Association Between High-density Lipoprotein Cholesterol and Renal Function in Elderly Hypertension

A Cross-sectional Study in Chinese Population

Ya-Ping Zhang, MD, PhD, Ming-Gen Lu, PhD, Dayue Darrel Duan, MD, PhD, Ying-Long Liu, MD, Meilin Liu, MD, Ying Li, MD, Ze-Min Kuang, PhD, Yao Lu, MD, Xing Liu, MD, Xiao-Hui Li, PhD, and Hong Yuan, MD, PhD

Abstract: Few studies have yet investigated the possible association between high-density lipoprotein cholesterol (HDL-C) and kidney function in elderly patients with primary hypertension. Accordingly, the aim of the present study was to evaluate the relationship between HDL-C and kidney function in elderly hypertension.

A total of 14,644 elderly hypertensive subjects were enrolled in our cross-sectional study. The patients were categorized based on serum HDL-C level and glomerular filtration rate (GFR) value, respectively. One-way analysis of variance was used to compare the parameters among different groups. Bonferroni correction was performed for multiple comparisons. Analysis of covariance was used to control for confounding factors. The significance of difference between 3 groups and more was determined by chi-square test for categorical variables.

Serum creatinine and uric acid were negatively related to HDL-C level, whereas GFR was positively related to HDL-C level in elderly hypertensive patients according to tertiles of HDL-C and tertiles of HDL-C/total cholesterol ratio (all P for trends <0.05). The male elderly hypertensive patients showed stronger relationship between HDL-C and renal function than the female elderly hypertensive subjects. Low HDL-C was associated with renal insufficiency and proteinuria in the hypertensive elderly ($P < 0.05$). The elderly ''renal-hyperfiltrator'' appeared to have lower HDL-C level, compared with the ''normal renal-filtrator'' ($P < 0.05$). There was an inverse ''V'' shape between HDL-C and GFR by GFR strata.

Our results point out that there is an association of low HDL-C level with impaired kidney function in elderly hypertensive patients. Glomerular hyperfiltration may also affect HDL-C level and sex might be an influential factor for the association of HDL-C with kidney function in elderly hypertension.

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Abbreviations: ApoA-I = apolipoprotein A-I, BMI = body mass index, BP = blood pressure, BUN = blood urea nitrogen, CKD = chronic kidney disease, CKD-EPI = chronic kidney disease epidemiology collaboration, DBP = diastolic blood pressure, ESRD = end-stage renal disease, GFR = glomerular filtration rate, HDL-C = high-density lipoprotein cholesterol, JNC = Joint National Committee, LDL-C = low-density lipoprotein cholesterol, MDRD = simplified modification of diet in renal disease, PP = pulse pressure, SBP = systolic blood pressure, Scr = Serum creatinine, SD = standard deviation, SR-B1 = scavenger receptor class B member 1, TC = total cholesterol, TG = triglyceride, UA = uric acid.

INTRODUCTION

The elderly population is susceptible to dyslipidemia of aging and renal dysfunction. Lipid abnormalities may lead to the progression of chronic kidney disease (CKD).[1] Emerging evidence showed the cardiovascular risk profile in the elderly is different from that in young people.[2,3] The increased risk of cardiovascular disease associated with high serum cholesterol in young men and middle-aged adults has been clearly established.[4] But the prospective studies have revealed controversial results about relationship of total serum cholesterol level with cardiovascular outcomes and kidney disease progression in the elderly.[5–7] Further investigation into the association of dyslipidemia with renal disease progression in aging population has been needed. High-density lipoprotein cholesterol (HDL-C) benefits kidney function and cardiovascular system by extracting tissue cholesterol. The general population-based studies showed that HDL-C level was associated with kidney function and the association between them gradually strengthened as estimated glomerular filtration rate (GFR) declined.[8,9] But it seems that renal function status, in turn, impacts the level and function of HDL-C. The HDL-C in patients with end-stage renal disease (ESRD) on hemodialysis is dysfunctional and dramatically less effective in accepting cholesterol from macrophages.[10] Both clinical and laboratory studies have revealed that ESRD decreased the levels of apolipoprotein A-I (ApoA-I) and HDL-C as well as altered HDL composition.[11,12] A very recent study demonstrated that even mild renal dysfunction was also tied to

low HDL-C level. In our previous study, we found that the hypertensive elderly had higher prevalence of dyslipidemia and renal dysfunction.[13] Thus, the present study was initiated to test the association of HDL-C with kidney function in elderly hypertensive subjects.

METHODS

The study protocol was approved by the medical ethics committee of the Third Xiang-Ya Hospital. All of the subjects enrolled in this study gave informed consent to participate in this study.

