박 사 학 위 논 문

Serum Uric Acid Levels and the Risk of Subclinical Atherosclerosis in Korean Adults without Previous History of Major Adverse Clinical Events

계 명 대 학 교 대 학 원

의 학 과

원 기 범

지도교수 허 승 호

2 0 2 1 년 2 월

Serum Uric Acid Levels and the Risk of Subclinical Atherosclerosis in Korean Adults without Previous History of Major Adverse Clinical Events

지도교수 허 승 호

이 논문을 박사학위 논문으로 제출함

2021년 2월

계명대학교 대학원

의학과 내과학 전공

원 기 범

원기범의 박사학위 논문을 인준함

주 심 김 형 섭

부 심 허 승 호

부 심 조 윤 경

부 심 이 철 현

부 심 안 서 희

계 명 대 학 교 대 학 원

２０２１년 ２월

Acknowledgement

2009년 석사 학위를 취득한 후 심장내과 전문의로 정신없이 보내왔던 시간들이 주마등처럼 떠오릅니다. 울산에 위치한 대학병원에서 진료를 하면서 학업을 같이 병행해야 했던 지난 과정이 개인적으로 그리 녹록치 않았습니다. 그런 와중에도 한 걸음 더 나아갈 수 있도록 이끌어 주시던 허승호 교수님과 더욱 좋은 논문이 될 수 있도록 지도해 주신 김형섭 교수님, 조윤경 교수님, 이철현 교수님, 그리고 안서희 교수님께 감사의 말씀을 전해드립니다. 또한 힘들 때마다 제게 많은 조언을 주셨던 울산대학교병원 심장내과 교수님들께도 감사의 마음을 전합니다. 무엇보다도 항상 저를 지지해주며 응원해준 부모님과 아내에게 고마운 마음을 전합니다. 오늘의 이 논문이 앞으로 제가 한걸음 더 나아갈 수 있는 소중한 기회가 되었음을 다시 한번 새기면서 감사의 글을 맺습니다.

2021년 2월

원 기 범

Table of Contents

List of Tables

List of Figures

1. Introduction

A number of epidemiological studies have suggested that serum uric acid (SUA) is an important risk factor for cardiovascular (CV) disease (1-6). It is well-known that increased levels of SUA are closely linked to metabolic disorders, including obesity, hyperlipidemia, and hypertension (7,8). However, the impact of SUA levels on CV disease has been suspected to be epiphenomenal due to this relationship (9).

Brachial-ankle pulse wave velocity (baPWV) has been considered a reproducible index of arterial elasticity and stiffness in clinical practice. Additionally, the measurement of carotid intima-medial thickness (IMT) and plaque of the carotid artery using high-resolution ultrasound is a useful method for evaluating subclinical atherosclerosis in the general population. The increased baPWV and carotid IMT, and high amounts of carotid plaque are important predictive markers for an increased risk of adverse CV events (10,11). The purpose of present study was to evaluate the relation of SUA levels to baPWV, carotid IMT, and carotid plaque in a 2560 relatively healthy subjects who participated in baseline health examinations for a community-based cohort study.

2. Materials and Methods

2.1. Subjects:

This prospective cross-sectional cohort study analyzed the data of 2560 adults who participated in health examinations in the Seoul area between April 2010 and November 2012. This study excluded subjects with a clinical history of CV and cerebrovascular disease, neurological abnormalities, or malignancies. The study protocol was approved by the local ethics committee, and informed consent for the procedure was obtained from each individual.

2.2. Laboratory and Clinical Information:

All blood samples were obtained after 8 hours of fasting and analyzed. Height and weight were measured while the subjects wore light clothing and no shoes. The body mass index (BMI) was calculated as weight (kg) / height (m^2). Hypertension was defined as blood pressure (BP) ≥ 140 / 90 mm Hg or a self-reported history of hypertension and / or the use of anti-hypertensive medication. Diabetes mellitus was defined as either a fasting glucose value ≥ 126 mg/dL, anti-diabetic treatment, or a referral diagnosis of diabetes. Hyperlipidemia was defined as total cholesterol ≥ 240 mg/dL or the use of an anti-hyperlipidemic treatment.

2.3. Measurement of Subclinical Atherosclerotic Parameters:

The baPWV was measured under the inhibition of caffeine-containing food or beverages for at least 45 minutes prior to the examination. The blood pressure and baPWV were measured with an automated waveform analyzer (Colin VP-2000, Colin Medical Instruments Corp., Komaki, Japan) after the patient rested in the supine position for at least 5 minutes in a quiet room. Pneumatic cuffs were wrapped around both upper arms and ankles and connected to a plethysmographic sensor to determine the volume pulse waveform. The mean baPWV of the values measured on both sides of each patient was used for analysis. Carotid IMT was measured using high-resolution B-mode ultrasonography (Acuson X300, Siemens, USA) with a transducer frequency of 1315 MHz. Image acquisition, processing, storage, and calculation of the IMT were performed with the Syngo Arterial Health Package (Siemens, USA). Automatic measurements of both common carotid arteries were made at the far wall of the 1-cm segment distal to the carotid bulbs. The mean value of the carotid IMT was used for analysis. The measurement of the carotid IMT was taken at sites free of any discrete plaques. Carotid plaque was defined as a focal region with a carotid IMT greater than 1.5 mm that protruded into the lumen and was distinct from the neighboring boundary or as the presence of focal wall thickening at least $\geq$50% than that of the surrounding vessel wall (12,13).

