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Research Article

Association of Brachial Artery Measures with Estimated GFR>60 mL/min/1.73 m^2 in a Cross-Sectional Study of the Community-Based Women

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ABSTRACT

Objective: The purpose of this study is to estimate whether early decline in kidney disease is correlated with brachial artery measures as surrogate markers of the endothelial function in community-based women.

Methods: We studied 36 women with estimated glomerular filtration rate (eGFR)>60 mL/min/1.73 m^2 in community-based population women were enrolled in this study. Brachial artery measures including Flow-Mediated Vasodilation (FMD), Nitroglycerin-Mediated Vasodilation (NMD), Brachial Artery Diameter (BAD), FMD/NMD ratio and Post-Nitroglycerin Brachial Artery Diameter (P-NTGD) examinations were measured in all subjects by using brachial artery ultrasonography. The eGFR was calculated using the Japanese GFR inference formula, which was developed by the Japanese Society of Nephrology.

Results: There was significantly positive correlation between eGFR and FMD (r=0.348, p=0.041), positive correlation between eGFR and FMD/NMD ratio (r=0.471, p=0.004) and negative correlation between eGFR and P-NTGD (r=-0.405, p=0.016) were recognized. Negative correlation between Serum Uric Acid (SUA) and eGFR (r=-0.335, p=0.049) and negative correlation between FMD and SUA (r=-0.34, p=0.045) were also demonstrated.

Conclusion: Mild renal dysfunction with eGFR>60 mL/min/1.73 m^2 was associated with endothelial dysfunction in women. The cardio-renal interrelationship may be also suggested under mild renal dysfunction. It can be suggested that mild renal dysfunction might be a cardiovascular risk factor in women. Though it should not be distinctly stated just based on the results of the study.

Keywords: Estimated glomerular filtration rate; Flow-mediated vasodilation; Endothelial dysfunction; Cardio-renal interrelationship; Mild renal dysfunction

INTRODUCTION

Flow-Mediated Vasodilation (FMD), an endothelium-dependent function, and Nitroglycerin-Mediated Vasodilation (NMD), an endothelium-independent function in the brachial artery is potent procedure for assessing vascular endothelial and Vascular Smooth Muscle Cell (VSMC) function [1]. Patients with severe Chronic Kidney Disease (CKD) have high risk of occurring Cardiovascular Disease (CVD) [2], but it has been reported that subjects with mild kidney dysfunction have also an increased CVD risk in the community-based study [3]. It has been suggested that the increased risk of CVD has been contributed not only to clustering of CV risk factors [4] but also to endothelial dysfunction [5,6] in subjects with CKD. Though the threshold eGFR at which CV risk increases is unclear, expert consensus have proposed a level of <60 mL/min/1.73 m^2 [7]. Studies have been reported that eGFR is associated with endothelial dysfunction in the community-based subjects [6,8-11]. With regard to the restricting analysis to subject with eGFR>60 mL/min/1.73 m^2 representing CKD stage 0-2, a few reports has been studied [9-11]. The cardio-renal interrelationship has been suggested under normal conditions [12]. It has been also reported that endothelial dysfunction is considered as one of the major pathophysiological mechanism contributing to the relation of CVD and CKD [6,13,14]. We think that early detection of cardio-renal interaction damage can contribute to the prevention of initiation or precipitation of diseases. According to the experts consensus proposed as a threshold of eGFR>60 mL/min/1.73 m^2, we evaluate whether early decline in kidney function with eGFR>60

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mL/min/1.73 m^2 value is correlated with brachial artery measures as indicators of the endothelial function. Except the relationship between endothelial dysfunction and eGFR value, Serum Uric Acid (SUA) is also an independent predictor of CKD in subject with eGFR>60 mL/min/1.73 m^2 [15,16]. Experimentally, some studies indicate that hyperuricemia cause systemic and glomerular hypertension, leading to endothelial dysfunction and contribute to an afferent renal arteriopathy and tubulointerstitial fibrosis in kidney [17-20]. We also add the estimation whether eGFR 60 mL/min/1.73 m^2 of renal function is related with SUA. Furthermore, experimental and clinical studies have also indicated the relationship between SUA and endothelial dysfunction [21-25]. Therefore, we have studied whether interrelationship among eGFR>60 mL/min/1.73 m^2, FMD and SUA are correlated. Meanwhile, carotid Intima-Media Thickness (IMT) is a marker to assess the largely medial hypertrophy of the vessel [26] and brachial-ankle Pulse Wave Velocity (baPWV) is a predictor to evaluate arterial stiffness [13]. In addition to the evaluation of endothelial function, we added the examinations whether eGFR>60 mL/min/1.73 m^2 value is correlated with different arterial trees at different sites.

