Turk Kardiyol Dern Ars 2017;45(4):348-354 doi: 10.5543/tkda.2017.05248

ORIGINAL ARTICLE

The relationship between serum lipid parameters and renal frame count in hypertensive patients with normal renal functions

Normal böbrek işlevi olan hipertansif hastalarda serum lipit parametreleri ile renal kare sayıları arasındaki ilişki

Emrah İpek,[1] M.D., Mustafa Yolcu,[2] M.D., Erkan Yıldırım,[1] M.D.

[1]Department of Cardiology, Erzurum Regional Training and Research Hospital, Erzurum, Turkey
[2]Department of Cardiology, Arel University Faculty of Medicine, İstanbul, Turkey

ABSTRACT

Objective: Atherosclerosis can contribute to renovascular disease, and high cholesterol level is an independent risk factor for disease progression. Renal frame count (RFC) is an objective angiographic method of measuring macrovascular blood flow in the main renal artery and its segmental branches. The aim of the present study was to demonstrate relationship between serum lipid parameters and RFC.

Methods: In this cross-sectional study, 116 hypertensive patients were allocated into 2 groups according to serum low-density lipoprotein (LDL) levels. Group 1 comprised 60 patients with LDL <130 mg/dL and Group 2 consisted of 56 individuals with LDL ≥130 mg/dL. The patients were also divided into 2 groups according to total cholesterol (TC) levels (52 patients in group with TC <200 mg/dL and 64 patients in group with TC ≥200 mg/dL).

Results: Group 2 had higher mean RFC than Group 1 (p<0.001). RFC of both kidneys in Group 2 was significantly higher than results in Group 1 (p<0.001 and p=0.023, respectively). We found similar significant results in comparison of TC-based patient groups. RFC had positive correlation with smoking, TC, and LDL (r=0.326, p=0.035; r=0.393, p=0.010; and r=0.386, p=0.012, respectively). In multivariate linear regression analysis, LDL, TC, smoking, and creatinine clearance were independent predictors of RFC.

Conclusion: In conclusion, in hypertensive patients with normal renal function, LDL, TC, and smoking may be predictors of RFC and aggressive risk factor modification may help to reduce the risk of renal failure.

ÖZET

Amaç: Ateroskleroz renovasküler hastalığa katkıda bulunabilir ve yüksek kolesterol düzeyleri hastalığın ilerlemesi için risk faktörüdür. Renal kare sayısı (RKS) ana renal arter ve segmental dallarındaki makrovasküler kan akımını gösteren nesnel bir yöntemdir. Bu çalışmada, serum lipit parametreleri ile RKS arasındaki ilişki incelendi.

Yöntemler: Kesitsel olarak kurgulanan çalışmaya 116 hipertansif hasta alındı ve hastalar serum LDL kolesterol seviyelerine göre iki gruba ayrıldı. Grup 1'de LDL<130 mg/dL olan 60, grup 2'de ise LDL seviyesi 130 mg/dL ve üzeri olan 56 hasta mevcuttu. Hastalar serum toplam kolesterol (TK) seviyelerine göre de iki gruba ayrıldı (TK <200 mg/dL olan 52 hasta grup 1'de, TK 200 mg/dL ve üzeri olan 64 hasta grup 2'de).

Bulgular: Ortalama RKS, grup 2'de grup 1'e kıyasla daha yüksekti (p<0.001). Her iki böbreğin RFK'ları ayrı ayrı grup 2'de grup 1'e göre daha yüksekti (sırasıyla, p<0.001 ve p=0.023). Toplam kolesterol temelli gruplarda da benzer sonuçlar elde edildi. RKS, sigara (paket yıl), TK ve LDL ile anlamlı pozitif ilişkiye sahipti (sırasıyla, r=0.326, p=0.035; r=0.393, p=0.010; r=0.386, p=0.012). Çoklu değişkenli lineer regresyon analizinde LDL, TK, sigara ve kreatinin klirensi, RKS'nin bağımsız tahmin ettiricileri olarak bulundu.

