

### 3.0T MR 弥散加权成像评价中晚期食管鳞癌放化疗的早期疗效

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**【摘要】目的:**探讨3.0 T磁共振(MR)弥散加权成像(DWI)在评价中晚期食管鳞癌放化疗早期疗效的应用价值。**方法:**收集2016年6月~2017年12月在泉州市第一医院拟行根治性放化疗的53例中晚期食管癌患者,于治疗前后不同时间点行常规MR平扫及DWI检查。根据近期疗效评价结果分为有效组和无效组,比较两组治疗前后肿瘤ADC值、 $\Delta$ ADC及肿瘤最大径变化,对ADC值变化率评价食管癌放化疗早期疗效进行ROC曲线分析。**结果:**本组53例患者,有效41例,无效12例。有效组与无效组在治疗1周末、治疗2周末及治疗结束时ADC值均逐渐增高( $P<0.05$ ),且有效组在上述各时点的 $\Delta$ ADC均显著高于无效组( $P<0.05$ )。两组在治疗1周末肿瘤最大径与治疗前比较差异无统计学意义( $P>0.05$ ),治疗2周末及治疗结束时较治疗前均明显减小( $P<0.05$ )。ROC曲线分析显示,治疗1周末ROC曲线下面积最大(0.785),以该时刻ADC值变化率(15.5%)为阈值,评价放化疗近期疗效是否有效的敏感性为86.5%、特异性为69.8%、阳性预测值为89.4%、阴性预测值为63.4%。**结论:**MR-DWI对评价食管鳞癌放化疗早期疗效有重要价值,治疗1周末的ADC值变化率可作为优选疗效预测时间点。

**【关键词】**磁共振;弥散加权成像;食管鳞癌/药物治疗;食管鳞癌/放射治疗;早期疗效

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### Evaluation of the early therapeutic effect of radiotherapy and chemotherapy for advanced esophageal squamous cell carcinoma by 3.0T MR diffusion weighted imaging

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**Abstract: Objective** To investigate the value of 3.0T magnetic resonance (MR) diffusion weighted imaging (DWI) in evaluating the early therapeutic effect of radiotherapy and chemotherapy for advanced esophageal squamous cell carcinoma. **Methods** A total of 53 patients with advanced esophageal cancer who were scheduled for radical radiotherapy and chemotherapy in the First People's Hospital of Quanzhou City from June 2016 to December 2017 were selected. Routine plain MR scan and DWI examination were performed at different time points before and after treatment. According to the short-term therapeutic effect, the patients were assigned into effective group and ineffective group. The changes of apparent diffusion coefficient (ADC) values,  $\Delta$ ADC and the maximum diameter of the tumor before and after treatment were compared between two groups. The change rate of ADC value in evaluation of early therapeutic effect of radiotherapy and chemotherapy for esophageal cancer was analyzed by receiver operating characteristic curve (ROC) curve. **Results** Forty-one cases were assigned into effective group and 12 cases in ineffective group. ADC values of effective group and ineffective group gradually increased after 1 week of treatment, after 2 weeks of treatment and at the end of treatment ( $P<0.05$ ), and  $\Delta$ ADC was significantly higher in effective group than in ineffective group at above time points ( $P<0.05$ ). There was no significant differences of the maximum diameter of the tumor in two groups before treatment and after 1 week of treatment ( $P>0.05$ ), but the diameter was significantly decreased after 2 weeks of treatment and at the end of treatment ( $P<0.05$ ). ROC curve analysis showed that the area under ROC curve was the largest after 1 week of treatment (0.785). With the change rate of ADC at this time point (15.5%) as the threshold, the sensitivity, specificity, positive predictive value and negative predictive value for evaluating the short-term therapeutic effect of radiotherapy and chemotherapy were 86.5%, 69.8%, 89.4% and 63.4%, respectively. **Conclusion** MR-DWI is of great value in evaluating the early therapeutic effect of radiotherapy and chemotherapy for esophageal squamous cell carcinoma. The change rate of ADC value after 1 week of treatment can be used as the optimal time point for predicting the therapeutic effect.