2.4. Statistical Analysis:

Continuous variables are expressed as the mean ± SD, and categorical

variables are presented as n (%). Continuous variables were compared using independent t-tests or Mann-Whitney U-tests, and categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Correlational analyses between the SUA levels, baPWV, and carotid IMT were performed using Pearson's correlation tests. Multivariate regression analyses were performed to identify the independent impact of the clinical variables on baPWV, carotid IMT, and carotid plaque. The forced entry method was used to enter independent variables into the multivariate regression analyses. SPSS version 18 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. All statistical tests were 2-tailed, and $p < 0.05$ was considered significant.

3. Results

3.1. Baseline Characteristics:

Table 1 shows the clinical characteristics of the study participants. All participants were stratified into four groups based on the quartiles of their SUA levels. The mean levels of SUA were 3.3 ± 0.4, 4.3 ± 0.2, 5.1 ± 0.3, and 6.6 ± 0.9 in group I (lowest), II, III, and IV (highest), respectively. There were significant differences in age, BMI, systolic and diastolic BP, serum levels of triglyceride and high-density lipoprotein cholesterol, sex, and smoking between the groups. The prevalence of hypertension and hyperlipidemia were significantly different between the groups.

3.2. SUA Levels and Subclinical Atherosclerosis:

Figure 1 shows that the mean baPWV (group I [lowest]: 1441 ± 271 vs. group II: 1444 ± 228 vs. group III: 1495 ± 255 vs. group IV [highest]: 1518 ± 250 cm/s), the mean carotid IMT (group I: 0.74 ± 0.15 vs. group II: 0.74 ± 0.16 vs. group III: 0.79 ± 0.20 vs. group IV: 0.79 ± 0.20 mm), and the incidence of plaque (group I: 28.9% vs. group II: 29.0% vs. group III: 36.2% vs. group IV: 41.0%) were significantly different between all groups (all $p < 0.001$). The SUA levels were significantly correlated with baPWV ($r = 0.142$; $p < 0.001$) and carotid IMT ($r = 0.140$; $p < 0.001$) (Figure 2). The results of the subgroup analysis for the risk of carotid plaque related to SUA levels are presented in Figure 3.

3.3. Impact of Clinical Variables on Subclinical Atherosclerosis:

The results of the multiple regression analyses for the association between clinical variables and subclinical atherosclerosis are described in Table 3. Age, BMI, SUA, high-sensitivity C-reactive protein level, hypertension, and diabetes mellitus were significantly associated with baPWV. Age, SUA, hypertension, and diabetes mellitus were significantly associated with carotid IMT. Age, SUA, hypertension, diabetes mellitus, and smoking were significantly associated with carotid plaque.

Table 1. Baseline Characteristics

	Quartiles of SUA				p
	I (lowest) (n = 662)	II (n = 689)	III (n = 643)	IV (highest) (n = 566)	
Age, years	59.6 ± 7.8	60.1 ± 7.4	61.0 ± 7.8	61.1 ± 8.5	0.001
Male, n (%)	63 (9.5)	120 (17.4)	247 (38.4)	412 (72.8)	<0.001
BMI, kg/m^2	24.0 ± 2.9	24.6 ± 2.9	25.0 ± 3.1	26.0 ± 2.8	<0.001
Heart rate, bpm	66.9 ± 8.8	67.2 ± 9.5	66.9 ± 10.1	67.0 ± 10.3	0.959
Systolic BP, mmHg	120.4 ± 15.2	120.8 ± 14.7	123.9 ± 14.8	126.7 ± 15.1	<0.001
Diastolic BP, mmHg	71.9 ± 10.1	72.3 ± 9.3	74.6 ± 8.9	77.5 ± 9.9	<0.001
Past history, n (%)					
Hypertension	271 (40.9)	303 (44.0)	331 (51.5)	368 (65.0)	<0.001
Diabetes mellitus	105 (15.9)	92 (13.4)	109 (17.0)	105 (18.6)	0.080
Hyperlipidemia	250 (37.8)	261 (37.9)	249 (38.7)	178 (31.4)	0.035
Smoking	62 (9.4)	102 (14.8)	211 (32.8)	320 (56.5)	<0.001
Laboratory test					
Total cholesterol, mg/dL	198.8 ± 34.8	199.2 ± 35.2	201.7 ± 37.7	197.3 ± 37.5	0.195
Triglyceride, mg/dL	109.7 ± 53.5	118.2 ± 59.9	134.8 ± 69.4	158.1 ± 88.9	<0.001
HDL cholesterol, mg/dL	58.8 ± 15.3	56.5 ± 14.4	52.8 ± 14.0	48.4 ± 13.0	<0.001
LDL cholesterol, mg/dL	120.2 ± 30.8	121.3 ± 32.2	124.0 ± 34.5	120.8 ± 34.3	0.170
Fasting glucose, mg/dL	100.8 ± 26.0	98.1 ± 17.6	103.0 ± 20.2	103.8 ± 16.5	<0.001
Uric acid, mg/dL	3.3 ± 0.4	4.3 ± 0.2	5.1 ± 0.3	6.6 ± 0.9	<0.001
hsCRP, mg/dL	1.3 ± 2.9	2.0 ± 8.0	1.8 ± 4.0	1.6 ± 3.1	0.375

