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超声造影定量与动态增强 MRI 定量在宫颈癌诊断中的应用价值*

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摘要 目的:探究超声造影定量与动态增强 MRI 定量在宫颈癌诊断中的应用价值。**方法:**选择 2016 年 1 月至 2019 年 1 月于我院接受治疗的 86 例疑似宫颈癌患者为实验组,另选取同期于我院接受治疗的 50 例宫颈良性病变患者为对照组,分别对两组患者实施超声造影定量检测及动态增强 MRI 检查,对比两组患者各参数组间差异性,同时以病理学检测结果为金标准,分析两种检查手段对宫颈癌的筛查效果并实施组间比较。**结果:**(1)比较显示实验组患者的峰值强度(peak intensity,PI)及时间-曲线下面积(area under curve,AUC)均高于对照组,达峰时间(time to peak,TTP)及平均渡越时间(mean transit time,MTT)均低于对照组($P<0.05$);(2)比较显示实验组患者的容积转移常数(volume transfer constant, K^{trans})、速率常数(rate constant, k_{ep})以及血管外细胞外容积分数(extravascular extracellular volume fraction, V_e)均高于对照组,表观扩散系数(apparent diffusion coefficient,ADC)低于对照组($P<0.05$);(3)以病理学检测结果为金标准,超声造影定量检测对宫颈癌检测一致性为 93.02%,灵敏度为 94.44%,特异度为 85.71%,增强 MRI 对宫颈癌检测一致性为 96.51%,灵敏度为 98.61%,特异度为 85.71%。**结论:**宫颈癌患者实施超声造影定量与增强 MRI 检测时检测参数与正常宫颈组织相比会出现明显的差异性,可将上述两种检测方式用于宫颈癌患者的筛查诊断中。

关键词:超声造影定量;动态增强 MRI;宫颈癌;诊断

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Contrast-enhanced Ultrasound Quantification and Dynamic Enhanced MRI Quantification in the Diagnosis of Cervical Cancer*

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ABSTRACT Objective: To explore the value of contrast-enhanced ultrasound quantification and dynamic contrast-enhanced MRI quantification in the diagnosis of cervical cancer; **Methods:** 86 patients with suspected cervical cancer who were treated in our hospital from January 2016 to January 2019 were selected as the experimental group. Fifty patients with benign cervical lesions treated in our hospital during the same period were selected as the control group. Quantitative contrast-enhanced ultrasound and dynamic enhanced MRI were performed on the two groups of patients, and the differences between the two groups of parameters were compared. The result is the gold standard. The screening effect of the two screening methods on cervical cancer is analyzed and the comparison between groups is performed. **Results:** The comparison shows that the peak intensity (PI) and time-curve area (AUC) of the experimental group are high. In the control group, the peak time (TTP) and mean transit time (MTT) were lower than the control group ($P<0.05$). The comparison showed that the volume transfer constant (K^{trans}) and rate constant (k_{ep}) of the experimental group of patients The extravascular extracellular volume fraction (V_e) was higher than that of the control group, and the apparent diffusion coefficient (ADC) was lower than that of the control group ($P<0.05$). Based on the pathological test results, the gold standard, Quantitative sonography for cervical cancer has a consistency of 93.02 %, sensitivity of 94.44 %, and specificity of 85.71 %. Enhanced MRI has a consistency of 96.51 %, sensitivity of 98.61 %, and specificity of 85.71 % for cervical cancer. **Conclusion:** The detection parameters of cervical cancer patients undergoing quantitative ultrasound contrast and enhanced MRI detection will show significant differences compared with normal cervical tissues. The above two detection methods can be compared. Used in the screening diagnosis of cervical cancer patients.

