论著·肝癌诊疗新策专题

增强MRI联合表观弥散系数在肝原发性黏膜相关淋巴组织淋巴瘤与肝细胞癌中的鉴别诊断价值

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[摘要] **目的** 探究增强MRI影像特征联合表观弥散系数(apparent diffusion coefficient, ADC)在肝原发性黏膜相关淋巴组织(mucosa-associated lymphoid tissue,MALT)淋巴瘤与肝细胞癌(hepatocellular carcinoma, HCC)中的鉴别诊断价值。**方法** 纳入1997年1月至2025年5月在陆军军医大学第一附属医院放射科经病理证实的10例肝原发性MALT淋巴瘤患者和20例HCC患者的临床资料,分析增强MRI图像,主要包括肿瘤数目、形态、信号特征、强化方式以及有无血管漂浮征,同时在ADC图测量ADC值,筛选有统计学意义的变量。采用Firth回归分析筛选肝原发性MALT淋巴瘤的独立预测因素。运用受试者工作特征(receiver operating characteristic,ROC)曲线下面积(area under the curve,AUC)评估诊断效能。**结果** 肝原发性MALT淋巴瘤组与HCC组对比,女性发病率更高(P=0.026),多数患者AFP<8 ng/mL(P<0.001),T2WI信号较低(P=0.001),ADC值更低(P<0.001),病灶多呈持续强化(P<0.001),更易出现血管漂浮征(P=0.008)。单因素Firth回归分析显示,性别(95%*CI*:1.36~52.10,P=0.020)、T2WI信号(95%*CI*:3.89~5 121.00,P<0.001)、AFP(95%*CI*:0~0.21,P<0.001)、ADC值(95%*CI*:0~0.21,P<0.001)、动态强化方式(95%*CI*:0~0.23,P<0.001)、血管漂浮征(95%*CI*:0~0.40,P=0.004)是诊断肝原发性MALT淋巴瘤的预测因素。多因素Firth回归分析显示,ADC值(95%*CI*:0.00~0.62,P=0.006)、AFP(95%*CI*:0~0.05,P=0.01)和动态强化方式(95%*CI*:0~0.39,P=0.005)是诊断肝原发性MALT的独立预测因素。ADC值诊断肝原发性MALT淋巴瘤的AUC为0.96(敏感性为0.8,特异性为1.0);AFP诊断肝原发性MALT淋巴瘤的AUC为0.85(敏感性为1.0,特异性为0.7);动态强化方式诊断肝原发性MALT淋巴瘤的AUC为0.85(敏感性为0.8,特异性为0.9)。**结论** 动态强化方式与ADC值可作为肝原发性MALT淋巴瘤与HCC的鉴别标志,为临床术前评估提供参考。

[关键词] 肝原发性黏膜相关淋巴组织淋巴瘤;增强磁共振成像;表观弥散系数

[中图法分类号] R445.2;R733.4;R735.7 [文献标志码] A

Differential value of enhanced MRI combined with ADC between hepatic primary mucosa-associated lymphoid tissue lymphoma and hepatocellular carcinoma

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[**Abstract**] **Objective** To investigate the value of enhanced MRI image features combined with apparent diffusion coefficient(ADC) in the differential diagnosis of primary hepatic mucosa-associated lymphoid tissue(MALT) lymphoma and hepatocellular carcinoma(HCC). **Methods** The clinical data of 10 patients with pathology-confirmed primary MALT lymphoma admitted in our hospital from January 1997 to

