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Diurnal variation of renal resistive index over 24-hour period in hypertensive patients and healthy controls

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Abstract

Purpose: There are no data in the literature to our knowledge related to changes in renal resistive index (RRI) values over 24-h period and the importance of detecting these changes in patients who have hypertension (HT). In this study, we aimed to investigate the variation of RRI values over 24-h period and its usability in hypertensive patients.
Methods: A total of 118 subjects (80 with HT and 38 healthy controls) were included in the study. Morning, midday, evening, and midnight RRI, renal pulsatility index, and accelerated time were measured by Doppler ultrasonography (US). B-mode US and elastograpic assessment were performed only in the morning.
Results: Temporal RRI varied significantly ($p < 0.001$). The highest and lowest levels were found in the morning and evening, respectively. All temporal RRI levels were significantly higher in patients with HT (both $p < 0.001$). The absolute and relative increases in RRI (ΔRRI) levels were similar in two groups. All temporal RRI measurements positively correlated with the patient age, pulse pressure, renal cortical thickness, and cortical stiffness. However, absolute-ΔRRI and relative-ΔRRI positively correlated with the age. Absolute-ΔRRI positively correlated with the pulse pressure and cortical stiffness, and no correlation was observed between relative-ΔRRI and these variables. Of the four temporal measurements, morning RRI were found to be independently associated with cortical stiffness ($p < 0.001$).
Conclusions: RRI measurements varied over 24-h period in patients with HT and/or healthy controls. Morning RRI was significantly higher than other day time, and it is also related to renal cortical stiffness.

Key words: Hypertension—Renal resistive index—Variation

In hypertensive patients, conventional renal ultrasonography (US) can be used to detect kidney size, cortical thickness, and parenchymal echogenicity and can reveal indicators of chronic morphologic changes that happen. However, all these changes are not quantitative and clear. Atrophic changes in patients with stages 3–4 chronic kidney disease (CKD) can be revealed by conventional renal US, but in patients with stages 1–2 CKD atrophic changes cannot be fully demonstrated. For this reason, conventional renal US is not adequate in determining the progression and the stages of hypertension (HT)-related early-stage CKD [1]. Renal Doppler US is a noninvasive, stable, and cost-effective US study that has been used in past 10 years to evaluate renal function, renal vascular disease and several types of intrinsic renal disorders [1–4]. The greatest advantage of renal resistive index (RRI) measurement is that it can reveal renal vascular and parenchymal abnormalities before renal morphological changes occurred. Also, RRI obtained by renal Doppler US has been shown to be a simple and practical technique that can be used in the detection of chronic morphological changes in renal transplanted patients, in renal tumors, in CKD due to HT, and in CKD staging [3–5]. RRI value was obtained by renal Doppler US of intrarenal artery (segmental or interlobar) and was calculated according to the formula (peak systolic velocity (PSV) − end-diastolic velocity (EDV))/PSV. Higher RRI was independently associated with

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target organ damage in hypertensive patients [6–8]. The renal Doppler US examination is available on every US device, and it can be done by every radiology specialist.

However, RRI is the most frequently used and acknowledged renal Doppler US parameter, but it is affected by many demographic, clinic, and systemic parameters [1, 9–14]. Studies have shown that many clinical and demographic parameters are associated with increased RRI. These parameters include age, female gender, increased body mass index (BMI), presence of diabetes mellitus (DM) and HT, use of beta-blocker as a medication and hypoxia, increased heart rate, increased systolic and diastolic blood pressure (SBP and DBP), and pulse pressure from clinical parameters [11, 12, 15–19]. Except demographic data, all other parameters should change during the day. For this reason, we think that the RRI may change at different times of the day. There are no data in the literature to our knowledge related to changes in RRI values over 24-h period and the importance of detecting these changes in patients who have HT.

In this study, we aimed to investigate the variation of RRI values at 6-h interval over 24-h period and its usability in hypertensive patients.

Methods

Study population

We enrolled 80 patients with HT (24 males, 56 females with average age 57.4 ± 18.6) and 38 healthy controls (13 males, 25 females with average age 58.5 ± 19.4). All of the patients who were included in the study were diagnosed with HT according to ESC 2013 guideline [20]. Follow-up and treatment of hypertensive patients were also regulated by ESC 2013 guidelines. Age and gender of the patients included in the control group were similar to the patient group. The control group was healthy individuals who did not have cardiovascular risk factors, who did not use any medication, and who were proven not to have HT by 24-h blood pressure monitoring. We excluded patients with HT who have reduced GFR $<$ 60 mL/min/1.73 m^2 or $>$ 30 mg/L proteinuria. Patients with coronary artery disease or history of myocardial infarction (MI), significant cardiac valvular disease, respiratory or heart failure, active thyroid disease, chronic liver disease, hematological disorders, renal artery stenosis, history of nephrectomy, secondary HT, history of malignancy, bleeding diathesis, active infection, hypertensive urgency, or emergency and pregnancy are excluded. This study followed the recommendations of ethical principles published in The Declaration of Helsinki developed by World Medical Association and approved by Local Ethical Committee. Informed consents were explained in details to patients, and patients were enrolled only after obtaining written consents. Patients and healthy individuals included in the study were followed up in the internal medicine clinic for 24 h. Risk factors were obtained after the detailed physical examinations. Demographic data included age, gender, presence of HT, DM, hyperlipidemia (HL), tobacco use were noted. Height and weight were measured, and BMI was calculated. SBP and DBP were measured, and pulse pressure was calculated. White blood cell counts, hemoglobin, fasting plasma glucose, HbA1c, blood urea nitrogen (BUN), and creatinine were measured using an automated analyzer using appropriate commercial kits.

