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ORIGINAL ARTICLE

Elevated Serum Uric Acid to HDL-Cholesterol Ratio is Related to Cardiovascular Risk in Patients Receiving Hemodialysis

Hemodiyaliz Hastalarında Yüksek Serum Ürik Asit/HDL-Kolesterol Oranı Kardiyovasküler Risk ile İlişkilidir

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ABSTRACT

Aim: Chronic kidney disease (CKD) is a progressive disease in which frequent cardiovascular (CV) comorbidities. High uric acid to HDL-cholesterol ratio (UHR) results were quite notable in patients receiving peritoneal dialysis. Thus, in this study, we aimed to evaluate the UHR results in dialysis patients.
Materials and Methods: This retrospective, multicenter, cross-sectional study was conducted with CKD patients, and the control group consisted of hypertensive patients with a normal glomerular filtration rate (GFR). Patients' laboratory, ambulatory blood pressure monitoring, and demographic records were obtained from the follow-up cases of two university hospitals' internal medicine and nephrology departments. The patients' group then were divided into five subsets according to GFR.
Results: A total of 124 CKD patients and 127 control participated in this study. All CKD patients were also identified as pre-dialysis and dialysis. The cases of UHR, non-dipper blood pressure pattern, and nocturnal heart rate (HR) were increased in CKD compared to the control group. Per disease progression, the non-dipper HR and nocturnal HR were more significant in patients receiving dialysis with high UHR than in the pre-dialysis subset. In diabetic patients with an on-targeted HbA1c, those with high UHRs still had nocturnal diastolic BP elevations. Finally, there was not an exact stage-specific result for pulse wave velocity.
Conclusions: Based on our results, dialysis patients with high UHRs have higher non-dipper pulse rate, nocturnal heart rate, and nocturnal diastole blood pressure, associated with CV risk. Despite well-managed diabetes, elevated UHR in dialysis patients may be associated with non-dipper hypertension.

Key words: Ambulatory blood pressure monitoring, Cardiovascular risk, Diabetes mellitus, Hemodialysis, High-density lipoprotein, Serum uric acid.

ÖZ

Amaç: Kronik böbrek hastalığı (KBH), kardiyovasküler (KV) komorbiditelerin sık olduğu ilerleyici bir hastalıktır. Yüksek ürik asit/HDL-kolesterol oranı (UHR) sonuçlarının periton diyalizi alan hastalarda dikkate değer bulunmuştur. Bu çalışmada bu nedenle diyaliz hastalarında UHR sonuçlarını değerlendirmeyi amaçladık.
Gereç ve yöntem: Bu retrospektif, çok merkezli, kesitsel çalışma KBH hastaları ile normal glomerüler filtrasyon hızına (GFR) sahip hipertansif hastaları içeren bir kontrol grubu ile yürütüldü. Laboratuvar, ayaktan kan basıncı takibi ve demografik kayıtları iki üniversite hastanesinin dahiliye ve nefroloji bölümlerinden temin edildi. Hasta grubu daha sonra GFR'ye göre beş alt gruba ayrıldı.
Bulgular: Çalışmaya toplam 124 KBH hastası ve 127 kontrol katıldı. Tüm KBH hastaları ayrıca prediyalitik ve diyalitik olarak tanımlandı. KBH'li grupta UHR, non-dipper kan basıncı paterni ve gece kalp hızı (KH) kontrol grubuna göre artmıştı. Non-nipper KH ve gece KH, yüksek UHR'si olan diyaliz hastalarında prediyalitik olanlara göre hastalık progresyonuyla daha anlamlıydı. HbA1c'si hedefte olan diyabetik hastalardan yüksek UHR'leri olanlarda hala gece diyastolik KB yükselmeleri vardı. Son olarak, nabız dalga hızı için evreye özel bir sonuç yoktu.
Sonuç: Sonuçlarımıza göre, yüksek UHR'leri olan diyaliz hastaları, KV riskle ilişkili olarak daha yüksek non-dipper nabız hızı, gece KH ve gece diyastol kan basıncına sahiptir. Ayrıca, iyi önetilebilen diyabete rağmen, diyaliz hastalarında UHR yüksekliği non dipper hipertansiyon ile ilişkili olabilir.

Anahtar kelimeler: Ambulatuar kan basıncı takibi, Diabetes mellitus, Hemodiyaliz, Kardiyovasküler risk, Yüksek yoğunluklu lipoprotein, Serum ürik asidi.

Introduction

Chronic kidney disease (CKD) is a progressive disease in which abnormal kidney function and structure changes are seen (1). Uncontrolled CKD has a rapid pathological progression process (2). CKD's main marked laboratory finding is a decrease in glomerular filtration rate (GFR) (3). Thus, hemodialysis is one of the

temporary treatment regimens in low GFR levels (<15 ml/min / 1.73 m2) (4).

