·临床研究·

MRI动脉期强化模式预测肝内胆管细胞癌患者的预后

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摘　要：【目的】探讨术前MRI增强扫描动脉期强化模式对肝内胆管细胞癌（ICC）无病生存时间（DFS）和术后总生存时间（OS）的预测价值。【方法】回顾性分析2018年1月至2021年12月在中山大学附属第一医院手术治疗，术后病理证实为ICC的93例患者的临床、术前增强MRI、术后病理、术后随访资料。采用Kaplan-Meier生存曲线分析比较MRI增强扫描动脉期强化模式不同的三组间的DFS和OS，Cox回归分析影响ICC术后DFS和OS的危险因素。【结果】不同动脉期强化模式组术后DFS和OS差别有统计学意义（Log-rank检验，$P < 0.05$）。MRI动脉期强化模式是ICC术后DFS的独立危险因素（以弥漫性高增强为参照，外周环形强化：HR = 3.550；95%CI：1.16 ~ 10.8；$P = 0.026$；弥漫性低增强：HR = 3.430；95%CI：1.04 ~ 11.3；$P = 0.042$）。MRI动脉期强化模式和肿瘤位置是ICC术后OS的独立危险因素（以弥漫性高增强为参照，弥漫性低增强HR = 8.500；95%CI：1.09 ~ 66.3；$P = 0.041$；以肝周为参照，肿瘤位置近肝门HR = 2.583，95%CI：1.14 ~ 5.83，$P = 0.022$）。动脉期强化模式预测术后1年、2年和3年DFS的受试者特征曲线（ROC）的曲线下面积（AUC）分别为0.722、0.748和0.617，预测患者术后1年、2年和3年OS的AUC分别为0.720、0.704和0.730，预测效能均优于AJCC-TNM分期系统。【结论】术前MRI动脉期强化模式是预测ICC术后DFS和OS的可靠指标，优于AJCC-TNM分期系统，有良好的预后预测效能，可用于ICC的临床管理。

关键词：肝内胆管细胞癌；磁共振成像；动脉期强化模式；预后
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Prognostic Value of MRI Arterial-phase Enhancement Pattern in Intrahepatic Cholangiocarcinoma Patients

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Abstract：【Objective】To investigate the prognostic value of the enhancement pattern in arterial phase of preoperative Gd-EOB-DTPA enhanced magnetic resonance imaging（MRI）in evaluating the disease-free survival（DFS）and overall survival（OS）in patients undergoing curative resection for intrahepatic cholangiocarcinoma（ICC）.【Methods】A retrospective analysis was done on the clinical，preoperative MRI findings and postoperative follow-up results of 93 pathologically confirmed ICC patients undergoing surgery in our hospital between January 2018 and December 2021. Kaplan-Meier survival curves and log-rank test were used to compare the DFS and OS of three groups with different arterial enhancement patterns. Cox regression analysis was used to identify the factors affecting DFS and OS.【Results】There were significant differences in DFS and OS among the 3 groups（log-rank test，$P < 0.05$）. The arterial enhancement pattern was an independent predictive factor for DFS（using diffuse hyperenhancement as a reference，peripheral rim enhancement：HR = 3.550；95%CI：1.16 ~ 10.8；$P = 0.026$；diffuse hypoenhancement：HR = 3.430；95%CI：1.04 ~ 11.3；$P = 0.042$）. The arterial

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enhancement pattern and tumor location were predictive factors for OS ((using diffuse hyperenhancement as a reference, diffuse hypoenhancement, HR = 8.500; 95%CI: 1.09-66.3; P = 0.041; using tumor distal location as a reference, tumor perihilar location HR=2.583, 95%CI: 1.14-5.83, P =0.022). The AUC of arterial enhancement patterns in predicting 1-, 2-, and 3- year DFS were 0.722, 0.748, and 0.617, respectively; in OS, 0.720, 0.704, and 0.730, respectively, which showed better prognostic efficacy than AJCC-TNM staging system.【Conclusion】Arterial-phase enhancement pattern of preoperative Gd-EOB-DTPA enhanced MRI is an independent predictive factor for DFS and OS of ICC patients, with a better prognostic value than AJCC-TNM staging system, and can be used for the clinical management of ICC patients.

