ONLINE FIRST

This is a provisional PDF only. Copyedited and fully formatted version will be made available soon.

arterial hypertension
JOURNAL OF THE POLISH SOCIETY OF HYPERTENSION

ISSN: 2449-6170

e-ISSN: 2449-6162

Serum uric acid level independently predicted metabolic syndrome in non-diabetic hypertensive patients

Authors: Ahmet Seyda Yılmaz, Fatih Kahraman, Elif Ergül, Haldun Koç, Mustafa Çetin

DOI: 10.5603/AH.a2022.0017

Article type: Original paper

Submitted: 2022-01-30

Accepted: 2022-11-06

Published online: 2022-11-07

Serum uric acid level independently predicted metabolic syndrome in non-diabetic hypertensive patients

Running head: Uric acid and Metabolic syndrome in hypertension

10.5603/AH.a2022.0017

Ahmet Seyda Yılmaz[1], Fatih Kahraman[2], Elif Ergül[1], Haldun Koç[1], Mustafa Çetin[1]

[1]*Recep Tayyip Erdogan University, School of Medicine, Rize, Turkey*
[2]*Kutahya Evliya Celebi Education and Research Hospital, Turkey*

Correspondence to: Ahmet Seyda Yılmaz, Recep Tayyip Erdogan University, School of Medicine, 53000 Rize, Turkey; e-mail: ahmetseydayilmaz@gmail.com

Abstract

Background: Arterial hypertension may accompany metabolic syndrome (MetS) which is strongly associated with cardiovascular diseases. Determining high-risk groups concerning MetS development is crucial to prevent this undesirable clinic. Serum uric acid level was demonstrated to be associated with development of hypertension and MetS in normal population. It was aimed to investigate the role of serum uric acid for the prediction of MetS in non-diabetic hypertensive individuals.

Material and methods: Patients who were diagnosed with arterial hypertension between January 2021 and June 2021 were included in the study. Diabetes mellitus was determined as an exclusion criteria. Metabolic syndrome was considered as the clustering of high blood pressure, elevated glucose level, abnormal cholesterol levels, and abdominal obesity conditions according to the National Cholesterol Education Program (NCEP) definition. Patients were divided into two groups by the presence of MetS.

Results: The mean age of 107 non-diabetic hypertensive patients was 48.5 ± 8.6 years and 50 (46.7%) of them were female. A total of 56 patients (52%) had MetS. Waist circumference (101.2 ± 11.3 *vs.* 106.7 ± 10.1 cm, p = 0.020), body mass index (30.6 ± 4.9 vs 32.8 ± 4.1, p = 0.016), E/e' ratio [9.2 (7.3–11.1) *vs.* 10.6 (9.1–13.4), p = 0.003], EAT [5.9 (4.8–8) *vs.* 7.9 (6–9.6), p = 0.006], and serum uric acid level (4.75 ± 1.10 *vs.* 5.82 ± 1.21 mg/dL, p < 0.001) were higher in MetS (+) group. Multivariable regression demonstrated that serum uric acid [(odds ratio) OR = 2.217, 95% confidence interval (CI): 1.300–3.783, p = 0.003] and body

mass index (OR = 1.214, 95% CI: 1.032–1.428, p = 0.019) were independent predictors of MetS presence.

Conclusion: Serum uric acid level predicted MetS presence in non-diabetic hypertensive individuals independently. This practical blood parameter can be used to evaluate those who are at risk of MetS development.

Key words: arterial hypertension; serum uric acid; metabolic syndrome; inflammation; insulin resistance

Introduction

Arterial hypertension (AH) is the leading preventable morbidity and mortality cause, despite the pharmacological and interventional management options are well developed. According to European reports, AH accounts for almost 10 million deaths and 200 million disabilities, globally [1]. Most particularly, metabolic syndrome (MetS) accompanying hypertension represents a higher risk group for adverse outcomes. MetS was described by World Health Organization (WHO) in 1998 firstly and following years, National Cholesterol Education Program (NCEP) devised the definition as the simultaneous presence of various metabolic conditions including abdominal obesity, high blood sugar, abnormal cholesterol levels, and high blood pressure [2]. Notwithstanding, this syndrome was shown to induce cardiovascular diseases in many previous studies since then [3]. Moreover, in those with hypertension, MetS is related to poorly controlled hypertension [4].

