论著

# Gd-EOB-DTPA增强 MRI对无周围胆管扩张 的肿块型肝内胆管癌中 的诊断价值\*

吴斐斐 张学琴 张 涛 陆 健 邢 飞\*

南通大学附属南通第三医院影像科 (江苏南通 226006)

【摘要】目的 探讨Gd-EOB-DTPA增强MRI对不伴有 周围胆管扩张的肿块型肝内胆管癌(IMCC)中的诊断 价值。方法回顾性分析本院术前行Gd-EOB-DTPA检 查术后经病理证实的33例孤立性无周围胆管扩张的 IMCC患者的基本MRI征象、动态多期增强强化特征 以及肝胆期(HBP)表现。根据肿瘤动脉期强化特点 分为经典型和富血供型,测量并计算HBP病灶及周 围肝实质的信号强度(SI)比,对比两型间的差异。结 果 33例无周围胆管扩张的IMCC,T<sub>2</sub>WI以混杂稍高 信号为主(26/33, 78.8%),伴中央高信号(13/26, 50.0%)或低信号区(7/26, 26.9%), 66.7%(22/33) DWI上呈"靶征", 75.8%(25/33)HBP呈"EOB 云"。其中,经典型(n=27)IMCC表现为周边环状强 化伴中心渐进性延迟强化;富血供型IMCC(n=6)表 现为全瘤(n=2)或近乎全瘤(n=4)强化伴持续性强化 (n=5)或廓清(n=1)表现。两型IMCC在慢性乙肝、肝 硬化感染率(11.1% vs 66.7%, P=0.011)及肿瘤大小 (3.9 cm vs 2.8 cm, P=0.019)具有统计学差异,在 伴随征象(肝包膜回缩、DWI靶征、"EOB云"征)、 周边廓清及HBP病灶/肝脏SI比(0.67 vs 0.58)无统计 学差异(P均>0.05)。结论无周围胆管扩张的IMCC根 据动脉期强化特点分经典型和富血供型,DWI "靶 征"及"EOB云"征有助于IMCC的诊断。较经典型 IMCC,富血供型IMCC常发生于慢性乙肝、肝硬化背 景下,瘤体相对偏小。

 【关键词】钆塞酸二钠;胆管细胞癌;肝细胞癌; 鉴别诊断
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# Diagnostic Value of Gd-EOB-DTPA-Enhanced MRI in Intrahepatic Mass-Forming Cholangiocarcinoma Without Peripheral Bile Duct Dilatation\*

WU Fei-fei, ZHANG Xue-qin, ZHANG Tao, LU Jiang, XING Fei<sup>\*</sup>. Department of Radiology, The Third Hospital Affiliated of Nantong University, Nantong 226006, Jiangsu Province, China

## ABSTRACT

Objective To evaluate the value of Gd-EOB-DTPA-enhanced MRI in mass-forming intrahepatic cholangiocarcinoma (IMCC) without peripheral bile duct dilatation. *Methods* 33 pathologically confirmed solitary IMCCs without peripheral bile duct dilatation were retrospectively analyzed for basic MRI signs, Gd-EOB-DTPA-enhanced images and hepatobiliary phase sign. Each IMCC was categorized into either the classic IMCC group or hypervascular IMCC group according to the enhancement patterns in the arterial phase, and the MRI features and HBP signal intensity (SI) ratio of both IMCC groups were compared. *Results* On the T<sub>2</sub>WI, IMCC mainly showed high mixed signal (26/33, 78.8%), with 50.0%(13/26) hyperintensity areas or 26.9%(7/26) hypointense areas. 66.7%(22/33) showed target-sign on DWI and 75.8%(25/33) showed "EOB cloud" on HBP. Classic IMCCs (n=27) showed peripheral rim enhancement at arterial phase with centripetal enhance in the delayed phases, Hypervascular IMCCs (n=6) showed complete (n=2) or nearcomplete (n=4) arterial enhancement and persistent enhancement (n=5) or washout (n=1) on delayed phases. Both IMCC groups have statistical differences in chronic hepatitis B infection rate (11.1% vs 66.7%, P=0.011) and tumor size (3.9 cm vs 2.8 cm, p=0.019), and no statistical differences in ancillary imaging features(tumor capsule retraction, target-sign on DWI and "EOB cloud" ), peripheral washout and HBP mean SI ratio (0.67 vs 0.58)(each P>0.05). Conclusion IMCCs without peripheral bile duct dilatation were categorized into either the classic IMCC group or hypervascular IMCC group according to the enhancement patterns in the arterial phase, target sign on DWI and "EOB cloud" on HBP are helpful for IMCC diagnosis. Compared with classic IMCCs, hypervascular IMCCs were often occured with hepatitis B cirrhosis and the median size of tumors was relatively smaller.