Key words: intrahepatic cholangiocarcinoma (ICC); magnetic resonance imaging (MRI); arterial-phase enhancement pattern; postoperative survival

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肝内胆管细胞癌(intrahepatic cholangiocarcinoma, ICC)是第二常见肝原发性恶性肿瘤,约占原发性肝癌的10% ~ 15%[1]。过去十年,全球ICC发病率呈明显上升趋势[2-3]。ICC恶性程度高,预后差,患者术后的中位总生存时间仅40个月,术后5年生存率低于40%[4-5]。ICC的准确预后评估对确定治疗方案和构建个体化监测策略非常重要,例如术前新辅助化疗[6]和术后经动脉化疗栓塞术等[7]。目前,ICC预后评估最常采用美国癌症联合委员会(American joint committee on cancer, AJCC)第8版TNM分期系统[8],纳入了肿瘤大小、数目、血管浸润,以及淋巴结转移等指标,主要依赖术后病理组织学结果,存在滞后性。MRI检查在ICC术前全面评估中发挥的重要作用已经得到广泛认可。有研究表明,MRI一些征象与ICC预后相关,如:动脉期强化模式[9-11]。进行更进一步的研究来探索并解释影像学特征与临床结局间的内在关联是非常必要的。本研究利用本中心接诊ICC病患的临床及MRI数据,探索术前MRI动脉期强化模式对行根治性切除治疗的ICC的DFS和OS的预测价值。

1 材料与方法

1.1 病例收集

回顾性收集2018年1月至2021年12月于中山大学附属第一医院治疗的ICC病例。研究病例纳入标准如下:①原发初治的ICC;②接受根治性肿瘤切除术;③术后病理结果证实为ICC。研究病例排除标准:①术前一月内未行上腹部Gd-EOB-DTPA增强MRI检查、MRI序列不全或图像质量不佳;②合并有其他恶性肿瘤的患者;③未能获得完整的临床和随访资料的患者;④术前未行任何针对肿瘤的其他干预治疗,如:介入治疗、放射治疗、化学药物治疗等。本回顾性研究方案经中山一院伦理委员会批准([2023]345),免除患者知情同意。

1.2 Gd-EOB-DTPA增强MR图像采集

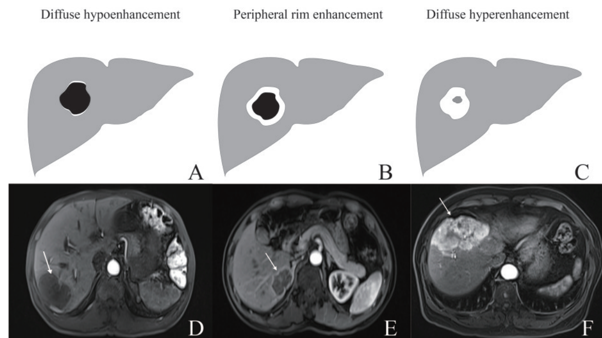
所有MRI检查均使用3.0TMR成像设备(siemens healthcare sector, Erlangen, Germany)。采用8通道体部线圈,取仰卧位进行图像采集,扫描范围覆盖膈顶至肝脏下缘。常规序列包括:屏气相T2WI(T2-weighted imaging)、Dixon序列、DWI(diffusion weighted imaging, b = 0,50,400,800 s/mm^2)。增强MRI采用的对比剂是钆塞酸二钠(gadoxetate disodium,Gd-EOB-DTPA,普美显,Bayer),使用剂量为0.025 mmol·kg^{-1},注射速率1 mL/s,注射对比剂后,采用T1WI压脂三维容积内插屏气检查(three dimensional volume interpolated breath-hold examination,3D-VIBE)序列扫描,共扫描7个期相,包括动脉期(2期,静脉注射后20 ~ 40 s内采集)、门静脉期(2期,50 ~ 70 s)、延迟期(2期,100 ~ 120 s)、肝胆特异期(hepatobiliary phase, HBP,静脉注射后20 min)。

1.3 增强MRI图像分析

由两位高年资(分别具有15年和8年的工作经验)腹部放射影像诊断医师盲法阅片评估并纪录影像指标。对于存在争议的指标,两位阅片者商议并最终达成共识。

评估的MR征象和指标有:①肿瘤大小(冠状位或轴位肿瘤最大径,结合肝胆期与T2WI测量);②动脉期强化模式(于动脉早期评估,共3种,为:弥漫性低增强:肿瘤高增强区域小于最大层面的10%;外周环形强化:肿瘤外周环形强化,环宽占最大径的10% ~ 70%;弥漫性高增强:肿瘤高增强区域大于最大层面的70%;图1);③动脉期瘤周高灌