Uric acid (UA) is an end-product of purine metabolism. It was revealed a robust link between UA level and cardiovascular diseases (CVD), mortality, atherosclerosis, and AH in previous studies [5, 6]. The main underlying cause of these undesired consequences was attended to endothelial dysfunction secondary to proinflammatory and oxidant properties of serum UA. Besides, plasma renin activity was shown to be increased in hyperuricemia [7]. In addition, also being an independent predictor of AH development, hyperuricemia was shown to be correlated with increased incidence of non-dipper pattern, a higher intense form, of the AH. Furthermore, serum UA level was also demonstrated to be associated with glucose intolerance and MetS in the normal population as well as in patients with diabetes mellitus (DM) [8]. Nevertheless, serum UA level has not been evaluated as a risk marker for MetS in non-diabetic and hypertensive individuals. Therefore, we aimed to investigate the role of serum UA levels on MetS development in those with hypertension unless the presence of DM.

Material and methods

Study population

This is a cross-sectional study performed between January 2021 and June 2021, included a total of 107 consecutive newly diagnosed hypertensive patients. Past medical histories, socioeconomic features, physical examinations, and laboratory and echocardiographic data of each participant were obtained at admission and noted into the hospital database system. The study was conducted following the principles stated in the Declaration of Helsinki. Informed consent was gained from all patients and the local ethics committee approved the study protocol.

At least 30 minutes prior to the blood measurements, patients were asked not to be exercised and not to take alcohol and caffein-based beverages. A calibrated electronic sphygmomanometer was used to measure systolic and diastolic blood pressure after the individuals were positioned at a sitting position and quite environment. The AH diagnosis was created according to the current guidelines [1]. Body mass index (BMI) was calculated through the obtained weight and height parameters.

Exclusion criteria

Secondary hypertension, diabetes mellitus, acute or chronic inflammatory disease, coronary artery disease, moderate to severe valvular heart disease, abnormal liver and kidney functions suggesting moderate to severe hepatic or renal failure, malignancy, and/or taking chemo- and/or radiotherapy were determined as exclusion criteria.

Blood analysis

Complete blood count, biochemical test including blood glucose and lipid profile, and C-reactive protein (CRP) were tested after at least 12 hours of fasting in the laboratory of the institute. Serum UA level was measured by Roche Cobas C analyzer with colorimetric uricase method (Roche Diagnostics, Indianapolis, IN).

Transthoracic echocardiographic evaluation

Two-dimensional M-mode echocardiography was performed for all patients by Philips EPIQ 7 ultrasound system. Left ventricular dimensions and wall thicknesses were obtained. Left ventricular ejection fraction (LVEF) was calculated using modified Simpson's method. LA volume was measured at end-systolic apical 2- and 4- chamber frames. Planimetric trace was conducted to measure the LA border within the left atrial wall and mitral annulus borderline. Pulmonary veins’ ostium and left atrial appendage were not included in the

measurement. Doppler sample volume was placed at the mitral valve tips at the apical window and mitral inflow peak E and A velocities were obtained. Tissue Doppler imaging recordings demonstrated early diastolic (e') and late diastolic (a') mitral annulus velocities obtained from the lateral wall of the left ventricle. E/e' was calculated by dividing mitral E velocity to lateral annulus e' velocity. In addition, the hyper-echoic space on the free right ventricular wall from the parasternal long-axis image, by using aortic annulus as an anatomic reference in the end-systolic phase, was determined as epicardial adipose tissue (EAT).