MATERIALS AND METHODS

Study population

Thirty six women with eGFR>60 mL/min/1.73 m^2 renal function in community-based population were retrospectively studied in this research (including: 8 cerebral infarction, 9 migraine, 2 cervical spondylosis, and 17 not otherwise). Thirty six subjects who fulfilled eGFR>60 mL/min/1.73 m^2 value were enrolled in the study between March 2008 and April 2014. All vasoactive medications were withheld for at least a few days. Women patients were allowed to perform ultrasonographic examinations either in luteal or follicular phase. For the FMD examination, patients fasted for 12 hours before the study and they were studied in a quiet, temperature-controlled room. The estimated glomerular filtration rate (eGFR) was calculated using Japanese eGFR equation [27].

Vascular reactivity

FMD of the brachial artery was determined using high resolution B-mode ultrasonographic system (UNEXEX 18G, Japan) with a linear transducer mid-frequency of 7.5 MHz, using the technique described previous report [28,29]. Briefly, this was followed by inflation pneumatic tourniquet of placed around forearm to higher pressure 50 mmHg more than systolic blood pressure and followed by deflation after 5 minutes. The scan was made by the procedure of auto calculation. Fifteen minutes were then allowed for vessel recovery and a further scan at rest was then recorded. An exogenous NO donor, such as a single high dose (0.3 mg) of NTG spray has been given to determine the maximum obtainable vasodilator response, and to serve as a measure of endothelium-independent vasodilation reflecting VSMC function, in accordance with the previous report [1,28,29]. Parameters including FMD, NMD and P-NTGD were expressed as previously described [28,29].

Carotid ultrasonography

The Intima-Media Thickness (IMT) of the bilateral Common Carotid Arteries (CCA) was measured by ultrasonography with a 10 MHz probe using an ultrasound system (Aplio SSA-700A, Toshiba Medical System, Tochigi, Japan). Measurement of IMT were performed on the visible CCA in either the near or the far wall, and maximum IMT was defined as IMT-C max. Measurement IMT were also made within a region free of plaque as previously described [26,28].

Brachial-ankle Pulse Wave Velocity (baPWV) measurement

baPWV was measured using a volume-plethysmographic apparatus (form PWV/ABI; Colin, Co.,Ltd., Komaki, Japan) and Ankle Brachial Pressure Index (ABI) is measured simultaneously by these machines in accordance with a described method [28-30].

Statistical analysis

Numerical variables were expressed as mean ± SD. Spearman's bi-variable correlation analysis was used to test the relationships between the numerical variables when appropriate. Statistical significance was defined as a p value of less than 0.05. The statistical analyses were performed using the SPSS software package (version 16.0; SPSS Inc., Chicago, IL).

RESULTS

Baseline characteristics of study population are summarized in (Table 1). Mean age of the participants was 55.4 ± 14.4 years (range: 19 to 80 years). Brachial artery measures of the participants were presented (Table 2).

Table 1: The Clinical and Biochemical Characteristics of the Participant (mean ± SD).

Variable	Value (n=36)
Age years	55.4 ± 14.4
Heart rate beats/min	69.7 ± 11.1
SBP mmHg	135.7 ± 24.4
DBP mmHg	80.3 ± 15.5
Weight kg	55.2 ± 9.7
BMI kg/m^2	22.9 ± 3.8
TC mg/dL	211.2 ± 39.9
TG mg/dL	99.8 ± 54.6
HDL-C mg/dL	65.1 ± 19.1
LDL-C mg/dL	125.2 ± 39.1
TC/HDL-C	3.5 ± 1.0
LDL-C/HDL-C	2.1 ± 0.8
Non-HDL-C mg/dL	145.1 ± 42.3
TG/HDL-C	1.8 ± 1.4
Glucose mg/dL	94.7 ± 8.5
HbA1c (NGSP)%	5.3 ± 0.3
UA mg/dL	4.3 ± 1.1
BUN mg/dL	12.9 ± 3.8
Cre mg/dL	0.6 ± 0.1
eGFR mL/min/1.73m^2	83.7 ± 12.1
Urine alb mg/day	28.2 ± 49.4
Renin pg/mL	8.3 ± 9.0

Table 2: Brachial Artery Measures (mean ± SD).

