

The Value of Magnetic Resonance Diffusion-Weighted Imaging in Evaluating the Efficacy of Concurrent Chemoradiotherapy in Patients with Hypopharyngeal Carcinoma

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Abstract

Objective: To investigate the application value of magnetic resonance diffusion-weighted imaging (DWI) combined with conventional magnetic resonance imaging (MRI) in evaluating the efficacy of concurrent chemoradiotherapy for hypopharyngeal carcinoma. **Methods:** A total of 20 patients with hypopharyngeal carcinoma diagnosed by pathological biopsy (who only received chemoradiotherapy without surgery) were collected. Before treatment, all patients underwent conventional MRI and DWI scanning, MRI characteristics of patients were analyzed, and maximum cross-sectional area of the tumor and average apparent diffusion coefficient (ADC) value were measured. One month after treatment, MRI was performed again to measure residual tumor area and ADC value, and the tumor remission rate was calculated. The changes in tumor ADC values before and after treatment were analyzed and their correlation with tumor remission rate was analyzed. The differences in ADC values and changes between complete response patients (CR group) and incomplete response patients (non-CR group) before and after treatment were analyzed. **Results:** The tumor area of 20 patients with hypopharyngeal cancer was 3.48 (0.93 - 5.6) cm² before treatment and 0.24 (0 - 0.9) cm² after treatment. There were 15 patients (15/20, 75%) in the CR group and 5 patients (5/20, 25.0%) in the non-CR group. The remission rate was 90.3% (6.0% - 100%). The average ADC value of the tumor before treatment was negatively correlated with the tumor remission rate after treatment ($r = -0.786, -0.813, P < 0.05$), and the average ADC value after treatment was positively correlated with the remission rate ($r = 0.669, P < 0.05$). The average ADC value of the non-CR group before treatment was higher than that of the CR group, and the average ADC value and the change of the average ADC value before

and after the treatment in the CR group were higher than those in the non-CR group, with statistical significance (all $P < 0.05$). **Conclusion:** The ADC value of tumor before treatment and the change of ADC value of tumor before and after treatment have a certain significance in evaluating the early remission rate of hypopharyngeal carcinoma after chemoradiotherapy.

Keywords

Hypopharyngeal Carcinoma, Magnetic Resonance Diffusion-Weighted Imaging, Radiotherapy, Chemotherapy

1. Introduction

Hypopharyngeal carcinoma is a common malignant tumor in the head and neck, mainly squamous cell carcinoma, and its incidence has been increasing gradually in recent years. Due to its complex anatomical structure, large surgical trauma, and difficult radical treatment, concurrent chemoradiotherapy is the main clinical treatment method, and a reasonable surgical plan combined with radiotherapy can preserve organ function and achieve better efficacy. Therefore, how to early predict and evaluate the sensitivity of tumors to chemoradiotherapy has important clinical significance for the development of individualized treatment plans. At present, many studies have shown that diffusion-weighted imaging (DWI) plays an important role in tumor diagnosis, identification, and differentiation of radioactive responses and tumor recurrence or residual [1] [2] [3], and provides quantitative indicators for tumor treatment effects. The value of apparent diffusion coefficient (ADC) calculated by DWI can reflect the diffusion ability of tissue water molecules and the microstructural characteristics such as tumor biology and cell structure, which has important reference value for the diagnosis of benign and malignant tumors, tumor invasiveness and prognosis [4]. The purpose of this study was to investigate the application value of ADC of DWI in the evaluation of curative effect and prognosis in patients with hypopharyngeal carcinoma.

2. Materials and Methods

2.1. General Information

A total of 20 patients with hypopharyngeal cancer who were treated in the Department of Radiation Head and Neck Synthesis of Shanxi Cancer Hospital from March 2015 to March 2018 were selected as the research objects, including 19 males and 1 female; aged 46 - 80 years old, with an average age of 60.8 years old; Tumor stage: 6 cases of T1 stage, 8 cases of T2 stage (patients refused surgery), 3 cases of T3 stage, and 3 cases of T4 stage. All patients were confirmed to be squamous cell carcinoma by laryngoscopy biopsy, and all received comprehensive chemoradiotherapy treatment without surgery. This study was approved by

the Ethics Committee of Shanxi Cancer Hospital. All patients were informed about the study before the examination and signed informed consent.