Study Subjects

There were 31,941 Chinese people aged >60 years who participated in annual physical examination in Health Management Center of the Third Xiang-Ya Hospital in Hunan Province between January 1, 2008 and December 31, 2010. In this study, inclusion criteria were age >60 years and hypertension. Exclusion criteria included: no available data on blood pressure (BP) value, glucose concentration, cholesterol level, blood urea nitrogen (BUN) level, uric acid (UA) level, serum creatinine (Scr) level, urine analysis, body weight, or height; diabetes; obesity; immune diseases; malignant diseases; use of lipid-lowering agents; history of primary renal diseases; renal artery stenosis; and duplicate cases. After the subjects with incomplete data were removed and duplicate cases were deleted, there were 28,258 people left. The 19,276 subjects were diagnosed to have hypertension among 28,258 people. After we removed the patients with diabetes, obesity, immune diseases, malignant diseases, primary renal diseases, or renal artery stenosis and we excluded the patients who took lipid-lowering agents 14,644 elderly hypertensive subjects were finally screened and eligible for this study. Hypertension was defined according to the Joint National Committee (JNC) 7 report.[14] People who had previously received a diagnosis of hypertension were also considered to have hypertension, although they had normal BP after taking antihypertensive drugs. Diabetes was diagnosed by either fasting blood glucose ≥ 7.0 mmol/L, or casual blood glucose ≥ 11.1 mmol/L.[15] Patients who had a previous diagnosis of diabetes were also considered to have diabetes, although they had normal blood glucose concentration after treatment. The presence of obesity was defined by body mass index (BMI) of 30 kg/m^2 or more.[16] The data for all subjects were obtained from annual physical examination database at the data center of the Health Management Center in the Third Xiang-Ya Hospital.

Measurements and Renal Function Estimates

The examination was carried out during outpatient visit including an interview to determine the history of hypertension, diabetes, hyperlipidemia, usage of medicine agents, and so on. After fasting overnight, BP was measured with an appropriately sized cuff and a mercury column sphygmomanometer in the sitting posture after a 10-min rest. Height and body weight were measured, and BMI was calculated as body weight divided by square of height. Venous blood sampling from all of the subjects was performed. Serum glucose, total cholesterol (TC), HDL-C, low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), BUN, Scr, and UA levels were determined using standard laboratory methods. Qualitative analysis of urinary protein was measured by sulfosalicylic acid method. GFR was estimated using the equations of simplified modification of diet in renal disease (MDRD)[17]

and chronic kidney disease epidemiology collaboration (CKD-EPI).[18] The GFR_{MDRD} was calculated as $186 \times Scr^{-1.154} \times Age^{-0.203}$ ($\times 0.742$ if female). The $GFR_{CKD-EPI}$ was calculated as recommended: for women with a Scr ≤ 0.7, $144 \times (Scr/0.7)^{-0.329} \times 0.993^{age}$; for women with a Scr >0.7, $144 \times (Scr/0.7)^{-1.209} \times 0.993^{age}$; for men with a Scr ≤ 0.9, $141 \times (Scr/0.9)^{-0.411} \times 0.993^{age}$; for men with a Scr >0.9, $141 \times (Scr/0.9)^{-1.209} \times 0.993^{age}$.

Protocol

The 14,644 elderly hypertensive subjects were first divided into 3 groups according to serum HDL-C and HDL-C/TC ratio, respectively. Then all the patients were categorized into 6 groups according to GFR_{MDRD} value and categorized into 5 groups based on $GFR_{CKD-EPI}$ value. The values of BMI, BP, TC, TG, HDL-C, LDL-C, glucose concentration, GFR, Scr, UA and BUN, prevalence of renal insufficiency and proteinuria prevalence were compared among different groups.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables were presented as percentage unless otherwise stated. One-way analysis of variance was used to compare difference of means of continuous variables among 3 groups or more. Bonferroni correction was performed for multiple comparisons. Analysis of covariance (ANCOVA) was used to control for confounding factors. The significance of difference between 3 groups and more was determined by chi-square test for categorical variables. P value <0.05 was considered to be statistically significant. Analysis was performed in statistical software package SPSS16.0 (SPSS Inc, Chicago, IL) for Windows.

RESULTS

Summary of Study Subjects

The clinical and laboratory characteristics of study subjects were shown in Table 1. Overall, 14,644 subjects with 67% male and at age of 70 ± 6 years were studied. Isolated systolic hypertension predominated among the hypertensive elderly. The HDL-C to TC ratio was 0.3 ± 0.1. Estimated GFR by MDRD formula was higher than that calculated by CKD-EPI equation ($P < 0.01$). GFR_{MDRD} was strongly correlated with $GFR_{CKD-EPI}$ ($r = 0.92$, $P < 0.01$).

