Apo A1 / Apo B Ratio and Acute Coronary Syndrome Among Peritoneal Dialysis Patients

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Research

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Abstract

Background: Acute coronary syndrome (ACS) is prevalent in continuous ambulatory peritoneal dialysis (CAPD) patients. But the association between apoprotein profile and ACS is not well known. Therefore, we aimed to investigate the relationship between apoproteins and ACS in CAPD patients.

Methods: Eighty-one CAPD patients were included in this retrospective study. The primary endpoint was ACS. Predictors were baseline apoprotein levels, particularly the ratio of apoprotein A1 (Apo A1) / apoprotein B (Apo B). Binary logistics regression was used to determine the relationship between Apo A1 / Apo B and ACS.

Results: During follow-up, 34 (41.98%) CAPD patients experienced an ACS. ACS patients had higher levels of total cholesterol ($p = 0.03$), LDL-C ($p = 0.04$), CRP ($p = 0.01$), and Apo B ($p < 0.01$). However, hemoglobin ($p = 0.01$) and the Apo A1 / Apo B ($p < 0.01$) were lower in the ACS group than the non-ACS group. Patients with Apo A1 / Apo B ≥ 1.105 experienced fewer ACS compared with those with Apo A1 / Apo B < 1.105 (33.33% vs. 75.56%, $p = 0.03$). In binary logistics regression, Apo A1 / Apo B (OR, 0.01; 95% CI, 0.00-0.77; $p = 0.04$) was independently associated with ACS.

Conclusions: Apo A1 / Apo B were strongly associated with ACS, and may be considered as a predictor of future ACS in CAPD patients.

Introduction

More than 10% of people worldwide have chronic kidney disease (CKD)[1]. As renal function declines, the incidence of cardiovascular disease (CVD) in patients increases significantly. A reduction in the estimated glomerular filtration rate is a major independent predictor of cardiovascular morbidity and mortality and all-cause mortality[2]. Many risk factors increase the CVD burden in CKD patients, including oxidative stress[3], chronic inflammation[4], endothelial dysfunction[5], renal anemia[6], lipid metabolism disorders[7], secondary hyperparathyroidism, and mineral metabolism disorders[8]. Dyslipidemia may directly affect the kidney by causing deleterious renal lipid derangement[9].

Hyperlipidemia is a recognized risk factor for CVD in the general population[10]. Dyslipidemia is the most important risk factor for coronary atherosclerosis, which in turn underlies acute coronary syndrome (ACS) lesions. However, in CKD patients, the relationship becomes more complex and may even be contradictory. CKD seems to weaken the classical relationship between abnormal lipid metabolism and CVD[11]. At this time, the apoprotein A1 (Apo A1) / apoprotein B (Apo B) ratio provides a better summary of the burden of dyslipidemia than conventional lipids and lipoproteins. Previous studies[19] have confirmed that apo A1 / apo B is closely related to CVD risk in maintenance hemodialysis patients. However, the relationship between apolipoprotein profile and ACS in continuous ambulatory peritoneal dialysis (CAPD) patients is poorly studied. Therefore, this study aimed to investigate the relationship between apo A1 / apo B and ACS in CAPD patients.

Patients And Methods

Study subjects

We finally enrolled 81 regular CAPD patients who were hospitalized in the Nephrology Department of our hospital from February 2014 to December 2017. Inclusion criteria included a diagnosis of uremia, age greater than 18 years, and regular peritoneal dialysis greater than or equal to 3 months. At the same time, patients who could not cooperate to complete the relevant index examination, missing data, had peritoneal dialysis failure during follow-up, and lost to follow-up were excluded. The study was carried out following the Declaration of Helsinki and approved by the Medical Ethics Committee of the Third Affiliated Hospital of Soochow University.

Data collection

Data on age, gender, body mass index (BMI), smoking, hypertension, diabetes, history of CVD, primary disease of CKD, use of statins, residual GRF, creatinine, urea nitrogen, lipid profile, albumin, and C-reactive protein (CRP) were collected from case records. The above laboratory parameters were measured by the central laboratory in an automatic system and a standardized method. The Apo A1 / Apo B ratio was obtained by dividing the absolute value of Apo A1 by the absolute value of Apo B.