Compared to other chronic diseases, CKD patients are more prone to complications in both pre-dialysis and dialysis stages (5-7). Complications such as impaired immune defense, an accelerated vascular deformation, accumulation of amyloid protein in an intercellular matrix, and formation of defects in neurons and support tissue repair should be expected in patients with poor control. This circumstance is more common in diabetic patients (8). Moreover, CKD is solitary associated with increased cardiovascular (CV) disease risk compared to the risk of coronary heart disease and diabetes mellitus (9, 10). Non-dipper circadian blood pressure (BP) rhythm also increases CV risk in patients with CKD (11, 12).

To date, many different criteria predicting CKD progression have been evaluated. High serum uric acid (sUA) levels are evaluated as a low prognostic factor in many diseases (13). Similarly, a low high-density lipoprotein (HDL) level is evaluated to indicate a poor prognosis in vascular diseases (14). In addition, the ratio of sUA to HDL is used as a new criterion in many cases with vascular events (15, 16). In this context, the sUA / HDL ratio (UHR) was associated with CV mortality in patients undergoing peritoneal dialysis (17).

This study thus aimed to compare UHR results in patients with CKD and evaluate UHR relations with the ambulatory blood pressure monitoring (ABPM) recordings associated with CV risk.

Methods

This research is a retrospective, cross-sectional study conducted in 2020. An approval numbered 2020/525 was obtained from the ethics committee of the university. Since the components of the calculated UHR results (sUA and HDL) in the study differ by gender, the reference values were re-defined according to gender and categorized accordingly. All GFRs were calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula, and results above 60 mL/min/1.73m3 were considered normal (18). In the study, a control group included the records of hypertensive patients over 18 years of age, have a normal GFR, without documented kidney damage, and the patient group had the records of the patients over 18 years of age, stage 1 to 5 CKD, and ongoing dialysis for stage 5. The last two years' patient records were obtained from two university hospitals' internal medicine and nephrology departments. The patients' demographic characteristics, the use of drugs that interact with uric acid and cholesterol metabolism, and the current laboratory results for CKD staging were noted. In the groups' creation, those with low GFRs within the last three months were chosen. As a result, two subgroups were formed as dialysis and non-dialysis patients in the patient group. The non-dialysis group was also divided into five subgroups according to renal clearance (Figure 1). Patients with a renal clearance below 15 mL/min/1.73m3 who have not yet received hemodialysis were also included in stage 5. Like the patient group, the used drugs that would interact with the UHR results (19, 20) and triglyceride results above 400 mg/dL (21) were excluded.

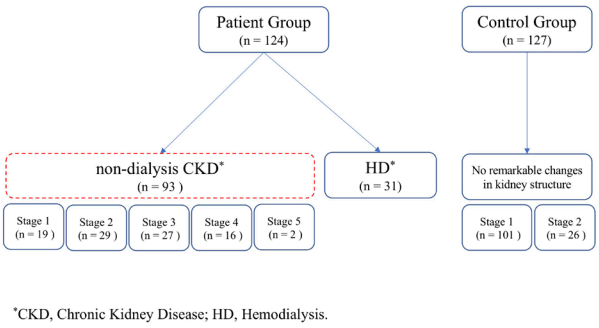

Figure 1: Study design of patients and control group.

All participants in the study were followed up with a brachial-based ABPM oscillometric device (Mobil-O-Graph, IEM, Stolberg, Germany) that registers BP, heart rate, (HR) and pulse wave velocity (PWV) every 15 minutes during the day and every 30 minutes at night. Accordingly, the mean, daytime, and nocturnal values of the systolic and diastolic BP, the HR, the pulse pressure were derived from the recorded data. Patients having invalid measurements of more than 20% were excluded from the study. In the records, a HR non-dipper status was defined as (daytime HR - nocturnal HR) / daytime HR < 0.1 (22).

In the UHR calculation, which is the focus of our study, as it is already known that there are differences in the reference values of both sUA and HDL according to gender, a laboratory database of a current study conducted in our country was taken as a local reference. A proper sUA and HDL reference levels were redefined for the male and female gender (23). Accordingly, all sUA and HDL values were classified as low, normal, or high. UHR results were calculated as the ratio of sUA (mg/dl) to HDL (mg/dl). Results are expressed as a percentage.

Statistical analysis: Statistical analyses were performed using SPSS version 21 (SPSS Inc., Chicago, IL, USA). The distribution of the data obtained was determined. The Pearson correlation was used to compare normally distributed data, whereas the Spearman correlation was used for non-normal data. An independent sample t-test was applied to identify the UHR results in significance between the patient and control groups. In subgroup analysis, nonparametric tests were preferred due to the decrease in the number of patients. An independent sample t-test was used in the group with a normal distribution to evaluate the difference between the predialysis group and the dialysis group.

In contrast, the Kruskal Wallis test and the Mann Whitney U test were used in non-dispersed data of

the predialysis subgroups. Intergroup significance evaluations were made using the chi-square test. For all statistical significance, the p-value <0.05 was considered significant.

Results

At first, 314 patient files were reviewed. Five patients received allopurinol for gout prophylaxis in the patient group, four patients' results were out of date, and twelve patients had low GFR for less than 6 months. In the control group, eleven patients were documented to have renal damage, fifteen patients' cholesterol results were not updated. Finally, the oscillometric data of sixteen patients from both groups did not match the minimum record criteria. They were all excluded from the study. As a result, 251 patient files, including the years 2019-2020, were evaluated. The demographic, clinical characteristics and ABPM results of both groups are summarized in Table 1 and 2.

