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FULL PAPER

Evaluation of renal cortical thickness by non-contrast-enhanced MR imaging with spatially selective IR pulses: comparison between cirrhotic and non-cirrhotic patients

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Objective: To compare renal cortical thicknesses between patients with and without cirrhosis with normal renal function based on serum creatinine using non-contrast-enhanced steady-state, free precession (SSFP) MRI with spatially selective inversion recovery (IR) pulses and to discuss the clinical implications of measuring renal cortical thickness in patients with cirrhosis.

Methods: 40 patients with and without cirrhosis who had normal renal function based on serum creatinine and underwent non-contrast-enhanced SSFP imaging with spatially selective IR pulses were included. The renal cortical thickness, renal width, renal cortical width ratio, serum creatinine levels and estimated glomerular filtration rates (eGFRs) were compared between cirrhotic and non-cirrhotic groups.

Results: The mean renal cortical thickness was significantly lower in the cirrhotic group (3.6 ± 0.9 mm) than in the non-cirrhotic group (4.9 ± 0.8 mm; $p < 0.001$). The mean renal cortical width ratio was significantly lower in

the cirrhotic group (0.07 ± 0.02) than in the non-cirrhotic group (0.10 ± 0.02 ; $p < 0.001$). The mean serum creatinine and mean eGFR did not show significant differences between the two groups.

Conclusion: Measurement of renal cortical thickness by means of non-contrast-enhanced SSFP MRI with spatially selective IR pulses may help evaluate renal function accurately in patients with cirrhosis, in whom it may be overestimated by serum creatinine and eGFR.

Advances in knowledge: (1) The renal corticomedullary junction was clearly depicted by non-contrast-enhanced SSFP MRI with spatially selective IR pulses in all patients with and without cirrhosis. (2) The mean renal cortical thickness measured on the optimal SSFP image with spatially selective IR pulses was significantly lower in the cirrhotic group (3.6 ± 1.0 mm) than in the non-cirrhotic group (4.9 ± 0.8 mm) ($p < 0.001$), although the mean eGFR did not show a significant difference between the two groups.

INTRODUCTION

Serum creatinine measurement is the most commonly accepted method for estimating renal function in clinical practice. However, several problems exist with the current techniques for assessing renal function based on serum creatinine in patients with cirrhosis because these patients have underlying conditions that result in falsely low serum creatinine levels, even in the presence of moderate to severe renal impairment. Such underlying conditions include decreased creatinine production secondary to decreased hepatic creatine synthesis and increased tubular secretion of creatinine converted from creatine.^{1–5} As a result, patients with cirrhosis often have normal serum creatinine concentrations while true glomerular filtration rate (GFR) is actually considerably decreased. Currently, new urinary biomarkers for the assessment of renal failure in patients

with cirrhosis have not been developed.² Meanwhile, renal cortical volumes and cortical thicknesses have been found to correlate with renal function.^{6–13} It has been reported that non-contrast-enhanced steady-state free precession (SSFP) MRI with a spatially selective inversion recovery (IR) pulse can emphasize the difference in T_1 values between the renal cortex and the medulla by suppressing the background signal and the target tissue signal. Therefore, compared with conventional MRI sequences, this technique can improve the visualization of renal corticomedullary differentiation and facilitate the measurement of renal cortical thickness even in patients with renal dysfunction compared with conventional MRI sequences.^{6,7,14}

In clinical practice, we have sometimes encountered patients with cirrhosis with a thin renal cortex even though

their serum creatinine levels were almost normal, suggesting masked renal dysfunction in patients with cirrhosis. The aim of the present study was to compare the renal cortical thicknesses using non-contrast-enhanced SSFP MRI with spatially selective IR pulses between patients with and without cirrhosis with normal renal function based on serum creatinine and to discuss the clinical implications of measuring renal cortical thickness in patients with cirrhosis.

