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The Role of Diffusion-Weighted MR Imaging in Detecting Malignant and Benign Pleural Thickening in Asbestos-Related Pleural Diseases

ORIGINAL INVESTIGATION

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ABSTRACT

Objective: The aim of this study was to evaluate the role of diffusion-weighted magnetic resonance imaging (dMRI) in differentiating between diffuse malignant and benign pleural thickening in asbestos-related pleural diseases.

Materials and Methods: Sixty-two patients were included in the study. Thirty-two had a benign form and 30 had malignant pleural mesothelioma (MPM). The patient files and records belonging to those who underwent dMRI on a 1.5 T MR system between May 2014 and January 2016 in our clinic were examined retrospectively. The dMRI was performed with 0, 500, and 1000 mm^2/s b-values. The apparent diffusion coefficient (ADC) map was generated, and means ADC values were determined from measurements of pleural thickening.

Results: The mean ADC values were $1.94\pm0.09\times10^{-3}$ mm^2/s and $0.84\pm0.05\times10^{-3}$ mm^2/s in benign pleural disease and MPM, respectively. The mean ADC value in the malignant group was significantly lower than in the benign group ($p<0.05$).

Conclusion: Our results show that dMRI and ADC values are useful for differentiating between benign and malignant pleural thickening in asbestos-related pleural diseases. dMRI gives clues for the interpretation of whether pleural thickening is benign or malignant and can assist in the early detection of MPM.

Keywords: Diffusion-weighted imaging, ADC measurement, pleura, asbestosis, mesothelioma

INTRODUCTION

Millions of people around the world have been exposed to asbestos. Asbestos-related chest diseases include benign pleural effusions, diffuse pleural thickening, pleural plaques, asbestosis, mesothelioma, and chest cancer. Asbestos is the most common cause of malignant pleural mesothelioma (MPM). Mesotheliomas are rare malignant diseases originating from pleural mesothelial cells and peritoneal tissues. Other rare sites of MPM are the pericardia of the heart and the scrotum tunicas.

Histopathological examination is necessary to establish an accurate MPM diagnosis. For diagnosis, efficacy is low in the cytology of pleural fluid (20%-35%), and needle biopsy from the pleura (20%-80%) and thoracic surgery are usually necessary (1, 2). Multislice computed tomography (MSCT) is used as the primary radiological modality for evaluating whether thickening of the pleura is benign or malignant. Major findings in MSCT are diffuse or nodular pleural thickening, pleural plaques, occasionally unilateral effusion, and adjacent tumor invasion.

Magnetic resonance imaging (MRI) can provide more detail than MSCT in assessing chest wall and diaphragm involvement due to excellent contrast resolution. Diffusion-weighted MRI (dMRI) of the chest has recently become feasible. In thorax imaging, dMRI has been used to characterize the lymph nodes, chest cancers, and lung metastases (3). The apparent diffusion coefficient (ADC) value has been demonstrated to have a negative correlation with the cellular density of the tumor. The cellular density of a malignant tumor is generally higher than a benign tumor and the normal surrounding tissue. As a result, when compared to benign tumors, in malignant tumors Diffusion-weighted imaging (DWI) also provides a bright signal reflecting the restricted diffusion, and there tend to be low ADC values in ADC mapping (4).

The aim of this study was to perform dMRI and to evaluate the role of ADC as a quantitative parameter in differentiating between diffuse malignant and benign thickening of the pleura in asbestos-related pleural diseases.

MATERIALS and METHODS

The study protocol was approved by the Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent is waived for this retrospective study.