The sUA results above 428 mmol/L (7,195 mg/dl) in men and 357 mmol/L (6.002 mg/dl) in women were considered high, whereas, the HDL results below 1.05 mmol/L (40 mg/dl) in men and 1.32 mmol/L (50 mg/dl) in women was considered low (23). Accordingly, for UHR, results above 0.12 for females and above 0.18 for males were considered high.

In the ungrouped data, UHR was negatively correlated with GFR (p = 0.001, r =-0.249), unlike positively correlated with BMI (p = 0.005, r = 0.176). In the patient group, UHR was positively correlated (p = 0.006, r = 0.245) with BMI and negatively correlated with non-dipper HR (p = 0.018, r =-0.213). Conversely, UHR was positively correlated with diastolic BP (p = 0.023, r =0.201) and mean arterial pressure (p = 0.033, r =0.189) and negatively correlated with GFR (p = 0.002, r =-0.271) in the control group.

In addition, an independent t-test showed a statistically significant difference between patients and control groups with a 95% confidence interval for UHR's (p = 0.007, Ƞ2 = 0.029), for non-dipper blood pressure pattern (p = 0.001, Ƞ2 = 0.077), for nocturnal HR (p = 0.001, Ƞ2 = 0.072), and for systolic blood pressure at night (p = 0.024, Ƞ2 = 0.020). When ABPM data were evaluated in the patient group, a Kruskal Wallis analysis revealed a statistical difference in non-dipper circadien rythym (p = 0.002), night HR (p = 0.001), and PWV results (PWVmean, p = 0.003; PWVdaylight, p = 0.019; PWVnight, p = 0.022) at disease stages. The most remarkable difference between CKD subgroups was between stages 1 and 4. Additionally, the increase in nocturnal diastolic BP at stage 5, the increase in non-dipper HR at stage 4, and the increase in systole and diastole BP at stage 3 were prominent. The same analysis did not present any statistical difference in the control group except for PWVdaylight (p = 0.003).

In subgroup analysis, there were differences in non-dipper HR (p = 0.015) and nocturnal HR (p = 0.011) between non-dialysis and hemodialysis groups with high UHR results (Figure 2a - 2b). In addition, an increase in nocturnal diastole BP was found in patients receiving dialysis with high UHR (p = 0.040) (Figure 3a). While there was no difference between the groups in men in a gender-based evaluation, there was a statistically significant increase in non-dipper HR (p = 0.009) (Figure 3b) and nocturnal HR (p = 0.019) in women (Figure 3c).

The number of diabetic patients in the patient group was 27 in the non-dialysis group and 7 in the dialysis group. In comparing diabetic treatment achievements, there was no effect of targeted HbA1c (>6.5 %, >7.77 mmol/L) (24) on ABPM results in patients with high UHR (Figure 4).

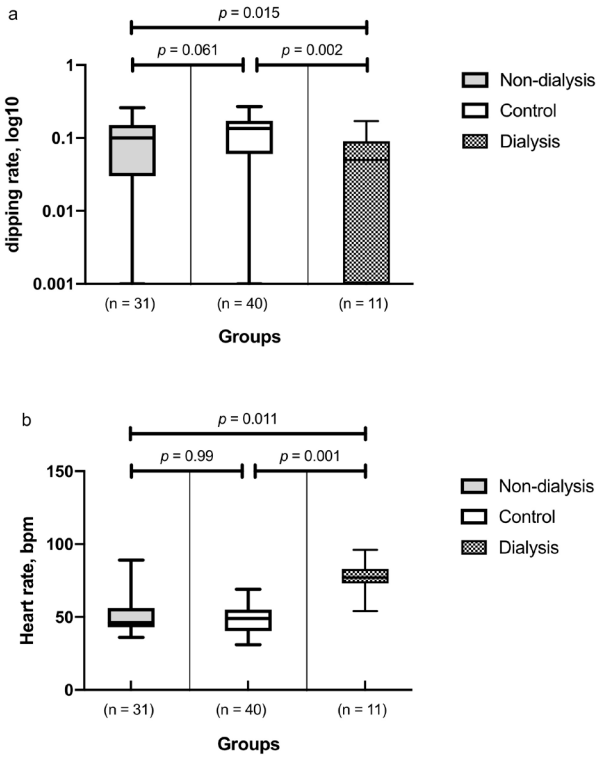

Figure 2: **a)** Dipping heart rates comparisons in all groups with high UHRs, **b)** Nocturnal heart rate distributions in all groups with high UHRs.

