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Research article

Pretreatment MR imaging radiomics signatures for response prediction to induction chemotherapy in patients with nasopharyngeal carcinoma

Guangyi Wang[a,1], Lan He[a,1], Cai Yuan[b], Yanqi Huang[a], Zaiyi Liu[a,*,2], Changhong Liang[a,*,2]

[a] Department of Radiology, Guangdong General Hospital, Guangdong Academy of Medical Sciences, Guangzhou, 510080, China
[b] Internal Medicine Residency, Florida Hospital, Orlando, FL, 32804, USA

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ABSTRACT

Purpose: This study aimed to investigate the capability of magnetic resonance (MR) imaging radiomics signatures for pretreatment prediction of early response to induction chemotherapy in patients with nasopharyngeal carcinoma (NPC).

Materials and methods: This was a retrospective study consisting of 120 patients with biopsy-proven NPC (stage II–IV). Texture features were extracted from the pretreatment morphological MR images for each case. Radiomics signatures were obtained with the least absolute shrinkage and selection operator method (LASSO) logistic regression model. The association between the radiomics signatures and the early response to induction chemotherapy was explored.

Results: From the contrast-enhanced T1-weighted MR imaging (CE T1WI), 5 features were selected by the LASSO model. The radiomics signature categorised patients with NPC into response and nonresponse groups ($P < 0.001$). The area under the receiver operating characteristic curve values (AUC), sensitivity, specificity, positive predictive value (PPV) and negative predictive value(NPV) were 0.715(95% CI 0.699–0.731), 0.940, 0.500, 0.568 and 0.897 respectively, where non-responders are true-positives. The AUC of 1000 bootstrap internal validation was 0.715. Furthermore, when the features of T1-weighted MR imaging (T1WI), T2-weighted MR imaging (T2WI), T2-weighted fat-suppressed MR imaging (T2WI FS) and CE T1WI were analysed together, 15 features were selected to develop the radiomics signature. The performance of this radiomics signature was better than that developed only from CE T1WI ($P < 0.05$). The AUC value was 0.822(95% CI 0.809–0.835) with sensitivity of 0.980, specificity of 0.529, PPV of 0.593 and NPV of 0.949. The AUC of 1000 bootstrap analysis was 0.821. From T1WI, T2WI, and T2WI FS images separately, no valuable features were selected.

Conclusions: Pretreatment morphological MR imaging radiomics signatures can predict early response to induction chemotherapy in patients with NPC.

1. Introduction

Nasopharyngeal carcinoma (NPC) prevails in Southeast Asia. There were about 86,700 new cases of NPC and 50,800 deaths in 2012 [1]. Radiotherapy is the primary treatment regimen for all stages NPC [2]. Patients with advanced stages can benefit from additional chemotherapy, which can significantly improve overall survival (OS) [3–11]. Therefore, concurrent chemoradiotherapy (CCRT) was recommended as the standard treatment for patients with NPC with advanced stages by the guidelines of the National Comprehensive Cancer Network (NCCN).

Recently, it had been proven that addition of induction chemotherapy (IC) followed by CCRT can significantly improve failure-free survival in advanced NPC compared with CCRT alone [12]. However, in clinical practice, not all patients with NPC respond well to IC [13,14]. Predicting the response to IC may play an important role in individualising the therapeutic strategy for NPC patients. Furthermore, the prediction of response to IC may help avoid unnecessary side effects caused by ineffective IC. Moreover, some studies have revealed that different responses to IC in patients with NPC had prognostic values for survival outcomes [14,15]. Therefore, there would be an advantage in finding reliable and practical predictive markers that can predict the response to IC for patients with NPC before treatment.

To date, at least 3 imaging modalities have been tried to predict the

* Corresponding authors.
E-mail addresses: zyliu@163.com (Z. Liu), cjr.lchh@vip.163.com (C. Liang).
[1] These authors contributed equally to this work and share first authorship.
[2] These authors contributed equally to this work and share last authorship.

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response to IC in patients with NPC. These include diffusion-weighted MR imaging (DWI) with an apparent diffusion coefficient (ADC) map [16,17], dynamic contrast-enhanced MR imaging (DCE-MRI) [18,19], and intravoxel incoherent motion diffusion-weighted MR imaging (IVIM-DWI) [20,21]. According to the results of these studies, the efficacy of DWI and DCE-MRI for predicting response to IC was controversial. Although the *D* (pure diffusion coefficient) values developed from IVIM-DWI may potentially predict the response to IC in patients with NPC before treatment, with sensitivity and specificity ranging from 0.647 to 0.658 and from 0.722 to 0.818, respectively [20,21], the specificity of these studies was relatively low.

Recently, some studies have indicated that quantitative MR imaging radiomics shows promise in tumour prognosis. Through MR imaging radiomics analysis, Nie et al. developed models to predict the pathological response after chemoradiotherapy for rectal cancer [22]. Breast cancer recurrence risk was predicted successfully by analysing MR imaging radiomics signatures [23]. Jia et al. tried to predict a treatment response to chemoradiotherapy in NPC by texture analysis based on MR images [24]. There was a study dealing with MR imaging radiomics signature and prediction of survival in NPC [25]. Their results are encouraging. The aim of our study was to evaluate the ability of MR imaging radiomics for pretreatment prediction of the response to IC in patients with NPC.

