The relationship between leukocyte level and hypertension in elderly patients with hyperuricemia.

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Research article

Keywords: Hyperuricemia, leukocyte, hypertension, inflammation

Posted Date: June 18th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-31127/v1

The relationship between leukocyte level and hypertension in elderly patients with hyperuricemia

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Abstract:

Background: The purpose of this study was to evaluate the change of leukocyte level caused by hyperuricemia and explore the relationship between leukocyte level and hypertension in elderly patients with hyperuricemia. **Methods:** A cross-sectional study of serum uric acid level was conducted in 1352 elderly people over 65 years old in Beichen District of Tianjin. Hyperuricemia was defined as uric acid (UA) >420μmol/L. The study samples were divided into three categories according to the tertiles of leukocyte: Tertile 1, leukocyte $\leqslant 5.2\times10^9$/L; Tertile 2, leukocyte=5.3~6.3$\times10^9$/L; and Tertile 3, leukocyte $\geqslant 6.4\times10^9$/L. Multiple logistic regression models were used for modeling relationships between leukocyte, hyperuricemia and hypertension. In vitro, human vascular endothelial cells (HUVECs) were treated by different concentrations of UA (0, 4, 8, 16 mg/dl) for 24 h, then cells were collected. Interleukin-1 beta (IL-1β), tumor necrosis factor-α (TNF-α), endothelial nitric oxide synthase (eNOS) and inducible nitric oxide synthase (iNOS) protein expression was measured by western blotting. Reactive oxygen species (ROS) were analyzed with a fluorescence microscope. **Results:** The levels of leukocyte were higher in elderly patients with hyperuricemia than without hyperuricemia(*P*<0.01). In multiple logistic regression, hyperuricemia was an independent risk factor of leukocyte in Tertile 3 (OR=1.657, 95%CI: 1.180～2.328, *P*=0.004). The prevalences of hypertension were higher in elderly patients with hyperuricemia than without hyperuricemia (77.0% vs 63.5%, χ^2=11.447, *P*=0.001). In multiple logistic regression (Model 1), hyperuricemia was an independent risk factor of hypertension (OR=1.536, 95%CI: 1.026～2.302, *P*=0.037). When leukocyte in Tertile 3 was further adjusted, the association between hyperuricemia and hypertension disappeared.

Leukocyte in Tertile 3 was an independent risk factor of hypertension in Model 2 (OR= 1.333, 95%CI: 1.031~1.724, *P*=0.028). Expression levels of IL-1β, iNOS and TNF-α were obviously higher in the 8mg/dl UA group and 16mg/dl UA group than that in the control group (*P*<0.05). Expression level of eNOS was obviously lower in the 8mg/dl UA group and 16mg/dl UA group than that in the control group (*P*<0.05). The production of ROS in the 8mg/dl UA group and in the 16mg/dl UA group were obviously higher than that in the control group (*P*<0.05). **Conclusion:** The present study demonstrated that hyperuricemia was associated with an increased risk for hypertension. The chronic inflammation caused by hyperuricemia maybe one of important pathogenesis of incident hypertension in patients with hyperuricemia.

Key words: Hyperuricemia; leukocyte; hypertension;inflammation.

Background

Hypertension is a long-term condition that the blood pressure in the arteries is persistently elevated. In China, hypertension is very common. In 2017, the prevalence of hypertension reached 37.2% and the rates of treatment and control were extremely low[1]. Hypertension maybe not cause symptoms. However, hypertension is not benign and causes significant target organ damage, such as cardiovascular diseases and stroke[2,3]. Hypertension-related cardiovascular diseases remains the leading cause of death in Chinese adults[4].

In humans, uric acid (UA) is the final product of purine metabolism. UA played an important role to maintain arterial blood pressure and guarantee sufficient blood supply to

important organs[5]. Cross-sectional studies found that hyperuricemia is associated with hypertension in Chinese adults[6]. Cohort studies further confirmed that hyperuricemia can predict the risk of incident hypertension, independent of traditional risk factors[7-9]. Hyperuricemia could induce hypertension by the following mechanisms, including activation of renal epithelial sodium channel, renal oxidative stress, renin-angiotensin-aldosterone system and peripheral insulin resistance[10-13]. Several clinical trials found that lowering of UA may assist reducing blood pressure. UA lowering treatment can lower blood pressure in patients with hyperuricemia, especially in patients with normal renal function or early stage of chronic kidney disease[14, 15].