METHODS AND MATERIALS

Subjects

Institutional review board approval was obtained for the retrospective review of MRI data and clinical data. The need for informed consent was waived for this retrospective analysis. This study included 20 patients with cirrhosis (11 males, 9 females; mean age, 70 years; age range, 39–86 years) and 20 patients without cirrhosis (6 males, 14 females; mean age, 68 years; age range, 42–86 years), who had normal serum creatinine concentrations (males, $0.6\text{--}1.10\text{ mg dl}^{-1}$; females, $0.45\text{--}0.80\text{ mg dl}^{-1}$) and underwent abdominal non-contrast-enhanced SSFP imaging with spatially selective IR pulses between May 2011 and October 2012. The causes of cirrhosis were viral infection in 16 patients [hepatitis B ($n = 4$), hepatitis C ($n = 12$)], alcohol abuse in 2, autoimmune hepatitis in 1 and unknown aetiology in 1. Based on the Child-Pugh classification, 14 patients were Class A and 6 were Class B. The final diagnosis of cirrhosis was established by pathological examination ($n = 4$) or based on a combination of the patient's clinical, laboratory and radiological data ($n = 16$).

Imaging technique

MRI was performed in the standard supine position using a 1.5-T scanner (EXCELART Vantage™ Powered by Atlas; Toshiba Medical Systems, Tochigi, Japan), equipped with the Atlas SPEEDER™ body coil. Non-contrast-enhanced SSFP MRI with spatially selective IR pulses was performed as a part of our routine abdominal protocol. The imaging parameters of the

non-contrast-enhanced SSFP sequence with fat-suppression were: repetition time/echo time = $4.2/2.1\text{ ms}$, number of acquisitions = 1, flip angle = 90° , receiver bandwidth = 977 Hz/pixel , slice thickness = 7 mm , field of view = $400 \times 400\text{ mm}$, acquisition matrix = 256×256 and acquisition time = 4 s during a single breath-hold. Parallel imaging technique was applied in SSFP sequences with a speeder factor of 2 in the phase-encoding direction. First, a non-contrast-enhanced coronal SSFP image without applying spatially selective IR pulses was obtained at nearly the centre of both kidneys, and this image was used to determine the position for the placement of the spatially selective IR pulse to the kidney. The width of a spatially selective IR pulse was set at 130 mm to cover the entire kidney (Figure 1). After that, non-contrast-enhanced SSFP MR images of the kidney with spatially selective IR pulses and various inversion times (TIs) were obtained using identical imaging parameters during breath-holding in the coronal plane. 9 TIs ($700, 800, 900, 1000, 1100, 1200, 1300, 1400$ and 1500 ms) were applied to investigate the optimal TI for the best visualization of renal corticomedullary differentiation. Each of these 9 images was obtained in a separate breath-hold.

Data analysis

2 radiologists (10 and 7 years of clinical experience in abdominal MRI, respectively), who were blinded to all of the subjects' clinical information, placed operator-defined regions of interest (ROIs) within the cortex and medulla in both the left and right kidneys, collaboratively. Each ROI was a circle or oval. The size of each ROI was chosen to be as large as possible. For each kidney, one ROI was placed in the cortex and one ROI was placed in the medulla on the same coronal image. The ROIs were drawn in almost the same location for each image. The mean signal intensity (SI) of the right and left renal cortex and medulla in each subject were recorded. The corticomedullary contrast ratio was calculated from the mean SI values of the renal cortex (SI_{cortex}) and the renal medulla (SI_{medulla}) as $SI_{\text{cortex}}/SI_{\text{medulla}}$. The corticomedullary contrast ratios among nine SSFP

Figure 1. (a) On a scout steady-state free precession (SSFP) image, the range of a spatially selective inversion recovery (IR) pulse with a 130-mm width to place on both kidneys (parallel horizontal lines) is determined. (b) Coronal SSFP image with a spatially selective IR pulse obtained with optimal inversion time (1000 ms) in the same patient. The renal corticomedullary junction is clearly visualized.