Sonuç: Normal böbrek işlevi olan hipertansif hastalarda LDL, TK ve sigara RKS'yı tahmin ettirebilir ve yoğun risk faktörü modifikasyonu böbrek yetersizliği riskini azaltabilir.

As the major contributor to cardiovascular disease, atherosclerosis is among the most important reasons for mortality all over the world. Atherosclerosis is a progressive disease, especially in patients with diabetes and multiple cardiovascular disease risk factors, such as hyperlipidemia.[1] Atherosclerotic renal artery stenosis (RAS), as a part of cardiovascular disease spectrum, is the most common cause of secondary hypertension.[1–3] Coronary angiography performed in patients exhibiting severe hypertension, unexplained

Received: October 31, 2016 *Accepted:* February 09, 2017

Correspondence: Dr. Emrah İpek. Erzurum Bölge Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, Çat Yolu Üzeri, Zemin Kat, 25070 Palandöken, Erzurum, Turkey.
Tel: +90 442 - 232 55 55 e-mail: dremrah21@yahoo.com

kidney failure, acute pulmonary edema with hypertension, or severe atherosclerosis, but who were not suspected of having RAS, revealed incidence of significant RAS of 14.3%.[4] At glomerular level, atherosclerotic process can also contribute to renal disease.[5] Serum lipids, as an important traditional risk factor, play an important role in pathogenesis of both coronary artery disease and renal artery atherosclerosis.[5] Correlation between progression of renal disease and dyslipidemia has been suggested in some experimental and clinical studies, and in humans, higher plasma cholesterol and triglyceride levels have been shown to be independent risk factors for progression of renal disease.[5] Renal frame count (RFC) is an objective angiographic method to quantify renal perfusion based on macrovascular blood flow in the main renal artery and its segmental branches as well as microvascular resistance of the cortex and medulla.[6] Aggressive management of cardiovascular risk factors, such as serum lipids, before overt renal artery atherosclerosis and renal failure occur may be a new focus.

In the present study, relationship between serum lipid parameters and RFC in hypertensive patients without critical renal artery stenosis was evaluated.

METHODS

This study was designed as a cross-sectional observational study of 116 hypertensive patients (blood pressure ≥140/90 mmHg despite treatment with 2 or more antihypertensives) who were admitted to our outpatient clinic between August 2012 and February 2015 and referred for coronary angiography with suspicion of stable coronary artery disease and eligible for selective renal angiography. All hospital archive data about pre-coronary angiography period of participants was examined. Demographic characteristics (age, gender) of the patients and risk factors, such as hypertension, diabetes mellitus, smoking, family history, and biochemical and hemogram values, were recorded.

Blood samples were collected to examine whole blood count, serum glucose, lipid profile, and renal function (blood urea nitrogen and creatinine) tests using Abbott Architect C16000 auto analyzer (Abbott Laboratories, Lake Bluff, IL, USA). Total and differential leukocyte counts were measured with automated hematology analyzer (Beckman Coulter, Inc., Brea, CA, USA). Creatinine clearance was calculated with Cockroft-Gault formula: (140-age) x mass (in kilograms) x (0.85 if female) / 72 x serum creatinine (in mg/dL).

Abbreviations:

GFR	*Glomerular filtration rate*
LDL	*Low-density lipoprotein*
RA	*Renal artery*
RAS	*Renal artery stenosis*
RFC	*Renal frame count*
TC	*Total cholesterol*

Transthoracic echocardiography was performed at admission to determine left ventricular ejection fraction and presence of valvular disease (Vivid 7; GE Healthcare, Inc., Chicago, IL, USA). Selective coronary angiography was performed using the Judkins technique through right femoral artery.