Renal ultrasonography

We obtained renal US by using high-resolution US machine (Philips EPIQ 7) and 5-1 MHz convex probe (Philips Health Care, Bothell, WA, USA). Images were obtained minimum of 5 h of fasting and at least 20 min of rest. Images were initially obtained with grayscale B-mode US in the early morning (06.00 a.m.). Kidney size, cortical thickness, and parenchyma echogenicity were assessed in gray scale. Kidney length was measured between upper and lower poles of kidney. The distance between renal hilum and renal capsule was measured in the middle pole in coronal plane. Cortical thickness was measured between pyramid base of renal medulla in the middle and renal capsule. Renal cortical echogenicity was scored from 0 to 2 by comparing renal echogenicity to the adjacent liver echogenicity; Grade 0: the renal echogenicity was less than that of the liver; Grade 1: the renal echogenicity equaled that of the liver; Grade 2: the renal echogenicity was greater than that of the liver.

PSV, EDV, and acceleration time (AT) in intrarenal artery (segmental or interlobar) were measured when Doppler angle was 30°–60° in right and left kidneys every 6-h interval: morning (06.00 a.m.), midday (12.00 a.m.), evening (6.00 p.m.), and midnight (12.00 p.m.) (Figs. 1, 2). For RRI measurements, repeated measurements were taken from different regions of the intrarenal arteries with renal Doppler US and at least five clear or acceptable waveforms were obtained (Figs. 1, 2). One of the obtained spectral waveforms was manually selected. Through the selected waveform, PSV and EDV measurements and RRI value were obtained automatically with PSV − EDV/PSV formula. Renal pulsatility index (RPI) is calculated on spectral waveform based on PSV − EDV/mean flow rate formula. AT is the measured time between the onset of increased systole and first peak point. All measurements were taken three times from right and left kidneys. Averages of six measurements were taken. Morning, midday, evening, and midnight mean values of RRI and only morning RPI and AT values from right and left kidneys were recorded. Images were initially obtained with grayscale B-mode ultrasound, and then, quantitative Doppler parameters were obtained. Absolute change in RRI (absolute-ΔRRI) over 6 h was calculated as the RRI value in the morning

