Original Investigation

Multi-model Analysis of Diffusion-weighted Imaging of Normal Testes at 3.0 T: Preliminary Findings

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Rationale and Objectives: This study aimed to establish diffusion quantitative parameters (apparent diffusion coefficient [ADC], DDC, α, D_{app}, and K_{app}) in normal testes at 3.0 T.

Materials and methods: Sixty-four healthy volunteers in two age groups (A: 10–39 years; B: ≥ 40 years) underwent diffusion-weighted imaging scanning at 3.0 T. ADC_{1000}, ADC_{2000}, ADC_{3000}, DDC, α, D_{app}, and K_{app} were calculated using the mono-exponential, stretched-exponential, and kurtosis models. The correlations between parameters and the age were analyzed. The parameters were compared between the age groups and between the right and the left testes.

Results: The average ADC_{1000}, ADC_{2000}, ADC_{3000}, DDC, α, D_{app}, and K_{app} values did not significantly differ between the right and the left testes ($P > .05$ for all). The following significant correlations were found: positive correlations between age and testicular ADC_{1000}, ADC_{2000}, ADC_{3000}, DDC, and D_{app} ($r = 0.516$, 0.518, 0.518, 0.521, and 0.516, respectively; $P < .01$ for all) and negative correlations between age and testicular α and K_{app} ($r = –0.363$, –0.427, respectively; $P < .01$ for both). Compared to group B, in group A, ADC_{1000}, ADC_{2000}, ADC_{3000}, DDC, and D_{app} were significantly lower ($P < .05$ for all), but α and K_{app} were significantly higher ($P < .05$ for both).

Conclusions: Our study demonstrated the applicability of the testicular mono-exponential, stretched-exponential, and kurtosis models. Our results can help establish a baseline for the normal testicular parameters in these diffusion models. The contralateral normal testis can serve as a suitable reference for evaluating the abnormalities of the other side. The effect of age on these parameters requires further attention.

Key Words: Testis; diffusion-weighted imaging; mono-exponential model; stretched-exponential model; diffusion kurtosis imaging.

INTRODUCTION

Ultrasound is the initial imaging method for testicular evaluation. However, magnetic resonance imaging (MRI), which provides anatomic information, is a powerful alternative imaging modality for testicular disease, especially ultrasound equivocal cases (1,2). Diffusion-weighted imaging (DWI), which assesses the random movement of water molecules within a tissue, is one of the primary components of MRI. DWI is a highly accurate cancer detection strategy and has been recommended as a biomarker for cancer identification (3).

The mono-exponential model, based on the assumption of free Brownian movement of molecular water, has been adopted for DWI analysis in most clinical studies. However, water molecules do not move freely in biological tissues because of many forms of hindrance, such as membranes and intracellular organelles, which influence diffusion (4). Furthermore, only one parameter can be obtained from the mono-exponential model, which limits the amount of information acquired from the DWI dataset. Therefore, new diffusion models have been developed to describe the complicated behavior of water diffusion; these models include the stretched-exponential and kurtosis models, among others (5,6). Previous studies have suggested that those new models might provide more useful information for disease detection or classification (7–9).

Despite the promising value of DWI, the use of DWI is still not widespread in testicular diseases. To date, only a few

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studies have evaluated the apparent diffusion coefficient (ADC) calculated from the mono-exponential model in testicular diseases at 1.5 T (2,10–12), and only two studies were performed at 3.0 T (13,14). There have been no reports regarding the stretched-exponential model and diffusion kurtosis imaging in testes at 1.5 T or at 3.0 T. A challenge to more widespread application of DWI is the lack of standardization. A better understanding of the normal values is required to successfully interpret DWI results, including those of testicular disease. To date, only one study systematically reported the ADC values of normal testes at 1.5 T, and no reference value for normal testes has been published with any available diffusion model at 3.0 T (15).

Furthermore, age-related changes in the structure and function of the testicle might induce variations in the values of diffusion parameters because a previous study suggested that the ADC values of normal testes change with age (15). Age-related changes in diffusion parameters seem likely to have a major impact on the use of DWI in the diagnosis of testicular diseases. Another important point requiring attention is the asymmetry between the left and the right testes. Whether the asymmetry between the left and the right testes induces differences in the quantitative parameters also requires evaluation.

