

A study of the relationship between gender/age and apparent diffusion coefficient values in spleen of healthy adults using diffusion-weighted magnetic resonance imaging

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Abstract

Background: Diffusion-weighted magnetic resonance imaging (DWI) systems are very effective in detecting strokes, and they also have shown significant promise in the detection of fibrosis and cirrhosis of the liver. However, such systems have the disadvantages of poor reproducibility and noise, which can diminish the accuracy of the apparent diffusion coefficients (ADCs) provided by the DWI process. The main aim of this study was to determine the relationship between the age and gender of healthy adults in terms of the ADC values of the spleen measured by DWI.

Methods: Sixty-nine subjects selected for this study from people who were referred to the Tabesh Medical Imaging Center in Tabriz, Iran, in 2013. Each subject underwent echo-planar DWI for her or his ADC values of the spleen with b-values of 50, 400, and 800 s/mm², and the resulting ADC values were evaluated.

Results: No significant differences were observed in ADC values of the spleen among the female and male participants or those from various ages ($P>0.05$).

Conclusions: Based on the findings of this study, it was concluded that the effect of age and gender on the spleen's ADC values can be omitted from the spleen-diagnosis procedure. In other words, the spleen's ADC values are not related to the age or the gender of healthy adults.

Keywords: spleen, diffusion-weighted magnetic resonance imaging, age, gender

1. Introduction

DWI is one of the primary diagnostic methods used for diagnosing acute cerebral infarction. Very recently, however, the application of DWI has emerged for diagnosing other organs and structures, including the spine, breasts, spleen, prostate gland, and liver (1). In images of the spleen taken by DWI, different b-values are calculated qualitatively for the purpose of differentiation between normal and pathologic cases, while the ADC maps are measured quantitatively. Currently, the splenic ADC values are used as the reference ADC values for evaluating cirrhosis and fibrosis of the liver (2, 3). As a lymphatic organ, the spleen's size and internal structure may change with age and physiological circumstances (4, 5).

The spleen's ADC values depend largely on the amount and the movements of water in the organ. If the assumption is true that the structure of the spleen varies by gender and age, this should be reflected in the ADC values. This retrospective, cross-sectional study is aimed at examining the effects of age and gender on the spleen's normal ADC values.

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2. Material and Methods

This study was conducted in 2013 at the Tabesh Medical Imaging Center in Tabriz, Iran. The 69 subjects who participated in the study were selected from female and male adults who were referred to the Tabesh Center for abdominal MRIs from July through December in 2013. The subjects included 40 females and 29 males, and, first, we obtained their medical histories. The exclusion criteria included: 1) having a pacemaker, aneurysm clips, an artificial heart valve, or other kinds of foreign bodies, 2) presence of splenic disease, such as tumors, cysts, and haemangioma.

Next, the subjects were requested to complete questionnaires that provided age and gender information, after which they underwent the spleen-imaging process. First, the subjects were asked to wear special clothing. After they were dressed appropriately, a phase array body coil was mounted on their abdomens, while two element spine coils were installed in a supine position to receive the signals from the subjects. The apparatus used in this study included a 1.5 Tesla (T) imaging system (Magnetom Avanto 18-channel, equipped with Syngo MR B17 software) with a 45 mT/m maximum gradient amplitude and a maximum slew rate of 200 T/m/s. The anatomy of the spleen was processed using T1-W_FLASH 2D_fatsat with a repetition time (TR)=188 ms, echo time (TE)=2.38 ms, field of view (FOV)=385 mm, average=1, T2-HASTE_fatsat Axial with TR=1450 ms, TE=123 ms, slice thickness of 6 mm, distance factor=0%, and FOV=385 mm. Also, the axial sequence of free-breathing, echo-planar DWI was used to analyze the functional status of the spleen. To improve the quality of the diffusion images, the following parameters were considered: 30 sections; section thickness=4 mm; intersection gap=0 mm; field of view=360 mm; matrix=192×192; in plane resolution=2.3×1.8 mm; bandwidth=290 Hz per pixel; optimized for minimal echo-spacing; partial Fourier factor 6/8; TR=5600 ms; TE=102 ms; number of signal averages=6; Diffusion gradient b-values of 50, 400, and 800 s/mm² were applied in three orthogonal directions.

After approval of the local ethics committee, the participants were briefed and assured of the safety of MRI imaging, and a written consent was obtained from each subject. Taking part in the study was voluntary and free of charge. Measurements of the spleens' ADC values were made on ADC map images. The measurement procedure consisted of selecting regions of interest (ROI) with areas of 20-25 mm² on the spleen ADC map to acquire the ADC values. To avoid random variability in the measurements and to minimize the impact of probable partial volume artifacts, the calculation of each individual ADC value was performed by obtaining the average value of three separate measurements, with adequate distance from the border of the spleen. The means and standard deviations (SDs) of the ADC values were calculated. The ADC map was formed automatically for each echo-planar DWI sequence on a pixel-by-pixel basis using MRI application software (Syngo MR B17, Siemens Healthcare). Figure 1 shows that the gray values of the pixels, which were linearly consistent with the ADC values, were expressed in mm²/sec.

