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3.0 TMRI Diffusion Weighted Imaging in Assessing the Efficacy of Cervical Cancer Chemo-radiotherapy

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Abstract: **To analyze DWI magnetic resonance imaging both anterior and posterior to cervical cancer chemotherapy and to explore the application of ADC and EADC values in predicting and monitoring the efficacy of cervical cancer chemotherapy. Perform conventional MR scanning and DWI on 52 cases of cervical cancer patients prior to chemotherapy and fifteen days, one month, and two months into chemotherapy. At different check points, measure ADC and EADC values and the maximum diameter of the tumor. Analyze differences in ADC and EADC values before and after chemotherapy. ADC changes take place earlier than morphological changes in tumor volume. ADC values are significantly higher than those before treatment while EADC values get lower. 2 months into the treatment, the reduction rate of the maximum tumor diameter is negatively correlated to ADC values before the treatment ($r = -0.658$, $P < 0.05$). 15 days into the treatment, the mean ADC values increase ($t = 11.119$, $p < 0.05$). EADC values decrease ($t = -9.916$, $p < 0.05$). And the maximum tumor diameter shows no significant change from that before the treatment ($t = -1.797$, $p > 0.05$). ADC and EADC values before cervical cancer chemotherapy may help predict the efficacy of cancer treatment. ADC and EADC values during the treatment may contribute to early detection and dynamic observation of therapeutic effect.**

Keywords: Cervical cancer; Magnetic resonance imaging; Diffusion weighted imaging; Chemo-radiotherapy

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1. Introduction

Cervical cancer mortality ranks the highest among all female genital tract malignancies. The preferred method of treatment for advanced cervical cancer is concurrent chemotherapy[1]. Early prediction and monitoring of chemotherapy sensitivity of cervical cancer patients has long been a hot issue in clinical research on gynecologic oncology. With diffusion weighted imaging (DWI) being widely applied in body diagnosis, more and more researchers begin to adopt ADC values to conduct quantitative analysis on water molecule diffusion movement in the diseased tissue . This study is to analyze dynamic changing trend of the maximum tumor diameter, DWI image features, ADC values, and EADC values at different time points after cervical cancer patients begin to receive chemotherapy, and to investigate the application of DWI in predicting the efficacy of cervical cancer chemotherapy.

2. Materials and Methods

2.1 General Materials

In the author's hospital from January, 2012 to November, 2014, 52 cases of cervical cancer having received or to receive chemo-radiotherapy, including 48 cases of squamous cell carcinoma and 4 cases of glandular cancer. The patients are aged from 37 to 75, (53.3±2.4) on average. The maximum diameter of the cancer before treatment is 23 ~ 89 mm, (47.2 ± 3.8) mm on average. Patients in the group never received any cancer treatment before the examination.

2.2 Examination method and imaging parameters

Use GE Signa3.0T MR Scanner. Perform conventional MR scanning and DWI on 52 patients prior to chemotherapy and fifteen days, one month, and two months into chemotherapy. The patients are required to fast for 8 ~ 12h before examination and to be in normal respiration during examination. Scan areas from the upper edge of the ilium to the lower edge of the pubic symphysis. All patients in turn undergo conventional MRI scanning and DWI. Conventional axial T1W, TR300 ~ 600ms, TE2 ~ 20ms; T2W, TR2000 ~ 8000ms, TE80 ~ 150ms; coronal T2W, TR2000 ~ 8000ms, TE80 ~ 150ms; axial DWI, TR2000 ~ 8000ms, TE80 ~ 150ms; layer thickness 6 mm, layer spacing 2 mm, matrix 230 × 256, FOV40 × 40, NEX4 times, b taking 0 and 800 s/mm2.

2.3 Image post-processing and measurement classification

Transmit original images onto AW 4.3 workstation.

Process images with FUNCTOOL analysis software. With reference to T2WI and DWI images, choose uniform signal areas on ADC maps as regions of interest (ROI).And measure ADC and EADC values. Based on Response Evaluation Criteria in Solid Tumors (RECIST) [2], divide patients into a complete remission (CR) group and a partial remission (PR) group.

2.4 Statistical analysis

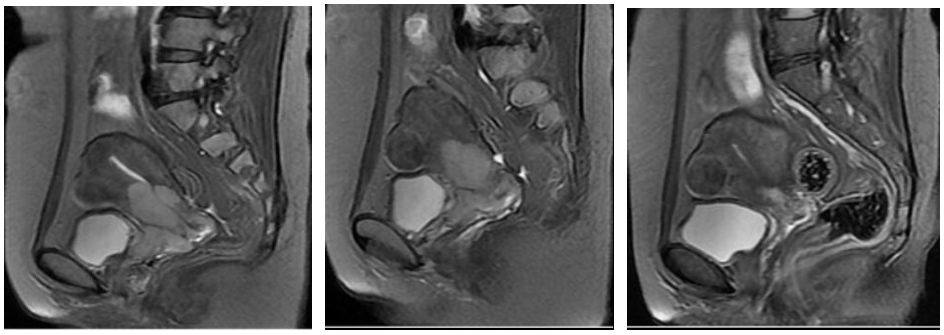
Use SPSS 19.0 software. Process data with two separate samplet tests. Conduct randomized block variance analysis and Pearson bivariate correlation analysis. P <0.05 is considered statistically significant.