Metabolic syndrome definition

National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) definition was regarded to define the presence of Mets: (I) Abdominal obesity defined by waist circumference ≥ 102 cm in males and ≥ 88 cm in females, (II) Triglyceride level ≥ 150 mg/dl, (III) High-density lipoprotein cholesterol (HDL-C) level < 40 mg/dl in male and < 50 mg/dl in female, (IV) Blood pressure >130/85 mm Hg, (V) Fasting glucose > 110 mg/dl. Each of abovementioned criteria was scored as one point and those with ≥ 3 points was considered to have MetS [2].

Statistical analysis

The SPSS 23.0 version software package (Chicago, IL) was employed to analyze the obtained data. A two-tailed p-value of ≤ 0.05 was accepted as statistical significance. The incidence of metabolic syndrome among patients with hypertension was obtained based on previous studies and sample size was calculated through the G. Power 3.1 software (power of test at 0.80, α error at 0.005, statistical significance level (double-sided) at 0.05). According to this analysis, it was needed 90 patients totally to evaluate metabolic syndrome, appropriately. While visual histograms and Kolmogrov-Smirnov test were carried to weigh the normality distribution of variables, Levene's test was used to test homogeneity of variances. Mean ± standard deviation scheme was used for normally distributed continuous variables; interquartile ranges for skew-distributed variables; and percentages for categorical variables. The categorical groups were compared by the Chi-square test. While the two-tailed Student t-test was carried for parameters that were normally distributed, the Mann-Whitney U test was conducted for non-normally distributed parameters. The univariate regression analysis was conducted to assess the effects of the various variables on MetS prediction. Unadjusted $p < 0.05$ was accepted as a cut-off value to determine confounding factors and these parameters were included in the full model of multivariable regression analysis to reveal independent

predictors of MetS. In addition, Pearson and Spearman analyses were used to evaluate the correlation co-efficiency between Serum UA level and other obtained parameters. Receiver operating characteristic (ROC) analysis was performed to estimate the value of serum UA and to determine the cut-off point of UA level in predicting MetS.

Results

A total of 107 non-diabetic hypertensive patients were included in the analysis. The mean age of the population was 48.5 ± 8.6 years and 50 (46.7%) of them were female. Patients were divided into two groups according to the presence of MetS and obtained parameters were compared between these groups. A total of 56 patients (52%) had MetS. Except waist circumference (101.2 ± 11.3 *vs.* 106.7 ± 10.1 cm, p = 0.020) and BMI (30.6 ± 4.9 *vs.* 32.8 ± 4.1, p = 0.016) were elevated in MetS (+) group, other demographical characteristics including age (p = 0.763), gender (p = 0.477), and hyperlipidemia rate (p = 0.053) were similar between groups (Tab. 1).

Among echocardiographic findings, interventricular wall thickness [11.2 (10.8–13.8) vs. 13 (11.6–14) mm, p = 0.035], posterior wall [10.8 (10–12.4) *vs.* 12 (11–13) mm, p = 0.018] thickness, E/e' ratio [9.2 (7.3–11.1) *vs.* 10.6 (9.1–13.4), p = 0.003], and EAT [5.9 (4.8–8) *vs.* 7.9 (6–9.6) mm, p = 0.006] were higher in MetS (+) group. When the participants were compared regarding laboratory data, while serum UA level (4.75 ± 1.10 *vs.* 5.82 ± 1.21 mg/dL, p < 0.001), lymphocyte count [2.2 (1.8–2.9) *vs.* 2.68 (2.02–3.15) 10^3/µL, p = 0.019], and triglyceride level [117.5 (80–152.7) *vs.* 176.5 (141–231.7) mg/dL, p < 0.001] were higher, HDL-C level [50.5 (43–58.7) *vs.* 42.5 (37.2–47) mg/dL, p = 0.001] was lower in MetS (+) group (Tab. 1).

Significantly differed parameters between groups were included in the fully adjusted regression model and serum UA [OR = 2.217, 95% CI: 1.300–3.783, p = 0.003] and BMI [OR = 1.214, 95% CI: 1.032–1.428, p = 0.019] were revealed to be independent predictors of MetS presence (Tab. 2).