2.2. Treatment Methods

Among the 20 patients, patients with T1 stage only received radiotherapy, the total dose of radiotherapy was 50 Gy, with 2 Gy for each time, 5 times a week, a total of 25 times. Patients with stage T2 - T4 were treated with induction chemotherapy first, and the patients were treated with TP regimen, TP: docetaxel 60 mg/m² for day 1, nedaplatin 30 mg/m² for day 1 - 3, with every 21 days as a cycle, a total of 2 cycles. After induction chemotherapy, concurrent chemoradiotherapy was performed. During concurrent chemoradiotherapy, TP regimen was used for chemotherapy, and intensity modulated radiotherapy was used. The total radiotherapy dose was 70 Gy, with 2.12 Gy for each time, 5 times a week, a total of 32 - 33 times.

2.3. Examination Method

All 20 patients were examined with a PHILIPS Achiva 3.0T TXMR scanner, and an 8-channel head and neck combined coil was used. The patient was placed in the supine position, breathing calmly, and coughing and swallowing were avoided as much as possible during the examination. All patients underwent conventional MRI plain scan, enhanced scan and DWI examination before and 1 month after treatment. Conventional MRI plain scan plus enhanced scan: Transverse plane TSE T1WI (TR 550 ms, TE 8.55 ms), coronal plane TSE T2WI (TR 3000 ms, TE 80 ms), transverse plane fat suppression sequence T2WI (TR 4650 ms, TE 85 ms), enhanced scanning of fat suppression T1WI in transverse, coronal and sagittal planes, contrast agent GD-DTPA (Bayer, Germany) was injected at a dose of 0.2 mL/kg. Layer thickness was 4 mm, layer spacing was 1 mm, the field of view (FOV) of transverse plane was 230 mm × 260 mm, matrix was 512 × 512; the scanning range was from the base of the skull to the root of the neck. DWI examination: single-shot SE-EPI sequence was used for transverse plane scanning, b = 0 and 1000 s/mm², FOV of 230 mm × 260 mm, matrix of 256 × 256, slice thickness of 4 mm, slice spacing of 1 mm.

2.4. Image Analysis

All MRI images were diagnosed, evaluated and measured by two radiologists with rich experience in MRI diagnosis without knowing the pathology and efficacy, and the diagnosis result was based on the joint opinion of two physicians. The MRI manifestations of the lesion area were observed before and after treatment. Region of Interest (ROI) selection and data measurement were based on plain T2WI and DWI sequences, and the maximum cross-sectional area of the tumor was measured on the transverse plane enhanced T1WI images before and after treatment. On the GE AW 4.5 workstation, Functool software was used to delineate the maximum cross-section of the tumor before treatment as ROI be-

fore treatment. Each ROI was measured 3 times, and the average value was taken as the final ADC value of each ROI. According to the ADC diagram of the maximum cross-section of the tumor, the highest and lowest ROI were delineated in the areas with the lightest and heaviest diffusion limitation (the area was 10 - 30 mm², pay attention to avoid hemorrhagic or necrotic areas), and the highest and lowest ADC values were obtained. The anatomical structure of the primary tumor area in the CR group after treatment was delineated. If no obvious tumor was found after treatment, the primary tumor area was delineated as ROI. The maximum cross-sectional area of residual tumors in the non-CR group was the ROI after treatment, and the average ADC value in this region was obtained.

2.5. Efficacy Evaluation Criteria

Two experienced radiologists evaluated tumor remission at the end of treatment (within 1 month after the end of treatment) when the efficacy of the tumor was unknown. According to the response evaluation criteria in solid tumors (RECIST) [5], the efficacy of the tumor remission in the lesion area was evaluated: 1) Complete response (CR): the tumor disappeared completely, and the tumor remission rate was 100%; 2) Partial response (PR): the tumor was partially relieved and not completely disappeared, but the tumor remission rate $\geq 30\%$; 3) Stable disease (SD): the tumor progressed steadily, and the tumor remission rate $< 30\%$. Tumor remission rate = (area before treatment - area after treatment) / area before treatment $\times 100\%$.