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May 2025 were retrospectively collected. Their enhanced MRI images were analyzed, mainly including the number of lesions, morphology, signal characteristics, enhancement methods, and presence or absence of vessel floating signs, and the ADC value was calculated in order to screen statistically significant variables. Firth regression analysis was used to screen independent predictors of primary MALT lymphoma in the liver. Receiver operating characteristic(ROC) curve was plotted, and the area under the curve(AUC) was calculated to evaluate the diagnostic efficacy. **Results** Compared with the HCC group, the primary MALT lymphoma group had significantly higher incidence in the females(P=0.026), alpha-fetoprotein(AFP) <8 ng/mL(P<0.001), lower T2WI signal(P=0.001), lower ADC value(P<0.001), and mostly continuously enhanced lesions (P<0.001), and more vessel floating signs(P=0.008). Univariate Firth regression analysis showed that sex (95%*CI*: 1.36~52.10, P=0.020), T2 value(95%*CI*: 3.89~5 121.00, P<0.001), AFP(95%*CI*: 0~0.21, P<0.001), ADC value(95%*CI*: 0~0.21, P<0.001), and dynamic reinforcement(95%*CI*: 0~0.23, P<0.001), and vessel floating sign(95%*CI*: 0~0.40, P=0.004) were diagnostic predictors for primary MALT lymphoma of the liver. Multivariate Firth regression analysis indicated that ADC value(95%*CI*: 0~0.62, P=0.006), AFP (95%*CI*: 0~0.047, P=0.01), and dynamic reinforcement(95%*CI*: 0~0.39, P=0.005) were independent predictors for primary MALT in the liver. ROC curve analysis indicated that the AUC value of ADC value in diagnosing primary MALT lymphoma was 0.96, with a sensitivity of 0.8 and a specificity of 1.0, and the AUC value of AFP level in diagnosing primary MALT lymphoma was 0.85, with a sensitivity of 1.0 and a specificity of 0.7. The AUC value of dynamic reinforcement in diagnosing primary MALT lymphoma was 0.85, with a sensitivity of 0.8, and a specificity of 0.9. **Conclusion** Dynamic reinforcement and ADC value can be used as differential markers for primary MALT lymphoma and HCC, providing reliable reference for clinical preoperative evaluation.

[**Key words**] primary hepatic mucosa-associated lymphoid tissue lymphoma; enhanced magnetic resonance imaging; apparent diffusion coefficient

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原发性肝淋巴瘤(primary hepatic lymphoma,PHL)是一种无肝外浸润的淋巴组织增生性疾病[1],发病率占所有非霍奇金淋巴瘤(non-Hodgkin lymphoma,NHL)病例的0.016%[2]。黏膜相关淋巴组织(mucosa-associated lymphoid tissue,MALT)淋巴瘤在所有非霍奇金淋巴瘤中占比7%~8%[3],是少见类型,主要发生部位是胃[4]。肝原发性MALT淋巴瘤极为罕见,且术前极易误诊为肝细胞癌(hepatocellular carcinoma,HCC)[5]。HCC常通过手术或射频消融进行治疗,术后5年生存率仅为40%~50%[6];而肝原发性MALT淋巴瘤通过化疗能达到良好的治疗效果[7],10年生存率高达90%[8]。由于二者在治疗及预后存在显著差异,术前准确诊断在治疗决策中具有重要临床意义。

增强MRI是肝脏占位检测和分析最有效的方法,其多序列成像在肝脏病变的鉴别诊断中具有独特优势[9]。定量MRI技术可提供反映肿瘤细胞性、增殖状态等相关特征的成像标志物;其中,磁共振弥散加权成像(magnetic resonance diffusion-weighted imaging, MR-DWI)以表观弥散系数(apparent diffusion coefficient, ADC)量化,可间接反映肿瘤的细胞密度构成[10]。较多研究报道,增强MRI与ADC值相结合可为肝脏占位鉴别诊断提供可靠依据[11-12]。

然而,关于肝原发MALT淋巴瘤及HCC的影像学相关文献较少。因此,本研究回顾性收集陆军军医大学第一附属医院肝原发性MALT淋巴瘤和HCC患者的临床资料,通过分析增强MRI图像与ADC值相结合,对比二者之间存在的差异,同时评估诊断效能,为临床术前评估提供可靠的理论参考。