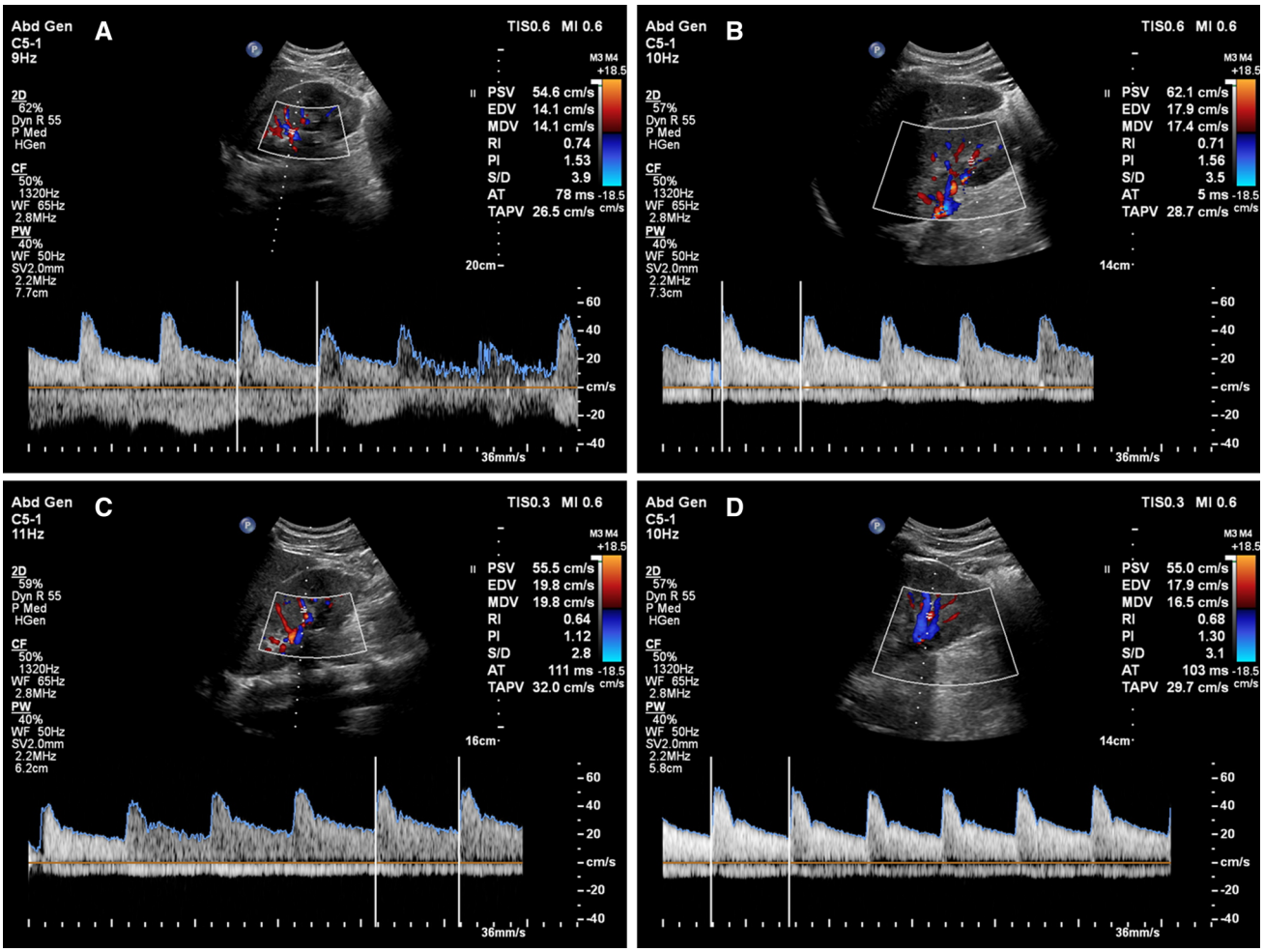

Fig. 1. In healthy control, renal resistive index (RRI) is measured by Doppler sonography in an right kidney intrarenal or intralobar artery and is the difference between the peak systolic (PSV) and end-diastolic (EDV) blood velocities divided by the peak systolic velocity (PSV) **A** highest RRI value was obtained in the morning (06.00 a.m.) as 0.74, **B** RRI value was 0.71 at midday (12.00 a.m.), **C** lowest RRI value was obtained at evening (18.00 p.m.) as 0.64, and **D** RRI value was 0.68 in midnight (24.00 p.m.).

minus the RRI value at the evening. Relative change in RRI (relative-ΔRRI) over 6 h was calculated as the absolute-ΔRRI divided by the RRI value at the evening.

Shear wave elastography evaluation was obtained with 5-1 MHz convex abdomen probe by using elastography point quantification (ElastPQ) technique. All renal cortical stiffness measurements were taken in early morning as explained previously. We obtained six valid measurements for each kidney and calculated the mean value. If reliability of measurement is low, the result will be seen with 0.00 kPa. Result is given as kPa value. Subjects were evaluated by a two well-experienced radiology specialists for B-mode, Doppler, and elastography examinations. Specialists had more than 12 years of experience in renal Doppler US studies and at least 500 renal Doppler US procedures in a year. During the RRI measurement, both radiology specialists were unaware of the clinical, laboratory, and medical treatment of individuals who were included in the study. Radiology specialists have not been involved in patient follow-up. Total time for all four US examinations was approximately 40–60 min.

Statistical analysis

All analyses were made by using SPSS 22.0 (Chicago, IL, USA) statistical software. Continuous variables in group data were referred as mean ± standard deviation. Categorical variables were referred as number and percentiles. Continuous variables that showed normal distribution were compared using the Student *t* test, whereas the Mann–Whitney *U* test is used to compare differences between two independent groups when the dependent variable is either ordinal or continuous, but not normally distributed. The Chi-square (χ^2) test was used to compare categorical variables. For multiple comparisons of