Severity of coronary artery disease was established using the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) and Gensini scores. SYNTAX score of the patients was calculated by 2 invasive cardiologists using Web-based computer program (http://www.syntaxscore.com).[7] Gensini scores were calculated in a similar manner. According to the scoring system designed by Gensini, 1 point is given for stenosis of 0% to 25%, 2 points for 25% to 50% stenosis, 4 points for 50% to 75% stenosis, 8 points for 75% to 90% stenosis, 16 points for 90% to 99% stenosis, and 32 points for total occlusion. Final score is obtained multiplying degree of angiographic stenosis by coefficients predefined for each main coronary artery segment and addition of the sums.[8]

Selective renal angiography of both renal arteries was performed with 6F right Judkins catheter. RFC was measured according to method described by Mulumudi et al.[6] Cineangiographic frames were taken at rate of 30 frames per second from time contrast dye reached proximal RA (contrast filling the transverse diameter of the artery) to distal landmark of the smallest cortical branch for each kidney. Mean RFC was calculated as arithmetic mean of right and left RFC.

Individuals with ≥30% RAS and those under statin therapy were excluded. Additionally, patients with chronic renal failure, ejection fraction <50%, valvular disease, previous renal artery disease, or history of renal stent were also excluded. The patients were allocated into 2 groups according to their serum low-density lipoprotein (LDL) and total cholesterol (TC) levels. Group 1 comprised 60 patients with serum LDL <130 mg/dL and Group 2 consisted of 56 indi-

viduals with serum LDL ≥130 mg/dL. There were 52 and 64 patients in TC-based groups of TC <200 mg/dL and ≥200 mg/dL, respectively.

All participants were informed about the study, and written consent was provided. The local ethics committee approved the study protocol and study performance complied with the Declaration of Helsinki.

Statistical analysis

Continuous variables were presented as mean±SD, while categorical variables were provided as percentages. Kolmogorov-Smirnov test was used to verify normality of distribution of continuous variables. Statistical analysis to determine difference in clinical data between 2 groups was performed using 2-sided Student's t-test. Categorical variables were compared

Table 1. Baseline demographic, clinical, and laboratory data of the patient groups based on serum low-density lipoprotein cholesterol level[a]

Variables	Group 1 (n=60) LDL <130 mg/dL	Group 2 (n=56) LDL >130 mg/dL	*p*
Age, years	59.2±10.7	61.7±10.4	0.697
Male (Gender), n (%)	31 (52)	27 (48)	0.710
Body mass index	29.4±4.4	32.1±3.9	<0.001
Smokers, n (%)	22 (36.6)	35 (62.5)	0.005
Smoking, package years	28.7±14.9	26.7±9.8	0.753
Diabetics, n (%)	27 (45.0)	30 (53.5)	0.356
Duration of hypertension, years	7.09±4.19	8.0±6.16	0.980
Systolic blood pressure (mmHg)	156.5±9.2	159.8±11.5	0.116
Diastolic blood pressure (mmHg)	92.4±12.5	91.5±8.3	0.224
Heart rate (bpm)	84.6±10.1	79.7±7.4	0.071
White blood cell (mm^3)	8.1±2.5	8.2±2.7	0.015
Hemoglobin (gr/L)	14.26±1.7	14.4±1.78	0.112
Platelet count (mm^3)	221.8±63.9	234.4±37.3	0.65
Mean platelet volume (fL)	8.6±1.06	8.41±0.58	0.789
Blood urea nitrogen (mg/dL)	38.02±1.5	36.9±2.4	0.285
Creatinine (mg/dL)	0.79±0.20	0.67±0.11	0.389
Creatinine clearance (mL/min)	111.2 ±11.1	107.8±9.6	0.932
Aspartate-amino transferase (U/L)	28.7±4.5	29.8±7.1	0.85
Alanine-amino transferase (U/L)	45.1±5.1	52.6±9.6	0.08
Triglyceride (mg/dL)	178±99.5	163.2±78.6	0.337
Total cholesterol (mg/dL)	169.1±23.3	239.2±32.7	<0.001
High density lipoprotein (mg/dL)	39.4±10.4	41.2±9.01	0.442
Low density lipoprotein (mg/dL)	107±28.4	170.9±25.9	<0.001
Glucose (mg/dL)	126.1±16.4	136.2±11.4	0.051
Ejection fraction (%)	58.4±3.2	61.2±1.1	0.052
SYNTAX score	6.12±8.71	6.13±7.58	0.385
Gensini score	16.77±26.13	20.92±26.66	0.631
Renal frame count of right kidney	20.08±6.08	23.51±6.02	<0.001
Renal frame count of left kidney	21.39±5.56	25.25±6.33	0.023
Mean renal frame count	20.73±5.32	24.38±5.59	<0.001