1 资料与方法

1.1 一般资料

回顾性收集1997年1月至2025年5月在陆军军医大学第一附属医院放射科的肝原发性MALT淋巴瘤患者及HCC患者。纳入标准:①经病理证实的肝原发性MALT淋巴瘤患者及HCC患者;②行增强MRI检查,且图像质量符合诊断标准;③临床资料、病理结果齐全;④未行任何临床治疗。排除标准:合并其他恶性肿瘤。根据纳排标准最终纳入30例患者,其中肝原

发性MALT淋巴瘤患者10例、HCC患者20例。本研究已通过陆军军医大学第一附属医院伦理委员会审查批准(BIIT2024177KX)。

1.2 增强MRI检查

采用Siemens Trio Tim 3.0T(德国西门子公司),相控阵线圈为18。扫描半傅里叶采集单次激发自旋回波(half-fourier acquisition single-shot turbo spin-echo,HASTE)序列冠状位、容积内插体部检查(volumetric-interpolated body examination,VIBE)序列平扫轴位、同反相位,从0和1 000 s/mm^{2}的b值(b=200、400、600、800)生成表观扩散系数图。注射剂量根据0.1 mL/kg Gd-EOB-DTPA于肘静脉,速度1.0 mL/s,于对比剂约平至胸主动脉下段水平时患者屏气开始进行动脉期扫描,持续20~30 s,门静脉期图像于延时70 s后获得,移行期图像于延迟180 s后获得,然后行磁敏感加权成像序列扫描,肝胆期图像于延时15 min后获得。

1.3 图像评估

由2名陆军军医大学第一附属医院放射科腹部组高年资医师(工作时间>8年)在未知病理结果情况下,采用盲法进行独立影像评估,若意见不一致,再邀请第三位高年资医师共同诊断,并且经过协商后完全达成一致。评估内容主要包括:肿瘤数目、形态、边缘、有无钙化、脂肪、囊变、出血、TIWI信号、T2WI信号、ADC值、MRI强化方式(轻度持续强化,快进快出强化)、有无血管穿透标志(定义为解剖学上预先存在的肝动脉、门静脉和肝静脉穿行于肿瘤)、有无肝胆期斑点状增强[16](定义为低信号肿瘤内的点状阳性造影剂摄取)。

1.4 统计学分析

采用SPSS 23.0软件进行统计分析,符合正态分布的计量资料以$\bar{x}\pm s$表示,两组比较采用独立样本t检验;不符合正态分布的计量资料用$M(P_{25},P_{75})$表示,两组比较采用Mann-Whitney U检验;分类变量比较采用Fisher精确检验。采用R 4.4.0软件Firth回归分析筛选肝原发性MALT淋巴瘤的独立预测因素,P<0.05为差异具有统计学意义。运用受试者工作特征曲线(receiver operating characteristic,ROC)评估各参数的诊断效能。利用R 4.4.0语言的ggplot2及ggrain包绘制云雨图,展示肝原发性MALT淋巴瘤和HCC组间ADC值的分布特征。

2 结果

2.1 临床资料及MRI增强特征

肝原发性MALT淋巴瘤、HCC组分别对性别、年龄、乙肝病毒感染史、AFP值、肿瘤最大径、病灶数量、肿瘤边界、病灶内有无囊变、脂肪、钙化、坏死信号、T1、T2WI信号、ADC值、动态强化方式、血管漂浮征以及肝脏期斑点状强化进行比较,结果提示:肝原发性MALT淋巴瘤组与HCC组对比,女性发病率更高(P=0.026),多数患者AFP<8 ng/mL(P<0.001),T2WI信号较低(P=0.001),ADC值更低(P<0.001),病灶多呈持续强化(P<0.001),更易出现血管漂浮征(P=0.008)。肝原发性MALT淋巴瘤组较HCC组对比,患者年龄、有无乙肝病毒感染、肿瘤最大径、病灶数量、肿瘤边界、病灶内有无囊变、脂肪、钙化、坏死信号、T1WI信号、及肝脏期斑点状强化差异无统计学意义,见表1。肝原发性黏膜相关淋巴组织淋巴瘤与肝细胞癌组间ADC值分布特征,见图1。