The Kolmogorov Smirnov test was used to evaluate the normality of the distribution of the parameters. The correlation coefficient was used to evaluate the correlation between age and the ADC values. Statistical data analyses concerning the effect of age and gender on the spleens' ADC values were performed using the t-test for individual samples and correlation coefficient analysis using SPSS software V. 21. A P-value of < 0.05 was deemed to be statistically significant.

3. Results

The Kolmogorov-Smirnov test indicated that there was a normal distribution of ADC values and age. Figure 1 shows scatter plots of the ADC values of the spleen correlated with age. The mean age of male patients with normal spleens was 52.5 (age range 11–84), and the mean age of female patients with normal spleens was 46.8 (age range 10–85). In addition, the distribution of the mean ADC values was similar for the male and female subjects (P=0.3), i.e., the mean ADC value of male patients with normal spleens was $0.724 \pm 0.099 \times 10^{-3}$ mm²/s (ADC range 0.518–0.88×10⁻³ mm²/s), and the mean ADC value of female patients with normal spleens was $0.750 \pm 0.113 \times 10^{-3}$ mm²/s (ADC range 0.194–0.892×10⁻³ mm²/s). The mean of the ADC values in the male subjects was 0.724×10^{-3} mm²/s, and it was $0.750 \pm 0.113 \times 10^{-3}$ mm²/s for the female subjects.

The identical ADC values in the male and female subjects of various ages showed that the spleen's ADC values could not be used as determinant diagnostic criteria (P-values>0.5). Table 1 provides the spleens' ADC values as they relate to gender and age. With our samples of ADC values (n=69), Pearson's correlation between the age and ADC values of the subjects with healthy spleens showed that the average ADC values of the normal adult spleen

across different ages were not age-dependent; there was no significant correlation between the ADC values of the spleens and age (correlation values=0.188, P=0.122).

Table 1. Results of student’s t-test to compare the ADC values in the spleens of healthy adult male and female subjects based on body mass index

Gender	Number	ADC ($\times 10^{-3}$ mm ² /s) \pm SD ^a	F-statistic value of F	Significance level
Male	29	0.724 \pm 0.099	-1.007	0.317
Female	40	0.750 \pm 0.113	-1.007	0.317

a: Standard deviation

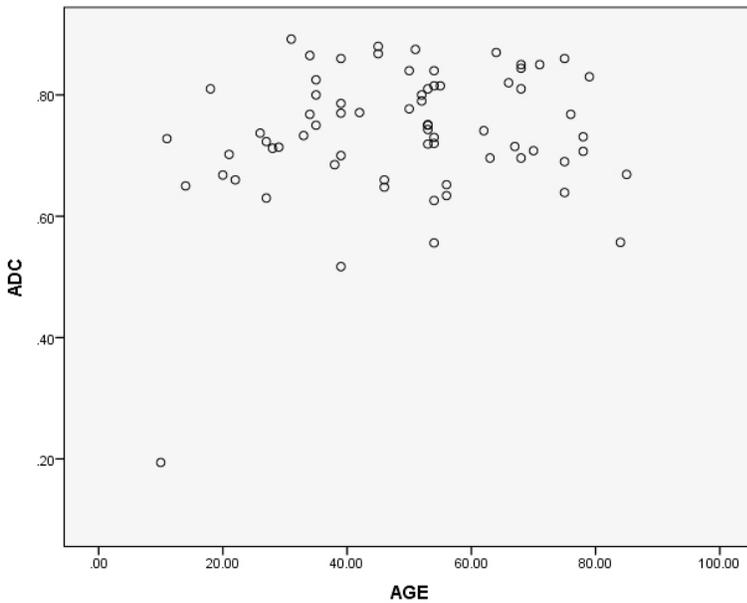


Figure 1. Scatter plots of the spleens’ ADC values with age

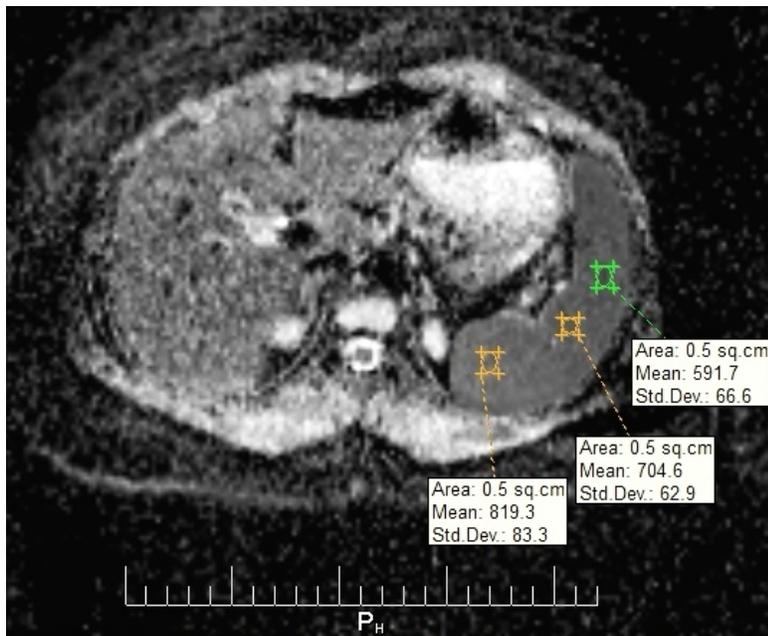


Figure 2. Spleen of a 30-year-old woman: An ADC-map image obtained with DWI axial images with b-values of 50, 400, and 800 s/mm².

