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磁共振灌注加权成像与弥散加权成像在脑胶质瘤分级诊断中的应用 *

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摘要 目的:探讨磁共振灌注加权成像(perfusion weighted imaging,PWI)与弥散加权成像(diffusion weighted imaging,DWI)在脑胶质瘤分级诊断中的应用价值。**方法:**选取 2012 年 1 月 -2017 年 6 月在我院就诊并经病理证实为脑胶质瘤患者 100 例,其中高、低级别胶质瘤患者各 44、56 例。对所有患者行 PWI、DWI 检查,比较肿瘤不同区域表观扩散系数(apparent diffusion coefficient,ADC)、局部脑血流量(regional cerebral blood flow,rCBF),不同级别肿瘤实质区、瘤周水肿区 rADC、rrCBF,根据 ROC 曲线分析 rADC、rrCBF 对不同级别胶质瘤的诊断阈值、敏感性、特异性。**结果:**与对侧相应正常脑实质比较,瘤周水肿区及肿瘤实质区 ADC、rCBF 均显著升高(*P<0.05*);与瘤周水肿区比较,肿瘤实质区 ADC、rCBF 均显著升高(*P<0.05*)。高级别肿瘤实质区 rADC 显著低于低级别肿瘤实质区(*P<0.05*),rrCBF 显著高于肿瘤实质区(*P<0.05*)。高级别瘤周水肿区与低级别瘤周水肿区 rADC 间无显著差异(*P>0.05*),高级别瘤周水肿区 rrCBF 显著高于低级别瘤周水肿区(*P<0.05*)。在对高、低级别脑胶质瘤的分级中,rADC、rrCBF 的曲线下面积(under the receiver operating characteristic curve,AUC)分别为 0.957、0.978,均 >0.9。rADC 诊断不同分级胶质瘤的敏感度是 90.12 %,特异度是 95.26 %,诊断阈值是 13.12;rrCBF 诊断不同分级胶质瘤的敏感度是 92.31 %,特异度是 98.57 %,诊断阈值是 2.62。rADC 与 rrCBF 诊断不同分级胶质瘤敏感度、特异度间无显著差异(*P<0.05*)。**结论:**PWI、DWI 能够为脑胶质瘤的分级诊断提供参考依据。

关键词:磁共振灌注加权成像;磁共振弥散加权成像;脑胶质瘤;表观扩散系数;局部脑血流量
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Application of Perfusion Weighted Imaging and Diffusion Weighted Imaging in the Grading Diagnosis of Glioma*

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ABSTRACT Objective: To explore the value of perfusion weighted imaging and diffusion weighted imaging in grading diagnosis of glioma. **Methods:** Selected 100 glioma patients in our hospital from January 2012 to June 2017. Pathologically confirmed high and low grade glioma patients each have 44, 56 cases. All patients underwent PWI, DWI examination. ADC and rCBF of different regions of glioma were compared. The rADC and rrCBF of different grades of tumor parenchyma and peritumoral edema of glioma patients were compared. According to ROC curve, the diagnostic threshold, sensitivity and specificity of rADC and rrCBF in different grades of gliomas were analyzed. **Results:** Compared with corresponding normal brain parenchyma, ADC and rCBF in peritumoral edema and tumor parenchyma were significantly increased (*P<0.05*). Compared with the peritumoral edema area, ADC and rCBF in the parenchyma of the tumor were significantly increased (*P<0.05*). The rADC of the high grade tumor was significantly lower than that of the low grade tumor (*P<0.05*) and rrCBF was significantly higher than that of the tumor (*P <0.05*). There was no significant difference between high-grade peritumoral edema and low-grade peritumoral edema rADC (*P>0.05*). The rrCBF in high-grade peritumoral edema was significantly higher than that in low-grade peritumoral edema (*P<0.05*). According to ROC curve analysis, the area under the curve of rADC and rrCBF under the classification of high and low grade gliomas were 0.957, 0.978. The sensitivity, specificity and threshold value of rADC in diagnosing different grade glioma were 90.12 %, 95.26 % and 13.12, respectively. The sensitivity, specificity and threshold value of rrCBF in diagnosing different grade glioma were 92.31 %, 98.57 % and 2.62 respectively. There was no significant difference between rADC and rrCBF in diagnosis of gliomas with different grading (*P<0.05*). **Conclusions:** PWI, DWI can provide a reference for the grading diagnosis of gliomas.

