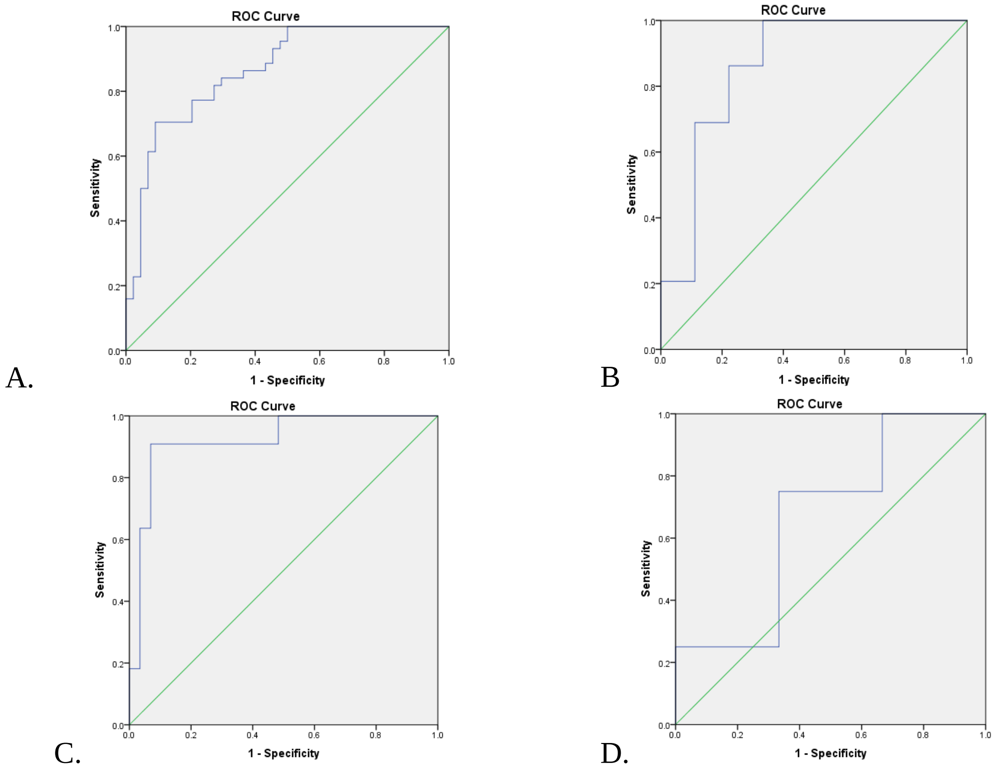

Figure 3: ROC curve of predictive value of tumor volume against peritumoral edema. A. In general (AUC = 0.865, p=0.001) B. Supratentorial non-basis cranii region (AUC = 862, p=0.001) C. Supratentorial basis cranii region (AUC 0.992, p=0.001) D. Infratentorial region (AUC = 0.667 p=0.394)

Table 2: Predicted cut off point tumor volume in general and by specific intracranial location, and bivariate analysis of the relationship between meningioma volume and the incidence of peritumoral edema.

			Spesific Location		
		General Location	**Supratentorial Non Basis Cranii**	**Supratentorial Basis Cranii**	**Infratentorial**
	***Cut Off* tumor volume (cm³)**	**≥ 44**	**≥ 22**	**≥ 54**	**≥ 19,75**
Diagnostic Value	Sensitivity	70,45%	86,21%	90,91%	75,00%
	Specificity	90,91%	77,78%	93,10%	66,67%
	Likelihood rasio (+)	7,75	3,88	13,18	2,25
	Likelihood rasio (-)	0,32	0,18	0,10	0,38
	Positif predictive value	88,57%	92,59%	83,33%	60,00%
	Negative predictive value	75,47%	63,64%	96,43%	80,00%
	Accuration	80,68%	84,21%	92,50%	70,00%
	Youden Index	0,614	0,640	0,840	0,417
***Chi Square* Analysis**	*p*	0,01	0,01	0,01	0,52
	RP	3,61	2,546	23,33	3,00
	CI 95%	2,22 – 5,88	1,16 – 5,61	3,35 – 162,57	0,45 – 101,57

Chi square test results of other variables including age, gender, tumor location, tumor margin, and degree of histopathology on the incidence of peritumoral edema showed a significant association between tumor margin and degree of histopathology with the incidence of peritumoral edema (p = 0.01). Meanwhile, the variables of age and gender did not have a significant difference in proportion with the incidence of peritumoral edema (p>0.05). Based on tumor location, there was no statistically significant association (p = 0.10) with edema incidence. However, clinically, tumors in the supratentorial non basis cranii region had a greater risk of peritumoral edema than tumors in the supratentorial basis cranii or infratentorial (RP 1.91 CI95% 0.88 - 4.16).