Renal Function According to Tertiles of HDL-C

The parameters of 3 groups according to tertiles of serum HDL-C level were demonstrated in Table 2. The subjects were younger in tertile 1 and tertile 2 than that in tertile 3. The females had higher HDL-C level, whereas males had lower HDL-C level. As HDL-C level elevated from tertile 1 to tertile 3, TC level increased, but TG and BMI levels decreased. The LDL-C level was highest in tertile 2 and lowest in tertile 1. Compared with tertile 2 and tertile 3, tertile 1 had higher glucose level. The systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse pressure (PP) were not different among 3 groups. The GFR, Scr, and UA values among 3 groups were presented in Figure 1. The Scr and UA levels were highest in tertile 1 and lowest in tertile 3, whereas the GFR_{MDRD} and $GFR_{CKD-EPI}$ values were lowest in tertile 1 and highest in tertile 3. There was no difference in BUN level among 3 groups ($P = 0.06$, data not shown). The prevalence of renal insufficiency and proteinuria

TABLE 1. Clinical and Laboratory Characteristics of Subjects

Variables	Values
N	14644
Age, y	70 ± 6
Male, %	66.7%
BMI, kg/m^2	24.2 ± 2.8
SBP, mmHg	148 ± 18
DBP, mmHg	81 ± 12
PP, mmHg	67 ± 16
TC, mmol/L	5 ± 0.9
TG, mmol/L	1.6 ± 1
HDL-C, mmol/L	1.3 ± 0.3
LDL-C, mmol/L	3 ± 0.8
Glucose, mmol/L	5.1 ± 0.7
BUN, mmol/L	5.4 ± 1.6
Scr, μmol/L	77.8 ± 27.7
UA, μmol/L	329.3 ± 88.4
GFR$_{CKD-EPI}$, mL/min/1.73m^2	81.7 ± 14.2
GFR$_{MDRD}$, mL/min/1.73m^2	88.4 ± 19.7
Renal insufficiency, %	6.1%
Proteinuria, %	14.2%
Hyperlipidemia, %	41.6%

BMI = body mass index, BUN = blood urea nitrogen, CKD-EPI = chronic kidney disease epidemiology collaboration, DBP = diastolic blood pressure, GFR = glomerular filtration rate, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, MDRD = simplified modification of diet in renal disease, PP = pulse pressure, SBP = systolic blood pressure, Scr = serum creatinine, SD = standard deviation, TC = total cholesterol, TG = triglyceride, UA = uric acid.

prevalence were lower in tertile 2 and tertile 3, compared with that in tertile 1 ($P < 0.05$, Figures 2A and 3A). Since sex was an influential factor for lipid and kidney function, we further categorized tertiles of HDL-C into female and male groups. We performed ANCOVA using age, BMI, TC, TG, LDL-C, and glucose concentration as confounding factors to explore the effect of HDL-C on kidney function (data shown in Table 3). As HDL-C level increased from tertile 1 to tertile 3, Scr and UA levels decreased while GFR value increased for male subjects. There was no difference in BUN, Scr and GFR values for female subjects among tertiles of HDL-C.

Renal Function According to Tertiles of HDL-C/TC Ratio

The GFR, Scr, and UA values among 3 groups according to HDL-C/TC ratio were presented in Figure 4. As HDL-C/TC ratio increased from tertile 1 to tertile 3, GFR$_{MDRD}$ increased and UA level decreased. But tertile 2 had highest GFR$_{CKD-EPI}$ and lowest Scr level. There was no significant difference in BUN level among 3 groups ($P = 0.052$, data not shown). The prevalence of renal insufficiency and proteinuria prevalence were lower in tertile 2 and tertile 3, compared with that in tertile 1 ($P < 0.05$, Figures 2B and 3B). The BUN, Scr, UA, and GFR values of male and female subjects from tertile 1 to tertile 3 were presented in Table 4. As HDL-C/TC ratio increased from tertile 1 to tertile 3, the Scr and UA levels decreased, but GFR value increased for male subjects. For female subjects, UA level gradually decreased from tertile 1 to tertile 3, but Scr, GFR, and BUN values did not change among different tertiles.

HDL-C Levels in Different GFR Strata

According to MDRD formula, GFR increased from sextile 1 to sextile 5 (all P for the trends < 0.05, Figure 5) and then eGFR decreased from sextile 5 to sextile 6 ($P < 0.05$, Figure 5). The GFR$_{CKD-EPI}$ increased from quintile 1 to quintile 4 (all P for the trends < 0.05, Figure 5) and then GFR$_{CKD-EPI}$ decreased from quintile 4 to quintile 5 ($P < 0.05$, Figure 5). The inverse ''V'' shape was observed between GFR and HDL-C (Figure 5). Either MDRD formula or CKD-EPI equation was used to calculate GFR.