注(peritumoral hyperenhancement in arterial phase, 动脉期瘤周斑片状高信号);④HBP瘤周高信号环(high signal rim in HBP);⑤瘤内坏死(增强扫描图像上持续性无增强区);⑥肿瘤位置(分为邻近肝门以及包膜下)和⑦DWI高信号(弥散受限区域,表现为高b值DWI上信号强度高于正常肝实质)。



Diagrams(A-C) of 3 enhancement patterns on arterial phase images and corresponding examples of MR images (D-F) of ICC. Diffuse hypoenhancement pattern, almost no enhancement, the peripheral hyperenhancement ring is less than 10% of the tumor cross-sectional area (A, D). Peripheral rim enhancement (ring-like enhancement) pattern, has a peripheral hyperenhancement ring, the enhancement area accounted about 10% ~ 70% of the tumor maximum cross-sectional area. (B, E). Diffuse hyperenhancement pattern (C, F), the tumor hyperenhancement area is greater than 70% of the tumor maximum cross-sectional area.

图1 ICC的MRI动脉期强化模式示意图

Fig. 1 Schematic diagram of the MRI arterial phase enhancement pattern of ICC

1.4 临床及病理指标收集

电子病历系统中摘录ICC病患以下特征:年龄、性别、乙肝病史、腹痛症状、术前肝功能Child-pugh分级,术前一周内血常规、肿瘤标志物(AFP、CA19-9、CEA、CA125)以及肝功能指标。计算的免疫炎症指标包括中性粒细胞与淋巴细胞比值(neutrophils to lymphocyte ratio, NLR)、血小板与淋巴细胞比值(platelet to lymphocyte ratio, PLR)。术后标本病理切片经病理科医师阅片记录以下指标:肝硬化(存在/不存在)、肿瘤数目、AJCC第八版TNM分期。

1.5 预后指标收集

随访信息通过对患者或家属的电话访查获得。患者术后常规复查项目包括体格检查、血常规、肝功能、肿瘤标志物和影像学检查,术后每3~6个月进行1次。随访的结局事件包括死亡和复发,无病生存时间(DFS)记录为从手术日期到首次复发或末次随访日期之间的时间,而总生存时间(OS)则记录为手术日期到死亡或末次随访日期之间的时间。

1.6 统计学方法

所有统计分析均使用R语言(版本号4.1.2,来自https://www.r-project.org)。计量资料符合正态分布的用均数±标准差表示,不符合正态分布则用中位数和四分位数 M (P_{25} ~ P_{75})表示,计数资料展示为频率(百分比)。依据MR动脉期强化模式分组,依据数据资料分布特征选择Fisher确切概率法、卡方检验、方差分析和Kruskal-Wallis检验进行组间差异性比较。两名放射科医生对影像征象评估的一致性评价采用kappa值(差,< 0.2;一般,0.2 ~ 0.4;中等,0.41 ~ 0.60;良好,0.61 ~ 0.80;极好,0.81 ~ 0.99)。绘制三组DFS和OS的Kaplan-Meier生存曲线,采用Log-rank检验行组间差异性比较。采用单因素和多因素Cox回归评价影响DFS和OS的危险因素,单因素Cox回归中 $P < 0.05$ 的变量被选入多因素Cox回归中。采用ROC曲线来评估变量的预测效能。所有检验均采用双侧检验,$P < 0.05$ 被认为具有统计学意义。

2 结果

2.1 临床及影像特征

本研究共收集246例ICC患者,排除无术前一月内Gd-EOB-DTPA增强MR检查资料78例,术前行其他辅助治疗40例,随访数据不完整35例,最终共纳入研究ICC 93例。其中男57例、女36例,年龄中位数为58岁(年龄范围:52 ~ 59岁)。ICC临床资料和MRI征象详见附表。癌灶的最大直径中位数5.4 cm(范围:4.1 ~ 8.1 cm)。AJCC-TNM分期:1期43例(46.2%),2期21例(22.6%),3期29例(31.2%)。

附表
Appendix table

MRI征象的观察者间一致性分析结果为良好至极好(κ = 0.65 - 0.95)。93例ICC根据MR动脉期强化模式分3组:弥漫性低增强组(n = 36)、外周环形强化组(n = 42)和弥漫性高增强组(n = 15)。3组的血小板计数、NLR和PLR的差异具统计学意义(H = 7.580, P = 0.023; H = 9.986, P = 0.007;