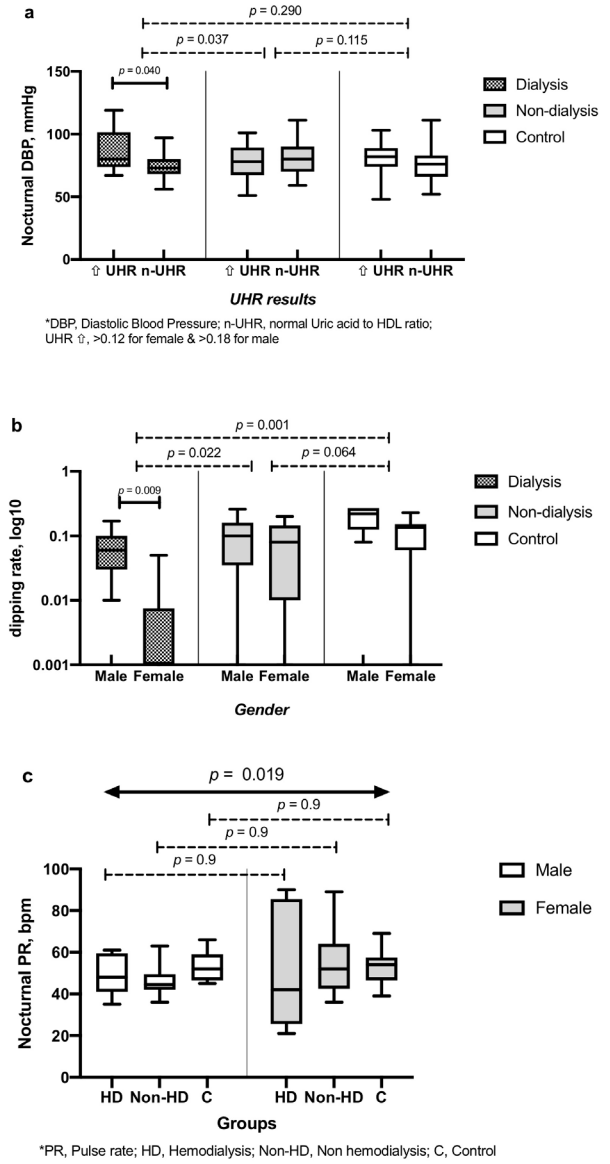

Figure 3: a) High UHR outcomes on nocturnal heart rate in dialysis and non-dialysis group compare to controls, b) The gender effect on dipping rate in all groups, c) Nocturnal pulse rate distributions in all groups per gender.

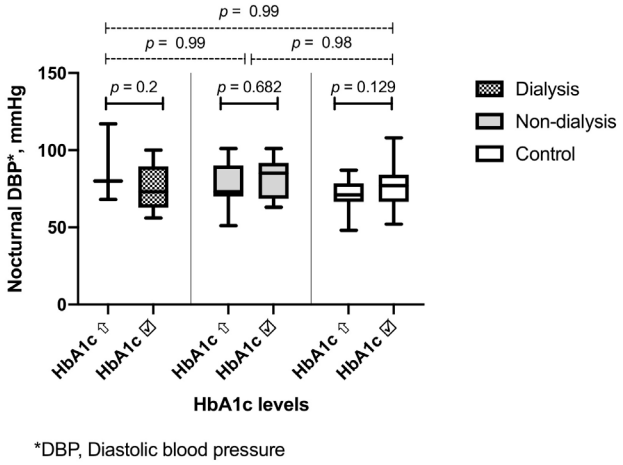

Figure 4: Nocturnal diastolic blood pressure levels in all groups according to the diabetes management achievement.

Discussion

In this retrospective, cross-sectional study, we found that; UHR is increased in patients with CKD; significantly higher UHR levels in patients receiving HD are associated with non-dipper BP and nocturnal HR. Moreover, the female gender was affected by this unfavorable condition.

Prior studies have noted the importance of more sUA and HDL in various vascular diseases. High levels of sUA and low HDL levels were directly related to mortality in patients receiving dialysis (25, 26). On the contrary, there is evidence that low SUA levels also contribute to mortality in hemodialysis patients (27). Therefore, new approaches are expressed on the sUA topic (28).

Similarly, remarkable researches have been done regarding HDL in vascular diseases (29-32). As in sUA, a high HDL result is considered a risk factor (33, 34). In other words, it seems that the risk factors related to diseases represented by the outliers of both sUA and HDL results are increasing. The results with the ratio of such mutable two parameters should be interpreted differently in various diseases. Contrary to expectations, HDL studies conducted with UHR reveal similar results (15, 16, 35). Nevertheless, it may be inconvenient to follow a standart reference interval in these two parameters, whose interpretation varies according to gender.

UHR was associated with determining mortality in patients undergoing peritoneal dialysis in a study conducted in terms of ratio, which was also inspired by our study (12). In the retrospective cohort study in which male patients were predominant, UHRs were divided into four quarters, and the least survival was detected in quarter 4 with the highest UHR results. In addition, UHR was negatively correlated with GFR and positively correlated with BMI and HbA1c in the study. In our retrospective study, we compared patients with CKD and those with normal kidney functions in terms of UHR. As a result, similar to the current study, we found a negative correlation between UHR and GFR, a positive correlation with BMI, and a statistically significant difference compared to the control group.