[a]Data are expressed as mean+SD, median (interquartile range), or frequency count (percentage), as appropriate. SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

Table 2. Correlation of study parameters to mean renal frame count

	Renal frame count	
	r	*p*
Variables		
Age	0.203	0.179
Body mass index	-0.182	0.072
Smoking pack years	0.326	0.035
Duration of hypertension	0.200	0.12
Platelet count	0.151	0.094
Mean platelet volume	0.083	0.476
Creatinine clearance	-0.513	<0.001
Triglyceride	0.023	0.846
Total cholesterol	0.393	0.010
High density lipoprotein	-0.128	0.175
Low density lipoprotein	0.386	0.012
SYNTAX score	0.141	0.140
Gensini score	-0.173	0.095

SYNTAX: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

using chi-square test. Statistical significance of degree of associations between continuous variables was evaluated using Pearson's or Spearman's correlation analysis, as applicable. Multivariate linear regression analysis using enter method was performed to evaluate association between RFC and independent variables, such as body mass index, smoking pack-years, platelet count, creatinine clearance, TC, LDL cholesterol and Gensini score, as determined by univariate analyses (p<0.1). Results were presented as regression coefficient (β) and with 95% confidence intervals (95% CI). SPSS for Windows, Version 17.0 (SPSS, Inc., Chicago, IL, USA) was used to conduct analyses, and 2-tailed p value <0.05 was considered statistically significant.

RESULTS

Baseline demographic, clinical, and laboratory data of the patients are presented in Table 1. There was no significant difference in terms of age, gender, duration of hypertension, smoking pack-years, number of diabetics, systolic and diastolic blood pressure, or heart rate between LDL cholesterol-based groups. Body mass index, number of smokers, white blood cell count, TC, and LDL level were found to be significantly greater in Group 2 compared to Group 1. There was no statistically significant difference in terms of ejection fraction, SYNTAX, or Gensini scores between groups. In comparison of mean RFC, Group 2 had higher mean RFC than Group 1 (p<0.001). RFC of right and left kidneys in Group 2 were significantly higher than seen in Group 1 (p<0.001 and p=0.023, respectively) (Table 1). Comparison of RFC in TC-based patient groups revealed similar relationship. Mean RFC and RFCs of right and left kidneys were significantly higher in Group 2, the patients with TC level >200 mg/dL (RFC of right kidney: 21.15±5.91 *vs*. 25.81±5.86, p=0.006; RFC of left kidney: 20.53±6.08 *vs*. 23.46±6.12, p=0.002; mean RFC: 20.84±5.64 *vs*. 24.64±5.28, p<0.001). In correlation analysis, RFC was observed to have positive and mod-

Table 3. Multivariate analysis demonstrating independent predictors of increased renal frame count

Independent variables	Dependent variable: Renal frame count	
	β (95% CI)	*p**
Low density lipoprotein	0.266 (0.012–0.520)	0.006
Total cholesterol	0.277 (0.083–0.471)	0.002
Smoking pack years	0.296 (0.099–0.493)	0.030
Creatinine clearance	-0.350 (-0.604– -0.096)	<0.001
Gensini score	-0.298 (-0.425– -0.171)	0.324
Platelet count	0.040 (-2.564–2.644)	0.753
Body mass index	-0.128 (-0.959–0.703)	0.056

*Linear regression analyses using the enter method were used for multivariate analysis of independent variables that were included if they were significantly different in the univariate analyses (p<0.1). CI: Confidence interval.

erate correlation to smoking pack-years, TC, and LDL level (r=0.326, p=0.035; r=0.393, p=0.010; r=0.386, p=0.012, respectively). Creatinine clearance had significant, negative, and moderate correlation with RFC (r=-0.513; p<0.001) (Table 2). Scatter plot graphics of significant correlations between mean RFC and the above parameters can be seen in Figures 1 to 4. In multivariate analysis, LDL level, TC, smoking pack-years, and creatinine clearance were demonstrated to be independent predictors of RFC (Table 3).

