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Differentiation between ICA and ECA Feeder Distributions in Meningioma Using MR Perfusion Original Image

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Objective: Preoperative information regarding tumor feeder distribution is important in meningioma surgery. We aimed to examine the relationship between the contrast-enhancement pattern in meningioma on magnetic resonance (MR) perfusion images and the feeder pattern.
Methods: The subjects were 21 patients diagnosed with meningioma who underwent MR perfusion imaging between 2017 and 2020.
Results: The distribution of feeders from the internal carotid artery (ICA) system or external carotid artery (ECA) system within the tumor based on angiograms was compared with that in areas of enhancement on original MR perfusion images in seven of 21 patients who underwent cerebral angiography. The aspect ratios of tumors, which was defined as the ratio of the area of contrast enhancement to the length of the enhanced area in contact with the tumor margin on the early-phase MR perfusion images, supplied by the ICA (pial feeder pattern) and ECA (dural feeder pattern) systems were 0.12 ± 0.11 and 7.21 ± 4.99 (mean ± standard deviation), respectively ($p < 0.0001$). MR perfusion imaging in all 21 patients revealed higher frequency of the pial feeder pattern in patients with peritumoral edema ($p = 0.0009$).
Conclusion: The distribution of pial and dural feeders within a meningioma could be distinguished by the aspect ratio based on original MR perfusion images.

Key words: angiography, meningioma, MRI, surgery, perfusion, brain

INTRODUCTION

Magnetic resonance (MR) perfusion imaging has been used to assess blood flow distribution in the brain parenchyma and involved lesions in patients with stroke or brain tumors [1, 2]. The possible relationships of tumor blood flow based on cerebral blood flow imaging and tumor vascular volume based on cerebral vascular imaging with the tumor location, the degree of histological malignancy and the likelihood of postoperative tumor recurrence in patients with gliomas and meningiomas have been reported in previous studies [1–3]. To avoid unexpected bleeding during surgery for meningioma, a preoperative evaluation to obtain information regarding the presence of pial feeders from the internal carotid artery (ICA) system is crucial [4] and is usually performed using cerebral angiography. We postulated that an analysis of unprocessed, original MR perfusion images in the early phase could clarify whether the blood supply distribution originates from the ICA or external carotid artery (ECA) system. Compared with cerebral angiography, MR perfusion imaging is less invasive and provides superior three-dimensional morphological features. In addition, a relationship between pial blood supply to a meningioma from the ICA system and peritumoral brain edema has been previously reported in several studies, although a variety of other factors are presumably also associated with cerebral edema [5, 6].

Hence, this study aimed to investigate whether original MR perfusion images in patients with meningioma could help distinguish the origin of blood supply, i.e., between the ICA and the ECA systems, and to determine the relationship between the presence of ICA feeder patterns on MR perfusion imaging and peritumoral brain edema.

MATERIALS AND METHODS

Patient population

In this study, we performed a retrospective search of clinical records to identify patients diagnosed with meningioma who underwent MR perfusion imaging at our hospital between 2017 and 2020. Patients with a maximum tumor diameter < 30 mm and those who had undergone previous surgery for the tumors were excluded. The study protocol was approved by the ethical board of our university hospital (IRB No.: 19R-299).

MR perfusion imaging analysis

All examinations were performed using a 1.5 T MR scanner (1.5 T Ingenia R5.3, Philips, Best, The Netherlands), which can operate at a maximum slew rate of 200 mT/m/ms and a maximum gradient

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strength of 80 mT/m. An eight-channel receive-only head coil was used to cover the whole brain. Perfusion sequence (two-dimensional [2D] single-shot echo-planar imaging [EPI]) was employed with the following parameters: repetition time (TR) = 1368 ms, echo time (TE) (first TE/second TE) = 7.9/54.8 ms, field of view = 224 × 224 mm, voxel size = 2.33 × 2.38 × 5.0 mm, flip angle = 75°, EPI factor = 47, sensitivity encoding factor = 2.0, number of excitations (NEX) = 1, dynamic scan = 70, and total acquisition time = 1 min 46 s. Gadolinium contrast agent (0.1 mmol/kg) was administered intravenously at a rate of 5 ml/s following the administration of normal saline (20 ml) at a rate of 5 ml/s.