Follow-up of CAPD patients

The enrolled CAPD patients were followed up by outpatient, inpatient, telephone, or home visited. The primary endpoint of this study was the occurrence of ACS during follow-up. ACS includes acute ST-segment elevation myocardial infarction, acute non-ST-segment elevation myocardial infarction and unstable angina pectoris, which were diagnosed by clinical symptoms, dynamic electrocardiogram changes and serum myocardial injury markers.

Statistical analysis

Statistical analysis was performed using SPSS software (v. 19.0, IBM Corp., Armonk, NY). Continuous variables were expressed as mean $\pm$ standard deviation, and categorical variables were presented as frequency and percentage. The cutoff values of Apo A1 / Apo B were analyzed using ROC curves. Survival curves according to Apo A1 / Apo B were determined by K-M survival analysis. Binary logistics regression analysis was performed to evaluate the association between Apo A1 / Apo B and ACS. A 2-tailed $p < 0.05$ was considered statistically significant.

Results

Comparison of demographic and clinical characteristics between ACS and non-ACS groups

During follow-up, a total of 34 (41.98%) patients experienced ACS. Patients were divided into two groups according to the presence or absence of ACS. No statistical differences were found in age ($p = 0.76$), sex ($p = 0.50$), BMI ($p = 0.86$), smoking ($p = 0.38$), hypertension ($p = 0.81$), diabetes ($p = 0.79$), history of CVD ($p = 0.51$), etiology of CKD ($p < 0.05$), use of statins ($p = 0.44$), total k_t/v_{urea} ($p = 0.07$), residual glomerular filtration rate (GFR) ($p = 0.55$), urea nitrogen ($p = 0.17$), creatinine ($p = 0.43$), triglycerides ($p = 0.11$), high-density lipoprotein-cholesterol (HDL-C) ($p = 0.22$), albumin ($p = 0.65$), and Apo A1 ($p = 0.09$) between the CVD and non-CVD groups. Moreover, as showed in Table 1, patients in the ACS group had higher levels of total cholesterol ($p = 0.03$), low-density lipoprotein-cholesterol (LDL-C) ($p = 0.04$), CRP ($p = 0.01$), and Apo B ($p < 0.01$). However, hemoglobin ($p = 0.01$) and the Apo A1 / Apo B ($p < 0.01$) were significantly lower in the ACS group than in the non-ACS group.

Table 1
Clinical data of 81 peritoneal dialysis patients.

Variables	Non-ACS (n = 47)	ACS (n = 34)	p value
Age	50.47 ± 12.54	49.74 ± 8.90	0.76
Female	18	16	0.50
BMI, kg/m ²	21.60 ± 2.42	21.48 ± 3.12	0.86
Smoking	10	4	0.38
Hypertension	28	22	0.81
Diabetes	12	7	0.79
History of CVD	5	6	0.51
CKD etiology			
Chronic glomerulonephritis	33	23	0.81
Diabetic nephropathy	9	8	0.78
Hypertensive nephropathy	1	3	0.30
Other	4	0	0.14
Use of Statins	33	27	0.44
Total k_t/v_{urea}	1.81 ± 0.53	2.05 ± 0.54	0.07
Residual GFR, ml/min/1.73 m ²	2.44 ± 1.95	2.75 ± 2.49	0.55
Urea nitrogen, mmol/L	17.86 ± 5.01	19.51 ± 5.66	0.17
Creatinine, umol/L	810.89 ± 195.76	773.62 ± 226.48	0.43
Triacylglycerol, mmol/L	2.62 ± 1.50	3.21 ± 1.84	0.11
Total cholesterol, mmol/L	3.98 ± 1.00	4.52 ± 1.09	0.03
LDL-C, mmol/L	2.16 ± 0.68	2.50 ± 0.76	0.04
HDL-C, mmol/L	0.96 ± 0.28	0.90 ± 0.18	0.22
Albumin, g/L	30.41 ± 4.78	29.90 ± 5.36	0.65
Hemoglobin, g/L	100.93 ± 13.70	92.82 ± 13.25	0.01
C-reactive protein, mg/L	6.37 ± 1.98	7.94 ± 3.05	0.01

ACS, acute coronary syndrome; BMI, body mass index; CVD, cardiovascular diseases; CKD, chronic kidney disease; GFR, residual glomerular filtration rate; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; Apo A1, apolipoprotein A1; Apo B, apolipoprotein B.