DISCUSSION

Results of this study indicate that serum lipid parameters may be related to RFC in hypertensive patients without significant renal arterial atherosclerotic lesions. Additionally, smoking period defined as pack-years and serum LDL level were found to be independent predictors of RFC.

There are several studies indicating role of increased serum lipids in atherosclerotic process and nephropathy. In a Danish study, serum cholesterol level was demonstrated to be predictive for progression of diabetic nephropathy in 301 type 1 diabetes patients who had overt nephropathy.[5,9] Circulating lipids bind to extracellular matrix molecules and undergo oxidation, which increases formation of reactive oxygen species, such as superoxide anion and hydrogen peroxide.[10,11] As a result, actions of endothelium-derived

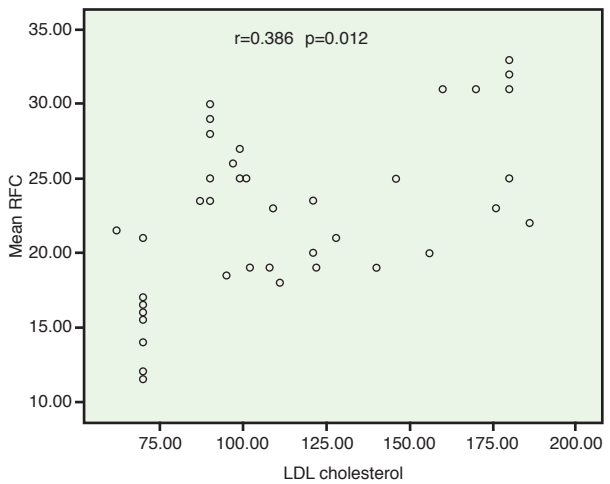

Figure 1. Scatter plot graphic of mean renal frame count and low-density lipoprotein cholesterol.

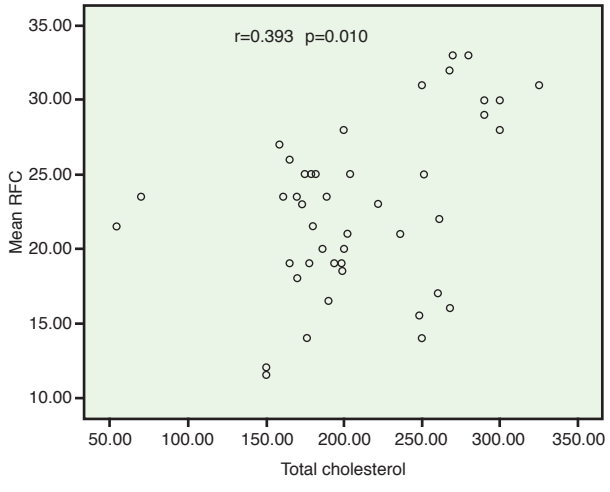

Figure 2. Scatter plot graphic of mean renal frame count and total cholesterol.

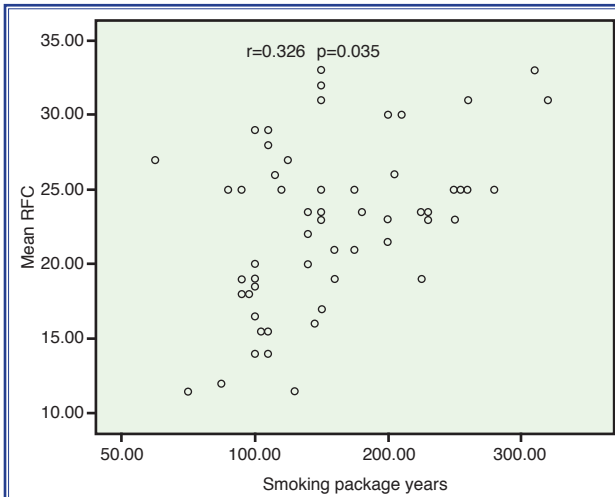

Figure 3. Scatter plot graphic of mean renal frame count and smoking pack-years.