In subgroup analysis, we found that the UHR was higher in patients receiving hemodialysis than in predialytics, and the female gender was affected in both cases. In evaluating the results of diabetic patients receiving dialysis, intriguingly, on-target HbA1c did not differ in terms of CV risk in patients with higher UHRs. However, the higher UHR results in patients whose more HbA1c was not on-targeted seemed to be related to low HDL rather than high sUA. This may be more likely that patients with abnormal HbA1c will cause low HDL due to cholesterol disorder. Nevertheless, high UHR may predict CV risk even if the diabetes treatment was accomplished.

Furthermore, there may be circumstances where peritoneal dialysis, which is one of the renal replacement therapies, is superior to hemodialysis (36). Because the dialysates used in peritoneal dialysis have an extra glucose load, the cholesterol balance may also worsen in patients receiving dialysis (37). Therefore, this can be expected that HDL results will be low, plus UHR results will be higher. In this context, cholesterol results will be more consistent in hemodialysis patients than in peritoneal dialysis.

A strong relationship between the effects of non-dipper BP and the CV system in patients with non-dialysis CKD has been reported in the literature (11). Accordingly, hypertension was the leading risk factor for the early prediction of CV disease progression (11). Findings were similar for patients receiving HD (38). There were numerous studies in the literature evaluating uric acid and HDL concurrently. Except for the study conducted by Liu et al., a ratio-based result such as the UHR that predicts CV risk in patients with CKD receiving renal replacement therapy has not been notified yet (17). Per the current findings, our study determined increases in non-dipper BP, nocturnal HR, and nocturnal diastolic BP results in hemodialysis patients with high UHR. Decreased renal clearance will increase diastolic BP (39), and BP was closely correlated with cardiac structure changes (11). Therefore, these undesired impacts would be more significant in CKD patients with advanced stages, especially in dialysis patients with non-dipper BP who often have other chronic diseases such as diabetes and hypertension with appending vascular complications (40). There was no statistical significance in the intergroup evaluation of PWV, which indicates another CV risk (41). However, this result may be attributed to the fact that the control group consisted of hypertensive patients. In addition, the PWV differences between CKD subgroups were not stage-specific. This uncertainty was likely to be due to multifactorial causes in CKD patients, especially per disease progression.

In addition, in contrast to current findings, the female gender is affected. This result may be explained by the fact that laboratory reference ranges vary according to gender; more proper reference ranges were used in the study, as in our case. We again ranked the reference intervals by gender for both sUA and HDL according to the local population (23). Another possible explanation for this is that the laboratory results in various studies were interpreted by gender; however, the same reference intervals should not be interpreted to both gender.

The first prominent lack in our study was that patients with diabetes were more likely to have high lipid levels due to abnormal blood glucose levels. However, we have included all comorbidities so that the study can cover all patients with CKD. Secondly, healthy individuals were not preferred in selecting the control group because it was clear that there would be bias for the UHR rate. Thus, the control group was formed from patients with HT. Finally, no objective cardiac evaluations have been performed to demonstrate cardiac risks correlated with abnormal results in ABPM.

In conclusion, higher UHR levels are associated with non-dipped BP and nocturnal HR elevation in patients receiving HD, indicating a higher CV risk. Moreover, the CV risk increased in diabetic dialysis patients with high UHRs even if HbA1c levels were on target.

Declarations

Financial support: No financial support was used in this study.

Conflict of interest: There was no conflict of interest between the authors in this study.

References

1.Meola M, Samoni S, Petrucci I. Clinical Scenarios in Chronic Kidney Disease: Kidneys' Structural Changes in End-Stage Renal Disease. Contrib Nephrol 2016;188:131-43.

2.Cha RH, Lee H, Lee JP, Kim YS, Kim SG. The influence of blood pressure patterns on renal outcomes in patients with chronic kidney disease: The long-term follow up result of the APrODiTe-2 study. Medicine (Baltimore) 2020;99(8):e19209.

3.Swinkels DW, Hendriks JC, Nauta J, de Jong MC. Glomerular filtration rate by single-injection inulin clearance: definition of a workable protocol for children. Ann Clin Biochem 2000;37 (Pt 1):60-6.

4.Vaidya SR, Aeddula NR. Chronic Renal Failure. StatPearls. Treasure Island (FL)2020.

5.Muniz-Junqueira MI, Braga Lopes C, Magalhaes CA, Schleicher CC, Veiga JP. Acute and chronic influence of hemodialysis according to the membrane used on phagocytic function of neutrophils and monocytes and pro-inflammatory cytokines production in chronic renal failure patients. Life Sci 2005;77(25):3141-55.

6.Mataradzija A, Resic H, Rasic S, Kukavica N, Masnic F. Risk factors for development of cardiovascular complications in patients with chronic renal disease and diabetic nephropathy. Bosn J Basic Med Sci 2010;10 Suppl 1:44-50.

7.Guerrero A, Montes R, Munoz-Terol J, et al. Peripheral arterial disease in patients with stages IV and V chronic renal failure. Nephrol Dial Transplant 2006;21(12):3525-31.

8.Zaoui P, Hannedouche T, Combe C. [Cardiovascular protection of diabetic patient with chronic renal disease and particular case of end-stage renal disease in elderly patients]. Nephrol Ther 2017;13(6S):6S16-6S24.