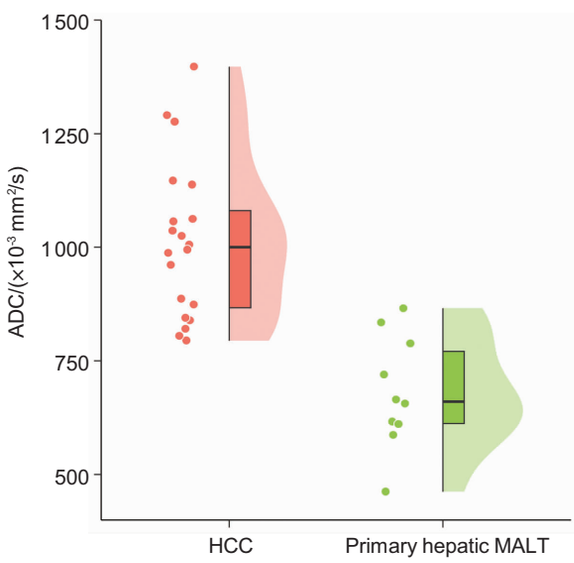


图1 肝原发性黏膜相关淋巴组织淋巴瘤与肝细胞癌组间ADC值分布特征的云雨图

Figure 1 Cloud-rain diagram of ADC distribution characteristics between hepatic primary MALT lymphoma and HCC groups

2.2 特征预测因素筛选

单因素Firth回归分析筛选诊断肝原发性MALT淋巴瘤的预测因素。结果显示,性别(95%CI:1.36~52.10,P=0.020)、T2WI信号(95%CI:3.89~5 121.00,P<0.001)、AFP(95%CI:0~0.21,P<0.001)、ADC值(95%CI:0~0.21,P<0.001)、动态强化方式(95%CI:0~0.23,P<0.001)、血管漂浮征(95%CI:0~0.40,P=0.004)是诊断肝原发性MALT淋巴瘤的预测因素。患者年龄、肿瘤最大直径、病灶数目(≥2个)、肿瘤边界、T1WI信号以及肝胆期斑点状增强与目标结局的关联均无统计学意义,见表2。

表1 肝原发性黏膜相关淋巴组织淋巴瘤与肝细胞癌的临床特征[例(%),$\bar{x}\pm s$,$M(P_{25},P_{75})$]

Table 1 Clinical features of hepatic primary MALT lymphoma and HCC [n(%),$\bar{x}\pm s$,$M(P_{25},P_{75})$]

Characteristics	Primary hepatic MALT(n=10)	HCC(n=20)	P	t/U
Gender			0.026	
male	5(50)	18(90)		
female	5(50)	2(10)		
Age/years	52.50±6.84	52.35±15.25	0.971	0.037
HBV infection			0.333[a]	
yes	9(90)	20(100)		
no	1(10)	0		
AFP>8 /(ng/mL)			<0.001[a]	
no	10(100)	6(30)		
yes	0	14(70)		
Maximum diameter /cm	3.00(1.68, 3.95)	3.40(2.58, 5.20)	0.344	78
Number of lesions			1[a]	
one	9(90)	19(95)		
⩾two	1(10)	1(5)		
Boundaries			0.419[a]	
clear	8(80)	12(60)		
unclear	2(20)	8(40)		
T1WI			0.074[a]	
low	10(100)	14(70)		
mixed	0	6(30)		
T2WI			0.001[a]	
high	0	13(65)		
mixed, slightly higher	10(100)	7(35)		
Calcification, Fat, Cystic			-	-
yes	0	0		
no	0	0		
Hemorrhage			0.074	
yes	10(100)	14(70)		
no	0	6(30)		
ADC($\times10^{-3}$ mm^2/s)	681.00±124.00	1 012.00±171.00	<0.001	−6.056
Dynamic reinforcement			<0.001[a]	
continue to strengthen	8(80)	2(10)		
fast in and out	2(20)	18(90)		
Vessel floating signs			0.008[a]	
yes	6(60)	20(100)		
no	4(40)	0		
Speckled enhancement			0.103[a]	
yes	8(80)	20(100)		
no	2(20)	0		