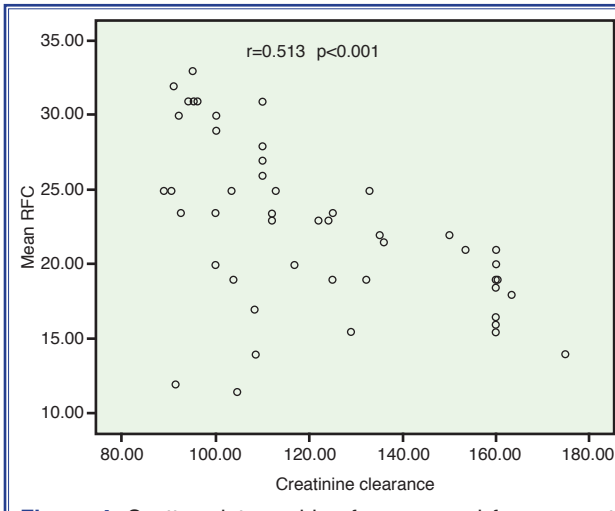

Figure 4. Scatter plot graphic of mean renal frame count and creatinine clearance.

vasodilators/growth inhibitors, such as prostacyclin and nitric oxide, decrease. This, in turn, leads to increased production of endothelium-derived vasoconstrictors/growth promoters, such as angiotensin II, endothelin-1, and plasminogen activator inhibitor-1, which has significant vascular and renal pathophysiological effects.[5] Phagocytosis of oxidized lipids by macrophages results in formation of foam cells that secrete cytokines, causing more macrophages to accumulate in the lesion and influence lipid deposition, endothelial cell function, and vascular smooth muscle cell proliferation.[5] Glomerular cells share some characteristics of atherosclerotic vessel wall endothelial cells, which lead progression of atherosclerosis and chronic kidney disease.[12] A rat study reported that hyperlipidemia increased glomerular and tubulointerstitial infiltration and aggravated glomerulosclerosis.[5,13] Another study with large nondiabetic population demonstrated positive and significant relationship between metabolic syndrome and risk for chronic renal disease and microalbuminuria.[14] In some studies, lipid-lowering therapy was reported to improve renal functions.[15–17] Satirapoj et al. reported that simvastatin treatment was associated with decrease in proteinuria in chronic kidney disease patients in addition to its lipid-lowering function.[16] Beneficial effects of statins may be result of inhibition of proliferation of cells such as mesangial, renal tubular, and vascular smooth muscle cells, and modulation of inflammatory response, inhibition of macrophage recruitment, activation, and fibrosis activity.[17] Although exact mechanism remains unclear, proliferation/apoptosis balance, down-regulation of inflammatory chemokines, and cytogenic messages mediated by Ras superfamily of GTPases may play some role in beneficial effects of lipid-lowering therapy.[15,17] However, data are scant and large-scale clinical trials are needed.

RFC, defined by Mulumudi et al., can be used as an indicator of renal perfusion, which is an indirect marker of renal function.[6] For optimal kidney perfusion, functional macrovascular and microvascular renal blood flow is required.[6,1819] Nuclear scintigraphy has traditionally been used to assess renal perfusion, and recently, computerized tomography, positron emission tomography, magnetic resonance imaging, and contrast-enhanced Doppler ultrasonography have been utilized to evaluate renal blood flow.[6] Mahmud et al. demonstrated that RFC decreased significantly after renal artery stenting, indicating recovery of renal perfusion.[1] In that study, high RFC value before renal artery stenting was accompanied by low creatinine clearance, which is indicator of glomerular filtration rate (GFR). This is an important finding that indicates role of high RFC as surrogate marker in clinical setting of decreased GFR. As a result of these studies, RFC can be assumed to be a practical measure of renovascular function.