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## 前言

弥散加权成像(Diffusion-weighted Imaging, DWI)作为一类新的磁共振(Magnetic Resonance, MR)功能成像技术在肿瘤放化疗领域展现出了良好的应用前景。有研究显示MR-DWI通过反映细胞分子水平病理生理改变而能够较好地评价多种肿瘤的放化疗早期疗效<sup>[1-3]</sup>。在食管癌研究上,最近亦有学者指出MR-DWI对食管癌治疗反应有着确切预测作用<sup>[4]</sup>。然而,目前国内外关于MR-DWI在食管癌放化疗领域的研究报道仍较为少见,亦未取得明确结论。本研究对食管癌患者放化疗前后进行MR-DWI检查,旨在探讨该MR技术在评价中晚期食管鳞癌放化疗早期疗效的应用价值,以期为临床提供指导。

## 1 资料与方法

### 1.1 一般资料

收集2016年6月~2017年12月泉州市第一医院收治的中晚期食管癌患者。纳入标准:(1)符合《实用肿瘤内科学》<sup>[5]</sup>中有关食管癌诊断标准,并均经病理组织诊断证实;(2)卡氏评分(KPS)在70分以上;(3)均接受MR常规及DWI检查;(4)临床分期为IIIa~IIIb期,均经会诊确定无法进行手术治疗,并拟行根治性放化疗;(5)既往无放化疗治疗史;(6)检查前均签署知情同意书。排除标准:(1)既往存在恶性肿瘤史者;(2)存在MR检查禁忌证;(3)未完成治疗者。共入组53例,其中男35例,女18例;年龄45~78岁,中位年龄60岁;肿瘤部位:颈段5例,胸上段14例,胸中段30例,胸下段4例;放化疗前食管钡餐造影显示肿瘤长度2.2~10.1 cm,中位长度5.9 cm;放化疗治疗前CT检查显示合并淋巴结转移者48例,未合并淋巴结转移者5例;病理类型均为鳞癌;临床分期:IIIa期25例,IIIb期28例。

### 1.2 放疗方法

所有患者均行CT模拟定位,将所获取的CT扫描图像传输至治疗计划系统(TPS),并行靶区及危及器官(OAR)勾画。肿瘤区(GTV)、临床靶区(CTV)、计划靶区(PTV)确定及外扩按照CT图像标准进行,并结合食管钡餐造影、内镜、DWI等多项检查信息综合确定。全组处方剂量为60 Gy,单次剂量2.0 Gy,分30次,5次/周,共6周。要求PTV 95%体积接受100%以上处方剂量照射,全肺 $V_5$ 不超过55%~60%, $V_{20}$ 不

超过25%~30%, $V_{30}$ 不超过18%,心脏平均剂量不超过30 Gy,脊髓最大剂量小于45 Gy,对治疗计划进行验证后开始治疗。

### 1.3 化疗方法

根据患者情况实施同期化疗或巩固化疗,采取FP方案(顺铂75 mg/m<sup>2</sup>,分3~5 d给予;氟尿嘧啶450~500 mg/m<sup>2</sup>,分5 d给予)或TP方案(紫杉醇135 mg/m<sup>2</sup>;d<sub>1</sub>,顺铂25 mg/m<sup>2</sup>,d<sub>2-4</sub>)。

### 1.4 MR扫描方法

采用Discovery 750 3.0T MR扫描仪(美国GE公司),8通道体部相控阵线圈。扫描时,患者取仰卧位,双臂平放,以头足位进入主磁场。常规平扫快速自旋回波(FSE)-T<sub>1</sub>加权成像(T<sub>1</sub>-Weighted Imaging, T<sub>1</sub>WI)(TR为250 ms, TE为2.3 ms,层厚为5 mm,层间距为0.5 mm,FOV为23 cm×46 cm,矩阵为384×180,采集次数为2次);FSE-T<sub>2</sub>加权成像(T<sub>2</sub>-Weighted Imaging, T<sub>2</sub>WI)(TR为6 316 ms, TE为97.2 ms,层厚为5 mm,层间距为0.5 mm,FOV为36 cm×42 cm,矩阵为320×224,采集次数为2次)。DWI采用单次激发自旋回波平面成像(SE-EPI)序列,横轴位,扫描参数:TR为8 000 ms, TE为65.5 ms, b=1 000 s/mm<sup>2</sup>, FOV为44 cm×48 cm,矩阵为96×130,层厚为5 mm,层间距为1 mm,采集次数为8次,弥散梯度方向为ALL模式。

