Original Article

Hyperuricemia Accompanied with Changes in the Retinal Microcirculation in a Chinese High-risk Population for Diabetes*

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Abstract

Objective To investigate the association of retinal vascular calibers with hyperuricemia in a middle-aged and elderly population.

Methods A cross-sectional design was applied in this study and 869 participants aged ⩾40 years from a high-risk group for diabetes were recruited. All participants received the anthropometrical measurements and laboratory tests. Retinal arteriolar and venular caliber of the participants were measured with a semi-automated system. Hyperuricemia was defined as a serum uric acid level >420 μmol/L in men and >360 μmol/L in women. Linear regression models were used to assess the association of hyperuricemia with retinal vascular calibers. These models were additionally adjusted for age, central obesity, hypertension, dyslipidemia, weekly activity, smoking status, and education.

Results Among the 869 participants, 133 (15.3%) suffered from hyperuricemia. The crude mean serum uric acid level was 312.3 μmol/L (Standard Deviation 79.5); mean concentration was 355.0 μmol/L (SD 75.5) in male participants, and 288.0 μmol/L (SD 71.1) in female participants (age-adjusted difference 58.1 μmol/L, 95% Confidence Internal 48.5, 67.6). After adjusting for additional covariates, male participants with hyperuricemia had 3.77 μm (95% CI -0.46, 8.00) smaller arteriolar caliber and 6.20 μm (95% CI 0.36, 12.04) larger venule than those without hyperuricemia; the corresponding numbers among female participants were 1.57 μm (95% CI -1.07, 4.21) for retinal arteriolar caliber and 2.28 μm (95% CI -1.72, 6.27) for retinal venular caliber.

Conclusion Hyperuricemia was associated with smaller retinal arteriolar caliber and larger venular caliber mainly in male participants in this study.

Key words: Cardiovascular disease; Hypertension; Hyperuricemia; Metabolic syndrome; Retinal photograph; Retinal vessels; Uric acid

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INTRODUCTION

Hyperuricemia has long been associated with hypertension, diabetes, metabolic syndrome, kidney disease, and cardiovascular disease[1-6]. The relative importance of these associations however remains controversial[3]. Several studies have suggested that an elevated uric acid level may lead to hypertension by causing changes in the microcirculation[3, 5-13], though direct

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in vivo observations of microcirculatory alterations in persons with hyperuricemia are lacking thus far.

Retinal vascular abnormalities have been considered as indicators for the severity of cardiovascular diseases[14-15]. Since the late 1990s, standardized methods for measuring retinal vascular caliber have been established and increasingly employed by many large population-based studies over the last decade[16-17]. Recent evidence indicated that changes in the retinal microcirculation such as arteriolar narrowing and venular dilatation were associated with hypertension[18-20], obesity[18-19, 21], impaired serum glucose level or diabetes, and proliferative diabetic retinopathy[18-19, 22-25].

As hyperuricemia has been linked to the occurrence of diseases with microvascular changes such as hypertension, we hypothesized that hyperuricemia might be associated with microvascular changes, which could ultimately lead to these cardiovascular diseases. Therefore, in the present study, we examined cross-sectionally the association of hyperuricemia with the retinal microcirculation in a Chinese urban middle-aged and elderly population who are at high risk for diabetes.

MATERIAL AND METHODS

Study Population

The present study was based on the High-risk for Diabetes Changfeng Study. Changfeng Community is an urban residential area in northwest Shanghai of China; the residents belong to middle socio-economic class in Shanghai. There were 41 626 residents (50.1% male) of the community covered by the service of a Community Health Service Center (Changfeng Community Health Service Center); 63% of them were 40 years or older. In accordance with the recommendations of the American Diabetes Association (ADA)[26], we intended to recruit persons aged 40 years or older who had (a) a family history of diabetes, or (b) a history of giving birth to a baby weighing > 4 kg, or a history of gestational diabetes mellitus (GDM), or (c) elevated glucose, triglycerides, or blood pressure levels in the past, or who suffered from (d) obesity (including increased waist circumference or fatty liver disease), coronary heart disease, myocardial infarction, or stroke. We did not include persons with a history of diabetes, and also excluded the newly diagnosed diabetic participants based on the definition of ADA[27]. The participants included were supposed to be at an increased risk of developing type 2 diabetes mellitus[28]. Inhabitants from 16 blocks of the community were invited to participate in the study by posting advertisements, on which the criteria were mentioned, on the walls of each building of the districts from March to December 2005. In total, 1 761 volunteers responded to the advertisement. Trained health workers checked all medical records of the respondents to ensure that the inclusion criteria were met. A small proportion of the respondents (n=85) were excluded because they failed to meet the inclusion criteria based on their medical records. For example, some respondents, who claimed to have coronary heart disease, but in fact had congenital heart disease based on their medical records, or others who responded to the advertisement had diabetes mellitus in fact.