2.6. Statistical Methods

SPSS 22.0 statistical software was used for statistical analysis. Kolmogorov-Smirnov *Z* test was used for normality test, and the normality test showed that the results of all relevant measurement items followed normal distribution ($P > 0.05$). Pearson linear correlation analysis was used to analyze the correlation between the ADC value of different tumor stages and the tumor remission rate. Two independent sample *T* tests were used to compare the difference of the average ADC values before and after treatment between the CR group and the non-CR group. $P < 0.05$ was considered statistically significant.

3. Results

3.1. MRI Manifestations before and after Treatment

Before treatment, tumors in different parts invaded the surrounding adjacent tissue structures (for example, tumors involved the posterior pharyngeal wall, posterior annulus area, piriform fossa, left and right ventricular bands, vocal cords, aryepiglottic fold and surrounding spaces, and mucosa was significantly thickened), showing uneven equal and low signal on T1WI, and uniform or uneven slightly high and high signal on T2WI. After enhancement, the lesions showed different degrees of obvious enhancement, showed slightly higher or higher sig-

nal on DWI, and obvious uneven enhancement after enhancement. After treatment, the tumors were significantly reduced or disappeared, the lesion area showed equal or slightly low signal on T1WI, slightly high or high signal on T2WI, uniform or uneven enhancement after enhancement, and equal or slightly higher signal intensity on DWI. As shown in **Figure 1**.

3.2. Changes in Lesion Area and Evaluation of Efficacy

The average maximum cross-sectional area of tumors in the 20 patients was 3.48 (0.93 - 5.6) cm² before treatment and 0.24 (0 - 0.9) cm² after treatment. In 11 patients, the tumor disappeared completely within 1 month after treatment. There were 15 patients (15/20, 75%) in the CR group and 5 patients (5/20, 25.0%) in the non-CR group. The remission rate was 90.3% (6.0% - 100%).

3.3. Comparison of ADC Value before and after Tumor Treatment

Compared with the ADC value before radiotherapy, the ADC value at the end of radiotherapy was significantly higher than that before treatment, but both were significantly lower than the ADC value of normal tissues. The difference was statistically significant ($P < 0.001$).