Low-grade systemic inflammation is implicated in the pathophysiology of hypertension. Leukocyte level count reflected low-grade systemic inflammation. Leukocyte count could independently predict hypertension in Chinese adults[16]. Two studies shown that hyperuricemia correlated with leukocyte count[17, 18]. Whether elevated leukocyte in patients with hyperuricemia correlated with hypertension? Very little information is currently available on the relationship between leukocyte and hypertension in hyperuricemia. In our study, we attempted to evaluate the change of leukocyte and related inflammatory factors caused by hyperuricemia and explore the relationship between leukocyte and hypertension in older adults with hyperuricemia.

Methods

Study Population

We performed a cross-sectional study about hyperuricemia. All subjects have medical examination in Beichen District of Tianjin between June 2018 and October 2018. All subjects

were men and women over 65 years old. The exclusion criteria included the following: 1) subjects with acute and chronic inflammation; 2) subjects with acute gout; 3) subjects with abnormal leukocyte (leukocyte<4×10^9/L or leukocyte>1×10^{10}/L); 4) subjects with secondary hypertension. This study was approved by the ethics committee of Tianjin Medical University Metabolic Diseases Hospital. All subjects provided written informed consent before study initiation.

Measurements

Anthropometric measurements, including height, weight, waist circumference (WC) and blood pressure were obtained. WC was accurately measured at the level of midway between the lowest rib and the top of the iliac crest. Blood pressure was measured with a mercury sphygmomanometer while the subjects were seated after 10 min of rest. Body mass index(BMI) was calculated by dividing weight (kg) by height squared (m^2).

After a 10-hour overnight fast, blood samples were collected from an antecubital vein into heparinised tubes. UA was measured using uricase method, fasting plasma glucose (FPG) concentration was measured using the glucose oxidase method, and serum lipid levels, as well as creatinine and alanine aminotransferase (ALT), were measured using enzymatic assays with an autoanalyzer (Hitachi, Tokyo, Japan). Estimate glomerular filtration rate (eGFR) = $175\times$creatinine (Cr, mg/dl)$^{-1.234}$ $\times$age(year)$^{-0.179}$($\times0.79$ if female)[19]. The automated hematology analyzer Beckman Coulter LH750 (Beckman Coulter Inc, Brea, CA) was used to evaluate the results of blood routine examinations (including leukocyte count).

Definition

Hyperuricemia was defined as UA>420μmol/L[20]. Hypertension was defined as subjects

with history of hypertension or systolic blood pressure (SBP) and/or diastolic blood pressure (DBP)≥140/90mmHg for three screenings. Abdominal obesity: WC≥90cm (male) and 85cm (female), abnormal glucose metabolism: FPG ≥ 6.1mmol/L or have been diagnosed with diabetes, hypertriglyceridemia: triglyceride (TG) ≥ 1.7mmol/L, low high density lipoprotein cholesterol (HDL-C): HDL-C <1.04mmol/L[21].

Cells culture and treatment

Human vascular endothelial cells (HUVECs, Beona chuanglian biotechnology co. LTD) were incubated in high-glucose DMEM medium (Gibco, USA) containing 10% fetal bovine serum (Gibco, USA) at 37 °C with 5% CO_2. When the adhering cells reached confluence, passage by trypsin digestion was conducted. After 3 to 5 passages, cells were treated with different concentrations of UA (0, 4, 8, 16 mg/dl) for 24 h, then cells were collected for western blotting.

Western blot analysis

HUVECs were collected and lysed with RIPA protein lysis buffer and the protein concentration was investigated by Bio Rad protein assay. Proteins were resolved by 12.5% SDS-PAGE and transferred to nitrocellulose membranes. Membranes were incubated with antibody targeting endothelial nitric oxide synthase (eNOS) (1:500, Abcam, England), inducible nitric oxide synthase (iNOS) (1:500, Abcam, England), interleukin-1 beta (IL-1β) (1:1000, Affinity, USA) and tumor necrosis factor-α (TNF-α) (1:1000, Abcam, England) at 4 °C overnight. After washing, the membranes were incubated with secondary antibody (1:4000) in TBST for 1 h at room temperature. ECL Plus detection system was used for immunodetection, and the density of the bands was detected by Image J software.