Variables	Non-ACS (n = 47)	ACS (n = 34)	<i>p</i> value
Apo A1, mg/dL	105.28 ± 14.17	100.03 ± 12.40	0.09
Apo B, mg/dL	86.11 ± 16.78	99.32 ± 14.63	< 0.01
Apo A1 / Apo B	1.26 ± 0.28	1.02 ± 0.16	< 0.01
ACS, acute coronary syndrome; BMI, body mass index; CVD, cardiovascular diseases; CKD, chronic kidney disease; GFR, residual glomerular filtration rate; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; Apo A1, apolipoprotein A1; Apo B, apolipoprotein B.			

Apo A1 / Apo B and ACS

ROC curve analysis was used to calculate the optimal cutoff value for Apo A1 / Apo B. As shown in Fig. 2, the optimal cutoff for Apo A1 / Apo B was 1.105. Patients with Apo A1 / Apo B $\geq$ 1.105 experienced fewer ACS during follow-up compared with those with Apo A1 / Apo B < 1.105 (Fig. 1; 33.33% vs. 75.56%, $p = 0.03$).

ACS, acute coronary syndrome; CVD, cardiovascular diseases; Apo A1, apolipoprotein A1; Apo B, apolipoprotein B.

Apo A1 / Apo B was associated with ACS

According to Fig. 2, the area under the ROC curve for Apo A1 / Apo B was 0.79 (95% CI: 0.69–0.88, $p < 0.01$). In binary logistics regression (Table 2), Apo A1 / Apo B (OR, 0.01; 95% CI: 0.00-0.77; $p = 0.04$) was independently associated with ACS in CAPD patients, Even after adjustment for age, smoking, history of CVD, triglycerides, LDL-C, HDL-C, total cholesterol, hemoglobin, and Apo B.

Bivariate correlation analysis was also used to evaluate the association between apoproteins and CRP. As a result, no correlation was found between CRP and Apo A1 ($r = -0.07$, $p = 0.53$), Apo B ($r = 0.21$, $p = 0.08$), and Apo A1 / Apo B ($r = -0.21$, $p = 0.07$).

Apo A1, apolipoprotein A1; Apo B, apolipoprotein B.

Table 2
Binary logistic regression analysis of ACS in peritoneal dialysis patients.

	OR	95% CI	p value
age	1.02	0.96–1.08	0.57
History of CVD	0.80	0.13-5.00	0.81
Smoking	1.48	0.26–8.43	0.66
Triacylglycerol, mmol/L	1.06	0.71–1.60	0.77
Total cholesterol, mmol/L	2.41	0.37–15.83	0.36
LDL-C, mmol/L	0.40	0.32–5.05	0.48
HDL-C, mmol/L	0.09	0.00-2.29	0.14
Hemoglobin, g/L	0.97	0.97 – 0.93	0.28
Apo B, mg/dL	1.01	0.96–1.07	0.70
Apo A1 / Apo B	0.01	0.00-0.77	0.04
ACS, acute coronary syndrome; CVD, cardiovascular diseases; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; Apo B, apolipoprotein B; Apo A1, apolipoprotein A1; OR, odds ratio.			

Discussion

Our study was the first time to demonstrate the relationship between the Apo A1 / Apo B ratio and ACS in CAPD patients. The association remained significant even after adjustment for traditional CVD risk factors such as age, prior CVD history, smoking, triglycerides, total cholesterol, HDL-C, LDL-C, hemoglobin, and Apo B. Moreover, Apo A1 / Apo B may be used as a predictor of the occurrence of future ACS.

Hyperlipidemia is a known risk factor for CVD in CKD patients. CKD appears to weaken the classical relationship between the lipid and CVD. Elevated very-low-density lipoprotein and low HDL-C have been shown to increase coronary heart disease risk in CKD patients [12, 13]. However, no significant association was found between LDL-C and cardiovascular outcomes. Moreover, some earlier studies [14–16] have failed to confirm an association between HDL-C, LDL-C, or triglyceride levels and CVD mortality. Similarly, our study indicated that total cholesterol and LDL-C were significantly higher in the ACS group than in the non-ACS group, but these two lipid parameters were not correlated with ACS. The study by *Chang et al* [17] even came to the opposite conclusion that an increased triglyceride / HDL-C ratio was associated with reduced CVD mortality in hemodialysis patients. Therefore, the association between dyslipidemia and CVD in the CKD population is very complicated.