DISCUSSION

To date, there is a paucity of studies, which are primarily aimed to determine the association of serum HDL-C level with renal function in elderly hypertensive patients. Our population-based study has demonstrated complex relationship between

TABLE 2. Parameters Among 3 Groups According to High-density Lipoprotein Cholesterol Level

Parameters	Tertile 1	Tertile 2	Tertile 3	P
N	2241	11783	620	
Age, y	69.7 ± 6	69.8 ± 6.2	$71 \pm 6.7^{*,\#}$	<0.01
Male, %	82.4%	64.8%*	47.6%$^{*,\#}$	<0.01
BMI, kg/m^2	25.2 ± 2.4	$24.1 \pm 2.7^*$	$21.6 \pm 3^{*,\#}$	<0.01
SBP, mmHg	148 ± 18	148 ± 18	147 ± 19	0.37
DBP, mmHg	81 ± 12	81 ± 12	80 ± 13	0.07
PP, mmHg	67 ± 16	67 ± 16	68 ± 17	0.72
TC, mmol/L	4.6 ± 0.9	$5.1 \pm 0.9^*$	$5.6 \pm 1^{*,\#}$	<0.01
TG, mmol/L	2.3 ± 1.7	$1.5 \pm 0.8^*$	$1 \pm 0.5^{*,\#}$	<0.01
HDL-C, mmol/L	0.9 ± 0.1	$1.4 \pm 0.2^*$	$2.2 \pm 0.2^{*,\#}$	<0.01
LDL-C, mmol/L	2.7 ± 0.8	$3 \pm 0.8^*$	$2.9 \pm 0.9^{*,\#}$	<0.01
Glucose, mmol/L	5.2 ± 0.7	$5.1 \pm 0.6^*$	$5.1 \pm 0.6^*$	<0.01

The HDL-C ranges in tertile 1, tertile 2, and tertile 3 were <1, 1–2, >2 mmol/L, respectively. Compared with tertile 1. BMI = body mass index, DBP = diastolic blood pressure, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, PP = pulse pressure, SBP = systolic blood pressure, TC = total cholesterol, TG = triglyceride.
* $P < 0.05$; Compared with tertile 2.
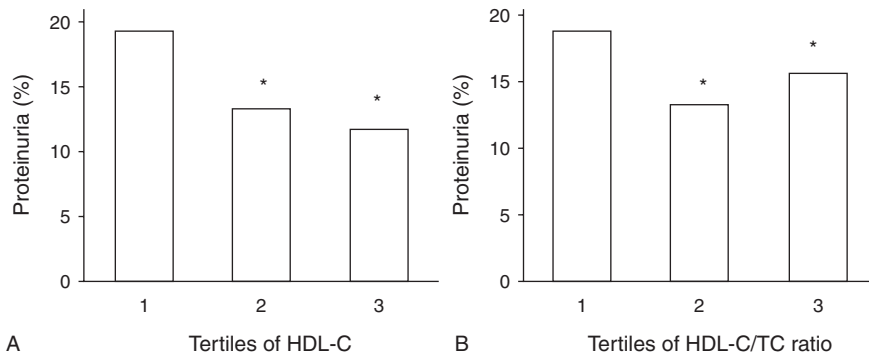$^\#$ $P < 0.05$.
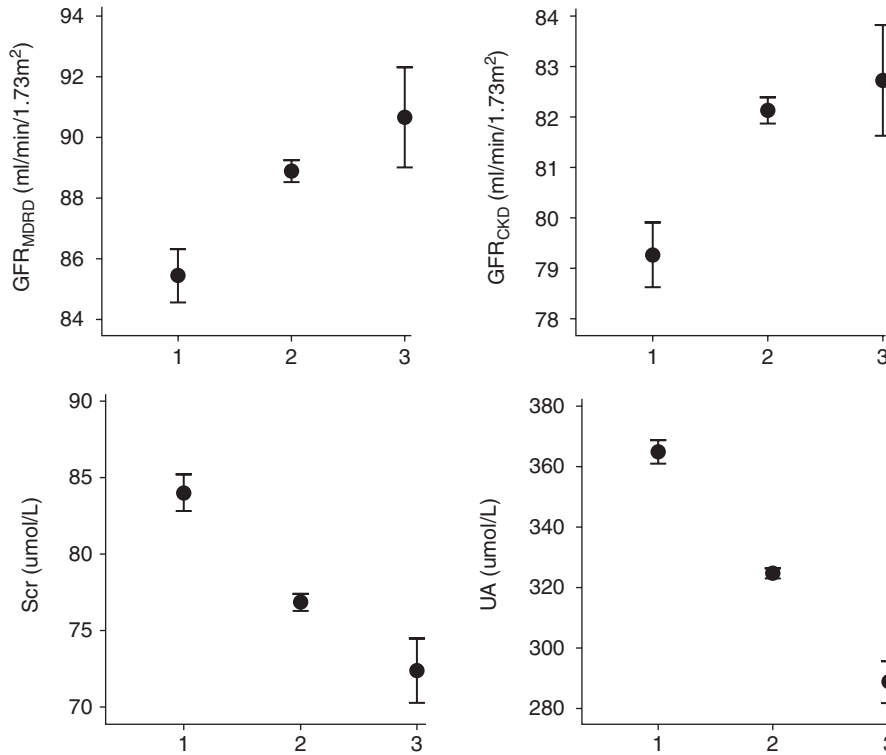
FIGURE 1. GFR_{MDRD}, $GFR_{CKD-EPI}$, Scr, and UA levels according to tertiles of HDL-C. Range 1, 2, and 3 of HDL-C in increasing tertiles were <1, 1–2, >2 mmol/L, respectively. The vertical bars represent 95% confidence interval for mean. All *P* for trends <0.05. CKD-EPI = chronic kidney disease epidemiology collaboration, GFR = glomerular filtration rate, HDL-C = high-density lipoprotein cholesterol, MDRD = simplified modification of diet in renal disease, Scr = Serum creatinine, UA = uric acid. n = 2241 for tertile 1, 11783 for tertile 2, and 620 for tertile 3.