	Value (n=36)
BAD-base mm	3.47 ± 0.58
BAD-max mm	3.67 ± 0.56
FMD mm	0.20 ± 0.11
FMD%	6.12 ± 3.94
NMD%	19.59 ± 8.54
P-NTGD mm	4.18 ± 0.52
FMD/NMD	0.36 ± 0.23

BAD: Brachial Artery Diameter; BAD-base: BAD Baseline Diameter; BAD-max: BAD Maximal Diameter; FMD: Flow-Mediated Vasodilation; NMD: Nitroglycerin-Mediated Vasodilation; P-NTGD: Post Nitroglycerin Brachial Artery Diameter

Table 3 shows Spearman's rank correlation coefficients of the brachial artery measures in participants. FMD% was significantly correlated with FMD/NMD ratio (r=0.68, p<0.001). Significant correlation between FMD% and P-NTGD was recognized (r=-0.37, p=0.03).

Table 3: Spearman's rank correlation coefficients of the brachial artery measures in participant with eGFR>60 mL/min/1.73 m^2.

	BAD-base	BAD-max	P-NTGD	FMD mm	FMD%	NMD%	FMD/NMD
BAD-base		0.97*	0.90*	-0.22	-0.42	-0.45	0.001
BAD-max	0.97*		0.88*	-0.06	-0.27	-0.42	0.10
P-NTGD	0.90*	0.88*		-0.19	-0.37	-0.24	-0.17
FMD mm	-0.22	-0.06	-0.19		0.96*	0.11	0.74*
FMD%	-0.42	-0.27	-0.37	0.96*		0.21	0.68*
NMD %	-0.45	-0.42	-0 24	0.11	0.21		-0.46
FMD/NMD	0.001	0.10	-0.17	0.74*	0.68*	-0.46	

*p<0.001.

Table 4 shows Spearman's rank correlation coefficients of the atherosclerotic parameters in participants. Negative correlation between FMD and right (rt) IMT (r=-0.664, p<0.001) and negative correlation between FMD and left (lt) IMT (r=-0.546, p=0.005) were also detected. Positive correlation between rt IMT and rt baPWV (r=0.432, p=0.027), positive correlation between rt IMT and lt baPWV (r=0.478, p=0.010), positive correlation between lt IMT and rt baPWV (r=0.498, p=0.010) and positive correlation between lt IMT and lt baPWV (r=0.527, p=0.006) were also recognized. Negative correlation between FMD and lt baPWV (r=-0.417, p=0.020) were observed, but there was no correlation between FMD and rt baPWV (r=-0.343, p=0.059).

Table 4: Spearman's rank correlation coefficients of the atherosclerotic parameters in participant with eGFR.60 mL/min/1.73m^2.

	FMD	NMD	FMD/NMD	Rt IMT	Lt IMT	Rt PWV	Lt PWV
FMD		0.21	0.68*	-0.66*	-0.55	-0.34	-0.42
NMD	0.21		-0.46	-0.17	-0.17	-0.17	-0.50
FMD/NMD	0.68*	-0.46		-0.39	-0.27	-0.05	-0.06
Rt IMT	-0.66*	-0.17	-0.39		0.64	0.43	0.48
Lt IMT	-0.55	-0.17	-0.27	0.64		0.50	0.53
Rt PWV	-0.34	-0.17	-0.05	0.43	0.50		0.97*
Lt PWV	-0.42	-0.50	-0.06	0.48	0.53	0.97*	

*p<0.001.

Table 5 shows Spearman's rank correlation coefficients for FMD, BAD, P-NTGD, NMD and FMD/NMD ratio with clinical and biochemical parameters in participants.