Of the remaining 1 676 eligible participants, 13 persons were excluded because their key variables (e.g. age, height, weight, etc.) were missing. A total of 164 newly diagnosed patients with diabetes were excluded. There were 312 persons who did not have fundus photographs due to too small pupils and/or opacities of refractive media. A total of 1 187 participants (79.2% of the eligible responders) had fundus photographs. Of them, 869 participants (58.0% of the eligible responders) had gradable fundus photographs, while the other 318 participants had non-gradable fundus photographs (Figure 1). Some families had more than 1 participant. Totally, there were 8 families (8 out of 773 families, 1.03%) which had more than 2 participants (together 28 participants, 3.22%). And 76 families (76 out of 773 families, 9.83%) had 2 participants, most of whom were spouses. All the data were collected between August 2005 and July 2007 by well-trained personnel from Zhongshan Hospital and health workers from the Community Health Service Center. The study was conducted according to the tenets of the Declaration of Helsinki and was approved by the institutional review boards at Zhongshan Hospital, Fudan University, Shanghai, China.

Data Collection

Retinal vascular caliber measurements Fundus photographs were taken centered on optic disc and/or macula lutea by using a nonstereoscopic, 45° nonmydriatic fundus camera (CR-DGI + Canon 20D, Canon Inc, Tokyo, Japan). For each participant, a masked grader (YZ Yuan) selected the fundus photographs with the best quality (either right or left eye). Right eye would be selected in case both

fundus photographs had same quality. Retinal vascular calibers were measured on the digital fundus photographs with a semi-automated system (IVAN; Optimate, Madison, WI; Department of Ophthalmology and Visual Science, University of Wisconsin-Madison, U.S.A.) by two trained graders masked to participants' characteristics according to a standardized protocol. The Parr-Hubbard-Knudtson formulas[16-17] were used to compute summary retinal arteriolar and venular calibers termed "central retinal arteriolar and venular equivalent (CRAE and CRVE)". The calculations were undertaken automatically by the programme. Quality control sessions were performed using two randomly selected sets of 35 and 33 fundus photographs. These were inserted into the regular workflow to assess intra- and inter-observer agreement. Intra-class correlation coefficients ranged from 0.88 to 0.92 for retinal arteriolar calibers and from 0.95 to 0.97 for retinal venular calibers.