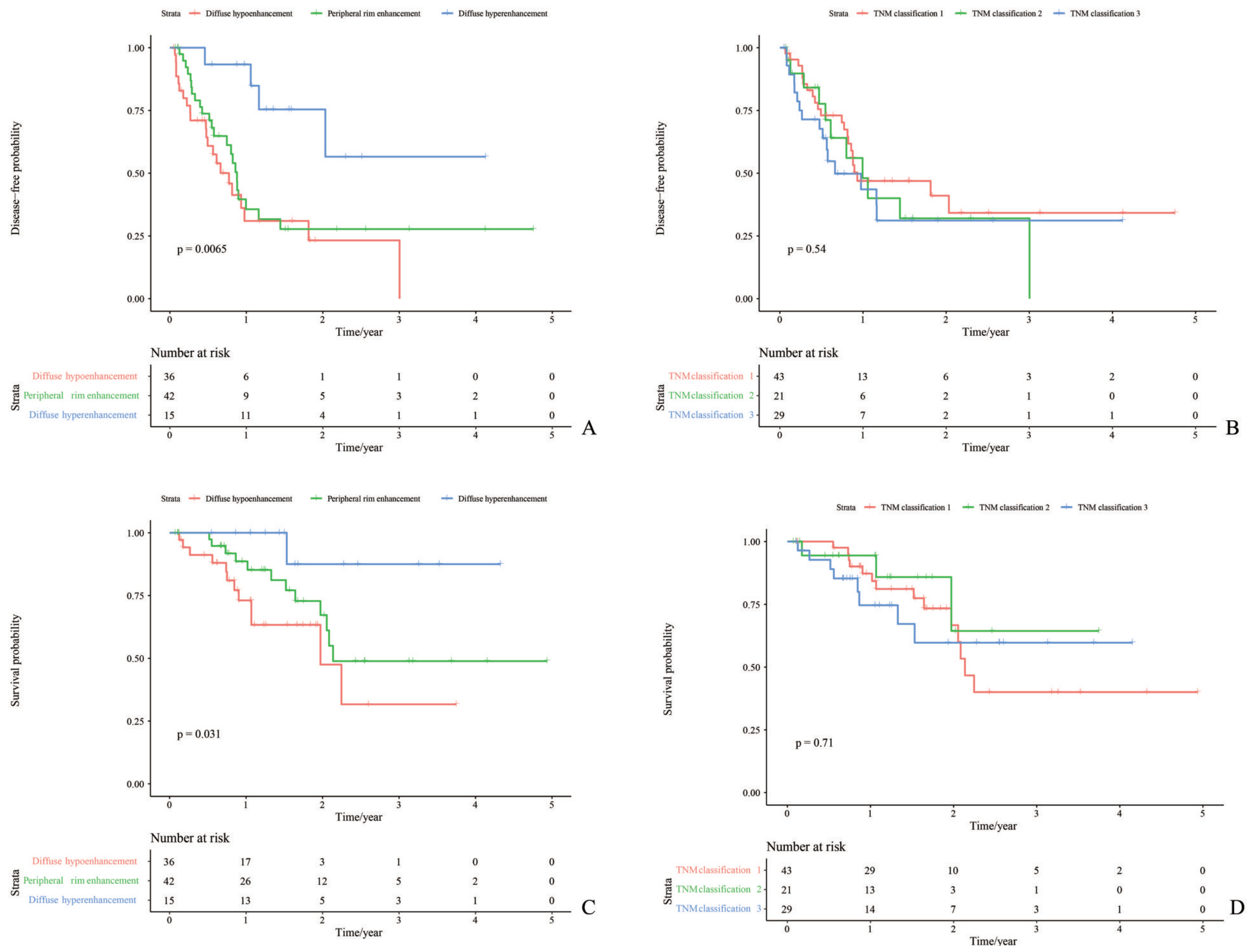
H = 10.095，P = 0.006)。其他MR征象中，瘤内坏死的差异具有统计学意义(P = 0.025)，动脉期弥漫性低增强组肿瘤坏死出现的比例高于其他两组。

2.2　比较MRI强化模式不同组间DFS和OS

93例ICC，中位随访时间15个月，随访时间范围为2至60个月。共49例(52.7%)出现复发。研究队列1年、2年和3年无病生存率分别为45.3%、35%和31.5%。共25例(26.9%)在随访过程中死亡。1年、2年和3年总生存率分别为84.8%、65.2%和51.5%。

