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FULL PAPER

ADC values in diffusion-weighted MRI and their relationship with age, gender and BMI in healthy people's pancreases

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Objective: The aim of this study is to use diffusion-weighted MRI to assess the apparent diffusion coefficient (ADC) values in head, body and tail sections of the pancreas in healthy subjects and the relationships between these values and age, gender and body mass index (BMI) of these cases.

Methods: This study was conducted on 82 participants who were referred to the Tabesh Medical Imaging Center, Tabriz, Islamic Republic of Iran, during 2013. Echo-planar diffusion-weighted imaging of the pancreas was carried out with *b*-values of 50, 400 and 800 s/mm², and ADC values were assessed for the head, body and tail sections of the pancreas.

Results: The ADC values for the head, body and tail sections of the pancreas in female participants were

significantly greater than those in male subjects ($p < 0.05$). ADC values for these parts among subjects with different BMI differed significantly ($p < 0.05$). Regarding age, there were no statistically meaningful differences among the ADC values for the three parts ($p > 0.05$).

Conclusion: Gender and BMI effect the ADC values of the three sections of the pancreas. Thus, knowledge of the basic values based on gender and BMI can improve diagnostics. Having looked at age factor, it seems that the ADC values were not significantly different.

Advances in knowledge: According to the results pancreatic ADC values appear to be influenced by gender and BMI but not by age.

Background

Usually referred to as "Brownian motion", diffusion is the result of random, thermal fluctuations. Diffusion-weighted imaging (DWI) is used as the first diagnostic method to investigate acute cerebral infarction. Recently, it has been used to investigate organs such as ovaries, breasts, pancreas, prostate and liver.¹ In diffusion-weighted (DW) images of the pancreas, different *b*-values are estimated in a qualitative way to differentiate between the normal and pathological status, while apparent diffusion coefficient (ADC) maps are evaluated by quantitative measures. For instance, lower ADC values are reported in cases of pancreatic cancer and pancreatitis.^{1,2} Therefore, DWI and its ADC values might help to differentiate between various diseases of the pancreas.

Statement of the problem

Routine sequences of MRI may assist to distinguish malignant lesions from benign types. But in three specific parts of the pancreas, DWI may be useful in investigation of and later identification of tumours, because it has the capability to show contrast between different tissues according

to molecular diffusion.³ DW images and their ADC values are not easy to use for pathological diagnoses and interpretations because such images are affected by various factors, such as the strength of the magnetic field, motion, *b*-factors, the types of pulse sequences and lack of standard ADC values for specific organs.^{4,5} Owing to conflicting findings of former studies regarding the impact of age and gender on ADC values and the probable effects of body mass index (BMI), a more multidimensional, accurate and detailed investigation seems to be necessary. Throughout the present study, we separately investigated the head, body and tail sections of the pancreas in healthy individuals by means of diffusion echo-planar sequence and ADC images, hoping that it would help to diagnose and segregate disease. We also determined and recorded ADC values and compared them according to age, gender and BMI.

Objective

The general objective of the present research was exclusively to investigate the relationship between the ADC values in DWI of the head, body and tail sections of the

pancreas of healthy individuals and to determine their link with age, gender and BMI of the subjects. However, we tried to divide the general aim into the following subobjectives:

- to compare ADC values in the head, body and tail sections of the pancreas among healthy male and female subjects
- to compare ADC values in the head, body and tail sections of the pancreas among healthy subjects of different ages
- to compare the ADC values in the head, body and tail sections of the pancreas based on BMI.

METHODS AND MATERIALS

Research design and setting

The present cross-sectional study was conducted in the Tabesh Medical Imaging Center, Tabriz, Islamic Republic of Iran, during 2013. The participants who had been referred to the centre for lumbar and abdominal MRI from July to December 2013 were recruited randomly.

Sampling

In this study, the mean and standard deviation of ADC values, required for the analysis of the samples, were derived from the results of Schoennagel *et al.*² Considering, 95% confidence interval and 80% statistical power, G*Power software indicated that the sample size should be at least 54 subjects. To ensure greater confidence, we used a sample size of 82 subjects (41 males and 41 females).

Selection criteria

In this study, the past medical backgrounds of subjects were obtained, and sonography of the pancreas was carried out. The inclusion criteria were:

- having no background of diabetes or pancreas disease
- having a healthy pancreas according to colour Doppler sonography
- having no pacemaker, aneurysm clips or artificial heart valves
- having no kind of foreign body
- not being pregnant.

Potential cases suspected to have claustrophobia, lesions observed in the anatomical images of the pancreas or patients with low quality pancreas images were also excluded from the study. Patients with diabetes were excluded from the study because we supposed ultrastructural abnormality in diabetics could affect its behaviour in diffusion studies.⁶ We used colour Doppler ultrasound to study patients, when patients showed any abnormality or suspicious findings in greyscale B scan.