a:*Fisher's* exact test

针对以上预测因素,分别构建2个多因素Firth回归模型,结果显示:ADC值(95%*CI*:0~0.62,*P*=0.006)、AFP(95%*CI*:0~0.05,*P*=0.010)和动态强化方式(95%*CI*:0~0.39,*P*=0.005)是诊断肝原发性MALT的独立预测因素,见表3。

2.3 基于Firth回归分析诊断效能评估

ADC值诊断肝原发性MALT淋巴瘤的曲线下面积为0.96(敏感性为0.8,特异性为1.0);AFP诊断肝原发性MALT淋巴瘤的AUC为0.85(敏感性为1.0,特异性为0.7);动态强化方式诊断肝原发性MALT淋巴瘤的AUC为0.85(敏感性为0.8,特异性为0.9),见表4、图2。

2.4 肝原发性MALT淋巴瘤患者与HCC患者MRI图像比较

肝原发性MALT淋巴瘤患者的增强MRI图像显

表2 单因素Firth回归分析肝原发性黏膜相关淋巴组织淋巴瘤与肝细胞癌的临床资料、MRI影像学特征

Table 2 Univariate Firth regression analysis of clinical data and MRI imaging characteristics of primary MALT lymphoma of the liver and HCC

Characteristics	*OR*	95%*CI*	*P*
Gender			
male	ref	ref	
female	7.40	1.36~52.10	0.020
Age	1.00	0.94~1.06	0.940
Maximum diameter	0.89	0.60~1.22	0.510
Number of lesions			
one	ref	ref	
≥two	2.05	0.15~28.00	0.620
Boundaries			
clear	ref	ref	
unclear	0.43	0.07~2.09	0.310
T1WI			
mixed	ref	ref	
low	9.41	0.93~1 278.00	0.060
T2WI			
mixed, slightly higher	ref	ref	
high	37.80	3.89~5 121.00	<0.001
ADC	0.02	0~0.21	<0.001
AFP(>8 ng/mL)			
no	ref	ref	
yes	0.02	0~0.21	<0.001
Dynamic reinforcement			
continue to strengthen	ref	ref	
fast in and out	0.04	0~0.23	<0.001
Vessel floating signs			
yes	ref	ref	
no	0.04	0~0.40	0.004
Speckled enhancement			
yes	ref	ref	
no	0.08	0~1.16	0.070

示:肿瘤T1WI呈低信号、T2WI呈高信号,边界较清,未见明显囊变、出血及坏死(图3A、B);肿瘤DWI明显增高(b=800),ADC明显减低(图3C、D);肿瘤动态增强可见轻度持续强化,并在增强各期存在血管飘浮征,肝胆期病灶边缘可见小结节状斑点样强化(图3E~H)。

HCC患者的增强MRI图像显示:肿瘤T1WI呈低信号、T2WI呈稍高信号,边界欠清,病灶内可见少许出血(图4A、B);肿瘤DWI增高(b=800),ADC稍减低(图4C、D);动态增强动脉期可见明显不均匀强化,门静脉期及移行期强化减低,呈快进快出强化方式,肝胆期病灶呈明显低信号,未见斑点样强化(图4E~H)。

表3 多因素Firth回归分析肝原发性MALT淋巴瘤与HCC的临床资料、MRI影像学特征

Table 3 Multivariate Firth regression analysis of clinical data and MRI imaging characteristics of primary MALT lymphoma of the liver and HCC