9.Tonelli M, Muntner P, Lloyd A, et al. Risk of coronary events in people with chronic kidney disease compared with those with diabetes: a population-level cohort study. Lancet 2012;380(9844):807-14.

10.Major RW, Cheng MRI, Grant RA, et al. Cardiovascular disease risk factors in chronic kidney disease: A systematic review and meta-analysis. PLoS One 2018;13(3):e0192895.

11.Che X, Mou S, Zhang W, et al. The impact of non-dipper circadian rhythm of blood pressure on left ventricular hypertrophy in patients with non-dialysis chronic kidney disease. Acta Cardiol 2017;72(2):149-55.

12.Baka T, Simko F. Nondipping heart rate: A neglected cardiovascular risk factor based on autonomic imbalance? Auton Neurosci 2018;210:83-4.

13.Pehlivanlar-Kucuk M, Kucuk AO, Ozturk CE, Er MC, Ulger F. The

Association Between Serum Uric Acid Level and Prognosis in Critically Ill Patients, Uric Acid as a Prognosis Predictor. Clin Lab 2018;64(9):1491-500.

14.Correia LC, Rocha MS, Esteves JP. HDL-cholesterol level provides additional prognosis in acute coronary syndromes. Int J Cardiol 2009;136(3):307-14.

15.Aktas G, Kocak MZ, Bilgin S, Atak BM, Duman TT, Kurtkulagi O. Uric acid to HDL cholesterol ratio is a strong predictor of diabetic control in men with type 2 diabetes mellitus. Aging Male 2019:1-5.

16.Zhang YN, Wang QQ, Chen YS, Shen C, Xu CF. Association between Serum Uric Acid to HDL-Cholesterol Ratio and Nonalcoholic Fatty Liver Disease in Lean Chinese Adults. Int J Endocrinol 2020;2020:5953461.

17.Liu R, Peng Y, Wu H, et al. Uric acid to high-density lipoprotein cholesterol ratio predicts cardiovascular mortality in patients on peritoneal dialysis. Nutr Metab Cardiovasc Dis 2021;31(2):561-9.

18.Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150(9):604-12.

19.Raja S, Kumar A, Aahooja RD, Thakuria U, Ochani S, Shaukat F. Frequency of Hyperuricemia and its Risk Factors in the Adult Population. Cureus 2019;11(3):e4198.

20.Dybro AM, Damkier P, Rasmussen TB, Hellfritzsch M. Statin-associated rhabdomyolysis triggered by drug-drug interaction with itraconazole. BMJ Case Rep 2016;2016.

21.Martin SS, Blaha MJ, Elshazly MB, et al. Friedewald-estimated versus directly measured low-density lipoprotein cholesterol and treatment implications. J Am Coll Cardiol 2013;62(8):732-9.

22.Cuspidi C, Meani S, Negri F, Valerio C, Sala C, Mancia G. Is blunted heart rate decrease at night associated with prevalent organ damage in essential hypertension? Blood Press Monit 2011;16(1):16-21.

23.Ozarda Y, Ichihara K, Aslan D, et al. A multicenter nationwide reference intervals study for common biochemical analytes in Turkey using Abbott analyzers. Clin Chem Lab Med 2014;52(12):1823-33.

24.Kowall B, Rathmann W. HbA1c for diagnosis of type 2 diabetes. Is there an optimal cut point to assess high risk of diabetes complications, and how well does the 6.5% cutoff perform? Diabetes Metab Syndr Obes 2013;6:477-91.

25.Zawada AM, Carrero JJ, Wolf M, et al. Serum Uric Acid and Mortality Risk Among Hemodialysis Patients. Kidney Int Rep 2020;5(8):1196-206.

26.Chang TI, Streja E, Soohoo M, et al. Association of Serum Triglyceride to HDL Cholesterol Ratio with All-Cause and Cardiovascular Mortality in Incident Hemodialysis Patients. Clin J Am Soc Nephrol 2017;12(4):591-602.

27.Li M, Ye ZC, Li CM, et al. Low serum uric acid levels increase the risk of all-cause death and cardiovascular death in hemodialysis patients. Ren Fail 2020;42(1):315-22.

28.Wang W, Liu W, Zhao Z, Zhao Y, Zhao C. High uric acid or low uric acid which is better for hemodialysis patients? Ren Fail 2020;42(1):759.

29.Igase M, Kohara K, Igase K, et al. Deep cerebral microbleeds are negatively associated with HDL-C in elderly first-time ischemic stroke patients. J Neurol Sci 2013;325(1-2):137-41.

30.Perrella J, Berco M, Cecutti A, Gerulath A, Bhavnani BR. Potential role of the interaction between equine estrogens, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) in the prevention of coronary heart and neurodegenerative diseases in postmenopausal women. Lipids Health Dis 2003;2:4.

31.Federici AB. HDL/ApoA-I: role in VWF-dependent thrombosis. Blood 2016;127(5):526-8.

32.Cetin EH, Cetin MS, Canpolat U, et al. Monocyte/HDL-cholesterol ratio predicts the definite stent thrombosis after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Biomark Med 2015;9(10):967-77.