In patients who required preoperative embolization at the discretion of the operators, preoperative cerebral angiography was performed to determine the origin of blood supply to the tumor. We compared the feeding artery identified on cerebral angiography with the area of enhancement on the original MR perfusion images to confirm whether the origin of blood supply is the ICA or ECA system. The second original image showed faint enhancement and the entire tumor was enhanced strongly on the fourth original image in most patients; thus, we selected the third original image for the evaluation in this study. As the margin of the enhanced area was poorly defined in some of the images, we used approximately 30% of the area of maximum intensity as the border of the enhanced area. The evaluation method for the enhanced areas is shown in Fig. 1D and E. The area showing contrast medium enhancement (A, B mm^2) and the length of the margin of the enhanced area, which shows the attachment of the tumor to the dura mater (a, mm) or the brain surface (b, mm), were measured. The ratio of the mean depth of the enhanced area (A/a or B/b) to the dural attachment length (a) or the surface length (b) of the enhanced area was expressed as an aspect ratio. Therefore, the aspect ratio was calculated using the following formula: A/a^2 or B/b^2. Two neurosurgeons (TS and MM) with > 30 years of experience in their specialties evaluated the areas of enhancement within each meningioma on the original MR perfusion images; they examined whether the origin of blood supply to the areas is the ICA or ECA system and compared their results with angiographic findings. Any differences in interpretation were resolved by consensus reading. Horos software (Mac-based; v. 3.3.6, an open-source version of OsiriX [Pixmeo, Switzerland]; https://horosproject.org) and MIPAV (open-source version 10.0.0; NIH, USA; https://mipav.cit.nih.gov) were used for the image analysis.

Peritumoral brain edema evaluation

Peritumoral brain edema was defined as an area of high signal intensity around a tumor and was evaluated on MR T2-weighted images (WI). 2D T2WI turbo spin echo sequence was used with the following parameters: TR = 4743 ms, TE = 100 ms, k-space trajectory = leaner ordering, field of view = 240 × 200 mm, voxel size = 0.75 × 0.91 × 5.0 mm, echo train length = 13, sensitivity encoding factor = 1.8, NEX = 1, and total acquisition time = 1 min 11 s.

Statistical analysis

Numerical data are expressed as mean ± standard deviation (S.D.). Statistical analysis was performed using chi-squared analysis and Fisher's exact probability test for categorical variables and Mann–Whitney U test for continuous variables. Differences were considered statistically significant at $p < 0.05$. SPSS v. 26 (IBM; Armonk, NY, USA) was used for statistical analyses.

RESULTS

Patients

MR perfusion imaging was performed in 42 patients with meningiomas during the study period. After excluding patients with a maximum tumor diameter < 30 mm (n = 8) and those who had undergone previous surgery for meningiomas (n = 7), and had susceptibility artifact that prevented imaging analysis (n = 6), a total of 21 patients (8 males [38%] and 13 females [62%]; mean age, 65.6 years; age range, 40–85 years) were included in the study. The meningioma locations were as follows: convexity, falx, tentorium, skull base, and parasagittal, in 10, 3, 3, 3, and 2 patients, respectively.