Influence of UA on the production of ROS

HUVECs were treated by different concentrations of UA (0, 4, 8, 16 mg/dl) for 12 h. Then cells were loaded with 10 μM working solution at 37 °C for 20 min and washed thrice with warm buffer according to the experimental protocol of reactive oxygen species (ROS) assay kit (Beyotime Biotechnology, China). After that, cells were analyzed with a fluorescence microscope.

Statistical Analyses

All analyses were performed using the SPSS 11.5 statistical software (SPSS 11.5 for Windows; SPSS, Inc., Chicago, IL). Values are expressed as mean with standard deviation, and analyzed using GraphPad Prism 8.0. The two groups were compared using the Student *t*-test. Comparison of prevalence data was performed by $\chi 2$ analysis. Multiple logistic regression models were used for modeling relationships between leukocyte, hyperuricemia and hypertension. The one-way analysis of variance (ANOVA) for multiple comparison was performed for differences analysis.$P<0.05$ was considered statistically significant.

Results

Clinical characteristics of the subjects.

This study enrolled 1352 elderly people (620 males and 732 females), age 72.4±6.4 years. The prevalence of hyperuricemia was 11.9% in our study. The prevalences of hyperuricemia were higher in males than in females (Males 16.1% vs Females 8.3%, $\chi^2=19.447$, $P<0.001$). The levels of hemoglobin, platelet, neutrophil (%), lymphocyte (%) and lymphocyte (10^9/L) were similar between elderly patients with or without hyperuricemia ($P>0.05$). The levels of neutrophil (10^9/L) and leukocyte (10^9/L) were higher in elderly patients with hyperuricemia than without hyperuricemia ($P<0.01$). The study samples were

divided into three categories according to the tertiles of leukocyte: Tertile 1 leukocyte $\leqslant$ 5.2×10^9/L, Tertile 2 leukocyte= 5.3~6.3×10^9/L, and Tertile 3 leukocyte $\geqslant$ 6.4×10^9/L. The frequencies of leukocyte in Tertile 3 were higher in elderly patients with hyperuricemia than without hyperuricemia (Table 1). In multiple logistic regression analysis, leukocyte (Tertile 3) was considered as the dependent variables with sex, age, BMI (0=BMI<24kg/m^2, 1=BMI 24~27.9kg/m^2, 2=BMI $\geqslant$ 28kg/m^2), abdominal obesity, abnormal glucose metabolism, hypertriglyceridemia, low HDL-C and hyperuricemia as independent variables. Hyperuricemia was an independent risk factor of leukocyte (Tertile 3) in elderly patients (OR=1.657, 95%CI: 1.180～2.328, *P*=0.004) (Table 2).

The prevalence of hypertension was 65.1% in our study. The prevalences of hypertension were similar between males and females (Males 63.2% vs Females 66.7%, χ^2=1.749, *P*=0.186). Patients with hypertension were older than patients without hypertension (*P*=0.006). The levels of ALT and eGFR were similar between two groups (*P*>0.05). The frequencies of BMI $\geqslant$ 28kg/m^2, abdominal obesity, abnormal glucose metabolism, hypertriglyceridemia, low HDL-C, hyperuricemia and leukocyte (Tertile 3) were higher in older adults with hypertension than without hypertension (*P*<0.01) (Table 3).

The prevalences of hypertension were higher in elderly people with hyperuricemia than without hyperuricemia (77.0% vs 63.5%, χ^2=11.447, *P*=0.001). In multiple logistic regression analysis (Model 1), hypertension was considered as the dependent variables with sex, age, BMI abdominal obesity, abnormal glucose metabolism, hypertriglyceridemia, low HDL-C and hyperuricemia as independent variables. Hyperuricemia was an independent risk factor of hypertension in older adults (OR=1.536, 95%CI: 1.026～2.302, *P*=0.037) (Table 4). When

leukocyte (Tertile 3) was further adjusted, the association between hyperuricemia and hypertension disappeared. Leukocyte (Tertile 3) was an independent risk factor of hypertension in Model 2 (OR= 1.333, 95%CI: 1.031～1.724, *P*= 0.028) (Table 5).

When the analysis was stratified by the status of UA, leukocyte (Tertile 3) was an independent risk factor of hypertension only in elderly people with hyperuricemia (OR= 2.364, 95%CI: 1.075～5.197, *P*= 0.032).

Effect of different concentrations of uric acid on the expression level of eNOS, iNOS, IL1-β and TNF-α in HUVECs.