Keywords: Gd-EOB-DTPA; Cholangiocarcinoma; Hepatocellular Carcinoma; Differential Diagnosis

周围局灶胆管受侵扩张是诊断肿块型肝内胆管癌(intrahepatic mass-forming cholangiocarcinoma, IMCC)的重要间接征象,但对不伴有周围胆管扩张的IMCC,影像 表现相对不典型,易与环形强化恶性肿瘤(如不典型肝细胞癌)相混淆<sup>[1-4]</sup>。研究发现,钆 塞酸二钠(gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid, Gd-EOB-DTPA)在IMCC诊断中具有重要价值<sup>[1-5]</sup>,但目前国内相关方面的研究报道甚少<sup>[6]</sup>。因此,本研究回顾性分析33例无周围胆管扩张的IMCC的Gd-EOB-DTPA增强MRI临床及影像资 料,以提高认识。

#### 1 资料与方法

**1.1 一般资料** 收集我院2015年9月至2020 年12月经手术病理证实的33例无周围胆管扩 张的IMCC患者,男15例,女18例,年龄39~80岁,中位年龄58岁,均为单发肿瘤。既 往有慢性乙肝、肝硬化7例,肝功能Child-Pugh分级为 A级(5例)或B级(2例),临床均无 黄疸,19例CA19-9升高。组织病理学显示,33例均为中、低分化腺癌,其中6例伴微血 管浸润(microvascular invasion, MVI)。

#### 1.2 方法

1.2.1 仪器设备 采用荷兰Philips 3.0 T超导多源发射MR机,16通道腹部线圈。MRI常规 平扫序列包括同、反相位T1WI、脂肪抑制T2WI和DWI。横轴面双回波T1WI序列参数: TR 130.00~250.00 ms,TE 4.50ms,层厚5.0mm,层间距1.0mm,矩阵256×160;横 轴面T2WI脂肪抑制序列参数:TR 2 000.00ms,TE 90.00ms,层厚5.0mm,层间距1.0 mm,矩阵256×160;DWI参数:TR 5 000.00 ms,TE 55.00ms,扫描范围、定位层厚 及层间距与T2WI一致,b=0、800 s/mm<sup>2</sup>,矩阵128×160。MRI增强扫描采用T1高分辨 率各向同性容积激发扫描(T1 high resolution isotropic volume excitation,THRIVE)序 列,对比剂采用Gd-EOB-DTPA(德国拜耳医药保健公司),注射对比剂后20s、60s、180 s分别采集动脉期(arterial phase, AP)、门静脉期(portal venous phase, PVP)及过渡期 (transitional phase, TP)图像,肝胆期(hepatobiliary phase, HBP)为注射对比剂后20 min扫描,剂量为0.1 mL/kg,注射流率为1.0~1.5 mL/s,经肘静脉快速推注。 1.2.2 诊断方法和标准 所有图像由2名高年资腹部影像专业医师独立阅片,当两者意见 不一致时,通过协商达成一致。主要观察并记录病灶以下内容:(1)一般特征,包括病灶

<sup>【</sup>第一作者】吴斐斐,女,主治技师,主要研究方向:腹部影像诊断。E-mail:552529250@qq.com

<sup>【</sup>通讯作者】邢 飞,男,主治医师,主要研究方向:腹部影像诊断。E-mail: ntyxxs123456@163.com

大小(最大径)、数目、形态(规则、不规则); (2)动态增强,根据 动脉期强化特点,将IMCC分为两型<sup>[7]</sup>(经典型:周边环形强化, 强化范围10%~70%;富血供型:全瘤或近乎全瘤强化,强化范 围>70%),周边廓清(PVP或TP时)及强化模式(渐进向心强化型、 持续强化型、快进快出型); (3)伴随征象,包括T<sub>2</sub>WI信号(均匀 稍高信号、混杂稍高信号伴中央高信号或低信号区)、DWI"靶 征"(周围高信号、中心低信号)、肝胆期"EOB云"征(中心高 信号区、周围低信号环)及肝包膜回缩; (4)肝胆期病灶信号强度 (signal intensity, SI病灶)和同层面背景肝实质SI肝脏,病灶感兴 趣区(region of interest, ROI)放置在病灶信号最高区域,肝实质 ROI避开大血管、瘤周低强化区,计算病灶与肝实质SI比。