Multivariate logistic regression test results and stratification of general tumor volume (≥ 44 cm3) and other variables on the incidence of peritumoral edema stated that simultaneously large tumor volume size (≥ 44 cm3) had the greatest influence on the incidence of peritumoral edema both clinically and statistically, while gender, tumor location, tumor margin, and histopathology did not have significant results (p>0.05).

Table 3. The results of multivariate analysis between variables and incidence of peritumoral edema

	Peritumoral Edema		
	p	**RP**	**CI 95%**
Tumor Volume			
≥ 44 cm^3	0,01	3,81	1,87 – 5,76
< 44 cm^3		1	
Gender			
Male	0,37	1,69	0,40 – 4,78
Female		1	
Tumor Location			
Supratentorial non-basis cranii	0,46	1,42	0,38 – 3,22
Supratentorial basis cranii	0,38	0,17	0,09 – 2,28
Infratentorial		1	
Tumor Margin			
Ireguler	0,71	1,21	0,47 – 2,87
Reguler		1	
Histopatology			
Grade 3	0,59	1,50	0,20 -5,01
Grade 2	0,44	0,61	0,42 – 2,63
Grade 1		1	

4. DISCUSSION

In this study, the overall tumor volume size without distinguishing tumor location using ROC obtained an AUC prediction value of 0.856, meaning that tumor volume has strong accuracy to predict peritumoral edema. There are several cut off values of tumor volume with varying sensitivity, specificity and Youden Index. The researcher chose a cut off point of 44 cm3 tumor volume because this study aims to predict the presence or absence of peritumoral edema so that it requires a high specificity value, relatively good sensitivity and strengthened by the value of Youden Index and the highest accuracy. If the tumor volume is assumed to be spherical, the tumor diameter is ± 4.4 cm. These results support previous research by Shin and colleagues (2021) on meningiomas in the convexity and parasagittal regions which stated that a meningioma volume of 13,953 cc or a diameter of ± 3 cm is the optimal cutoff value for predicting the incidence of PTBE in meningiomas in these regions. Shin and colleagues (2021) also stated that a tumor diameter of 3 cm has clinical significance in determining clinical decisions regarding the choice of meningioma therapy in the convexity and parasagittal regions, which has only been determined by implicit agreement between clinicians (6). Differences in patient characteristics between health care facilities are suspected to have a role in differences in tumor size variations that have an impact on the outcome of peritumoral edema events.

The results of the analysis of the comparative relationship between meningioma volume in general and the incidence of peritumoral edema stated that subjects with large tumor volume size (≥44 cm3) had a risk of experiencing peritumoral edema 3.61 times (95% CI = 2.22 - 5.88, p = 0.01) compared to subjects with tumor volume size <44 cm3. These results support previous research which states that there is a strong correlation (r = 0.627 and p value = 0.001) between tumor size and the incidence of peritumoral edema (7). Liyanage and colleagues (2020) also stated that the strongest predictor of perilesional edema was the maximum diameter of meningioma with an Odds Ratio of 1.46 (95% CI = 0.95-2.39) (10).

The results of bivariate analysis of other variables affecting the incidence of edema stated that tumor margins and histopathological grade had a statistically and clinically significant relationship with the incidence of peritumoral edema. Irregular tumor margins reflect tumor invasion into the cerebral cortex. The integrity of the tumor boundary with the cerebral parenchyma under tumor conditions without surgery or radiation is influenced by tumor size (11,12,13). High-grade meningioma will infiltrate the surrounding brain parenchyma and cause cortex disruption, thus positively correlating with the incidence of peritumoral brain edema (14,15). However, multivariate test results showed that simultaneously, large tumor volume size (≥44 cm3) had the greatest influence on the incidence of peritumoral edema both clinically and statistically.

