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Original Article

Combined diffusion-weighted MRI and MR spectroscopy: Feasibility to improve the MRI capability in differentiation between benign and malignant neck lymphadenopathy

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ABSTRACT

The study aims to evaluate the additional value of MRS and DWI in differentiating malignant and benign neck lymphadenopathy.

Materials and methods: Thirty-three patients with enlarged neck lymph nodes of malignant suspicious underwent DWI and MRS. ADC values, presence of Cho peak and Cho/Creatine ratio of the dominant node were assessed and results were compared with histopathological results.

Results: the patients were classified into benign (n = 9) and malignant (n = 24: 17 metastases and 7 lymphoma). The mean ADC values of the benign, metastasis and lymphoma patients were 1.56 ± 0.23, 1.01 ± 0.23 and 0.71 ± 0.02 × 10^{-3} mm^2/s respectively. It was significantly higher in benign than malignant ($p < 0.0001$) and in metastatic than lymphomatous ($p = 0.001$) as well as in well- and moderately than poorly differentiated metastatic ($p = 0.01$) lymph nodes. Using the receiver operating characteristic (ROC), cutoff value of 1.15 × 10^{-3} mm^2/s of ADC could differentiate benign from malignant nodes with sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of 91.6%, 77.7%, 91.9%, 77.7%, KAPPA = 0.69 and $p < 0.001$ respectively.

Malignant nodes showed a significant choline peak (n = 24, 100%) while benign nodes showed choline peak in only two cases (22%). Mean Cho/Cr ratio was significantly higher in malignant nodes than benign ones (2.64 ± 1.16 versus 1.09 ± 0.04) ($p < 0.0001$), furthermore it was significantly higher in lymphoma versus metastatic (4.3 ± 0.35 versus 1.94 ± 0.34, $p < 0.001$) as well as poor versus Well- to moderately differentiated metastases (2.3 ± 0.11 versus 1.69 ± 0.18, $p < 0.01$). The MRS sensitivity, specificity, PPV, NPV and Kappa in differentiating benign and malignant cervical lymph nodes were 100.0, 77.7, 92.3, 100.0% and 0.83 and p value = 0.001.

Combination of DWI and MRS showed higher diagnostic value than DWI or MRS alone with sensitivity, specificity, PPV, NPV and Kappa of 100, 88.9, 96, 100% and 0.92 respectively ($p < 0.0001$).

Conclusion: ADC and MRS can help in the differentiation between malignant and benign neck lymph nodes. Combination of both techniques achieved higher diagnostic performance.

1. Introduction

Discrimination of benign and malignant neck lymph nodes are crucial especially in the presence of head and neck malignancy as it is needed for proper staging and designing treatment plane as well as follow up evaluation [1–5].

Conventional imaging relies on the morphological pattern of lymph nodes as short axis diameter, lymph node hilum loss and necrosis together with heterogenous pattern of post contrast enhancement and perinodal infiltrative process [6–9]. Ultrasound (US), computed tomography (CT) and conventional magnetic resonance (MR) can detect cervical lymphadenopathy, yet their ability in the discrimination between benign and malignant lymph nodes is not highly accurate. Positron emission tomography (PET) and PET/CT depend on the metabolic imaging and can aid in this differentiation but it is limited by low spatial resolution, as well as false physiological and inflammatory uptake. Fine needle aspiration

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cytology (FNAC) is invasive with a risk of false results as its operator dependent [10–13].

Proton (1H) MR spectroscopy (1H MRS) is a noninvasive technique that depends on the evaluation of the metabolism at cell level and measures the chemicals and metabolites in the body. 1H MRS has been shown as a valuable tool in the cancer evaluation with accumulating literatures validated its usage in variable types of body cancers [14–19].

The large water and lipid resonances at 4.7 and 1.3 ppm (ppm) has to be suppressed for proper assessment of the metabolites of interest. Shimming is needed to make the magnetic field is as homogeneous as possible. The spectrum of MRS has horizontal axis corresponds to the metabolite resonance frequency in respect to the water resonance peak at 4.7 ppm. On the other hand the vertical axis corresponds to the relative metabolite signal amplitude in arbitrary units. MRS shows quantitative data (presence or absence of metabolites) and semi-quantitative (amplitude of metabolites or its ratio relative to control) [20–24].

On the other hand, diffusion-weighted MRI (DWI) is considered also as a non-invasive technique that can analyze the water molecules motion to characterize the tissues. These signal changes can be quantified and reflected by apparent diffusion coefficient (ADC) [25–30].