Values are given as the mean ± standard deviation or number (%).

BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein.

Table 2. Multivariate Regression Analyses for the Association of Clinical Variables with Subclinical Atherosclerosis

	baPWV		Carotid IMT		Carotid plaque	
	β (95% CI)	p	β (95% CI)	p	OR (95% CI)	p
Age, per 1 year	12.029 (10.543−13.514)	<0.001	0.009 (0.008−0.010)	<0.001	1.070 (1.052−1.088)	<0.001
Male	11.407 (-27.697−50.511)	0.567	0.001 (-0.027−0.029)	0.931	1.001 (0.661−1.515)	0.998
BMI, per 1 kg/m^2	-5.197 (-9.394−-1.000)	0.015	0.001 (-0.002−0.004)	0.584	0.993 (0.950−1.038)	0.754
Uric acid, per 1 mg/dL	12.267 (1.235−23.299)	0.029	0.013 (0.005−0.021)	0.001	1.125 (1.004−1.261)	0.043
hsCRP, per 1 mg/dL	3.042 (0.675−5.408)	0.012	-0.002 (-0.003−0.001)	0.075	0.994 (0.962−1.028)	0.729
Hypertension	111.155 (84.971−137.340)	<0.001	0.032 (0.013−0.050)	0.001	1.530 (1.160−2.018)	0.003
Diabetes mellitus	85.701 (54.009−117.393)	<0.001	0.039 (0.016−0.062)	0.001	1.677 (1.223−2.300)	0.001
Hyperlipidemia	-1.191 (-26.834−24.453)	0.927	0.009 (-0.009−0.028)	0.325	1.243 (0.949−1.629)	0.114
Smoking	-3.120 (-41.814−35.575)	0.874	-0.007 (-0.035−0.021)	0.638	1.633 (1.089−2.448)	0.018

baPWV, brachial-ankle pulse wave velocity; BMI, body mass index; CI, confidence interval; hsCRP, high-sensitivity C-reactive protein; IMT, intima-medial thickness; OR, odds ratio.

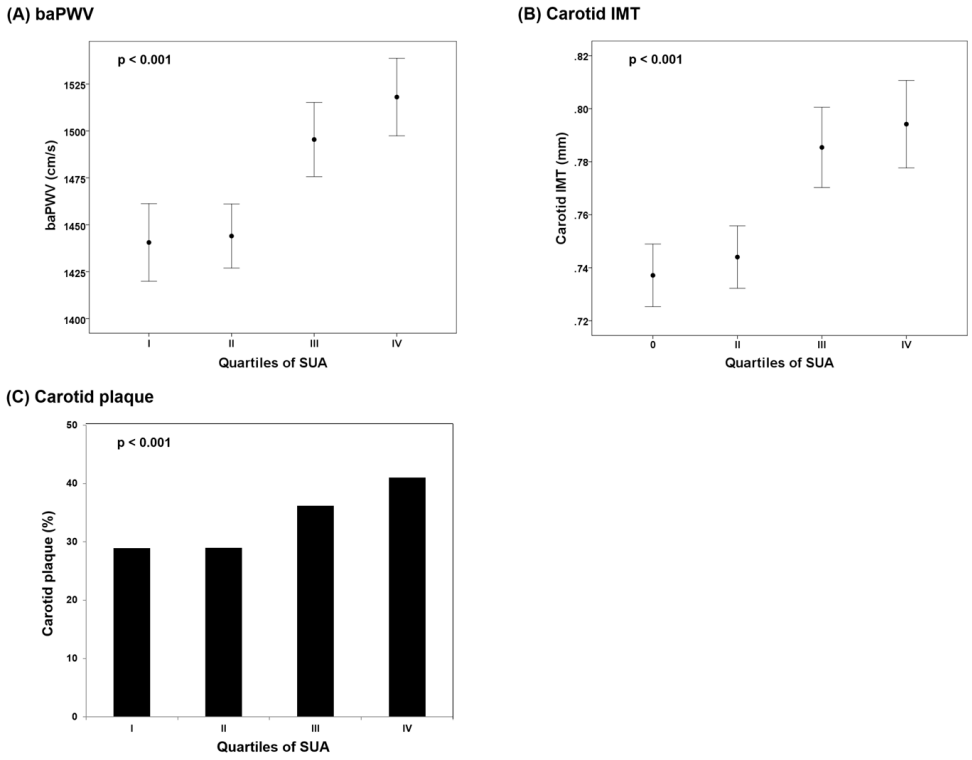

Figure 1. Comparison of subclinical atherosclerosis according to the quartiles of SUA levels.

