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Dynamic contrast-enhanced magnetic resonance imaging in Head and Neck Cancer: differentiation of new H&N cancer, recurrent disease, and benign post-treatment changes☆,☆☆

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ABSTRACT

Purpose: To determine if dynamic contrast-enhanced (DCE)-magnetic resonance imaging (MRI) parameters such as permeability surface area (PS) and blood volume (BV) allow differentiating between new head and neck (HN) cancer, recurrent HN cancer, and post-treatment benign changes.
Method: A total of 35 patients with newly diagnosed, recurrent, and benign post-treatment benign changes underwent DCE-MRI. PS and BV were calculated.
Results: PS values of the lesion were $2.3\times10^4\pm5.8\times10^4$ for the newly diagnosed cancer group, $3.3\times10^4\pm1.7\times10^4$ for the recurrent cancer group, and $4.8\times10^4\pm8.1\times10^4$ for the post-treatment benign change group ($P=.031$).
Conclusion: Post-treatment benign changes in the HN region had significantly high permeability property than newly diagnosed or previously treated recurrent tumor.

1. Introduction

With widespread adaptation of organ preservation, advanced stage head and neck cancer is treated with chemoradiation therapy. Local recurrence is the most frequent type of the failure after initial therapy of head and neck cancers [1]. Early detection of a recurrence is crucial to facilitate prompt and successful salvage therapy. The early detection of a recurrent tumor by a clinical examination is limited to superficial or mucosal surface lesions that are accessible by visual inspection or endoscopy. Consequentially, the diagnostic imaging plays an important role with a great emphasis on evaluation of treatment response and early detection of recurrent cancers [2,3].

Computed tomography (CT) and magnetic resonance imaging (MRI) are the standard imaging studies commonly performed as a part of initial staging and surveillance study for patients with head and neck cancer. However, these conventional CT and MRI studies based on the morphology of disease have limited capacity of discriminating residual or recurrent cancer from post-treatment benign changes. Dynamic contrast-enhanced (DCE)-MRI utilizes fast T1-weighted imaging following a bolus injection of gadolinium contrast agent that provides hemodynamic information of tumor, such as blood flow, blood volume (BV), and time to peak. Time–intensity curve (TIC) obtained from DCE-MRI shows different patterns between benign and malignant tumors or between post-treatment benign changes and recurrent tumors [4–6]. Therefore, hemodynamic parameters obtained from DCE could potentially shed lights on tumor biology and physiology.

There is emerging evidence about quantitative parameters serving as surrogates of microcirculation environment of various cancers. One such a parameter among them is permeability surface area (PS) product. PS is a measure of contrast medium exchange between intravascular plasma and interstitial compartment in a lesion, which shows leakiness and disorganization of blood vessels [7]. It has been reported to be useful in predicting tumor response to therapy and post-treatment prognosis and also to differentiate benign from malignant tumors [8–14].

We hypothesized that quantitative DCE-magnetic resonance (MR) parameters might be useful to differentiate post-treatment benign changes from tumor recurrence due to the difference in hemodynamic characteristics. Contrast medium continues to leak in post-treatment benign changes until late phase without early wash-in or wash-out, while that of tumor shows typically early peak and relatively early wash-out [4–6]. The aim of this study was to investigate the potential value of quantitative DCE-MR parameters in differentiating new head and neck cancer, recurrent head and neck cancer, and post-treatment benign changes.

2. Materials and methods

2.1. Patients

The institutional review board approved this retrospective study and waved the requirement to obtain written informed consent from patients. This study population included 51 patients who had DCE-

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MRI for newly diagnosed malignant tumors or suspected recurrent tumors in the head and neck region. Indication for DCE-MRI was determined at clinical discretion to obtain the further characterization of a lesion in addition to routine sequences. We excluded non-head and neck cancer ($n=4$; melanoma, neuroblastoma, chordoma, and lymphoma), adenoid cystic cancer ($n=4$), thyroid cancer ($n=1$), a patient under 20 years old ($n=1$), a patient who underwent MRI performed immediately after surgery ($n=1$), and patients with no obvious lesion on a surveillance examination ($n=5$).

The final study population consisted of 35 patients including 29 men and 6 women, with a mean age of 57.7 years (range: 39–72). There were 25 patients with newly diagnosed head and neck cancer, 4 patients with confirmed recurrent head and neck cancer, and 6 patients with lesions initially suspected of a local recurrence, however, later proven to be benign post-treatment benign changes.

The diagnosis of newly diagnosed head and neck cancer was confirmed pathologically: squamous cell cancer ($n=24$) and poorly differentiated cancer ($n=1$). The primary tumor locations were base of tongue ($n=9$), nasopharynx ($n=5$), oropharynx ($n=6$), hypopharynx ($n=5$), and maxillary sinus ($n=1$). Three out of five nasopharyngeal cancer patients were positive for Epstein-Barr virus, one was negative, and immunohistochemistry was not performed for one patient. Three out of 11 oropharyngeal and hypopharyngeal cancer patients were positive for p16, three were negative, and immunohistochemistry was not performed for five patients. Three out of four patients with recurrent cancer were confirmed pathologically, and the other one was diagnosed by progressive growth on subsequent follow-up examinations. Their primary pathological diagnoses were squamous cell cancer. The primary tumor locations for recurrent cancer were base of tongue ($n=3$) and external auditory canal ($n=1$). The treatments prior to recurrence for these patients include surgery alone in one patient, radiation therapy in one patient, and chemoradiotherapy in two patients. Six patients with post-treatment benign changes as diagnosed by DCE-MRI had subsequent clinical and imaging follow-up of the index lesion for a minimum of 24 months (24–60 months, mean: 38 months), ensuring benign etiology. The primary tumor locations before treatment were base of tongue ($n=1$), oropharynx ($n=2$), hypopharynx ($n=1$), and maxillary sinus ($n=1$). The initial treatments prior to DCE-MR for these patients include surgery and radiation in four patients, surgery alone in one patient, and chemoradiotherapy in one patient. The mean time between completion of treatment and DCE-MRI was 16 months for the recurrent cancer group (range, 6–24 months) and 4.5 months for the post-treatment benign change group (range, 3–12 months).