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The files and records of patients who underwent chest MRI on a 1.5 T MR system between May 2014 and June 2015 in our clinic were examined retrospectively. Patients with MPM and benign pleural thickening were selected for our study. The study included 62 patients (33 men and 29 women), and the mean age was 44 years (range: 35-73 years). Thirty-two had a benign form and 30 had MPM. Eight of the men were exposed to asbestos occupationally, and the rest of the subjects had a history of environmental exposure. Histological diagnosis was made in MPM from resection material (n=7), core biopsy (n=13), or fine needle aspiration cytology (n=10). The chest dMRI of patients with pleural thickening and who had any malignancy were included in the benign group. All dMRI examinations were made on a 1.5 T MRI superconducting system (Siemens Magnetom Symphony, Erlangen, Germany). A body phased-array coil was used, and patients were examined in a supine position. Cardiac gating and respiratory compensation techniques were routinely used. Transverse dMRI image were generated from a single-shot echo-planar image (TR/TE: 5000/139 ms, slice thickness: 6 mm, interval: 2 mm, FOV: 350×350 mm, and matrix: 256×512) with a scan time <2 minutes with 0, 500, and 1000 b-values.

Apparent diffusion coefficient maps were created and ADC measurements were made using region of interest (ROI) with OsiriX MD software (v.6.5). Three circular ROIs with diameters of 1.0 cm each were overlaid onto the pleural thickening, and the mean pleural ADC was calculated. The ADC value was expressed as 10^{-3} mm^2/s, and the mean ADC values of the lesions were noted. ROIs were placed around areas of pleural thickening unless pleural fluid was present. The DW images and ADC maps were analyzed by two radiologists with 10 year's experience each.

The statistical analysis was done using the Statistical Packages for the Social Sciences (SPSS) version 12.0 (SPSS Inc.; Chicago, IL, USA). The data were described using standard deviations and mean deviations. Mean ADC values of MPM and benign pleural thickening were compared with unpaired two-tailed Student's *t*-tests, and $p<0.05$ was considered significant. In order to calculate the diagnostic accuracy of ADC values, receiver operating characteristic (ROC) analysis was used. Cut-off values were calculated around the optimal cut-off with maximum sensitivity and specificity for the differentiation of benign and malignant thickenings.

RESULTS

Appropriate ADC maps were obtained from all 62 patients. The mean ADC values in benign pleural thickenings were $1.96\pm0.18\times10^{-3}$ mm^2/s, and the corresponding values in MPM were $0.84\pm0.05\times10^{-3}$ mm^2/s (Figure 1-2). The mean ADC values for MPM were significantly lower than for benign pleural thickening ($p<0.05$). The average ADC values are shown in the table. The optimal cut-off point for the ADC value was 1.28×10^{-3} mm^2/s. For this value, the sensitivity was 92.6% and the specificity was 85%. The negative and positive predictive values and the diagnostic accuracy were determined to be 84%, 87%, and 86%, respectively.

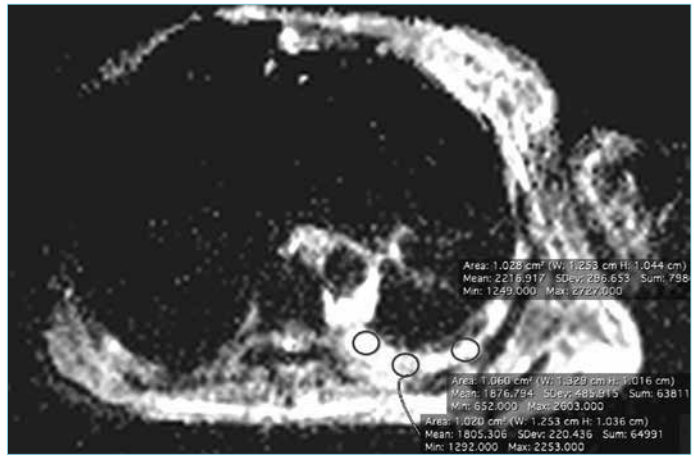

Figure 1. ADC measurements were made using ROI on the ADC map from the left of the benign pleural thickening

