J Surg Med. 2023;7(1):86-90.
DOI: 10.28982/josam.7627

Research article

Journal of Surgery and Medicine
e-ISSN: 2602-2079
https://jsurgmed.com/

The relationship between renal resistive index and hypertensive end-organ damage: A cross-sectional study

Düriye Sıla Karagöz Özen [1], Mehmet Maruf Aydın [2], İpek Genç [3], Mehmet Derya Demirağ [1]

[1] Clinic of Internal Medicine, Samsun University, Samsun Research and Training Hospital, Samsun, Turkey
[2] Clinic of Radiology, Samsun University, Samsun Research and Training Hospital, Samsun, Turkey
[3] Clinic of Ophthalmology, Samsun University, Samsun Research and Training Hospital, Samsun, Turkey

ORCID ID of the author(s)

DSK: 0000-0001-7852-2114
MMA: 0000-0001-7706-0819
İG: 0000-0002-3291-4654
MDD: 0000-0001-5667-1805

Corresponding Author
Düriye Sıla Karagöz Özen
Clinic of Internal Medicine, Samsun Research and Training Hospital, Samsun, Turkey
E-mail: silakaragoz@yahoo.com

Ethics Committee Approval
The study was approved by Health Sciences University Samsun Research and Training Hospital ethics committee (date: 1 June 2021, decision number: GOKA/2021/11/5).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2023 January 22

Abstract

Background/Aim: The prevalence of hypertension increases with age and one out of every three adults over the age of 40 has hypertension. Hypertensive end-organ damage is an important predictive factor for patient morbidity and mortality. This study aimed to investigate the role of the renal resistive index (RI) in predicting retinopathy and nephropathy in hypertensive patients.
Methods: This study was cross-sectional in design. Sixty hypertensive patients who were followed in Samsun Research and Training Hospital Internal Medicine outpatient clinic were included in the study. In all patients, a routine ophthalmological examination, including visual acuity, anterior segment examination, and dilated ocular fundus examination, was performed. Urinary albumin to creatinine ratio (mg/g) was measured in spot urine samples, and a level ≥30 mg/g was accepted as the presence of proteinuria. Renal Doppler ultrasonography was performed using Esaote mylab x 9 model sonography device vovex probe (C1-8) 3.5 MHz. RI values were measured using Xflow Doppler at the level of interlobular or arcuate arteries of both kidneys. First, the patients were divided into two groups (with or without retinopathy). The patients who had retinopathy were then divided into two groups according to their retinopathy degree. Hypertensive retinopathy was graded according to the Scheie classification. The patients were also divided into two groups according to their proteinuria status (with or without proteinuria).
Results: The mean of renal RI was 0.59 (0.04) in patients without retinopathy (n=15), 0.63 (0.05) in patients with grade 1 hypertensive retinopathy (n=29), and 0.66 (0.04) in patients with grade 2 hypertensive retinopathy (n=15). The difference between groups was statistically significant (overall P=0.001). It has been shown that proteinuria develops more frequently in cases in which the renal value is above 0.7, and these results were statistically significant (P=0.034).
Conclusion: This study indicates that renal RI increase is a valuable tool for estimating retinopathy and proteinuria in hypertensive patients.

Keywords: hypertensive end-organ damage, renal resistive index, retinopathy, nephropathy

How to cite: Karagöz Özen DS, Aydın MM, Genç I, Demirağ MD. The relationship between renal resistive index and hypertensive end-organ damage: A cross-sectional study. J Surg Med. 2023;7(1):86-90.