Thus, the purpose of our study was to investigate the quantification of diffusion models (mono-exponential model, stretched-exponential model, and kurtosis model) in normal testes to establish baseline values for further clinical studies and to evaluate age-related differences and asymmetry between the right and the left testes.

PATIENTS

This prospective study was approved by the institutional review board, and informed content was obtained from each participant. From May 2014 to May 2017, 64 volunteers with no known or prior scrotal abnormalities (mean age, 38.60 years; age range, 11–80 years) were enrolled in this study.

MRI PROTOCOL

All MR images were acquired with a 3.0 T MR scanner (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany) with an 18-element body matrix coil combined with a 32-channel spine coil. Patients were positioned in a feet-first supine position. Transverse T2-weighted turbo spin-echo sequences with the following parameters were used: a repetition time/echo time range of 6500/104 ms, a slice thickness of 3 mm, an inter-slice gap of 0 mm, a field of view of 180×180 mm^2, and a matrix of 384×320. Axial DWI was performed using a single-shot echo-planar imaging pulse sequence with the following parameters: repetition time, 5300 ms; echo time, 78 ms; slice thickness, 3 mm; inter-slice gap, 0 mm; field of view, 220×176 mm^2; matrix, 90×90; bandwidth, 2058 Hz/px; acceleration factor of 2; and 8 b-values (number of excitations) of 50 (1), 100 (2), 500 (2), 1000 (4), 1500 (4), 2000 (6), 2500 (6), and 3000 (6) s/mm^2. The total acquisition time was 7 minutes and 9 seconds.

MRI DATA ASSESSMENT

MRI post-processing was performed using ImageJ (Version 1.46r, NIH, https://imagej.nih.gov/ij/). One observer with 5 years of experience in pelvic MRI analysis evaluated the MR images. The regions of interest (ROIs) were placed on the largest slice of the testes on the image with b-value = 50 s/mm^2. The ROIs were drawn within the outer border for each side (right and left) of the testes. The ROIs were copied from images with b-value = 50 s/mm^2 to other b-value images on the same location. The mean signal intensity value for each b-value was recorded for each ROI. For the ROI drawing method, please see Figure 1.

MODELING

All analyses in our study were conducted at the ROI level. We performed nonlinear least-square fitting based on the Levenberg-Marquardt algorithm using MATLAB 2014a (MathWorks, Natick, MA) to fit the following Equations (1)–(3) to the mean signal of each ROI (Fig 1j). ADC, DDC, α, D_{app}, and K_{app} were estimated in the normal testes. As the maximum b-value primarily affects the ADC value, the b-value used in clinical settings may change. To calculate ADC values, the data were divided into three groups by the maximum b-values, namely, ADC_{1000}, ADC_{2000}, and ADC_{3000}.

1. Mono-exponential model

$$S(b)/S_{50} = \exp[-(b-50)\cdot ADC] \quad (1)$$

2. Stretched-exponential model

$$S(b)/S_{50} = \exp\{-[(b-50)\cdot DDC]^{\alpha}\} \quad (2)$$

3. Diffusion kurtosis imaging

$$S(b)/S_{50} = \exp\left[-(b-50)\cdot D_{app} + (b-50)^2\cdot {D_{app}}^2\cdot K_{app}/6\right] \quad (3)$$

S(b) is the DWI signal intensity at a particular b-value, and S_{50} is the DWI signal intensity at b = 50 s/mm^2. ADC represents the diffusion coefficient calculated from the mono-exponential model. DDC represents the diffusion coefficient, and α represents the water diffusion heterogeneity index (between 0 and 1) calculated from the stretched-exponential model. D_{app} represents the diffusion coefficient, and K_{app} is the apparent kurtosis calculated from the kurtosis model.

STATISTICAL ANALYSIS

To provide reference values for diffusion parameters for different age ranges, the volunteers were divided into two groups according to age: 10–39 years (group A, 36 men), ≥40 years (group B, 28 men). The cutoff value of the group was based