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磁共振扩散加权成像联合血清 AFP、CA125、CEA、CA199 检测 在早期原发性肝癌中的诊断价值研究 *

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摘要 目的:研究磁共振扩散加权成像(DWI)联合血清甲胎蛋白(AFP)、糖类抗原125(CA125)、癌胚抗原(CEA)、糖类抗原199(CA199)检测在早期原发性肝癌(PHC)中的诊断价值。**方法:**选取我院自2017年9月开始至2020年5月收治的63例早期PHC患者纳入研究,记作肝癌组,再取同期我院收治的61例良性肝病患者记作对照组。对所有受试者均实施DWI扫描,比较两组DWI图像信号强度。检测并比较两组血清AFP、CA125、CEA、CA199水平,以受试者工作特征(ROC)曲线分析上述各项血清学指标水平检测和DWI诊断早期PHC的效能。另外,比较PHC淋巴结转移患者和无淋巴结转移患者血清AFP、CA125、CEA、CA199水平。**结果:**肝癌组DWI信号强度为高信号人数占比高于对照组(均P<0.05)。肝癌组血清AFP、CA125、CEA、CA199水平均高于对照组(均P<0.05)。血清AFP、CA125、CEA、CA199水平联合DWI诊断早期PHC的曲线下面积、灵敏度以及特异度均高于上述各检查方式单独检测。PHC淋巴结转移患者的血清AFP、CA125、CEA、CA199水平均高于无淋巴结转移患者(均P<0.05)。**结论:**DWI联合血清AFP、CA125、CEA、CA199检测诊断早期PHC的价值较高,且淋巴结转移患者的血清AFP、CA125、CEA、CA199水平明显升高。

关键词:原发性肝癌;磁共振扩散加权成像;甲胎蛋白;癌胚抗原;糖类抗原125;糖类抗原199;转移

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The Diagnostic Value of Diffusion - weighted Magnetic Resonance Imaging Combined with Serum AFP, CA125, CEA and CA199 in Early Primary Liver Cancer*

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ABSTRACT Objective: To study the diagnostic value of diffused-weighted magnetic resonance imaging (DWI) combined with serum alpha-fetoprotein (AFP), carbohydrate antigen 125 (CA125), carcinoembryonic antigen (CEA) and carbohydrate antigen 199 (CA199) in early primary liver cancer (PHC). **Methods:** 63 patients with early PHC admitted to our hospital from September 2017 to May 2020 were included in the study, which were labeled as liver cancer group. Another 61 patients with benign liver disease admitted to our hospital during the same period were taken as the control group. DWI scans were performed on all subjects, the signal intensity of DWI images between the two groups were compared. The levels of serum AFP, CA125, CEA and CA199 were detected and compared between the two groups. Receiver operating characteristic (ROC) curve was used to analyze the efficacy of the above serological indicators and DWI in the diagnosis of early PHC. In addition, the levels of serum AFP, CA125, CEA and CA199 in patients with and without PHC lymph node metastasis were compared. **Results:** The proportion of patients with high DWI signal intensity in liver cancer group was higher than that in control group (all P<0.05). The levels of serum AFP, CA125, CEA and CA199 in the liver cancer group were all higher than those in the control group (all P<0.05). The area under curve, sensitivity and specificity of serum AFP, CA125, CEA and CA199 combined with DWI in early PHC diagnosis were all higher than those of the above inspection methods independently detected. The levels of serum AFP, CA125, CEA and CA199 in patients with PHC lymph node metastasis were all higher than those in the non-metastasis group (all P<0.05). **Conclusion:** The value of DWI combined with serum AFP, CA125, CEA and CA199 in the detection and diagnosis of early PHC is relatively high, and the serum AFP, CA125, CEA and CA199 levels in patients with lymph node metastasis are significantly increased.

