Original Investigation

Differentiation of Diffuse Large B-cell Lymphoma From Follicular Lymphoma Using Texture Analysis on Conventional MR Images at 3.0 Tesla

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Rational and Objectives: Diffuse large B-cell lymphoma (DLBCL) represents the most common type of aggressive non-Hodgkin lymphoma (NHL); follicular lymphoma (FL) is the most frequent indolent NHL. The aim of this study was to investigate whether texture-based analysis of conventional magnetic resonance imaging (MRI) allows discrimination of DLBCL from FL, and further, to correlate the MRI texture features with diffusion-weighted imaging apparent diffusion coefficient (ADC) value and tumor tissue cellularity.

Materials and Methods: Forty-one patients with histologically proven NHL (30 DLBCL and 11 FL) underwent conventional MRI and diffusion-weighted imaging examination before treatment. Based on regions of interest, texture analysis was performed on T1-weighted images pre- and postcontrast enhancement and on T2-weighted images with and without fat suppression, and features derived from the run-length matrix- and co-occurrence matrix-based methods were analyzed. Receiver operating characteristic curves were performed for the three most discriminative texture features for the differentiation of the two most common types of lymphoma. The analyzed MRI texture features were correlated with the ADC value and the tumor tissue cellularity.

Results: We found that on T1-weighted images postcontrast enhancement, run-length matrix-based texture analysis for lesion classification differentiated DLBCL from FL, with specificity and sensitivity of 76.6% and 76.5%, respectively. There was no correlation between the texture features and the ADC value or tumor tissue cellularity.

Conclusions: DLBCL and FL can be differentiated by means of texture analysis on T1-weighted MRI postcontrast enhancement. These results could serve as a basis for the use of the texture features on conventional MRI as adjunct to clinical examination to distinguish DLBCL from FL.

Key Words: Non-Hodgkin lymphoma; diffuse large B-cell lymphoma; follicular lymphoma; texture analysis; MRI; diffusion-weighted imaging; apparent diffusion coefficient; cellularity.

INTRODUCTION

Non-Hodgkin lymphoma (NHL) is a diverse group of malignant lymphoid neoplasms with variable clinical behavior and prognosis; it can be divided into an indolent group and an aggressive lymphoma group in clinical practice. The correct characterization of the tumor histology is essential for appropriate treatment planning, because the treatment strategies are different for aggressive and indolent lymphomas. Imaging studies have played an important role in the early diagnosis, accurate staging, and treatment response evaluation of lymphomas. Contrast-enhanced computed tomography (CT) and conventional magnetic resonance imaging (MRI) are commonly used in detecting the sites of the disease and in monitoring morphological changes after treatment. However, they rely on size criteria and could not differentiate between malignant and benign lesions. Diffusion-weighted imaging (DWI) allows quantification of the random motion of water molecules in tissue by means of apparent diffusion coefficient (ADC) measurements. Recently, DWI has been introduced as a new imaging modality that provides both morphological and functional information regarding

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characterization of lymphomas, and it has been used in detecting and staging malignant lymphomas, as well as in monitoring the response to therapy (1,2). However, it could not distinguish between diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL) (3,4). Positron emission tomography with the use of 2-deoxy-2-[^{18}F]fluoro-d-glucose tracer could differentiate aggressive from indolent lymphoma and guide biopsies in the detection of histological transformation of indolent lymphoma (5,6). However, it is relatively expensive, time-consuming, and involves exposure to ionizing radiation.