Introduction

The prevalence of hypertension varies in the adult population and increases with age. One out of every three adults over the age of 40 has hypertension. Hypertensive end-organ damage is an important problem that causes morbidity and mortality. For this reason, in the latest international hypertension guidelines, medical treatment is recommended in addition to lifestyle modifications for people whose end-organ damage risk is increased and whose blood pressure level is above 130/85 mmHg [1,2]. Hypertension-related end-organ damage is an important predictive factor for cardiovascular risk [3]. The length of time that a patient has been hypertensive and his/her arterial blood pressure are major determinants of hypertension-related organ damage. To investigate the effects of high blood pressure, a 24-h ambulatory blood pressure measurement was performed on 130 hypertensive patients, and it was found that myocardial wall thickness and peripheral vascular resistance were higher in patients with higher mean systolic blood pressure [4]. The European Society of Cardiology hypertension diagnosis and management guidelines strongly suggest using the Systematic COronary Risk Evaluation (SCORE) system during the treatment of hypertensive patients [1]. This scoring system aims to identify high-risk patients in the early period and to initiate medical treatment earlier for patients with high cardiovascular risk. Predicting cardiovascular risk, especially in young patients or newly diagnosed hypertensive patients, is possible using this scoring system.

Hypertensive retinopathy, hypertensive nephrosclerosis, hypertension-related cerebrovascular changes, and left ventricular hypertrophy are the major hypertension-related end-organ injuries. The risk of stroke in patients with retinopathy is a frequently studied topic because of the close relationship between retinal and cerebral vascularity. It has been previously shown in a study that the presence of hypertensive retinopathy is associated with an increased risk of stroke, and the risk of stroke increases as the retinopathy degree increases [5]. In another study, in which hypertensive retinopathy was divided into severe and mild, it was shown that the risk of hemorrhagic stroke correlated with the severity of retinopathy [6].

Considering studies examining the relationship between hypertensive retinopathy and coronary artery disease, Duncan et al.'s study concerning middle-aged male patients revealed that retinal microvascular changes led to an increase in the risk of coronary artery disease and related events that are 2.1 times in the high-risk versus the low-risk patient group [7].

The pathogenesis of hypertensive retinopathy is believed to consist of complex and intertwined phases rather than progressing via sequential steps. These phases are defined as the vasoconstrictive, exudative, sclerotic, and complicated sclerotic phases [8].

The presence of microalbuminuria in hypertensive patients at the time of diagnosis is a risk factor for the presence of left ventricular hypertrophy [9]. It has been shown that in patients with a diagnosis of essential hypertension, an elevation in the the renal resistive index (RI) occurs. The index is correlated with carotid intima–media thickness and microalbuminuria [10]. The RI is the ratio of peak systolic velocity to end-diastolic velocity in the flow pattern of vascular structure and is an indicator of vascular resistance.

This study aimed to investigate the role of the renal RI in predicting retinopathy and nephropathy in hypertensive patients.

Materials and methods

This study was cross-sectional in design. Sixty hypertensive patients who were monitored in the Samsun University, Samsun Research and Training Hospital Internal Medicine outpatient clinic were included in the study. The patients were divided into three groups according to their retinopathy development status: (1) those who did not develop retinopathy, (2) those who developed stage 1 retinopathy, and (3) those who developed stage 2 retinopathy. All patients were also divided into two groups according to their proteinuria status.

To determine the number of patients to be included in the study, a power calculation was done, and the minimum number of patients recommended for study inclusion was found to be 60 with 80% power and 95% confidence interval at a $P < 0.05$ significance level [11]. In all patients, a routine ophthalmological examination, including visual acuity, anterior segment examination, intraocular pressure measurement, and dilated ocular fundus examination, was performed. Fundus examination was done after instilling tropicamide 1% and cyclopentolate 1% eye drops, and retinal abnormalities were noted and graded according to Scheie classification (*): (1) Grade 0: No visible changes; (2) Grade 1: barely detectable arterial narrowing; (3) Grade 2: obvious arterial narrowing with focal irregularities; (4) Grade 3: grade 2 plus retinal hemorrhage, exudates, cotton wool spots, or retinal edema; and (5) Grade 4: grade 3 plus papilloedema [12].