Characteristics	Expβ	95%*CI*	*P*
Model 1			
Gender			
male	ref	ref	
female	6.00	0.11~4 912.00	0.400
T2WI			
mixed, slightly higher	ref	ref	
high	12.20	0.89~1 710.00	0.060
ADC	0.10	0~0.62	0.006
Model 2			
AFP(>8 ng/mL)			
no	ref	ref	
yes	0.02	0~0.05	0.010
Dynamic reinforcement			
continue to strengthen	ref	ref	
fast in and out	0.03	0~0.39	0.005
Vessel floating signs			
yes	ref	ref	
no	0.09	0~2.83	0.200

表4 临床资料、MRI影像征象在肝原发性MALT淋巴瘤与HCC的诊断效能

Table 4 Diagnostic efficacy of clinical data and MRI imaging signs in primary MALT lymphoma of the liver and HCC

Predictors	AUC	95%*CI*	Sensitivity	Specificity
AFP	0.85	0.747~0.953	1.0	0.7
ADC	0.96	0.897~1.000	0.8	1.0
Dynamic reinforcement	0.85	0.703~0.997	0.8	0.9

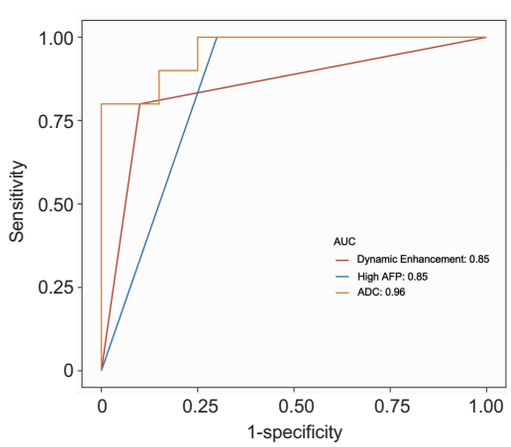
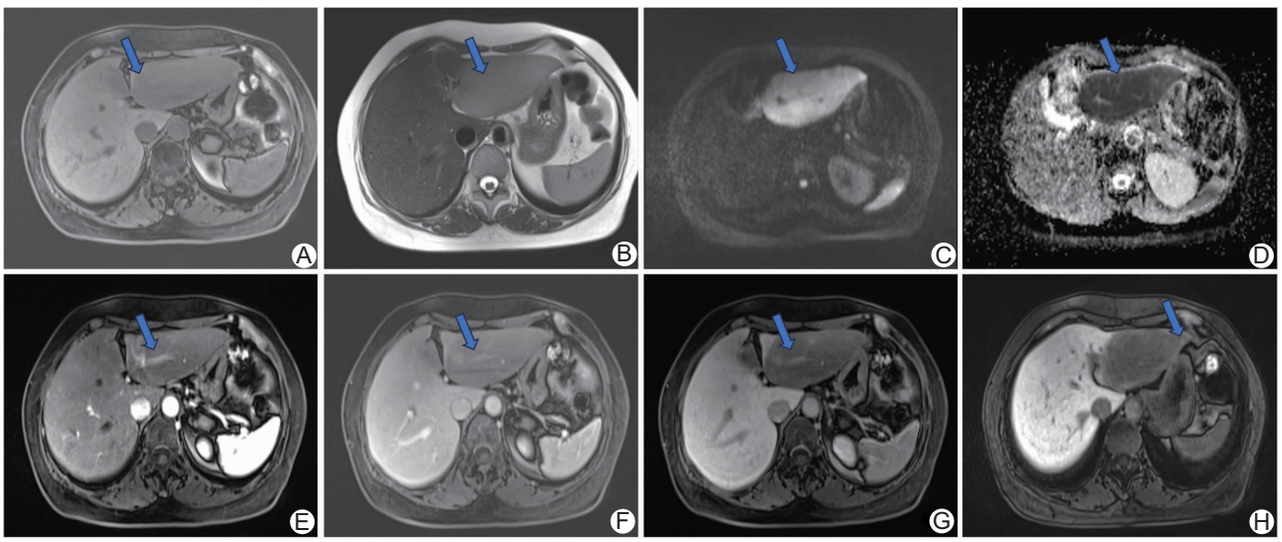


