Advanced MRI prediction of meningioma histopathological classification: a literature review and case presentations

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ABSTRACT

Meningioma is not uncommon case; however, the differentiation of high-grade from low-grade meningioma is important. The rate of recurrence of grade I meningioma is 7-20%, but in grade II meningioma is 30-40% and in grade III 50-80%. Non-invasive MRI techniques that can differentiate high-grade from low-grade meningiomas before surgery are useful for surgical planning and subsequent treatment. We present a review article and some case studies of low-grade (WHO grade I) and high-grade (WHO grade II and grade III) meningioma with conventional MRI and continue with advanced MRI; we performed diffusion weighted imaging (DWI) with apparent diffusion coefficient (ADC) value, dynamic susceptibility contrast (DSC), dynamic contrast-enhanced (DCE) magnetic resonance (MR) perfusion and 3D ASL. From these three cases show that advanced magnetic resonance imaging with ADC value, DSC, DCE, and 3D arterial spin-labelling (ASL) is an essential sequence to differentiate high-grade from low-grade meningioma.

Keywords: Meningioma, Conventional MRI, ADC Value, DSC, DCE, 3D ASL.

INTRODUCTION

Meningiomas are the most common intracranial tumours, accounting for 13-26% of all primary intracranial tumours in adults, with three grades of meningioma. WHO grade I or typical meningioma accounted for 80-90% cases, WHO grade II or atypical meningioma 5-15% cases, and WHO grade III or malignant meningioma 1-3% cases. The treatment of choice is surgery, curative surgery of grade I with a recurrence rate of 7-20%, but the recurrence rate of grade II meningioma is 30-40% and grade III 50-80%.

Non-invasive techniques that can differentiate low-grade from high-grade meningioma are very useful for surgical planning and subsequent treatment. Patients with WHO grade II/III meningioma are more beneficial when surgery is performed earlier, so the detection of high-grade meningiomas is important for early resection and postoperative handlers.

LITERATURE REVIEW

Conventional magnetic resonance imaging shows a picture of meningioma with homogeneous or heterogeneous contrast enhancement and perilesional oedema, as well as a dural tail, but cannot predict the degree of tumour malignancy. Advanced magnetic resonance imaging can illuminate the classification of meningioma, DSC MR perfusion to noninvasively measure brain perfusion through hemodynamic measurements such as cerebral blood volume and cerebral blood flow from intracranial tumours, while DCE MR perfusion noninvasively measures contrast enhancement patterns in tumour tissue by evaluating time intensity curve (TIC) and permeability studies Ktrans (wash-in rate), Kep (wash-out rate), initial area under gadolinium contrast (IAUGC) and volume of extravascular and extracellular space (ve).

ASL as an endogenous tracer, imaging of relative cerebral blood flow (rCBF), does not require contrast media, it is a non-invasive technique, very suitable for patients who require repetitive follow-up, patients with impaired renal function, and paediatric patients. ASL shows different rCBF in meningioma and other extra-axial tumours such as schwannoma, macroadenoma, or extra-axial metastatic tumour. ASL shows a different pattern of rCBF in low-grade meningiomas and high-grade meningiomas, in low grade shows a diffuse increase in rCBF, and in high grade shows a heterogeneous increase in rCBF due to hypoperfusion. The ADC values could help differentiate high-grade from low-grade meningioma, in high-grade meningioma the ADC value is lower than that in low-grade meningioma.

DCE MR perfusion, also widely referred to as ‘permeability’ MRI, is based on the acquisition of serial T1-weighted images before, during, and after administration of low-molecular-weight extracellular MR contrast media, such as a gadolinium-based contrast agent.
The resulting signal intensity–time curve reflects a combination of tissue perfusion, vessel permeability, and extravascular-extracellular space. DCE MR perfusion allows for the determination of the permeability, or ‘leakiness’, of tumour vasculatures such as the transfer coefficient ($K^{\text{trans}}$) and the extravascular extravascular extracellular space volume fraction (ve). In a normal brain with an intact blood-brain barrier (BBB), $K^{\text{trans}} = 0 \text{ min}^{-1}$ and ve is unmeasurable. In contrast to conventional, static contrast-enhanced, T1-weighted MRI, which displays contrast enhancement at a single point in time, DCE MR perfusion imaging depicts the wash-in, plateau, and wash-out contrast kinetics of the tissue, providing insight into the nature of the bulk tissue properties at the microvascular level.

