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Correlation of human papilloma virus status with quantitative perfusion/diffusion/metabolic imaging parameters in the oral cavity and oropharyngeal squamous cell carcinoma: comparison of primary tumour sites and metastatic lymph nodes

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AIM: To investigate the differences in perfusion/diffusion/metabolic imaging parameters according to human papilloma virus (HPV) status in the oral cavity and oropharyngeal squamous cell carcinoma (OC-OPSCC), separately in primary tumour sites and metastatic lymph nodes.

MATERIALS AND METHODS: This retrospective study comprised 41 patients with primary OC-OPSCCs and 29 patients with metastatic lymph nodes. The perfusion/diffusion/metabolic imaging parameters were measured at the primary tumour and the largest ipsilateral metastatic lymph node. The quantitative parameters were compared between the HPV-positive and -negative groups.

RESULTS: The HPV-positivity was 39% (16 patients) for the primary tumours and 51.7% (15 patients) for the metastatic lymph nodes. Patients with HPV-positive tumours had a lower T stage (p=0.034). The metastatic lymph nodes for the HPV-positive patients were bulkier (p=0.016) and more frequently had cystic morphology (p=0.005). The perfusion parameters were not different, regardless of HPV status. The diffusion parameter (ADC_{min}, p=0.011) of the metastatic lymph nodes in the HPV-positive groups was lower and metabolic parameter (metabolic tumour volume p=0.035 and total lesion glycolysis p=0.037) were higher than those in HPV-negative groups.

CONCLUSION: The diffusion and metabolic parameters of metastatic lymph nodes from OC-OPSCC were different according to HPV status. The perfusion parameters did not clearly represent HPV status.

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Introduction

Over the past few decades, the incidence of oral cavity and oropharyngeal squamous cell carcinoma (OC-OPSCC) has increased despite declining tobacco consumption and decreasing incidence of other cancers of the head and neck. This is due to an increase in human papilloma virus (HPV)-associated oropharyngeal cancers.[1] HPV-associated OC-OPSCC seems to be a distinct disease entity. Clinically, patients with HPV-positive tumours tend to be younger and of advanced nodal stage; however, they respond more favourably to standard treatment and, consequently, show better survival than those with HPV-negative tumours.[2,3] The newly released 8th edition of American Joint Committee on Cancer (AJCC) staging manual, head and neck section, separate the staging algorithm for HPV-positive oropharyngeal cancer from that of HPV-negative cancer as a result of prognostic difference.[4,5]

Imaging parameters from dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) and diffusion-weighted MRI (DWI), and metabolic parameters from 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG) positron-emission tomography (PET), have been shown to reflect the biological characteristics of tumours and are useful for early treatment assessment of head and neck carcinoma.[6–12] Some conflicting studies have analysed the relationship between perfusion, diffusion, metabolic parameters, and HPV status.[13–21] In these reports, the correlations were mainly analysed for the primary tumour site, although cystic nodal metastasis is one of the most obvious imaging characteristics of HPV-positive tumours.[22–25] Whereas other studies evaluated only one type of imaging technique or parameter, the current study evaluated various imaging parameters in primary OC-OPSCCs and metastatic lymph nodes with HPV status. The purpose of this study was to investigate the correlation between MRI quantitative perfusion and diffusion parameters, metabolic parameters from FDG PET, and HPV status simultaneously in the same population. Furthermore, the correlations were analysed not only in the primary tumour sites but also in the metastatic lymph nodes of patients with OC-OPSCC.

Materials and methods

Patients

This study was approved by the Ethics Committee of Ajou University School of Medicine, and the requirement for written informed consent was waived due to its retrospective nature.

Fifty-two consecutive patients were reviewed retrospectively (from May 2012 to March 2016) with histopathologically proven squamous cell carcinoma (SCC) of the oral cavity or oropharynx, who underwent pretreatment work-up MRI including DCE-MRI, DWI sequences, and combined FDG PET/computed tomography (CT). Among them, 10 patients were excluded because the primary lesion was not visible on MRI or was <0.5 cm^3. One patient was excluded because the primary lesion was distorted on MRI due to a dental artefact. As a result, 41 patients were enrolled for analysis of the primary SCC. Among the 52 patients, 30 had lymph node metastasis. Of these, one patient was excluded because the metastatic lymph node was <0.5 cm^3, leaving 29 patients to be evaluated on the basis of imaging characteristics and quantitative parameters of metastatic lymph nodes.

The demographic data of the enrolled patients were obtained from electronic medical records. T and N classifications were staged according to the 7th edition of American Joint Committee on Cancer (AJCC) staging system for comparing of TN stage base on HPV status.

MRI acquisition

All patients underwent MRI using a 1.5 T MRI system (Signa HDxt; GE Healthcare, Milwaukee, WI, USA) with a 12-channel neurovascular head and neck coil. Axial fat-saturated T2-weighted imaging (WI; 3,700 ms repetition time [TR]/102 ms echo time [TE]) and axial T1WI (517 ms TR/11 ms TE), as well as coronal T2 and sagittal T1WI, were acquired before contrast agent administration with a field of view (FOV) of 200 mm, matrix of 320 $\times$ 256, and section thickness of 4 mm with a 1 mm intersection gap; 26 sections were acquired. After gadolinium contrast (gadobutrol; Gadovist, Bayer HealthCare, Berlin, Germany) injection (0.2 mmol/kg; flow rate of 2.5 ml/s) using a power injector immediately followed by a 20 ml saline flush, fat-saturated axial and coronal T1WI were acquired. DCE-MRI was performed using a three-dimensional (3D) fast spoiled gradient-echo sequence with the following parameters: 5.2 ms TR/1 ms TE, 200 mm FOV, 160$\times$128 matrix, 25° flip angle, 5 mm section thickness, 26 sections acquired, 55 dynamic cycles, 5 s temporal resolution, and total acquisition time of 5 minutes 35 seconds. The DCE-MRI included two pre-contrast T1WI with different flip angles (5° and 15°) to determine the T1 relaxation time in the blood and tissue. DWI was performed using periodically rotated overlapping parallel lines with enhanced reconstruction (PROPELLER) sequences to reduce imaging distortion and artefacts (b-values of 0 and 1,000 s/mm^2; 8,000 ms TR/85 ms TE, 200 mm FOV, 128$\times$128 matrix, 26 sections acquired, 4 mm section thickness, 1 mm intersection gap, 20 echo train length, and 1.5 excitations).

FDG PET/CT image acquisition

All patients fasted for at least 6 hours and were preconditioned to have a blood glucose level <200 mg/dl at the time of injection of FDG. PET/CT was performed using a dedicated PET/CT system (Discovery STE; GE Healthcare). Before PET, unenhanced CT was performed 60 min after a 5 MBq/kg FDG injection using 16-section helical CT (120 keV; 30–100 mA in the Autom A mode; section width, 3.75 mm). An emission scan was acquired from the thigh to the head for 2.5 minutes per frame in the three-dimensional (3D) mode. Attenuation-corrected PET images using CT data

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