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前言

原发性肝癌(PHC)是常见恶性肿瘤之一,且随着人们生活方式的不断改变以及生活环境的日益恶化,PHC 的发病率呈逐年上升的趋势^[1-3]。由此可见,对 PHC 患者进行早期准确的诊断和治疗具有极其重要的意义,亦是提高患者存活率的重中之重。然而,在临床实际工作中,由于 PHC 早期发病的病灶体积相对较少,且表现不典型,部分肝脏良性局灶性病灶动态增强扫描表现和 PHC 相似,从而导致 PHC 的早期诊断仍存在一定的难度。磁共振扩散加权成像(DWI)主要是通过检测机体组织内水分子扩散运动,继而实现对疾病进行诊断的一种影像学手段,在多种恶性肿瘤诊断过程中起着极其重要的作用^[4-6]。此外,甲胎蛋白(AFP)、糖类抗原 125(CA125)、癌胚抗原(CEA)、糖类抗原 199(CA199)均是目前临幊上广泛用于恶性肿瘤诊断的肿瘤标志物,在多种恶性肿瘤中均存在异常高表达^[7-9]。鉴于此,本文通过研究 DWI 联合血清 AFP、CA125、CEA、CA199 检测在早期 PHC 中的诊断价值,旨在为临床 PHC 的早期诊断提供参考依据,现作以下报道。

1 对象与方法

1.1 一般资料

将我院自 2017 年 9 月开始至 2020 年 5 月收治的 63 例早期 PHC 患者纳入研究,记作肝癌组。其中男女分别有 37 例、26 例;年龄范围 25~82 岁,平均年龄(58.15 ± 10.66)岁。淋巴结转移 23 例(转移组),无淋巴结转移 40 例(未转移组)。再选取同期我院收治的 61 例良性肝病患者记作对照组;其中男女分别有 38 例、23 例;年龄范围 24~83 岁,平均年龄(57.22 ± 10.71)岁。肝癌组和对照组性别及年龄无差异($P > 0.05$),均衡可比。入选标准:(1)所有受试者均符合《原发性肝癌诊疗规范(2017 版)》^[10]中所制定的相关诊断标准,肝癌分期为 I a 期~II b 期;(2)年龄 ≥ 24 岁;(3)均经手术病理活检确诊;(4)入院前并未接受相关抗肿瘤治疗。排除标准:(1)精神异常者;(2)存在其他恶性肿瘤者。纳入对象均已签同意书,本研究获得我院伦理委员会批准。

1.2 研究方法

(1)DWI: 使用仪器为 GE HDxt3.0 磁共振扫描仪,8 通道

体部相控阵线圈,对受试者肝区实施横断面和冠状面扫描。相关参数设置如下:TR 为 3200 ms,TE 为 94ms,FOV 为 350 mm \times 350 mm,矩阵为 128 \times 128,激励次数为 3 次。待常规扫描结束后,通过肘静脉注射 15 mL 的对比剂,随后在注射后 25s、60s 以及 200s 时进行动脉期、静脉期及延迟期扫描。相关参数设置如下:TR 为 1200 ms,TE 为 78.9 ms,层厚取 5.0 mm,层间距取 2 mm,FOV 为 400 mm \times 400 mm,矩阵为 128 \times 128,激励次数为 1 次,b 值为 500 s/mm²。最后将所有扫描数据传输至处理系统中实施分析,观察病灶边界、形状、信号强度等特征。所有图像数据分析均由我院 2 名经验丰富的放射诊断科医师以双盲法进行。(2)血清 AFP、CA125、CEA、CA199 水平检测:采集受试者空腹静脉血 5 mL,随后进行离心半径 12 cm、时长 10 min 的 3000 r/min 离心处理。取血清开展酶联免疫吸附法检测,步骤遵循试剂盒说明书完成,试剂盒由上海晶抗生物工程有限公司提供。

1.3 观察指标

比较两组 DWI 图像信号强度,血清 AFP、CA125、CEA、CA199 水平,分析血清 AFP、CA125、CEA、CA199 水平与早期 PHC 患者淋巴结转移的关系。

1.4 评价标准^[11]

血清 AFP、CA125、CEA、CA199 水平临床参考范围:AFP < 25 ng/mL, CA125 < 35 U/mL, CEA < 5 μ g/L, CA199 < 37 U/mL。检查结果超出正常参考值范围上限即为阳性。

1.5 统计学方法

以 SPSS 22.0 软件完成数据的分析,采用[n(%)]表示计数资料,实施 χ^2 检验,采用($\bar{x} \pm s$)表示计量资料,实施 t 检验。血清 AFP、CA125、CEA、CA199 水平及 DWI 诊断早期 PHC 的效能予以受试者工作特征(ROC)曲线分析。 $P < 0.05$ 即差异有统计学意义。

2 结果

2.1 两组 DWI 图像信号强度对比

肝癌组 DWI 信号强度为高信号人数占比高于对照组,而低或稍低信号、等信号人数占比均低于对照组(均 $P < 0.05$),见表 1。

表 1 两组 DWI 图像信号强度对比[n(%)]