Table 5: Spearman's rank correlation coefficients for FMD, BAD, P-NTGD, NMD and FMD/NMD with clinical and biochemical parameters in participants with eGFR>60 mL/min/1.73 m^2.

	FMD	BAD	P-NTGD	NMD	FMD/NMD
Age years	-0.56*	0.39*	0.30	-0.43*	-0.19
TC mg/dL	-0.23	0.43*	0.26	-0.55*	0.19
TG mg/dL	0.10	0.10	-0.003	-0.52*	0.33
HDL-C mg/dL	-0.22	-0.15	-0.28	0.17	-0.19
TC/HDL-C	0.08	0.27	0.27	-0.41*	0.28
LDL-C/HDL-C	0.003	0.33	0.32	-0.37*	0.23
LDL-C mg/dL	-0.10	0.36*	0.25	-0.47*	0.24
Non-HDL-C mg/dL	-0.08	0.36*	0.26	-0.54*	0.27
TG/HDL-C	0.14	0.13	0.12	-0.42*	0.28
Glucose mg/dL	-0.28	0.33	0.25	-0.45*	0.06
HbA1c (NGSP) %	-0.18	0.44*	0.39*	-0.47*	0.20
Weight kg	-0.02	0.46*	0.48*	-0.41*	0.28
BMI kg/m^2	-0.08	0.32	0.34	-0.46*	0.30
Waist cm	-0.04	0.42*	0.42*	-0.41*	0.32
UA mg/dL	-0.34*	0.11	-0.07	-0.03	-0.22
SBP mmHg	-0.14	0.22	0.14	-0.43*	0.09
DBP mmHg	0.07	0.05	0.06	-0.12	0.10
HR bpm	-0.17	0.05	0.05	-0.12	-0.08
BUN mg/dL	-0.05	0.23	0.19	-0.21	-0.19
Cre mg/dL	-0.01	0.01	0.21	0.42*	-0.38*
eGFR mL/ in/1.73m^2	0.35*	-0.24	-0.41*	-0.18	0.47*
Urine alb mg/day	0.08	-0.04	-0.10	-0.26	0.25
Renin pg/mL	-0.09	0.01	-0.11	-0.14	0.06

*p<0.05.

There was significantly positive correlation between FMD and eGFR (r=0.348, p=0.041; Figure 1) and positive correlation between FMD/NMD ratio and eGFR (r=0.471, p=0.004; Figure 2). Negative correlation between P-NTGD and eGFR (r=-0.405, p=0.016; Figure 3) was recognized. There was weak negative correlation between FMD and SUA (r=-0.340, p=0.045).

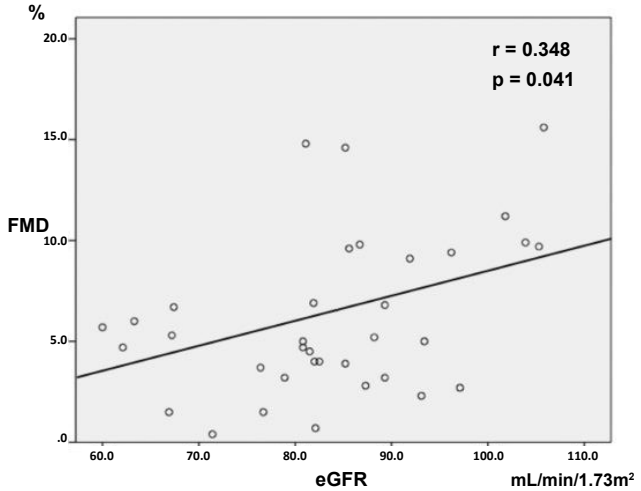

Figure 1: Positive correlation between FMD and eGFR was significantly observed.