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前言

脑胶质瘤是源自神经上皮的肿瘤，也称为胶质细胞瘤，占颅脑肿瘤的 40-50 %，是颅脑中枢神经系统最常见的原发性肿瘤[1-3]。脑胶质瘤在发生初期并没有典型的症状，随着肿瘤的不断扩大会出现颅内压增高、头痛、呕吐、视力衰减、癫痫等症状，脑组织受到肿瘤的压迫、浸润和破坏会产生局部症状，症状会因肿瘤生长位置的不同而有差异[4-6]。按照世界卫生组织(world health organization，WHO)2007 年分类标准，胶质瘤可分为低级别胶质瘤 I、II 级和高级别胶质瘤 III、IV 级共 4 级，随着级别数的升高胶质瘤的恶性程度随之升高[7]。针对不同恶化程度的胶质瘤患者需要选择与之相适的治疗方案和手术疗法，故脑胶质瘤的准确分级对临床治疗及预后有很重要的价值[8-10]。临床上采用的常规磁共振成像(magnetic resonance imaging，MRI)可对胶质瘤进行定性诊断，但对不同级别胶质瘤的分级准确性不高、效果不够明显，PWI 和 DWI 是对 MRI 诊断脑胶质瘤的很好补充[11-13]。本研究应用 PWI 和 DWI 对脑胶质瘤患者进行分级诊断，旨在为脑胶质瘤的诊断分级提供参考，现报道如下。

1 材料与方法

1.1 一般资料

选取 2012 年 1 月 -2017 年 6 月 100 例在我院就诊并经病理证实为脑胶质瘤患者，其中男性、女性分别有 68、32 例，年龄 22-78 岁，平均年龄(53.63 6.57)岁。按照 WHO(2000 年)病理分级标准：低级别胶质瘤 56 例 (WHO I 级 26 例，WHO Ⅱ级 30 例)，其中男性 37 例，女性 19 例，平均年龄(52.26 7.84)岁；高级别胶质瘤 44 例(WHO Ⅲ级 9 例，Ⅳ级 35 例)，其中男性 31 例，女性 13 例，平均年龄(54.68 6.47)岁。所有患者术前均行 PWI、DWI 检测，本研究已通过我院伦理委员会审核和批准。

1.2 纳入及排除标准

纳入标准：① 检查前未经放射或药物治疗；② 经病理证实为原发性胶质瘤；③ 患者资料完整、图像清晰；④ 患者本人及家属对本研究知情且已签署同意书。

排除标准：① 合并重大器官疾病者；② 不可行行常规磁共振平扫、PWI 及 DWI 检测者；③ 存在其他炎症性疾病，局部有坏死或钙化灶；④ 资料不全、图像不清晰者。

1.3 方法

使用 1.5T 磁共振成像仪(美国 GE Discovery MR750)和 8 通道相控阵头线圈(美国 GE Medical System)进行检查，造影剂使用钆贝葡胺(Gd-BOPTA)。

DWI：采用单次自旋回波成像序列，弥散敏感梯度依次施加 P(相位编码方向)、M(测量编码方向)、S(频率编码方向)三个不同的方向。扫描参数：TR 5000 ms，TE 104 ms，层厚 6.5 mm，层间距 1.5 mm，视野(FOV)230 mm，矩阵 256× 256，共 16 层，弥散系数 b 值分别为 0、1000。

PWI：采用梯度回波 EPI 成像序列，根据常规 T2WI 上病变范围选择 7-10 个层面，每层采集 100 幅图像，成像时间 41s。扫描参数：TR 1500ms，TE 26 ms，层厚 6 mm，层间距 0.1 mm，视野(FOV)240 mm，矩阵 130× 128，激励数 1.00。成像时间 68 s，翻转角 90° 。