Kaplan-Meier生存曲线显示，三组不同强化模式的DFS和OS的差异有统计学意义(log-rank检验：DFS，χ^2 =10.100，P = 0.0065；OS，χ^2 = 6.901，P = 0.031)。弥漫性高增强组的DFS高于外周环形强化组和弥漫性低增强组。弥漫性高增强组的1年、2年和3年总无病生存率分别为93.3%、75.4%和56.6%；外周环形强化组和弥漫性低增强组分别为35.6%、27.7%和27.7%和31.0%、23.2%和23.2%(图2A)。弥漫性高增强组的OS高于外周环形强化组和弥漫性低增强组；弥漫性高增强组的1年、2年和3年总生存率分别为100%、87.5%和87.5%，而外周环形强化组和弥漫性低增强组的相应总生存率分别为88.6%、67.2%和48.9%和73.1%、47.5%和31.7%(图2C)。

TNM不同分期的DFS和OS之间的差异均无统计学意义(log-rank检验：DFS，χ^2 = 1.200，P = 0.541；OS，χ^2 = 0.701，P = 0.715)。



Statistical significance was assessed by using the log-rank test. A: Kaplan-Meier survival curves of DFS and C: OS according to MRI arterial-phase enhancement pattern. B: Kaplan-Meier survival curves of DFS and D: OS according to AJCC-TNM staging system. TNM staging systems were evaluated according to the eighth edition of the American joint committee on cancer.

图2　ICC术前MR动脉期强化模式及AJCC-TNM分期与DFS和OS的生存曲线

Fig. 2　Kaplan - Meier curves for overall survival and Disease-free survival according to Arterial-phase enhancement pattern and AJCC-TNM-staging system in ICC

2.3 MRI动脉期强化模式是预测ICC术后DFS和OS的独立危险因素

单变量Cox回归分析表明MRI动脉期强化模式(外周环形强化,HR = 3.669,P = 0.017;弥漫性低增强,HR = 4.980,P = 0.003)、性别(女性,HR = 2.029,P = 0.018)、腹痛症状(HR = 1.989,P = 0.019)、CA125水平(高水平,HR = 2.109,P = 0.032)、CA199水平(高水平,HR = 2.919,P = 0.003)、PLT(HR = 1.000,P = 0.047)和NLR(HR = 1.080,P = 0.035)是预测ICC术后DFS危险因素(均P < 0.05)。经多变量Cox分析,MRI动脉期强化模式对ICC术后DFS的影响仍显著(外周环形强化,HR = 3.550,P = 0.026;弥漫性低增强,HR = 3.430,P = 0.042;表1)。

单变量Cox回归分析表明MRI动脉期强化模式(弥漫性低增强,HR = 9.410,P = 0.032)和肿瘤位置(近肝门,HR = 2.750,P = 0.013)是预测ICC术后OS危险因素(均P < 0.05)。经多变量Cox分析,MRI动脉期强化模式(弥漫性低增强,HR = 8.500,P = 0.041)和肿瘤位置(近肝门,HR = 2.583,P = 0.022)对ICC术后OS的影响仍显著(表2)。本研究结果表明MRI动脉期强化模式是ICC术后DFS和OS的独立危险因素。

表1 影响ICC术后DFS的多变量Cox回归分析

Table 1 Multivariate Cox analysis of potential prognostic factors associated with DFS

Variable	b	S_b	Wald χ^2	P	HR	HR 95% CI
Arterial.phase.enhancement.type						
Diffuse hyperenhancement					1.000	(1.00,1.00)
Peripheral rim enhancement	1.27	0.569	4.97	0.026	3.550	(1.16, 10.8)
Diffuse hypoenhancement	1.23	0.608	4.12	0.042	3.430	(1.04, 11.3)
Sex						
M					1.000	(1.00,1.00)
F	0.633	0.328	3.72	0.053	1.883	(0.99, 3.58)
Abdominal.pain						
No					1.000	(1.00,1.00)
Yes	0.581	0.339	2.96	0.086	1.788	(0.92, 3.48)
CA125						
Low					1.000	(1.00,1.00)
High	0.292	0.392	0.556	0.456	1.339	(0.62, 2.89)
CA199						
Low					1.000	(1.00,1.00)
High	0.735	0.382	3.69	0.054	2.086	(0.99, 4.41)
NLR	0.038	0.048	0.627	0.428	1.038	(0.95, 1.14)
PLT	0.000 07647	0.002	0.001 3	0.971	1.000	(1.00, 1.00)

HR: Hazard Ratio; CI: Confidence Interval. The first item of each categorical variable was treated as the reference category. Variables with P < 0.05 in univariable analysis were selected as corrected factors in multivariable analysis.

