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MRI predictive score of pial vascularization of supratentorial intracranial meningioma

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Abstract

Objective Meningiomas are highly vascularized tumors which may recruit pial blood supply. Pial supply complicates tumor treatment in numerous ways. The objective of this study was to establish a reliable MRI-based diagnostic score to predict the existence of pial blood supply in supratentorial intracranial meningiomas and then correlate the score with clinical and surgical outcomes and histopathological findings.

Methods We performed a retrospective analysis of supratentorial histologically proven meningiomas in our institution from 2010 to 2018. A score was built based on MRI criteria and correlated with digital subtraction angiography (DSA) pial vascularization assessment. The score was then validated on a second independent population recruited with the same modalities.

Results Logistic regression identified four parameters related to pial blood supply which were used to build the score: skull base location, tumor size > 45 mm, peritumoral flow voids, and incomplete cerebrospinal fluid rim. The overall diagnostic performance in predicting pial blood supply was as follows: sensitivity 97.8%, specificity 76.9%, predictive positive value 88.2%, negative predictive value 95.2%, and accuracy 90.3%. Inter-reader agreement and Cohen's kappa were good, respectively, of 90.7% and 0.69. A high score was associated with aggressive meningioma (World Health Organization II–III) ($p = 0.04$) and with greater importance of pial supply relative to dural supply.

Conclusions We have identified a reliable way to use MRI to predict the existence of pial blood supply in supratentorial intracranial meningiomas. A higher score also predicted higher grade meningioma.

Key Points

- *Accurate and reproducible MRI score composed of four items to predict the existence of pial blood supply in supratentorial meningioma.*
- *High score is associated with high-grade meningioma (WHO II–III) but also with greater importance of pial supply relative to dural supply.*

Keywords Magnetic resonance imaging · Meningioma · Retrospective studies · Supratentorial neoplasms

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Abbreviations

DSA Digital subtraction angiography
ECA External carotid artery
PTBE Peritumoral brain edema
WHO World Health Organization

Introduction

Meningiomas are highly vascularized tumors which develop from the leptomeninges [1]. Meningiomas are usually primarily vascularized by external carotid artery (ECA) branches (i.e., middle meningeal artery) but may also recruit pial blood supply [1, 2]. Pial supply complicates tumor treatment in a number of ways. First, pial blood supply prevents complete tumor devascularization during pre-operative embolization [3] which can make surgical operations more challenging. Pial vascular supply is also associated with higher tumoral adhesion to brain parenchyma [4, 5], lower rates of extrapial cleavage during surgery [5, 6], higher rates of recurrence, and potentially higher rates of complications during surgical resection [6, 7]. Furthermore, pial supply has been reported to be associated with the presence of peritumoral brain edema [8–10] and to a higher World Health Organization (WHO) grade [8].

Given the numerous challenges associated with pial blood supply to supratentorial meningiomas, it appears imperative to figure out the tumoral arterial supply before surgery and to identify pial vascularization in order to appropriately plan a safer surgical procedure and weigh the indication of pre-surgical embolization [11]. Cerebral angiography is the gold standard for the evaluation of meningioma vascularization, but this procedure involves some risks including cerebral ischemia [12] and is not systematically performed in the management of meningioma patients. On the other hand, MRI is almost always performed in cases of intracranial meningiomas and could offer a means to assess the presence or absence of pial supply [13].

The objective of this study was to establish a reliable diagnostic score based on MRI examination to predict the existence of pial blood supply in supratentorial intracranial meningioma. We studied the correlation between this score and both clinical and surgical outcomes as well as histopathological findings.

Methods

Data collection

Following Institutional Review Board approval, we performed a retrospective analysis of our prospective database for all consecutive patients who underwent pre-surgical cerebral angiography for supratentorial histologically proven meningioma from 2010 to 2018.

In order to get a more homogeneous population, patients with at least one of the following criteria were excluded: previously operated tumors with tumor recurrence, multiple and voluminous simultaneous meningiomas, and “en-plaque” subtype [14].