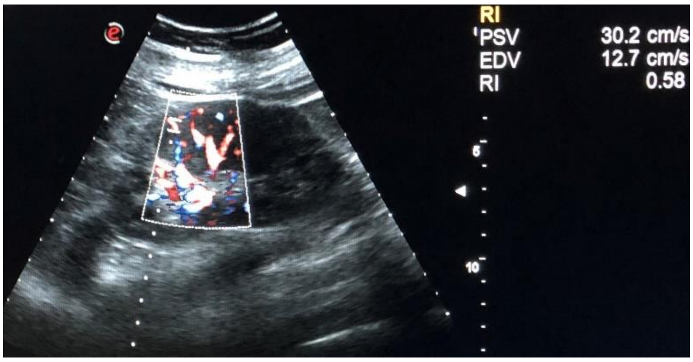
Venous blood samples following 12 h of fasting were collected to measure blood glucose, creatinine, and glycosylated hemoglobin levels. Urinary albumin to creatinine ratio (mg/g) was also measured and calculated in spot urine samples. Conditions that could cause false positive measurements in urinary albumin excretion were evaluated and the measurement was repeated after that. Albumin to creatinine ratio ≥30 mg/g was accepted as the presence of albuminuria [13].

Renal doppler ultrasonography was performed using Esaote mylab x9 model sonography device vovex probe (C1-8) 3.5 MHz. The patients were examined under supine and bilateral decubitus positions. Bilateral renal parenchymal thickness and length were measured in the long axis plane with B-mode. RI values were measured at the level of interlobular or arcuate arteries from the upper, middle, and lower parenchyma of the kidney with Xflow Doppler, and measurements were taken at least three times after which average values were obtained (as shown in Figure 1).

The duration of hypertension and patients' demographic characteristics were recorded to evaluate the risk factors affecting retinopathy. Patients with a diagnosis of secondary hypertension, those with known chronic kidney disease, those with a diagnosis of diabetes mellitus, and/or those under the age of 18 were excluded from the study.

The ethical evaluation of our study was performed by Samsun University Samsun Research and Training Hospital ethics committee, and it was approved on 1.6.2021 with the decision number GOKA/2021/11/5.

Figure 1: X-Doppler image of resistive index (RI) measurement at the level of the interlobular and arcuate arteries



Statistical analysis

The statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) Program Version 22.0. Normally distributed continuous variables were expressed as mean (standard deviation), while non-normally distributed continuous variables were expressed as median (lowest–highest). Categorical variables were expressed as n (%). A chi-squared test was used to compare the variables between groups. One-way analysis of variance (ANOVA) and post hoc Tukey honestly significant difference (HSD) tests were used to compare continuous variables between the groups. A receiver operating characteristic (ROC) curve analysis was done to determine the RI cut-off value. A *P*-value of less than 0.05 was considered statistically significant.

Results

A total of 60 hypertensive patients, including 38 women, and 22 men, were included in the study. The mean age was 52.6 (11.8) years. The median duration of hypertension in the patients was 4 years (0–40 years). According to the calculated urinary albumin excretion (UAE), the number of patients with a UAE of 30 mg/g and above was 22 (36.7%) while the number of patients without proteinuria was found to be 38 (63.3%).

The number of patients without retinopathy was 15 (25%), the number with grade 1 retinopathy was 29 (48.3%), and the number with grade 2 retinopathy was 16 (26.7%).

RI measurements were obtained from all 60 patients, and 18 (30%) patients with a mean renal RI value below 0.61 and 42 (70%) patients with RI value above 0.61 were noted.

According to the ROC curve analysis, the RI cut-off value to determine retinopathy was determined as 0.61 with a sensitivity of 76% and specificity of 67%. The area under the curve (AUC) was 0.761 with 95% confidence interval (CI) values for AUC ranging from 0.619 to 0.903. The ROC curve is shown in Figure 2. It was shown that in patients with a greater RI level, hypertensive retinopathy frequency significantly increased (Table 1).