In addition, correlation analysis showed that serum UA was positively correlated with EAT and left atrial volume measurements. On the other hand, office systolic and diastolic blood pressures were positively correlated with BMI and EAT (Tab. 3).

The receiver operating curve (ROC) analysis was performed to demonstrate the sensitivity and specificity of serum UA levels for predicting MetS and found that an optimal cutoff value of serum UA level was 5.35 mg/dL with 65% sensitivity and 75% specificity [area under curve (AUC): 0.733, 95% CI: 0.633–0.833, p < 0.001] (Fig. 1).

Discussion

In the present study, it was demonstrated that serum UA and BMI were independent predictors of MetS in non-diabetic hypertensive individuals. Along being a heavy contributor to AH development, UA is also inducing MetS in hypertension.

MetS was firstly described by Reaven in 1988 as ‘Syndrome X’ which was based on insulin resistance as the main underlying cause of the syndrome [9]. However, it is quantified with specific criteria by WHO in 1998 and by NCEP in 2001 [2]. After a certain definition, it was demonstrated to be associated with a vastly increased risk of cardiovascular diseases including AH, stroke, atherosclerosis, and kidney diseases [10, 11]. On the other hand, a huge amount of the western population was revealed to have MetS unwittingly. Unfortunately, MetS prevalence is on the rise by the time, especially linked to a sedentary lifestyle, increased life expectancy, and even an increase in antihypertensive drug usage [12]. Although it is not the obligated criteria to have MetS, AH is one of the components of MetS presence and accompanies other criteria mostly. All-cause mortality, end-organ damage including retinopathy and nephropathy, and other cardiovascular events were shown to be more frequent among these patients than those without MetS [13]. On the other hand, another study demonstrated that the presence of MetS induced blood pressure increase furtherly and after the MetS development, it is getting difficult to control blood pressure adequately. In addition, without treatment, AH has a strong potential to attract other criteria of MetS subsequently [4]. Hence, it is crucial to prevent the AH leading to MetS, for sure. Therefore, determining high-risk groups for the development of MetS and keep them under close observation should be ensured.

The pathophysiological mechanism of MetS became the focus of research interest since was shown to be related to cardiovascular diseases. Prevailing instruments of MetS were proposed as to be insulin resistance, sympathetic system activation, obesity, sodium retention, and oxidative stress up to date [11, 14]. Since the current population is non-diabetic, remained mechanisms come into prominence. Indeed, BMI was an independent predictor of MetS in this study, compatible with postulated pathways. Actually, increased BMI induces all these other mechanisms indirectly. Interestingly, when we look at other conventional parameters that we tested in routine practice including physical examination findings, echocardiography, and laboratory data, there was no independent predictor of MetS except BMI. Hence it is needed to investigate other clinical parameters that contributor to MetS with further studies.

On the other hand, serum UA level was an independent predictor of MetS coexistence in the current study. UA is a degradation product of purine metabolism. Although serum UA was well established to be caused nephrolithiasis and gout, it is more vitally related to cardiovascular diseases, especially AH and MetS [14]. Congestive heart failure, chronic kidney disease, nonalcoholic fatty liver disease, myocardial infarction, stroke, and all-cause mortality rates were also shown to be increased in patients with elevated UA [17]. Hyperuricemia was also found to be common in malignant hypertension [15]. In addition, child patients with hypertension were shown to have hyperuricemia frequently [18]. Moreover, severe forms of hypertension such as preeclampsia and non-dipper type were demonstrated to be associated with hyperuricemia [19]. Besides, plasma renin-angiotensin activity was elevated in people with hyperuricemia, which was confirmed by experimental studies. In addition, UA level was correlated with oxidative stress. Moreover, UA has deleterious effects on cardiovascular cells by promoting inflammation, depleting nitric oxide, endothelial dysfunction, and proliferating vascular smooth muscle cells [17]. These UA-related pathways are also the same as the underlying mechanism of MetS. Thus, it is elucidative that the serum UA level predicted MetS in this study. And also, some studies demonstrated that UA lowering medications might be beneficial in the control of blood pressure and adverse outcome [20]. Whereas thiazide diuretics were shown to have negative effects on cardiovascular outcomes in hypertensive patients. Metabolic side effects and an increase in serum UA level might lead to adverse outcomes [21]. Thus, it may be avoided to use thiazide diuretics in patients with increased serum UA levels to prevent MetS.