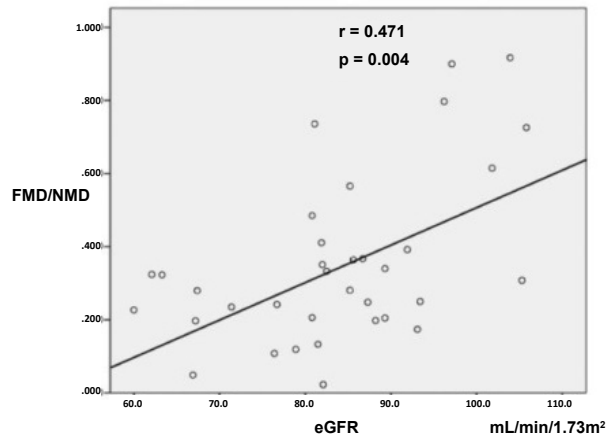

Figure 2: Significant positive correlation between FMD/NMD ratio and eGFR was shown.

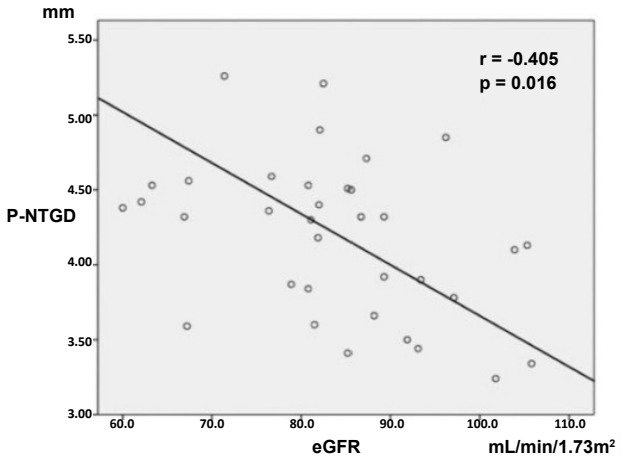

Figure 3: Significant negative correlation between P-NTGD and eGFR was observed.

Table 6 shows Spearman's rank correlation for carotid IMT, baPWV and Ankle Brachial Pressure Index (ABI) with clinical and biochemical parameters in participants.

Table 6: Spearman's rank correlation coefficients for IMT, baPWV and ABI with clinical and biochemical parameters in participant with eGFR>60 mL/min/1.73 m^2.

	IMT (Rt)	IMT (Lt)	PWV (Rt)	PWV (Lt)	ABI (Rt)	ABI (Lt)
Age years	0.58*	0.45*	0.68*	0.76*	0.40*	0.28
TC mg/dL	0.34	0.50*	0.39*	0.40*	0.34	0.15
TG mg/dL	0.18	0.01	0.43*	0.40*	0.05	-0.08
HDL-C mg/dL	-0.13	0.06	-0.18	-0.13	-0.003	0.14
LDL-C mg/dL	0.30	0.35	0.41*	0.42*	0.12	-0.03
Non-HDL-C mg/dL	0.33	0.44*	0.45*	0.48*	0.13	-0.03
Glucose mg/dL	0.62*	0.57*	0.57*	0.57*	0.15	0.04
HbA1c (NGSP) %	0.27	0.31	0.32	0.34	0.30	0.02
Weight kg	0.24	0.20	0.07	0.03	0.07	-0.07
BMI kg/m^2	0.22	0.30	0.18	0.18	0.09	-0.02
Waist cm	0.49*	0.25	0.24	0.22	0.05	-0.08
UA mg/dL	0.61*	0.64*	0.06	0.09	-0.32	-0.12
SBP mmHg	0.46*	0.47*	0.67*	0.60*	-0.06	-0.20
DBP mmHg	0.37	0.51*	0.31	0.22	-0.08	-0.21
HR bpm	0.07	0.17	0.18	0.17	0.02	-0.04
BUN mg/dL	0.16	0.34	0.22	0.17	0.12	-0.09
Cre mg/dL	0.29	0.002	-0.18	-0.18	0.05	0.17
eGFR mL/min/1.73m^2	-0.51*	-0.23	-0.14	-0.18	-0.25	-0.26
Urine alb mg/day	0.42	0.32	0.23	0.21	-0.13	-0.32*
Renin pg/mL	0.03	0.18	0.06	0.06	0.05	0.16

*p<0.05.

Negative correlation between eGFR and rt IMT (r=-0.509, p=0.009) was detected, but here was no correlation between eGFR and ltIMT (r=-0.229, p=0.271). Correlation between eGFR and rt baPWV and between eGFR and lt baPWV were not shown. Positive correlation between SUA and rt IMT (r=0.613, p=0.001) and positive correlation between SUA and lt IMT (r=0.638, p=0.001) were also recognized.