**1.3 统计学方法** 采用IBM SPSS 22.0统计软件进行处理。计量资料以中位数(上、下四分位数)表示,采用Mann-Whitney U检验。 计数资料以频数或率表示,比较采用 Fisher确切概率法。P<0.05 为差异有统计学意义。

# 2 结 果

33例IMCC,均为单发,病灶最大径1.6~12.1 cm,平均4.6 cm。MRI平扫,T<sub>2</sub>WI以混杂稍高信号为主(26/33,78.8%),

伴中央高信号(13/26,50.0%)或低信号区(7/26,26.9%); 66.7%(22/33)DWI上呈"靶征";75.8%(25/33)肝胆期呈"EOB 云",病灶-肝脏SI比为0.59(0.37~0.91);12.1%(4/33)的病灶表 现包膜回缩。

依据动脉期强化特点,分为经典型IMCC(见图1)和富血供型 IMCC(见图2)。经典型IMCC(27/33,81.8%),最大径为1.9~12.1 cm,中位数3.9 cm,动脉期呈周边环状强化伴中心渐进性延迟 强化,T<sub>2</sub>WI信号多不均质(中央高信号13个,中央低信号5个), 20个DWI表现"靶征",10个增强时表现为周边廓清,22个肝胆 期表现"EOB云",病灶-肝脏SI比为0.67(0.40~0.91)。富血供型 IMCC(6/33,18.2%),最大径为1.6~4.9 cm,中位数为2.8 cm, 动脉期呈全瘤(n=2)或近乎全瘤(n=4)强化伴持续性强化(n=5)或廓 清(n=1)表现,3个T2WI表现为均质稍高信号,2个DWI表现"靶 征",2个表现周边廓清,3个肝胆期表现"EOB云",病灶/肝 脏SI比为0.58(0.37~0.86)。

两型IMCC在慢性乙肝、肝硬化感染率(11.1% vs 66.7%, P=0.011)及肿瘤大小(3.9 cm vs 2.8 cm, P=0.019)具有统计学差异, 在伴随征象(肝包膜回缩、DWI靶征、"EOB云"征)、周边廓清及肝 胆期病灶SI比(0.67 vs 0.58)无统计学差异(P均>0.05)(见表1)。

		经典型IMCC(n=27)	富血供型IMCC(n=6)	P值
临床特征	慢性乙肝、肝硬化	3(11.1%)	4(66.7%)	0.011
	CA19-9升高	17(62.9%)	2(33.3%)	0.363
影像特征	最大径(cm)	3.9(1.9~12.1)	2.8(1.6~4.9)	0.019
	包膜回缩	3(11.1%)	1(16.7%)	1.0
T <sub>2</sub> WI表现	均匀稍高信号	3(11.1%)	3(11.1%)	0.093
	混杂稍高信号			
	伴中央高信号区	13(48.1%)	1(16.7%)	0.209
	伴中央低信号区	5(18.5%)	1(16.7%)	1.0
DWI靶征		20(74.1%)	2(33.3%)	0.146
周边廓清		10(37.0%)	2(33.3%)	1.0
"EOB云"征		22(81.5%)	3(50.0%)	0.137
SI <sub>病灶</sub> /SI <sub>肝脏</sub>		0.67(0.40~0.91)	0.58(0.37~0.86)	0.093