The results showed that there was no significant difference in eNOS protein expression between the 4mg/dl UA group and the control group (*P*=0.9639). Expression level of eNOS was obviously lower in the 8mg/dl UA group (*P*=0.0022) and in the 16mg/dl UA group (*P*=0.0003) than that in the control group. Expression levels of eNOS tested by Western blot in the 8mg/dl UA group (*P*=0.0013) and in the 16mg/dl UA group (*P*=0.0002) were obviously lower than that in the 4mg/dl UA group. Expression level of iNOS was obviously higher in 4mg/dl UA group (*P*=0.0021), 8mg/dl UA group (*P*=0.0210) and 16mg/dl UA group (*P*=0.0111) than that in the control group. There was no significant difference in iNOS protein expression between the 4mg/dl UA group, 8 mg/dl UA group (*P*=0.3281) and 16 mg/dl UA group (*P*=0.5593).

The results showed that there was no significant difference in IL1-β protein expression between the 4mg/dl UA group and the control group (*P*=0.0687). Expression levels of IL1-β in the 8mg/dl UA group and in the 16mg /dl UA group were obviously higher than that in the control group (*P*<0.0001). Expression levels of IL1-β in the 8mg/dl UA group and in the 16mg /dl UA group were obviously higher than that in the 4 mg/dl UA group (*P*<0.0001) .

The results showed that there was no significant difference in TNF-α protein expression between the 4mg/dl UA group and the control group (*P*=0.3260). Expression levels of TNF-α in the 8mg/dl UA group and in the 16mg /dl UA group were obviously higher than that in the control group (*P*<0.0001). Expression levels of TNF-α in the 8mg/dl UA group and in the 16mg /dl UA group were obviously higher than that in the 4 mg/dl UA group (*P*=0.0001).

Comparison of ROS content in different uric acid concentration groups.

The results showed that there was no significant difference in ROS content between the 4mg/dl UA group and the control group (*P*=0.7230). The production of ROS in the 8mg/dl UA group (*P*=0.0370) and in the 16mg /dl UA group (*P*<0.0001) were obviously higher than that in the control group (*P*<0.05).

Discussion

In this study, we found that hyperuricemia has higher level of leukocyte than patients with normal uric acid. Elevated leukocyte level induced by hyperuricemia was associated with hypertension in elderly people with hyperuricemia.

As a marker of inflammation, elevated leukocyte count reflected a low-grade systemic inflammation in hyperuricemia. Consistent with previous research[17, 18], the frequencies of the highest tertile of leukocyte was higher in elderly people with hyperuricemia. As we known, subjects with hyperuricemia often accompany abdominal obesity, abnormal glucose metabolism, hypertriglyceridemia, etc. These factors were also associated with chronic inflammation. In our study, we adjusted these confounding factors, hyperuricemia still correlated with leukocyte count. Elevated UA can promote the expression of inflammatory proteins by triggering complex proinflammatory cascades that damage cells and tissues[22].

UA lowering treatment can improve systemic inflammation in asymptomatic hyperuricemia[23].

In whole sample, hyperuricemia was an independent risk factor of hypertension. However, after leukocyte adjusted, the association between hyperuricemia and hypertension disappeared. Among older adults with hyperuricemia, elevated leukocyte was independently associated with hypertension. These results implied that inflammation may be involved in the development of hypertension associated with hyperuricemia in elderly people. Leukocyte was correlated with coronary heart disease risk in Chinese adults aged 40~85 years old with hyperuricemia[24]. Similar result was also observed in Japanese men[25].

Endothelial dysfunction plays an important role in pathogenesis of hypertension. Hyperuricemia caused endothelial dysfunction through inflammation, which may induce hypertension[26]. UA promoted vascular inflammation, which was characterized by up-regulating of cytokines and enhanced monocyte adhesion[27]. Anti-inflammatory intervention can attenuate UA-induced endothelial injury[28]. Therefore, we further verified the effect of high levels of uric acid on inflammatory factors and endothelial function at the cellular level. In this study, we found that UA could significantly increase the level of IL-1β and TNF-α in HUVECs. Several reports in the literature suggested that the monosodium urate activated several inflammatory mediators, such as IL-1β, IL-6, and TNF-α[29]. IL-1β, a member of interleukin-1 cytokine superfamily[30]. TNF-α is most important player in inflammatory reactions, can further activating production of additional inflammatory cytokines[29]. It was reported that endothelial cells damage induced by inflammatory factors plays a key role in the pathogenesis of vascular diseases. The increase of IL-1β and TNF-α