With pharmacokinetic modelling of DCE MR perfusion data, several metrics are commonly derived: the transfer constant ($K^{\text{trans}}$), the fractional volume of the extravascular extravascular extracellular space (ve), the rate constant (kep, where kep = $K^{\text{trans}} / \text{ve}$) and the fractional volume of the plasma space (vp). The most frequently used metric for DCE MR perfusion is $K^{\text{trans}}$. It can have different interpretations depending on blood flow and permeability. When there is very high permeability, the flux of the gadolinium-based contrast agent is limited only by flow and thus $K^{\text{trans}}$ mainly reflects blood flow. In situations in which there is very low permeability, the gadolinium-based contrast agent cannot easily leak into the extravascular extracellular space and thus $K^{\text{trans}}$ mainly reflects permeability.

In intra-axial tumours, they have an endothelial tight junction as the blood-brain barrier, but for extra-axial tumours, there are no endothelial tight junction and permeability barriers. Armed with these techniques, we can more clearly and confidently differentiate between benign and malignant lesions using DCE MR perfusion imaging with permeability studies. Classification for the time-intensity curve (TIC) in DCE MR perfusion shown in Figure 1: Type 1, no enhancement; type 2, gradual enhancement followed by a plateau phase; type 3, rapid enhancement followed by a washout phase; and type 5, rapid enhancement followed by slowly increasing enhancement (e) [13].

![Figure 1.](image)

**Classification for the time-intensity curve (TIC):** Type 1, no enhancement (a); type 2, gradual enhancement (b); type 3, rapid enhancement followed by a plateau phase (c); type 4, rapid enhancement followed by a washout phase (d); and type 5, rapid enhancement followed by slowly increasing enhancement (e) [13].

**CASE PRESENTATION**

We present three cases of meningioma, one malignant meningioma (WHO grade III), one atypical meningioma (WHO grade II), and one typical meningioma (WHO grade I). All patients underwent routine conventional magnetic resonance imaging, followed by 3D ASL, and continued with DCE perfusion with permeability studies. MRI examinations were performed with a 3.0 Tesla MRI (Signa Pioneer; GE Medical Systems, Milwaukee, WI, USA) using a 21-channel TDI head-neck coil. Magnetic resonance imaging examination is divided into two parts: before injection contrast and after injection contrast. Before contrast injection, the protocols used were axial, sagittal, coronal T2 weighted images, axial T2 flair, T1 flair, DWI b-value 1000, axial 3D acquisition in SWAN, high resolution T2 cube, and ASL. The 3D-ASL sequence with the following parameters; Post-label delay (PLD) values were chosen as 1525, 2025, and 2525 ms. TR 4387 ms (PLD 1525 ms), 4630 ms (PLD 2025 ms) and 5344 ms (PLD 2525 ms), scanning times were 4 min and 15 seconds (PLD 1525 ms), 4 min and 29 seconds (PLD 2025 ms) and 4 min and 51 seconds (PLD 2525 ms), FOV 24 cm × 24 cm, TE = 10.9 ms, NEX = 3, matrix = 512 x 512.

**Table 1. The ADC value, rCBV, 3D ASL, TIC and Peritumoral $K^{\text{trans}}$ in case 1, case 2 and Case 3**

| Advanced MRI | WHO grade III Meningioma Presurgery (Case 1) | WHO grade III Meningioma Recidive (Case 1) | WHO grade II Meningioma (Case 2) | WHO grade I Meningioma (Case 3) |
|--------------|---------------------------------------------|------------------------------------------|---------------------------------|---------------------------------|
| ADC Value    | 0.714-0.799                                 | 0.666-0.849                              | 0.747-0.790                     | 0.809-1.046                     |
| rCBV         | 12.22-15.44                                 | 14.02-17.77                              | Heterogenous pattern            | Homogenous pattern              |
| 3D ASL       | Heterogenous pattern                        | Type 4 with increase of maximum slope    | Type 4 with increase of maximum slope | Type 3                         |
| TIC          |                                             | 0.0594                                   | 0.0279                          | 0.0200                          |

ADC value = Apparent Diffusion Coefficient value, rCBV = relative Cerebral Blood Volume, 3D ASL = 3 Dimension Arterial Spin Labelling, TIC = Time Intensity Curve, $K^{\text{trans}}$ = Transfer Constant contrast from intravascular to extravascular extracellular space.
CASE REPORT