33.Brown WV. The disparity between the very strong performance of high-density lipoprotein (HDL) cholesterol as a risk factor and the very weak effects. Foreword. J Clin Lipidol 2010;4(1):1.

34.Espinosa-Larranaga F, Vejar-Jalaf M, Medina-Santillan R, Latin American G. The importance of low serum levels of high-density lipoprotein cholesterol (HDL-C) as a cardiovascular risk factor. Diab Vasc Dis Res 2005;2 Suppl 1:1-8.

35.Onat A, Can G, Ornek E, Altay S, Yuksel M, Ademoglu E. Elevated serum uric acid in nondiabetic people mark pro-inflammatory state and HDL dysfunction and independently predicts coronary disease. Clin Rheumatol 2013;32(12):1767-75.

36.Sinnakirouchenan R, Holley JL. Peritoneal dialysis versus hemodialysis: risks, benefits, and access issues. Adv Chronic Kidney Dis 2011;18(6):428-32.

37.Wei X, Wen Y, Zhou Q, et al. Hyperlipidemia and mortality associated with diabetes mellitus co-existence in Chinese peritoneal dialysis patients. Lipids Health Dis 2020;19(1):234.

38.Rahman M, Griffin V, Heyka R, Hoit B. Diurnal variation of blood pressure; reproducibility and association with left ventricular hypertrophy in hemodialysis patients. Blood Press Monit 2005;10(1):25-32.

39.Hamrahian SM, Falkner B. Hypertension in Chronic Kidney Disease. Adv Exp Med Biol 2017;956:307-25.

40.MacRae C, Mercer SW, Guthrie B, Henderson D. Comorbidity in chronic kidney disease: a large cross-sectional study of prevalence in Scottish primary care. Br J Gen Pract 2021;71(704):e243-e9.

41.Sequi-Dominguez I, Cavero-Redondo I, Alvarez-Bueno C, Pozuelo-Carrascosa DP, Nunez de Arenas-Arroyo S, Martinez-Vizcaino V. Accuracy of Pulse Wave Velocity Predicting Cardiovascular and All-Cause Mortality. A Systematic Review and Meta-Analysis. J Clin Med 2020;9(7).

Table 1. Demographics characteristics and laboratory findings of the groups			
	Patient (n = 124)	Control (n = 127)	*P* value
Characteristics			
Males, n (%)	69 (55.6)	62 (48.8)	0.381
Age	52.6±15.4	51.3±12.6	0.464
BMI	28.3±5.6	27.6±4.3	0.254
DM, n (%)	34 (27)	29 (23)	0.468
HT, n (%)	124 (96)	127 (100)	0.117
CKD stage			
Stage 1, n (%)	19 (15.3)	101 (79.5)	0.021
Stage 2, n (%)	29 (23.4)	26 (20.5)	0.001
Stage 3, n (%)	27 (21.8)	-	NA
Stage 4, n (%)	16 (12.9)	-	NA
Stage 5, n (%)	33 (26.6)	-	NA
Stage 5- HD, n (%)	31 (93.94)	-	NA
Laboratory tests			
Glucose, mg/dL	99.5 (65 - 436)	97 (76 - 351)	0.114
HbA1c, %	8.23±2.29	7.14±1.66	0.049
Urea, mg/dL	67 (15 -294)	29 (15 -74)	0.001
Creatinine, mg/dL	1.32 (0.4 - 12)	0.74 (0.48 – 1.29)	0.001
eGFR (mL/min/1,73m^3)	56 (4.6 - 126)	102 (65 - 142)	0.001
Uric acid, mg/dL	6.38±1.65	5.48±1.35	0.001
Na, mEq/L	137.1±3.2	138.4±2.4	0.001
K, mEq/L	4.47±0.5	4.31±0.4	0.036
Ca, mg/dL	9.10±0.8	9.60±0.4	0.001
P, mg/dL	3.7 (1.7 – 7.6)	3.3 (2.3 – 5.3)	0.012
Albumin, g/dL	3.71±0.7	4.31±0.3	0.001
Mg, mg/dL	2.03±0.2	2.03±0.1	0.465
PTH, pg/mL	83 (15 - 758)	50.5 (9.1 - 126)	0.001
WBC, x10^9/L	7.71±2.15	7.48±1.7	0.893
Hb, g/dL	12.4±2.5	13.84±1.7	0.001
ANC, x10^9/L	5.01±1.8	4.48±1.6	0.806
ALC, x10^9/L	1.90±0.72	2.24±0.5	0.003
N/L r (%)	2.44 (1 – 9.46)	1,77 (0.9 – 5.94)	0.001
Platelet, x10^9/L	222 (105 - 723)	269 (130 - 420)	0.008
Cholesterol, mg/dL	211.6 (99 - 443)	211.7 (130 - 305)	0.614
Triglyseride, mg/dL	155 (43 - 386)	160 (48 - 348)	0.460
LDL, mg/dL	133.8 (54 - 345)	133.9 (68 -209)	0.784
HDL, mg/dL	47.5±13.5	46.9±11.2	0.692
Non-HDL, mg/dL	167.5±51.6	161.5±31.2	0.268
UHR (%)	14.41±5.7	12.80±4.4	0.007