The mean of renal RI values was 0.59 (0.04) in patients without retinopathy (n=15), 0.63 (0.05) in patients with grade 1 hypertensive retinopathy (n=29), and 0.66 (0.04) in patients with grade 2 hypertensive retinopathy (n=15). The difference between groups was statistically significant (overall *P*=0.001). In the post hoc analysis, it was determined that this difference was due to the difference between those without retinopathy and those with grade 1 retinopathy (*P*=0.047) and those without retinopathy and those with grade 2 retinopathy (*P*=0.001). No statistically significant difference between the grade 1 and the grade 2 retinopathy groups was found (*P*=0.11).

Figure 2: Receiver operating characteristic (ROC) curve to determine retinopathy

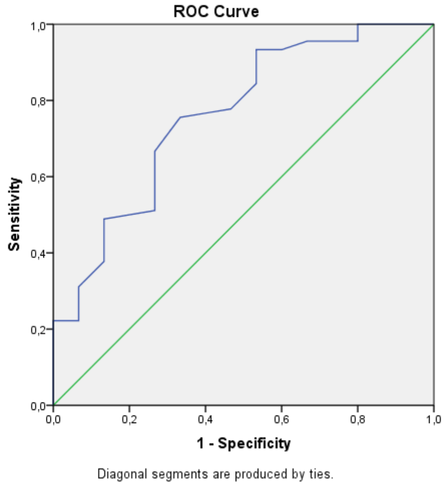


Table 1: The effect of the renal resistive index (RI) on retinopathy

	Retinopathy (-) n (%)	Retinopathy (+) n (%)	*P*-value*
Renal resistive index			
<0.61	8 (44.4)	10 (55.6)	0.023
≥0.61	7 (16.7)	35 (83.3)	
Renal resistive index	**Grade 0-1 retinopathy n (%)**	**Grade 2 retinopathy n (%)**	
<0.61	17 (94.4)	1 (5.6)	0.015
≥0.61	27 (64.3)	15 (35.7)	

*Pearson Chi-Squared Test

According to the ROC curve analysis, RI cut-off value to determine proteinuria was determined as 0.63 with a sensitivity of 64% and specificity of 5%. The AUC was 0.620 with a 95% CI range for the AUC ranging from 0.465 to 0.774 The ROC curve is shown in Figure 3.. A significant relationship between RI increase and proteinuria status could not be shown (Table 2). Moreover, Spearman's test showed that renal RI levels did not correlate with the level of proteinuria (r=0.226; *P*=0.09).

Figure 3: ROC curve according to determine microalbuminuria

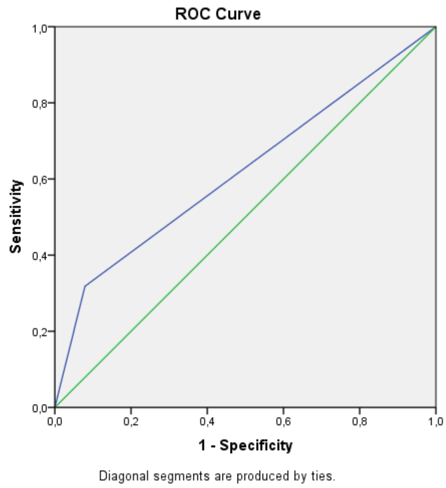


Table 2: The effect of the renal resistive index on proteinuria

	UAE <30 mg/g n (%)	UAE ≥30 mg/g n (%)	*P*-value*
Renal resistive index			
<0.63	22 (73.3)	8 (26.7)	0.108
≥0.63	16 (53.3)	14 (46.7)	

UAE: urinary albumin excretion

Discussion

Hypertension-related end-organ damage is an important marker of cardiovascular risk. Retinal, glomerular, and cerebral vascular damage due to hypertension constitute the trivet of microvascular complications. Mild hypertensive retinopathy (grades 1 and 2) is associated with an increase in cardiovascular and stroke risks [14].