Key words: Quantitative contrast-enhanced ultrasound; Dynamic contrast-enhanced MRI; Cervical cancer; Diagnosis

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前言

宫颈癌是妇科常见恶性肿瘤之一,其发病率仅次于乳腺

癌,位居女性恶性肿瘤发病率第二位,近些年,随着近些年居民生活方式与起居习惯的改变,宫颈癌的发病率呈现逐年上升趋势,统计数据显示,全球每年新增宫颈癌患者约为 50 万例,死

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亡例数约为 23.1 万例,我国每年宫颈癌新发病例高达 13.15 万,其发病率与死亡率均位居国内女性恶性肿瘤之首^[1-3]。病毒感染、多次分娩、吸烟等因素都可能会诱发宫颈癌,且由于早期宫颈癌临床症状不明显,多数患者在发现时宫颈癌已发展至中后期,现阶段对宫颈癌的治疗主要包括手术治疗、化学治疗与放射治疗等^[4-6],早期对宫颈癌的诊断及干预是提高患者预后的重要手段,对制定个体化治疗方案也具有重要意义。超声造影定量和动态增强 MRI 都是近些年临床上新兴的影像学检查手段,超声造影定量检测在肿瘤动态观测方面具有较好的技术优势,能够用于肿瘤血管程度动脉改变评估中,是一种无创性的微循环血管造影^[7,8];动态增强 MRI 则主要是在常规 MRI 平扫的基础上加用增强扫描,通过改变局部组织的磁环境而间接增强信号,用于肿瘤检测的手段^[9,10]。本研究旨在分析超声造影定量与动态增强 MRI 定量在宫颈癌中的诊断价值,为宫颈癌的筛查治疗提供进一步的理论依据,现详述如下。

1 资料与方法

1.1 一般资料

选择 2016 年 1 月至 2019 年 1 月于我院接受治疗的 86 例疑似宫颈癌患者为实验组,另选取同期于我院接受治疗的 50 例宫颈良性病变患者为对照组。

纳入标准:(1)意识清晰能够配合进行调研;(2)病历资料齐全;(3)调研经医院伦理学会批准实施;(4)患者及其家属对本次调研过程、方法、原理清楚明白并签署知情同意书;(5)实验组患者经初步检测拟诊断为宫颈癌且出现相应临床症状。

排除标准:(1)合并精神疾病患者;(2)合并其他恶性肿瘤患者;(3)合并全身感染性疾病患者;(4)合并严重心脑血管疾病患者;(5)妊娠或哺乳期女性;(6)已采取手术或放化疗治疗的宫颈癌患者。

1.2 干预方法

分别对两组患者实施超声造影定量及动态增强 MRI 定量

检测,超声造影定量检测选择仪器为西门子 ACUSON X150 系列彩色多普勒超声诊断仪,选择 4C1 型凸阵探头,设置探头频率为 6.0~7.0 MHz,选择第二代微泡造影剂(声诺维,生产厂家:瑞士 Bracco Suisse SA,规格 59 mg,注册号:国药准字 J20130045),患者检测时取仰卧位,检查者首先实施二维超声检测,采集数据后切换至增强造影模式,将造影剂由患者肘静脉注入,并同步观察病灶动态过程,记录 PI、AUC、TTP、MTT 等参数;1 周内再对患者实施动脉增强 MRI 检测,选择仪器为飞利浦 Ingenia 1.5T 型磁共振成像仪,分别对患者的常规轴位、矢状位进行扫描,设置层厚为 4 mm、间距为 1 mm,扫描矩阵为 256×256,重建矩阵为 512×512,记录两组患者的 ADC、 K^{trans} 、 k_{ep} 、 V_e ;两组患者的上述指标均由同一组影像学医师采取双盲形式进行判读,并最终以病理学检测结果为金标准,判读两种检测方式对宫颈癌筛查的价值。

1.3 观察指标及评测标准

分别记录两组患者实施超声造影定量及动态增强 MRI 定量时各参数的差异性,并以病理学检测结果为金标准(86 例患者中阳性 72 例,阴性 14 例),比对两种检测方式对宫颈癌的筛查诊断价值。

1.4 统计学方法

将采集的数据录入至 SPSS 20.0 软件中实施统计学分析,对于计量数据采取 $(\bar{x} \pm s)$ 的形式来表示,组间的差异性比较应用 t 检验,对于计量资料采取[n(%)]的形式表示,组间的差异性比较采用卡方检验,取 $P < 0.05$ 为差异具有统计学意义^[11]。

