Atherosclerosis 210 (2010) 602–606

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Decrease in glomerular filtration rate by plasma low-density lipoprotein cholesterol in subjects with normal kidney function assessed by urinalysis and plasma creatinine

Yasuko Morita[a], Yasuhiko Homma[a,*], Mihoko Igarashi[a], Ryuusuke Miyano[a], Hiroshi Yamaguchi[a], Momoo Matsuda[a], Toshimori Tanigaki[a], Yutaka Shiina[a], Koichiro Homma[b]

[a] Health Evaluation and Promotion Center, Tokai University Hospital, 143 Shimokasuya, Isehara 259-1193, Japan
[b] Department of Internal Medicine, Keio University School of Medicine, 35 Shinanomachi, Shinjuku, Tokyo 160-8582, Japan

ARTICLE INFO

Article history:
Received 16 July 2009
Received in revised form
27 November 2009
Accepted 15 December 2009
Available online 29 December 2009

Keywords:
e-GFR
LDL cholesterol
Coronary risk factors
Blood pressure
Plasma glucose

ABSTRACT

Objective: It has not been well defined whether plasma low-density lipoprotein cholesterol (LDL-C) progresses arteriolosclerosis (arteriosclerosis of small arteries) or not. Estimated glomerular filtration rate (e-GFR) is an indicator of the function of renal arterioles and capillaries of glomeruli. The relationship between e-GFR and plasma LDL-C was studied to estimate the effect of plasma LDL-C on the function of renal arterioles and capillaries of glomeruli to speculate the effect of plasma LDL-C on arteriolosclerosis.
Methods and results: Major coronary risk factors; blood pressure, plasma lipids, and fasting plasma glucose were compared among 4 groups of examinees of a health evaluation and promotion center separated by e-GFR, namely, Control group, Group 1, 2, 3 from highest e-GFR to lowest e-GFR. Numbers of total male and female subjects were 4602 and 2920, respectively. Plasma LDL-C levels were significantly high in Group 2 and 3 in all male subjects and high in Group 1, 2, and 3 in male subjects with age of fifties, compared with Control group. Plasma LDL-C levels were significantly high in Group 1, 2, and 3 in all female subjects and high in Group 2 and 3 in female subjects with age of fifties, compared with Control group. Plasma levels of LDL-C were not significantly different at each years of age in subjects with age of fifties in both sex. BMI and waist circumference were higher in male subjects with low e-GFR but not in female subjects. Blood pressure and fasting plasma glucose were not high in subjects in Group 1, 2, and 3, compared with Control group in all subjects and subjects with age of fifties in both sex.
Conclusions: We concluded that the high plasma level of LDL-C was the major risk factor among coronary risk factors to reduce GFR probably due to impairing the function of renal arterioles and capillaries of glomeruli in subjects with normal kidney function assessed by urinalysis and plasma creatinine.

1. Introduction

Kidney function is assessed routinely by urinalysis and plasma levels of creatinine and urea nitrogen (UN). Recently, estimated glomerular filtration rate (e-GFR) has been used as a marker of kidney function [1,2]. Many subjects whose kidney function are determined normal with urinalysis and plasma levels of creatinine and UN have low e-GFR. Some coronary risk factors, namely, hypertension and diabetes mellitus (DM), metabolic syndrome (MS) are known to impair the kidney function [3–6]. However, it has not been well defined which factor is most important to decrease e-GFR in subjects with normal kidney function assessed by urinalysis and plasma creatinine and UN.

The Health Evaluation and Promotion Center, Tokai University Hospital has approximately 17,000 examinees a year. We investigated the correlation between e-GFR and coronary risk factors in subjects with normal kidney function assessed by urinalysis and plasma creatinine to speculate the mechanism of early stage of kidney impairment except the inflammation and to speculate the effects of coronary risk factors on arteriolosclerosis (arteriosclerosis of small arteries).

2. Materials and methods

This study was made in conformity with the ethical guide of Tokai University Hospital.