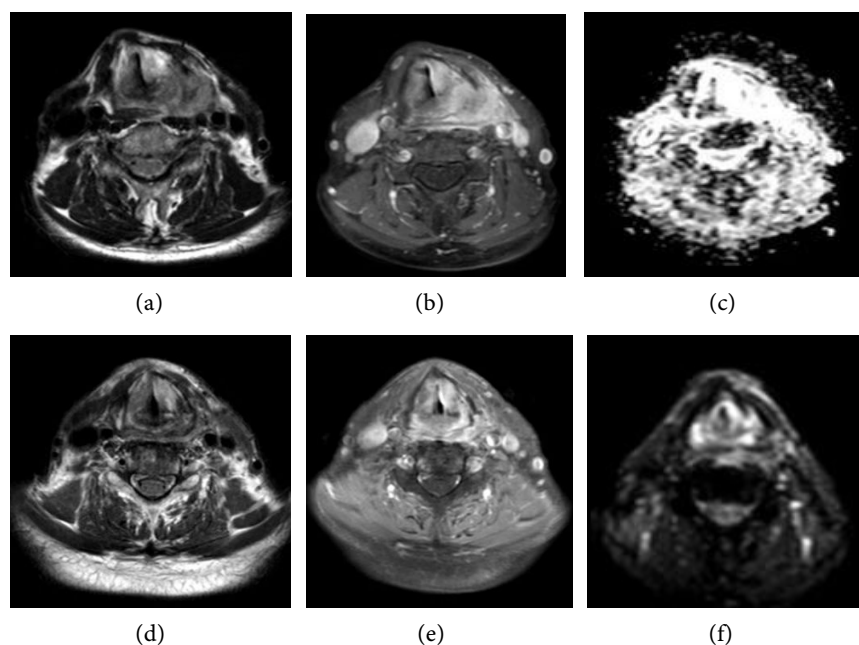


Figure 1. A 66-year-old male patient, hypopharyngeal carcinoma (T4N1M0). Note: Before treatment ((a)-(d)): (a): T2WI showed that the lesion was located in the left hypopharynx, involving the left laryngeal ventricle and left thyroid cartilage; enlarged lymph nodes were seen in the left area, about 1.3 cm in size; (b): Enhanced scan showed uneven enhancement of the lesion, and the maximum axial cross-sectional area was 2.1×3.4 cm²; (c): DWI showed obvious high signal of the lesion; (d): The average ADC value of the lesion was 0.94×10^{-3} mm²/s. After treatment ((d), (e) and (f)): (e): (T2WI) and (f): (enhanced scan) showed that the mass shrunk after treatment, the maximum axial cross-sectional area was 1.0×1.2 cm², and the original enlarged lymph node was significantly reduced (about 0.6 cm in size), with no definite manifestation. The tumor remission rate was 85%.

3.4. Correlation Analysis between ADC Value and Tumor Remission Rate

The average and maximum ADC values of all patients before treatment were negatively correlated with the remission rate, while the average ADC values after treatment were positively correlated with the remission rate. As shown in **Table 1**.

3.5. Comparison of ADC Values of Tumor between CR Group and Non-CR Group

The average ADC value of the tumor in the non-CR group before treatment was higher than that in the CR group, and the average ADC value of the tumor in the CR group after treatment and the change in the average ADC value of the tumor before and after treatment in the CR group were higher than those in the non-CR group, and the differences were statistically significant ($P < 0.001$). As shown in **Figure 2** and **Figure 3**.

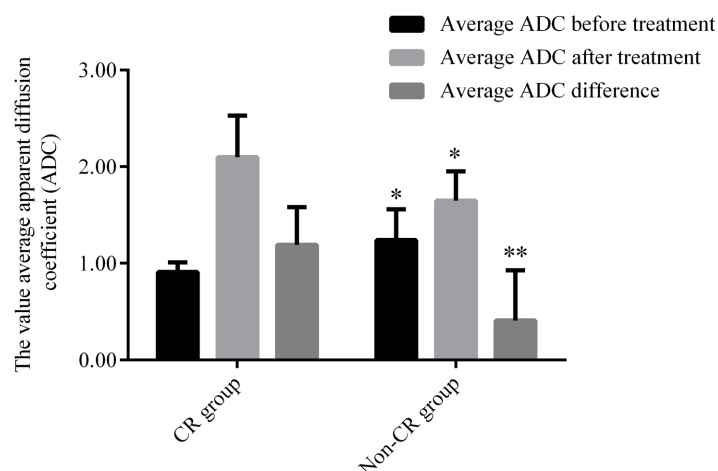


Figure 2. Comparison of the average ADC values before and after treatment in the CR group and the non-CR group. Note: There were 15 patients in the CR group and 5 patients in the non-CR group, * represents compared with CR group, $P < 0.05$; ** represents compared with CR group, $P < 0.01$.

Table 1. The correlation coefficient between the average ADC value before and after treatment and the tumor remission rate after treatment in different T stages.

T stage (cases)	Average ADC before treatment	Average ADC after treatment
T1 (3)	0.877	0.744
T2 (10)	-0.786*	0.669*
T4 (5)	-0.813*	0.300
Total cases (20)	-0.714*	0.673*

Note: There were only 2 cases in T3 stage, so no correlation analysis could be performed, * represents $P < 0.05$ for correlation analysis.