Pial supply analyses on DSA

Digital subtraction angiography (DSA) was performed with a biplane angiography unit (Artis Zee Biplane, Siemens) with a six-axis angiography by two experienced interventional neuroradiologists. Acquisitions consisted in anteroposterior and lateral projections in both right and left internal and external carotids as well as left vertebral.

Pial supply was defined as the presence of tumoral blush fed by the internal carotid arteries or the vertebro-basilar vascularization or any vascularization dedicated to brain supply. The importance of this pial supply was also semi-quantitatively assessed as absent, inferior or equal to dural supply, or superior to dural supply based on the system used by Pistolesi et al [8]. This assessment of pial supply was performed by an 8-years-experience interventional neuroradiologist blinded for MRI results.

Pre-surgical MRI examinations

MRI examinations were performed with two different systems: Philips Achieva 3.0 T (Philips Healthcare) and Siemens Area 1.5 T (Siemens Medical Solutions). Patients were allocated to one of the two machines without any specific criterium. MRI protocols are detailed in Supplemental Digital Content 1. Table 1. MRI analyses were performed by two independent readers blinded to the presence or absence of pial supply on DSA. Inter-reader variability was evaluated with inter-reader agreement and Cohen’s kappa. A consensus was obtained between the two readers in case of discordance. Further analyses were performed with the consensual results.

MRIs were systematically analyzed for criteria previously described in the literature as related to the presence of pial blood supply: tumor size [10], peritumoral brain edema (PTBE) [8–10], alteration of the tumor-brain interface [4, 13]. Tumor size was reported with the measurement of the tumoral great axis in centimeters on 3D T1-gadolinium-enhanced images (Dotarem 0.5 mmol/ml: 0.01 mmol/kg IV, Guerbet). PTBE was assessed semi-quantitatively on 2D axial T2 FLAIR images. It was considered as extensive when edema volume (T2 FLAIR hyperintensity) was greater than tumor volume. Edema volume was measured on Advantage Workstation 4.2, General Electrics Healthcare. Semi-automatic contouring of peritumoral T2 FLAIR hyperintensity was performed on each slice with a manual correction of aberrations. Edema volume was then extracted by the software. Tumor-brain interface was evaluated on 2D

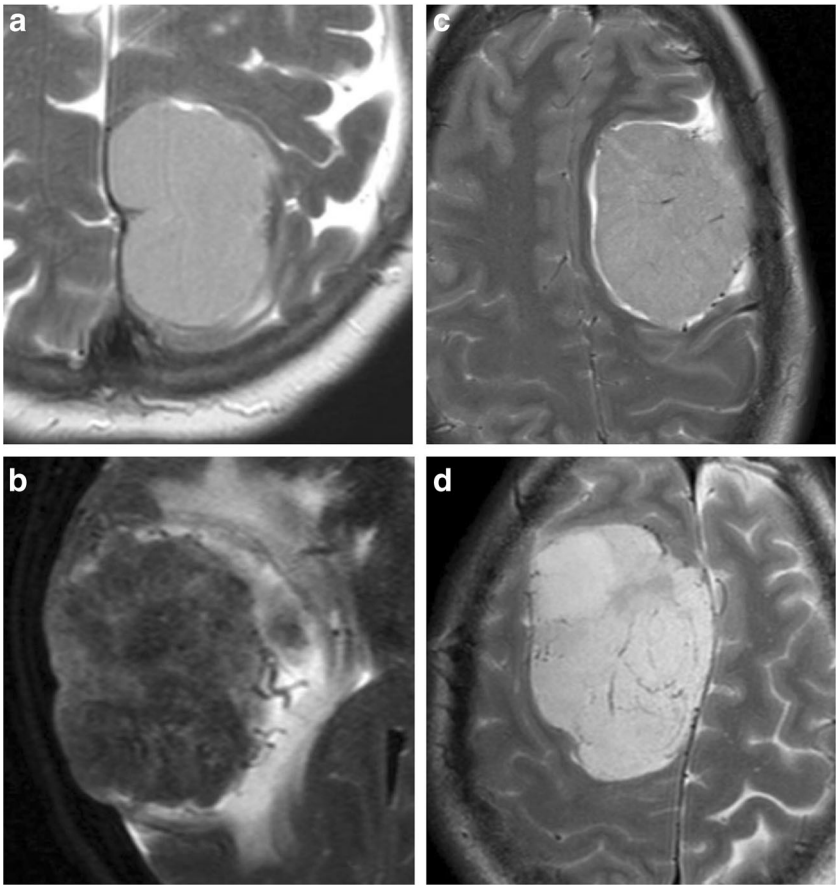

Fig. 1 Absence of peritumoral flow voids (**a**). Numerous peritumoral flow voids (**b**). Complete CSF rim (**c**). Absent CSF rim (**d**)