In our study, patients with chronic hypertension using 2 or more antihypertensive drugs were evaluated. Significantly increased RFC in patients with LDL >130 mg/dL and TC >200 mg/dL may raise the need for more aggressive or earlier lipid-lowering therapy in these patient cohorts. Our findings regarding serum lipid parameters and RFC are interesting, as there was no overt renal failure or decrease in GFR beyond physiological limits. RFC was found to increase as exposure to smoking defined as pack-years. Similar to the catastrophic role of smoking in atherosclerotic coronary artery disease, it may have cumulative deleterious effect on renal functions, both at macro- and microvascular level. It has previously been reported that smoking is one of the most important factors in pathogenesis of hypertensive nephropathy.[20–22] In study conducted by Muhlhauser, risk of developing progressive kidney disease in diabetics who were smokers was much higher than for nonsmokers.[23] Additionally, relationship between chronic smoking and impairment of renal function, which was independent of age, has also been reported in studies.[24,25] Research of Regalado et al. indicated that smoking was the strongest independent risk factor for decrease in renal function in patients with severe essential hypertension.[26] In hypertensive patients, serum LDL, TC, and smoking pack-years were observed to be independent predictors of RFC in our study. Also, as a negatively independent predictor of RFC, creatinine clearance, a strong indicator of GFR, provides rationale to use RFC as a surrogate marker of GFR. These findings are important and may be useful in clinical practice to encourage smoking cessation, lifestyle and dietary modifications, and earlier initiation of antihyperlipidemic therapy using lower cut-off limits in hypertensive patients.

Study limitations

The major limitation of the current study is the relatively small sample size. Lack of assessment of urinary microalbumin to determine subtle renal failure

is another limitation. Also, we could not assess renal function with renal Doppler ultrasonography or renal blush grade, which would have added some much power to our statistical analyses. Large-scale studies that include antilipidemic therapy with follow-up renal angiograms in this patient cohort would be complimentary.

Conclusion

We can conclude that in hypertensive patients with normal GFR and renal function, serum LDL and TC levels may be predictors of increased RFC or decreased renal perfusion. In addition to serum lipid parameters, as traditional risk factor, smoking is an independent predictor of decreased renal perfusion. As a result, aggressive lipid-lowering therapy and smoking cessation may help to reduce risk of overt kidney failure by increasing renal perfusion.

Conflict-of-interest: None declared.