Table 1 ADC and EADC Values of CR Group and PR Group in Different Treatment Phases

Treatment Phase	CR Group		PR Group	
	ADC (×10-3mm2/s)	EADC	ADC (×10-3mm2/s)	EADC
Before Treatment	0.764±0.073	0.546±0.033	0.986±0.049	0.457±0.018
15 Days into Treatment	1.703±0.044**	0.258±0.009*	1.577±0.047**	0.289±0.012**
1 Month into Treatment	1.730±0.024**	0.251±0.005*	1.674±0.025**	0.261±0.005**
2 Months into Treatment	1.799±0.035**	0.237±0.007*	1.752±0.009**	0.246±0.002**
* Significantly different from that before treatment, p＜0.05. ** p＜0.01				

Table 2 - ADC and EADC Values and Maximum Tumor Diameter in Different Treatment Phases

Treatment Phase	ADC(×10-3mm2/s)	EADC	Maximum Tumor Diameter (mm)
Before Treatment	0.944±0.046	0.474±0.017	47.21±3.83
15 Days into Treatment	1.601±0.040**	0.283±0.010**	46.86±3.77
1 Month into Treatment	1.685±0.097**	0.259±0.004**	21.57±1.50**
2 Months into Treatment	1.761±0.047**	0.244±0.002**	6.48±1.09**
* Significantly different from that before treatment, p＜0.01.			



A B C

Figure 1. Female patient with cervical squamous cell carcinoma: the sagittal T2WI images A) before treatment, B) after 15 days of treatment, and C) after 2 months of treatment.

3. Results

3.1 Efficacy assessment and ADC and EADC values

tumor change did not reach 30%. Table 1 shows ADC and EADC values of CR group and PR group prior to chemotherapy and fifteen days, one month, and two months into chemotherapy. Before treatment, ADC variance between CR group and PR group was statistically significant (P <0.05). And EADC variance was also statistically significant (P <0.05).

After two months of treatment, MR showed that the tumor completely disappeared in 9 cases (CR group) and partially disappeared in 42 cases. (Tumor size in PR group decreased by at least 30%). Only in case the

3.2 Maximum tumor diameter changes

Table 2 shows the average maximum tumor

diameter at different check points. The maximum diameter 15 days into treatment shows no significant difference from that before treatment. The maximum diameter 1 month and 2 months into treatment shows significant difference from that before treatment. (Figure A, B and C.) Thus, it is concluded that morphological changes lag behind changes in ADC and EADC values after treatment. 15 days into treatment, changes in ADC and EADC values become significant. Among all 52 cases, the average ADC value before treatment is (0.944±0.046) × 10-3mm2/s. After two months of treatment, the average maximum diameter reduction ratio is (85.69±2.38) %. ADC values before treatment are negatively correlated to the maximum diameter reduction ratio after two months of treatment (r = -0.658, P <0.05). After 15 days of treatment, the ADC changing rate is (40.24 ± 3.24) %. After a month of treatment, the ADC changing rate is (44.03 ± 2.51) %. Both values are positively correlated to the maximum diameter reduction ratio after two months of treatment (r = 0. 783, P=0. 000; r=0. 676, P=0. 001).

4. Discussion

Different proliferation characteristics of water molecules in tumor and normal tissues constitute the theoretical basis for DWI to differentiate between tumor and normal tissues[3]. The density of tissue cells is closely related to the signal intensity on DWI and ADC values [4]. Naganawa et al [5] have showed that the average ADC value of cervical lesions and normal cervical tissues are respectively (1.09 ± 0.20) × 10-3mm2/s and (1.79 ± 0.24) × 10-3mm2/s. The main reason for the difference is that cancer cells are mostly exuberant, causing the cell to increase both internal external water content and cell density. The adsorption of water molecules in proteins is also enhanced so that the intracellular space increases. The effective movement of water molecules within the tumor is limited, resulting in increased DWI signal and decreased ADC value [6]. Through effective anti-tumor therapy, cancer cells in cervical cancer tissues die through apoptosis and necrosis, with cell membrane integrity disappearing, extracellular space increasing, cell density decreasing, DWI signal lowering and ADC values increasing [7]. The goal of cancer treatment is to maximally kill tumor cells and reduce damage to normal tissues. Thus, tissue functions change prior to morphological changes. Therefore, it is feasible to apply DWI to early efficacy evaluation before any tumor size changes. As ADC value of tumor tissue is related to the degree of tumor regression or the slacking growth rate after treatment, it is thus possible to predict tumor sensitivity to treatment at early stages [8]. After treatment, ADC value of tumor tissue is gradually getting close to that of normal cervical tissue [5]. Meanwhile, DWI technique is simple and less time consuming. When effectively combined with other approaches, it has a high clinical value in the early evaluation of the efficacy of cervical cancer treatment.

This study shows that, after 15 days of cancer treatment, ADC values get significantly higher while EADC values get significantly lower. Meanwhile, the narrowing of maximum tumor diameter is not obvious, indicating that changes in the value of ADC and EADC take place earlier than changes in tumor volume. With ongoing therapy, ADC values continue to rise. CR and PR group demonstrate significant difference after 15 days and a month of treatment. Therefore, it can be concluded that, after chemotherapy, ADC value of cervical cancer manifests a gradually increasing trend while EADC value a gradually decreasing trend. ADC value before treatment is negatively correlated to the changing rate of the maximum tumor diameter after treatment. For those with good efficacy, the change in measurement magnitude is relatively big. And for those with poor efficacy, small measurement change ensues. Before treatment, ADC value of CR group is lower than that of PR group. Therefore, DWI examination in the early stage of treatment may not only conduct an early evaluation on the efficacy of chemotherapy, but also dynamically monitor the effect of chemotherapy on cervical cancer.

In previous studies, the morphological changes of the tumor were used to assess the effect of cancer treatment and to predict the sensitivity to cervical cancer chemotherapy. But the morphological changes come later than quantitative indicators which are highly effective in the early prediction of treatment efficacy [9]. And the effect of monitoring is closely related to functional magnetic resonance imaging.

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