4. Discussion

To date, DWI has proven to be the only safe method of examining the movements of water molecules (Brownian motion) within the human body. The previous literature has shown that any variability in composition and/or cellularity of the tissues of organs (the spleen in this case) can affect the diffusion of water molecules in the body in the *in vivo* MR determination (6) and that employing DWI can help to diagnose certain diseases by quantifying such changes, as represented by the variability of the ADC values. The measurement techniques used by DWI and ADC recently have been improved substantially (7), including fast parallel imaging approaches, physiological gating, and breath-holding, resulting in even broader usage of such systems in the diagnosis of abdominal diseases (7-10). Note that recent findings have indicated that measuring the ADC maps using single-direction DWI for spleen imaging is possible and preferable to the traditional and prolonged trace-based DWI procedure. Good evidence of this feasibility is the spleen's parenchyma, representing acceptable consistency in the average ADC maps that used single-shot, breath-hold DWI, whether in one diffusion direction (z) or three orthogonal diffusion directions (x, y, and z). Some other similar results have been presented in the literature in connection with the spleen and other abdominal organs, such as the liver and others (11). Despite the above improvements, DWI images can be subject to blurring effects because of the prolonged readout interval and the artifacts associated with movements. It is promising, though, to say that three-direction DWI with considerably maximized imaging time provides adequate diagnostic quality for abdominal imaging. Hence, this study can assuredly affirm that three-direction DWI can be used to examine and determine the characteristics of the impact of age and gender on the ADC values in the spleens of healthy adults. In particular, the results of this study indicated that the ADC values of normal adults' spleens were not significantly dependent on either gender or age ($p > 0.05$). Conversely, G. Li et al. (11) concluded that there was a negative correlation between ADC values and the higher ages of the healthy adult volunteers and younger people when using breathing echo-planar DWI. The differences in the results of the two studies can be traced back to the b-values. We used b-values of 50, 400, and 800 s/mm². Thus, the two studies can be said to be complementary, not contradictory. It is well known that some organs in the human body attain steady state around ages in the mid-teens or twenties (12); therefore, it is probable that the spleen's ADC maps are lower in the adolescent years but develop to the steady state in the twenties. Structural and functional variations with age have been investigated using numerous methods, including ultrasonography, computed tomography (CT), and MRI (13). The findings indicated that there was an increase in fibrous connective tissue, progressive pancreatic lobulation, a loss of acinar cells, and changes consistent with fatty pancreatic degeneration.

The results showed that the spleen's ADC values did not differ significantly for male and female subjects. Currently, researchers use the splenic ADC values as a reference for evaluating cirrhosis and fibrosis of the liver (2). Some reports (2, 11) in the literature acknowledged that normalizing of liver ADC with the spleen's ADC values could improve diagnostic accuracy in detecting fibrosis and cirrhosis of the liver. The spleen is a lymphatic organ, and, as such, its size and internal structure change with age and physiological condition (4, 5). Despite the expectation that the ADC values should decrease with age, particularly in patients over 60, there was no correlation between the two in this study. In addition, no significant correlation was observed between age and the ADS map.

Other factors that affect the diffusion of water molecules, include the density of the tissue, intravoxel perfusion, and the T2-shinethrough effect (9). Accordingly, the effect of changes in the density of the tissue with age and the T2 effect on the estimation of ADC values were not considered. This study also had several limitations, e.g., it is not known that whether the ADC values vary with age. The Pearson correlation coefficient analysis showed that the spleen's ADC values did not change with age. Difficulty in obtaining tissue samples was the major obstacle for the researcher in tracing the physiological changes of the normal spleen associated with age. To our knowledge, the spleen's hematopoietic function shifts to the bone marrow as humans age, but the blood volume decreases in older adults, which is accompanied by a relatively considerable increase in the volume of the spleen. No correlation between the changes in the spleen's ADC values with age was found in this study. To summarize, in this DWI-focused study, we found that the ADC values of the normal adult spleen obtained through imaging did not exhibit significant dependence on gender or age.

5. Conclusions

The main aim of this study was to investigate the relationship between the changes in the spleen's ADC values and gender/age in healthy female and male adults. Since the findings of the study indicated that the ADC values of the spleen in normal healthy adults did not differ significantly due to the subjects' differences in gender and age, it can be concluded that the ADC values cannot be considered to be reliable diagnostic criteria.

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Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

Both authors contributed to this project and article equally. Both authors read and approved the final manuscript.

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