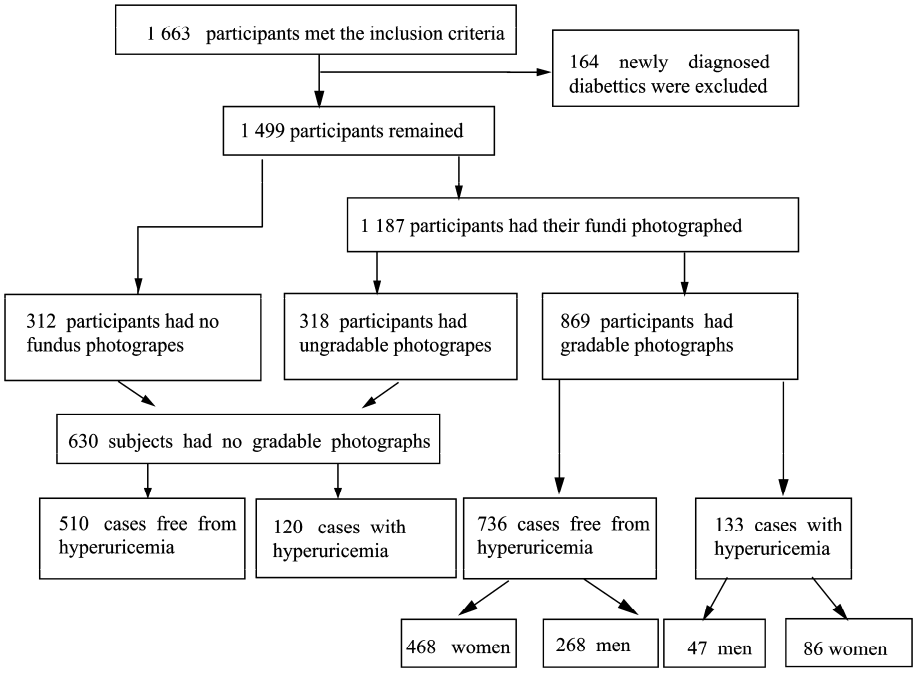

Figure 1. Flowchart of the study population.

Other Cardiovascular Risk Factors

All participants were examined using a standardized protocol including anthropometrical measurements. Waist circumferences (WC) were measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest. Body mass index (BMI) was calculated as weight (kg) divided by height (m) square. Each participant had the systolic and diastolic blood pressures measured 3 times using a mercury sphygmomanometer, and then the average was calculated. Fasting blood samples were collected after at least 10-h overnight fasting. Serum uric acid was assessed by uricase enzymatic method. The blood glucose was measured by the glucose oxidase method. Fasting blood lipid profile, HDL cholesterol and Triglyceride (TG) were determined by using the enzymatic method (Hitachi 7170A, Hitachi Co., Tokyo, Japan). An oral glucose tolerance test was performed in each participant to detect undiagnosed diabetes and impaired glucose regulation (IGR). First morning urine was collected to detect urine protein.

Potential confounders such as education, smoking status and physical activity were assessed by questionnaires. Educational levels were categorized into secondary school education or above and primary school education or below. Smoking status was classified into never smoking and ever smoking. We documented weekly physical activity time in hours.

Definitions of Hyperuricemia and Other Cardiovascular Diseases

Hyperuricemia was defined as a serum uric acid level > 420 μmol/L in men and 360 μmol/L in women [3].

ADA definition was used to diagnose diabetes mellitus[27]. International Diabetes Federation (IDF) consensus worldwide definition was used to define metabolic syndrome, central obesity, dyslipidemia, and hyperglycemia[29-30]. Specifically, central obesity was defined as waist circumference≥90 cm in man and≥80 cm women; dyslipidemia was defined as serum triglycerides≥1.7 mmol/L or HDL-cholesterol <1.03 mmol/L; and hyperglycemia was defined as fast serum glucose≥5.6 mmol/L. Hypertension was defined as average systolic blood pressure≥140 mm Hg and/or average diastolic blood pressure≥90 mm Hg and/or participants who were on treatment for previously diagnosed hypertension.

Statistical Analysis

Analysis of covariance (ANCOVA) was used to compare the demographic characteristics of participants with and without gradable fundus photographs, and participants with and without the hyperuricemia. Student's T-test was used to compare difference of age between men and women, while ANCOVA was used to compare the age-adjusted difference in serum uric acid levels across genders.

We studied serum uric acid levels both as continuous variable [per standard deviation (SD)] and categorized (gender-specified definition for hyperuricemia) using linear regression models. These models were additionally adjusted for age, gender, smoking status (never smoke *vs.* ever smoke), education (more than primary school education *vs.* primary school education or lesser), weekly activity (hours), central obesity, hypertension, hyperglycemia, and dyslipidemia. As described previously, retinal arteriolar and venular calibers were mutually adjusted for[31]. All analyses were performed by using SPSS (Windows ver. 15.0; SPSS Inc., Chicago, IL).

RESULTS

Demographic Characteristics of the participants

Figure 1 shows the flowchart of the study population. Among the 1 499 eligible participants, 869 (58.0%) had gradable fundus photographs, while the other 630 had no gradable photographs.

Table 1 shows the demographic characteristics of the participants with and without gradable fundus photographs. Most of the differences were subtle and insignificant, though the non-gradable group tended to have more women and had a slightly higher triglycerides and lower HDL-cholesterol levels.

The mean age of the participants with gradable fundus photographs (n=869) was 59.3 years (SD 9.8), and 36.3% were men. The mean age of men and women were 60.5 (SD 9.9) and 58.6 (SD 9.7) years (Student's t-test, t=-2.73, P<0.01), respectively.