Table 1 Signal intensity comparison of DWI images between the two groups[n(%)]

Groups	n	Low or slightly low signal	Equisignal	High signal
Liver cancer group	63	0(0.00)	0(0.00)	63(100.00)
Control group	61	5(8.20)	9(14.75)	47(77.05)
χ^2	-	5.381	10.023	16.299
P	-	0.020	0.002	0.000

2.2 两组血清 AFP、CA125、CEA、CA199 水平对比

(均 $P<0.05$), 见表 2。

肝癌组血清 AFP、CA125、CEA、CA199 水平均高于对照组

表 2 两组血清 AFP、CA125、CEA、CA199 水平对比($\bar{x}\pm s$)

Table 2 Comparison of levels of serum AFP, CA125, CEA and CA199 in the two groups($\bar{x}\pm s$)

Groups	n	AFP(ng/mL)	CA125(U/mL)	CEA(μg/L)	CA199(U/mL)
Liver cancer group	63	542.05±44.27	80.93±15.53	14.98±2.34	102.74±21.32
Control group	61	6.33±1.09	12.73±1.77	2.41±0.58	25.12±3.45
t	-	94.113	20.364	9.479	14.236
P	-	0.000	0.000	0.000	0.000

2.3 血清 AFP、CA125、CEA、CA199 水平及 DWI 诊断早期 PHC 的效能

血清 AFP、CA125、CEA、CA199 水平联合 DWI 诊断早期

PHC 的曲线下面积、灵敏度以及特异度均高于上述各检查方式单独检测, 见表 3、图 1。

表 3 血清 AFP、CA125、CEA、CA199 水平及 DWI 诊断早期 PHC 的效能

Table 3 Serum levels of AFP, CA125, CEA and CA199 and the efficacy of DWI in diagnosing early PHC

Diagnosis mode	Area under the curve	Sensitivity(%)	Specificity(%)	Youden index
AFP	0.611	63.12	60.05	0.232
CA125	0.624	63.97	60.42	0.244
CEA	0.619	63.23	61.01	0.242
CA199	0.630	66.30	59.04	0.253
DWI	0.713	75.16	69.25	0.444
4 items serum combined with DWI	0.856	89.46	81.24	0.707

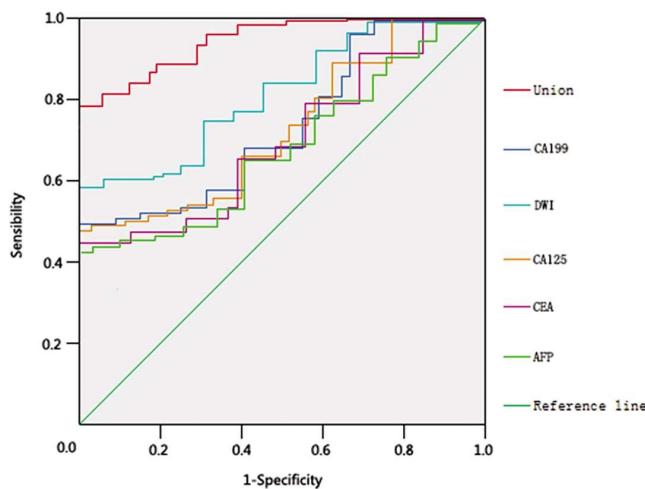


图 1 血清 AFP、CA125、CEA、CA199 水平及 DWI 诊断 PHC 的 ROC 曲线
Fig.1 Serum AFP, CA125, CEA, CA199 levels and ROC curve of DWI in diagnosis of early PHC

2.4 血清 AFP、CA125、CEA、CA199 水平与早期 PHC 患者淋巴结转移的关系分析

转移组患者的血清 AFP、CA125、CEA、CA199 水平均高于未转移组(均 $P<0.05$), 见表 4。

3 讨论

PHC 患者往往无特异性临床表现, 部分患者存在食欲减退、乏力以及腹胀等症状, 而当其一旦出现黄疸、肝区疼痛以及腹水等典型症状时,普遍已处于局部晚期或远处转移,彻底丧失了手术根治的最佳时机^[12-14],由此可见,在病情早期准确的诊断对 PHC 患者而言具有极其重要的意义。DWI 作为新型影像学手段之一,主要是通过表观扩散系数值进行组织病生理改变的评估,目前已被广泛应用于临床多种肿瘤疾病的诊断中,且效果明显^[15,16]。曹博等^[17]的研究表明,DWI 联合 AFP 可以提高 PHC 的诊断率;齐杰等^[18]的研究表明 DWI 联合 AFP 在 PHC 的早期诊断中具有较高的灵敏度、特异度及阳性似然度,为临床