DLBCL represents the most common type of aggressive NHL; FL is the most frequent indolent NHL, and it accounts for more than 50% of NHL cases (7). About 40% of patients with an indolent lymphoma eventually experience a relapse with a more aggressive histology (8). Histological transformation of FL to a more aggressive NHL, most commonly DLBCL, is a pivotal event in the natural history of FL and is associated with poor outcome (9). If transformation from indolent to aggressive lymphoma is clinically suspected, it is mandatory to perform a biopsy for the histological confirmation. However, the lymphomatous site that contains the tumor cells with the highest malignancy grade can be missed by biopsy; as a result, multiple or repeated biopsies may sometimes be needed. Texture analysis is an image postprocessing approach that extracts quantitative information from a digital image based on mathematical analysis. It evaluates interpixel relationships that generate characteristic organizational patterns in an image, many of which, such as coarseness and regularity, are beyond the ability of visual perception (10). Many promising studies have been reported with MRI texture analysis in the classification of pathological tissues from normal tissues in liver (11), muscles (12), and brain (13–15), and in the classification of different pathological tissue types in breast cancer (16,17) and liver tumor (18), as well as in monitoring lymphoma pathological changes after treatment (19). We hypothesize that the textural gray-level patterns on conventional MR images may indirectly reflect tumor histopathological heterogeneity, because microscopic level differences can be expected to manifest at a more macroscopic level by imaging analysis. The purpose of this study was to investigate whether MRI texture analysis allows discrimination of DLBCL from FL before treatment, and further, to correlate the MRI texture features with ADC value and tumor tissue cellularity.

MATERIALS AND METHODS

Patients

Patients were enrolled from our prospective clinical study investigating the potential of positron emission tomography/CT and MRI for early chemotherapy response evaluation in patients with NHL. The inclusion criteria were at least 18 years of age, histologically proven DLBCL and FL, and World Health Organization performance scale (Zubrod score) better than 4. The exclusion criteria were concomitant previous malignant disease, primary central nervous system lymphoma, human immunodeficiency virus infection or acquired immunodeficiency syndrome, diabetes, or other serious medical conditions that would prevent the imaging examinations. The study was approved by the Ethics Committee of Tampere University Hospital, and all patients gave written informed consent prior to study entry.

All patients underwent anamnestic and physical examinations, standard laboratory tests, and CT scans of the chest, abdomen, and pelvis. In addition, unilateral bone marrow aspiration and trephine biopsy were performed on each patient. Biopsy specimens were examined by an expert hematopathologist and classified according to the World Health Organization/Revised European-American Lymphoma classification of lymphoid neoplasm (20). An experienced physician selected the target tumor mass of interest (the region containing the largest tumor or the greatest number of >1 cm lymph nodes) for texture analysis based on clinical presentation and CT examination. Clinical prognostic indexes, such as Ann Arbor stage, International Prognostic Index, and Follicular Lymphoma International Prognostic Index, were also evaluated.

Tumor Cellularity Analysis

Biopsy specimens were fixed in buffered formalin, processed for paraffin embedding, and sectioned at 5-μm thickness. The cellularity was estimated for each biopsy site from the hematoxylin and eosin-stained sections. Two slides were obtained from different areas of the tumor (×20 objective), and digital photomicrographs were taken from the qualitatively assessed representative region of highest cellular packing density by the same expert hematopathologist using the Leica DMD108 digital microimaging network instrument (integrated camera). The images were segmented and the number of nuclei was counted using BioImageXD software (21); the method has been described in detail in our previous publication (3).

MR Image Acquisition

MRI was acquired using a 3 Tesla MR System (Siemens Trio-Tim, Erlangen, Germany) with the manufacturer's body and spine array coils. The body matrix coil had six elements. It was used in combination with the spine matrix coil that had 24 elements. Additionally, a neck coil with four elements was used for the cervical region examination. The MRI consisted of a whole-body examination from the level of the skull base to the floor of the pelvis in the coronal plane using a parallel acquisition technique; the reduction factor was 2. The coronal MRI sequences included a T1-weighted turbo spin-echo imaging and a T2-weighted inversion-recovery imaging. For the purpose of quantitative analysis, high-resolution axial images and DWI were acquired from the target tumors. Total acquisition time was about 25–30 minutes. The axial MRI sequences included a T1-weighted three-dimensional volumetric interpolated breath-hold examination with fat suppression