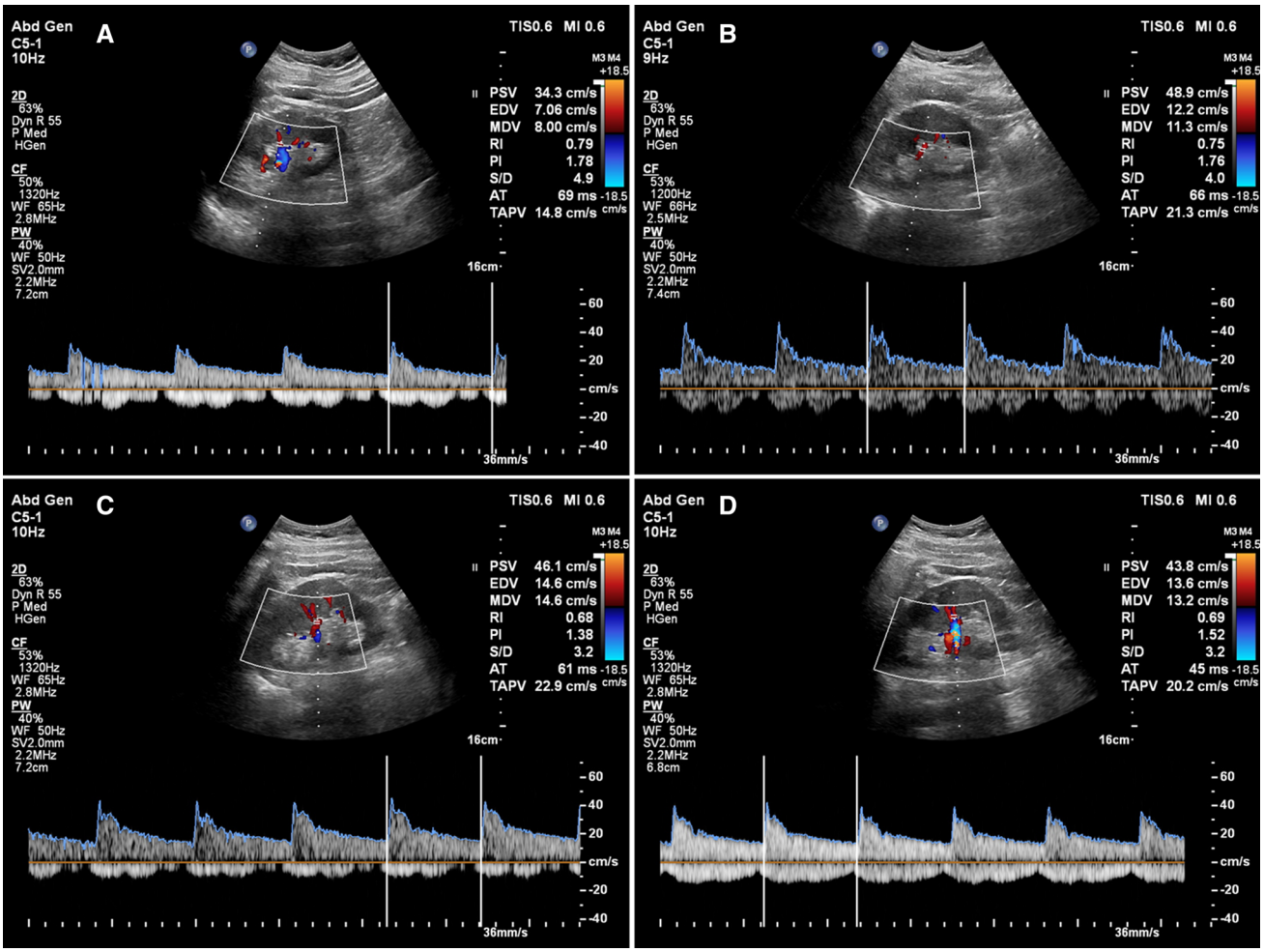

Fig. 2. In hypertensive patient, renal resistive index (RRI) is measured by Doppler sonography in an right kidney intrarenal or intralobar artery and is the difference between the peak systolic (PSV) and end-diastolic (EDV) blood velocities divided by the peak systolic velocity (PSV) **A** highest RRI value was obtained in the morning (06.00 a.m.) as 0.79, **B** RRI value was 0.75 at midday (12.00 a.m.), **C** lowest RRI value was obtained at evening (18.00 p.m.) as 0.68, and **D** RRI value was 0.69 in midnight (24.00 p.m.).

groups' proportions, we used Bonferroni corrected z test. For the comparison of RRI value that was obtained at different times of the day, repeated-measures analysis of variance was applied. Pearson's correlation and Spearman's correlation were used to examine the relationship between continuous variables. Significant variables in univariate analysis at a $p < 0.1$ level were entered in linear regression analysis. Linear regression analysis was performed with parameters significantly related to all RRI. It was determined as statistically significant if $p < 0.05$. Data are expressed as mean ± SD for continuous variables and percentage for categorical variables.

Results

All demographic parameters in two patient groups with HT and healthy controls were compared. Patients with HT had significantly elevated SBP, DBP, pulse pressure, heart rate, BMI, blood glucose, HbA1c, and BUN levels and low hemoglobin levels compared to healthy controls (Table 1). Presence of DM and HL was significantly higher in hypertensive patients (Table 1). It was determined that 55% of the patients with HT who were included in the study reached the blood pressure target. In our study, in patients with HT, 31 of them (38.8%) were using angiotensin converting enzyme inhibitors, 35 of them (43.6%) were using angiotensin receptor blockers, 18 of them (22.5%) were using beta-blockers, 22 of them (27.5%) were using calcium channel blockers, and 26 of them (32.5%) were using diuretic, when renal B-mode, Doppler US, and elastography findings were compared between patients with HT and healthy controls. Patients with HT had increased cortical echogenicity in B-mode renal US compared the healthy controls (Table 2). Cortical stiffness level obtained with renal elastography technique was significantly higher in hypertensive pa-