The risk of stroke in patients with retinopathy is a frequently studied topic because of the close relationship between retinal and cerebral vascularity [5]. Duncan et al.'s study on middle-aged male patients revealed that retinal microvascular changes lead to an increase in the risk of coronary artery disease and related events that is 2.1 times more in the high-risk patient group versus normal subjects [7].

In a study conducted on hypertensive individuals over the age of 65, it was shown that the risk of hypertensive retinopathy increases as the UAE level increases [15]. In another study on renal resistive index and hypertension, it was shown that as RI increases, the incidence of proteinuria and carotid intima–media thickness increases in hypertensive individuals [10]. However, not enough studies examining the role of RI in predicting hypertensive retinopathy have been published..

Diabetic patients were not included in our study due to the increased incidence of retinopathy in diabetic patients and the fact that it is not always possible to reveal the underlying cause of retinopathy and nephropathy development in the presence of hypertension in this patient group. To exclude diabetic patients, the patients were questioned in terms of their past medical history, and venous plasma glucose and glycosylated hemoglobin values were measured in all patients after 12 h of fasting. If the patients were diagnosed with diabetes mellitus according to the new measurements, they were excluded from the study.

Previous studies demonstrated that the renal RI increases in the presence of diabetic retinopathy compared to the healthy population [16]. We think that exclusion of diabetic patients in our study is valuable for measuring the relationship between the renal RI and hypertensive end-organ damage. It was shown in a previous study that ambulatory arterial stiffness index increase was correlated with hypertensive end-organ damage. In that study, the effect of ambulatory arterial stiffness index on hypertensive end-organ damage did not differ between those patients who were on antihypertensive medications and those who were not [17].

It is also known that renal RI values increase due to glomerulosclerosis development in the presence of chronic renal failure [18]. For this reason, the glomerular filtration rate (GFR) was calculated by measuring the creatinine level of all patients included in the study.

As a result of the analysis of 60 patients who met these criteria, it was observed that the frequency of retinopathy was higher if the RI value was 0.61 and above. Renal RI values greater than 0.61 may predict hypertensive retinopathy with 77.8% sensitivity and 83.4% positive predictive value. For this reason, we think that RI can be used to indicate end-organ damage in hypertensive patients; thus, cardiovascular risk factors should be reviewed more carefully in patients with high RI levels.

Proteinuria and ultimately nephrosclerosis are important end-organ damage events in patients with hypertension. Ozmen et al. [19] reported that renal RI values increase in patients with diabetic nephropathy, and the levels of proteinuria were found to correlate well with intrarenal RI.. Our results show that proteinuria is slightly increased in patients with higher renal RI levels. It was shown in our study that proteinuria develops more frequently in cases in which the renal RI value is above 0.7, and these results were statistically significant. Our result is compatible with some other studies in the literature in which the risk of proteinuria increases above an RI cut-off value of 0.7 [20,21].

However, some investigators mention that RI cut-off levels should be determined according to the patient group and for this reason, we performed an ROC curve analysis to determine the best cut-off level [22,23]. Unfortunately, when we re-evaluated the results according to the measured cut-off level ROC curve analysis, no significant difference between the patients with and without microalbuminuria was found.

Limitations

In our study, no patient with advanced stage (grade 3/4) retinopathy participated in the study. We would like to point out this situation as the most important limitation of our study. To generalize the results of the study, we think that prospective studies are needed by including more patients with all four stages of hypertensive retinopathy.

Conclusion

This study shows that renal RI levels increase in hypertensive nondiabetic patients who have retinopathy. Renal RI starts to increase earlier than the glomerular filtration decline in hypertensive patients who have retinopathy. This increase is an important point for identifying patients at high risk for hypertensive end-organ damage.

