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Utility of intravoxel incoherent motion diffusion-weighted imaging in predicting early response to concurrent chemoradiotherapy in oesophageal squamous cell carcinoma

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AIM: To investigate the utility of intravoxel incoherent motion diffusion-weighted imaging (IVIM-DWI) in predicting the early response to concurrent chemoradiotherapy (CRT) in oesophageal squamous cell carcinoma (OSCC).

MATERIALS AND METHODS: Thirty-three patients with OSCC who received CRT underwent IVIM-DWI at three time points (before CRT, at the end of radiotherapy 20 Gy, and immediately after CRT). After CRT, the patients were divided into the responders (complete response or partial response) and the non-responders (stable disease) based on RECIST 1.1. The IVIM-DWI parameters (apparent diffusion coefficient [ADC], true diffusion coefficient [D], the pseudo-diffusion coefficient [D*], and the perfusion fraction [*f*]) values and their percentage changes (Δvalue) at different time points were compared between the responders and the non-responders. Receiver-operating characteristic (ROC) curve analysis was used to determine the efficacy of IVIM-DWI parameters in identifying the response to CRT.

RESULTS: The tumour regression ratio showed negative correlations with ADC_{pre} (r=−0.610, p=0.000), $ADC_{20\ Gy}$ (r=−0.518, p=0.002), D_{pre} (r=−0.584, p=0.000), and $D_{20\ Gy}$ (r=−0.454, p=0.008), and positive correlation with $\Delta D_{20\ Gy}$ (r=0.361, p=0.039) and ΔD_{post} (r=0.626, p=0.000). Compared to the non-responders, the responders exhibited lower ADC_{pre}, D_{pre}, $ADC_{20\ Gy}$, and $D_{20\ Gy}$, as well as higher $\Delta ADC_{20\ Gy}$, $\Delta D_{20\ Gy}$, and ΔD_{post} (all $p<0.05$). D_{pre} had the highest sensitivity (92.9%) and value of area under the ROC curve (0.865) in differentiating the responders from the non-responders.

CONCLUSION: Diffusion-related IVIM-DWI parameters (ADC and D) are potentially helpful in predicting the early treatment effect of CRT in OSCC.

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Introduction

Oesophageal cancer is one of the most common malignant tumours; it has the fourth highest morbidity rate in China and a 5-year survival rate of <40% worldwide.[1] A majority of patients with oesophageal cancer are diagnosed at an advanced stage because of the lack of obvious early symptoms.[2] Currently, chemoradiotherapy (CRT) is considered an effective treatment regimen for locally advanced or unresectable oesophageal cancer, and it may improve the survival rate[3,4]; however, not all patients benefit equally from CRT, because their outcomes mainly depend on the response to chemotherapy and/or radiotherapy.[5,6] Therefore, early prediction of therapeutic response is important for making appropriate and timely adjustments to therapy regimens.

Traditional imaging techniques, including computed tomography (CT), magnetic resonance imaging (MRI), oesophageal barium meal, and endoscopic ultrasound, rely mainly on morphological changes to evaluate the therapeutic response of oesophageal cancer. Usually, therapy-induced early changes in the tumour microenvironment occur prior to morphological changes, and the former changes cannot be detected by traditional imaging techniques. Combined positron-emission tomography and CT and dynamic contrast-enhanced MRI, as functional imaging approaches, have been used for evaluating the therapeutic response to CRT in patients with oesophageal cancer[7–9]; however, these approaches are difficult to popularise because of their exorbitant expense or contraindications to the administration of gadolinium contrast agents.