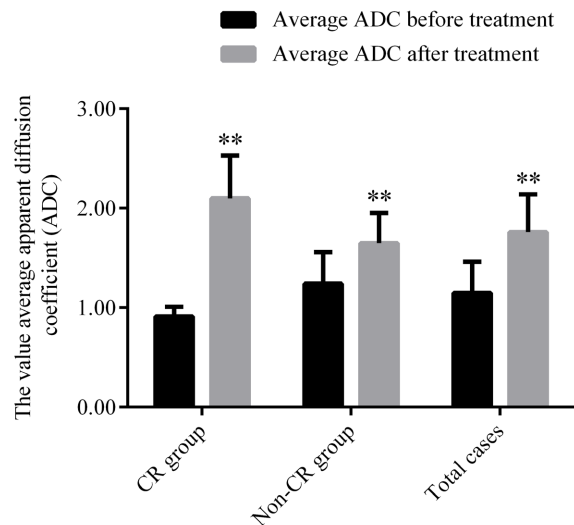


Figure 3. Comparison of the average ADC values before and after treatment in the CR group and the non-CR group. Note: There were 15 patients in the CR group and 5 patients in the non-CR group, * represents compared with CR group, $P < 0.05$; ** represents compared with CR group, $P < 0.01$.

4. Discussions

At present, CT, MR and dynamic enhanced MR examinations are mostly used to identify complications and tumor recurrence after treatment of hypopharyngeal carcinoma, but they cannot meet the needs of clinical differential diagnosis. MRI technology makes up for this defect to a certain extent. MRI DWI can provide more microscopic anatomical information, help to identify benign and malignant lesions, assist lymph node staging, and predict the efficacy of chemoradiotherapy in early stage, identify local granulation tissue hyperplasia, radioactive reaction, infection and tumor recurrence after tumor treatment [5] [6]. MRI plays an important role in the selection and optimization of therapeutic strategies for head and neck tumors. Its ADC value can provide quantitative indicators of tumor conditions before and after treatment. DWI measures changes in tissue signal intensity by applying diffusion-sensitive gradient field, reflecting microscopic movement of water molecules in living tissues under physiological and pathophysiological states. It provides histopathological information of tumor cell density and cell membrane integrity, which is sensitive to changes in the microenvironment before and after tumor treatment, and can monitor changes in tissue components and pathological changes during tumor treatment [7] [8]. DWI uses ADC to quantitatively describe the diffusion and motion state of water molecules in vivo. Malignant tumor cells tend to grow in accumulation, with increased cell density, reduced extracellular space, and severe restriction diffusion of water molecules. Therefore, they are often characterized by high DWI signal and reduced ADC value [9].

At present, a large number of studies at home and abroad have proved that the ADC value of most malignant tumors is significantly lower than that of be-

nign tumors and tumor-like lesions; moreover, the lower the degree of cell differentiation, the lower the ADC value of tumors. Zhang W *et al.* [10] found that among malignant lesions, the ADC value of malignant lymphoma was lower than that of squamous cell carcinoma. In benign lesions, the ADC value of adenomas is lower than that of benign cysts. Song *et al.* [11] reported that DWI can be used to differentiate nasopharyngeal carcinoma from nasopharyngeal lymphoma. The ADC value of nasopharyngeal lymphoma is about $(0.75 \pm 0.19) \times 10^{-3} \text{ mm}^2/\text{s}$, while that of NPC is about $(0.98 \pm 0.16) \times 10^{-3} \text{ mm}^2/\text{s}$, so the ADC value of nasopharyngeal lymphoma is lower than that of NPC. Similarly, when neck lymph node metastasis occurs in head and neck squamous cell carcinoma, DWI can be used as a method to distinguish neck lymph node metastasis from inflammatory lymphadenopathy. Pang B *et al.* [12] showed that the ADC value of metastatic lymph nodes was lower than that of inflammatory lymph nodes, that of metastatic lymph nodes was about $0.850 \times 10^{-3} \text{ mm}^2/\text{s}$, and that of inflammatory lymph nodes was about $1.448 \times 10^{-3} \text{ mm}^2/\text{s}$. When the ADC value was $1.03 \times 10^{-3} \text{ mm}^2/\text{s}$, the sensitivity and specificity in differentiating benign and malignant lymph nodes were 100% and 92.9%. Yang FJ *et al.* [13] studied 40 patients with head and neck squamous cell carcinoma, and found that the ADC values of complete remission and partial remission before treatment were $1.04 \pm 0.19 \times 10^{-3} \text{ mm}^2/\text{s}$ and $1.35 \pm 0.30 \times 10^{-3} \text{ mm}^2/\text{s}$ respectively, and the complete remission was significantly lower than the partial remission, and the two were statistically significant ($P < 0.05$). At the same time, it was found that the ADC value increased in the first week of concurrent chemoradiotherapy, and the increase was greater in complete remission than in partial remission. These results indicate that the measurement of ADC value before treatment and the change of ADC value after treatment can predict the effect of chemoradiotherapy for head and neck malignant tumor. A foreign study [14] monitored the changes of ADC values in patients with head and neck squamous cell carcinoma before treatment and after concurrent chemoradiotherapy, and found that the changes of ADC values in patients with complete remission were more significant than those in patients with recurrence in the early stage of treatment ($P < 0.01$). Lin M *et al.* [15] used DWI to study 65 patients with nasopharyngeal carcinoma undergoing concurrent chemoradiotherapy, and the results showed that the ADC value before treatment had a high predictive value for the efficacy of nasopharyngeal carcinoma, and the average and highest ADC values before treatment were negatively correlated with the tumor regression rate ($P < 0.001$). The average ADC value before tumor treatment was used as the cut-off value to predict tumor CR, indicating that DWI and ADC value can better predict the therapeutic effect of nasopharyngeal cancer, which can provide a basis for the individualized treatment of nasopharyngeal cancer. However, there are controversies in some studies on the conclusion of ADC value in predicting the efficacy of head and neck squamous cell carcinoma. Whether such differences are related to the selection of p-value or pathological type needs to be confirmed by further studies [16]