HDL-C and kidney function in elderly hypertension. Our results agree with some data previously reported by several studies. The general population-based studies showed HDL-C was associated with kidney function and the association gradually strengthened as GFR value declined.[8] A longitudinal follow-up study revealed that HDL-C level was the only lipid parameter that affected the progression of CKD independently of the presence of diabetes and that low HDL-C levels were associated with earlier entry in dialysis or doubling of the Scr level.[19] Serum cholesterol efflux mediated by scavenger receptor class B member 1 (SR-B1) was significantly reduced in CKD patients with low HDL-C levels and then HDL functionality is also impaired in renal dysfunction.[19] Some studies showed that a decrease in HDL-C or ApoA-I levels is observed in renal dysfunctional individuals and may be associated with the down-regulation of ApoA-I synthesis in the liver.[20–24] Our study
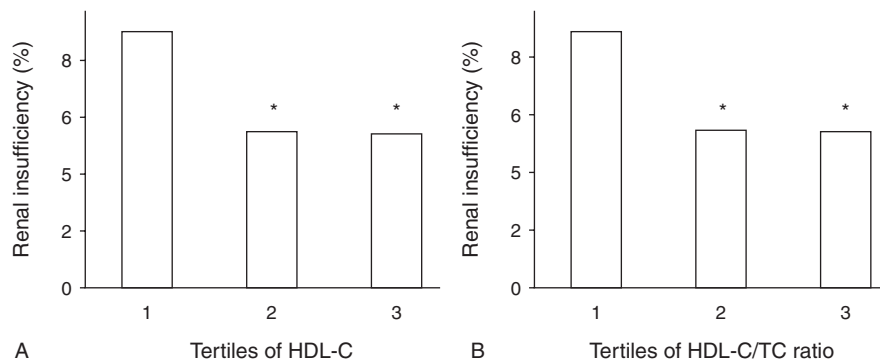
FIGURE 2. (A) Prevalence of renal insufficiency according to tertiles of HDL-C. Range 1, 2 and 3 of HDL-C in increasing tertiles of HDL-C were <1, 1–2, >2 mmol/L, respectively. (B) Prevalence of renal insufficiency according to tertiles of HDL-C/TC Ratio. Range 1, 2, and 3 of HDL-C/TC ratio in increasing tertiles of HDL-C/TC ratio were <0.2, 0.2–0.4, >0.4, respectively. Renal insufficiency was defined as GFR <60 mL/min/1.73m² by MDRD equation. *$P < 0.05$ vs tertile 1. HDL-C = high-density lipoprotein cholesterol, MDRD = simplified modification of diet in renal disease, TC = total cholesterol. n = 2241 for tertile 1, 11783 for tertile 2 and 620 for tertile 3 according to HDL-C level, n = 2458 for tertile 1, 11418 for tertile 2, and 768 for tertile 3 according to HDL-C/TC Ratio.