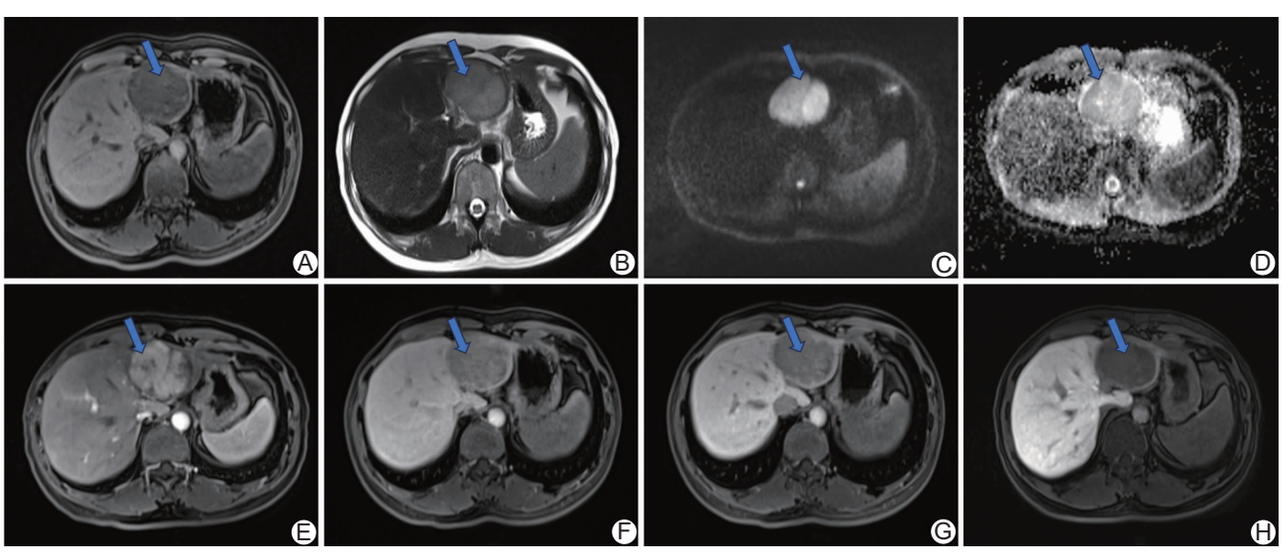
图2 临床资料、MRI影像征象在肝原发性MALT淋巴瘤与HCC诊断效能ROC曲线

Figure2 ROC curve analysis for clinical data, MRI imaging signs in the diagnosis of hepatic primary MALT lymphoma of the liver and HCC



Blue arrows: primary MALT lymphoma in the left lobe of the liver
A and B: T1 and T2 images at the cross-sectional position; C and D: Cross-sectional diffusion-weighted images; E~H: Cross-sectional MRI enhanced images (arterial, portal vein, transitional, hepatobiliary)

图3 原发性MALT淋巴瘤患者的增强MRI图像
Figure 3 Enhanced MRI images of a patient with hepatic primary MALT lymphoma



Blue arrows: HCC in the left lobe of the liver
A and B: T1 and T2 images at the cross-sectional position; C and D: Cross-sectional diffusion-weighted images; E~H: Cross-sectional MRI enhanced images (arterial, portal vein, transitional, hepatobiliary)

图4 HCC患者的增强MRI图像
Figure 4 Enhanced MRI images of a HCC patient

3 讨论

本研究讨论了增强MRI影像特征联合ADC在肝原发性MALT淋巴瘤与HCC中的鉴别诊断价值。结果表明,增强MRI联合ADC值具有良好的诊断效能,能够为临床术前诊断提供可靠的诊断评估。