表 4 血清 AFP、CA125、CEA、CA199 水平与早期 PHC 患者淋巴结转移的关系分析($\bar{x}\pm s$)

Table 4 Analysis of the relationship between the levels of serum AFP, CA125, CEA, CA199 and lymphatic metastasis of early PHC patients($\bar{x}\pm s$)

Groups	n	AFP(ng/mL)	CA125(U/mL)	CEA(μg/L)	CA199(U/mL)
Metastasis group	23	625.25±52.33	99.55±20.55	19.62±4.42	123.08±24.59
Non-metastasis group	40	494.21±41.39	70.23±12.19	12.31±2.94	91.05±317.48
t	-	11.245	4.670	2.956	3.249
P	-	0.000	0.000	0.004	0.002

诊断该疾病具有重要的参考价值。然而,DWI在临床实际应用中受呼吸运动、扫描时间等因素的影响,从而可能对其检查结果造成干扰,降低了诊断的灵敏度以及特异度。故此,DWI单独应用存在一定的局限性,可考虑联合其它检查手段进行PHC的诊断,以期提高临床诊断效能。此外,AFP是目前广泛用于肝癌诊断的一种血清标志物,可实现对PHC的早期诊断,但其存在灵敏度以及特异度均较低的特点,可能导致漏诊以及误诊情况的发生,继而促使患者无法得到及时有效的治疗,预后不良^[19]。因此,寻找更多积极有效的肿瘤标志物对PHC进行早期诊断显得尤为重要,亦是目前临床广大医务人员共同关注的热点。CA125、CEA及CA199作为常见的肿瘤标志物,目前已被应用于多种恶性肿瘤的诊断中,且具有一定的价值。

本文结果发现,肝癌组DWI信号强度为高信号人数占比高于对照组,这在陈斐等人的研究报道中得以佐证^[20],提示了PHC患者DWI主要表现为高信号。分析原因,磁共振成像扫描相较于传统B超或CT扫描而言,具有软组织分辨率较高等优势,可通过DWI序列扫描,实现对病灶性质的鉴别诊断。然而,DWI扫描仍存在一定的漏诊以及误诊几率,其主要原因可能和呼吸、心脏搏动引起的伪影有关^[21,22],因此,往往需综合其他检查方式完成诊断。此外,肝癌组血清AFP、CA125、CEA、CA199水平均高于对照组,提示了上述各项血清学指标水平在PHC患者中存在异常高表达。究其原因,AFP是一种于胎儿肝脏内合成的糖蛋白,于成人中的表达水平升高主要见于肝癌以及胃癌等恶性肿瘤,已成为国内外广泛应用于肝癌早期诊断的标志物^[23-25]。CA125作为肿瘤相关抗原家族成员之一,主要源自体腔上皮组织,于PHC中具有较高的敏感度,亦是目前临床上应用较为广泛的PHC诊断肿瘤标记物之一^[26]。CA199作为一种糖类蛋白肿瘤标志物,其在PHC中呈高表达^[27,28]。CEA是一种肿瘤胚胎抗原,于正常生理状态下几乎不表达,而在肿瘤患者的血液中存在明显异常升高^[29,30]。另外,血清AFP、CA125、CEA、CA199水平联合DWI诊断PHC的曲线下面积、灵敏度以及特异度均高于上述各检查方式单独检测,可能是由于联合检测具有一定的协同互补作用,从影像学表现以及血清肿瘤标志物两个方面实现对PHC的诊断,继而可提高诊断价值。本文结果还显示了早期PHC淋巴结转移患者的血清AFP、CA125、CEA、CA199水平均高于无淋巴结转移患者,提示了随着淋巴结转移的发生,患者上述血清学指标水平升高,考虑原因可能是随着淋巴结转移的发生,肿瘤细胞会发生侵袭,并且侵入血液循环之中,从而使上述各项肿瘤标志物水平的异常升高。

综上所述,DWI联合血清AFP、CA125、CEA、CA199检测可作为早期诊断PHC的可靠手段,且上述血清学指标水平可在一定程度上反映淋巴结转移情况。

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