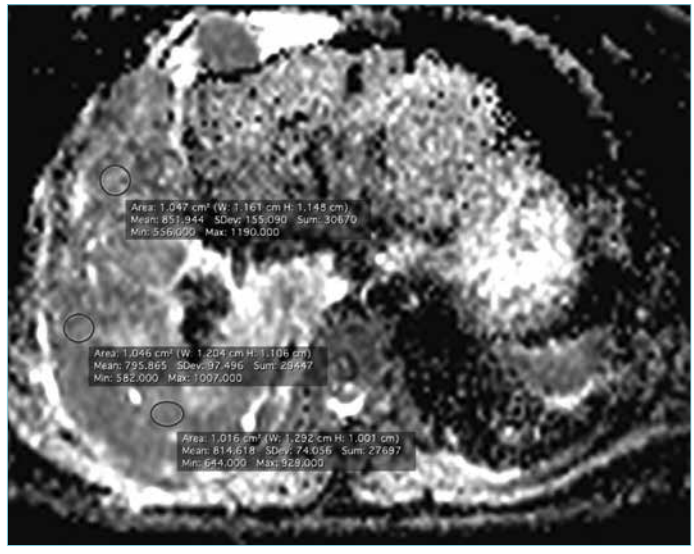

Figure 2. ADC measurements were made using ROI on the ADC map from the right of the malignant pleural thickening

Table 1. Mean ADC values of pleural lesions

Pathology	No. of patients	Mean ADC value (10^{-3} s/mm^2)
Benign lesion	32	1.95±0.08
Malignant lesion	30	0.84±0.05

ADC: apparent diffusion coefficient

DISCUSSION

It is usually difficult to diagnose MPM with confidence despite supporting clinical evidence, a history of asbestos exposure, and helpful imaging markers. In order to diagnose MPM, clinical and radiological findings must be assessed carefully in addition to a confirmed tissue biopsy with cytological examination of the pleural fluid. However, only about 5% of patients are suitable for curative operations at the time of diagnosis.

In our study, we used dMRI to determine if it is possible to differentiate between malignant and benign thickening of the pleura

in asbestos-related pleural diseases. The mean ADC values were $1.94\pm0.09\times10^{-3}$ mm^2/s and $0.84\pm0.05\times10^{-3}$ mm^2/s in benign pleural disease and MPM, respectively. The mean ADC values of MPM were significantly lower than benign pleural thickening ($p<0.05$). Our findings suggested that the dMRI and ADC measurement can be useful for the differentiation of malignant and benign thickening of the pleura.

The use of dMRI to assess extracranial diseases is growing, and DWI is becoming popular for evaluating cancer patients. DWI does not require contrast agent ingestion, and this technique can be combined with other assessments without a significant increase in examination time. Moreover, not only qualitative, but also quantitative information can be obtained via DWI, and this can be useful for tumor assessment (5).

Diffusion-weighted imaging provides a functional assessment of microstructure. The flow of water movements causes phase dispersion, and this result in a loss of signal intensity that can be quantified by calculating the ADC. The ADC value is an indication of the extent of diffusion, and the main determinant of the ADC signal is the amount of diffusion in the tissues. However, perfusion and blood flow also affect the ADC signal, although only by a small amount. The ADC value has been demonstrated to have a negative correlation with cellular density of the tumor, and the densities of malignant tumor cells are generally higher than benign tumors and the normal surrounding tissue. As a result, when compared to benign tumors, DWI in malignant tumors provides a bright signal reflecting the constrained diffusion, with low ADC values in the ADC mapping (3, 6, 7).

In order to stage MPM and decide on treatment options, imaging modalities such as MSCT, MRI, and positron emission tomography-computed tomography (PET-CT) are employed (8, 9). Due to the diffusion of water molecules in tissues, DWI can reveal tissue characteristics. Loss of signal can be quantitatively determined by calculating the ADC, and this process depends on the restriction of water molecule diffusion from the cell membrane and macromolecules and provides indirect quantification of high cell density (10, 11). DWI has been widely employed for assessing central nervous system disorders like acute cerebral infarction, tumors, and demyelinating disease (12). It is also being used to evaluate multiple intrathoracic and abdominal organs (13, 14).