Comparison between cerebral angiography and MR perfusion imaging

Seven of the 21 patients underwent preoperative cerebral angiography. The distribution of feeders from the ICA and/or ECA systems within the tumor was identified on cerebral angiography and compared with the areas of enhancement on the original MR perfusion images of the tumor. Fig. 1 shows a representative case of both the ICA and ECA feeder types. In the ECA feeder type, the contrast medium outlines a feeder from the ECA system (usually the middle meningeal artery) that penetrates the tumor internally before spreading to the periphery (Fig. 1C). In the ICA feeder type, the contrast medium fed from the ICA system covers the tumor margin widely before spreading gradually into the tumor (Fig. 1B). On each axial MR perfusion image showing a tumor, we classified the tumor blood supply as ICA or ECA system (Fig. 1E). Among the seven patients who underwent angiography, the blood supply to the meningioma was from the ICA system in five patients and the ECA system in seven patients. Fig. 2 shows the relationship between the feeding system and the aspect ratio of the enhanced area on the MR perfusion images, which showed the meningioma in seven patients; ICA feeders were noted in 35 slices and ECA feeders in 29 slices. The aspect ratios of the enhanced areas supplied by the ICA and ECA systems were 0.12 ± 0.11 (range, 0.02–0.50) and 7.21 ± 4.99 (range, 0.93–17.92) (mean ± S.D.), respectively; the former was significantly smaller than the latter ($p < 0.0001$). Based on this result, the blood supply to the enhanced areas with an aspect ratio < 1 was termed pial pattern, and the blood supply to those with an aspect ratio ≥ 1 was termed dural pattern.

Presence of peritumoral brain edema and pial supply pattern in the enhanced area

Peritumoral brain edema was identified in 14 of 21 patients. Table 1 shows the relationship between the presence of peritumoral brain edema and the supply pattern in the 21 patients. The presence of peritumor-