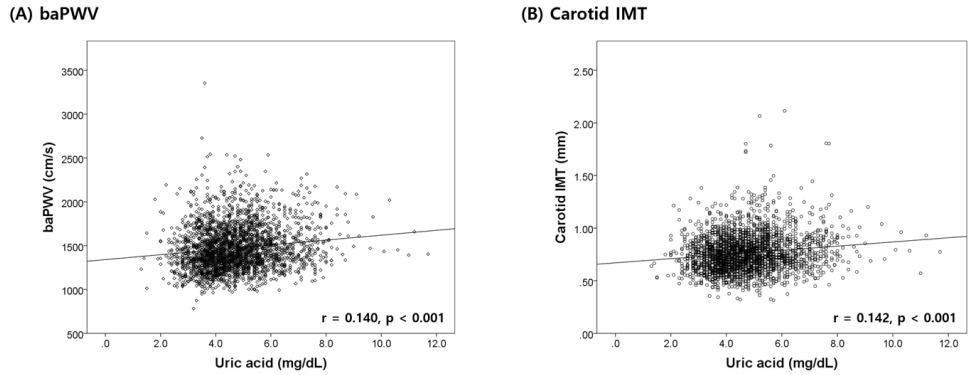

Figure 2. Correlations between SUA levels and subclinical atherosclerosis.

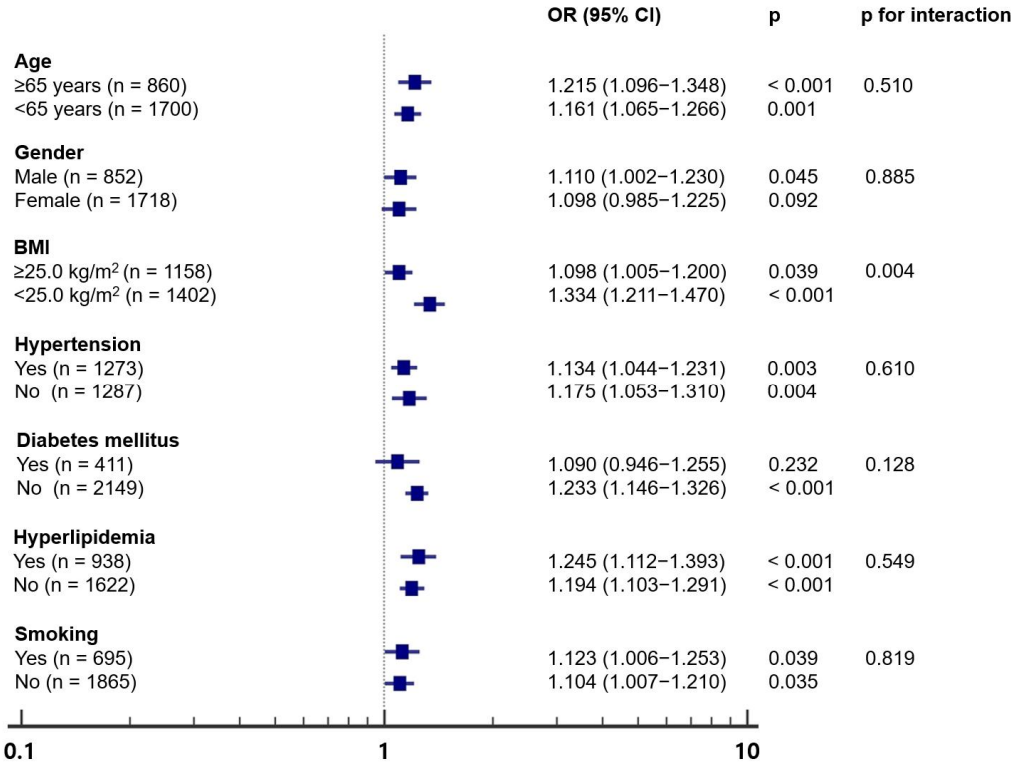

Figure 3. Subgroup analyses for the impact of SUA levels on carotid plaque.

4. Discussion

In this prospective cohort study, we identified that SUA levels had a positive correlation with carotid IMT and baPWV and were associated with an increased risk for carotid plaque. After adjusting for confounding clinical factors, SUA levels had an independent impact on all subclinical atherosclerotic parameters.