The use of MSCT might facilitate the differentiation between benign and malignant diseases. While the presence of pleural calcification signifies a benign process, different findings such as peripheral and pleural nodular thickening and mediastinal involvement of the pleura might be indicative of malignancy (15, 16). Pleural diseases like asbestosis, chest infection, and pleural malignancy with MPM can result in diffuse pleural thickening and effusion (15). Hierholzer et al. (16) studied 42 cases of pleural disease and found that peripheral thickening and irregular pleural contour, mediastinal involvement, and chest wall invasion or infiltration of the diaphragm are the most common indicators of malignant cases. Calcification in the pleura with MSCT is a sign of a benign case. However, it is difficult to distinguish between benign and malignant disease from pleural thicknesses less than 1 cm.

To differentiate between benign and malignant pleural diseases, MRI has proven to be better than MSCT. High signal intensity on T2-weighted images or strong contrast agent enhancement in T1-weighted images is an indicator of malignancy. Moreover, the contrast-enhanced and fat-suppressed T1-weighted sequence is a very sensitive method. Susceptibility and aliasing artifacts with motion artifacts are the most critical elements affecting the resolution of chest MRI. Respiratory compensation techniques and optimal cardiac gating can be used to reduce thoracic motion artifacts. In order to verify subtle positive findings, clear resolution in the pleura of adjacent structures and an appropriate gate are all required (15).

Functional examination with PET-CT facilitates the noninvasive evaluation of proliferation and tumor metabolism. Compared to normal tissues, the increased glucose metabolism in cancer cells can be identified with the use of fluorodeoxyglucose (FDG). The use of FDG in PET-CT has proven to be effective in differentiating between malignant and benign lesions, and these techniques can also be used for staging of cancer and for observing metabolic responses to treatment. The usefulness of PET-CT using 18F FDG in assessing chest diseases has been evaluated, but this must be researched further (17). This method has been suggested to allow for the differentiation between benign and malignant pleural lesions with MPM staging, and it can also be used as a guide for the biopsy of metabolically overactive neoplastic tissue. It was also shown to be better than other imaging techniques because it can determine the local spread of the disease and can even detect distant metastases (18).

Only a few studies have assessed asbestos-related pleural pathologies and MPM using 18F FDG PET-CT. Moreover, only a few studies have looked at the effectiveness of 18F FDG PET-CT for observing responses to treatments (19). Basu et al. (20) proposed that the use of 18F FDG uptake in results estimation in the differentiation of benign lesions from MPM, the evolution of responses to therapy, and the analysis of post-treatment recurrence are crucial MPM research areas. It has been shown that 18F FDG PET-CT has high precision and that it is good at specifying the local extension of the disease, lymph node involvement, and metastasis (21).

This study has a number of limitations. It is quite difficult to avoid susceptibility artifacts on DWI of pulmonary lesions. We faced image distortion artifacts related to the echo-planar image and macroscopic movement even though we employed a phased-array coil with respiratory compensation and cardiac gating techniques that are designed to improve the acquisition speed and quality of the image.

Diffusion-weighted imaging has some advantages. For example, it is a totally noninvasive imaging method and there is no need for contrast agent ingestion or for ionizing radiation, and the patients feel no discomfort.

CONCLUSION

Diffusion-weighted magnetic resonance imaging has been employed for the diagnosis and characterization of mediastinal and pleural tumors, and it has a role in characterizing the differences between benign and malignant diseases. In this study, we suggest that ADC values can be a useful tool for the differential diagnosis between benign and malignant thickening of the pleura.

Ethics Committee Approval: Ethics committee approval was received for this study from The Institutional Ethics Committee.

Informed Consent: Informed consent is not necessary due to the restors rective nature of the study.

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