Original Article

Serum Apolipoprotein B-48 Concentration Is Associated with a Reduced Estimated Glomerular Filtration Rate and Increased Proteinuria

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Aim: Apolipoprotein B-48 (apoB-48) is a constituent of chylomicrons and their remnants (chylomicron remnants). A high concentration of serum apoB-48 is suspected to be a major risk factor for the development of atherosclerotic cardiovascular disease. Proteinuria and a reduced estimated glomerular filtration rate (eGFR) are independent risk factors for cardiovascular events and renal dysfunction. In the present study, we examined whether the serum apoB-48 concentration is associated with renal dysfunction.

Methods: A total of 264 patients was enrolled and classified into four groups according to the eGFR and level of proteinuria: a high eGFR (>60 mL/min/1.73 m²) without proteinuria ($\geq 1+$ by urine dipstick) ($n=50$); a high eGFR with proteinuria ($n=75$); a low eGFR (>60 mL/min/1.73 m²) without proteinuria ($n=74$); and a low eGFR with proteinuria ($n=65$). Biochemical markers of lipid metabolism, including the fasting serum apoB-48 concentration, were compared between the four groups.

Results: The serum log-apoB-48 and log-apoB-48/TG levels were significantly higher in the patients with a high eGFR with proteinuria, low eGFR with proteinuria and low eGFR without proteinuria than in those with a high eGFR without proteinuria, with the most significant differences for these parameters. The eGFR was found to be significantly correlated with the log-apoB-48 and log-apoB-48/TG levels, whereas urinary protein was found to be significantly correlated with the log-apoB-48 level only. A multiple regression analysis indicated that the log-apoB-48/TG level was a significant determinant of a reduced eGFR.

Conclusions: Both a low eGFR (<60) and proteinuria ($\geq 1+$) are independent determinants of a high apoB-48 concentration. Taken together, the present results suggest that an increased serum apoB-48 concentration contributes to an increased risk of cardiovascular events.

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Key words: Apolipoprotein B-48, Chylomicron remnants, Chronic kidney disease, eGFR, Proteinuria

Introduction

Proteinuria is an independent risk factor for the

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progression of chronic kidney disease (CKD) and the development of cardiovascular disease (CVD)^{1, 2)}. Patients with CKD are at a substantially increased risk of developing atherosclerosis, and approximately 40% of CKD patients have CVD even before they reach end-stage renal failure requiring hemodialysis³⁾. The cardiovascular mortality is 30 times higher among hemodialysis patients than individuals from the general population⁴⁾. In an effort to standardize the stage

of CKD, a system was recently developed based on the calculation of the estimated glomerular filtration rate (eGFR) using the serum creatinine level and age⁵⁾. Recent data have demonstrated the impact of albuminuria, as well as eGFR, on the incidence of CVD, and it is evident that both measurements together confer an enhanced risk of CVD⁶⁾. Recently, the prevalence of CKD has been increasing, approximately 13.3 million adults with CKD living in Japan⁷⁾. Therefore, CKD is a major health problem worldwide, and its prevention is an urgent issue.

Dyslipidemia associated with CKD is characterized by an increased level of serum triglycerides (TG) and a decreased level of high-density lipoprotein (HDL) cholesterol (HDL-C)⁸⁾. A high level of low-density lipoprotein (LDL) cholesterol (LDL-C) has been established as a strong risk factor for CVD; however, it is not consistently observed among patients with CKD⁹⁾. It has also been reported that individuals with CKD have elevated levels of TG-rich lipoproteins (TRL), including chylomicrons (CM), very-low-density lipoproteins (VLDL) and their remnant lipoproteins⁵⁾. Furthermore, many basic studies have suggested that remnant lipoproteins are associated with an increased risk of cardiovascular disease¹⁰⁾. The accumulation of CM remnant (CM-R) particles, the hydrolyzed products of CMs produced by lipoprotein lipase (LPL), are related to foam cell formation among macrophages and may promote the development of atherosclerosis in the arterial wall^{11, 12)}. It is presumed that measurements of the serum apoB-48 concentration can be used to evaluate the synthesis and metabolism of CM and CM-R, as each contains one apolipoprotein B-48 (apoB-48) molecule per particle¹³⁾. We previously developed a novel enzyme-linked immunosorbent assay (ELISA)^{14, 15)} and chemiluminescent enzyme immunoassay (CLEIA)¹⁶⁾ for conveniently determining the serum apoB-48 concentration. In our previous study, we reported that the serum apoB-48 concentrations are substantially elevated in patients with CKD of stage 4 (eGFR: 15-29 mL/min/1.73 m²) and 5 (eGFR: <15 mL/min/1.73 m²)¹⁷⁾. Recently, Japanese guidelines for the diagnosis and treatment of CKD¹⁸⁾ were released that indicate that both an increased GFR and the existence of proteinuria may exacerbate the pathogenesis of CKD. However, few studies conducted to date have investigated the association between the fasting serum apoB-48 concentration and proteinuria and/or eGFR.