In this study, clinically, tumor location in the supratentorial non-base cranii region had a 1.91 times greater risk of peritumoral edema than tumors in the supratentorial base cranii or infratentorial (CI95% 0.88-4.16). This is related to the theory of cerebral compression and the greater amount of substantia alba in the superficial region, which facilitates the spread of PTBE. In addition, the location of the tumor in the basis cranii tends to be close to the cranial nerves and vasculature so that it will provide signs and symptoms that are of concern to patients so that an early examination can be carried out (5,13).

Meningiomas are tumors that can occur at various intracranial locations. The relationship between meningioma and PTBE has substantial tumor site heterogeneity (6). Therefore, this study attempted to reduce the effect of site heterogeneity on the association between meningioma and PTBE and obtain cut off values at each site to predict the incidence of peritumoral edema.

Based on the specific intracranial location, there are differences in the cut off size of tumor volume to predict and assess the clinical risk of peritumoral edema. The optimal cut off value of tumor volume in supratentorial non basis cranii is 22 cm3 with a prevalence ratio of 2.54, while the optimal cut off value of tumor volume in supratentorial basis cranii is 54 cm3 with a prevalence ratio of 23.33. The basis cranii region required a larger tumor volume to predict the onset of edema than the non-basis cranii supratentorial area. These results suggest the role of tumor-brain interaction in edema formation and the important role of subarachnoid space in edema resolution. Cerebri edema depends not only on the rate of production but also on the reabsorption of extravasated fluid into the ventricles and subarachnoid LCS (16,17).

In the infratentorial area using 10 samples, a cut off value of 19.75 cm3 was obtained. This cut off value has a weak predictive power and the results of bivariate analysis showed no statistically or clinically significant relationship with the incidence of peritumoral edema. This is due to the small sample size in this region. Epidemiologically, based on previous studies, the incidence in the infratentorial area is only 10% and most intracranial meningiomas arise in the supratentorial area (90%) (18).

This study has advantages including the measurement of tumor volume and edema using semiautomatic segmentation techniques so as to produce more precise measurements compared to manual methods (ellipsoid). Determination of edema is done objectively by looking at the relationship between tumor volume and edema volume using the Edema Index (IE). In this study, the cut off value of tumor volume and predictive power, sensitivity and specificity were measured to obtain accurate cut off values both in general and specifically based on each location to reduce the effect of heterogeneity. In addition, relationship assessment and prevalence ratio measurement were also carried out overall and per location based on the cut off value of each region so as to obtain statistically and clinically accurate prediction of the incidence of peritumoral edema. This study also stratified other variables including gender, location, tumor margin and histopathological grade so that the role of each variable on the incidence of peritumoral edema can be clearly seen.

There are limitations that researchers found in this study, namely sampling was only carried out at 1 central public hospital. In the infratentorial location, only a small number of samples were obtained so that the results of the assessment in the region could not represent the relationship between the tumor and the incidence of peritumoral edema.

5. CONCLUSIONS

The chemotherapy regimen patterns at In general, the cut off value of intracranial meningioma tumor volume to predict the incidence of peritumoral edema is 44 cm3. Large meningioma volume ≥44 cm3 had a risk of peritumoral edema incidence of 3.61 times. Large tumor volume (≥ 44 cm3) had the greatest influence on the incidence of peritumoral edema.

There were differences in the cut off value of meningioma tumor volume based on the specific intracranial location to predict the incidence of peritumoral edema. The cut off value of meningioma volume in the supratentorial region of non basis cranii and basis cranii were 22 cm3 and 54 cm3 respectively with prevalence ratios of 2.54 times and 23.33 times to experience peritumoral edema. The cut off value of meningioma volume in the infratentorial region was 19.75 cm3, but had weak predictive power for the incidence of peritumoral edema.

Further research is needed with a study population that includes several health facilities to obtain a larger sample size. In addition, further research can be conducted on the impact of peritumoral edema on the preoperative clinical picture as well as postoperative outcomes and progonosis of meningioma recurrence.

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