3.1 ADC在肝原发性MALT淋巴瘤的诊断价值

通过DW-MRI对ADC进行定量已在许多研究中用于局灶性肝脏病变的非侵入性评估[13-14],具有良好的诊断性能。ADC值反映水分子在组织内的随机扩散运动状况。良性肿瘤通常细胞密度较低,细胞间隙较大,水分子扩散受限程度低,故ADC值较高。淋巴

瘤的恶性风险与其肿瘤细胞的增殖、浸润及转移等生物学行为密切相关。由于这些行为显著影响组织细胞密度和微观结构,水分子扩散速度可作为评估相关生物学特性的影像学指标。有研究表明淋巴瘤通常比大多数其他癌症或炎症过程具有更大的弥散受限[15]。COLAGRANDE等[16]比较肝原发性恶性淋巴瘤与HCC的平均ADC值,将0.918×10^{-3} mm^2/s为诊断临界值,其敏感性为91.9%,特异性为100%。HYODO等[17]收集了5例肝原发性MALT患者研究提示,其平均ADC值相对于HCC比较,具有更高的弥散受限,平均ADC值不超过0.823×10^{-3} mm^2/s。本研究发现,肝原发性MALT淋巴瘤组ADC值显著低于HCC组,这与上述报道的淋巴瘤ADC值差异趋势一致,其临界值(0.791×10^{-3} mm^2/s)较先前研究更低,可能由于COLAGRANDE等[16]研究主体以弥漫大B细胞淋巴瘤为主,侵袭性较强,而本研究中,主体为肝原发性MALT淋巴瘤,肝原发性MALT淋巴瘤为惰性淋巴瘤[18],肿瘤生物特性存在显著差异。这表明ADC值有助于鉴别肝原发性MALT淋巴瘤及HCC,并且ADC值的大小可以一定程度上区分病灶肿瘤某些生物特性[13]。

3.2 动态强化方式在肝原发性MALT淋巴瘤的诊断价值

肝原发性MALT淋巴瘤组多表现为“轻度持续强化”,与既往研究报道基本相符[4]。实质性脏器淋巴瘤细胞核仁较大,富含液体的胞质较少,同时肿瘤细胞间排列密集,肿瘤血管及间质成分相对较少,对比剂进入瘤体时较缓慢,故部分肝脏淋巴瘤增强扫描呈现出渐进性轻中度强化[19]。但肝原发性MALT淋巴瘤组更易出现血管漂浮征及肝胆期斑点状增强。由于肝原发性MALT淋巴瘤起源于肝脏间质,部分肿瘤内可见肝脏固有血管,其在动态增强MRI中显示为血管穿行于肿瘤内但未受侵犯的特征,反映MALT惰性生物学行为[20]。HYODO等[17]的研究中,在80%的病例中观察到,并认为这种斑点状增强是由于保留在肿瘤内的肝细胞簇对肝细胞特异性造影剂的阳性摄取,反映了边缘区B细胞淋巴瘤细胞的侵袭性较低,并且从未在HCC或其他侵袭性肿瘤中观察到这种影像改变。在本组患者所有病变中,均未观察到无脂肪、钙化、囊变,表明斑点状增强并不代表血管间隙中造影剂的积聚,从而这进一步证实了其强化方式,与HCC存在差异。

本研究尚存在一些局限性:①由于该病的罕见性,样本量较少,研究结果可能存在一定的偏倚,未来仍需要进行多年回顾或多中心收集、进一步扩大样本量;②对于ADC值b值选取较为单一,缺乏对于肝原发性MALT淋巴瘤的病理特征相结合,后续工作将纳入更多b值及病理相关性探究。

综上所述,动态强化方式与ADC值可作为肝原发性MALT淋巴瘤与HCC的鉴别标志,为临床术前评估提供可靠的理论参考。

利益冲突 本文所有作者声明不存在利益冲突

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