In the current study, we examined whether the serum apoB-48 concentration is associated with renal dysfunction in patients with a low eGFR and/or proteinuria.

Materials and Methods

Subjects

The study subjects included 264 patients who attended the outpatient clinic of Osaka University Hospital (Osaka, Japan) or who were admitted to the hospital. Subjects taking lipid-lowering medications and those with heart, liver or thyroid disease were excluded. All subjects provided their informed consent, and the research protocol was approved by the Ethics Committee of Osaka University Hospital.

Measurements of the Renal Function, Serum Lipids and Apolipoproteins

In each subject, a sample of blood was drawn from the cubital vein after an overnight fast (over 12 hours), and the serum was collected following brief centrifugation. The basal performance of the recently developed CLEIA for apoB-48 measurement kit (Fujirebio Inc., Tokyo, Japan) used in this study has been previously reported¹⁶⁾, and the assay was carried out on the Lumipulse fully automated immunoassay analyzer (Fujirebio, Inc.). The serum total cholesterol (TC), TG and HDL-C levels were determined according to enzymatic methods, while the serum LDL-C levels were determined using the direct method (Sekisui Medical Co., Ltd., Tokyo, Japan). The non-HDL-cholesterol levels were calculated by subtracting the value of HDL-C from that of serum TC. The serum creatinine levels were measured using a photometric assay (Wako, Osaka, Japan). The urine test results were classified as (-), ($\pm$), (+), (2+) or (3+).

The eGFR values were subsequently estimated using the new equation proposed by the Japanese Society of Nephrology¹⁹⁾: $\text{eGFR (mL/min/1.73 m}^2\text{)} = 194 \times \text{S-Cr}^{-1.094} \times \text{Age}^{-0.287}$ (for female patients, the total value was multiplied by 0.739). An eGFR of <60 mL/min/1.73 m² is generally considered to be indicative of CKD; therefore, subjects with an eGFR of <60 mL/min/1.73 m² (eGFR <60) were defined as having a low eGFR. As for proteinuria, (-) and ($\pm$) urine test results were defined as normal; all other results [($\geq 1+$); (+), (2+) or (3+)] were defined as indicating proteinuria. All samples were treated in accordance with the Helsinki Declaration.

Statistical Analysis

Before the analysis, skewed variables (TG, apoB-48 and apoB-48/TG ratio) were logarithmically transformed to improve data normalization. The data are expressed as the mean $\pm$ SD for continuous variables and percentages for categorical variables. The significance of differences in the systolic BP, diastolic BP,

Fig. 1. Distribution of the fasting serum apoB-48 concentrations in the subjects with and without urinary protein, the subjects with a low and high eGFR and the subjects with both eGFR and proteinuria.

Serum apoB-48 concentration = 1 represents a concentration between 0.0 and 1.0 $\mu\text{g/mL}$.

A) Fasting serum apoB-48 concentrations in the subjects without urinary protein (open squares, $n = 124$) and with urinary protein (closed squares, $n = 140$).

B) Fasting serum apoB-48 concentrations in the subjects with a high eGFR (open squares, $n = 125$) and a low eGFR (closed squares, $n = 139$).

C) Fasting serum apoB-48 concentrations in the subjects with a combination of a high eGFR without urinary protein (open squares, $n = 50$) and a high eGFR with urinary protein (closed squares, $n = 75$).

D) Fasting serum apoB-48 concentrations in the subjects with a combination of a low eGFR without urinary protein (open squares, $n = 74$) and a high eGFR with urinary protein (closed squares, $n = 65$).