induced by UA probably account for vascular endothelium damage. Studies demonstrated that hypertension may develop as a result of increased ROS. Hypertensive effects of oxidative stress are mostly due to endothelial dysfunction resulting from disturbances of vasodilator systems[31]. The eNOS is a vascular smooth muscle relaxing factor that plays an important role in the regulation of blood pressure[32]. Animal studies have shown that mice genetically deficient in eNOS (eNOS−/−) are hypertensive, indicated that the importance of eNOS to blood pressure regulation. A population-based study with Brazilian women showed that genetic polymorphisms of eNOS was significantly associated with a higher prevalence of hypertension[33]. In the present study, we determined that the high concentration of UA induced intracellular ROS accumulation, increasing iNOS, and reduced eNOS in a dose-dependent manner. In conclusion, the present study confirmed previous reports that high levels of UA trigger endothelium impairment and vascular dysfunction by increase the expression of inflammatory cytokines and ROS content，inducing iNOS and reducing eNOS，which may induce hypertension.

Limitations

There are two limitations to our study. First, because of the cross-sectional design of this study, we could not identify the causal relationship between hyperuricemia, leukocyte and hypertension. Second, it is well known that some antihypertensive agents can affect the level of UA. Antihypertensive agents were not analyzed in our study.

Conclusion

In conclusion, the present study demonstrates that hyperuricemia is associated with an increased risk for hypertension. The chronic inflammation caused by hyperuricemia maybe

one of important pathogenesis of incident hypertension in patients with hyperuricemia.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Abbreviations

UA: Uric Acid

WC: Waist Circumference

BMI: Body Mass Index

FPG: Fasting Plasma Glucose

HUVECs: Human Vascular Endothelial Cells

IL-1β: Interleukin-1 Beta

TNF-α: Tumor Necrosis Factor-α

eNOS: Endothelial Nitric Oxide Synthase

iNOS: Inducible Nitric Oxide Synthase

ROS: Reactive Oxygen Species

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Ethics declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Tianjin Medical University Metabolic Disease Hospital (No.DXBYYhMEC2018-17). Written informed consent was obtained from all the participants.

Consent for Publication

Not applicable.

Competing interests

The author declare that they have no competing interests.

Funding

No funding was provided for this study.

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Lijin Shen, Mingzhen Li, Bei Sun, Zhichao Zhou, Jing Zhang, Yanjie Liu, Ya Dong, Wei Zhao

Contributions

WZ contributed to the design of the study. MZL, ZCZ, YJL and YD contributed to the data collection process. WZ and BS performed the statistical data analyses. WZ and LJS drafted the manuscript. JZ performed the experiment part. The author(s) read and approved the final manuscript.