P values are the comparison of patient and control groups. (Mann-Whitney U test, Independent-Samples t-test or the chi-square test); Data is the median n (%), or n/N (%); BMI, Body-mass index; CKD, Chronic kidney disease; DM, Diabetes Mellitus; HT, Hypertension; eGFR, Estimated glomerular filtration rate; HD, Hemodialysis; Na, Sodium; K, Potassium; Ca, Calcium; P, Phosphorus; Mg, Magnesium; PTH, Parathyroid hormone; WBC, White blood cell; Hb, Hemoglobin; ANC, Absolute neutrophil count; ALC, Absolute lymphocyte count; N/L r: Neutrophil-lymphocyte ratio; LDL, low-density lipoprotein; HDL, High-density lipoprotein; UHR, Uric acid to HDL ratio; NA, Not applicable.

Table 2: The distribution of UHRs of the CKD patients and control group per Holter Monitor (24 h) records.

Groups	CKD					Control
	Stage 1 (n = 19)	Stage 2 (n = 29)	Stage 3 (n = 27)	Stage 4 (n = 16)	Stage 5 (n = 33)	(n = 127)
Sistolic BP_{mean}, mmHg	129.42±19.68	136.10±13.74	136.92±16.33	138.12±16.90	137.72±21.08	131.32±13.82
Sistolic BP_{day}, mmHg	131.57±19.61	138.13±14.49	138.66±16.16	138.18±17.02	133.21±21.23	133.37±13.97
Sistolic BP_{night}, mmHg	122.26±20.22	130.58±15.03	130.59±18.25	140.25±19.19	131.15±22.60	125.62±15.46
Diastolic BP_{mean}, mmHg	83.63±12.18	86.27±13.85	83.77±9.22	82.25±11.39	84.03±16.05	82.44±11.48
Diastolic BP_{day}, mmHg	85.36±11.89	87.96±14.18	85.44±9.64	82.56±11.95	84.54±16.16	84.28±11.82
Diastolic BP_{night}, mmHg	78.10±14.20	81.06±15.03	78.59±9.10	81.87±12.04	83.48±16.35	77.43±12.34
MAP_{mean}, mmHg	104.57±14.80	108.96±12.99	108.11±10.78	100.5±26.21	106.21±17.39	104.85±11.91
MAP_{day}, mmHg	106.52±14.64	110.89±13.57	106.18±22.02	107.06±11.02	106.24±18.86	105.98±14.76
MAP_{night}, mmHg	98.31±16.41	103.82±13.98	102.48±11.67	107.31±13.46	105.03±18.30	99.50±13.14
HR_{mean}, bpm	79.21±7.24	76.31±10.41	76.48±10.98	84.43±17.63	84.42±10.52	75.88±10.07
HR_{day}, bpm	81.73±7.92	79.24±10.89	78.29±11.49	84.50±17.85	85.06±10.98	78.72±10.68
HR_{night}, bpm	71.68±7.80	69.20±9.48	69.40±11.30	79.56±17.43	79.93±11.66	67.66±9.46
PP_{mean}, mmHg	45.84±12.22	49.75±9.57	53.11±14.05	56.0±15.01	48.45±12.74	48.85±8.36
PP_{day}, mmHg	46.10±13.11	50.06±9.36	53.07±13.62	55.87±15.50	48.66±12.56	49.10±8.61
PP_{night}, mmHg	44.31±10.24	49.41±11.45	52.0±16.26	57.68±14.97	48.30±14.73	48.31±9.20
PWV_{mean},m/s	6.59±1.32	7.77±1.51	8.46±1.91	9.44±1.73	8.09±2.35	7.65±1.47
PWV_{day}, m/s	6.57±1.37	8.08±1.68	8.11±1.89	9.16±1.96	7.31±2.22	7.73±1.40
PWV_{night}, m/s	6.31±1.43	8.00±1.76	7.90±1.98	9.18±2.14	7.17±2.07	7.56±1.40
ND-PR, bpm	0.120±0.073	0.123±0.076	0.108±0.105	0.058±0.053	0.059±0.079	0.13±0.06
ND-PR, n (%)	5 (26.3)	11 (37.9)	13 (48.1)	12 (75)	25 (75.8)	34 (26.8)
ND-SBP, bpm	7.16 (0.63-10.95)	5.34 (0.36–10.6)	5.72 (0.1-12.7)	-1.74 (-3.33-2.84)	1.46 (-3.2–6.4)	5.74 (1.22-11.25)
ND-SBP, n (%)	12 (63.2)	21 (72.4)	18 (66.7)	15 (93.8)	28 (84.8)	89 (70.1)
UHR, mg/dL	0.118±0.035	0.141±0.048	0.154±0.046	0.137±0.052	0.152±0.066	0.126±0.039

BP, Blood pressure; CKD, Chronic kidney disease; MAP, Mean arterial pressure; ND, Non-dipping; PP, Pulse pressure; HR, Heart rate; PWV, Pulse wave velocity; UHR, Uric acid / HDL ratio