Then, followed by contrast injection with DCE MR imaging, a three-dimensional fast spoiled gradient-echo (3D-FSPGR) sequence with the following parameters was performed: TR = 6 ms, TE = 1.3 ms, FOV = 24 cm x 16.8 cm, matrix = 256 x 160, slice thickness 6 mm without spacing, NEX = 0.77, flip angle = 20, acquisition time 5 minutes 50 seconds. A total of 30 dynamic acquisitions and the contrast material is a bolus of 1.0-mmol/l gadobutrol formula (Gadovist; Schering Bayer Pharma), contrast is injected bolus when acquisition starts. After dynamic studies, post-contrast T1-weighted 3D cube images and axial T1 flair images were obtained.

Post-processing of image results from the 3D-ASL study and DCE study using Ready View and GenIQ software (Advance Workstation AW Volume Share 7; GE Medical System). Ready View to analyse 3D-ASL results for rCBF and GenIQ software is an application based on DCE-MRI data sets for pharmacokinetic analysis.

The purpose of GenIQ is to evaluate tissue flow, permeability, and contrast leakage from the vascular space to the extravascular extracellular space (EES) and then slowly leak back into the vascular space. Permeability is a parameter related to the level of leakage of contrast agent from the blood plasma space to the EES. Tumours performed by DCE-MRI are sensitive to MRI contrast, which is higher and faster. GenIQ to show and analyze the permeability study, we evaluate the peritumoral Ktrans in each case. The results of the ADC value, rCBV, 3D ASL, TIC and Peritumoral Ktrans in case 1, case 2 and Case 3 were shown in Table 1.

CASE 1

F, 63 years with left parietal convexity meningioma, post-surgery, histopathology confirmed WHO grade III meningioma, recurrent meningioma in the surgical bed six months after surgery (Figure 2). The case diagnosis was concluded as meningioma, rhabdoid type; WHO grade III. Present infiltration into brain parenchyma. There was recurrent meningioma at the surgical bed in six months post-surgery (Figure 3).

CASE 2

M, 73 years with left para-midline frontal meningioma, histopathology confirmed atypical meningioma, WHO grade II (Figure 4). This case was concluded as atypical meningioma, WHO Grade II with present infiltration into brain parenchyma.

CASE 3

F, 51 years with left parieto-occipital convexity meningioma, a histopathological finding confirmed metaplastic meningioma, WHO grade I (Figure 5). The last case was concluded as metaplastic meningioma (WHO grade I).

DISCUSSION

Conventional magnetic resonance imaging in all three cases shows a picture of meningioma with homogeneous or heterogeneous contrast enhancement and perilesional oedema, as well as a dural tail, but cannot differentiate high-grade from low-grade meningioma.

DWI with characterization of the ADC value shows that high-grade meningiomas reveal lower ADC values than low-grade meningiomas. High-grade meningioma shows high cellularity with restricted diffusion and decreased ADC value. In case 1 patient with malignant meningioma (WHO grade III) shows a decrease in the ADC value compared to WHO grade II and WHO grade I meningioma. 3D ASL shows a different pattern of rCBF in low-grade and high-grade meningioma, in case 3 patient with low-grade meningioma shows a diffuse pattern of rCBF while in cases 1 and 2 high-grade meningioma shows a heterogeneous pattern of rCBF due to hypoperfusion. DSC MR perfusion shows a decrease in the rCBV value in high-grade meningioma and an increase in the rCBV in low-grade meningioma.

Case 1 and case 2, patient with high-grade meningioma shows type 4-time intensity curve with a fast wash in and wash out while case 3, patient with low-grade meningioma shows type 3 time intensity curve with a fast wash in and plateau phase wash-out, high-grade meningioma shows an increase in peritumoral Ktrans compared to low-grade meningioma, in case 1 and case 2, patients with high-grade meningioma the Ktrans are higher than case 3 with low-grade meningioma.

The grade of a meningioma has important therapeutic and prognostic implications. Therefore, prospective identification of the histological grade of a meningioma by DCE MR perfusion may be clinically beneficial. In most cases, total surgical resection is planned when technically feasible. Preoperative knowledge that one is dealing with atypical or malignant meningioma can lead to alterations in the planned size, shape, and extent of a craniotomy to ensure clean margins. Preoperative knowledge of an atypical and malignant meningioma can also change the risk-benefit assessment of a neurosurgeon. In other words, a surgeon may employ more aggressive surgical technique to achieve a complete Simpson grade I resection.