REFERENCES

1. Mahmud E, Smith TW, Palakodeti V, Zaidi O, Ang L, Mitchell CR, et al. Renal frame count and renal blush grade: quantitative measures that predict the success of renal stenting in hypertensive patients with renal artery stenosis. JACC Cardiovasc Interv 2008;1:286–92. [CrossRef]
2. Safian RD, Textor SC. Renal-artery stenosis. N Engl J Med 2001;344:431–42. [CrossRef]
3. Spitalewitz S, Reiser IW. Atherosclerotic renovascular disease. Am J Ther 1996;3:21–8. [CrossRef]
4. Buller CE, Nogareda JG, Ramanathan K, Ricci DR, Djurdjev O, Tinckam KJ, et al. The profile of cardiac patients with renal artery stenosis. J Am Coll Cardiol 2004;43:1606–13. [CrossRef]
5. Trevisan R, Dodesini AR, Lepore G. Lipids and renal disease. J Am Soc Nephrol 2006;17:S145–7. [CrossRef]
6. Mulumudi MS, White CJ. Renal frame count: a quantitative angiographic assessment of renal perfusion. Catheter Cardiovasc Interv 2005;65:183–6. [CrossRef]
7. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. Eurointervention 2005;1:219–27.
8. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol 1983;51:606. [CrossRef]
9. Hovind P, Rossing P, Tarnow L, Smidt UM, Parving HH. Remission and regression in the nephropathy of type 1 diabetes when blood pressure is controlled aggressively. Kidney Int 2001;60:277–83. [CrossRef]
10. Abrass CK. Cellular lipid metabolism and the role of lipids in progressive renal disease. Am J Nephrol 2004;24:46–53.
11. Chait A, Heinecke JW. Lipoprotein modification: Cellular mechanisms. Current Opin Lipidol 1994;5:363–70. [CrossRef]
12. Wheeler DC, Chana RS. Interaction between lipoproteins, glomerular cells and matrix. Miner Electrolyte Metab 1993;19:149–64.
13. Scheuer H, Gwinner W, Hohbach J, Gröne EF, Brandes RP, Malle E, et al. Oxidant stress in hyperlipidemia-induced renal damage. Am J Physiol Renal Physiol 2000;278:63–74.
14. Chen J, Muntner P, Hamm LL, Jones DW, Batuman V, Fonseca V, et al. The metabolic syndrome and chronic kidney disease in US adults. Ann Intern Med 2004;140:167–74. [CrossRef]
15. Oda H, Keane WF. Recent advances in statins and the kidney. Kidney Int Suppl 1999;71:2–5. [CrossRef]
16. Satirapoj B, Promrattanakun A, Supasyndh O, Choovichian P. The Effects of Simvastatin on Proteinuria and Renal Function in Patients with Chronic Kidney Disease. Int J Nephrol 2015;2015:485839. [CrossRef]
17. Buemi M, Senatore M, Corica F, Aloisi C, Romeo A, Cavallaro E, et al. Statins and progressive renal disease. Med Res Rev 2002;22:76–84. [CrossRef]
18. Radermacher J, Chavan A, Bleck J, Vitzthum A, Stoess B, Gebel MJ, et al. Use of Doppler ultransonography to predict the outcome of therapy for renal-artery stenosis. N Engl J Med 2001;344:410–7. [CrossRef]
19. Myers DI, Poole LJ, Imam K, Scheel PJ, Eustace JA. Renal artery stenosis by three-dimensional magnetic resonance angiography in type 2 diabetics with uncontrolled hypertension and chronic renal insufficiency: prevalance and effect on renal function. Am J Kidney Dis 2003;41:351–9. [CrossRef]
20. Tylicki L, Puttinger H, Rutkowski P, Rutkowski B, Horl WH. Smoking as a risk factor for renal injury in essential hypertension. Nephron Clin Pract 2006;103:121–8. [CrossRef]
21. Orth SR, Ritz E. The renal risk of smoking: an update. Curr Opin Nephrol Hypertens 2002;11:483–8. [CrossRef]
22. Orth SR. Effects of smoking on systemic and intrarenal hemodynamics: influence on renal function. J Am Soc Nephrol 2004;15:S58–63. [CrossRef]
23. Muhlhauser I. Cigarette smoking and diabetes:an update. Diabet Med 1994;11:336–43. [CrossRef]
24. Gambaro G, Verlato F, Budakovic A, Casara D, Saladini G, Del Prete D, et al. Renal impairment in chronic cigarette smokers. J Am Soc Nephrol 1998;9:562–7.
25. Pinto-Sietsma SJ, Mulder J, Janssen WM, Hillege HL, de Zeeuw D, de Jong PE. Smoking is related to albuminuria and abnormal renal function in nondiabetic persons. Ann Intern Med 2000;133:585–91. [CrossRef]
26. Regalado M, Yang S, Wesson DE. Cigarette smoking is associated with augmented progression of renal insufficiency in severe essential hypertension. Am J Kidney Dis 2000;35:687–94.

Keywords: Cholesterol; hypertension; low-density lipoprotein; renal frame count; smoking.

Anahtar sözcükler: Kolesterol; hipertansiyon; düşük yoğunluklu lipoprotein; renal kare sayısı; sigara.