Table 7 shows correlation between SUA and other parameters in participant. There was weak negative correlation between SUA and eGFR (r=-0.335, p=0.049).

Table 7: Correlation between serum uric acid and other parameters in the participant with eGFR>60 mL/min/1.73 m^2

Variable	Correlation Coefficients	p values
Age years	0.0721	0.680
Waist cm	0.352*	0.048
Weight kg	0.263	0.133
BMI kg/m^2	0.382*	0.037
AST U/L	0.385*	0.022
ALT U/L	0.448*	0.007
BUN mg/dL	0.016	0.942
Creatinine mg/dL	0.330	0.053
eGFR mL/min/1.73m^2	-0.335*	0.049
FMD%	-0.340*	0.045
FMD/NMD	-0.221	0.202
NMD%	-0.033	0.850
P-NTGD mm	-0.066	0.704
Rt IMT mm	0.613*	0.001
Lt IMT mm	0.638*	0.001

*p<0.05.

DISCUSSION

Previous studies have suggested that eGFR is associated with endothelial dysfunction in community-based [6,8-11]. Though the threshold eGFR at which CV risk increases is not clear, expert consensus have proposed a level of <60 mL/min/1.73 m^2 [7], namely, the National Kidney Foundation clinical practice guidelines define CKD as the presence of eGFR less than 60 mL/min/1.73 m^2 with or without kidney damage for at least 3 months [7]. With regard to the restricting analysis to subject with eGFR>60 mL/min/1.73 m^2, a few reports have been studied [9-11]. The Hoorn Study indicated that the inverse correlation between eGFR and biomarkers of endothelial function, namely plasma Von Willebrand Factor (VWF), soluble Vascular Cell Adhesion Molecule-1 (VCAM-1) and the urinary albumin-creatinine ratio in subjects unselected for CKD

in a population-based cohort [6]. The Framingham Heart Study indicated that endothelial dysfunction estimated with FMD is not a major correlate of moderate CKD in subjects with stage 3 CKD, suggesting the focus on other mechanism such as inflammation and arterial stiffness [8]. The Multi-Ethnic Study of Atherosclerosis (MESA) showed no association between FMD and renal function in subjects with eGFR>60 mL/min/1.73 m^2 [10]. Nerpin et al. reported that eGFR is associated with endothelial function in subjects with normal kidney function, but that this association is mainly explained by confounding CV risk factors [11]. However, study of Health in Pomerania (SHIP) indicated that FMD was associated with renal dysfunction in females with eGFR>60 mL/min/1.73 m^2 [9].

They suggest that very mild renal dysfunction is considered as a risk factor for the early atherosclerosis disease process in women [9]. Our data showed that mild renal dysfunction assessed by eGFR value is respectively associated with endothelial function evaluated with FMD, FMD/NMD ratio which represents more sensitive parameter than FMD [31] and P-NTGD [32]. P-NTGD value [32] which is without vascular tone and shows more stable marker than BAD [33]. BAD is the plausible surrogate marker of FMD. Our results indicated that correlation between mild renal dysfunction and endothelial function in the restricting study to subject with eGFR>60 mL/min/1.73 m^2 was shown in women in cross-sectional study.

It has been suggested that the interaction between the heart and the kidney may occur in the setting of processes and diseases such as advanced age, hypertension, diabetes mellitus and atherosclerosis [14]. The cardio-renal interrelationship by fine-turning by neuro-humoral activity, namely Atrial Natriuretic Peptide (ANP), Renin-Angiotensin-Aldosterone System (RAAS) and Sympathetic Nervous System (SNS) has been also reported under normal conditions [14]. Our result indicated that the cardio-renal relation may be also observed through endothelial dysfunction under mild renal dysfunction. While, it has been reported that endothelial dysfunction is considered as one of the pathophysiological major mechanism contributing to the relation of CVD and CKD [6,13,14]. Cytogenetically, Shang et al. reported microRNA-92a as a crucial link between CKD and CVD by mediated uremia-impaired endothelial dysfunction [34]. In addition to classic CVD risk factors, it can be suggested that mild renal dysfunction might be a CVD risk factor in women.