images with spatially selective IR pulses obtained with different TI values (700–1500 ms) were compared to determine the optimal TI for the visualization of the renal corticomedullary junction. The highest corticomedullary contrast ratio among the nine SSFP images was fixed as the optimal TI. Then, the optimal SSFP image was determined as the SSFP image with a spatially selective IR pulse obtained with the optimal TI in each patient (Figure 1), and it was used for the measurement of renal cortical thickness and maximal transverse renal width. The renal cortical thickness was measured at the mid portion of both kidneys, and the averaged value of both kidneys was used for data analysis. The maximal transverse renal width and renal cortical thickness were measured to calculate the renal cortical width ratio (cortical thickness/maximal renal width) (Figure 2).¹⁵ The renal cortical thickness and renal cortical width ratio were compared between patients with and without cirrhosis. Additionally, patients' medical records were reviewed to compare serum creatinine levels and estimated GFRs (eGFRs) between patients with and without cirrhosis.

Statistical analysis

SPSS® v. 17.0 J (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) for Windows® was used for all statistical analyses. The renal cortical thickness, renal width, renal cortical width

Figure 2. Coronal steady-state free precession image with a spatially selective inversion recovery pulse obtained with optimal inversion time in a 65-year-old female without liver disease. a, Cortical thickness; b, maximal transverse renal width.

ratio, serum creatinine levels, eGFRs and age were compared between patients with and without cirrhosis using Mann–Whitney tests. *p*-values <0.05 were considered significant.

RESULTS

There was no significant difference in the mean age between the cirrhotic and non-cirrhotic groups (70.1 ± 10.6 years *vs* 67.6 ± 11.7 years, $p = 0.490$). The mean serum creatinine concentration was 0.68 ± 0.14 mg dl⁻¹ in the cirrhotic group and 0.65 ± 0.08 mg dl⁻¹ in the non-cirrhotic group; this difference was not significant ($p = 0.440$). Similarly, the mean eGFR was not significantly different between the cirrhotic and non-cirrhotic groups (78.3 ± 11.0 ml (min 1.73 m²)⁻¹ *vs* 79.0 ± 12.6 ml (min 1.73 m²)⁻¹) ($p = 0.808$).

The renal corticomedullary junction was clearly depicted by non-contrast-enhanced SSFP MRI with a spatially selective IR pulse using the optimal TI in all patients with and without cirrhosis. Regarding the measurement on the optimal SSFP image with spatially selective IR pulses, the mean renal cortical thickness was significantly lower in the cirrhotic group (3.6 ± 1.0 mm) than in the non-cirrhotic group (4.9 ± 0.8 mm) ($p < 0.001$) (Figure 3). The mean renal cortical width ratio was significantly lower in the cirrhotic group (0.07 ± 0.02) than in the non-cirrhotic group (0.10 ± 0.02) ($p < 0.001$). The mean renal width was not significantly different between the cirrhotic and the non-cirrhotic groups (50.1 ± 6.4 mm *vs* 51.7 ± 3.4 mm, $p = 0.176$).

DISCUSSION

Although there were no significant differences between the cirrhotic and non-cirrhotic groups in serum creatinine and eGFR, the cirrhotic group had a significantly lower renal cortical thickness and renal cortical width ratio. This contradictory result may be due to overestimation of renal function by creatinine-based methods in patients with cirrhosis. Previous studies showed that patients with cirrhosis had significantly lower measured creatinine clearances than healthy volunteers despite having identical serum creatinine values¹⁶ and that the sensitivity of the serum creatinine level in detecting renal impairment (inulin clearance <80 ml min⁻¹) was only 18.5% in patients with cirrhosis.¹⁷ It has been shown that in patients with cirrhosis, creatinine is produced at approximately one-half the rate of that produced in patients with normal hepatic function.^{5,18} Therefore, decreased creatinine production may contribute to a falsely low serum creatinine level in the setting of decreased true GFR, thereby rendering creatinine-based methods for estimating renal function unreliable in patients with cirrhosis.³ As with a number of these previous studies, the present results suggest that the renal function of patients with cirrhosis may be overestimated by serum creatinine and eGFR. It should be assumed that true GFR may be lower (by >50%) than apparent renal function based on either measured or calculated creatinine clearance in patients with cirrhosis.³