Other noteworthy results of the study were as follows: (I) E/e’ ratio was increased and significant even after univariate analysis in MetS (+) side, despite the fully model eliminated its predictive value. E/e' rate was established to be one the best noninvasive indicators of LV filling pressure and diastolic function which was demonstrated to be an eminent predictor of future left ventricular dysfunction [22]. Hypertensive patients with MetS might be assessed with E/e’ ratio regarding myocardial involvement; (II) serum UA level was correlated with EAT and left atrial volume. It is difficult to estimate the causal link between UA levels and echocardiographic parameters. However, these two parameters were shown to be associated with adverse outcomes in many previous studies [23]. Thus, these factors might be other underlying mechanisms of UA-related cardiovascular incidents and modifying each of these parameters may improve others.

Limitations

There are multiple limitations to admit. Firstly, this was a single-center study and included a limited number of participants. Secondly, MetS presence was evaluated according to the National Cholesterol Education Program (NCEP) definition. WHO definition might affect the results. Thirdly, a dietary intake assessment was not implemented, which may alter the serum UA level. Fourthly, although medications did not differ between groups, their possible effects on serum UA level were ignored.

Conclusion

Serum UA level is a cost-effective and easily obtainable parameter in MetS prediction and can be used to define high-risk patient groups among hypertensive individuals. Even though the DM is not present, it should be kept in mind that MetS may develop considerably, among hypertensive individuals and should take precautions to prevent it.

Conflicting interests

The authors declare that they have no conflict of interest.

Funding

The author(s) received no specific funding for this work.

Author contribution

All authors contributed equally to: (1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the version to be published.

References

1. Williams B, Mancia G, Spiering W, et al. Authors/Task Force Members:, ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018; 39(33): 3021–3104, doi: 10.1093/eurheartj/ehy339, indexed in Pubmed: 30165516.

2. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001; 285(19): 2486–2497, doi: 10.1001/jama.285.19.2486.

3. Kachur S, Morera R, De Schutter A, et al. Cardiovascular Risk in Patients with Prehypertension and the Metabolic Syndrome. Curr Hypertens Rep. 2018; 20(2): 15, doi: 10.1007/s11906-018-0801-2, indexed in Pubmed: 29511907.

4. Katsimardou A, Imprialos K, Stavropoulos K, et al. Hypertension in Metabolic Syndrome: Novel Insights. Curr Hypertens Rev. 2020; 16(1): 12–18, doi: 10.2174/1573402115666190415161813, indexed in Pubmed: 30987573.

5. Mazidi M, Katsiki N, Mikhailidis DP, et al. Lipid and Blood Pressure Meta-Analysis Collaboration (LBPMC) Group. Associations of serum uric acid with total and cause-specific mortality: Findings from individuals and pooling prospective studies. Atherosclerosis. 2020; 296: 49–58, doi: 10.1016/j.atherosclerosis.2019.07.019, indexed in Pubmed: 32032905.

6. Cortese F, Scicchitano P, Cortese AM, et al. Uric Acid in Metabolic and Cerebrovascular Disorders: A Review. Curr Vasc Pharmacol. 2020; 18(6): 610–618, doi: 10.2174/1570161118666191217123930, indexed in Pubmed: 31845632.

7. Kanbay M, Segal M, Afsar B, et al. The role of uric acid in the pathogenesis of human cardiovascular disease. Heart. 2013; 99(11): 759–766, doi: 10.1136/heartjnl-2012-302535, indexed in Pubmed: 23343689.