2 结果

2.1 一般临床资料比较

经评估比对发现,两组患者一般临床资料诸如年龄、体重、BMI、教育程度等比对差异不具有统计学意义($P > 0.05$),具体数据如表 1 所示。

表 1 两组患者一般临床资料比较

Table 1 Comparison of general clinical data between two groups of patients

Index		Experimental group (n=86)	Control group(n=50)
Age(year)		46.18±3.33	46.21±3.21
Weight(kg)		61.21±3.22	61.31±3.19
BMI(kg/m ²)		22.19±2.11	22.21±2.21
Education level	Illiteracy	5	3
	Primary school	12	5
	Junior high school	35	22
	High school and above	34	20
Marital status	Married	81	46
	Not married	7	4
Hypertension	Yes	14	8
	no	72	42
Diabetes yes	Yes	11	5
	No	75	45

- 2.2 两组患者超声造影血流灌注参数差异性比较 低于对照组,组间比较差异具有统计学意义($P<0.05$),具体数据如表 2 所示。

表 2 两组患者超声造影血流灌注参数比较($\bar{x}\pm s$)Table 2 Comparison of perfusion parameters of contrast-enhanced ultrasound blood flow in two groups ($\bar{x}\pm s$)

Groups	n	PI(%)	AUC	TTP(s)	MTT(s)
Experimental group	86	72.88 $\pm$ 1.54*	6711.28 $\pm$ 2011.28*	37.19 $\pm$ 1.43*	63.01 $\pm$ 10.21*
Control group	50	67.18 $\pm$ 1.44	5569.87 $\pm$ 1012.21	41.28 $\pm$ 1.23	67.18 $\pm$ 11.01

Note: compare with the control group, * $P<0.05$.

- 2.3 两组患者动态增强 MRI 定量参数差异性比较 对照组,组间同一指标比较差异具有统计学意义($P<0.05$),具体数据如表 3 所示。

表 3 两组患者动态增强 MRI 检测定量参数比较($\bar{x}\pm s$)Table 3 Comparison of quantitative parameters of dynamic enhanced MRI detection between in two groups ($\bar{x}\pm s$)

Groups	n	ADC	$K^{\text{trans}}/(\text{min})$	$k_{ep}/(\text{min})$	V_e
Experimental group	86	0.818 $\pm$ 0.132	0.298 $\pm$ 0.121	0.531 $\pm$ 0.112	0.521 $\pm$ 0.123
Control group	50	1.322 $\pm$ 0.121	0.039 $\pm$ 0.018	0.198 $\pm$ 0.014	0.291 $\pm$ 0.113

Note: compare with the control group, * $P<0.05$.

- 2.4 超声造影定量及动态增强 MRI 定量对宫颈癌诊断价值分析 增强 MRI 对宫颈癌检测一致性为 96.51%,灵敏度为 98.61%,以病理学检测结果为金标准,超声造影定量检测对宫颈癌检测一致性为 93.02%,灵敏度为 94.44%,特异度为 85.71%,

表 4 超声造影定量对宫颈癌诊断价值分析

Table 4 Analysis of diagnostic value of contrast-enhanced ultrasound in cervical cancer

Detection method	Pathologically positive(n=72)	Pathologically negative(n=14)
Contrast-enhanced ultrasound	positive(n=70)	68
	negative(n=16)	4
Dynamic enhanced MRI quantification	positive(n=73)	71
	negative(n=13)	1

3 讨论

宫颈癌是发病率仅次于乳腺癌的女性恶性肿瘤,据世界卫生组织国际癌症研究署(International Agency for Research on Cancer, IARC)报道,全球每年新发宫颈癌约有 53 万例,占有癌症发病例数的 5%,数据显示,据世界卫生组织下属国际癌症研究机构发布的 2018 年最新的宫颈癌数据显示,宫颈癌女性发病率占第 2 位,每年全球有 20 万妇女因宫颈癌死亡,中国占 10%左右^[12-14]。近些年随着居民生活方式的改变及饮食结构的调整,宫颈癌呈现年轻化趋势,给女性身心健康带来较大的威胁。早期的准确诊断是及时干预的前提,也是改善宫颈癌患者预后的重要基础,目前对宫颈癌诊断的方式包括病理检测、影像学检查、生化检测、基因检测等,其中病理检测和基因检测周期长、费用昂贵,不适宜临床推广,生化检测受个体激素水平影响较大,前后检测可能会出现明显的差异性,影像学检测具有无创、可重复性好、实施简单等优点,因而在临床上得以推广应用^[15,16]。

