Research paper

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The pattern of renal artery Doppler indices in patients with sickle cell disease

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sickle cell disease; pulsatility index (PI); renal artery Doppler; resistive index (RI)

Abstract

Aim: To evaluate the pattern of renal artery Doppler indices in patients with sickle cell disease who do not have laboratory evidence of renal impairment. **Material and methods:** A case-control study was carried out after enrolling 50 patients with sickle cell disease (HbSS phenotype) (sickle cell disease group) and 50 control subjects (control group). All the participants underwent ultrasound and color Doppler examination, and the pulsatility index and resistive index values of the main renal artery, segmental artery, and interlobar artery in both kidneys were recorded and compared. **Results:** The Doppler measurements of the main renal artery, segmental artery, and interlobar artery were compared between the control and sickle cell disease groups. It was found that both pulsatility index and resistive index were significantly higher in the sickle cell disease group, as compared to the control group, for the main renal artery, segmental artery, and interlobar artery (p <0.0001, p <0.0001, and p <0.0001, respectively). The optimal cut-off points for mean pulsatility index and resistive index, as measured by the Youden index, were found to be >1.08 (72% sensitivity and 88% specificity) and >0.635 (66% sensitivity and 98% specificity), respectively. **Conclusions:** Resistive index and pulsatility index values in renal Doppler sonography can serve as early radiologic predictors of renal vascular changes in sickle cell disease patients who do not have laboratory evidence of renal impairment.

Introduction

Sickle cell disease (SCD) is an autosomal recessive disorder caused by an alteration in the molecular structure of hemoglobin: a single-pair DNA mutation encoding the β-globin molecules results in the substitution of valine for glutamic acid at the sixth position of the β-globin chain[1]. Sickle cell disease is a multisystem condition that affects practically all the body tissues, but in its later stages, it can also cause renal impairment and eventually sickle nephropathy[2,3]. Given the high incidence of the disorder in some populations, renal vascular alterations must be identified early before chronic vasculopathy results in permanent organ damage[4].

According to earlier research, the resistive index (RI), which assesses the resistance of renal arterial blood flow to the kidney, and the pulsatility index (PI), which reflects the variability of blood velocity in a vessel, can be used to predict renal vascular abnormalities in sickle cell disease at an early stage when renal changes are still treatable[5]. Color Doppler ultrasonography of the main renal arteries (extrarenal Doppler ultrasound) is generally used to identify pathologies of the major vascular structures, such as renal artery stenosis in the native and transplanted kidney or intrarenal arteriovenous fistula[6–8]. In contrast, color Doppler ultrasonography of the segmental and interlobar arteries (intrarenal Doppler ultrasound) is more useful in evaluating pathologies involving the renal parenchyma. Changes in intrarenal arterial waveforms are associated with several intrinsic renal disorders, such as renal transplant rejection, acute tubular necrosis, hemolytic-uremic syndrome, diabetic nephropathy, lupus nephritis, and progressive systemic sclerosis[9–11].

This study aimed to determine whether the renal PI and RI would be helpful as early radiologic predictors of renal impairment in sickle cell disease patients with otherwise normal standard laboratory tests.

Materials and methods

The study was approved by our institution's Institutional Ethics Committee. Written informed consent was taken from the participants or parents/guardians.

A case-control study was carried out after enrolling 50 patients with sickle cell disease (HbSS phenotype) (SCD group) and 50 control

subjects (control group). The inclusion criteria were as follows: any patients seven years and older diagnosed with sickle cell disease (HbSS phenotype). The exclusion criteria were: (1) participants with elevated serum creatinine levels (>1.5 mg/dl); (2) acute illness or history of blood transfusion within six months; (3) known hypertensives and diabetics; (4) tachycardia at the time of sonography; (5) blood pressure greater than 140/90 mm Hg on the day of sonography; (6) congenital renal anomalies; (7) active urinary tract infections; and (8) participants not cooperating for the ultrasonography examination. The control subjects were age and sex-matched with the patient group (within one year), and had no laboratory, clinical, or radiologic evidence of renal disease. A general physical examination was performed for all participants, and blood tests including blood urea, serum creatinine, and routine urinary laboratory pathologic tests were ordered.