8. Zoppini G, Targher G, Bonora E. The role of serum uric acid in cardiovascular disease in type 2 diabetic and non-diabetic subjects: a narrative review. J Endocrinol Invest. 2011; 34(11): 881–886, doi: 10.1007/BF03346733, indexed in Pubmed: 22322536.

9. Reaven GM, Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes. 1988; 37(12): 1595–1607, doi: 10.2337/diab.37.12.1595, indexed in Pubmed: 3056758.

10. Saklayen MG. The Global Epidemic of the Metabolic Syndrome. Curr Hypertens Rep. 2018; 20(2): 12, doi: 10.1007/s11906-018-0812-z, indexed in Pubmed: 29480368.

11. Samson SL, Garber AJ. Metabolic syndrome. Endocrinol Metab Clin North Am. 2014; 43(1): 1–23, doi: 10.1016/j.ecl.2013.09.009, indexed in Pubmed: 24582089.

12. Lavie CJ, Ozemek C, Carbone S, et al. Sedentary Behavior, Exercise, and Cardiovascular Health. Circ Res. 2019; 124(5): 799–815, doi: 10.1161/CIRCRESAHA.118.312669, indexed in Pubmed: 30817262.

13. Saeed S, Waje-Andreassen U, Nilsson PM. The association of the metabolic syndrome with target organ damage: focus on the heart, brain, and central arteries. Expert Rev Cardiovasc Ther. 2020; 18(9): 601–614, doi: 10.1080/14779072.2020.1807327, indexed in Pubmed: 32757786.

14. Rochlani Y, Pothineni NV, Kovelamudi S, et al. Metabolic syndrome: pathophysiology, management, and modulation by natural compounds. Ther Adv Cardiovasc Dis. 2017; 11(8): 215–225, doi: 10.1177/1753944717711379, indexed in Pubmed: 28639538.

15. Sanchez-Lozada LG, Rodriguez-Iturbe B, Kelley EE, et al. Uric Acid and Hypertension: An Update With Recommendations. Am J Hypertens. 2020; 33(7): 583–594, doi: 10.1093/ajh/hpaa044, indexed in Pubmed: 32179896.

16. Bonakdaran S, Kharaqani B. Association of serum uric acid and metabolic syndrome in type 2 diabetes. Curr Diabetes Rev. 2014; 10(2): 113–117, doi: 10.2174/1573399810666140228160938, indexed in Pubmed: 24588601.

17. Ndrepepa G, Ndrepepa G, Cassese S, et al. Association of uric acid with mortality in patients with stable coronary artery disease. Metabolism. 2012; 61(12): 1780–1786, doi: 10.1016/j.metabol.2012.05.014, indexed in Pubmed: 22749121.

18. Kubota M. Hyperuricemia in Children and Adolescents: Present Knowledge and Future Directions. J Nutr Metab. 2019; 2019: 3480718, doi: 10.1155/2019/3480718, indexed in Pubmed: 31192008.

19. Bellos I, Pergialiotis V, Loutradis D, et al. The prognostic role of serum uric acid levels in preeclampsia: A meta-analysis. J Clin Hypertens (Greenwich). 2020; 22(5): 826–834, doi: 10.1111/jch.13865, indexed in Pubmed: 32338457.

20. Liu X, Zhai T, Ma R, et al. Effects of uric acid-lowering therapy on the progression of chronic kidney disease: a systematic review and meta-analysis. Ren Fail. 2018; 40(1): 289–297, doi: 10.1080/0886022X.2018.1456463, indexed in Pubmed: 29619870.

21. Fujimori S, Oka Y, Ogata N, et al. Effects of losartan/hydrochlorothiazide on serum uric acid levels and blood pressure in hypertensive patients. Nucleosides Nucleotides Nucleic Acids. 2011; 30(12): 1030–1034, doi: 10.1080/15257770.2011.628356, indexed in Pubmed: 22132952.

22. Park JH, Marwick TH. Use and Limitations of E/e' to Assess Left Ventricular Filling Pressure by Echocardiography. J Cardiovasc Ultrasound. 2011; 19(4): 169–173, doi: 10.4250/jcu.2011.19.4.169, indexed in Pubmed: 22259658.