[17]. In conclusion, DWI plays an important role in the diagnosis of primary tumor and metastatic lymph node of head and neck squamous cell carcinoma before treatment, efficacy evaluation during treatment, and early detection of recurrence and complications after treatment.

We have been looking for non-invasive and efficient examination methods to evaluate and predict the therapeutic effect of concurrent chemoradiotherapy in patients with hypopharyngeal cancer, so as to provide a basis for the development of individualized strategies for tumor treatment. The results of this study showed that the average ADC value of tumors before treatment was negatively correlated with the remission rate, while the average ADC value of tumors after treatment was positively correlated with the remission rate ($P < 0.05$). The average ADC value of the non-CR group before treatment was higher than that of the CR group, and the average ADC value of the CR group after treatment and the change in the average ADC value of the tumor before and after treatment of the CR group were higher than those of the non-CR group, the difference was statistically significant ($P < 0.001$). These results indicate that chemoradiotherapy leads to degeneration and necrosis of tumor cells, enlargement of extracellular space, decreased limitation of water molecule diffusion, increased ADC value, hypoxic areas, and areas insensitive to chemoradiotherapy in tumors, and changes in ADC before and after treatment can be used as an evaluation index of treatment effect. However, there are many shortcomings in this study: 1) only the changes of tumors before and within one month after treatment were studied, which is a short-term follow-up; 2) The number of cases was small, and the individual analysis of patients with PR and SD was lacking; 3) In the selection of ROI, the human factor is relatively large, and the deviation of the location and the delineation of the region will affect the results; 4) After treatment, some patients may have local edema and acute radiation injury, resulting in high ADC value after treatment, which will affect the effect of ADC value change on the judgment of efficacy. In the future, it will be improved to expand the number of cases and obtain more accurate data to provide a clinical treatment basis and guide treatment.

5. Conclusion

In conclusion, the ADC value of the tumor before treatment and the change of the ADC value of the tumor before and after treatment have a certain significance for evaluating the early remission rate of patients with hypopharyngeal carcinoma after chemoradiotherapy. However, since the background signal is suppressed on DWI, it is difficult to identify the normal anatomical structure, which is not conducive to the accurate localization of the lesion. Therefore, it is necessary to combine the conventional MR to accurately judge the anatomical structure. The lack of specificity is the biggest defect in the clinical application of DWI technology. ADC value is a comprehensive index, which only reflects the random movement of water molecules in the intercellular space of microscopic tissues in a limited and specific time period. At present, DWI images alone can-

not be used for clinical diagnosis. It is only used as an auxiliary to MRI for clinical diagnosis, which needs to be further studied.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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