Among the 869 participants with gradable photographs, 133 (15.3%) met the criteria of hyperuricemia. Table 2 shows the demographic characteristics of the participants with and without hyperuricemia. The participants with hyperuricemia had a higher prevalence of central obesity, dyslipidemia, hypertension, hyperglycemia and metabolic syndrome.

The Distribution of Serum Uric Acid Levels of the participants

The mean serum uric acid was 312.3 μmol/L (SD 79.5). Its concentration in men was 355.0 μmol/L (SD 75.5), and 288.0 μmol/L (SD 71.1) in women. Age-adjusted difference between men and women was 63.2 μmol/L (95% CI 53.5-73.0). Figure 2 shows the different serum uric acid levels in men and women, which in both cases were approximately normally distributed.

Retinal Vascular Calibers and Hyperuricemia

Mean values for retinal arteriolar caliber was 139.7 μm (SD 14.4), and for retinal venular caliber, the value was 210.9 μm (SD 20.9) (Table 2).

Serum uric acid levels were linearly associated with retinal vascular caliber. After adjustment for age and gender, per SD increase of uric acid was associated with 2.23 μm (95% CI 1.45, 3.01) narrower arteriolar calibers, and 1.51 μm (95% CI 0.26, 2.76) wider venular calibers. Further adjustments for central obesity, dyslipidemia, hypertension, hyperglycemia, weekly activity, smoking status, and education did not alter the associations significantly: the corresponding numbers were 1.91 μm (95% CI 0.97, 2.84) and 1.51 μm (95% CI 0.11, 2.91).

Analyses were stratified for gender when we used the gender-specified definitions for hyperuricemia. Table 3 shows the associations of retinal arteriolar and venular caliber with hyperuricemia. After adjustment for age (Model I in Table 3), men with hyperuricemia had a 5.52 μm (95% CI 1.60, 9.43) smaller arteriole and a 7.08 μm (95% CI 1.68, 12.48) larger venule than those without hyperuricemia. In women, the changes were less significant: women

with hyperuricemia had a 1.81 μm (95% CI -0.73, 4.34) smaller retinal arteriolar caliber, and a 2.57 μm (95% CI -1.24, 6.38) larger retinal venular caliber. Further adjustments for central obesity, dyslipidemia, hypertension, hyperglycemia, smoking status, weekly activity and education, did not change these associations (Model II in Table 3): men with hyperuricemia had a 3.77 μm (95% CI -0.46, 8.00) smaller arteriolar caliber and a 6.20 μm (95% CI 0.36, 12.04) larger venular caliber, and in women the corresponding numbers were 1.57 μm (95% CI -1.07, 4.21) and 2.28 μm (95% CI -1.72, 6.27), respectively.

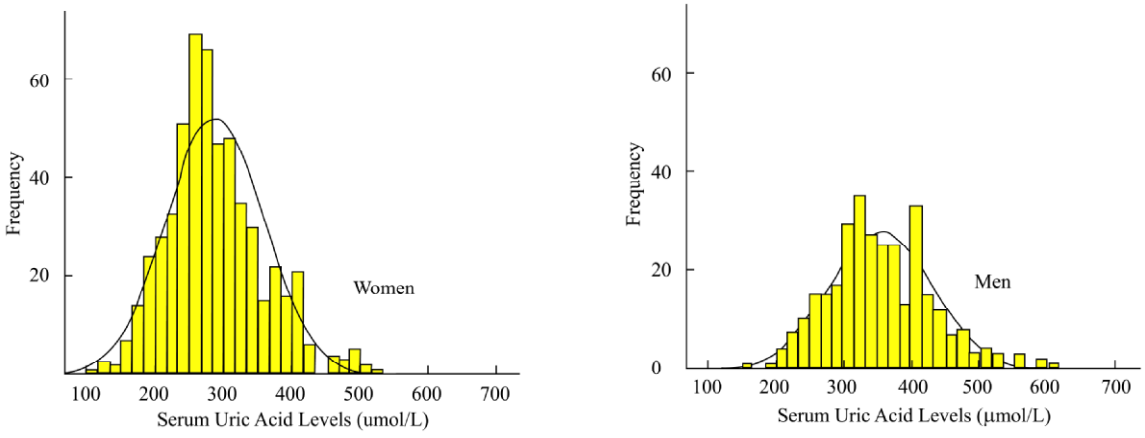

Figure 2. Histogram of serum uric acid levels specified by gender.