axial T2WI slices according to the presence or absence of a complete or quasi-complete cerebrospinal fluid (CSF) rim around the tumor. Other parameters studied on MRI included the presence of peritumoral flow voids (PTFV) on 2D axial T2WI slices [15], tumor location (skull base vs. non-skull base), and tumor T2 intensity [4]. Peritumoral flows voids were graded as present or absent. Tumoral intensity on 2D axial T2WI images was stated as hypo-, iso-, or hyperintense compared with cerebral cortex. Figures 1 and 2 show examples of MRI examination.

Pathological, surgical, and clinical outcomes

For all the patients, several outcome parameters were collected: rate of surgical complications, resection completeness (completeness according to Simpson's resection grade and MRI post-operative examination), hospitalization duration after surgery, return home or rehabilitation care after surgery, rate of recurrence (defined by the rise of a measurable lesion on any follow-up MRI after total resection). Histopathological findings collected included WHO grading and brain parenchyma invasion. For this analysis, we also included retrospectively additional consecutive patients from our institution without pre-surgical angiography but with pre-surgical MRI.

Statistical analysis

Data were analyzed using R version 3.4.0 for Windows V17.0 (R Foundation for Statistical Computing). Logistic regression was conducted in order to isolate the explanatory variables of pial vascularization. According to El Sanharawi et al [16], univariate analysis on each MRI criterion was performed in order to isolate all the parameters likely to be associated with the presence of pial blood supply on DSA. Then, a multivariate analysis was performed on these selected parameters. A p value < 0.05 was considered as the significance threshold. The diagnostic score was built using a point allocation system based on the resultant logistic regression model. Inter-reader variability was evaluated by inter-reader agreement as well as Cohen's kappa.

Score validation

In order to assess the validity of the proposed score, we evaluated the score in another retrospective series of consecutive patients from a second institution who underwent pre-surgical cerebral angiography for supratentorial histologically proven meningioma between 2012 and 2018. Those patients were selected with the same exclusion criteria. DSA was performed exactly the same way as in our institution. MRI and DSA data