1.4 图像分析

经 DWI 和 PWI 扫描后，使用 GE Advantage Workstation 4.2 (AW4.2)工作站对所得的原始图像进行处理。① 测量肿瘤实质区、瘤周水肿区及对侧相应正常脑实质的表观扩散系数(apparent diffusion coefficient，ADC)、局部脑血流量(regional cerebral blood flow，rCBF)；② 计算相对 ADC (relative ADC，rADC)、相对 rCBF(relative rCBF，rrCBF)，相对值 = 肿瘤实质区(或瘤周水肿区)量化值 / 对侧相应正常脑实质量化值；③ 通过 ROC(receiver operating characteristic)曲线分析比较 ADC、rCBF 值对诊断高、低级别脑胶质瘤的准确性，确定诊断阈值，计算敏感度与特异度。

1.5 统计学分析

用 SPSS 20.0 软件对数据进行分析，计量资料用($\bar{x}\pm s$)表示，组间进行 t 检验或单因素方差分析，以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 病理学检查结果

按照世界卫生组织 (world health organization，WHO)(2007 年)的病理分级标准，低级别脑胶质瘤患者有 56 例，I 级 26 例，Ⅱ级 30 例；高级别脑胶质瘤患者有 44 例，Ⅲ级 9 例，Ⅳ级 35 例。

2.2 肿瘤不同区域 ADC、rCBF 值的比较

与对侧相应正常脑实质比较，瘤周水肿区及肿瘤实质区 ADC、rCBF 均显著升高($P<0.05$)；与瘤周水肿区比较，肿瘤实质区 ADC、rCBF 均显著升高($P<0.05$)。见表 1。

2.3 不同级别肿瘤实质区 rADC、rrCBF 值的比较

高级别肿瘤实质区 rADC 显著低于低级别肿瘤实质区($P<0.05$)，rrCBF 显著高于肿瘤实质区($P<0.05$)，见表 2。

2.4 不同级别瘤周水肿区 rADC、rrCBF 值的比较

高级别瘤周水肿区与低级别瘤周水肿区 rADC 间无显著差异($P>0.05$)，高级别瘤周水肿区 rrCBF 显著高于低级别瘤周水肿区($P<0.05$)，见表 3。

2.5 ROC 曲线分析 rADC、rrCBF 值诊断脑胶质瘤的价值

根据 ROC 曲线分析，在对高、低级别脑胶质瘤的分级中，rADC、rrCBF 的曲线下面积(under the receiver operating characteristic curve，AUC)分别为 0.957、0.978，均 >0.9。rADC 诊断不同分级胶质瘤的敏感度是 90.12 %，特异度是 95.26 %，诊断阈值是 13.12；rrCBF 诊断不同分级胶质瘤的敏感度是 92.31 %，特异度是 98.57 %，诊断阈值是 2.62。rADC 与 rrCBF 诊断不同

表 1 肿瘤不同区域 ADC、rCBF 值的比较 ($\bar{x}\pm s$)

Table 1 Comparison of the ADC and rCBF values among different tumor areas ($\bar{x}\pm s$)

Areas	ADC (× 10^{-10} m^2/s)	rCBF (mL/(100 g· min))
Normal brain parenchyma	7.780.83	235.3456.82
Peritumoral edema area	11.013.18[a]	347.73121.57[a]
Tumor parenchyma	14.743.32[ab]	672.84237.25[ab]
P	0.000	0.000

Note: compared with normalbrain parenchyma, [a]*P<0.05*; compared with peritumoral edema area, [b]*P<0.05*.

表 2 不同级别肿瘤实质区 rADC、rrCBF 值的比较 ($\bar{x}\pm s$)

Table 2 Comparison of the rADC and rrCBF values among different grades of tumor parenchyma($\bar{x}\pm s$)

Grade	Cases	rADC	rrCBF
Low level	56	2.120.33	1.610.41
High level	44	1.430.26[a]	4.521.12[a]
P		0.000	0.000

Note: compared with low level grade, [a]*P<0.05*.