Table 1. Demographic Characteristics of Participants with and without Gradable Fundus Photographs

Variables	Participants without Gradable Photograph	Participants with Gradable Photographs	Differences[†]
n(%)	630 (42.0%)	869 (58.0%)	
Age (yrs)	59.5 (10.2)	59.3 (9.8)	0.2 (-0.8, 1.2)
Gender (% male)	31.1	36.3	-5.1 (-10.0, -0.3)[*]
Current smoking (%)	13.8	16.7	-0.6 (-3.7, 2.5)
Education (% more than primary school education)	81.1	85.0	-2.8 (-6.1, 0.6)
Metabolic Syndrome (%)	36.6 (230/630)	32.9 (286/869)	3.1 (-1.7, 7.9)
Waist Circumference (cm)	83.4 (9.4)	83.0 (9.3)	0.7 (-0.2, 1.6)
Body mass index (kg/m^2)	24.4 (3.3)	24.4 (3.2)	-0.0 (-0.4, 0.3)
Waist-to-hip ratio	0.88 (0.07)	0.87 (0.07)	0.01 (0.01, 0.02)[*]
Central Obesity (%)	51.8	48.0	2.9 (-2.1, 8.0)
Hyperglycemia (%)	31.2	31.0	0.3 (-4.4, 5.1)
Mean arteriolar blood pressure (mmHg)	98.2 (11.9)	99.2 (12.6)	-0.7 (-2.0, 0.5)
Total serum cholesterol (mmol/L)	4.97 (1.06)	5.00 (1.05)	-0.06 (-0.16, 0.05)
Serum Triglycerides (mmol/L)	1.73 (1.25)	1.60 (1.05)	0.13 (0.02, 0.25)[*]
Serum HDL-cholesterol (mmol/L)	1.36 (0.39)	1.41 (0.40)	-0.05 (-0.09, -0.01)[*]
Fasting blood glucose (mmol/L)	5.32 (0.51)	5.34 (0.53)	-0.03 (-0.08, 0.03)
Postprandial blood glucose(OGTT 2h) (mmol/L)	6.51(1.58)	6.45 (1.62)	0.05 (-0.12, 0.21)

Note. Data are presented as unadjusted means (SD) or percentages. [†]Age- and gender adjusted differences (95% confidence interval). [*] $P<0.05$.

Table 2. Demographic Characteristics of Participants with and without Hyperuricemia

Variables	Without Hyperuricemia	With Hyperuricemia	Differences[†]
n (%)	736 (84.7%)	133 (15.3%)	
Age (yrs)	58.5(9.7)	63.4(9.7)	-4.8(-6.6, -3.0)[*]
Gender (% male)	36.4	35.3	1.1(-7.8, 10.0)
Ever smoker (%)	23.1	22.9	-2.1(-7.9, 3.6)
Education (% above primary school education)	85.8	80.5	-2.3(-8.3, 3.8)
Weekly activity time (hours)	7.5(8.8)	7.3(7.4)	0.3(-1.3, 1.9)
BMI (kg/m^2)	24.1(3.1)	26.0(3.3)	-1.9(-2.5, -1.3)[*]
Metabolic syndrome (%)[‡]	28.3	58.7	-27.0(-35.5, -18.5)[*]
Central Obesity (%)[‡]	43.1	75.2	-28.8(-37.8, -19.8)[*]
Waist circumference (cm)	82.1(9.1)	87.6(8.7)	-5.0(-6.6,-3.4)[*]
Dyslipidaemia (%)[‡]	48.2	72.9	-22.8(-32.1, -13.6)[*]
Serum triglycerides (mmol/L)	1.47(0.87)	2.28(1.56)	-0.78(-0.97, -0.59)[*]
HDL-cholesterol (mmol/L)	1.42(0.40)	1.34(0.42)	0.08 (0.01, 0.16)[*]
Hypertension (%)[‡]	45.2	75.2	-24.8(-33.7, -15.9)[*]
Mean arteriolar blood pressure (mmHg)	98.1(12.4)	104.9(12.5)	-6.2 (-8.4, -3.9)[*]
Hyperglycemia (%)[‡]	28.4	45.1	-14.1(-22.7, -5.6)[*]
Fasting blood glucose (mmol/L)	5.31(0.52)	5.51(0.59)	-0.16(-0.26, -0.61)[*]
Postprandial blood glucose(OGTT 2h) (mmol/L)	6.35(1.56)	7.03(1.81)	-0.51(-0.80, -0.21)[*]
Retinal arteriolar diameter (μm)	140.23(14.27)	136.66(14.47)	2.19(-0.46, 4.83)
Retinal venular diameter (μm)	210.88 (20.66)	211.20(22.05)	-2.47(-6.31, 1.37)