Data collection

Imaging of the pancreas was carried out after the completion of questionnaires on the participants' height, weight, age and BMIs. According to the standard criteria of the World Health Organization, BMIs $<8.5 \text{ kg m}^{-2}$ were considered as underweight, $8.5\text{--}24.9 \text{ kg m}^{-2}$ as normal, $25\text{--}30 \text{ kg m}^{-2}$ as overweight and $>30 \text{ kg m}^{-2}$ as obese.⁷ After putting on special imaging clothes, a six-element body coil was used over the abdomen and two-element spine coil was used for signal reception from cases in a supine position. 1.5-T imaging system (MAGNETOM® Avanto 18-channel SQ engine; Siemens Healthcare, Erlangen, Germany) with a 45 mT m^{-1} maximum gradient amplitude and a maximum

slew rate of $200 \text{ T m}^{-1} \text{ s}^{-1}$ was applied. It used Syngo® MR B17 software (Siemens Healthcare). The parameters of turbo spin echo sequences that we used for lumbar spine MRI were T_2 weighted (T_2 -W) sagittal [repetition time (TR) = 300 ms; echo time (TE) = 103 ms; number of signal averages (NSA) = 2; field of view (FOV) = 314 mm; image matrix = 261×384 pixels]; T_1 weighted (T_1 -W) sagittal (TR = 510 ms; TE = 11 ms; NSA = 4; FOV = 315 mm; image matrix = 239×384 pixels) and T_2 -W axial (TR = 2900 ms; TE = 94 ms; NSA = 2; FOV = 270 mm; and image matrix = 180×256 pixels).

In order to process anatomy of the pancreas, we used T_1 -W_FLASH 2D_fatsat, with TR = 178 ms, TE = 2.38 ms, FOV = 380 mm, and average = 1, and T_2 -HASTE_fatsat in cross-section TR = 1400 ms, TE = 9 ms, slice thickness of 6 mm, distance factor = 0%, and FOV = 380 mm (Figure 1). For analysing the functional status, axial sequence of free breathing echo-planar DWI was implemented. In order to improve the quality of diffusion images, the following parameters were used: 30 sections; section thickness = 4 mm; intersection gap = 0 mm; FOV = 350 mm; matrix = 192×192 pixels; in-plane resolution = 2.3×1.8 mm; bandwidth = 290 Hz per pixel; optimized for minimal echo-spacing; partial Fourier factor 6/8; TR = 5700 ms; TE = 103 ms; number of signal averages = 9; diffusion gradient b -values of 50, 400 and 800 s mm^{-2} were applied in three orthogonal directions.

Ethical consideration

We followed the ethical research rules of Shahid Beheshti University of Medical Sciences and Health Services, Paramedical School, Tehran, Islamic Republic of Iran.

Image analysis

ADC values were measured by putting a region of interest (ROI) on the head, body and tail sections of the pancreas, at least 6 mm away from the pancreas side in order to prevent volume averaging effects. For each echo-planar DWI sequence, the ADC map was automatically formed on a pixel-by-pixel basis by a MRI software system (Syngo MR B17; Siemens Healthcare). The gray value of a pixel was linearly consistent

Figure 1. The pancreas of a 33-year-old male: a T_1 -Flash_fatsat image shows the anatomical regions of the pancreas.

with the ADC values, which were expressed in square millimetres per second. The T_1 and T_2 images were used to investigate pathological items and as a guide to put the ROI on the ADC map. Finally, the average value for each ROI was calculated (Figure 2).

Statistical analysis

Statistical analysis of the data was conducted utilizing the independent samples t -test, the analysis of variance (ANOVA) and the general linear model (GLM) run by SPSS® v. 21 (SPSS Inc., Chicago, IL). The analysis was about the effect of age, gender and BMI on the ADC values of the head, body and tail sections of the pancreas among two groups of both sexes. In order to investigate the significant differences between the averages of the parameters, Tukey's honestly significant difference (HSD) test was utilized, approximating to confidence level of 95%, the significant p -value was >0.05 .

RESULTS

Apparent diffusion coefficient values in head, body and tail of the pancreas

Here, ADC values of the head, body and tail sections of the pancreas of males and females are presented in Table 1. Clearly, it can be inferred that the ADC values were significantly different (Table 1).

Apparent diffusion coefficient values in the normal, overweight and obese groups

The analysis of one-way ANOVA revealed significant differences among the ADC values of the pancreas head, body and tail sections in normal, overweight and obese groups ($p < 0.05$). The results of the Tukey's HSD test are depicted in Table 2.