### 1.5 图像处理

将扫描图像上传至MRI后处理工作站AW4.1上,并采用系统软件Functool 2.0行DWI图像后处理,获取表观扩散系数(ADC)图。由2名高年资影像科医师评估DWI图像用于诊断及肿瘤ADC值测量的可行性。感兴趣区(ROI)的选择参照T<sub>2</sub>WI图像显示病变部位、形态,在含有病变的DWI图像上不规则划线圈入全部高信号病变区,尽可能避开不均质低信号。对肿瘤所有层面ADC值进行测量,并计算平均ADC值。对病变所有层面肿瘤最大径进行测量,并计算平均最大径。ADC值变化率指放化疗前后肿瘤平均ADC值差值占放化疗前肿瘤平均ADC值的比率,即 $\Delta ADC = (ADC_{放化疗后} - ADC_{放化疗前}) / ADC_{放化疗前} \times 100\%$ 。肿瘤最大径缩小率指放化疗前后肿瘤最大径差值占放化疗前肿瘤最大径百分比,即 $\Delta \text{肿瘤最大径} = (\text{肿瘤最大径}_{放化疗前} - \text{肿瘤最大径}_{放化疗后}) / \text{肿瘤最大径}_{放化疗前} \times 100\%$ 。

1.6 近期疗效评价

依据食管癌放疗后近期疗效评价标准,肿瘤完全消失,维持时间不少于4周,为完全缓解(CR);肿瘤最大径缩小 $\geq 30\%$ ,维持时间不少于4周,为部分缓解(PR);肿瘤最大径变化介于上述PR与PD之间,为疾病稳定(SD);肿瘤最大径增大 $\geq 20\%$ ,为疾病进展(PD),将CR、PR纳入有效组,SD、PD纳入无效组。

1.7 统计学方法

应用SPSS 20.0软件进行统计学分析,计量资料均满足正态分布,采用均数 $\pm$ 标准差表示,采用方差齐性分析、成组 $t$ 检验进行统计分析及变化描述;用

ROC曲线分析ADC值变化率对食管癌放化疗疗效的评价价值;以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 治疗反应情况

本组53例患者经治疗后,CR 21例(39.62%),PR 20例(37.74%),SD 12例(22.64%),治疗总有效率为77.36%(41/53)。

2.2 治疗前后食管癌T<sub>2</sub>WI图、DWI图及ADC图

典型患者影像资料见图1。

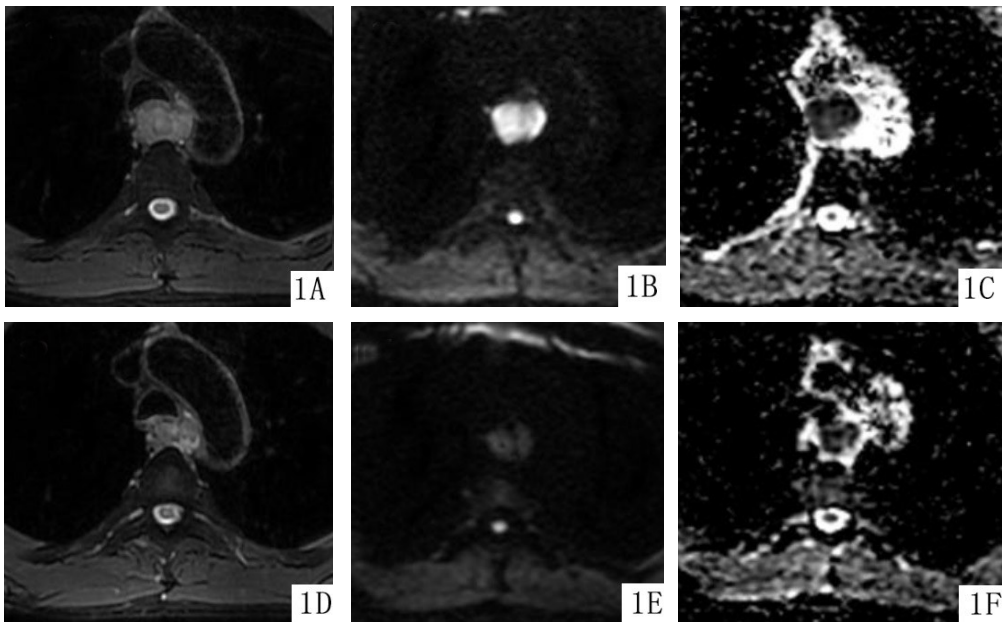


图1 患者,男,47岁,食管胸上段鳞癌

Fig.1 A 47-year-old male with squamous cell carcinoma of the upper-thoracic esophagus