2.1. Subjects

Examinees at the Health Evaluation and Promotion (HEP) Center, Tokai University Hospital from January, 2007 to June, 2007

* Corresponding author. Tel.: +81 463 93 1121; fax: +81 463 94 9310.
E-mail address: homma@is.icc.u-tokai.ac.jp (Y. Homma).

0021-9150/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.atherosclerosis.2009.12.025

Table 1
e-GFR and coronary risk factors in all male subjects.

Group	Control	1	2	3	p^1
Numbers	1159	1142	1161	1140	
e-GFR (mL/min/1.73 m^2)	85.5 ± 1.8[2]	73.1 ± 1.6[a]	65.5 ± 1.8[a]	58.7 ± 2.7[a]	<0.001
Range	76.1–138.9	69.6–75.8	63.0–69.6	52.6–62.9	
Age (y/o)	50.8 ± 10.6	57.1 ± 9.0[a]	53.2 ± 7.7[a]	59.3 ± 10.2[a]	<0.001
Creatinine (mg/dL)	0.73 ± 0.06	0.81 ± 0.03[a]	0.90 ± 0.02[a]	0.97 ± 0.04[a]	<0.001
BMI (kg/m^2)	23.0 ± 3.1	22.9 ± 2.7	23.4 ± 2.8[b]	23.3 ± 2.7[c]	<0.001
Waist cir (cm)	81.5 ± 8.5	81.8 ± 7.7	82.5 ± 8.0	82.6 ± 7.8	0.002
S BP (mmHg)	123.1 ± 18.7	124.2 ± 19.7	123.4 ± 18.3	123.9 ± 18.8	0.493
DBP (mmHg)	76.2 ± 11.5	77.1 ± 11.8	77.0 ± 11.3	76.6 ± 11.3	0.291
FPG (mg/dL)	104.3 ± 19.0	105.4 ± 18.9	102.7 ± 13.9	103.9 ± 14.4	0.002
TC (mg/dL)	201.5 ± 32.3	203.3 ± 31.1	203.6 ± 31.1	206.8 ± 30.0	0.001
TG (mg/dL)	124.8 ± 82.2	122.3 ± 86.9	126.2 ± 76.2	125.4 ± 74.4	0.067
HDL-C (mg/dL)	63.1 ± 17.4	63.3 ± 16.2	61.5 ± 16.3	60.9 ± 15.3[b]	0.001
LDL-C (mg/dL)	124.7 ± 82.2	124.1 ± 27.8	125.6 ± 28.2[c]	129.4 ± 27.6[a]	<0.001

1: Statistical significance by ANOVA. 2: Mean ± S.D. Statistical significance by multiple comparison analysis vs. Control: a; $p < 0.001$, b; $p < 0.01$, c; $p < 0.05$.

whose plasma creatinine levels were lower than 1 mg/dL for men and lower than 0.8 mg/dL for female without albuminuria were subjected for this study. Numbers of subjects were 4602 for male and 2920 for female. Examinees of the HEP Center consisted of the workers of companies and their spouses, school teachers and their spouses, and habitants of Isehara area. Hypertensive, hyperlipoproteinemic, and diabetic subjects without medicine were involved in this study but those subjects with medical treatment were excluded.

2.2. e-GFR formula [2]

$$\text{e-GFR (mL/min/1.73 m}^2\text{)} = 175 \times \text{age (y/o)}^{-0.203} \times \text{plasma creatinine (mg/dL)}^{-1.154} \text{ for male}$$

$$\text{e-GFR} = \text{e-GFR for men} \times 0.742 \text{ for female}$$

2.3. Protocol

Subjects were separated unintentionally into 4 groups of equal numbers of subjects with e-GFR in descending order. The group of subjects with highest e-GFR was designated as Control group. BMI, blood pressure, plasma total cholesterol (TC), low-density lipoprotein (LDL)-C, high-density lipoprotein (HDL)-C, triglyceride (TG), and fasting plasma glucose (FPG) were compared among 4 groups. Plasma lipids and FPG were measured with autoanalyzers at the Central Laboratory of Tokai University Hospital. Plasma LDL-C concentration was estimated by a direct determination but not by the calculation [7,8].