CONCLUSIONS

Advanced magnetic resonance imaging with ADC value, 3D ASL, DCE MR perfusion, DSC MR perfusion are useful for the diagnosis of high-grade and low-grade meningioma, confirmed with histopathological findings, and helps neurosurgeons plan surgical resection preoperatively.

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STATEMENT OF ETHICS

The authors confirmed that written informed consent was obtained from the patient for the publication of the case (including publication of images). All procedures performed in this study were reviewed and approved by the ethical committee standard of Dr. Soetomo General Hospital with letter of exemption reference number: 0731/LOE/301.4.2/ XII/2021.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.
Figure 2. Presurgery, Female, 63 yo with convexity meningioma at left parietal convexity, attach to the dura, the mass shows slight hypointense in T1 and T2 (A, B), post-contrast shows heterogeneous contrast enhancement with dural tail sign (C, D), peripheral slight restricted diffusion in DWI with ADC values range from 0.714 – 0.799 X 10⁻³ (E, F), DSC MR perfusion shows an increase of rCBV with ratio rCBV compare to the normal brain 7.275 (G, H). Histopathological examination: (I, J) Sections show tumor tissue composed of cells with rounded nuclei, moderately pleomorphic, eccentrically located with abundant cytoplasm giving rhabdoid features. There are also tumor cells having nuclei with pseudonuclear inclusion, and forming a whorls-like pattern, with some psammoma bodies. Mitotic count is 8/10 HPF in the cellular area. Tumor cells islands infiltrate into brain parenchyma.

Figure 3. Recurrent meningioma at surgical bed post-surgery, conventional MRI with contrast study reveals heterogeneous contrast enhancement besides the tumor also along the dura bed (A, B), DWI shows slightly restricted diffusion with ADC value 0.666 – 0.849 X 10⁻³ (C, D), 3D ASL with ratio tumor/normal brain 1.248 (E), DCE MR perfusion TIC type 4 with high increase of maximum slope (F, G), Ktrans peritumoral 0.0594 (H), DSC MR perfusion rCBV 2.979 (I, J)

Figure 4. Left frontal convexity meningioma, well defined border, slight hypointense in T2FSE, heterogeneous contrast enhancement (A-F), 3D ASL rCBF heterogeneous pattern with rCBF 166.6-167.2 (G, H), ADC value 0.747-0.790 (I, J), DCE MR perfusion shows type 4 time- intensity curve with high increase of maximum slope (K, L), Ktrans peritumoral 0.0279 (M). Histopathological examination: (N, O) Cellular tumor tissue forming sheets, syncytium, and whorls structures. Tumors are composed of meningothelial cells with rounded to oval nuclei, some atypical and hyperchromatic, pseudo nuclear inclusions are noted in tumor cells. The Mitotic count is 6/10 HPF. There is infiltration of tumor cells into the brain parenchyma.
Figure 5. Left parieto-occipital convexity meningioma, post-contrast conventional MRI reveals heterogenous contrast enhancement, mild perifocal edema, compression of left lateral ventricle with right midline shift (A,B), 3D ASL shows rCBF 180.4 – 208.9 (C), DWI with ADC value 1.031-1.046 (D,E), DCE MR perfusion TIC type 3 (F,G), Ktrans peritumoral 0.0200 (H), DSC MR perfusion reveals rCBV 28.69 – 36.39 (I,J,K). Histopathological examination (L,M): Microscopic images show pieces of tumor tissue consisting of proliferation of round-oval-infused meningothelial cells, fine chromatin, sufficient cytoplasm, partly with nuclear pseudo inclusion, arranged in sheets, partly forming a whorl pattern. Some tumor cells showed xanthoma degeneration. Mitosis 1/10 HPF. There were no signs of malignancy.

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AUTHOR CONTRIBUTIONS
Sri Andreani Utomo contributed to preparing the research design, collecting and analyzing the patient’s data, writing and submitting the manuscript. Abdul Hafid Bajamal contributed to reviewing this article and advising methodology design. Irwan Barlian contributed to reviewing reports and data collection. Vivid Umi Varidha contributed to reviewing this article and completing the data of the patient. Dyah Fauziah contributed to reviewing this article and the histopathology of the patient Eunike Serfina Fajarini contributed to technical application for MR sequence.

DATA AVAILABILITY STATEMENT
The case report data used to support the findings of this study are included in the article.