采用ROC曲线评估ICC术前MRI动脉期强化模式对DFS和OS的预测效能,结果显示动脉期强化模式预测患者术后1年、2年和3年DFS的AUC分别为0.722、0.748和0.617,而AJCC-TNM分期预测患者术后1年、2年和3年DFS的AUC分别为0.516、0.582和0.568(图3A-C)。动脉期强化模式预测患者术后1年、2年和3年OS的AUC分别为0.72、0.704和0.73;TNM分期预测患者术后1年、2年和3年OS的AUC分别为0.651、0.483和0.452(图3D-E)。

3 讨论

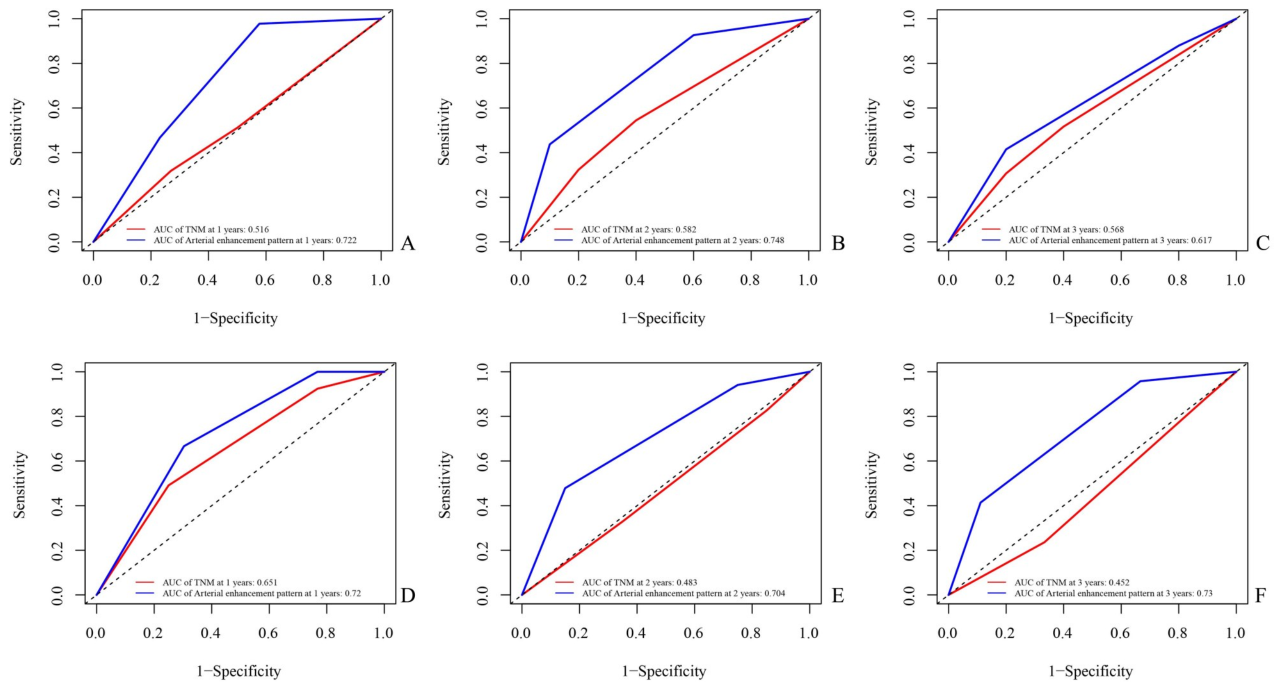
术前MRI肿瘤动脉期强化模式是ICC术后DFS和OS的独立危险因素。随着动脉期强化程度

表2　影响ICC术后OS的多变量Cox回归分析

Table 2　Multivariate cox analysis of potential prognostic factors associated with OS

Variable	b	S_b	Wald χ^2	P	HR	HR 95% CI
Arterial enhancement pattern						
Diffuse hyperenhancement					1.000	(1.00, 1.00)
Peripheral rim enhancement	1.75	1.04	2.83	0.093	5.775	(0.75, 44.6)
Diffuse hypoenhancement	2.14	1.05	4.17	0.041	8.500	(1.09, 66.3)
Location						
Distal					1.000	(1.00, 1.00)
Perihilar	0.949	0.416	5.22	0.022	2.583	(1.14, 5.83)

HR: Hazard Ratio; CI: Confidence Interval. The first item of each categorical variable was treated as the reference category. Variables with $P < 0.05$ in univariable analysis were selected as corrected factors in multivariable analysis.