An ultrasound machine (GE Voluson S8) was used for the examination, with grayscale, color, and Doppler imaging done using a 2–5 MHz curvilinear transducer. A lateral or posterolateral approach was used to obtain optimal renal images and appropriate Doppler tracing. Ultrasound gel was applied to the area of interest to transmit the ultrasound waves better. Both kidneys were examined, and echogenicity was assessed first to establish its normality compared to the liver and spleen. The sagittal plane was used to measure the renal length with the patient in either the supine or prone position. The maximum length of each kidney was measured from the highest point of the upper pole to the lowest point of the lower pole. The cortical thickness was measured from the base of the medullary pyramid to the outer cortex.

Then, color imaging was obtained to evaluate the blood flow in the kidneys. The main renal, segmental, and interlobar arteries were evaluated, and Doppler parameters, including PI and RI, were recorded for each kidney. In the case of interlobar arteries, three readings were taken from the upper pole, mid-pole, and lower pole regions, and their mean was taken for each kidney. Doppler tracing was obtained at an insonation angle of 0° to 60° and using a Doppler gate of 2–4 mm.

Statistical analysis was done using the Statistical Package for Social Sciences (SPSS) version 21.0. The Kolmogorov-Smirnov test was performed on continuous data to determine normal distributions. Independent sample T-test was used to detect the mean difference between the patient and control groups. A p-value <0.05 was considered to be significant. The Receiver Operating Characteristic (ROC) curve was plotted using the mean PI and RI taken from the main renal artery, segmental artery, and interlobar artery in the control and SCD groups. Using the Youden index, optimal cut-off points for mean PI and RI were calculated.

Results

The mean age of the patients was 22.5 ± 6.42 years (range 14–38 years). It was observed that the mean renal length and cortical thickness (Tab. 1) of both kidneys were greater in SCD patients as compared to controls, which was highly significant (p <0.0001) for both the right and left sides.

A comparison of Doppler parameters of the main renal, segmental, and interlobar arteries (Fig. 1, Fig. 2, Fig. 3) between the control and SCD groups (Tab. 2) found that both PI and RI were significantly elevated for the main renal, segmental, and interlobar arteries (p <0.0001, p <0.0001, and p <0.0001, respectively) in the SCD group compared to the control group.

The ROC curve was plotted using the mean PI and RI taken from the main renal artery, segmental artery, and interlobar artery in the control and SCD groups. Using the Youden index, the optimal cut-off points for mean PI and RI were observed to be >1.08 (72% sensitivity and 88% specificity) (Fig. 4) and >0.635 (66% sensitivity and 98% specificity) (Fig. 5), respectively.

Discussion

Initially, renal Doppler sonography was used for renovascular disease screening in the middle of the 1980s[12]. Numerous studies showing the possibility of Doppler sonographic assessment of various renal disorders have now been reported. It is widely known that renal Doppler sonography can identify renal artery stenosis in hypertensive individuals[12]. Sickle cell disease is a progressive vasculopathy that can damage any organ in the body, including the kidneys, and result in sickle cell nephropathy. Since it is impossible to identify a subset of patients who are predisposed to developing clinical renal disease despite rigorous investigation, Doppler evaluation of the renal arteries in SCD patients with normal renal functions is crucial.

Tab. 1. Comparison of renal length and cortical thickness for both kidneys in the control and SCD groups

	Control		SCD		*p*-value	
Parameter	**Right**	**Left**	**Right**	**Left**	**Right**	**Left**
Renal length (cm)	8.97 ± 0.85	9.23 ± 0.7	9.79 ± 1.11	10.08 ± 1.23	<0.0001	<0.0001
Cortical thickness (cm)	0.82 ± 0.15	0.88 ± 0.11	0.91 ± 0.12	0.93 ± 0.12	<0.0001	0.0100

Tab. 2. Comparison of Doppler parameters of the main renal, segmental, and interlobar arteries between the control and SCD groups