Uric acid is the final product of purine nucleotide metabolism that is finally eliminated by the kidney (14). Although an increased SUA level has been considered a risk marker rather than an independent risk factor for atherosclerosis, recent data strongly suggested that SUA levels are not only markers of the catabolic rate but may also be actively involved in the inflammatory process (15-17). In addition, there is evidence that hyperuricemia impairs endothelial dysfunction by reducing nitric oxide synthase in animal experiments (18). Some large cohort studies also suggested that SUA levels are significant risk factors for CV disease. The Progetto Ipertensione Umbria Monitoraggio Ambulatoriale (PIUMA) study reported that an increased SUA levels were a strong risk factor for subsequent CV disease and mortality in untreated subjects with essential hypertension (19). Bos et al. also reported that SUA levels were powerful risk markers for developing myocardial infarction and stroke in the Rotterdam study (20).

The strengths of the present study are to evaluate the association between SUA levels and subclinical atherosclerosis in an asymptomatic general population with a large sample size using diverse, validated, useful markers for subclinical atherosclerosis, including arterial stiffness and the combination of carotid IMT and plaque (10,11). Several recent studies evaluated the impact of SUA levels on subclinical

atherosclerosis, but the results were somewhat inconsistent. Cicero et al. reported that SUA levels were significantly correlated to hypertension and carotid IMT but not to arterial stiffness in 619 participants in the Brisighella Heart Study (21). However, the number of participants in this study was relatively small. Chen et al. reported that SUA levels were positively associated with carotid IMT in 10281 middle-aged and elderly Chinese subjects (22). Despite the large sample size in this study, the association between SUA levels and the risk of carotid plaque was not investigated. Other studies evaluated the relationship of SUA levels and coronary artery calcification, but the results were different (23,24). In the present study, we identified that SUA levels had an independent impact on arterial stiffness and carotid IMT and plaque in an asymptomatic Korean population after adjusting for traditional CV risk factors. Our results suggest that controlling SUA levels is important to prevent the development of subclinical atherosclerosis. Further prospective longitudinal studies with larger sample sizes are necessary to address the effect of uric acid-lowering agents on atherosclerosis.

The exact mechanism of SUA related to the development and progression of atherosclerosis has been uncertain. One possible mechanism is the inflammatory properties of SUA that cause arteriosclerosis. Nod-like receptor family protein 3 inflammasome is activated by urate crystal engulfed macrophages (25). Via this pathway, urate-stimulated macrophages secrete interleukin-1β and lead to inflammation, which cause the development of arteriosclerosis. Another possible mechanism is the expression of urate transporters in blood vessels, which move urate through glucose transporter 9 and voltage-driven urate efflux transporter 1, causing inflammation in the vessels (26). Further investigation should be necessary to fully

understand the mechanism.

This study has some limitations. First, the present study included only a Korean population. Second, we could not control the possible effects of underlying medications on subclinical atherosclerosis because of the observational nature of the study design. Finally, we did not have information from the participants on environmental risk factors, such as physical activity, exercise, or diet. Despite these limitations, we identified the independent impact of SUA levels on subclinical atherosclerosis using established imaging tools to evaluate atherosclerosis.

5. Summary

High SUA levels were independently associated with an increased risk for subclinical atherosclerosis, as reflected in the baPWV and carotid IMT and plaque, in a relatively healthy Korean adult population.

References

1. Fang J, Alderman MH: Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971-1992. National Health and Nutrition Examination Survey. JAMA 2000; 283: 2404-10.

2. Levine W, Dyer AR, Shekelle RB, Schoenberger JA, Stamler J: Serum uric acid and 11.5-year mortality of middle-aged women: findings of the Chicago Heart Association Detection Project in Industry. J Clin Epidemiol 1989; 42: 257-67.

3. Fessel WJ: High uric acid as an indicator of cardiovascular disease. Independence from obesity. Am J Med 1980; 68: 401-4.

4. Staessen J: The determinants and prognostic significance of serum uric acid in elderly patients of the European Working Party on High Blood Pressure in the Elderly trial. Am J Med 1991; 90(suppl 3A): 50S.

5. Freedman DS, Williamson DF, Gunter EW, Byers T: Relation of serum uric acid to mortality and ischemic heart disease. The NHANES I Epidemiologic Follow-up Study. Am J Epidemiol 1995; 141: 637-44.

6. Culleton BF, Larson MG, Kannel WB, Levy D: Serum uric acid and risk for cardiovascular disease and death: the Framingham Heart Study. Ann Intern Med 1999; 131: 7-13.

7. Burack RC, Keller JB, Higgins MW: Cardiovascular risk factors and obesity: are baseline levels of blood pressure, glucose, cholesterol and uric acid elevated prior to weight gain? J Chronic Dis 1985; 38: 865-72.

8. Osgood K, Krakoff J, Thearle M: Serum uric acid predicts both current and future components of the metabolic syndrome. Metab Syndr Relat Disord 2013; 11: 157-62.