FIGURE 3. (A) Proteinuria prevalence according to tertiles of HDL-C. Range 1, 2, and 3 of HDL-C in increasing tertiles of HDL-C were <1, 1–2, >2 mmol/L, respectively. (B) Proteinuria prevalence according to tertiles of HDL-C/TC Ratio. Range 1, 2, and 3 of HDL-C/TC ratio in increasing tertiles of HDL-C/TC ratio were <0.2, 0.2–0.4, >0.4, respectively. $^*P < 0.01$ vs tertile 1. HDL-C = high-density lipoprotein cholesterol, TC = total cholesterol. n = 2241 for tertile 1, 11783 for tertile 2 and 620 for tertile 3 according to HDL-C level, n = 2458 for tertile 1, 11418 for tertile 2, and 768 for tertile 3 according to HDL-C/TC Ratio.

supports that Scr and UA are negatively related to HDL-C level, whereas GFR is positively related to HDL-C level in elderly hypertensive patients according to tertiles of HDL-C. The male elderly hypertensive patients show stronger relationship between HDL-C and renal function than the female elderly hypertensive subjects. Low HDL-C is associated with renal insufficiency and proteinuria in the elderly. However, the elderly patients with too high GFR (GFR$_{MDRD}$ >140 mL/min/1.73m^2 or GFR$_{CKD-EPI}$ >120 mL/min/1.73m^2) have significantly decreased HDL-C levels by both GFR$_{MDRD}$ and GFR$_{CKD-EPI}$ strata in current study. Our results also show there is an inverse ''V'' relationship between GFR and HDL-C according to GFR strata in elderly hypertensive population. It reveals that glomerular hyperfiltration might reduce HDL-C level in the elderly, which has been proposed in young healthy men.[25]

Glomerular hyperfiltration is a phenomenon that occurs in various clinical conditions including hypertension and kidney diseases. To date, there is no exact definition of glomerular hyperfiltration. A very recent review revealed that 88.4% of studies involving glomerular hyperfiltration threshold used a single threshold and 11.6% of them used numerous thresholds to define glomerular hyperfiltration.[26] The glomerular hyperfiltration threshold ranged from 90.7 to 175 mL/min/1.73 m^2. The pathophysiological process of glomerular hyperfiltration, which may vary with the underlying diseases, has not been well explored. Glomerular hyperfiltration might be both a cause and a consequence of renal injury. Renal hyperfiltration has been reported in subjects with obesity and metabolic syndrome.[25,27–30] The ''hyperfiltrators'' in a general population at age ranging from 40 to 72 years were actually at elevated cardiovascular risk. Glomerular hyperfiltration independently predicted the combined outcomes of total death and cardiovascular events at roughly a 3-fold relative risk, irrespective of estimating GFR by the CKD-EPI formula or the MDRD equation.[31] The ''hyperfiltrators'' had higher plasma atherogenic index (TG/HDL-C ratio), but lower HDL-C and UA levels, compared with the ''nonhyperfiltrators''.[31] In this study, although sextile 6 (GFR$_{MDRD}$ >140 mL/min/1.73 m^2) and quintile 5 (GFR$_{CKD-EPI}$ >120 mL/min/1.73m^2) had higher GFR values, their HDL-C levels significantly decreased. It is well known that hypertensive patients usually have high blood

TABLE 3. Kidney Function Among Tertiles of High-density Lipoprotein Cholesterol in Male and Female Subjects

Variables		Tertile 1	Tertile 2	Tertile 3	P
BUN, mmol/L	Male	5.5 ± 1.6	5.5 ± 1.6	$5.8 \pm 1.8^{*,\dagger}$	0.03
	Female	5 ± 1.5	5.1 ± 1.5	5.2 ± 1.3	0.81
Scr, µmol/L	Male	87.8 ± 29.5	$83.9 \pm 26.6^*$	$80.9 \pm 20.4^*$	0.03
	Female	65.2 ± 18.7	63.9 ± 23.3	64.5 ± 28.6	0.63
UA, µmol/L	Male	375.8 ± 85.4	$348.4 \pm 82.8^*$	$331.8 \pm 82.9^{*,\dagger}$	0.00
	Female	313.5 ± 77.5	$280.9 \pm 76^*$	$249.6 \pm 72.1^{*,\dagger}$	0.01
GFR$_{CKD-EPI}$, mL/min/1.73m^2	Male	78.7 ± 15.6	$80.9 \pm 13.8^*$	$82 \pm 14^*$	0.00
	Female	82.9 ± 15.1	84.3 ± 13.6	83.3 ± 13.8	0.16
GFR$_{MDRD}$, mL/min/1.73m^2	Male	85.1 ± 20.6	$88.2 \pm 19.2^*$	$91.6 \pm 21.8^{*,\dagger}$	0.01
	Female	88 ± 21.2	90.2 ± 19.7	89.8 ± 20	0.32