	Control		SCD		*p*-value	
Parameter	**Right**	**Left**	**Right**	**Left**	**Right**	**Left**
Main renal artery PI	1.02 ± 0.16	1.05 ± 0.18	1.15 ± 0.22	1.24 ± 0.31	<0.0001	<0.0001
Main renal artery RI	0.61 ± 0.07	0.62 ± 0.07	0.66 ± 0.07	0.67 ± 0.09	<0.0001	<0.0001
Segmental artery PI	1 ± 0.17	0.93 ± 0.17	1.14 ± 0.21	1.15 ± 0.25	<0.0001	<0.0001
Segmental artery RI	0.6 ± 0.06	0.57 ± 0.06	0.66 ± 0.06	0.67 ± 0.1	<0.0001	<0.0001
Interlobar artery PI	0.92 ± 0.15	0.91 ± 0.16	1.13 ± 0.23	1.16 ± 0.22	<0.0001	<0.0001
Interlobar artery RI	0.57 ± 0.05	0.56 ± 0.07	0.64 ± 0.07	0.64 ± 0.07	<0.0001	<0.0001

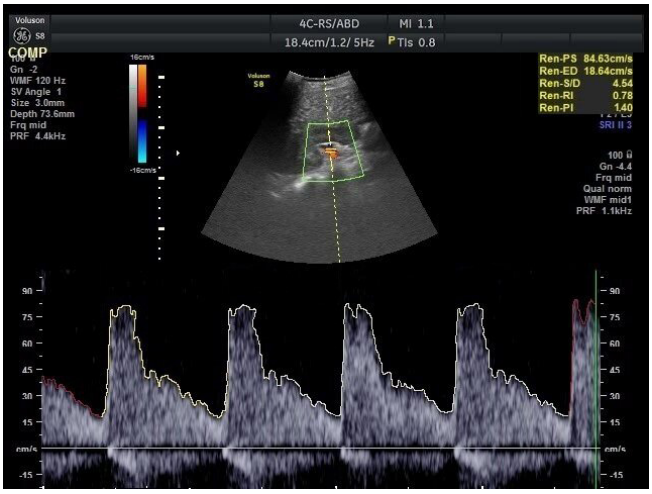

Fig. 1. *Renal Doppler ultrasonography demonstrates high-impedance flow in the right main renal artery of a 26-year-old female patient, as indicated by high PI and RI values (1.40 and 0.78, respectively)*

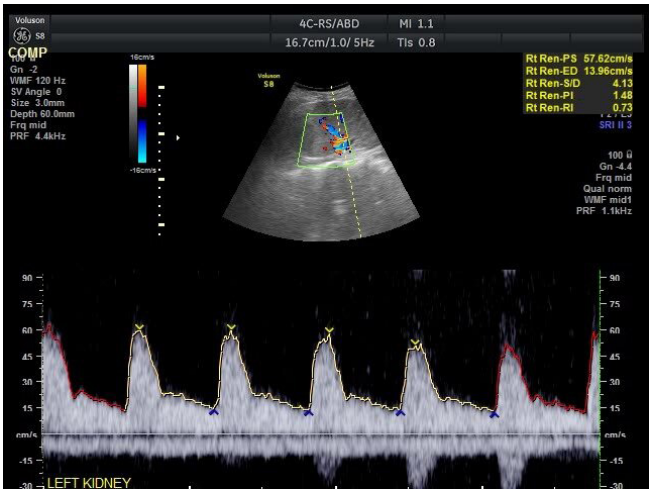

Fig. 2. *Renal Doppler ultrasonography demonstrates high-impedance flow in the left segmental artery of a 15-year-old male patient, as indicated by high PI and RI values (1.48 and 0.73, respectively)*

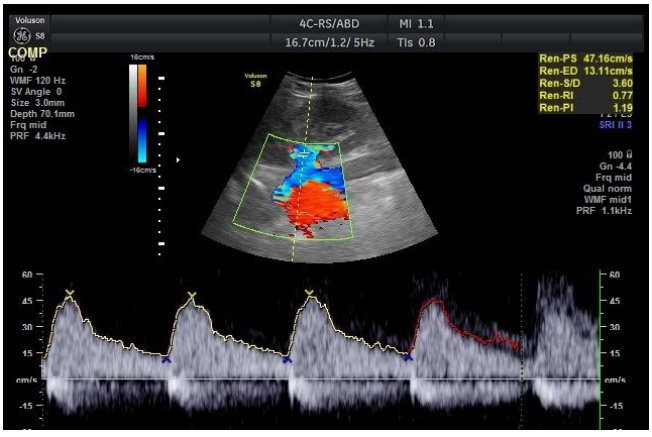

Fig. 3. *Renal Doppler ultrasonography demonstrates high-impedance flow in the right interlobar artery of a 17-year-old male patient, as indicated by high PI and RI values (1.19 and 0.77, respectively)*