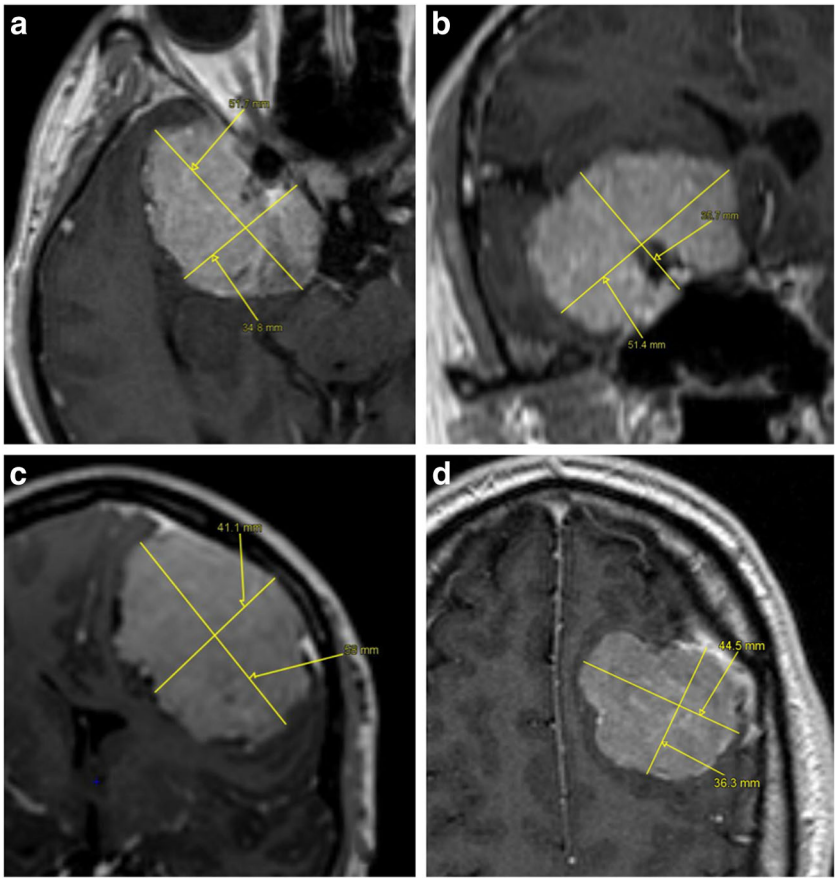

Fig. 2 Assessment of tumor great axis on a skull base meningioma (**a**, **b**) and on a non-skull base meningioma (**c**, **d**)

were evaluated by a unique reader, different from the two readers from institution 1, trained to use the score on a sample and were used to test the performances of the score on a different population. The assessment of the MRI score was performed prior to the assessment of pial supply on DSA.

Ethic statements

This study was approved by the Institutional Review Board (IRB) of our institution. Written informed consent was not obtained from participants because of the retrospective design of this study; therefore, the IRB of the hospital waived the need for written informed consent from participants.

Results

Logistic regression and score building

Fifty-four patients with supratentorial meningioma for whom both MRI and DSA were available in our institution were included. Average time between MRI and DSA was 22 ± 33 days. Flow

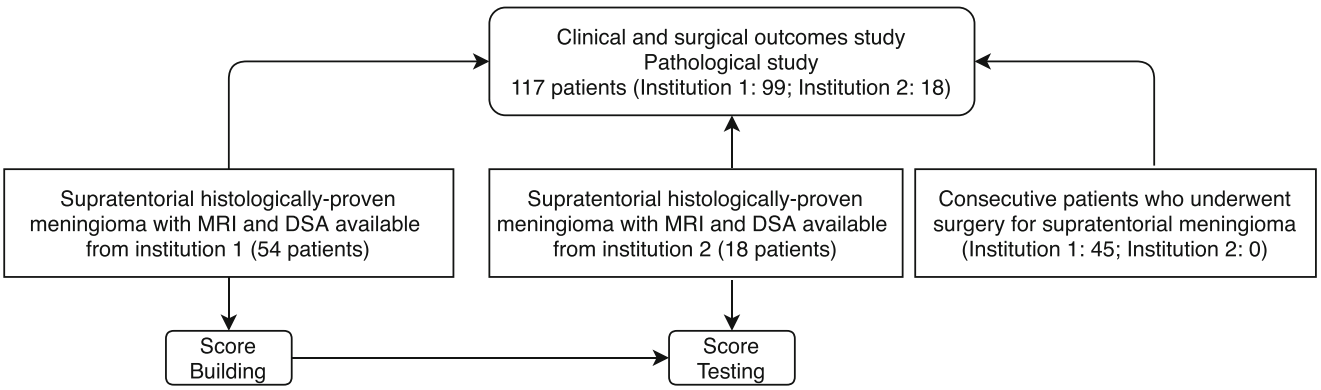

Fig. 3 Flow chart

chart is displayed in Fig. 3. Mean age was 58.5 ± 14.0 years. Sex distribution was as follows: male (29.6%; 16/54) and female (70.4%; 38/54). Mean tumor size was 57.6 ± 17.1 mm. Pial supply was present on DSA in 70.4% of the patients (38/54). Detailed characteristics are reported in Table 1.

Tumor size ($p < 0.001$; Mann-Whitney), peritumoral flow voids ($p < 0.001$; chi-square), and incomplete peritumoral CSF rim ($p < 0.001$; Fisher exact test) were significantly associated with the presence of pial supply on univariate analysis. ROC analysis showed that a tumor size > 45 mm was the best threshold to assess the existence of pial supply. A non-significant negative relation was found between pial supply and skull base location ($p = 0.19$). All these parameters were included in the multivariate analysis. Detailed results of the univariate and multivariate analyses are displayed in Table 2.