表1 经典型IMCC与富血供型IMCC临床及影像特征比较

注: CA 19-9: 糖抗原 19-9(正常值0~27 U/m1); \*P<0.05



## 3 讨 论

**3.1 一般MRI影像特征** 肝内胆管癌(intrahepatic cholangiocarcinoma, ICC)是原发于肝内胆管上皮的恶性肿瘤, 恶性程度较高,占原发性肝癌的10%~20%,近年来发病率呈逐 年上升趋势<sup>[8]</sup>。根据病灶大体形态和生长方式分为三类,即肿 块型、管周浸润型和管内生长型,以肿块型最常见(60%)。本组 IMCC均为肿块型,同时不伴有周围胆管扩张,具有以下MRI影 像特征表现:(1)T<sub>2</sub>WI以混杂稍高信号为主(78.8%),其内信号强 度变化与肿瘤成分如纤维组织、黏液及坏死组织的构成有关。当 纤维组织多,黏液坏死组织少,内部为低信号区(硬癌型);当纤 维组织少,黏液、坏死组织为主,内部为高信号区(髓质型),特 别是分泌大量黏液时,形成"黏液湖",病灶中心信号十分明 亮,甚至高于水的信号<sup>[9]</sup>;(2)本研究66.7%的病灶DWI显示"靶 征",IMCC外周肿瘤组织丰富,扩散受限呈高信号,而中心区域 以纤维间质及成纤维细胞为主伴有黏液变性或坏死、肿瘤细胞稀 疏,表现为低信号,部分肿瘤虽小,该特征也依然存在<sup>[3]</sup>;相关 研究结果显示DWI "靶征"在IMCC的出现率为68.6%~83.5%<sup>[10-</sup> <sup>il</sup>; (3)动态增强,经典型IMCC,瘤体偏大,病灶周边有大量成活 肿瘤细胞,增强早期呈环状强化,而内部因大量纤维组织成分呈 现渐进向心性"云雾状"延迟强化,部分患者(37.0%)在TP表现 为周边廓清;富血供型IMCC,整个瘤体因含大量肿瘤细胞而仅有 轻中度纤维组织,动脉期表现为全瘤或近乎全瘤强化,当门脉期 呈廓清表现时很容易误诊为肝细胞癌(hepatocellular carcinoma, HCC)<sup>[11]</sup>,此型IMCC并不少见(12.5~47%)<sup>[7]</sup>,常发生在慢性肝 炎、肝硬化背景下<sup>[12]</sup>,瘤体偏小(一般<3 cm),术后累积死亡率及 肿瘤复发率明显低于经典型IMCC<sup>[13]</sup>。

**3.2 肝胆期影像特征** Gd-EOB-DTPA作为肝胆特异性对比剂,能够通过影像特征反映病灶药代动力学特点和功能改变,尤其肝胆期 "EOB云"对IMCC的诊断及鉴别诊断具有重要提示价值<sup>[1-6]</sup>。

"EOB云"征在IMCC显示率较高(43.8%~85.7%)<sup>[1.7.9,14]</sup>,这与 IMCC的病理基础有关。通常,病灶中心由松散的结缔组织和丰 富的细胞间基质组成导致对比剂在细胞外间隙的蓄积、滞留,随 着时间延迟,中央"云雾状"强化逐渐明显或称为"假摄取"现 象;而病变外周由于纤维成分较少而呈相对低信号((对比剂"假 洗脱"现象),形成约2.5mm厚的低信号环<sup>[6]</sup>。Teo等<sup>[5]</sup>研究指出 IMCC肿瘤中心"EOB云"的信号强度会随着纤维基质间隙空间的 数量增多而增加。本研究中,"EOB云"征在无周围胆管扩张的 IMCC出现率为75.8%,两型IMCC在"EOB云"征显示率及病灶-肝脏SI比无明显差异。

**3.3 鉴别诊断** DWI "靶征"尤其肝胆期 "EOB云" 征有助于无周 围胆管扩张IMCC的诊断,但以下病变也可有类似表现,需鉴别: (1)少数含纤维成分较多的硬化型HCC、CK19阳性的HCC也呈

"靶征"表现,T2WI多灶性高信号、强化包膜及纤维间隔可帮助 鉴别<sup>[15]</sup>;(2)混合型肝细胞胆管细胞癌(combined hepatocellular cholangiocarcinoma, cHCC-CC),病理组织学肿瘤内同时存 在HCC及ICC的成分,总体强化方式与IMCC接近<sup>[16]</sup>,但cHCC-CC动脉期强化相对更明显、肝胆特异期强化程度不如IMCC; (3)来源于乳腺癌、胃肠道腺癌或间质瘤的肝脏单发转移瘤肝胆 期也可因对比剂蓄积形成靶征,体素不相干运动弥散加权成像 (Intravoxel incoherent motion diffusion weighted imaging, IVIM-DWI)定量指标有助于两者的鉴别<sup>[17]</sup>;(4)少数(约15%)的肝 脏原发淋巴瘤<sup>[18]</sup>,病灶中心因变性、坏死呈"靶征"表现,较 低的ADC值(0.56~0.918×10-3 mm<sup>2</sup>/s)、较高的氟脱氧葡萄糖 (fluorodeoxyglucose, FDG)摄取(SUVmax 19.6)以及正常水平的 肿瘤学标记物可能提示其恶性淋巴瘤的诊断。

综上所述,无周围胆管扩张的IMCC根据动脉期强化特点分 经典型和富血供型,DWI "靶征"及肝胆期 "EOB云" 征有助于

IMCC的诊断。较经典型IMCC,富血供型IMCC常发生于慢性乙 肝、肝硬化背景下,瘤体相对偏小。

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