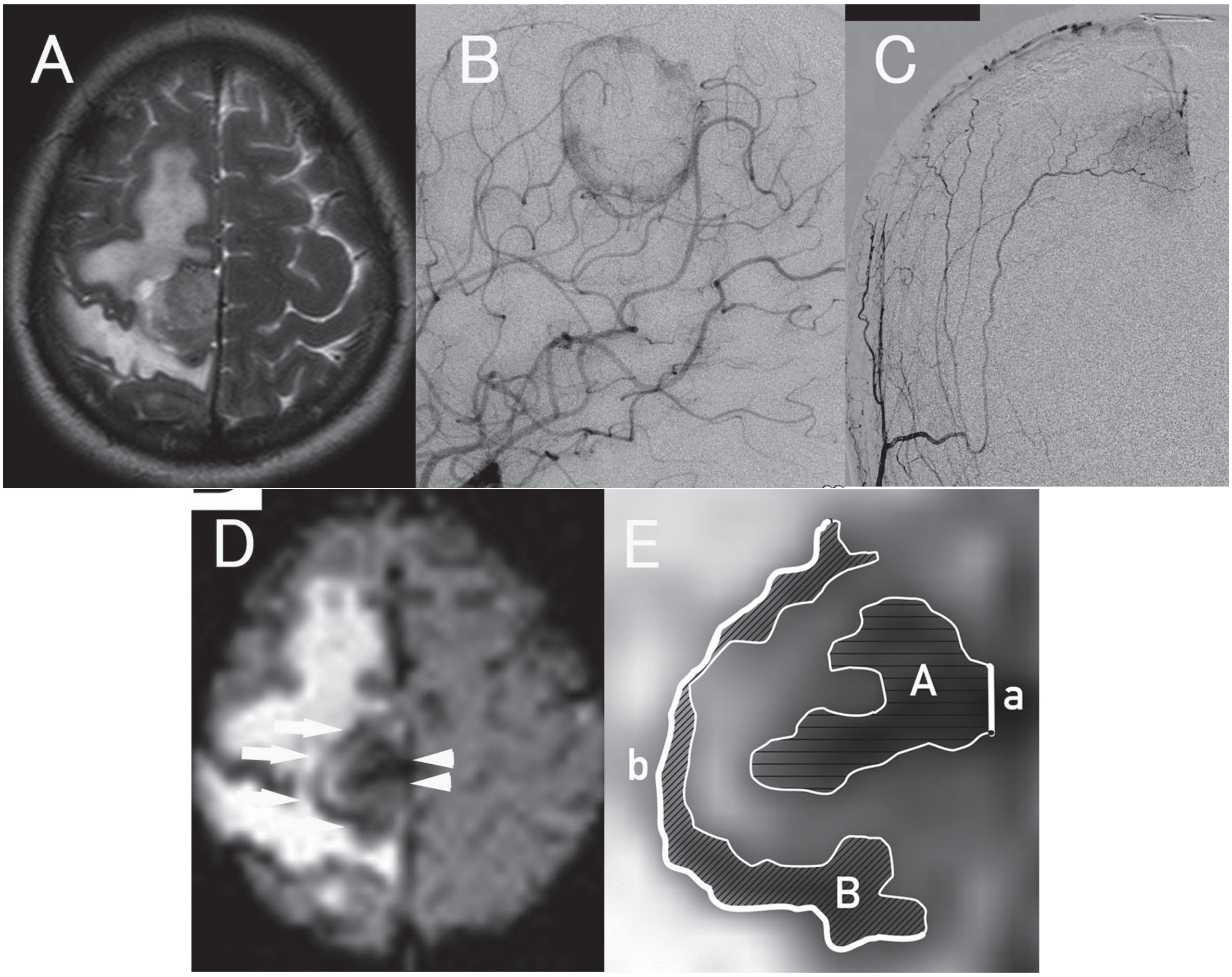

Fig. 1 Neuroradiological studies in a patient with a right falx meningioma
A: Magnetic resonance (MR) T2-weighted image showing a meningioma with extensive peritumoral edema.
B: Right internal carotid angiogram (lateral view) showing the contour of the tumor in contrast to pial feeders fed by the internal carotid artery (ICA).
C: Right external carotid angiogram (anteroposterior view) showing tumor staining fed by dural feeders from the external carotid artery (ECA).
D: Early-phase MR perfusion image showing heterogeneous contrast enhancement within the tumor. Two types of enhancement patterns are apparent within the tumor: a thin and wide area of low intensity that spreads along the tumor margin (arrows) and an area of low intensity with a relatively small attachment to the dura matter that extends laterally from the midline (arrow heads). The former and latter patterns correspond to the areas of enhancement fed by the ICA and ECA systems, respectively, according to the angiographic findings. For the ICA systems, the blood supply to the meningioma is distributed widely from the tumor surface into the shallow depth of the tumor (Fig. 1B). Feeders from the ECA systems supply blood from the dural attachment toward the main part of the tumor (so-called sun-bust appearance) (Fig. 1C).
E: Method of aspect ratio calculation for the enhanced areas on an enlarged image D showing the tumor area. Each enhanced area was traced over a threshold value of 30% of the maximum intensity within the area. The enhanced areas (A and B) and the length of the tumor margins within the enhanced areas (a and b) were measured. The ratio of the mean depth of the enhanced area (A/a and B/b) to the surface length of the enhanced area (a and b) was expressed as the aspect ratio. Therefore, the aspect ratios were calculated as follows: A/a^2 and B/b^2.

al edema was significantly associated with the pial pattern ($p = 0.0009$). Furthermore, in 13 patients with peritumoral edema associated with the pial pattern, the enhanced areas were adjacent to the peritumoral edema based on the original MR perfusion images (Fig. 1D).

DISCUSSION

The novelty of this study lies in the identification of three-dimensional blood supply distributions according to the distinctive characteristics of ICA and ECA feeders within a meningioma using original MR perfusion images.

Pial and dural supply patterns on original MR perfusion images

This study achieved the differentiation of feeding arteries in a meningioma, i.e., between the ICA and ECA systems, using original MR perfusion images. We found that for an aspect ratio ≥ 1, the area of enhancement was supplied from the ECA system (dural supply pattern), and for an aspect ratio < 1, the area was fed from the ICA system (pial supply pattern). In the dural supply pattern, the angiographic distribution shows the