Based on the resultant multivariate logistic regression equation, we developed a diagnostic score based on a point allocation system presented in Table 3. Three points were added in the case of a tumor size > 45 mm. Four points were added either in the case of an alteration of the CSF rim or abnormal peritumoral flow voids. Finally, 2 points were subtracted in the case of skull base location. A score > 6 was considered predictive of pial supply.

Diagnostic performances

This score was applied to the 54 patients of our institution and to 18 patients from the second institution. The contingency tables and test's performances are reported in Supplemental Digital Content 2. Table 2.

The overall performance on the 72 patients was as follows: a sensitivity of 97.8%, a specificity of 76.9%, a predictive positive value of 88.3%, a negative predictive value of 95.2%, and an accuracy of 90.3%. Details are displayed in Table 4. Inter-reader agreement and Cohen's kappa were respectively of 90.7% and 0.69.

Table 1 Description of the studied population

Mean age (years)	58.5 (SD, 14.0)
Tumor size (mm)	57.6 (SD, 17.1)
Pial supply	70.4% (38/54)
Extensive PTBE	48.1% (26/54)
Incomplete CSF rim	81.4% (44/54)
Sex	
Male	29.6% (16/54)
Female	70.4% (38/54)
Location	
Skull base	18/54 (33.3%)
Non-skull base	36/54 (66.6%)

PTBE, peritumoral brain edema; *CSF*, cerebrospinal fluid

Table 2 Univariate and multivariate analyses

Parameter	Univariate analysis *p* value	Multivariate analysis *p* value
Tumor size (great axis)	< 0.001*	–
Great axis > 45 mm	< 0.001†	< 0.01
Peritumoral flow voids	< 0.001‡	0.04
Incomplete CSF rim	< 0.001‡	< 0.01
Skull base location	0.19†	0.20
Vol. E/Vol. T	0.83*	–
Tumor T2 hyperintensity	0.75‡	–
Age	0.52*	–
Sex (male)	0.41†	–

*Mann-Whitney. † Chi-square. ‡ Fisher's exact test. *CSF*, cerebrospinal fluid; *Vol.*, volume

Mean score was 4.06 ± 3.54 in the case of absent pial supply, 9.33 ± 1.63 in the case of pial supply ≤ dural supply, and 9.85 ± 1.46 in the case of pial supply > dural supply ($r_s = 0.62$; $p < 0.01$; Spearman).

Influence on clinical and surgical outcomes

We studied clinical and surgical outcomes among these 72 patients but also on 45 consecutive patients from our institution who underwent surgery for supratentorial meningioma. Characteristics of these 117 patients are presented in Supplemental Digital Content 3. Table 3. We did not find any significant relationship between the score and the following outcomes: rate of surgical complications, Simpson's resection grade, hospitalization duration in acute care after surgery, return home or rehabilitation care after surgery, and recurrence rate (mean follow-up was 37 ± 31 months). Detailed results are available in Supplemental Digital Content 4. Table 4.

Correlation with pathologic criteria

Forty-one of the 117 meningiomas (36.3%) were graded WHO II–III. Brain invasion was histologically observed among 13.7% (16/117) of the patients. A score > 6 was significantly associated with WHO II–III meningioma ($p = 0.04$; chi-square). We identified a non-statistically significant

Table 3 Diagnostic score

Size > 45 mm	+ 3 points
Peritumoral flow voids	+ 4 points
Incomplete CSF rim	+ 4 points
Skull base meningioma	− 2 points
Diagnostic threshold	> 6 points

CSF, cerebrospinal fluid

Table 4 Overall diagnostic performances

	Pial supply	No pial supply
Score > 6	45	6
Score ≤ 6	1	20
	Value	CI95
Se	97.8%	(88.5–99.9)
Sp	76.9%	(56.3–91.0)
PPV	88.2%	(78.8–93.8)
NPV	95.2%	(74.0–99.3)
Acc	90.3%	(80.1–96.0)

CI95, 95% confidence interval; *Se*, sensitivity; *Sp*, specificity; *PPV*, predictive positive value; *NPV*, negative predictive value; *Acc*, accuracy

relation between a score > 6 and brain invasion (16.9% vs. 7.5%; $p = 0.25$; Fisher's exact test).