References

1. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018 Sep 1;39(33):3021-104. doi: 10.1093/eurheartj/ehy339. Erratum in: Eur Heart J. 2019 Feb 1;40(5):475. PMID: 30165516.
2. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension. 2020 Jun;75(6):1334-57. doi:10.1161/HYPERTENSIONAHA.120.15026. Epub 2020 May 6. PMID: 32370572.
3. Vernooij JW, van der Graaf Y, Nathoe HM, Bemelmans RH, Visseren FL, Spiering W. Hypertensive target organ damage and the risk for vascular events and all-cause mortality in patients with vascular disease. J Hypertens. 2013 Mar;31(3):492-9; discussion 499-500. doi: 10.1097/HJH.0b013e32835cd3cd. PMID: 23303394.
4. Mulè G, Nardi E, Andronico G, Cottone S, Raspanti F, Piazza G, et al. Relationships between 24 h blood pressure load and target organ damage in patients with mild-to-moderate essential hypertension. Blood Press Monit. 2001 Jun;6(3):115-23. doi: 10.1097/00126097-200106000-00001. PMID: 11518833.
5. Chen X, Liu L, Liu M, Huang X, Meng Y, She H, et al. Hypertensive Retinopathy and the Risk of Stroke Among Hypertensive Adults in China. Invest Ophthalmol Vis Sci. 2021 Jul 1;62(9):28. doi: 10.1167/iovs.62.9.28. PMID: 34283210; PMCID: PMC8300046.
6. Thiagarajah R, Kandasamy R, Sellamuthu P. Hypertensive Retinopathy and the Risk of Hemorrhagic Stroke. J Korean Neurosurg Soc. 2021 Jul;64(4):543-51. doi: 10.3340/jkns.2020.0285. Epub 2021 Jul 1. PMID: 34237912; PMCID: PMC8273771.
7. Duncan BB, Wong TY, Tyroler HA, Davis CE, Fuchs FD. Hypertensive retinopathy and incident coronary heart disease in high risk men. Br J Ophthalmol. 2002 Sep;86(9):1002-6. doi: 10.1136/bjo.86.9.1002. PMID: 12185127; PMCID: PMC1771277.
8. Tso MO, Jampol LM. Pathophysiology of hypertensive retinopathy. Ophthalmology. 1982 Oct;89(10):1132-45. doi: 10.1016/s0161-6420(82)34663-1. PMID: 7155524.
9. Nabbaale J, Kibirige D, Ssekasanvu E, Sebatta ES, Kayima J, Lwabi P, et al. Microalbuminuria and left ventricular hypertrophy among newly diagnosed black African hypertensive patients: a cross sectional study from a tertiary hospital in Uganda. BMC Res Notes. 2015 May 14;8:198. doi: 10.1186/s13104-015-1156-2. PMID: 25971452; PMCID: PMC4434545.
10. Pontremoli R, Viazzi F, Martinoli C, Ravera M, Nicolella C, Berruti V, et al. Increased renal resistive index in patients with essential hypertension: a marker of target organ damage. Nephrol Dial Transplant. 1999 Feb;14(2):360-5. doi: 10.1093/ndt/14.2.360. PMID: 10069189.
11. Dhand NK, Khatkar MS. Statulator: An online statistical calculator. Sample Size Calculator for Comparing Two Independent Means. Accessed 10 September 2021 at http://statulator.com/SampleSize/ss2M.html