Fig.1 A, B and C were the T<sub>2</sub>-weighted imaging, diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) images before treatment. Fig.1 D, E and F were the T<sub>2</sub>-weighted imaging, DWI and ADC images after treatment. DWI image showed significantly high signals before treatment, and the average ADC value of the tumor was  $1.68 \times 10^{-3} \text{ mm}^2/\text{s}$ . The maximum diameter of the tumor was significantly reduced after treatment. The high signals on DWI image were significantly decreased after treatment, and the average ADC value of the tumor was  $2.08 \times 10^{-3} \text{ mm}^2/\text{s}$ .

2.3 有效组与无效组治疗前后ADC值比较

两组在治疗1周末、治疗2周末及治疗结束时ADC值均逐渐增高( $P<0.05$ ),且有效组在治疗1周末、治疗2周末及治疗结束时的 $\Delta$ ADC均显著高于无效组( $P<0.05$ )。见表1、2。

2.4 有效组与无效组治疗前后肿瘤最大径比较

两组在治疗1周末肿瘤最大径与治疗前比较差异无统计学意义( $P>0.05$ ),治疗2周末及治疗结束时较治疗前均明显减小( $P<0.05$ )。见表3。

表1 有效组与无效组治疗前后ADC值比较( $\times 10^{-3} \text{ mm}^2/\text{s}$ ,  $\bar{x} \pm s$ )

Tab.1 Comparison of ADC values between effective group and ineffective group before and after treatment ( $\times 10^{-3} \text{ mm}^2/\text{s}$ ,  $\text{Mean} \pm \text{SD}$ )

Group	Before treatment	After 1 week of treatment	After 2 weeks of treatment	At the end of treatment	F value	P value
Effective (n=41)	1.58 $\pm$ 0.48	1.93 $\pm$ 0.51 <sup>a</sup>	2.09 $\pm$ 0.53 <sup>a</sup>	2.94 $\pm$ 0.61 <sup>a</sup>	17.232	<0.05
Ineffective (n=12)	1.43 $\pm$ 0.26	1.60 $\pm$ 0.23 <sup>a</sup>	1.74 $\pm$ 0.28 <sup>a</sup>	2.16 $\pm$ 0.49 <sup>a</sup>	15.467	<0.05

Compared with before treatment, <sup>a</sup> $P<0.05$



表2 有效组与无效组治疗后各时间点ΔADC比较(% ,  $\bar{x} \pm s$ )

Tab.2 Comparison of ΔADC between effective group and ineffective group at each time point after treatment (% , Mean±SD)

Group	After 1 week of treatment	After 2 weeks of treatment	At the end of treatment
Effective (n=41)	22.15±6.84	32.28±8.74	78.28±13.21
Ineffective (n=12)	11.89±3.42	21.68±6.54	54.12±9.87
t value	4.992	3.884	5.858
P value	<0.05	<0.05	<0.05

表3 有效组与无效组治疗前后肿瘤最大径比较(mm,  $\bar{x} \pm s$ )

Tab.3 Comparison of the maximum diameter of the tumor in effective group and ineffective group before and after treatment (mm, Mean±SD)

Group	Before treatment	After 1 week of treatment	After 2 weeks of treatment	At the end of treatment	F value	P value
Effective (n=41)	67.21±15.36	63.34±16.69	45.47±13.84 <sup>a</sup>	23.59±9.14 <sup>a</sup>	24.127	<0.05
Ineffective (n=12)	71.25±9.46	69.37±11.54	61.28±7.13 <sup>a</sup>	55.36±6.72 <sup>a</sup>	19.244	<0.05