Note. Data are presented as unadjusted means (SD) or percentages. [†]Age- and gender adjusted differences (95% confidence interval). Retinal arteriolar and venular diameters were also mutually adjusted for. [‡]International Diabetes Federation (IDF) consensus worldwide definition was used to defined metabolic syndrome, central obesity (waist circumference≥90cm in man and≥80 cm women), dyslipidemia (serum triglycerides ≥1.7 mmol/L or HDL-cholesterol<1.03 mmol/L), and hyperglycemia (fast serum glucose≥5.6 mmol/L). Hypertension was defined as average systolic blood pressure≥140 mm Hg and/or average diastolic blood pressure≥90 mm Hg and/or participants who were on treatment for previously diagnosed hypertension. [*]P<0.05.

Table 3. Changes in Retinal Vascular Calibers in Association with Hyperuricemia

Variables		Crude Analysis		Men		Women	
		Δ(μm) (95% CI)	*P*	Δ(μm) (95% CI)	*P*	Δ(μm) (95% CI)	*P*
Retinal arteriolar caliber [†]	Model I[‡]	-3.12 (-5.27, -0.97)	0.01	-5.52 (-9.43, -1.60)	0.01	-1.81 (-4.34, 0.73)	0.16
	Model II[§]	-2.40 (-4.64, -0.15)	0.04	-3.77 (-8.00, 0.46)	0.08	-1.57 (-4.21, 1.07)	0.24
Retinal venular caliber [†]	Model I[‡]	4.20 (1.06, 7.34)	0.01	7.08 (1.68, 12.48)	0.01	2.57 (-1.24, 6.38)	0.19
	Model II[§]	3.92 (0.63, 7.20)	0.02	6.20 (0.36, 12.04)	0.04	2.28 (-1.72, 6.27)	0.26

Note. ΔAdjusted difference in retinal vascular caliber (μm) between groups with *vs.* without hyperuricemia. [†]Retinal arteriolar and venular calibers were mutually adjusted. [‡]Model I: adjusted for age and retinal venular/arteriolar caliber. [§]Model II: adjusted for age, retinal venular/arteriolar caliber, central obesity, dyslipidemia, hypertension, hyperglycemia, weekly activity, smoking status, and education. International Diabetes Federation (IDF) consensus worldwide definition was used to defined central obesity (waist circumference≥90 cm in man and≥80 cm women), dyslipidemia (serum triglycerides≥1.7 mmol/L or HDL-cholesterol<1.03 mmol/L), and hyperglycemia (fast serum glucose≥5.6 mmol/L). Hypertension was defined as average systolic blood pressure≥140 mm Hg and/or average diastolic blood pressure≥90 mm Hg and/or participants who were on treatment for previously diagnosed hypertension.

DISCUSSION

The present study has shown that hyperuricemia is associated with narrower retinal arterioles and wider venules independently from other known cardiovascular risk factors mainly in Chinese men.

Population-based studies have demonstrated that an elevated level of uric acid predicts the development of hypertension, obesity, diabetes, metabolic syndrome, and other cardiovascular disease[3]. In accordance with previous studies, we have also found that persons with hyperuricemia have a higher prevalence of cardiovascular risk factors, including central obesity, dyslipidemia, hypertension, hyperglycemia, and the metabolic syndrome (Table 2). Furthermore, we have found that participants with hyperuricemia in this study have a narrower retinal arteriolar caliber and a wider retinal venular caliber (Tables 2 and 3). The microvascular changes described in the present study might be a chain that links hyperuricemia with hypertension and cardiovascular disease.