Apparent diffusion coefficient values of pancreas head, body and tail among age groups

One-way ANOVA was used to compare the ADC values in the head, body and tail sections of the pancreas among the age groups. The results of the test showed that there were no statistically significant differences between the ADC values based on age ($p = 0.061$, 0.102 and 0.489 for the head, body and tail sections, respectively).

The relation between the apparent diffusion coefficient values of the pancreas sections and age, gender and body mass index

We utilized GLM test to investigate the simultaneous relationship of age, gender and BMI. Test results showed significant affinity between gender variables and BMI groups with ADC values of the pancreas head ($p < 0.001$). However, there was no significant relationship between the age groups and the ADC values of the pancreas head ($p = 0.704$). There was significant linkage between gender variables and the BMI groups with ADC values of the pancreas body ($p < 0.001$), but such significance was not seen among the age groups ($p = 0.704$). However, there was significant linkage between gender and BMI and the ADC values of the pancreas tail ($p = 0.001$ and 0.003 , respectively), but it was not significant in terms of age and ADC values of the pancreas head ($p = 0.529$) (Table 3).

DISCUSSION

DWI is a non-invasive method to analyse Brownian motion of water molecules in the human body. It can detect the diffusion of water molecules *in vivo* and indirectly reflects the micro-structural changes. Changes in structure or tissue of cells have an effect on the diffusion of water molecules in the body, and this effect can be evaluated quantitatively by ADC of DWI.^{1,3,4} Remarkable progress has been made in techniques available for the diagnosis of abdominal disease, including physiological gating, parallel imaging methods, breath-holding techniques, utilization of DWI and application of ADC measurements.⁸ DWI may help to diagnose the types of lesions, the segregation of inflammation that results from chronic infections caused by tumours and the exocrine function mode. In studies conducted by DWI to identify the type of disease, relatively high interference of several factors has resulted in suboptimal specificity.^{9–11}

The apparent diffusion coefficient values of pancreas sections in two separate male and female groups

The findings of the study showed that in the head, body and tail sections of the pancreas, the ADC values among females were

Figure 2. The pancreas of a 33-year-old male: an apparent diffusion coefficient (ADC)-map image obtained with diffusion-weighted imaging axial images with b -values of 50, 400 and 800 s mm^{-2} from the different sections of the pancreas. The measured ADC within region of interest. FoV, field of view; max, maximum; min, minimum, SD, standard deviation; TE, echo time; TR, repetition time.

Table 1. Results of Student's *t*-test to compare the apparent diffusion coefficient (ADC) values in head, body and tail sections of the pancreas among healthy male and female subjects

Index	Gender	Number	ADC ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) $\pm$ standard deviation	<i>F</i> -statistic value of <i>F</i>	Significance level
Head of pancreas	Male	41	0.984 ± 0.2	-3.058	0.003
	Female	41	1.104 ± 0.152		
Body of pancreas	Male	41	0.897 ± 0.245	-3.056	0.003
	Female	41	1.04 ± 0.148		
Tail of pancreas	Male	41	0.867 ± 0.184	-2.107	0.038
	Female	41	0.943 ± 0.135		

greater than those for males. A study conducted on a larger number of subjects using CT and autopsies showed fat deposition in males when they reach their forties, but in females it continued from their twenties to the nineties. Here, both gender-related differences in the pancreas exocrine function and the differences in the changes in the pancreas tissue and fat volume could possibly be the reason for the partial decrease in ADC values in the male subjects.¹² Such results are in agreement with the results by Herrman *et al* (2012) in which the ADC values in females were greater than those in males.¹³ However, the study by Ma *et al*¹⁴ showed no significant relationship between the values of ADC in male and female subjects.⁴ This could probably be owing to the number of participants or the methods, for example, *b*-values of 0 and 500 s mm^{-2} in the ADC images.

The apparent diffusion coefficient values in pancreas sections in normal, overweight and obese groups
The present study showed meaningful differences in averages of the ADC values of the pancreas head, body and tail sections among the overweight and normal subjects ($p < 0.05$). They also showed that the average difference of the ADC values in body and tail of the pancreas both among the normal/obese subjects and overweight/obese groups were significant

($p < 0.05$). The structure of the pancreas may depend on the physical status of individuals, for example, the volumes of pancreatic parenchyma and fat would be greater in male and overweight female subjects.¹⁵ The effects of BMI on the ADC values in the head, body and tail sections of the pancreas were not examined in former studies. However, as BMI increased, the ADC values in these three parts decreased, and this might be owing to the ratio of fat volume to the pancreatic parenchyma volume. In an autopsy by Klöppel *et al*,¹⁶ it was found that the volume of the pancreas in obese subjects was double that of other subjects, which might explain the decrease in ADC values.