Table 1. Clinical and laboratory parameters in patients with hypertension and healthy controls

	Patients with HT $n = 80$	Healthy controls $n = 38$	p
Age (years)	57.4 ± 18.6	58.5 ± 19.4	0.771
Gender (male/female)	24/56	13/25	0.675
Systolic BP (mmHg)	153.1 ± 15.2	115.3 ± 10.0	< 0.001
Diastolic BP (mmHg)	91.2 ± 10.5	79.7 ± 7.9	< 0.001
Pulse pressure (mmHg)	56.9 ± 12.8	35.5 ± 7.8	< 0.001
Heart rate (beat/min)	82.6 ± 11.6	71.2 ± 10.1	< 0.001
BMI (kg/m^2)	27.5 ± 4.2	24.6 ± 3.13	< 0.001
Smoking, n (%)	8 (10)	4 (11)	0.988
Diabetes mellitus, n (%)	12 (15)	0 (0)	0.007
Hyperlipidemia, n (%)	24 (30)	0 (0)	< 0.001
Glucose (mg/dL)	120.2 ± 63.5	87.6 ± 5.7	< 0.001
HbA1c (%)	5.7 ± 1.1	5.1 ± 0.6	< 0.001
BUN (mg/dL)	33.2 ± 11.8	28.2 ± 9.1	0.012
Creatinine (mg/dL)	0.76 ± 0.15	0.71 ± 0.14	0.071
WBC count ($1000/mm^3$)	8.7 ± 2.6	8.5 ± 2.0	0.779
Hemoglobin (g/dL)	12.0 ± 1.31	12.9 ± 1.2	0.003

BUN, blood urea nitrogen; BMI, body mass index; BP, blood pressure; HT, hypertension; WBC, white blood cell

Table 2. Ultrasonographic parameters in patients with hypertension and healthy controls

	Patients with HT $n = 80$	Healthy controls $n = 38$	p
Morning RRI	0.77 ± 0.08	0.69 ± 0.03	< 0.001
Morning RPI	2.43 ± 1.20	1.90 ± 1.01	0.014
Morning renal AT (m/s)	107.4 ± 30.5	135.9 ± 29.1	< 0.001
Midday RRI	0.72 ± 0.07	0.64 ± 0.03	< 0.001
Evening RRI	0.71 ± 0.06	0.62 ± 0.02	< 0.001
Midnight RRI	0.73 ± 0.07	0.64 ± 0.02	< 0.001
Absolute-ΔRRI	0.07 ± 0.04	0.07 ± 0.02	0.906
Relative-ΔRRI	10.0 ± 5.7	10.9 ± 3.1	0.290
RRI over 24 h ≤ 0.70, n (%)	17 (21)	26 (68)	< 0.05
RRI over 24 h ≤ 0.70 or > 0.70, n (%)	28 (35)	12 (32)	> 0.05
RRI over 24 h > 0.70, n (%)	35 (44)	0 (0)	< 0.05
Kidney length (cm)	98.6 ± 12.7	94.9 ± 13.1	0.204
Kidney width (cm)	48.3 ± 7.9	45.9 ± 7.7	0.106
Cortical thickness (mm)	12.1 ± 1.9	11.6 ± 2.4	0.462
Cortical echogenicity Grade 0–1–2, n	64–12–4	35–3–0	0.024
Cortical stiffness (kPa)	5.80 ± 1.32	3.92 ± 1.20	< 0.001

HT, hypertension; RRI, renal resistive index; RPI, renal pulsatility index; AT, acceleration time

tients (Table 2). Morning, midday, evening, and midnight RRI, morning RPI, and morning AT values determined with renal Doppler US during the day were found to be significantly higher in hypertensive patients (Table 2).

The RRI measurements differed greatly throughout the day: The most significant difference was between the morning and evening measurement ($p < 0.001$, Fig. 3). In two groups, maximum and minimum RRI measurements were taken in the morning and in the evening, respectively. According to this finding, for calculating the absolute-ΔRRI and relative-ΔRRI, the difference between the morning and midday RRI was used. Except for eight patients in the HT group and four in the healthy control group, morning measurements were higher than other measurements. All four temporal mean RRI measurements were significantly higher in the HT group, whereas no significant difference was observed for the absolute-ΔRRI and relative-ΔRRI in two groups (Table 2). Four different RRI values were obtained at different times of the day in hypertensive patients and controls. These were grouped into the following categories: (1) all RRI were normal ≤ 0.70, (2) RRI were > 0.70 and ≤ 0.70, and (3) all RRI were > 0.70. In the hypertensive patient group, there were less of the daytime RRI values < 0.70 compared to the control group (21% vs. 68% and $p < 0.05$), RRI values > 0.70 or ≤ 0.70 at different times during the day were similar between two groups (35% vs. 32% and $p > 0.05$), and the all RRI values > 0.70 were higher in hypertensive patient group (44% vs. 0% and $p < 0.05$, Table 2).