By contrast, renal cortical thickness was significantly thinner in the cirrhotic group than in the non-cirrhotic group in the setting of equivalent serum creatinine and eGFR values in the current study. This fact suggested that measurement of renal cortical thickness may be a potential alternative for the

Figure 3. Coronal steady-state free precession image with a spatially selective inversion recovery pulse obtained with optimal inversion time in (a) a 62-year-old male with cirrhosis and in (b) a 64-year-old female without liver disease. Renal cortical thickness is thinner in the patient with cirrhosis than in the patient without cirrhosis (2.4 vs 5.3 mm). The serum creatinine level and estimated glomerular filtration rate are 0.72 mg dl^{-1} and $85 \text{ ml (min} \cdot 1.73 \text{ m}^2)^{-1}$, respectively, for the patient with cirrhosis, and 0.63 mg dl^{-1} and $72 \text{ ml (min} \cdot 1.73 \text{ m}^2)^{-1}$, respectively, for the patient without cirrhosis.

assessment of renal function in patients with cirrhosis. It has been reported that decreased renal cortical thickness would be induced by atrophy and fibrosis of nephrons predominantly located in the renal cortex in patients with renal dysfunction.¹⁹ Using CT, Zhou et al²⁰ reported that the renal cortical thickness/renal parenchyma ratio was significantly lower in patients with cirrhosis than in patients without cirrhosis. A previous study using ultrasound also showed that renal cortical thickness was considered a surrogate marker of renal function because renal cortical thickness decreased with decreasing renal function in patients with chronic kidney diseases.⁹ However, renal cortical thickness was sometimes difficult to measure on ultrasound because the renal corticomedullary junction can be difficult to identify in patients with renal dysfunction in whom corticomedullary differentiation is poor. Meanwhile, non-contrast-enhanced SSFP MRI with spatially selective IR pulses can visualize the renal corticomedullary junction to measure renal cortical thickness even in patients with renal insufficiency.¹⁴ Therefore, measurement of renal cortical thickness by the non-contrast-enhanced SSFP MRI with spatially selective IR pulses used in the present study may contribute to simple, accurate and non-invasive assessment of the renal function of patients with cirrhosis without depending on serum creatinine concentrations and eGFR, although this assumption should be validated using a larger patient population. In addition, future areas of investigation may include determination of a threshold cortical thickness to distinguish normal from impaired renal function or development of a predictive range of renal function given a particular cortical thickness.

Accurate assessment of renal function in patients with cirrhosis is vital because any significant insult to the kidneys, either acute or sustained, may induce the onset of hepatorenal syndrome,

with its high-associated mortality rate.²¹ Therefore, measurement of renal cortical thickness by means of non-contrast-enhanced SSFP MRI with spatially selective IR pulses may contribute to choosing the therapeutic and diagnostic interventions and appropriate dosing of many medications and to substantially decreasing morbidity and mortality.

The present study had a number of limitations. First, it was a single-centre study with a small number of patients; it will be necessary to investigate a greater number of patients in the future. Second, accurate GFR determination using inulin clearance or radioactive tracer was not conducted in the present study. In particular, inulin clearance currently represents the gold standard for estimation of GFR. However, these procedures are technically difficult, expensive and not widely available and, thus, are less than ideal for routine clinical care.^{3,10} In a future study, the detailed correlation between renal cortical thickness and true GFR will need to be determined in patients with cirrhosis. Third, the subjects of the present study were limited to patients with normal serum creatinine levels. Investigation of patients with even more greatly reduced renal function will be also necessary.

In conclusion, measurement of renal cortical thickness by means of non-contrast-enhanced SSFP MRI with spatially selective IR pulses may facilitate accurate evaluation of renal function, which may be overestimated by serum creatinine and eGFR in patients with cirrhosis. In evaluating patients with cirrhosis, it is important to remember that, although renal function may seem normal based on commonly used creatinine-based methods, in reality, it may be severely impaired when decreased renal cortical thickness is observed on non-contrast-enhanced SSFP MRI with spatially selective IR pulses.

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