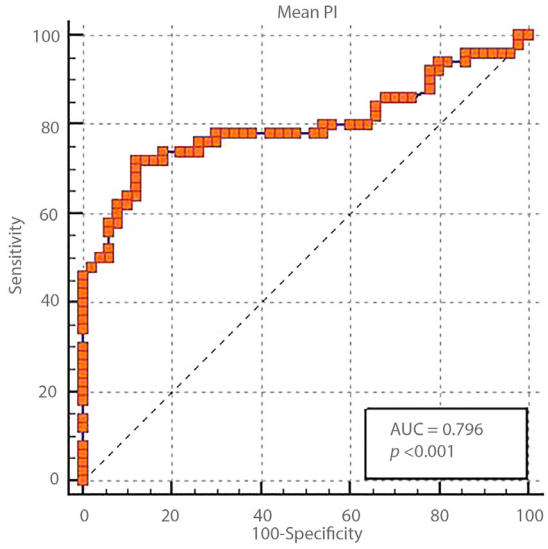

Fig. 4. *Receiver operating characteristic (ROC) curve for mean PI*

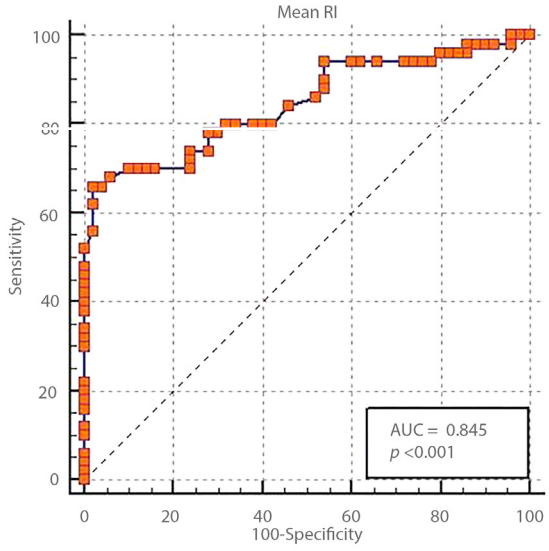

Fig. 5. *Receiver operating characteristic (ROC) curve for mean RI*

Our study observed that the mean renal length and cortical thickness in both kidneys were greater in SCD patients than in controls. The exact mechanism of renal enlargement is unknown. Vascular dilatation, artery engorgement, glomerular hypertrophy, elevated blood volume, and interstitial edema have all been implicated in the enlargement of sickle cell kidneys[13]. Increased cortical thickness in sickle cell disease may be attributed to glomerular hypertrophy and increased blood flow commonly seen in patients with sickle cell disease[13]. However, our study population consisted of individuals with variable BMI, which could be a contributing factor to changes in mean renal length. Consequently, further studies on patients with similar BMI could be done to corroborate the results of our study.

Compared to the control group, our study found that patients with SCD had significantly higher PI and RI in the main renal artery, segmental artery, and interlobar artery. This phenomenon might be

brought on by sickle-affected kidneys having higher renal vascular tone due to different vascular occlusive mechanisms. These processes include frank vasospasm, thrombosis, altered vascular reactivity, and vascular intimal hyperplasia[14].

In our study, the optimal cut-off points for mean PI and RI were observed to be >1.08 (72% sensitivity and 88% specificity) and >0.635 (66% sensitivity and 98% specificity), respectively. The cut-offs of 0.7–1.4 for PI and 0.5–0.7 for RI are used for the normal population[15]. However, no such values had been established in patients with SCD. Therefore, our study suggests using cut-offs for PI and RI of >1.08 and >0.635, respectively, in SCD patients for early identification of renal vascular changes.

Conclusions

Our study shows that RI and PI values can be early indicators of renal vascular alterations in renal Doppler sonography in SCD patients who otherwise have no laboratory evidence of renal impairment. Renal Doppler sonography can thus direct clinicians towards more rigorous laboratory value monitoring and the initiation of appropriate treatment at an early stage when the effects of the disease are still reversible.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Author contributions

Original concept of study: VP. Writing of manuscript: NC. Analysis and interpretation of data: VP, NC. Final approval of manuscript: VP. Collection, recording and/or compilation of data: NC. Critical review of manuscript: VP.

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