表 3 不同级别瘤周水肿区 rADC、rrCBF 值的比较($\bar{x}\pm s$)

Table 3 Comparison of the rADC and rrCBF values among different stages of peritumoral edema($\bar{x}\pm s$)

Grade	Cases	rADC	rrCBF
Low level	56	1.220.21	1.130.25
High level	44	1.150.24	1.520.31[a]
P		0.123	0.000

分级胶质瘤敏感度、特异度间无显著差异(x^2_1=0.244，P_1=0.621；x^2_2=2.749，P_2=0.097)。

3 讨论

不同级别的胶质瘤的治疗方法有所差异，脑胶质瘤患者需要根据高低级别选择是否在手术切除后联合放疗或化疗进行治疗，高级别胶质瘤患者需要而低级别患者不需要，故脑胶质瘤的准确分级对于临床治疗及预后有着重要的影响[14,15]。常规 MRI 在检测脑胶质瘤的出血、坏死、展位效应及瘤周水肿等有一定帮助，有报道显示低级别胶质瘤常规 MRI 影像学表现出信号均匀、多无强化、占位效应不明显、瘤周水肿轻等，而高级别胶质瘤常规 MRI 影像学表现出信号不均匀、明显强化、占位效应明显、瘤周水肿明显等，以上特征对于胶质瘤的分级具有一定帮助[16-18]。以往临床中常将肿瘤强化与否作为鉴别良恶性胶质瘤的重要指标，但有时高、低级别胶质瘤在 T1 加权成像(T1 weighted image，T1WI)和 T2 加权成像(T2 weighted image，T2WI)序列上有相似的影像学表现，且有报道显示 10-20 %的低级别胶质瘤会表现出强化，月 10-38 %高级别胶质瘤不强化或仅有轻度强化，说明肿瘤强化与恶性程度并非完全一致，故常规 MRI 对不同级别胶质瘤的分级准确性不高、应用效果不明显[19-21]。

PWI 是一种无创性测量脑灌注的新技术，通过特定脑区血流的比对剂(包括内源性和外源性)引起的信号变化来测量局部脑血容量、脑血流量、毛细血管通透性等微观血流动力学相关信息，可以反映组织血流灌注功能及血管生成情况。由于肿瘤恶性程度与微血管结构、肿瘤细胞增值情况密切相关，故 PWI 较常规 MRI 课提供更多的胶质瘤分级的鉴别诊断信息[22-24]。本研究结果显示与对侧相应正常脑实质比较，肿瘤实质区、瘤周水肿区 rCBF 显著升高；与瘤周水肿区比较，肿瘤实质区 rCBF 显著升高。以上结果说明胶质瘤患者肿瘤组织的局部脑血流量相较于正常脑组织显著加大。对于不同级别胶质瘤患者，本研究结果显示高级别肿瘤实质区、瘤周水肿区 rrCBF 显著高于低级别肿瘤实质区；根据 ROC 曲线分析，在对高、低级别脑胶质瘤的分级中，rrCBF 诊断不同分级胶质瘤的敏感度是 92.31 %，特异度是 98.57 %，诊断阈值是 2.62。以上结果说明 PWI 技术的 rrCBF 对高低级别胶质瘤的诊断与鉴别效果较好。

DWI 通过水分子的微观弥散运动基于平面回波技术进行成像，可以反映活体组织的空间组成信息以及组织在病理状态下成分间的分子交换的功能状况，是一种无创性磁共振技术[25-27]。本研究结果显示与对侧相应正常脑实质比较，肿瘤实质区、瘤周水肿区 ADC 显著升高；与瘤周水肿区比较，肿瘤实质区 ADC 显著升高。以上结果表明胶质瘤患者肿瘤组织的表观扩散系数相较于正常脑组织显著加大。有报道显示高级别胶质瘤除了因血脑屏障被破坏、血管的渗透性增加而引起的间质水分增加外，还有肿瘤细胞的浸润，而低级别胶质瘤的肿瘤侵袭较少，瘤周肿瘤细胞的浸润也较少，故二者的组织结构变化不同、水分子扩散能力的变化也有差异[28-30]。本研究结果中，不同级别及不同部位的 ADC 值表现可以用以上叙述进行解释。对于不同级别胶质瘤患者，本研究结果显示高级别肿瘤实质区 rADC 显著高于低级别肿瘤实质区，而不同级别瘤周水肿区的

rADC 差异不显著。另外，根据 ROC 曲线分析，在对高、低级别脑胶质瘤的分级中，rADC 诊断不同分级胶质瘤的敏感度是 90.12 %，特异度是 95.26 %，诊断阈值是 13.12。以上结果说明 DWI 技术的 rADC 对高低级别胶质瘤的诊断与鉴别效果较好。综上所述，PWI 和 DWI 这两种无创性磁共振技术均可为脑胶质瘤的分级诊断提供帮助。

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