23. Çırakoğlu ÖF, Yılmaz AS. Systemic immune-inflammation index is associated with increased carotid intima-media thickness in hypertensive patients. Clin Exp Hypertens. 2021; 43(6): 565–571, doi: 10.1080/10641963.2021.1916944, indexed in Pubmed: 33858279.

Figure *1*. Sensitivity and specificity of uric acid level in predicting metabolic syndrome

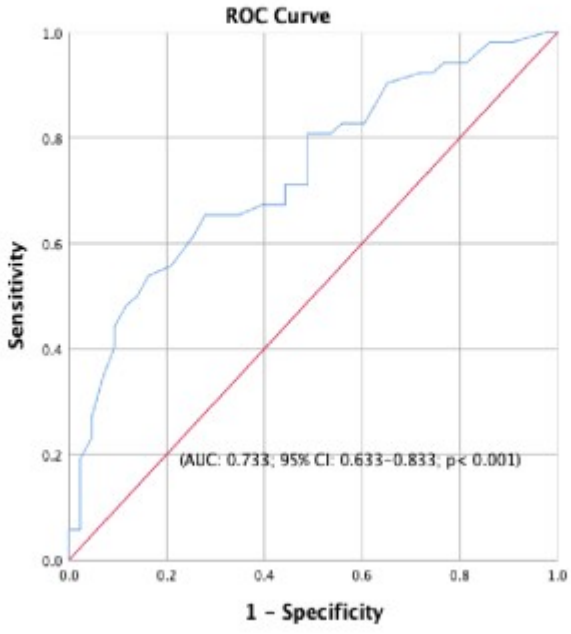

Table 1. Baseline characteristics of the study population

Variable	**Metabolic syndrome (-) (n=51)**	**Metabolic syndrome (+) (n=56)**	**All patients (n=107)**	**P value**
Demographic data				
Age (year)	48.2 ± 7.6	48.7 ± 9.6	48.5 ± 8.6	0.763
Gender (Female) n(%)	22 (43.1)	28 (56)	50 (46.7)	0.477
Smoking n(%)	15 (29.4)	19 (33.9)	34 (31.8)	0.616
Hyperlipidemia n(%)	24 (47.1)	37 (66.1)	61 (57)	0.053
Office SBP [mm Hg]	156.3 ± 14.6	156.6 ± 15.6	156.1 ± 15.4	0.846
Office DBP [mm Hg]	97.2 ± 7.9	99.3 ± 9.8	98.1 ± 9.1	0.055
Waist circumference [cm]	101.2 ± 11.3	106.7 ± 10.1	104.2 ± 11	0.020
Length [cm]	167.5 ± 8.7	167.7 ± 9.7	167.6 ± 9.2	0.912
Weight [kg]	86 ± 14.3	92.4 ± 13.6	89.2 ± 14.2	0.020
BMI [kg/m^2]	30.6 ± 4.9	32.8 ± 4.1	31.7 ± 4.6	0.016
Echocardiographic findings				
LA Volume [mL]	40.3 ± 13.2	46 ± 13.1	43.3 ± 13.2	0.097
LV EF (%)	65 ± 3.4	64.7 ± 4	64.9 ± 3.7	0.825
IVSD [mm]	11.2 (10.8–13.8)	13 (11.6–14)	12 (11–13.9)	0.035
PWD [mm]	10.8 (10–12.4)	12 (11–13)	11.2 (10.3–12.5)	0.018
E/e’	9.2 (7.3–11.1)	10.6 (9.1–13.4)	10.1 (8.4–12.2)	0.003
EAT [mm]	5.9 (4.8–8)	7.9 (6–9.6)	6.3 (5.6–8.7)	0.006
Laboratory data				
WBC [10^3/µL]	7.2 ± 1.3	7.6 ± 1.5	7.4 ± 1.4	0.136
Hemoglobin [g/dL]	14.8 (13–15)	14.9 (14–15)	14.7 (13.5–15)	0.988
Neutrophil [10^3/µL]	4.06 ± 1.09	4.16 ± 1.08	4.11 ± 1.07	0.866
Lymphocyte [10^3/µL]	2.2 (1.8–2.9)	2.68 (2.02–3.15)	2.56 (1.9–2.95)	0.019
Fasting glucose [mg/dL]	96.5 (93.2–101)	99 (92–110)	98 (92–108)	0.275
Creatinine [mg/dL]	0.82 ± 0.13	0.80 ± 0.10	0.81 ± 0.12	0.442
Uric acid [mg/dL]	4.75 ± 1.10	5.82 ± 1.21	5.28 ± 1.26	<0.001
CRP [mg/dL]	0.30 (0.18–0.64)	0.40 (0.26–0.63)	0.33 (0.22–0.63)	0.162
Total cholesterol [mg/dL]	215.9 ± 41.1	227.3 ± 37.3	222.1 ± 39.8	0.375
Triglyceride [mg/dL]	117.5 (80–152.7)	176.5 (141–231.7)	145 (98.5–191)	<0.001
LDL [mg/dL]	137.5 ± 31.9	144.3 ± 42.2	141.4 ± 37.3	0.606
HDL [mg/dL]	50.5 (43–58.7)	42.5(37.2–47)	45 (41–54)	0.001
Medication				
Beta Blocker n (%)	8 (15.7)	7 (12.7)	15 (14.2)	0.662
ACEI n (%)	13 (26)	9 (16.4)	22 (21)	0.241
ARB n (%)	16 (31.4)	16 (29.1)	32 (30.2)	0.835
CCB n (%)	10 (19.6)	8 (14.5)	18 (17)	0.607