Corresponding author

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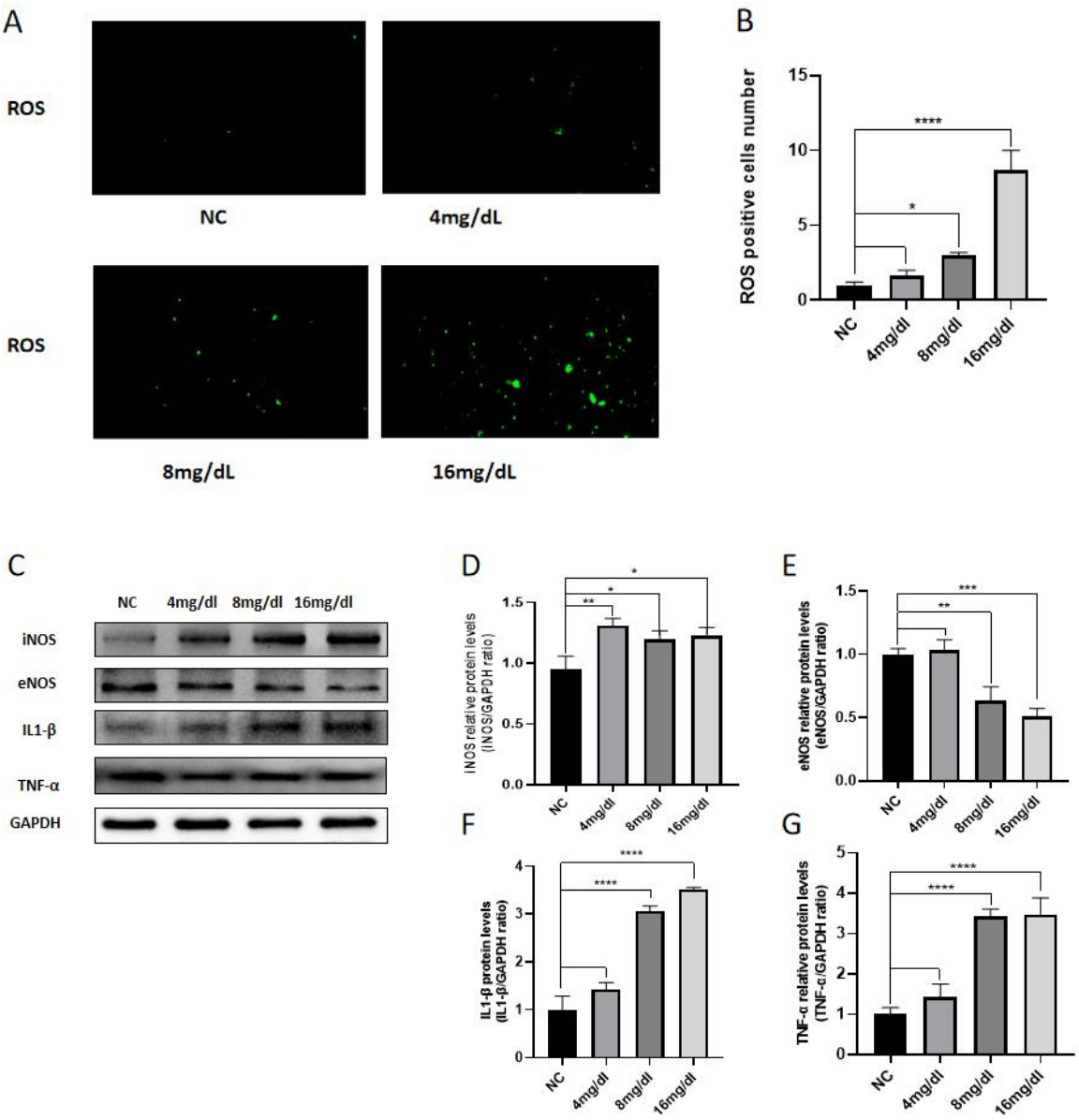
Acknowledgements

Not applicable.

Figure legends:

Figure A-G. Effect of different concentrations of uric acid on the expression of eNOS, iNOS, IL1-β, TNF-α and ROS content in human vascular vein endothelial cells (HUVECs).

(A and B) Effect of uric acid (UA) on intracellular reactive oxygen species (ROS) generation in human vascular vein endothelial cells (HUVECs). (C、D、E、F and G) iNOS, eNOS, IL1-β and TNF-α protein levels were measured by western blot analysis in HUVECs incubated with 4 mg/dl, 8 mg/dl and 16 mg/dl UA.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8mg/dl
16mg/dl
C
NC
4mg/dl
8mg/dl
16mg/dl
iNOS
eNOS
IL1-β
TNF-α
GAPDH
D
iNOS relative protein levels (iNOS/GAPDH ratio)
1.5
1.0
0.5
0.0
*
*
**
NC
4mg/dl
8mg/dl
16mg/dl
E
eNOS relative protein levels (eNOS/GAPDH ratio)
1.5
1.0
0.5
0.0
***
**
NC
4mg/dl
8mg/dl
16mg/dl
F
IL1-β protein levels (IL1-β/GAPDH ratio)
4
3
2
1
0
****
****
NC
4mg/dl
8mg/dl
16mg/dl
G
TNF-α relative protein levels (TNF-α/GAPDH ratio)
5
4
3
2
1
0
****
****
NC
4mg/dl
8mg/dl
16mg/dl

Figure A-G.

Table 1 Hematological parameters of the subjects in each group.

Variable		Non-Hyperuricemia Group (n=1191)	Hyperuricemia Group (n=161)	t or χ^2	P
Hemoglobin (g/L) mean (SD)		138.7(14.9)	137.8(18.5)	0.537	0.592
Platelet (10^9/L) mean (SD)		226.8(55.9)	221.7(55.7)	1.094	0.274
Neutrophil (%) mean (SD)		58.4(8.8)	59.3(8.1)	1.255	0.210
Lymphocyte (%) mean (SD)		33.6(8.1)	32.4(7.7)	1.745	0.081
Neutrophil (10^9/L) mean (SD)		3.51(1.00)	3.78(1.01)	3.158	0.002
Lymphocyte (10^9/L) mean (SD)		1.99(0.59)	2.04(0.61)	0.935	0.350
Leukocyte (10^9/L) mean (SD)		5.97(1.22)	6.33(1.32)	3.247	0.001
Leukocyte (10^9/L)[n(%)]	Tertile 1($\leqslant$ 5.2)	389(32.7)	40(24.8)	11.960	0.003

Tertile 2(5.3~6.3)	424(35.6)	48(29.8)
Tertile 3(≥ 6.4)	378(31.7)	73(45.3)

SD: standard deviation.