The aim of our study was to evaluate the additional value of using MRS and DWI in the differentiation between malignant and benign neck lymphadenopathy.

2. Patients and methods

2.1. Patients

This prospective study had included 33 patients (17 male and 16 female patients, their mean age 53.1 ± 8.7 years) with enlarged neck lymph nodes clinically suspicious of malignancy before going to histopathological examination either by neck dissection (n = 11), core biopsy (n = 10) or surgical (n = 12). Approval from our institutional review board was achieved and patient informed written consents were taken.

2.2. MR imaging protocol

2.2.1. Conventional MRI

MR examination was done using a 1.5-T MR (Achieva, Philips Medical Systems, Netherland B.V.). A standard head and neck coil was used.

Axial, coronal and sagittal localizer images were obtained first then conventional study was completed including T1-weighted images (repetition time (TR)/echo time (TE) = 600–600/8–10 ms) and T2-weighted fast spin echo images (TR/TE = 3000–4000/80–100).

Planes included axial and coronal planes with a slice thickness of 3–4 mm, an inter-slice gap of 2 mm, a field of view (FOV) of 250–300 mm, an acquisition matrix 256 × 224 and a flip angle of 90 degree. T1-weighted images were performed with and without fat saturation after IV injection of 15 ml of gadopentetate dimeglumine.

2.2.2. Diffusion weighted MR

Acquisition of diffusion-weighted images using single shot echo planar imaging (EPI) sequence was achieved in the axial plane before the administration of contrast with 3–4 mm slice thickness, 1 mm intersection gap, FOV 250–300 mm, TR/TE = 2000–2600/70 ms. Application of the diffusion sensitizing gradient was done in the three orthogonal planes (X, Y, Z). The b values used were 0 and 1000 s/mm^2.

2.2.3. 1-H MR spectroscopy

Magnetic resonance spectroscopy was done for all patients. Homogeneity of the magnetic field before recording the spectrum was achieved by application of automatic shimming, when the automatic shimming was difficult due to significant susceptibility differences the manual shimming was applied with a linewidth of 12–14 Hz.

Point resolved spectroscopic sequence (PRESS) – single voxel technique was obtained with the following parameters; TR/TE = 2000/135 ms, signal acquisition 64, spectral bandwidth 1000 Hz, and number of points 512. Water suppression using chemical shift-selective suppression was done. The acquired data was processed automatically with an average scan time of 4:48 min.

The dominant solid node was selected for the analysis. The volume of interest (VOI) was positioned on the solid part of the node in three planes (axial, sagittal and coronal planes) to limit inclusion of surrounding fat as much as possible.

Spectra are assessed for the presence of choline (Cho) and Creatine (Cr) peak at 3.22 and 3.03 ppm respectively and Cho/Cr ratio was calculated automatically.

2.2.4. Calculation of the ADC value

A region of interest (ROI) was positioned on the ADC map on the same location as the VOI.

Automatic calculation of apparent diffusion coefficient (ADC) maps was achieved by MRI machine software incorporated in same sequence of diffusion weighted image.

2.3. Image analysis and data interpretation

MR images were evaluated independently by the two radiologists sharing this study without any previous knowledge of its pathology. Conventional MRI image were analyzed to evaluate of the lesion.

MRI results were compared to the results of pathological examination of the biopsy.

Topographic correlation was applied by recording the maximum lymph node short axis and its exact location and anatomical relations to ensure that the surgically removed node is the same subjected to analysis.

2.4. Statistical analysis

According to the histopathological results of lymph nodes, the patients in this study were categorized into benign and malignant (metastasis either well/moderately or poorly differentiated and lymphoma). Statistical analysis was done using SPSS version 17. The mean and standard deviations for ADC and Cho/Cr ratio were calculated for each group.

One way analysis of variance (ANOVA) and post hoc analysis were applied to analyze the difference in ADC and Cho/Cr ratio among the different histolopathological types. T-test was used to assess the difference in ADC values and Cho/Cr ratio between well and moderately differentiated and poorly differentiated metastasis.

Receiver operating characteristic (ROC) curve was applied to evaluate the diagnostic ability of the ADC value. Multiple thresholds of ADC values were analyzed to rule out the cutoff value determined by Kappa test to differentiate benign from malignant nodes.

The sensitivity, specificity, positive predictive value (PPV) negative predictive value (NPV) and Kappa test of DWI, MRS and combined DWI + MRS in differentiating benign and malignant cervical lymph nodes were calculated.

The probability (p value) of <0.05 was considered significant.

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