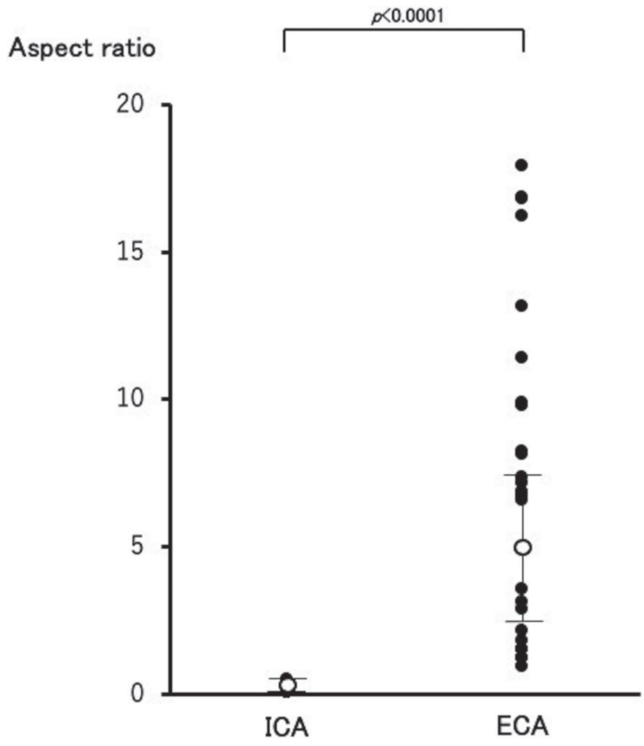

Fig. 2 Comparison of the aspect ratios of contrast-enhanced areas between internal carotid and external carotid artery blood supplies
The aspect ratios of the enhanced areas fed by the internal carotid artery (ICA) and by the external carotid artery (ECA) were 0.12 ± 0.11 and 7.21 ± 4.99 (mean ± standard deviation), respectively ($p < 0.0001$). The aspect ratio was calculated for each slice. The black circle indicates the aspect ratio; the white circle indicates the mean aspect ratio; and the bars indicate the standard deviation.

Table 1 Relationship between pial supply pattern on magnetic resonance (MR) perfusion imaging and peritumoral brain edema on MR T2-weighted images

	Peritumoral brain edema n = 14	No edema n = 7
Presence of pial supply pattern n = 14	13 patients	1 patient
No pial supply pattern n = 7	1 patient	6 patients

middle meningeal artery piercing the dural attachment into the tumor before spreading to the periphery, with a sunburst appearance. By contrast, the appearance of the pial supply pattern approximates that of the angiographic tumor stain of a meningioma, in which the supply to a wide tumor margin adjacent to the brain parenchyma is via many small pial branches of the ICA system. To the best of our knowledge, no previous study has reported the use of MR perfusion imaging to identify the origin of the feeding artery for meningiomas.

Preoperative information on the blood supply distribution of meningiomas is essential for surgical planning. Several studies have reported significantly stronger tumor–brain adhesion and more difficult tumor detachment during surgery in patients with a pial feeder to the meningioma on angiography than in those with a dural feeder alone [7, 8]. Alvernia *et al.* reported that the pial feeder location coincided with the intraoperative findings on the location of cortical invasion of the tumor [9]. Analysis of original MR perfusion images, which is less invasive than cerebral angiographic examination, may enable the identification of the presence and location of pial feeders, which may in turn allow surgeons to predict the locations of adhesion between the tumor and brain parenchyma and prevent excessive intraoperative bleeding.

Moreover, MR perfusion imaging method could be useful in the decision-making regarding preoperative embolization of a meningioma and in estimating residual blood flow distribution within the meningioma after embolization. The need for preoperative embolization has previously been determined based on the angiographic findings of the feeding arteries to a meningioma. In our study, the MR perfusion method, which is less invasive than conventional angiography, helped evaluate the necessity for preoperative embolization without performing an angiographic procedure. Residual blood flow distribution from the ICA system after embolization of ECA feeders could be estimated prior to embolization, although the exact amount of blood flow could not be predicted as it depends partially on the embolic procedure and embolic material used.

In this study, MRI perfusion images were obtained at approximately 1.5 s intervals. The third original image used for evaluation showed contrast enhancement approximately 3–4.5 s after initiation of a contrast agent entering a tumor. On cerebral angiography, an arterial phase usually continues up to 3 s after injection of a contrast agent, then transfers into a capillary phase and an early venous phase. Therefore, the third original image is supposed to be compatible to a late arterial phase to a capillary phase and an early venous phase on cerebral angiography. On a cerebral angiogram of a meningioma, a tumor stain usually appeared in a late arterial phase to an early venous phase, which is demonstrated in the MRI perfusion image evaluated in this study.