2.2. Imaging

MRI was performed with a 3T scanner (Intera Achieva; Philips Medical Systems, Best, The Netherlands) using either 16-channel neurovascular head and neck coil ($n=31$) or Q-body (Quadrature Detection Transmit/Receive) coil, which is integrated in the magnet ($n=4$).

Before DCE-MRI, routine diagnostic MRI sequences (T1-weighted fast spin-echo image and fat-suppressed T2-weighted fast spin-echo image) were acquired. DCE-MRI was performed using fat-suppressed three-dimensional T1-weighted fast field echo sequence. The scanning parameters were as follows: TR/TE, 5.5/1.3; flip angle, 15°; field of view, 212 mm; slice thickness/overlap, 6 mm/3 mm for neurovascular coil and 10 mm/5 mm for body coil; imaging matrix, 208×151 for neurovascular coil and 108×78 for body coil. The coverage volume (slice number) was set depending on the size of primary tumor, area of enhancing lesion, or the distribution of lymph node metastases to include the entire lesion with some margins. Gadolinium-based contrast agent (0.1 mmol/kg, MultiHance; Bracco Diagnostics, Milan, Italy) was injected via 20-gauge catheter inserted into the antecubital vein at a flow rate of 5 ml/s, followed by a 20-ml saline flush using a power injector. In total, 100 dynamic phases with a temporal resolution of 2.6 s were acquired. Total acquisition time is 4 min 17 s. After DCE, post-contrast fat-suppressed T1-weighted spin-echo images were obtained.

2.3. Image analysis

Two board-certified neuroradiologists who were blinded to results evaluated MR images in agreement. Image processing was performed on dedicated software (FSL version 5.4, Oxford University). Four regions of interest (ROIs) were drawn in common or internal carotid artery for each patient on DCE-MRI images. The averaged signal intensity value at each dynamic phase was used for arterial input function. Then, volume of interest for an entire mass or enhancing lesion was drawn for each patient on DCE-MRI images mainly based on post-contrast T1-weighted image referring to pre-contrast T1- and T2-weighted images. First, ROIs were drawn for each axial image of BV map image because the contour of tumor was readily identified and similar to post-contrast images. Then, the software automatically propagated these ROIs onto the PS map images. Three ROIs (at least 10 cm^2) were drawn on the posterior neck muscle for each patient and used for normalization of the BV values of the lesion (Fig. 1).

Time-series statistical analysis was then carried out to calculate permeability parametric maps after pre-processing using in-house software [15]. PS maps were principally based on the two-compartment pharmacokinetic model proposed by Tofts and Kermode [7] and were calculated using the algorithm developed by Demsar et al. [16]. The fractional leak rate of contrast medium from vessels was determined from the slope of the line resulting when the concentration of contrast medium in the vessels was divided by the concentration of the contrast agent into the extravascular space. This methodology uses a model assuming that little or none of the contrast agent that enters the extravascular space returns to the intravascular compartment during the image acquisition. This technique has been used with small molecular size (gadolinium-based contrast media) as well as macromolecular contrast agents [16].

BV is most commonly used parameters for MR perfusion application to oncology. BV is defined as the total volume of blood traversing a given region of tissue, measured in milliliters of blood per 100 g of tissue (ml/100 g). The change in MR signal caused by perfusion of gadolinium is computed on a voxel-by-voxel basis and used to construct a TIC. The degree of MR signal change is then assumed to be proportional to the tissue concentration of gadolinium so that relative concentration time curves can be obtained. A relative measure of BV can be estimated from the integral of the signal intensity versus time curve resulting from the passage of contrast through a tumor [17]. Although this technique is mainly developed for brain tumors, the same general physiologically principles of BV still apply to head and neck tumors. Baseline of the TIC was determined from that of artery using arterial input function. Since absolute BV values depend on the duration of scan time after contrast reached to tumor, the BV value was normalized by that of the posterior neck muscle and showed as a ratio of the lesion to the posterior neck muscle.

2.4. Statistical analysis

All continuous variables were expressed as the median±S.D. (range). PS and BV values were compared among three groups, newly diagnosed cancer, recurrent cancer, and post-treatment benign change groups using the Kruskal–Wallis test using commercially available statistical software (SPSS version 19, IBM, New York). For all statistical analyses, $P<.05$ was considered statistically significant.

3. Results

All results were summarized in Table 1.

PS values of the lesion were $2.3\times10^4\pm5.8\times10^4$ for the newly diagnosed cancer ($n=25$), $3.3\times10^4\pm1.7\times10^4$ for the recurrent cancer