Statistical significances were obtained by analysis of covariance. The covariates included age, BMI, TC, TG, LDL-C, and glucose concentration. The HDL-C ranges in tertile 1, tertile 2, and tertile 3 were <1, 1–2, >2 mmol/L, respectively. Compared with tertile 1. BMI = body mass index, BUN = blood urea nitrogen, CKD-EPI = chronic kidney disease epidemiology collaboration, GFR = glomerular filtration rate, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, MDRD = simplified modification of diet in renal disease, Scr = serum creatinine, TC = total cholesterol, TG = triglyceride, UA = uric acid.
* $P < 0.05$; compared with tertile 2.
† $P < 0.05$.
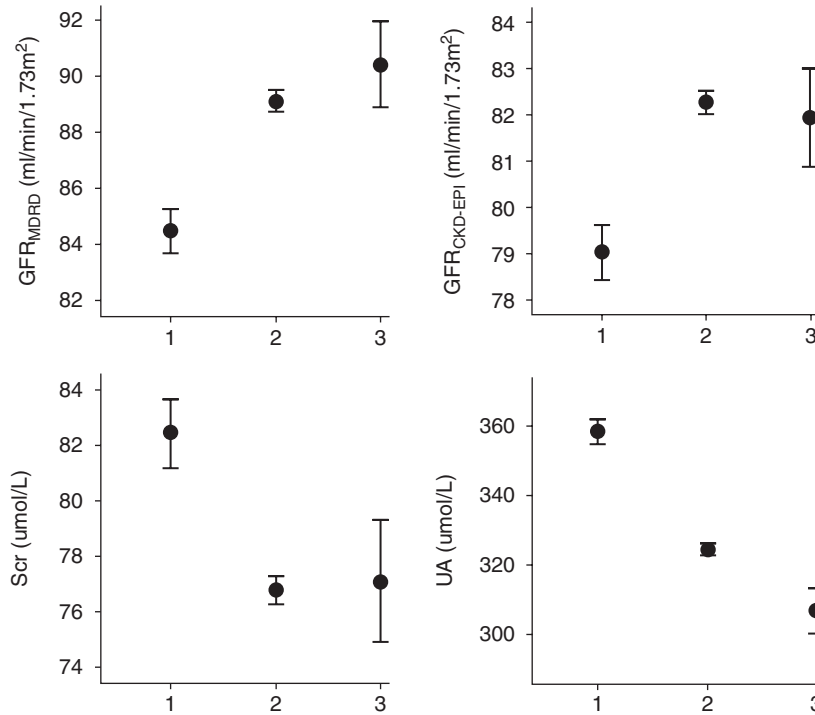
FIGURE 4. GFR$_{MDRD}$, GFR$_{CKD-EPI}$, Scr, and UA levels according to tertiles of HDL-C/TC Ratio. Range 1, 2, and 3 of HDL-C/TC ratio in increasing tertiles were <0.2, 0.2–0.4, >0.4, respectively. The vertical bars represent 95% confidence interval for mean. All *P* for trends <0.05. CKD-EPI = chronic kidney disease epidemiology collaboration, GFR = glomerular filtration rate, HDL-C = high-density lipoprotein cholesterol, MDRD = simplified modification of diet in renal disease, Scr = Serum creatinine, TC = total cholesterol, UA = uric acid. n = 2458 for tertile 1, 11418 for tertile 2, and 768 for tertile 3.

volume and enhanced vasoconstriction both of which lead to increased glomerular pressure.[32] Increased glomerular pressure may predict an early manifestation of hypertension and directly contribute to the progression of CKD.[33] In experimental studies, glomerular hypertension has been shown to mediate progressive kidney damage following a variety of initiating injuries.[34–36] However, the pathophysiological mechanism of low HDL-C

associated with glomerular hyperfiltration has not been well explored currently, although lower HDL-C level was observed in ''hyperfiltrators'' based on some studies. The involved mechanism remains to be elucidated in future studies to develop new therapeutic strategies.

The current study has several advantages. The larger number of elderly hypertensive population makes the results

TABLE 4. Kidney Function Among Tertiles of High-density Lipoprotein Cholesterol to Total Cholesterol Ratio in Male and Female Subjects

Variables		Tertile 1	Tertile 2	Tertile 3	*P*
BUN, mmol/L	Male	5.5 ± 1.6	5.5 ± 1.6	5.7 ± 1.9	0.08
	Female	5.1 ± 1.5	5.1 ± 1.4	5.1 ± 1.6	0.80
Scr, μmol/L	Male	88.1 ± 24.6	83.8 ± 27.6*	83 ± 26*	0.00
	Female	67.6 ± 18.8	63.5 ± 18.2	64.6 ± 22.6	0.10
UA, μmol/L	Male	378.3 ± 84	348.5 ± 82.5*	332.6 ± 90.2*,†	0.00
	Female	306.1 ± 79.6	279.1 ± 75.4*	252.3 ± 75.7*,†	0.00
GFR$_{CKD-EPI}$, mL/min/1.73m²	Male	78 ± 14.9	81.1 ± 13.9*	81.5 ± 14.9*	0.00
	Female	81.7 ± 14.8	84.4 ± 13.5	84.3 ± 14.5	0.10
GFR$_{MDRD}$, mL/min/1.73m²	Male	83.8 ± 19.3	88.5 ± 19.4*	90 ± 21.8*	0.00
	Female	86.3 ± 20.3	90.4 ± 19.7	91.8 ± 21	0.47