Table 3 shows the correlation of RRI measurements during the day with the clinical, laboratory, B-mode US, and elastography parameters. All temporal RRI measurements positively correlated with the patient age, BMI, pulse pressure, renal cortical thickness, and cortical

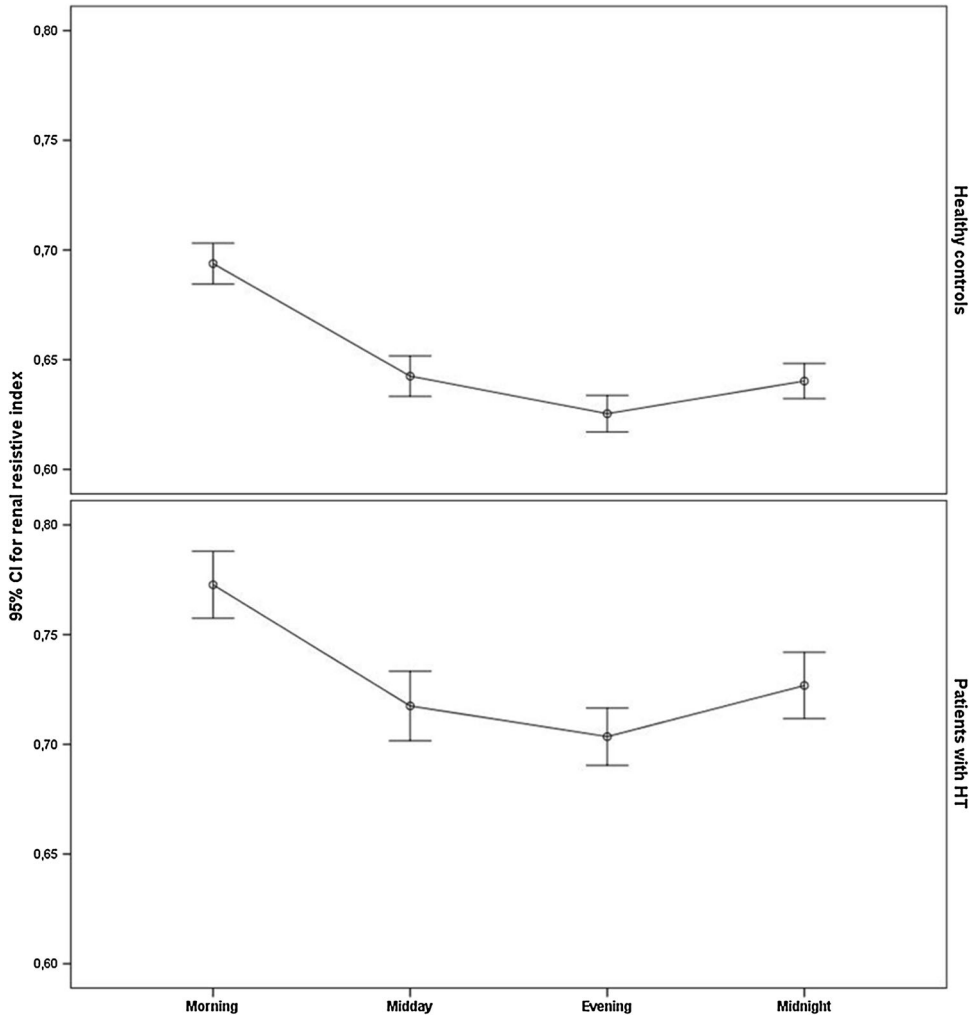

Fig. 3. Temporal variation of mean renal resistive index (RRI) in patients with hypertension and healthy controls.

Table 3. Correlation of renal resistive index measurements during the day with clinical and laboratory parameters

	Morning RRI		Midday RRI		Evening RRI		Midnight RRI		Absolute-ΔRRI		Relative-ΔRRI	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Age	0.531	< 0.001	0.503	< 0.001	0.398	< 0.001	0.492	< 0.001	0.353	< 0.001	0.258	0.005
Pulse pressure	0.0563	< 0.001	0.556	< 0.001	0.471	< 0.001	0.452	< 0.001	0.284	0.002	0.183	0.048
Body mass index	0.217	0.018	0.176	0.056	0.311	0.001	0.325	< 0.001	− 0.126	0.175	− 0.169	0.067
Creatinine	0.132	0.156	0.196	0.033	0.064	0.489	0.097	0.298	0.149	0.107	0.141	0.128
Cortical thickness	0.403	< 0.001	0.340	< 0.001	0.390	< 0.001	0.325	< 0.001	0.107	0.248	0.028	0.760
Cortical stiffness	0.737	< 0.001	0.621	< 0.001	0.646	< 0.001	0.662	< 0.001	0.319	< 0.001	0.192	0.037

RRI, renal resistive index

stiffness. However, absolute-ΔRRI and relative-ΔRRI positively correlated with the age. Absolute-ΔRRI positively correlated with the pulse pressure and cortical stiffness, and no correlation was observed between relative-ΔRRI and these variables (Table 3).