Table 2 The risk factors of elevated leukocyte in older adults.

Variable	OR	95%CI	*P*
Abdominal obesity	1.595	1.249～2.038	<0.001
Abnormal glucose metabolism	1.380	1.091～1.746	0.007
Hypertriglyceridemia	1.404	1.105～1.785	0.006
Hyperuricemia	1.657	1.180～2.328	0.004

Elevated leukocyte was defined as leukocyte in Tertile 3($\geqslant 6.4 \times 10^9$/L)。 Multiple logistic regression analysis, elevated leukocyte was considered as the dependent variables in a multiple logistic regression analysis with sex, age, BMI(0=BMI<24kg/m^2, 1=BMI 24~27.9kg/m^2, 2=BMI $\geqslant$ 28kg/m^2), abdominal obesity, abnormal glucose metabolism, hypertriglyceridemia, low HDL-C and hyperuricemia as independent variables. OR: odds ratio; CI: confidence interval; BMI: body mass index; HDL-C: high density lipoprotein cholesterol.

Table 3 Clinical characteristics of older adults with or without hypertension.

Variable		Non-Hypertension Group (n=472)	Hypertension Group (n=880)	*t* or χ^2	*P*
Sex(males/females)		228/244	392/488	1.749	0.186
Age (years) mean (SD)		72.2(6.3)	73.7(6.8)	2.760	0.006
ALT (U/L) mean (SD)		20.7(15.3)	21.7(14.5)	0.763	0.445
eGFR (ml*min-1*1.73m-2) mean (SD)		94.5(14.6)	93.2(15.9)	0.928	0.354
BMI[n(%)]	<24kg/m^2	190(40.3)	225(25.6)	35.434	<0.001
	24~27.9kg/m^2	173(36.7)	352(40.0)		
	⩾28kg/m^2	109(23.1)	303(34.4)		
Abdominal obesity[n(%)]		245(51.9)	573(65.1)	22.424	<0.001
Abnormal glucose metabolism[n(%)]		134(28.4)	435(49.4)	55.809	<0.001
Hypertriglyceridemia[n(%)]		149(31.6)	343(39.0)	7.286	0.007

Low HDL-C[n(%)]	52(11.0)	171(19.4)	15.794	<0.001
Hyperuricemia[n(%)]	37(7.8)	124(14.1)	11.447	0.001
Leukocyte (Tertile 3)[n(%)]	130(27.5)	321(36.5)	11.033	0.001

SD: standard deviation; ALT: alanine aminotransferase; eGFR: estimate glomerular filtration rate; BMI: body mass index; HDL-C: high density lipoprotein cholesterol.

Table 4 The risk factors of hypertension in older adults (Model 1).

Variable		OR	95%CI	*P*
BMI	<24kg/m^2	1		
	24~27.9kg/m^2	1.829	1.382～2.422	<0.001
	⩾28kg/m^2	2.261	1.662～3.076	<0.001
Abnormal glucose metabolism		2.319	1.812～2.969	<0.001
Low HDL-C		1.608	1.134～2.280	0.008
Hyperuricemia		1.536	1.026～2.302	0.037

Multiple logistic regression analysis, hypertension was considered as the dependent variables in a multiple logistic regression analysis with sex, age, BMI(0=BMI<24kg/m^2, 1=BMI 24~27.9kg/m^2, 2=BMI ⩾ 28kg/m^2), abdominal obesity, abnormal glucose metabolism, hypertriglyceridemia, low HDL-C and hyperuricemia as independent variables. OR: odds ratio; CI: confidence interval; BMI: body mass index; HDL-C: high density lipoprotein cholesterol.

Table 5 The risk factors of hypertension in older adults (Model 2).