Except the correlation between endothelial dysfunction and eGFR, Sonoda et al. reported the SUA as an independent predictor of future development of CKD in subject with eGFR>60 mL/min/1.73 m^2 [15]. It has been also suggested that SUA was independently related to the eGFR in the subject with eGFR>60 mL/min/1.73 m^2 [16]. Experimentally, some studies indicated that hyperuricemia causes systemic and glomerular hypertension, leading to endothelial dysfunction and experimental hyperuricemia also contribute to an afferent renal arteriopathy and tubulointerstitial fibrosis in the kidney by activating the RAAS [17-20]. It is plausible that elevated SUA may contribute to endothelial dysfunction, inflammation, oxidative stress and Renin-Angiotensin System (RAS) activation [17] and leading to systemic atherosclerosis and/or reduced eGFR, namely, initiation and progression of CKD. As our data showed the weak inverse relationship between SUA and eGFR, the increased SUA level, even in physiological range, may be a risk factor for impaired eGFR in subjects with mild renal dysfunction.

The evidence of SUA to stimulate oxidant production has already been studied in both adipocytes [35] and VSMC [36]. In addition to these studies, Yu et al. [21] have reported that SUA can induce oxidative stress and activation of local RAS system leading to senescence and apoptosis, showing a mechanism of uric acid-induced human umbilical vein endothelial dysfunction. Clinical studies have also indicated the relationship between SUA and endothelial dysfunction [22-25]. As our data showed a weak inverse correlation between SUA and endothelial function, the raised SUA, even in physiological range, may reflect he endothelial dysfunction.

Kanbay et al. have reported that allopurinol lowering SUA showed decreased SUA level, increased FMD value and increased eGFR level [24]. Our result may suggest that raised SUA level, in physiological range, contribute to both decreased FMD and impaired eGFR. It is putative that the interrelationship among SUA, endothelial dysfunction and eGFR, subsequently leading to systemic and/or renal atherosclerosis.

Meanwhile, atherosclerosis and arteriosclerosis which are different vascular pathologies are present in CKD [13]. It has reported that progressive deterioration of renal function in CKD is related with the uremic toxins, oxidative stress and inflammation, and develop the initiation of endothelial dysfunction and progression of atherosclerosis [13]. Endothelial dysfunction also cause arteriosclerosis, a disease affecting the media of large and middle sized arteries with an increased collagen:elastin ratio, calcification and hyperplasia and hypertrophy of VSMCs, leading to the occurrence of increased arterial stiffness measured by PWV [13].

On the other hand, IMT is a marker which reflects not only early atherosclerosis, but also non-atherosclerotic compensatory remodeling with largely medial hypertrophy [26]. In addition to the endothelial function assessed by brachial artery measures, we add the study whether eGFR>60 mL/min/1.73 m^2 value is correlated with these indicators. Negative correlation between eGFR and rt IMT was detected, but there was no correlation between eGFR and lt IMT. Correlation between eGFR and baPWV was not shown.

The interrelationship among FMD, IMT and baPWV which are different artery trees at different sites and different indicators of atherosclerosis were also evaluated. Our data suggested correlations between FMD and IMT and between IMT and baPWV, respectively.

STUDY LIMITATION

There were some limitations in this study. Our results indicated that correlation between mild renal dysfunction and endothelial function in the restricting study to subject with eGFR>60 mL/min/1.73 m^2 was shown in women in cross-sectional study. But several confounding factors related to endothelial dysfunctions as well as renal dysfunction were present. The differences in risk factors are important to address as they are likely independently related to endothelial dysfunction as well as renal dysfunction. However, our study sample size is relatively small; we did not adjust using confounding factors. Future prospective studies are warranted to obtain more specific conclusion.

CONCLUSION

It can be suggested that mild renal dysfunction might be a cardiovascular risk factor in women. Though, it should not be distinctly stated just based on the study results.

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COMPLIANCE WITH ETHICAL STANDARDS

Informed consent was obtained from patients in this study and the study was approved by the Ethics Committee of NIihon University School of Medicine.

CONFLICT OF INTEREST

Authors declare that they have no conflicts of interest.

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