Conventional diffusion-weighted imaging (DWI), another functional MRI approach, is potentially helpful in predicting the response to CRT in oesophageal cancer[10–14]; however, the prediction potency of the apparent diffusion coefficient (ADC) derived from conventional DWI, especially the initial ADC, was inconsistent across different studies.[15,16] The signal intensity on DWI is also believed to be influenced by perfusion besides diffusion.[17] Therefore, a weakness of conventional DWI in quantitating microenvironmental information of tissues is that the influence of microcirculation perfusion on diffusion signal intensity is completely ignored by the mono-exponential decay model, which is the basis of conventional DWI. On the basis of the bi-exponential model,[18] intravoxel incoherent motion DWI (IVIM-DWI) can simultaneously obtain diffusion and perfusion information from tissues, without the administration of an exogenous contrast agent. In recent years, several studies have demonstrated that IVIM-DWI has an advantage over conventional DWI in predicting the therapeutic response in a variety of tumours, such as rectal cancer,[19] nasopharyngeal carcinoma,[20] and metastatic bone tumours[21]; however, the utility of IVIM-DWI in evaluating the early response to CRT in oesophageal cancer has not been well understood. Considering that oesophageal squamous cell carcinoma (OSCC) is the main pathological type of oesophageal cancer in China,[22] the purpose of this pilot study was to investigate the feasibility of IVIM-DWI in predicting the early response to concurrent CRT in patients with OSCC.

Materials and methods

Patient selection and treatment procedure

This study was approved by the Medical Ethics Committee of Hunan Cancer Hospital and the Affiliated Cancer Hospital of Xiangya School of Medicine and all patients signed written informed consent forms. Patients were enrolled into the study if they (i) had histopathologically confirmed OSCC via endoscopic examination, with a clinical stage of II–IV; (ii) did not receive any anti-tumour therapy before enrolment; (iii) were >18 years of age; (iv) were scheduled for concurrent CRT; and (v) had a Karnofsky score ≥80. Patients were excluded if they (i) did not sign the informed consent form; (iii) had any contraindication to MRI or CRT; or (iii) had irregular respiratory rhythm during MRI examinations. Between September 2015 and May 2017, 41 patients with OSCC were initially enrolled into this study.

The clinical stages of all patients were determined by an experienced oncologist doctor (with >15 years of experience in thoracic radiotherapy), with reference to the 7th edition of the Union for International Cancer Control/American Joint Committee on Cancer staging system.[23] According to the National Comprehensive Cancer Network guideline, all patients received two cycles (a dose of 50 mg/m^2 paclitaxel plus 25 mg/m^2 nedaplatin on days 1 and 8) of weekly chemotherapy, accompanied by concurrent intensity-modulated radiation therapy (2 Gy/fraction/day; five fractions per week; total radiation dose, 40 Gy).

Conventional MRI and IVIM-DWI protocols

All patients with OSCC received conventional MRI and IVIM-DWI examinations at three time points (before CRT, at an accumulated radiation dose of 20 Gy, and immediately after CRT). MRI examinations were performed using a 1.5 T MRI system (Optima MR360, GE Healthcare, Milwaukee, WI, USA) using an eight-channel phased-array body coil, and the signal acquisition coordinated cardiac and respiratory gating. Shallow slow breath training was provided to every patient before they underwent MRI examinations.

The conventional MRI sequences were as follows: axial T1-weighted spin-echo sequence (230 ms repetition time [TR], 2.1 ms echo time [TE], 24 sections, 5 mm section thickness, 1 mm intersection gap, 40 cm field of view, 256×192 matrix, number of excitations=1); axial T2-weighted spin-echo sequence with fat suppression (7,500 ms TR, 85.6 ms TE, 24 sections, 5 mm section thickness, 1-mm intersection gap, 40 cm field of view, 320×224 matrix, number of excitations=2); and three-dimensional T1-weighted spoiled gradient echo sequence (liver acquisition with volume acceleration; 3.2 ms TR, 1.5 ms TE, 24 sections, 5-mm section thickness, 1 mm intersection gap, 40 cm field of view, 256×192 matrix, number of excitations=1). Intravenous injection of 0.1 mmol/kg body weight gadodiamide (Omniscan, GE Healthcare AS, Shanghai, China) was performed at a rate of 3 ml/s, followed by a 20-ml saline flush with a power injector.

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