12.Scheie HG. Evaluation of ophthalmoscopic changes of hypertension and arteriolar sclerosis. AMA Arch Ophthalmol. 1953 Feb;49(2):117-38. doi: 10.1001/archopht.1953.00920020122001. PMID: 13007237.
13.Awua-Larbi S, Wong TY, Cotch MF, Durazo-Arvizu R, Jacobs DR Jr, Klein BE, et al. Retinal arteriolar caliber and urine albumin excretion: the Multi-Ethnic Study of Atherosclerosis. Nephrol Dial Transplant. 2011 Nov;26(11):3523-8. doi: 10.1093/ndt/gfr095. Epub 2011 Mar 11. PMID: 21398363; PMCID: PMC3247797.
14.Li J, Kokubo Y, Arafa A, Sheerah HA, Watanabe M, Nakao YM, et al. Mild Hypertensive Retinopathy and Risk of Cardiovascular Disease: The Suita Study. J Atheroscler Thromb. 2022 Nov 1;29(11):1663-71. doi: 10.5551/jat.63317. Epub 2022 Jan 15. PMID: 35034920; PMCID: PMC9623077.
15.Jian G, Lin W, Wang N, Wu J, Wu X. Urine Albumin/Creatinine Ratio and Microvascular Disease in Elderly Hypertensive Patients without Comorbidities. Biomed Res Int. 2021 Feb 13;2021:5560135. doi: 10.1155/2021/5560135. PMID: 33628790; PMCID: PMC7899778.
16.Jinadu YO, Raji YR, Ajayi SO, Salako BL, Arije A, Kadiri S. Resistivity index in the diagnosis and assessment of loss of renal function in diabetic nephropathy. Cardiovasc J Afr. 2022 Jan-Feb 23;33(1):26-32. doi: 10.5830/CVJA-2021-032. Epub 2021 Jul 26. PMID: 34309616; PMCID: PMC9198679.
17.García-García A, Gómez-Marcos MA, Recio-Rodriguez JI, González-Elena LJ, Parra-Sanchez J, Fe Muñoz-Moreno M, et al. Relationship between ambulatory arterial stiffness index and subclinical target organ damage in hypertensive patients. Hypertens Res. 2011 Feb;34(2):180-6. doi: 10.1038/hr.2010.195. Epub 2010 Oct 21. PMID: 20962781.
18.Boddi M. Renal Ultrasound (and Doppler Sonography) in Hypertension: An Update. Adv Exp Med Biol. 2017;956:191-208. doi: 10.1007/5584_2016_170. PMID: 27966109.
19.Ozmen ND, Mousa U, Aydin Y, Deren T, Unlu EB. Association of the renal resistive index with microvascular complications in type 2 diabetic subjects. Exp Clin Endocrinol Diabetes. 2015 Feb;123(2):112-7. doi: 10.1055/s-0034-1390448. Epub 2014 Oct 24. PMID: 25343266.
20.Miyoshi K, Okura T, Tanino A, Kukida M, Nagao T, Higaki J. Usefulness of the renal resistive index to predict an increase in urinary albumin excretion in patients with essential hypertension. J Hum Hypertens. 2017 Jan;31(1):66-9. doi: 10.1038/jhh.2016.38. Epub 2016 Jun 9. PMID: 27278927.
21.Faubel S, Patel NU, Lockhart ME, Cadnapaphornchai MA. Renal relevant radiology: use of ultrasonography in patients with AKI. Clin J Am Soc Nephrol. 2014 Feb;9(2):382-94. doi: 10.2215/CJN.04840513. Epub 2013 Nov 14. PMID: 24235286; PMCID: PMC3913238.
22.Boddi M, Natucci F, Ciani E. The internist and the renal resistive index: truths and doubts. Intern Emerg Med. 2015 Dec;10(8):893-905. doi: 10.1007/s11739-015-1289-2. Epub 2015 Sep 4. PMID: 26337967.
23.Ponte B, Pruijm M, Ackermann D, Vuistiner P, Eisenberger U, Guessous I, et al. Reference values and factors associated with renal resistive index in a family-based population study. Hypertension. 2014 Jan;63(1):136-42. doi: 10.1161/HYPERTENSIONAHA.113.02321. Epub 2013 Oct 14. PMID: 24126174.

The National Library of Medicine (NLM) citation style guide has been used in this paper.