A−C: ROC curves of Arterial enhancement pattern and TNM staging system for 1, 2, and 3−year DFS in ICC. D−F: ROC curves of Arterial enhancement pattern and AJCC−TNM staging system for 1, 2, and 3−year OS in ICC.

图3　ROC曲线比较动脉期强化模式与TNM分期的预后预测效能

Fig. 3　Predictive efficacy comparison between Arterial−phase enhancement pattern and AJCC−TNM staging system about 1−, 2−, and 3−year DFS and OS using ROC curves

的降低(从弥漫性高增强到外周环形强化再到弥漫性低增强),ICC术后OS及DFS缩短,弥漫性低增强组的DFS和OS最差。术前MRI肿瘤动脉期强化模式可以作为一种无创性预测指标,用于术前ICC总生存时间和术后无病生存时间的预判,合理进行术前患者沟通、个性化评估及最终治疗方案的选择,具一定临床应用价值。

弥漫性低增强组的患者所对应的AJCC−TNM分期在三组内最晚,肝功能相关指标最差,这也对应了该组的不良预后,这一结果与Panettieri等的研究一致[11−13]。他们发现弥漫性低增强组的肿瘤分化程度更差,微血管浸润比例更高,T分期和N分期也更晚。这意味着肿瘤的生物学行为更恶性,更容易发生侵袭和转移,从而降低患者的治疗效果,

导致预后不良。有研究表明,ICC术前MRI最常见的动脉期强化模式为外周环形强化,其病理基础可能是ICC中央区存在丰富的纤维性基质,而癌细胞主要分布于肿瘤外周,这一病理结构区域分布的差异造成磁共振对比剂自外周向瘤中央灌注时间的逐渐延长。在延迟期MRI图像上,ICC因对比剂的潴留而表现为向心性、渐进性强化[14-15]。早期外周强化及中心延迟强化等征象反映了MR对比剂逐渐填充于纤维基质的分布过程。因此,动脉期弥漫性高增强和弥漫性低增强这两种强化模式分别反映了肿瘤细胞丰富的ICC和基质成分丰富的ICC。Fujita等[9]研究发现,与外周环形强化组和动脉期高增强组相比,动脉期低增强组更常见于近肝门型ICC,其淋巴、血管、神经浸润率为三组中最高,且预后最差。Nam等[16]研究显示,动脉期高增强这一影像特征提示ICC组织学类型为小导管型,与良好预后相关。这些结果表明不同强化模式的肿瘤表现出不同的生物学行为。动脉期强化程度越低(从弥漫性高增强到外周环形强化再到弥漫性低增强),瘤内基质成分占比越高,提示不良预后。越来越多的证据表明,纤维基质在促进ICC进展和耐药产生等方面起着重要作用[17-18],ICC内部纤维基质比例增高与预后呈负相关[19]。近年来逐渐有成纤维生长因子受体抑制剂应用于ICC治疗[20]报道,确定较好的治疗效果,这提示抗纤维基质生成是治疗ICC潜在有效靶点。我们的研究结果提示动脉期强化模式可能间接反映了ICC的细胞外基质存在及分布特征,可据此预测肿瘤的生物学行为,为制定个性化治疗决策提供重要的参考。未来需要更多研究进一步探索影像特征与病理特征的关联,辅助筛选可能获益于靶向治疗的患者,实现精准治疗。

AJCC-TNM分期系统(第八版)应用于ICC临床预后预测已经被广泛接受,近年来关于预后分层能力及效力高低的争议也多有报道[21-24]。Li等[22]建议纳入新的预后指标,如CA199、AFP等。一项回顾性多中心研究对比了第7版和第8版AJCC肝内胆管细胞癌分期系统的预后预测效能,发现第7版AJCC分期系统预测ICC术后OS的C-index为0.642,而第8版AJCC分期系统预测ICC术后OS的C-index为0.667[25]。Kang等[26]在回顾性的大样本研究(N = 626)中评估了第8版AJCC分期系统的预后预测效能,发现其预测ICC术后OS的C-index为0.625,预测ICC术后DFS的C-index为0.628。本文虽未计算C-index,但计算的AUC也表明该分期系统预后分层效果不佳,预测ICC术后1,2,3年DFS及OS的AUC均小于0.7,劣于MRI动脉期强化模式。本研究TNM分期系统预测预后的AUC较低,可能是由于本研究样本量较小,不足以反映真实情况。但总体而言,该分期系统对ICC术后预后的预测效能仍不尽人意,需要进一步改进和完善。MRI影像征象作为术前可获得的可靠指标,具有无创、易获得,提供信息全面的优势,从而可以为术前ICC患者及家属的沟通及治疗方案的选择提供重要参考。