9. Rich MW. Uric acid: is it a risk factor for cardiovascular disease? Am J Cardiol 2000; 85: 1018-21.

10. Hodis HN, Mack WJ, LaBree L, Selzer RH, Liu CR, Liu CH, et al.: The role of carotid arterial intima-media thickness in predicting clinical coronary events. Ann Intern Med 1998; 128: 262-9.

11. Yamashina A, Tomiyama H, Arai T, Hirose K, Koji Y, Hirayama Y, et al.: Brachial-ankle pulse wave velocity as a marker of atherosclerotic vascular damage and cardiovascular risk. Hypertens Res 2003; 26: 615-22.

12. Roman MJ, Naqvi TZ, Gardin JM, Gerhard-Herman M, Jaff M, Mohler E: Clinical application of noninvasive vascular ultrasound in cardiovascular risk stratification: a report from the American society of echocardiography and the society of vascular medicine and biology. J Am Soc Echocardiogr 2006; 19: 943-54.

13. Hunt KJ, Sharrett AR, Chambless LE, Folsom AR, Evans GW, Heiss G: Acoustic shadowing on B-mode ultrasound of the carotid

artery predicts CHD. Ultrasound Med Biol 2001; 27: 357-65.

14. Wu XM, MuznyDM, Lee CC, Caskey CT: Two independent mutational events in the loss of urate oxidase during hominoid evolution. J Mol Evol 1992; 34: 78-84.

15. Frohlich ch M, Imhof A, Berg G, Hutchinson WL, Pepys MB, Boeing H: Association between C-reactive protein and features of the metabolic syndrome: a population-based study. Diabetes Care 2000; 23: 1835-9.

16. Ruggiero C, Cherubini A, Ble A, Bos AJ, Maggio M, Dixit VD: Uric acid and inflammatory markers. Eur Heart J 2006; 27: 1174-81.

17. Ruggiero C, Cherubini A, Miller E 3rd, Maggio M, Najjar SS, Lauretani F, et al.: Usefulness of uric acid to predict changes in C-reactive protein and interleukin-6 in 3-year period in Italians aged 21 to 98 years. Am J Cardiol 2007; 100: 115-21.

18. Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C, Mu W, et al.: Hyperuricemia induces endothelial dysfunction and vasoconstriction. Kidney Int 2005; 67: 1739-42.

19. Verdecchia P, Schillaci G, Reboldi G, Santeusanio F, Porcellati C, Brunetti P: Relation between serum uric acid and risk of cardiovascular disease in essential hypertension. The PIUMA study. Hypertension 2000; 36: 1072-8.

20. Bos MJ, Koudstaal PJ, Hofman A, Witteman JC, Breteler MM: Uric

acid is a risk factor for myocardial infarction and stroke: the Rotterdam study. Stroke 2006; 37: 1503-7.

21. Cicero AF, Salvi P, D'Addato S, Rosticci M, Borghi C: Association between serum uric acid, hypertension, vascular stiffness and subclinical atherosclerosis: data from the Brisighella Heart Study. J Hypertens 2014; 32: 57-64.

22. Chen Y, Xu B, Sun W, Sun J, Wang T, Xu Y, et al.: Impact of the serum uric acid level on subclinical atherosclerosis in middle-aged and elderly Chinese. J Atheroscler Thromb 2015; 22: 823-32.

23. Coutinho TA, Turner ST, Peyser PA, Bielak LF, Sheedy PF 2nd, Kullo IJ: Associations of serum uric acid with markers of inflammation, metabolic syndrome and subclinical coronary atherosclerosis. Am J Hypertens 2007; 20: 83-9.

24. Santos RD, Nasir K, Orakzai R, Meneghelo RS, Carvalho JA, Blumenthal RS: Relation of uric acid levels to presence of coronary artery calcium detected by electron beam tomography in men free of symptomatic myocardial ischemia with versus without the metabolic syndrome. Am J Cardiol 2007; 99: 42-5.

25. Gicquel T, Robert S, Loyer P, Victoni T, Bodin A, Ribault C, et al.: IL-1beta production is dependent on the activation of purinergic receptors and NLRP3 pathway in human macrophages. FASEB J 2015; 29: 4162-73.

26. Mishima M, Hamada T, Maharani N, Ikeda N, Onohara T, Notsu T,

et al.: Effects of uric acid on the NO production of HUVECs and its restoration by urate lowering agents. Drug Res (Stuttg) 2016; 66: 270-4.