Linear regression analysis was performed with parameters significantly related to all RRI (Table 4). In linear regression analyses, all temporal RRI measurements were found to be independently associated with the patient age. Morning, midday, and midnight RRI were correlated with pulse pressure. Only morning RRI was independently correlated with cortical thickness. Of the four temporal measurements, morning RRI value was most significantly correlated cortical stiffness

Table 4. A linear regression analysis for parameters significantly correlated with renal resistive index

	Morning RRI		Midday RRI		Evening RRI		Midnight RRI		Absolute-ΔRRI		Relative-ΔRRI	
	β	p	β	p	β	p	β	p	β	p	β	p
Age	0.329	< 0.001	0.307	< 0.001	0.222	0.002	0.294	< 0.001	0.278	0.002	0.227	0.015
Pulse pressure	0.201	0.001	0.304	< 0.001	0.145	0.067	0.147	0.045	0.109	0.280	0.058	0.534
Cortical thickness	0.149	0.002	0.109	0.125	0.170	0.056	0.108	0.136	0.010	0.919	0.047	0.646
Cortical stiffness	0.476	< 0.001	0.376	< 0.001	0.439	< 0.001	0.424	< 0.001	0.228	0.013	0.116	0.222

RRI, renal resistive index

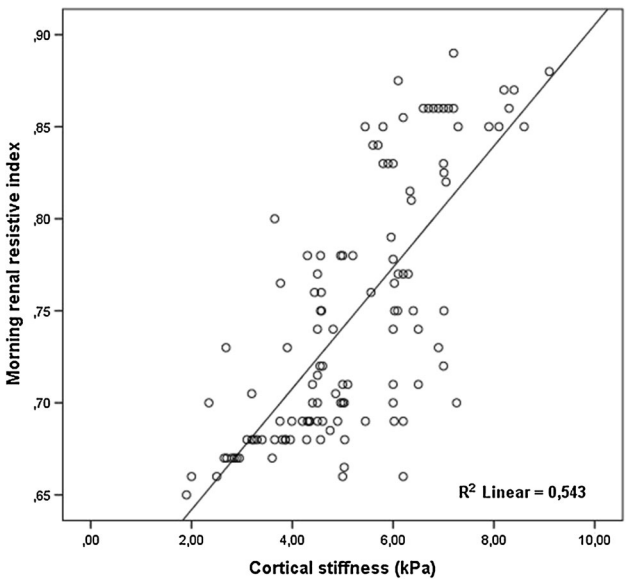

Fig. 4. Relationship between morning RRI and cortical thickness.

($p < 0.001$, $\beta = 0.737$ and 95% CI 13.719–19.281). The relationship between morning RRI and cortical stiffness is shown in Fig. 4.

Discussion

Our study shows significant variation in RRI measurement over 24-h period, in both hypertensive patient group and healthy controls. Early morning RRI was markedly higher than the other RRI values in patients with and without HT. Another important finding was that patients with HT had significantly increased RRI regardless of the measurement time, which is similar to previous studies that reported high RRI in hypertensive patients. Moreover, early morning RRI is independently related to increased cortical stiffness. Therefore, it is thought that RRI can be used as an objective parameter in renal cortical stiffness determination in patients with HT. To our knowledge, this is the first study in the literature that inspects this relation.

Cardiovascular events are the most common cause of death worldwide. HT is a substantial and known risk factor for cardiovascular event development. The most important target organ damage in HT is coronary artery disease, heart failure, atrial fibrillation, retinopathy, nephropathy, or renal failure and stroke. In clinical practice, the presence of albuminuria and reduction in eGFR is checked for target organ damage in HT-related renal diseases. At the same time, these two target organ damages are associated with cardiovascular prognosis. However, in recent years, RRI measurements for earlier target organ damage have been taken in hypertensive patients. RRI > 0.70 is associated with albuminuria, decreased GFR, hyperuricemia, and inflammation in hypertensive patients with normal renal function [6, 21].