Discussion

Score performance

Our study is the first to propose a score able to predict the existence of pial blood supply in supratentorial meningiomas. With an overall sensitivity of 97.8% and a specificity of 76.9%, the score reliably predicts the existence of pial blood supply for supratentorial meningioma and appears to be reproducible as no major differences were observed between its diagnostic performance across two institutions. Moreover, a higher score is predictive of a more important pial supply relative to dural supply. These findings are important as they suggest that our scoring system could be used to help radiologists and neurosurgeons routinely identify the presence of pial blood supply pre-operatively. This might be useful to plan a safer surgical time but also to take the decision of pre-surgical embolization.

A number of prior studies have studied the relationship between meningioma imaging features and vascular supply. Tumor size has previously been reported to be associated with the presence of pial supply [10]. This finding was confirmed in our study. Intra-tumoral flow voids have been associated with tumoral hypervascularity but not type of vascular supply (i.e., pial vs. dural) [15]. We found an association between peritumoral flow voids and pial blood supply. It is likely that peritumoral flow voids have a stronger association with pial supply than intra-tumoral flow voids because the recruitment of pial vessels occurs mostly at the periphery of the meningioma [1, 2]. The relationship between pial supply and tumor location has to our knowledge not been studied. The negative correlation between skull base location and pial supply might be explained by differences in vascularization of these meningiomas, relying mostly on proximal dural branches from the internal carotid artery.

Contrary to the previous literature, we did not identify PTBE as a variable associated with the presence of pial supply in our model. Pial vascularization has been widely correlated with the development of PTBE [8–10]. This result in our study might be related to the dichotomic evaluation of pial supply limited to its presence or absence in our model. Though, the semi-quantitative approach showed a non-statistically significant correlation.

Clinical and surgical outcomes

We expected that a high score would be associated with poorer surgical and clinical outcomes given the previously described relation between pial vascularization and tumor cleavability as well as the association between pial supply and poorer results associated with pre-surgical embolization. However, no significant association was observed which might again be explained partly by our dichotomic approach of pial supply, but also by the many factors influencing clinical outcomes such as adjunct radiotherapy or pre-surgical embolization.

Pathologic study

The relation between a score > 6 and high-grade meningioma is concordant with data from the literature as pial supply is related to WHO II–III meningioma [8]. The higher rate of brain invasion found in cases of score > 6 might be associated with the positive correlation between arachnoid disruption and pial vascularization described by Nakasu et al [9].

Limitation

This study is limited by its retrospective nature. The score has also been established on a population mostly composed of patients addressed for a pre-surgical embolization which can result in a selection bias in our results. In our institution, according to the literature review of Dubel [2], pre-surgical embolization is generally proposed in the case of large meningioma (> 5 cm), in surgically challenging locations (skull base and particularly sphenoid wing or middle crania fossa). As shown in Table 1, mean tumor size was 57 mm and a third was located to skull base.

Also, our study did not evaluate the importance of pial supply compared with dural supply for the score building which is a key parameter to take into account when discussing the outcomes of pre-surgical embolization [2]. Nevertheless, we added a semi-quantitative study showing that a higher score is associated with a more important pial supply relative to dural supply.

Acquisition of MRI images with two different machines (1.5 T and 3 T) might be a limitation concerning the score reproducibility. Nevertheless, we think that the criteria included in the score are not so prone to assessment's variations depending on protocols and machines. This statement is particularly true concerning tumor size and location. This might

be more discussable for peritumoral flow voids and alteration of the CSF rim although these two criteria's assessment is neither subtle nor quantitative and might work in a very similar way on two different machines.

Conclusion

This study provides a reliable way to predict on MRI exam the existence of pial blood supply in supratentorial intracranial meningiomas. A higher score also predicted a higher grade meningioma. Further studies are needed to validate our scoring system and determine its clinical relevance.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Aymeric Rouchaud.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Retrospective
- Diagnostic or prognostic study/observational
- multicenter study

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