Serum Uric Acid Levels and the Risk of Subclinical Atherosclerosis in Asymptomatic Korean Adults without Previous History of Major Adverse Clinical Events

Won, Ki-Bum

Department of Internal Medicine
Graduate School

Keimyung University

(Supervised by Professor Seung-Ho Hur)

(Abstract)

Data on the association between serum uric acid (SUA) levels and diverse atherosclerotic parameters in asymptomatic general population is limited. The present study aimed to evaluate the relation of SUA levels with brachial-ankle pulse wave velocity (baPWV), carotid intima-medial thickness (IMT), and carotid plaque in 2560 asymptomatic adults (60 ± 8 years, 33% men) without a previous history of cardiovascular or cerebrovascular disease, neurological abnormalities, or malignancies and who participated in health examinations for a community-based cohort study between April 2010 and November 2012. All participants were stratified into four groups based on the quartiles of their SUA levels. The mean baPWV (group I: 1441 ± 271 vs. group II: 1444 ± 228 vs.

group III: 1495 ± 255 vs. group IV: 1518 ± 250 cm/s), carotid IMT (group I [lowest]: 0.74 ± 0.15 vs. group II: 0.74 ± 0.16 vs. group III: 0.79 ± 0.20 vs. group IV [highest]: 0.79 ± 0.20 mm), and incidence of carotid plaque (group I: 28.9% vs. group II: 29.0% vs. group III: 36.2% vs. group IV: 41.0%) were significantly different between all groups (all $p < 0.001$). The SUA levels were significantly correlated with baPWV ($r = 0.142$) and carotid IMT ($r = 0.140$) (all $p < 0.001$). Multiple regression analyses showed that SUA levels were significantly associated with baPWV ($\beta = 12.267$), carotid IMT ($\beta = 0.013$) and the risk of carotid plaque (odds ratio 1.125; 95% confidence interval 1.004-1.261) (all $p < 0.05$). In conclusion, SUA levels have an independent association with subclinical atherosclerosis in a relatively healthy Korean adult population.

중요한 임상 사건의 병력이 없는 무증상 성인 한국인에서 혈청 요산 수치와 잠재적 동맥경화의 위험성

원 기 범
계명대학교 대학원
의학과 내과학 전공
(지도교수 허 승 호)

(초록)

무증상 성인에서 혈청 요산 수치와 다양한 동맥경화 지표와의 연관성에 대해서는 잘 알려져 있지 않다. 본 연구는 2010년 4월부터 2012년 11월까지 지역 기반 코호트 연구 건강 검진에 참여했던 심혈관 및 뇌혈관 질환, 신경학적 이상, 또는 악성종양 질환에 대한 과거력이 없는 무증상 성인 2560명을 대상으로 혈청 요산 수치와 상완-발목간 맥파전달속도, 경동맥 내막-중막 두께 및 경동맥 동맥경화반의 연관성을 조사했다. 모든 연구 참여자들은 혈청 요산 수치의 사분위수를 확인한 후 네 군으로 구분하였다. 각 군의 평균 상완-발목간 맥파전달속도 (1군 [가장 낮은]: 1441 ± 271 cm/s, 2군: 1444 ± 228 cm/s, 3군: 1495 ± 255 cm/s, 4군 [가장 높은]: 1518 ± 250 cm/s), 평균 경동맥 내막-중막 두께 (1군: 0.74 ± 0.15 mm, 2군: 0.74 ± 0.16 mm, 3군: 0.79 ± 0.20 mm, 4군: 0.79 ± 0.20 mm), 및 경동맥 동맥경화반의 빈도 (1군: 28.9%, 2군: 29.0%, 3군: 36.2%, 4군: 41.0% cm/s)는 각각

유의한 차이를 보였다 (all p <0.001). 혈청 요산 수치는 상완-발목간 맥파 전달속도 (r = 0.140) 및 경동맥 내막-중막 두께 (r = 0.142)와 유의한 양의 상관관계를 보였다 (all p <0.001). 다변량 회귀분석에서 혈청 요산 수치는 상완-발목간 맥파전달속도 (β = 12.267), 경동맥 내막-중막 두께 (β = 0.013) 및 경동맥 동맥경화반의 위험도 (odds ratio 1.125; 95% confidence interval 1.004-1.261)와 유의한 연관성을 보였다 (all p <0.05). 따라서 혈청 요산 수치는 비교적 건강한 무증상 성인에서 잠재적인 동맥경화와 독립적으로 연관되어 있을 것으로 판단된다.

□ 저자 약력

1978년 대구 출생
계명대학교 의과대학 의학과 졸업
동국대학교 대학원 내과학 석사
연세대학교 심장내과 전임의
St. Luke's International Hospital 연구원 (해외연수)
계명대학교 심장내과 임상조교수
울산대학교 심장내과 조교수(현)

□ 논문 및 저서

「High serum advanced glycation end-products predict coronary artery disease irrespective of arterial stiffness in diabetic patients」 Korean Circ J 2012; 42: 335-40.

「Differential impact of metabolic syndrome on subclinical atherosclerosis according to the presence of diabetes. Cardiovasc Diabetol 2013; 12: 41.

「Metabolic syndrome does not impact long-term survival in patients with acute myocardial infarction after successful percutaneous coronary intervention with drug-eluting stents」 Catheter Cardiovasc Interv 2014; 83: 713-20.