There is a clear diurnal variation of the onset time of cardiovascular events. Clinical and epidemiological evidence suggests that cardiovascular events such as MI [22], stroke [23], and sudden cardiac death [24] occur most frequently in the morning. This clinical condition is associated with increased blood pressure and heart rate, especially in the morning hours. A lot of different renal and extra renal parameters were used to determine RRI. Among them renal determinants related to decreased RRI were renal artery stenosis, and increased RRI were renal vasoconstriction, arteriolosclerosis, increased interstitial pressure, and venous pressure, and among extra renal determinants with decreased RRI were valvular aortic stenosis, tachycardia, hypervolemia, parasympathetic activation, and increased RRI were sympathetic or adrenergic hyperactivity, bradycardia and increased aortic stiffness, SBP, DBP, and aortic pulse pressure [1, 5, 16]. Many of these parameters, especially all blood pressures, heart rate, sympathetic and parasympathetic activation, show significant temporal variation over 24-h period [1, 5, 25, 26]. For this reason, the RRI associated with these parameters may also change during the day. To the best of our knowledge, temporal RRI variation in patients with HT had not been demonstrated previously during the day. Ideally morning measurement is recommended because the change in RRI during the day cannot be demonstrated clearly. During the day, changes in RRI levels may affect risk group identification according to the RRI level recommended by HT guidelines and follow-up resources. Because the available evidence does not indicate that the

RRI level varies during the day, day to day or seasonally. In our study, in patients with HT, the RRI level showed an average change of 86%, and 35% of the patients were found to be at different risk groups (> 0.70) at the same day recommended by guidelines. For this reason, the same patient was diagnosed as having a high risk group according to the RRI level during the day and some follow-up and treatment approaches were needed but the other measurement shows that the same patient is in the low risk group and does not require strict follow-up and treatment. A similar situation is in the healthy control group, where 32% of patients in this group have RRI > 0.70 or ≤ 0.70 at different times during the day.

In our study, the highest value of RRI measurement was found in the early morning hours and this finding is closely related to renal cortical stiffness, an indicator of HT target organ involvement, relative to other RRI levels, because of the RRI's daytime changes, we routinely suggest morning fasting measurement. Moreover, patients with HT had significantly increased RRI regardless of the measurement time, which is similar with previous studies that reported high RRI in hypertensive patients [3–9].

Doppler US provides information about intrarenal hemodynamic changes resulting from structural and/or functional disorders. RRI detected with renal Doppler US is an objective indicator of renal tissue changing that occurs from renal vascular resistance, compliance, arteriolosclerosis, and interstitial fibrosis in both native and transplanted kidneys [27–29]. RRI is used as a prognostic and diagnostic parameter for many vascular and renal diseases. The most important goal of RRI measurement in hypertensive patients is early recognition of renal damage in patients with normal renal function. An increased RRI (> 0.70) in primary hypertensive patients is related to worse renal and cardiovascular complications [30]. Optimal RRI reference values and systematic factors influencing measurement values are not well known. Most of them have described an increase in RRI with age and even suggested a value > 0.7 as being pathological [1, 5, 25, 26, 31]. Many authors use > 0.70 to evaluate RRI values as abnormal or increased. An increased RRI that > 0.8 in CKD with or without HT is an indicator for worsening kidney functions [31]. In patients with renal artery stenosis, RRI > 0.73 in the other kidney is an indication that it is more difficult to revert renal function impairment [30]. In addition, different studies have reported different limit values for the use of RRI measurement at different times in diseases such as HT and DM. We determined that hypertensive patients had different RRI values during the day, while our study was not working to determine the limit value. The most important finding of our study is that all hypertensive patients' RRI measurement should be done in the morning hours. If morning measurement is not possible, hypertensive patients followed up with RRI should be monitored at the same time as the previous RRI measurement.

Our study has some limitations. The present study examined the diurnal variation of RRI in hypertensive patients and healthy controls in a cross-sectional fashion. We included a relatively small number of subject but, nevertheless, demonstrated that RRI measurements varied over 24-h period in patients with HT and/or healthy controls. Same medications affect arteriolar vasomotor properties (beta-blockers, nitroglycerine, or captopril), and these have also been reported to change RRI [15]. In our study, all patient were previously diagnosed HT and we did not found drug effect on RRI. Patient groups who were included in our study were in relatively younger than in previous HT studies. As it is known and as in our study, it is reported that RRI is closely related to age and RRI increases with increasing age. If our study was performed with an older patient group, different results could be obtained. In our study, all RRI measurements were taken by a single radiology specialist if the all measurements were taken by two different radiologists and the interobserver variability was evaluated, the results could be more meaningful. We did not make Doppler US examination of the abdominal aorta and main renal artery because these assessments were done for renal artery stenosis before [32]. Therefore, diurnal changes in the aortic and main renal artery resistive index and their relation with intrarenal RRI were not evaluated. Furthermore, our study was not a follow-up study, so the effect of variation of RRI on prognosis was not considered.

In conclusion, similar to the change in blood pressure, heart rate, sympathetic and parasympathetic activity in hypertensive patients, the widely used RRI measured by renal Doppler US also changes in day time period. According to the data of our study, when the RRI measurement is taken in the patient, due to intraday RRI change it should be measured at the earliest possible morning and this measurement should be used for following the patient.

Compliance with ethical standards

Funding No funding was received for this study.

Conflict of interest There is no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the Ethical Standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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