Variable		OR	95%CI	*P*
BMI	<24kg/m^2	1		
	24~27.9kg/m^2	1.839	1.389～2.434	<0.001
	⩾28kg/m^2	2.271	1.670～3.088	<0.001
Abnormal glucose metabolism		2.256	1.762～2.889	<0.001
Low HDL-C		1.654	1.168～2.341	0.005
Leukocyte (Tertile 3)		1.333	1.031～1.724	0.028

Multiple logistic regression analysis, hypertension was considered as the dependent variables in a multiple logistic regression analysis with sex, age, BMI(0=BMI<24kg/m^2, 1=BMI 24~27.9kg/m^2, 2=BMI ⩾ 28kg/m^2), abdominal obesity, abnormal glucose metabolism, hypertriglyceridemia, low HDL-C, hyperuricemia and leukocyte (Tertile 3) as independent variables. OR: odds ratio; CI: confidence interval; BMI: body mass index; HDL-C: high density lipoprotein cholesterol.

Figures

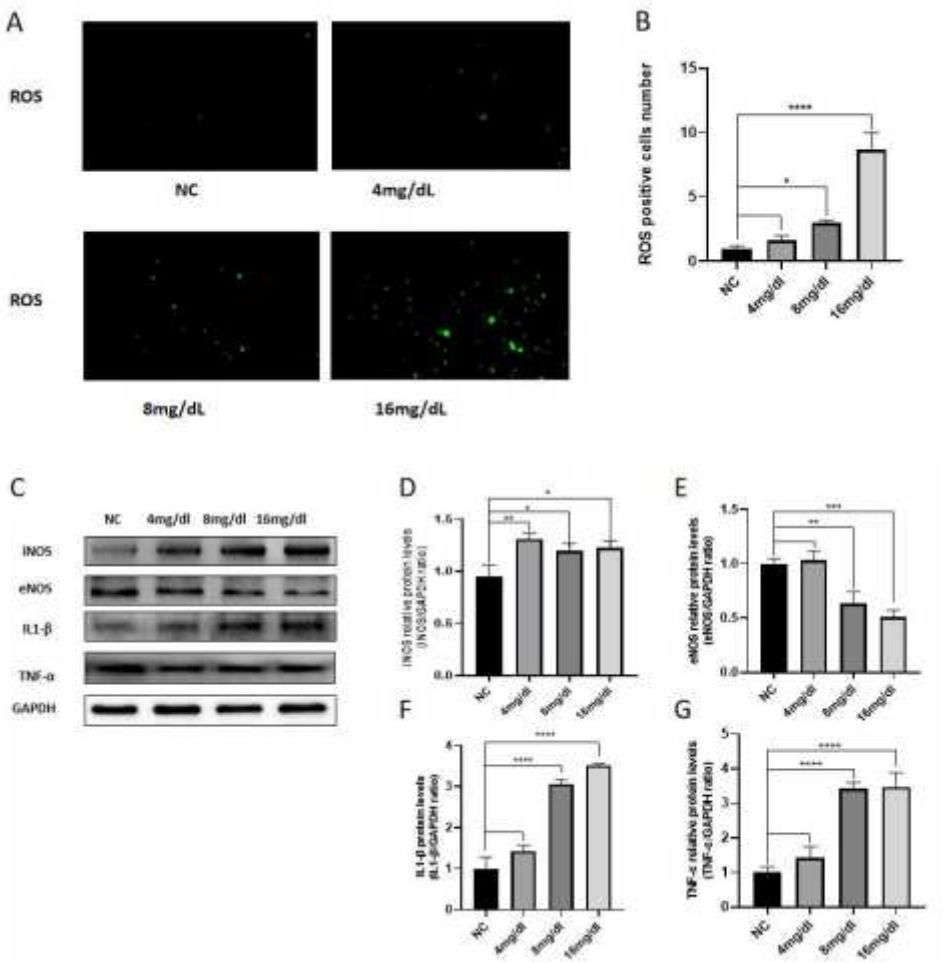

Figure 1

Effect of different concentrations of uric acid on the expression of eNOS, iNOS, IL1-β, TNF-α and ROS content in human vascular vein endothelial cells (HUVECs). (A and B) Effect of uric acid (UA) on intracellular reactive oxygen species (ROS) generation in human vascular vein endothelial cells (HUVECs). (C□D□E□F and G) iNOS, eNOS, IL1-β and TNF-α protein levels were measured by western blot analysis in HUVECs incubated with 4 mg/dl, 8 mg/dl and 16 mg/dl UA.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfiles.pdf
- STROBEchecklistv4combined.pdf