UA, TC, TG, HDL-C, LDL-C, non-HDL-C, log-apoB-48 and log-apoB-48/TG values between the four groups was tested using an analysis of variance (ANOVA) with the least significant difference (LSD) test as a post hoc test and the Bonferroni correction for multiple comparisons. The significance of differences with respect to the prevalence of diabetes and drug treatment were tested using the χ^2 test. Correlations between the kidney function parameters (eGFR and urinary protein) and various other parameters

were analyzed using Spearman's rank correlation coefficient, and a stepwise multiple logistic regression analysis was performed to determine independent predictors of CKD. The statistical analyses were conducted using the JMP8 software program (SAS Institute, Cary, NC). Statistical significance was established at a p value of < 0.05 .

Table 1. Clinical characteristics of the four groups based on eGFR and proteinuria

	High eGFR (≥ 60 mL/min/1.73 m ²)		Low eGFR (< 60 mL/min/1.73 m ²)		<i>p</i> values ^a
	without proteinuria	with proteinuria	without proteinuria	with proteinuria	
Age (year)	60 $\pm$ 15	61 $\pm$ 17	65 $\pm$ 12	63 $\pm$ 13	0.215
Sex (m/f)	26/24	38/37	39/35	35/30	0.88
BMI (kg/m ²)	22 $\pm$ 4	22 $\pm$ 3	23 $\pm$ 3	23 $\pm$ 4	0.362
Diabetes (%)	16 (32)	27 (36)	21 (28)	24 (37)	0.581
Prevalence of drug-treated patients (%)	7 (14)	10 (14)	10 (14)	13 (20)	0.666
Systolic BP (mmHg)	123 $\pm$ 24	122 $\pm$ 18	122 $\pm$ 21	136 $\pm$ 23 ^{bcd}	<0.001
Diastolic BP (mmHg)	76 $\pm$ 13	74 $\pm$ 11	72 $\pm$ 10	77 $\pm$ 14	0.052
Prevalence of drug-treated patients (%)	10 (20)	26 (35)	30 (41)	43 (66) ^{bcd}	<0.001
eGFR (mL/min/1.73 m ²)	80 $\pm$ 18	79 $\pm$ 16	36 $\pm$ 16 ^c	34 $\pm$ 17 ^c	<0.001
UA (mg/dL)	5.3 $\pm$ 1.2	5.3 $\pm$ 1.5	6.8 $\pm$ 1.3 ^{bc}	7.0 $\pm$ 1.6 ^{bc}	<0.001
Prevalence of drug-treated patients (%)	8 (16)	7 (9)	10 (14)	25 (38) ^{cd}	<0.001
TC (mg/dL)	194 $\pm$ 42	205 $\pm$ 58	296 $\pm$ 47	205 $\pm$ 70	0.648
Log-TG	2.0 $\pm$ 0.2	2.2 $\pm$ 0.2 ^b	2.1 $\pm$ 0.2 ^b	2.1 $\pm$ 0.2 ^b	<0.001
HDL-C (mg/dL)	62 $\pm$ 16	55 $\pm$ 19	57 $\pm$ 16	60 $\pm$ 26	0.209
LDL-C (mg/dL)	109 $\pm$ 44	121 $\pm$ 49	114 $\pm$ 41	117 $\pm$ 48	0.495
Non-HDL-C (mg/dL)	133 $\pm$ 40	150 $\pm$ 55	139 $\pm$ 33	145 $\pm$ 63	0.301
Log-ApoB-48	0.57 $\pm$ 0.28	0.74 $\pm$ 0.29 ^b	0.78 $\pm$ 0.32 ^b	0.89 $\pm$ 0.26 ^{bc}	<0.001
Log-ApoB-48/TG	0.28 $\pm$ 0.13	0.35 $\pm$ 0.13 ^b	0.35 $\pm$ 0.16 ^b	0.41 $\pm$ 0.11 ^{bc}	<0.001

Data represent the means $\pm$ S.D. Comparisons between patients were divided into 4 groups based on eGFR and proteinuria. We divided all subjects ($n=264$) into low (< 60 mL/min/1.73 m²) and high (≥ 60 mL/min/1.73 m²) eGFR levels; these two groups were also divided into those without or with proteinuria (by dipstick). *P* values refer to the results after analysis after adjusting for age, gender, and BMI. BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; UA, uric acid; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol.