超声造影定量是在二维超声和彩色多普勒超声基础上发展起来的影像学检测手段,通过向受试者静脉内团注造影剂,

能够明显增强患者组织器官和血流灌注的显像程度,进而补充和提高血管超声成像,为疾病的诊断治疗提供可靠依据^[17-19]。临床实践发现^[20],超声造影定量相比 MRI 价格更为低廉,且安全性高,过敏反应发生率更低,近些年新一代的超声造影定量甚至能够实现血管高精度检测和血液灌注定量分析,已在多种恶性病变的诊断中取得了较好的应用效果^[21,22]。MRI 具有较好的软组织分辨率,在宫颈癌浸润深度判定、宫旁组织侵犯以及淋巴结转移方面具有较好的应用效果,而动态增强 MRI 则能够动态显示宫颈癌病灶的血供特点,强化病变特征,为临床诊断提供更准确的理论依据^[23,24]。

本研究通过设立不同分组的方式,就超声造影定量与动态增强 MRI 定量在宫颈癌诊断中的应用价值进行了探究,结果显示,相比于良性宫颈病变患者,疑似宫颈癌患者的超声造影定量中 PI 及 AUC 均高于对照组, TTP 及 MTT 均低于对照组,本研究与刘薇等学者的研究类似,该学者探究了超声造影与动态增强 MRI 在乳腺病灶诊断价值,结果显示超声造影与动态增强 MRI 在诊断乳腺病灶中具有较好的一致性,可以成为动态增强 MRI 的可替代检查方法^[25],有研究指出,宫颈癌患者行超声造影是会呈现处不同的增强特征,主要表现包括高增强、

非均匀、向心性等特征^[26,27]。我们分析认为,出现上述差异的原因主要为,与正常或良性病变宫颈组织相比较,恶性病变宫颈组织中的新生微血管密度大大增加,同时血管走向较为紊乱,这就导致了病灶内血管走向不一致、分布不均匀,而这种变化体现在造影定量检测上就表现在达峰时间短、峰值强度高^[28,29]。研究指出,恶性肿瘤内存在大量新生血管,这些新生血管因缺乏管壁肌层,血管壁较薄,同时由于走行弯曲,易与周边的小动脉形成瘘管,因而造影剂能够在较短的时间内流入病灶区域,缩短达峰时间^[30,31]。文中的研究结果还显示,实验组患者的 K^{trans} 、 k_{ep} 以及 V_e 均高于对照组,ADC低于对照组,目前,国内外还没有报道与此结果类似的研究,多数研究只应用动态增强磁共振成像定量评价对肿瘤的诊断价值^[32]。我们分析认为,肿瘤的快速生长依赖于血管的供应,已有较多的研究证实肿瘤中的微血管密度要明显高于正常组织,而动态增强MRI定量参数 K^{trans} 、 k_{ep} 以及 V_e 值是检测部位血管密度和组织密切联系的,如血流量、血管密度、血管渗透性、间质压力等都会影响检测结果。宫颈癌组织虽然新生血管较多,但血管多较不成熟,血管壁不成熟导致通透性增加,使得单位时间内对比剂从血管进入组织的速度大大提高,在静脉内对比剂被廓清的速度也大大提高,因而宫颈癌患者的 K^{trans} 、 k_{ep} 以及 V_e 值均明显高于正常组织。文中还就两种检测方式在评估宫颈癌准确性方面进行了对比,结果显示虽然动态增强MRI定量对宫颈癌筛查的一致性、灵敏度和特异度均高于超声造影定量,但两种检测方式间的差异不大,提示两种检测方式在宫颈癌诊断方面均具有较好的应用价值。本研究将超声造影定量与增强MRI检测创新性的用于宫颈癌患者的筛查诊断中,取得了一定的诊断价值,为以后宫颈癌的早期的准确诊断提供了新的方法。但是本研究也存在一定的不足,样本量少,仅仅重点观察可疑病灶,缺乏全面性、系统性、直观性。后续研究需要综合考虑,优化选择检查方法。

综上所述,宫颈癌患者实施超声造影定量与增强MRI检测时检测参数与正常宫颈组织相比会出现明显的差异性,可将上述两种检测方式用于宫颈癌患者的筛查诊断中,有助于为临床诊断提供更准确的理论参考依据,值得进行临床推广应用。

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