2.4. Statistical analysis

Statistical comparison of parameters among 4 groups was made first with ANOVA to know the trends. Further comparison of each parameters among 4 groups was made with multiple comparison analysis.

3. Results

Results of all male subjects are shown in Table 1. Age and plasma creatinine were significantly high in Group 1, 2, and 3, compared with Control group because those were variables for calculating e-GFR. BMI and waist circumference (Waist) were significantly higher in low e-GFR groups than in Control group by ANOVA. BMI was slightly but significantly higher in Group 2 and 3 than in Control group but Waist was not different among 4 groups by multiple comparison analysis. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) and fasting plasma glucose (FPG) were not high in Group 1, 2, and 3, compared with Control group. Plasma TC levels were higher in low e-GFR groups than in Control group by ANOVA but were not higher in Group 1, 2, and 3 than in Control group by multiple comparison analysis. Plasma TG levels were not different among 4 groups. Plasma HDL-C was significantly lower in low e-GFR groups than in Control group by ANOVA and lower in Group 3 than in Control group by multiple comparison analysis. Plasma LDL-C was significantly higher in low e-GFR groups than in Control group by ANOVA. Plasma LDL-C was significantly higher in Group 2 and 3 than in Control group and in Group 3 than in Group 2 by multiple comparison analysis.

Table 2
e-GFR and coronary risk factors in all female subjects.

Group	Control	1	2	3	p^1
Numbers	738	722	707	753	
e-GFR (mL/min/1.73 m^2)	89.7 ± 9.6[2]	76.3 ± 1.2[a]	66.8 ± 2.9[a]	58.9 ± 4.0[a]	<0.001
Range	78.7–138.9	73.4–78.4	63.8–73.7	50.8–63.7	
Age (y/o)	48.8 ± 10.1	57.1 ± 5.2 [a]	52.1 ± 9.7[a]	60.1 ± 8.9[a]	<0.001
Creatinine (mg/dL)	0.54 ± 0.05	0.60 ± 0.01[a]	0.69 ± 0.02[a]	0.75 ± 0.05[a]	<0.001
BMI (kg/m^2)	22.0 ± 3.3	22.0 ± 3.1	22.0 ± 3.0	22.0 ± 3.1	0.467
Waist cir (cm)	74.3 ± 9.5	75.9 ± 25.0	73.8 ± 8.9	7 5.1 ± 9.2	0.049
S BP (mmHg)	116.6 ± 20.5	118.8 ± 21.0	116.4 ± 20.5	120.5 ± 21.2[b]	<0.001
DBP (mmHg)	70.7 ± 12.6	72.7 ± 11.8	71.1 ± 12.0	72.9 ± 12.1	<0.001
FPG (mg/dL)	97.2 ± 14.4	99.1 ± 11.3	96.0 ± 10.0	99.5 ± 11.9	<0.001
TC (mg/dL)	204.4 ± 32.3	219.8 ± 30.0[a]	213.3 ± 33.9[a]	220.1 ± 31.5[a]	<0.001
TG (mg/dL)	83.5 ± 45.6	94.4 ± 49.2	88.3 ± 49.0	94.8 ± 45.4	<0.001
HDL-C (mg/dL)	74.9 ± 17.4	75.5 ± 16.9	75.6 ± 17.7	75.2 ± 17.1	0.865
LDL-C (mg/dL)	119.6 ± 28.3	132.9 ± 28.0[a]	1257.3 ± 30.9[a]	133.3 ± 29.3[a]	<0.001

1: Statistical significance by ANOVA. 2: Mean ± S.D. Statistical significance by multiple comparison analysis vs. Control: a; $p < 0.001$, b; $p < 0.01$, c; $p < 0.05$.