Apo A1 is the main component of HDL and is closely related to CVD. A study [18] of 299 patients with ST-segment elevation myocardial infarction (STEMI) found that high baseline apoA1 levels were associated

with reduced risk of STEMI. Apo B is present on the surface of LDL, and cellular recognition and uptake of LDL are mainly achieved by recognition of Apo B. Higher level of Apo B can increase the incidence of coronary heart disease, even if LDL levels are normal. Moreover, Apo B was significantly associated with CVD-related mortality[19]. Our study suggested that Apo A1 levels were higher in the non-ACS group than in the ACS group, while Apo B showed the opposite. Unfortunately, we did not conclude that Apo A1 or Apo B was associated with ACS.

The Apo A1 / Apo B ratio provides a better summary of the burden of dyslipidemia than conventional lipids and lipoproteins. Some studies have confirmed that the Apo B / Apo A1 ratio was superior to LDL and HDL cholesterol in predicting cardiovascular events. *Bodde MC et al*[18] found that elevated Apo B / Apo A1 ratio was associated with an increased risk of STEMI, but not LDL-C, after adjustment for age, sex, and statin therapy. In maintenance hemodialysis patients, each SD increase in the Apo B / Apo A1 ratio increased all-cause mortality or CVD-related mortality by 16%[19]. In our study, similar results were found, adjusted for traditional CVD influencing factors, Apo A1 / Apo B and ACS were independently associated. Furthermore, the area under the ROC curve for Apo A1 / Apo B was 0.79 (95% CI: 0.69–0.88, $p < 0.01$). This suggests that Apo A1 / Apo B may be well used as a predictor for the future occurrence of ACS in CAPD patients.

Inflammation may affect Apo A1 metabolism to some extent in patients with renal failure, and CRP was also found to be significantly higher in the CVD group than in the non-CVD group[20]. However, no correlation was found between CRP and Apo A1, Apo B, and Apo A1 / Apo B in the binary correlation analysis. Therefore, apolipoproteins do not simply mediate the occurrence of ACS through an inflammatory state, and the specific mechanism requires further investigation.

Our study has some limitations. This study was a retrospective small sample study, and the conclusion needs to be confirmed by prospective large sample studies in the future. Secondly, due to the voluntary principle, the enrolled patients pay more attention to their physical health than the non-enrolled patients, so the research population may have a certain degree of selection bias, which cannot well represent the general CAPD patients. Finally, it was unclear how dyslipidemia affected the development of ACS.

Conclusion

In conclusion, we found that the Apo A1 / Apo B ratio was independently associated with ACS in CAPD patients. Our study suggested that the ratio of Apo A1 / Apo B may be considered as a predictor of future ACS risk compared with traditional lipid measures. The role of apolipoproteins in predicting ACS in CKD patients and their specific mechanisms require further investigation.

Abbreviations

ACS, acute coronary syndrome; CAPD, continuous ambulatory peritoneal dialysis; BMI, body mass index; CVD, cardiovascular diseases; CKD, chronic kidney disease; GFR, residual glomerular filtration rate; LDL-C,

low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; Apo A1, apolipoprotein A1; Apo B, apolipoprotein B. CRP, C-reactive protein; OR, odds ratio; STEMI, ST-segment elevation myocardial infarction

Declarations

Acknowledgments

None.

Author contributions

Tianlei Chen proposed the design of the study, completed the collection, management, and analysis of data, contributed to the conceptualization of the manuscript, and wrote the first draft of the manuscript. Min Yang was mainly responsible for supervision, review, and editing of the first draft, and did part of the work on the writing of the discussion section. All authors reviewed and approved the manuscript.

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Availability of data and materials

The original data used to support the results of this study are available from the corresponding author upon request.

Ethics approval and consent to participate

The study was carried out following the Declaration of Helsinki and approved by the Medical Ethics Committee of the Third Affiliated Hospital of Soochow University.

Consent for publication

Written informed consent was obtained from all participants.

Competing interest

The authors declare that they have no competing interests.

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Figures

Kaplan-Meier survival curve according to Apo A1 / Apo B

Figure 1

ACS free survival curves according to Apo A1 / Apo B.

Figure 2

ROC curves analysis for Apo A1 / Apo B.