Apparent diffusion coefficient values in the head, body and tail of the pancreas among age groups
Study findings showed no significant differences in the ADC values of different age groups. Also, there were no meaningful discrepancies in the ADC values of healthy individuals in the pancreas body and tail of the age groups below 20, 20–40 and above 40 years. Indeed, some organs in the human body reach a steady state in the mid-teens or twenties.¹⁴ Thus, it is possible that ADC values in the pancreas can be lower in the early years and reach steady state in the twenties. Different imaging methods, such as sonography, CT scan and MRI,

Table 2. Results of Student's *t*-test to compare the apparent diffusion coefficient (ADC) values in the head, body and tail sections of the pancreas based on body mass index (BMI)

Index	BMI	Number	ADC ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) $\pm$ standard deviation	<i>F</i> -statistic value of <i>F</i>	Significance level
Head of pancreas	Normal	23	1.142 ± 0.161	7.804	0.0001
	Overweight	31	1.051 ± 0.183		
	Obese	28	0.952 ± 0.169		
Body of pancreas	Normal	23	1.083 ± 0.159	11.047	0.000
	Overweight	31	0.993 ± 0.179		
	Obese	28	0.838 ± 0.221		
Tail of pancreas	Normal	23	0.999 ± 0.154	9.783	0.000
	Overweight	31	0.915 ± 0.123		
	Obese	28	0.815 ± 0.170		

Table 3. Results of Student's *t*-test to compare the apparent diffusion coefficient (ADC) values in the head, body and tail sections of the pancreas among age groups

Index	Age groups (years)	Number	ADC ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) $\pm$ standard deviation	F-statistic value of F	Significance level
Head of pancreas	Under 20	4	1.123 ± 0.16	0.721	0.489
	21–40	37	1.058 ± 0.189		
	Over 40	41	1.023 ± 0.186		
Body of pancreas	Under 20	4	1.14 ± 0.284	2.348	0.102
	21–40	37	0.989 ± 0.229		
	Over 40	41	0.926 ± 0.181		
Tail of pancreas	Under 20	4	0.973 ± 0.147	2.906	0.061
	21–40	37	0.944 ± 0.169		
	Over 40	41	0.862 ± 0.154		

have shown that an increase of fibrous connective tissue and progressive lobulation of the pancreas and changes in fatty degeneration can occur as age increases.^{14,17,18} Although it was expected that the ADC values decrease by increases in age, our study showed no significant linkage in this respect. No significant linkage was found between the ADC values and the three age groups owing to lobulation of pancreas tissue or decreases in the accuracy of ROI measurements. In the present study, the calculated ADC values with low and high *b*-values (50, 400 and 800 s mm^{-2}), theoretically, were affected by diffusive perfusion.³ Meanwhile, in a previous analysis of adult subjects, the selection of a set of *b*-values (50/400, 50/800, 400/800 and 50/400/800 s mm^{-2}) revealed no significant effect on the ADC values.² In a study conducted by Ma et al, the effect of age on ADC values was examined, and results showed no significant relationship between age and ADC values.¹⁷ In that study, 36 older cases (aged between 62 and 85 years) who were not able to hold their breath were excluded from the study.¹⁹

A study conducted by Herrmann et al¹³ on subjects under the age of 25 years old revealed that there was a negative affinity between the pancreas ADC values in healthy adults and children, *i.e.*, the ADC values decreased as age increased. The variations between the results of the present study and Herrmann's study might be owing to the number of samples and the age groups involved.

Age and body mass index relationship with apparent diffusion coefficient values

The results of this study showed that there were no significant relationships among the ADC values of the pancreas head, body and tail and age. However, ADC values of these three parts consequently decreased as the BMI increased, which could be the result of increasing fat in the pancreas. The volume of pancreas fat in overweight and obese cases was greater than that

in the normal subjects by 68% and 32%, respectively, and the volume of pancreatic parenchyma was greater than that of normal subjects with 7% and 13%, respectively.¹⁵

CONCLUSIONS

The aim of the present research, was to investigate the effect of age, gender and BMI on the ADC values of the pancreas in healthy subjects. The findings showed that the ADC values of the pancreas in healthy females were lower than those in males. The differences in the ADC values in the three pancreas sections mentioned among the age groups were not significant. The ADC values of the pancreas of obese subjects were lower than those of fit subjects. The findings of the study also indicated that the clinical application of ADC values must be appropriately standardized according to diffusion protocols, such as *b*-values and the ADC measuring methods. In the analysis of the ADC values of the pancreas, the subject's gender and BMI were focused in differential diagnosis; however, the age factor should not be included in the analysis of the ADC values. Since the research samples did not include underweight subjects, it is recommended that further studies must be conducted. An appropriate direction for future research on this subject matter would be to analyse ADC values of the pancreas among insulin-dependent/independent patients with diabetes and a control group.

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