慢性炎症和免疫反应在恶性肿瘤的发生发展中扮演重要角色,与细胞增殖、分化、细胞外基质重塑、血管生成和免疫逃避等过程密切相关[27]。外周血中性粒细胞、淋巴细胞和血小板计数是三种简单、易得、低成本的炎症和免疫相关指标,可以从常规血液检查中获得。研究表明,中性粒细胞可产生基质降解蛋白酶及分泌促炎因子,如IL-12、TNF-α和GM-CSF等,通过降解细胞外基质、促进新生血管形成和免疫抑制等过程促进肿瘤生长、侵袭和转移[28-29]。肿瘤细胞可激活血小板并刺激血小板聚集,活化。活化的血小板可分泌VEGF等细胞因子,促进上皮间充质-转化,调控肿瘤生长、转移和血管生成等过程[30-31]。此外,淋巴细胞的减少可能导致机体对肿瘤细胞的免疫反应不足[32],Galon等证明淋巴细胞的浸润是结肠癌患者预后良好的指标[33]。因此,中性粒细胞、淋巴细胞和血小板可以作为抗肿瘤活性、预后和治疗反应的指标。这些炎性细胞的组合,如中性粒细胞与淋巴细胞比值(NLR)和血小板与淋巴细胞比值(PLR),在包括肝细胞癌、肾脏、乳腺癌、结肠癌和转移性黑色素瘤在内的多种恶性肿瘤中都显示出其预后价值[34-35],其升高与较差的OS和DFS相关。也有少数研究报道NLR和PLR在肝内胆管癌中的预后价值。Buettner等[36]探讨了NLR和PLR与ICC术后预后的相关性,发现高NLR水平是ICC术后OS的独立危险因素,而高PLR水平和低PLR水平组之间的OS差异无统计学意义。Chen等[37]则得出了相反的结论,发现高PLR水平是ICC术后OS和RFS的独立危险因素。在Huh等[38]的研究中,高PLR水平是ICC行化疗后OS和PFS的独立危险因素。总体而言,研究者们尚未明确NLR和PLR在ICC中的预后价值,研究结果之间存在争议。本研究中三种强化模式组间血小板计数、NLR和PLR的差异具统计学意义,血小板计数、NLR和PLR在弥漫性低增强组中最

高,在弥漫性高增强组中最低,与其OS和DFS的高低趋势相仿。然而,在本研究中,炎症细胞(中性粒细胞、淋巴细胞、血小板)计数、NLR和PLR均不是ICC术后OS的独立风险因素。高血小板和高PLR水平与ICC术后较差的DFS相关,但在多因素Cox回归校正后,其影响不显著。本研究结果同其他结果的不一致可能与患者的选择偏倚相关,包括手术方式、肿瘤分期和就诊年份等。因此,有必要在大样本、多中心研究中进一步探讨血小板、NLR和PLR在ICC中的预后价值和影响患者预后的相关机制。

本文研究结果显示,ICC瘤内坏死的出现不是ICC患者术后预后的独立危险因素,这与Min等[11]的研究结果不同。他们认为肿瘤坏死与肿瘤分化程度负相关,是预测术后DFS的独立危险因素。这可能是因为本研究定义的肿瘤坏死是单纯影像征象,表现为肿瘤内无对比剂进入,不强化的区域,这与病理上所直接观察到的坏死并不完全对应。但是,本研究发现肿瘤坏死在三组的差异具有统计学意义,MRI上弥漫性高增强的ICC出现肿瘤坏死的比例最低,ICC瘤内坏死的影像-病理相关性尚需进一步研究验证,MRI上ICC瘤内坏死出现与否对ICC预后的价值亦需后续研究证实。

本研究存在一些不足之处。首先,这是一项回顾性的单中心研究,可能存在人群的选择偏倚。未来需要更大的样本量及多中心研究验证我们的发现。此外,因为本研究的预后分析是基于病灶可切除的人群,这限制了本研究结果在病灶不可切除的ICC患者中的应用。未来研究需进一步扩大研究群体,全面精准预测ICC患者预后。

综上所述,术前MRI动脉期强化模式是ICC术后DFS和OS的可靠预测因素的预后,较AJCC-TNM分期系统预后预测效能更优,有助于ICC临床管理、治疗决策及预后分层。

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