^a*p* values for ANOVA test or χ^2 test.

^bBonferroni's post-hoc analysis < 0.05 vs High eGFR without proteinuria.

^cBonferroni's post-hoc analysis < 0.05 vs High eGFR with proteinuria

^dBonferroni's post-hoc analysis < 0.05 vs Low eGFR without proteinuria

Results

Distribution of the Serum ApoB-48 Concentrations in the Patients with Proteinuria and a Low eGFR

The distribution of the serum apoB-48 concentrations in the patients with proteinuria was significantly shifted toward higher values as compared with that observed in the patients without proteinuria (**Fig. 1-A**). Meanwhile, in the patients with a low eGFR, the distribution was significantly shifted toward higher values as compared with that observed in the patients with a high eGFR (**Fig. 1-B**).

Comparison of Clinical Profiles between the High eGFR Subjects without Proteinuria, High eGFR Subjects with Proteinuria, Low eGFR Subjects without Proteinuria and Low eGFR Subjects with Proteinuria

Table 1 shows the characteristics of the four

groups of subjects: those with a high eGFR without proteinuria ($n=50$), high eGFR with proteinuria ($n=75$), low eGFR without proteinuria ($n=74$) and low eGFR with proteinuria ($n=65$). The serum uric acid (UA) levels were significantly higher in the subjects with a low eGFR with and without proteinuria than in the age-, sex- and body mass index (BMI)-matched subjects with a high eGFR with and without proteinuria (**Table 1**). The fasting serum apoB-48 concentrations ranged from 0 to 17.0 μ g/mL in the subjects with a high eGFR with or without proteinuria (**Fig. 1-C**), from 0 to 15.0 μ g/mL in those with a low GFR without proteinuria and from 0 to 20.0 μ g/mL in those with a low GFR without proteinuria (**Fig. 1-D**). The serum log-apoB-48 and log-apoB-48/TG levels were significantly higher in the patients with a high eGFR with proteinuria, low eGFR without proteinuria and low eGFR with proteinuria than in those with a high eGFR without proteinuria. The

Table 2. Correlation coefficients (r) between the urine protein levels and various parameters in all subjects

	Coefficient	Univariate <i>p</i> value
Age	-0.1123	0.0826
BMI	-0.0195	0.7653
Systolic BP	-0.2034	0.0017
Diastolic BP	-0.1151	0.0782
eGFR	-0.0240	0.7057
TC	0.0515	0.4262
Log-TG	0.2876	<0.0001
HDL-C	-0.1475	0.0220
LDL-C	0.0954	0.1398
Non-HDL-C	0.0930	0.1502
Log-ApoB-48	0.2622	<0.0001
Log-ApoB-48/TG	0.0876	0.1751

A univariate analysis was performed using Pearson's correlation analysis. Abbreviations; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; BP, blood pressure; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol.

average levels of serum log-apoB-48 and log-apoB-48/TG were higher in the patients with a low eGFR with proteinuria than in any of the other groups (Table 1).

Correlations between the Kidney Function and Various Parameters

The correlations between the renal function parameters (urinary protein and eGFR) and various other parameters were analyzed using a logistic regression analysis. According to Pearson's correlation analysis, significant correlations with urinary protein were observed for systolic blood pressure (BP), log-TG, HDL-C and log-apoB-48 (Table 2), while significant correlations with eGFR were observed for age, non-HDL-C, log-apoB-48 and log-apoB-48/TG (Table 3). A multiple regression analysis indicated that the log-apoB-48/TG levels were a significant determinant of a reduced eGFR among the various lipid parameters, with the most significant differences observed for these parameters (Table 4).