Statistical significances were obtained by analysis of covariance (ANCOVA). The covariates included age, BMI, TG, LDL-C, and glucose concentration. The HDL-C ranges in tertile 1, tertile 2 and tertile 3 were <0.2, 0.2–0.4, >0.4, respectively. Compared with tertile 1. BMI = body mass index, BUN = blood urea nitrogen, CKD-EPI = chronic kidney disease epidemiology collaboration, GFR = glomerular filtration rate, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, MDRD = simplified modification of diet in renal disease, Scr = serum creatinine, TG = triglyceride, UA = uric acid.
* *P* < 0.05; compared with tertile 2.
† *P* < 0.05.
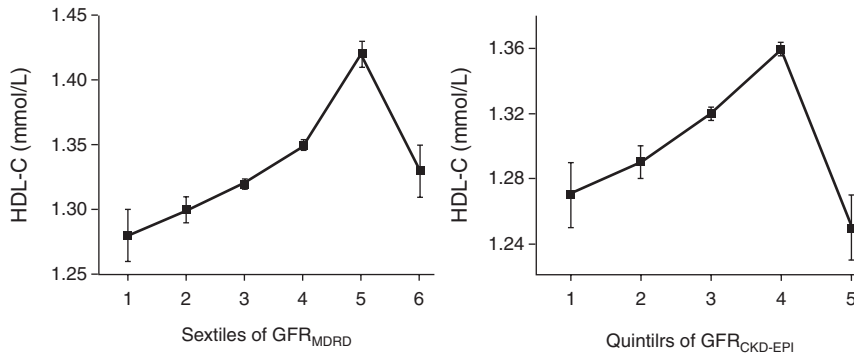
FIGURE 5. Inverse ''V'' shape between GFR and HDL-C. Range 1, 2, 3, 4, 5, and 6 of GFR_{MDRD} in increasing sextiles of GFR_{MDRD} were <30, 30–60, 60–90, 90–120, 120–140, >140 mL/min/1.73m^2, respectively. Range 1, 2, 3, 4, and 5 of $GFR_{CKD-EPI}$ in increasing quintiles of $GFR_{CKD-EPI}$ were <30, 30–60, 60–90, 90–120, >120 mL/min/1.73m^2, respectively. All P for trends <0.05. CKD-EPI = chronic kidney disease epidemiology collaboration, GFR = glomerular filtration rate, HDL-C = high-density lipoprotein cholesterol, MDRD = simplified modification of diet in renal disease. n = 79 for sextile 1, 807 for sextile 2, 7166 for sextile 3, 5831 for sextile 4, 602 for sextile 5, and 159 for sextile 6 according to GFR_{MDRD}, n = 90 for quintile1, 1073 for quintile 2, 8763 for quintile 3, 4629 for quintile 4, and 89 for quintile 5 according to $GFR_{CKD-EPI}$.

more reliable and replicable. MDRD equation was developed for estimating kidney function of subject with GFR >60 mL/min/1.73m^2. Compared with MDRD equation, CKD-EPI formula was aimed to evaluate higher GFR.[17,18] In our study, we used both of them to estimate GFR due to their accuracy in different ranges of GFR. It is shown that kidney function is influenced by diabetes and obesity. Therefore, this study excluded the patients with diabetes and obesity. To minimize the number of confounding factors, we also excluded the subjects who took lipid-lowering agents.

Our study also has some limitations. The primary limitation of this study is that cross-sectional data do not allow us to observe the impact of risk factors over time and distinguish between reason and consequence. Another limitation is that we do not have the information on how long hypertension and low HDL-C statuses last. The older subjects are likely to have longer history of risk factors, which may influence the association of HDL-C with kidney function. In addition, the information on some chronic diseases such as recent infection and chronic inflammatory diseases was not inquired and recorded in current study. Recent infection and chronic inflammatory diseases as confounding factors may influence HDL-C level and renal function. Those chronic disease states should be excluded in the future further study. Finally, our study used eGFR rather than directly measured GFR. But direct measurement of GFR is rarely used in clinical practice. Given those limitations, further longitudinal cohort studies are needed to observe and analyze the causative relationship of HDL-C and renal function in the hypertensive elderly.

In summary, our results support the possibility that low HDL-C level is associated with renal function decline in elderly hypertension. Sex may be a pivotal factor for the association of HDL-C level with GFR value. Glomerular hyperfiltration (GFR_{MDRD} >140 mL/min/1.73m^2 or $GFR_{CKD-EPI}$ >120 mL/min/1.73m^2) may also affect serum HDL-C level. There is an inverse ''V'' shape between GFR and HDL-C based on GFR stratification in elderly hypertension.

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