Compared with before treatment, <sup>a</sup>P<0.05

2.5 ROC 曲线分析

对治疗1周末、治疗2周末、治疗结束时ADC值变化率进行ROC曲线分析,其中治疗1周末ROC曲线下面积最大,此时诊断效能最高,以该时刻ADC值变化率(15.5%)为阈值,评价放化疗近期疗效是否有效的敏感性、特异性、阳性预测值、阴性预测值依次为86.5%、69.8%、89.4%、63.4%。

3 讨论

放化疗是中晚期食管癌的主要治疗手段,寻找有效手段评价食管癌放化疗早期疗效对及时调整治疗方案、改善患者预后有着重要意义。目前,临床常采取测量肿瘤体积的方式进行抗肿瘤治疗反应评价,但由于食管管腔呈不规则形状,常规影像在测量肿瘤体积上存在较大难度,且放化疗早期根据肿瘤体积减小或缩小率来评价治疗有效性仍缺乏可靠报道。MR-DWI基于其特殊的成像原理,能够从分子水平上描述组织内水分子弥散运动的分子生物学特征,并以ADC对扩散程度进行量化,从而呈现与组织含水量相关的形态、病理改变<sup>[6-7]</sup>。目前关于MR-DWI已被报道应用于预测多种恶性肿瘤的抗肿瘤治疗反应中,但未取得一致结论,这可能与各类型肿瘤病理生理基础及不同研究资料存在差异有关<sup>[8-9]</sup>。在食管癌研究中,关于治疗前ADC值与抗肿瘤治疗反应的研究结论各家报道亦存在较大差异<sup>[10-11]</sup>。

研究表明经有效治疗后,肿瘤ADC值可出现增高,并指出这与治疗后肿瘤组织密度减小有关<sup>[12]</sup>。治疗前,食管癌组织由于肿瘤细胞大量增殖,组织密

度较高,细胞外隙空间较小,加之细胞生物膜限制等多种因素,限制了水分子扩散,从而使得ADC值较低;而放化疗治疗后,肿瘤细胞膜遭到破坏,细胞大量死亡,细胞外隙空间扩大,易于水分子扩散,故而ADC值增高<sup>[13]</sup>。本研究结果显示,有效组与无效组在治疗1周末、治疗2周末及治疗结束时ADC值均逐渐增高,这与既往研究报道保持一致。有研究认为治疗后ADC值升高是治疗初期普遍发生的反应,与病理类型及治疗方法无关<sup>[14-15]</sup>。本研究比较有效组与无效组在治疗1周末、治疗2周末及治疗结束时的ADC值增长率,结果显示有效组在上述3个时间点的ΔADC均明显高于无效组。由此,笔者认为无效组并非不受放化疗影响,而是肿瘤对放化疗敏感性较之有效组要低,两组放化疗后ΔADC差异是由肿瘤对抗肿瘤治疗敏感性不同而引起的。王澜等<sup>[16]</sup>研究结果显示不同疗效组放化疗后ΔADC无明显差异,但该研究比较的CR组与PR组ΔADC差异,这可能是造成两项报道存在差异的原因之一。本研究还显示治疗1周末,有效组与无效组肿瘤最大径较治疗前无显著变化,故可认为相比于肿瘤体积变化,治疗后肿瘤ADC值变化更早,亦更为可靠。

本研究还进行了ADC值变化率评价食管癌放化疗早期疗效的ROC曲线分析,结果显示治疗1周末ROC曲线下面积最大(0.785),此时诊断效能最高,以该时刻ADC值变化率(15.5%)为阈值,评价放化疗近期疗效是否有效的敏感性、特异性、阳性预测值、阴性预测值依次为86.5%、69.8%、89.4%、63.4%。考虑到两疗效组治疗1周末肿瘤最大径均无显著变化,故

笔者认为,放化疗1周末ADC变化率或许是评价食管癌治疗反应的理想时间点,较之形态学评估更为可靠,因此,建议食管癌放化疗1周末行MR-DWI复查,获取ADC值数据,为治疗策略制定提供指导。然而关于ADC变化率阈值的确定仍有待开展多中心、大样本量研究加以探讨。

综上所述,MR-DWI作为一种新型功能成像手段,在评价中晚期食管鳞癌放化疗早期疗效上有重要价值,治疗1周末的ADC值变化率是理想的监测时间点。

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