Discussion

Dyslipidemia in patients with CKD is characterized by increased levels of TRL and TG and a decreased level of HDL-C⁸⁾. However, it is interesting to note that the serum LDL-C level is usually normal or slightly reduced in CKD patients⁹⁾. In order to evaluate the accumulation of CM and CM-R quantitatively, we developed the system to measure the

Table 3. Correlation coefficients (r) between eGFR and various parameters in all subjects

	Coefficient	Univariate <i>p</i> value
Age	-0.3938	<0.0001
BMI	-0.1121	0.0843
Systolic BP	-0.1208	0.0646
Diastolic BP	-0.0223	0.7341
Urin protein	-0.0244	0.7057
TC	0.0489	0.4498
Log-TG	-0.0218	0.7359
HDL-C	-0.0270	0.6764
LDL-C	-0.0106	0.8704
Non-HDL-C	-0.2693	<0.0001
Log-ApoB-48	-0.3090	<0.0001
Log-ApoB-48/TG	-0.3161	<0.0001

A univariate analysis was performed using Pearson's correlation analysis. Abbreviations; BMI, body mass index; BP, blood pressure; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol.

apoB-48 concentration. Both an eGFR of <75 mL/min/1.73 m² and the presence of trace urinary protein or more on a dipstick test are independently associated with all-cause mortality, cardiovascular mortality and kidney events in the general population²⁰⁾. In the current study, we measured the fasting apoB-48 concentrations in CKD patients. As in our former study¹⁷⁾, the apoB-48 concentrations were significantly higher in the patients with CKD of Stage 4 (eGFR: 15-25 mL/min/1.73 m²) and CKD of Stage 5 (eGFR: <15 mL/min/1.73 m²) than in those with CKD of Stage 1 (>90 mL/min/1.73 m²). In accordance with the new Japanese CKD guidelines both a decreased GFR and the existence of proteinuria may exacerbate the pathogenesis of CKD and induce the development of end-stage renal disease¹⁸⁾. In the current study, we found that the apoB-48 concentrations were higher in the patients with proteinuria (≥1+) than in those without proteinuria, and the existence of proteinuria increased the apoB-48 concentrations in patients with both a high and low eGFR (Table 1). Recently, many studies have shown that proteinuria is clustered with a number of risk factors, including hypertension, dyslipidemia, renal dysfunction, hyperhomocysteinemia and various inflammatory and oxidative stress markers, and this parameter has been demonstrated to be an independent predictor of adverse cardiovascular events, even after adjusting for these factors²⁰⁻²²⁾. These results indicate that the existence of proteinuria impairs remnant lipoprotein metabolism and enhances

Table 4. A stepwise multiple regression analysis of the eGFR and various parameters

	Model 1		Model 2	
	<i>F</i> value	<i>p</i> value	<i>F</i> value	<i>p</i> value
Age	37.38	< 0.001	Not included	
BMI	Not remain		Not included	
Systolic BP	Not remain		Not included	
Diastolic BP	Not remain		Not included	
HDL-C	Not remain		Not remain	
Non-HDL-C	Not remain		3.48	0.063
Log-ApoB-48/TG	17.13	< 0.001	28.19	< 0.001

A stepwise multiple regression analysis was used to determine eGFR with the *p* value-to-enter and *p* value-to-remain set at 0.20. Abbreviations; BMI, body mass index; BP, blood pressure; HDL-C, high density lipoprotein-cholesterol.

the accumulation of CM-R and that both proteinuria and accumulated CM-R deteriorate the renal function in CKD patients, synergistically leading to the development of end-stage renal disease.

We also calculated the apoB-48/TG ratio in the current study. In the postprandial serum, the TG moiety of CMs is promptly hydrolyzed by LPL, resulting in the subsequent production of CM-R of various sizes. Small CM-R particles contain a smaller amount of TG than do large CM-R particles; however, both sizes of CM-R contain one molecule of apoB-48. Therefore, it has been suggested that a high apoB-48 concentration is related to the accumulation of CM-R of all sizes, while a high apoB-48/TG ratio is related to the accumulation of small CM-R particles. Indeed, we previously found that the apoB-48/TG ratios are significantly higher in patients with type III hyperlipidemia, whose remnant lipoproteins accumulate due to a genetic abnormality in apolipoprotein E, than in those with other types of HL, although the subjects received lipid-lowering medications²³. In the current study, the eGFR values were found to be significantly correlated with the log-apoB-48 and log-apoB-48/TG levels, whereas urinary protein was found to be correlated with the log-apoB-48 level only. These results suggest that the number of small CM-R particles is increased in patients with a low eGFR, while the number of large CM-R particles is increased in patients with a high eGFR and proteinuria. Apolipoprotein C-III (ApoC-III) has been shown to inhibit the LPL and hepatic triglyceride lipase (HTGL) activity as well as the uptake of TRLs and CM-Rs by hepatic lipoprotein receptors²⁴. The plasma apoC-III concentrations are significantly elevated in patients with CKD²⁵. Unfortunately, we did not measure other apolipoproteins, although it is suspected that these changes may hydrolyze CM particles insufficiently, resulting in an