「Prognostic usefulness of metabolic syndrome compared with diabetes in Korean patients with critical lower limb ischemia treated with percutaneous transluminal angioplasty」 Yonsei Med J 2014; 55: 46-52.

「Safety and cost-effectiveness of bridge therapies for invasive dental

procedures in patients with mechanical heart valves」 Yonsei Med J 2014; 55: 937-43.

「Differential association between metabolic syndrome and coronary artery disease evaluated with cardiac computed tomography according to the presence of diabetes in a symptomatic Korean population」 BMC Cardiovasc Disord 2014; 14: 105.

「Differential association between obesity and coronary artery disease according to the presence of diabetes in a Korean population」 Diabetol Metab Syndr 2014; 6: 134.

「Evaluation of the predictive value of coronary artery calcium score for obstructive coronary artery disease in asymptomatic Korean patients with type 2 diabetes mellitus」 Coron Artery Dis 2015; 26: 150-6.

「Inverse association between central obesity and arterial stiffness in Korean subjects with metabolic syndrome: a cross-sectional cohort study」 Diabetol Metab Syndr 2015; 7: 3.

「Comparison of 2-year mortality according to obesity in stabilized patients with type 2 diabetes mellitus after acute myocardial infarction: results from the DIAMOND prospective cohort registry」 Cardiovasc Diabetol 2015; 14: 141.

「Clinical outcomes in patients with deferred coronary lesions according to disease severity assessed by fractional flow reserve」 J Korean Med Sci 2016; 31: 1929-36.

「Metabolic Syndrome predicts long-term mortality in subjects without established diabetes mellitus in asymptomatic Korean population: a propensity score matching analysis from the Korea Initiatives on Coronary Artery Calcification (KOICA) registry」 Medicine (Baltimore)

2016; 95: e5421.

「Evaluation of the impact of statin therapy on the obesity paradox in patients with acute myocardial infarction: A propensity score matching analysis from the Korea Acute Myocardial Infarction Registry」 Medicine (Baltimore) 2017; 96: e7180.

「Comparison of long-term mortality according to obesity in patients with successful percutaneous chronic total occlusion interventions using drug-eluting stents」 Catheter Cardiovasc Interv 2018; 91: 710-6.

「Evaluation of the impact of glycemic status on the progression of coronary artery calcification in asymptomatic individuals」 Cardiovasc Diabetol 2018; 17: 4.

「The relationship of insulin resistance estimated by triglyceride glucose index and coronary plaque characteristics」 Medicine (Baltimore) 2018; 97: e10726.

「Impact of optimal glycemic control on the progression of coronary artery calcification in asymptomatic patients with diabetes」 Int J Cardiol 2018; 266: 250-3.

「Relationship of insulin resistance estimated by triglyceride glucose index to arterial stiffness」 Lipids Health Dis 2018; 17: 268.

「Longitudinal assessment of coronary plaque volume change related to glycemic status using serial coronary computed tomography angiography: A PARADIGM (Progression of AtheRosclerotic PlAque DetermIned by Computed TomoGraphic Angiography Imaging) substudy」 J Cardiovasc Comput Tomogr 2019; 13: 142-7.

「Longitudinal quantitative assessment of coronary plaque progression related to body mass index using serial coronary computed

tomography angiography」 Eur Heart J Cardiovasc Imaging 2019; 20: 591-9.

「Independent role of low-density lipoprotein cholesterol in subclinical coronary atherosclerosis in the absence of traditional cardiovascular risk factors」 Eur Heart J Cardiovasc Imaging 2019; 20: 866-72.

「Association between insulin resistance, hyperglycemia, and coronary artery disease according to the presence of diabetes」 Sci Rep 2019; 9: 6129.

「Relationship between the optimal cut-off values of anthropometric indices for predicting metabolic syndrome and carotid intima-medial thickness in a Korean population」 Medicine (Baltimore) 2019; 98: e17620.

「High HDL-C levels reduce the risk of obstructive coronary artery disease in asymptomatic diabetics who achieved optimal glycemic control」 Sci Rep 2019; 9: 15306.

「Triglyceride glucose index is a useful marker for predicting subclinical coronary artery disease in the absence of traditional risk factors」 Lipids Health Dis 2020; 19: 7.

「Triglyceride glucose index is an independent predictor for the progression of coronary artery calcification in the absence of heavy coronary artery calcification at baseline」 Cardiovasc Diabetol 2020; 19: 34.

「High-density lipoprotein cholesterol and the risk of obstructive coronary artery disease beyond low-density lipoprotein cholesterol in non-diabetic individuals」 Eur J Prev Cardiol 2020; 27: 706-14.

「Quantitative assessment of coronary plaque volume change related to triglyceride glucose index: The Progression of AtheRosclerotic PlAque

DetermIned by Computed TomoGraphic Angiography Imaging (PARADIGM) registry」 Cardiovasc Diabetol 2020; 19: 113.