2. Materials and methods

2.1. Patient selection and clinical characteristics

Data were obtained from our institute. The research protocol was approved by the institutional review board. Since all the data were de-identified, informed patient consent was waived.

Between August 2009 to May 2016, 155 consecutive patients who were biopsy-proven NPC at our institute were recruited retrospectively. The exclusion criteria for our study were: (1) unmeasurable (< 5 mm) nasopharynx lesion on pre-treatment MR(n = 7). (2) chosed to get treatment elsewhere (n = 12). (3) without pre- or post-IC MR examination (n = 7). (4) no IC or had inadequate IC (n = 9). A total of 120 (mean age 46.81 ± 10.89, range 22–70, male = 95, female = 25, stage II = 10, stage III = 70, stage IV = 40) were studied in this research.

2.2. Assessment of tumour stage

Patients were staged according to the latest seventh edition of the International Union Against Cancer/American Joint Committee on Cancer (UICC/AJCC) staging manual [26]. All medical images and clinical records were reviewed by two radiologists separately, and disagreements were resolved by discussion.

2.3. Induction chemotherapy

All the patients accepted IC every 3 weeks for 2 cycles (n = 16) or 3 cycles (n = 104). Each cycle IC protocol consisted of cisplatin (60 mg/m^2) on days 1–3, 5-fluorouracil (600 mg/m^2) on days 1–5, and docetaxel (60 mg/m^2) on day 1.

2.4. Criteria for tumour response

Tumour response was evaluated by two radiologists separately using MR images obtained before treatment and one week after the second cycle of IC respectively. Tumour response was defined according to RECIST 1.1 criteria [27]. Both of the radiologists blinded to the patients' clinical data. Disagreements were resolved by their discussion. Maximum diameters of target lesions were measured on CE T1WI with tools of the picture archiving and communication system (PACS), (Carestream, Ontario, Canada). Complete response (CR) was defined as the disappearance of all target lesions. Partial response (PR) was defined as at least a 30% decrease in the sum of the diameters of the target lesions, taking as reference the baseline sum diameters. Progressive disease (PD) was defined as at least a 20% increase in the sum of the diameters of the target lesions, taking as reference the smallest sum on study. Stable disease (SD) was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters. Both CR and PR patients were defined as response patients; SD and PD were defined as nonresponse patients.

2.5. MR images acquisition protocol

All patients underwent nasopharynx and cervical region contrast-enhanced MR examination using head and neck coils with 1.5T MR scanners (Magnetom Espree, Siemens Medical Solutions, Erlangen, Germany, or Achieva, Philips Healthcare, Best, the Netherlands). T1-weighted fast spin-echo images in the axial plane (repetition time [TR] = 450 ms; echo time [TE] = 8.8 ms, flip angle = 90°; matrix = 256 × 168, slice thickness = 4 mm; spacing between slices = 5 mm), T2-weighted fast spin-echo MR images in the axial plane (TR = 6000 ms; TE = 95 ms; flip angle = 90°; matrix = 256 × 168; slice thickness = 4 mm; spacing between slices = 5 mm), and T2-weighted fat-suppressed spin-echo sequence (TR = 6360 ms; TE = 95 ms; flip angle = 90°; matrix = 256 × 168; slice thickness = 4 mm; spacing between slices = 5 mm) were obtained before contrast was administrated. After bolus injection of contract (0.1 mmol/kg body weight; Magnevist, Schering, Berlin, Germany), axial T1-weighted fast spin-echo sequences were performed (with the same parameters as before contrast).

2.6. Images retrieval procedure

The DICOM format images of T1WI, T2WI, T2WI FS, and CE T1WI for each case were retrieved from the PACS (Carestream, Ontario, Canada).

2.7. Image intensity normalisation

Because signal intensity in morphological MR images is a relative number and not an absolute number, normalisation would have been necessary even using the same protocol. All image intensities were normalised according to the following equation:

$$I_{new} = (I - I_{Min})\frac{I_{newMax} - I_{newMix}}{I_{Max} - I_{Min}} + I_{newMin} \quad (1)$$

Normalisation transforms an MR image *I* with intensity values in the range (I_{Min}, I_{Max}) into a new image I_{new} with intensity values in the range (I_{newMin}, I_{newMax}). Here we I_{newMin} = 0, I_{newMax} = 1000 defined

2.8. Texture analysis

Using ImageJ 1.50i (Wayne Rasband, National Institutes of Health, Bethesda, MD, USA), a region of interest (ROI) was drawn around the entire tumour outline on the largest primary tumour cross-sectional area from the CE T1WI images by a radiologist who was blinded to the clinical outcome and had 10 years of experience in head and neck MR interpretation. Only tumour components within nasopharynx were included in the ROI. The ROI was then copied and applied on the same level slices of T1WI, T2WI, and T2WI FS (Fig. 1). Textures were then extracted from T1WI, T2WI, T2WI FS, and CE T1WI images, respectively, using an in-house texture analysis algorithm applied in Matlab 2010a (MathWorks, Natick, MA, USA).