Diuretics n(%)	21 (41.2)	18 (32.7)	39 (36.8)	0.423

SBP — systolic blood pressure; DBP — diastolic blood pressure; BMI — body mass index; LVEF — left ventricular ejection fraction; IVSD — interventricular septum diameter, PWD — posterior wall diameter; EAT — epicardial adipose tissue; CIMT — carotid intima-media thickness; WBC — white cell count; CRP — C-reactive protein; LDL — low-density lipoprotein; HDL — high-density lipoprotein; continuous variables are given as mean ± standard deviation (SD)

Table 2. Independent predictors of metabolic syndrome

	Univariate			**Multivariable**		
	OR	**CI 95%**	**p**	**OR**	**CI 95%**	**p**
Waist circumference	1.051	1.007–1.096	0.022			
BMI	1.114	1.019–1.218	0.018	1.214	1.032–1.428	0.019
EAT	1.234	1.034–1.473	0.020			
IVSD	1.163	0.945–1.432	0.154			
PWD	1.305	1.003–1.698	0.047			
E/e’	1.387	1.132–1.700	0.002			
Lymphocyte	2.101	1.136–3.885	0.018			
Uric acid	2.048	1.391–3.014	< 0.001	2.217	1.300–3.783	0.003
Triglyceride	1.008	1.002–1.014	0.011			
HDL	0.933	0.893–0.974	0.002			

OR — odds ratio; CI — confidence interval; BMI — body mass index; EAT — epicardial adipose tissue; IVSD — interventricular septum diameter; PWD — posterior wall diameter; HDL — high-density lipoprotein

Table 3. Correlation coefficients (r value) between continues variables

	Uric acid	**Office SBP**	**Office DKB**	**BMI**	**EAT**	**Left atrial volume**
Uric acid	1					
Office SBP	0.120	1				
Office DKB	0.186	0.410*	1			
BMI	–0.100	0.273*	0.356*	1		
EAT	0.305*	0.335*	0.244*	0.447*	1	

Left atrial volume	0.398*	0.076	0.120	0.115	0.491 *	1

SBP — systolic blood pressure; DBP — diastolic blood pressure; BMI — body mass index; EAT — epicardial adipose tissue; CIMT — carotid intima-media thickness; *significant relationship was found between related parameters