increased level of large-sized CM-Rs. Remnant particles are taken up by the liver via LDL receptors and LDL receptor-related proteins (LRPs)^{26, 27}. A previous study demonstrated a decrease in the LDL-receptor mRNA levels in rats with chronic renal failure²⁸. Therefore, the clearance of hydrolyzed small-sized CM-Rs by LDL-receptors may be delayed. Therefore, the decreased activity of LPL and HTGL, as well as the downregulation of LDL-receptors, may be attributed to the increase in large- and small-sized CM-Rs in subjects with a low eGFR. The urinary loss of apolipoprotein C-II (apoC-II), an activator of LPL, in the setting of proteinuria-dominant CKD, may decrease the LPL activity²⁹. A recent study demonstrated the downregulation of LDL-receptors in the liver in nephrotic rats³⁰. However, patients with nephrotic syndrome do not exhibit a decreased LDL apoB fractional catabolic rate³¹. Therefore, the decreased activity of LPL, but not decreased catabolism of CM-Rs, may be associated with the increased level of large CM-R particles observed in subjects with a high eGFR and proteinuria.

A number of studies have suggested that CM-Rs have highly atherogenic properties and that CM-R accumulation correlates with the development of atherosclerotic cardiovascular disease¹², whereas a reduced eGFR and proteinuria are independent risk factors for the development of cardiovascular disease. According to our multiple regression analysis, the log-apoB-48/TG level was found to be a significant determinant of a reduced eGFR. Therefore, an increased serum CM-R level may exacerbate atherosclerotic cardiovascular disease in patients with a reduced eGFR and/or proteinuria.

The present study is associated with some limitations. First, the subjects had already been treated with antidiabetic drugs, antihypertensive drugs and antihy-

peruricemic drugs. In particular, the subjects with a low eGFR and proteinuria were treated with antihypertensive and antihyperuricemic drugs at a high frequency. However, it has not been reported whether the serum apoB-48 concentration is affected by treatment with any antihypertensive or antihyperuricemic agents. Second, we did not measure the levels of other apolipoproteins, which play a key role in regulating CM catabolism. Finally, it was not possible to clarify whether an increased serum apoB-48 concentration contributes to atherosclerosis and CHD in patients with CKD. In our recent study, a high concentration of fasting apoB-48 was found to be significantly correlated with the intima-media thickness in subjects with normal but relatively high TG levels ($100 < \text{TG} \leq 150$ mg/dL) and the fasting serum apoB-48 concentration was found to be significantly correlated with the prevalence of coronary artery disease^{32, 33}.

In conclusion, both a low eGFR (< 60) and proteinuria ($\geq 1+$) are independent determinants of a high apoB-48 concentration. Taken together, the present results suggest that an increased serum apoB-48 concentration contributes to an increased risk of cardiovascular events.

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Disclosures

S. Yamashita and D. Masuda received lecture fees in 2010 from FUJIREBIO, INC. FUJIREBIO, INC. shared the cost for the apoB-48 measurements as a joint research. The other authors have nothing to disclose.

Conflicts of Interest

There is nothing to disclose, except that FUJIRE-

BIO, INC. shared the cost for the apo B-48 measurements as a joint research.

List of Abbreviations

apo: apolipoprotein
 BMI: body mass index
 CKD: chronic kidney disease
 CLEIA: chemiluminescence enzyme immunoassay
 CM: chylomicron
 CM-R: chylomicron remnant
 CVD: cardiovascular disease
 eGFR: estimated glomerular filtration rate
 ELISA: enzyme-linked immunosorbent assay
 HDL-C: high-density lipoprotein cholesterol
 HTGL: hepatic triglyceride lipase
 LDL-C: low-density lipoprotein cholesterol
 LPL: lipoprotein lipase
 LRP: LDL receptor-related protein
 TC: total cholesterol
 TG: triglyceride
 TRL: TG-rich lipoprotein
 VLDL: very-low-density lipoprotein
 VLDL-R: very-low-density lipoprotein remnant
 UA: uric acid

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