Relationship between pial supply and peritumoral brain edema

Peritumoral brain edema is frequently observed to be adjacent to a meningioma. The factors reported to influence the development of peritumoral edema include tumor blood supply (presence or absence of pial feeders from the ICA system), tumor size, tumor location, brain–tumor interface character (smooth or not), signal intensity of the tumor on MR T2WI, histological subtype of the tumor, cyst formation, and vascular endothelial cell growth factor (VEGF) expression [5, 6, 10].

Our study identified a significant relationship between the presence of a pial supply pattern and the development of peritumoral edema. Several studies have investigated the relationship between pial blood supply and peritumoral edema in patients with meningioma [5, 11]. Bitzer *et al.* found that peritumoral edema is significantly more prevalent in tumors with pial feeders and that the location of blood flow from the pial feeder to the tumor is correlated with that of peritumoral edema, which is consistent with the findings of our study [12]. In addition, the degree of peritumoral edema has been reported to be correlated with the blood flow from pial feeders to the tumor [7]. Several mechanisms regarding the relationship of the presence of pial feeders with the development of peritumoral edema have been postulated. Takeguchi *et al.* reported an association between peritumoral edema and adhesion of the tumor to the brain during surgery [13]; the degree of adhesion was significantly stronger in patients with disrupted continuity of the rim surrounding the tumor based on MR T1WI and T2WI. They also reported relationships among tumor adhesion, the presence of pial feeders on cerebral angiography, and the presence of peritumoral edema. Their results suggested that the rim preserves the pial membrane structures on the surface of the brain that is in contact with the tumor and that rim disruption is indicative of tumor invasion and adhesion. Moreover, Schmid *et al.* reported that the presence of pial feeders and VEGF expression are correlated with the development of peritumoral edema surrounding a meningioma [10]. In the development of peritumoral edema around a meningioma, VEGF is considered to play an important role as both an angiogenic and vascular permeability-increasing factor [14]. VEGF is secreted by tumor cells in the area surrounding the tumor as well as within the tumor and binds to the VEGF receptors of the pial vessels surrounding the tumor, which in turn triggers the proliferation of pial vessels and promotes their penetration through the arachnoid membrane into the tumor.

Study limitations

Most meningiomas in this study were relatively large and/or symptomatic and thus were candidates for surgical removal. Hence, the patients in this study may not be representative of a cohort of patients with meningiomas. This method cannot be applied for a small sized meningioma. The timing of the first appearance of the contrast enhancement in the source image and the actual timing of the entry of the contrast agent to the brain was not exactly consistent in each patient, which could be explained by the 1.5-s interval in the former. Furthermore, the rate of contrast agent entry into the brain depends on the cardiovascular condition of each patient. Nevertheless, these factors did not affect the major findings, because the enhancement distribution pattern was evaluated in this study and not the rate of contrast entry and contrast volume. In addition, this study was conducted in a single center with a small number of cases, which may have biased the results. However, the statistically significant p values were extremely small such that the number of cases could not have affected the results of the study. The third MRI perfusion original image was used for evaluation in this study. Feeding arteries of the ECA go through the dura mater into the tumor, on the other hand, feeders of the ICA from the brain parenchyma into the tumor. Therefore, chronological assessment of MRI perfusion original image series from initiation of the tumor enhancement up to the entire tumor enhancement might to assist the differentiation whether ECA or ICA is the original feeder of the contrast areas.

CONCLUSIONS

The distribution of pial feeders within a meningioma could be distinguished from that of dural feeders using the aspect ratio based on original MR perfusion images. Aspect ratios < 1 were derived exclusively from the ICA (pial feeder pattern) and aspect ratios ≥ 1 were derived mostly from the ECA (dural feeder pattern). Pial feeders may contribute to the mechanism of peritumoral edema formation. This method could possibly facilitate the decision-making on the surgical strategy for meningioma and assist in the evaluation for the need for preoperative embolization.

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