Studies have shown that elevated serum uric acid level can lead to hypertension. A hyperuricemic animal model has revealed that secondary hypertension is caused by uric acid-mediated renal vasoconstriction resulting from a reduction in endothelial levels of nitric oxide with activation of the rennin-angiotensin system[7-9]. Additionally, uric acid induces cellular proliferation, inflammation, oxidative stress, and activation of the local rennin-angiotensin system in cultured vascular smooth muscle cells[3,7,10-11]. A correlation between elevated serum uric acid levels and endothelial dysfunction and rennin activity in humans has also been reported[3,12]. Fazlıoğlu et al. found in patients with stable angina that serum uric acid was independently associated with arterial elasticity measured by applanation tonometry[32]. To our knowledge, the present study is the first one in the worldwide literature showing an association of serum uric acid levels with the microcirculation in humans by directly visualizing the retinal microcirculation *in vivo*. Although causality cannot be established from a cross-sectional study, our findings added further to the concept that hyperuricemia could lead to hypertension.

Larger retinal venular caliber has been found to be associated with cardiovascular disease[15,19,33], obesity[18-19,21], impaired fasting glucose or type2 diabetes[22-24], and proliferative diabetic retinopathy[25]. In the present study, a positive correlation has also been found between serum uric acid levels and retinal venular caliber. Data from population-based studies have shown a consistent correlation between increased inflammatory markers and retinal venular dilatation[15, 21, 34-35]. Animal studies have supported the hypothesis that inflammation leads to venular widening. Lipid hydroperoxide administration in the vitreous of rats has been shown to result in an increase in the number of leukocytes in the retinal microvasculature and in an increase in the diameter of retinal venules instead of arterioles[36]. Evidences have indicated that nitric oxide synthase (iNOS) could be induced by pro-inflammation cytokines like interleukin-1β(IL-1β), tumor necrosis factor-α(TNF-α), and interferon-γ(IFN-γ), etc[37]. Free radicals produced by oxidized low-density lipoproteins or activated leukocytes can damage and disrupt the endothelial surface layer and cause endothelium dysfunction[7,15,33,35,37]. Uric acid is not only an important pro-inflammation factor[3,38], but also a pro-oxidant, either by generating radicals during its degradation or by stimulating NADPH oxidase[3]. Therefore, inflammatory and oxidative stress processes may underlie the correlation between venular widening and hyperuricemia.

Gender differences in serum uric acid levels and possibly its impact on retinal vascular calibers have been witnessed in the present study. Gender differences in cardiovascular risk factors have been increasingly recognized. It has been reported that the associations of serum uric acid levels with cardiovascular disease[39], insulin resistance and plasma glucose levels[40] are generally stronger in women than in men. In the present study, however, the association of hyperuricemia with retinal vascular calibers has been found to be more pronounced and significant in men than in women (Table 3). In this study women were younger than men (58.6 years in women *vs.* 60.5 years in man, $P<0.01$). It is not yet clear whether this age difference could fully explain the discrepancy. Studies of larger sample size are called for to confirm this result.

Strengths of the present study include the population-based design, and the use of well-measured cardiovascular risk factors. Furthermore, a standardized semi-automated retinal vessel grading system ensures the precision and reproducibility of the vessel measurement. In addition, grading of retinal vascular calibers is

masked for the participants' characteristics.

Some limitations of this study should be discussed. First, because of the cross-sectional setting of the present study, interpretation of the temporal sequence of associations found in this study is not feasible. Second, information on an important confounder, alcohol consumption, had not been collected in this study. Third, using volunteers might introduce some selection bias, because they are in general healthier than those who did not participate. This might have caused an underestimation of the reported associations. Finally, generalization of these findings to the general population should be made with caution because the current study population consisted of a group of people at an increased risk of developing type 2 diabetes.

In summary, elevated serum uric acid is associated with smaller retinal arteriolar caliber and larger retinal venular caliber after adjusting for other cardiovascular risk factors. The associations are more pronounced in men than in women. These findings further add to the notion that hyperuricemia might play a role in the development of cardiovascular diseases, through its interaction with the microcirculation.

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CONFLICT OF INTEREST

No authors have any financial/conflict interest to disclose.

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