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Research Article

Apolipoprotein B as a Risk Factor of DKD Progression to Renal Replacement Therapy

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Abstract

Objective: To Analyze the Value of Apolipoprotein B (ApoB) in the risk of progression to Renal Replacement Therapy (RRT) in patients with CKD 3-5 stage Diabetic Kidney Disease (DKD).

Method: 149 cases of DKD patients were followed-up for 2 years; they were divided into non-RRT group (95 cases) and RRT group (54 cases) on the basis of entering into the renal replacement therapy, logistic regression analyzed risk factors of DKD progression into RRT.

Result: The between-group variances of HGB, HCT, MCV, TC, TG, HDL, ApoA, ApoB, ALB, SCr, urea nitrogen, serum cystatin, serum calcium had statistical significance($P<0.05$). The increase of ApoB and serum creatinine in the multi-factors logistic regression analysis were the independent risk factors for DKD patients evolved into RRT in the two-year follow-up.

Conclusion: ApoB is the risk predictive factor of RRT progression in DKD patients of CKD 3-5 stages. For every 1-unit increase of ApoB mean the risk of progression to RRT increasing by 2.745 times.

Keywords: Apolipoprotein B; Diabetic kidney disease; Renal replacement therapy; Risk factor

Background

Dyslipidemia is common problem among patients with CKD [1]. Dyslipidemia may affect the kidney directly by causing deleterious renal lipid disturbances, as well as indirectly through systemic inflammation and oxidative stress, vascular injury, and other signaling molecules with renal action [2,3]. Decreased renal function is associated with many disruptions in lipoprotein metabolism, leading to dyslipidemia and accumulation of atherogenic particles [4,5] and progress to Renal Replacement Therapy (RRT). Several studies [6,7] show that LDL-C and ApoB were not independently associated with the progression of Chronic Kidney Disease (CKD). The CRIC study prompted that the blood lipid had no independent association with the CKD progression, ApoB/A1 was associated with CKD progression, ApoB had no association with CKD progression, while there are few studies on the association between ApoB and kidney disease among DKD patients. The increase of ApoB in patients with diabetes, the lipid-lowering therapy can postpone the decrease of eGFR in patients with diabetes complicated with proteinuria [8].

Therefore, the function of ApoB in the progression of renal functions in DKD patients was studied in this research, the ApoB as a risk factor of DKD progressing into RRT was analyzed by logistic regression model.

Subjects and Methods

Study Design

149 cases of DKD patients had hospitalized in the Nephrology Department of the Third Affiliated Hospital of Sun

Yat-Sen University, Yuedong Hospital, clinical data were collected, there were 90 male cases and 59 female cases, with ages from 27 to 88 years (65.58±11.47). On the basis of progressing into RRT, they were divided into non-RRT group (95 cases) and RRT group (54 cases). eGFR was calculated by CKD-EPI formula (Table 1).

Variable		Non-RRT group	RRT group	P-Value
		N=95 (constituent ratio)	N=54(constituent ratio)	
sex	male	52(54.7%)	38(70.4%)	0.081
	female	43(45.3%)	16(29.6%)	
Age (years)		64.59±11.76	67.31±10.84	0.164
Smoking history		30(31.6%)	14(25.9%)	0.576
Drinking history		12(12.6%)	8(14.8%)	0.804
BMI(kg/m^2)		25.36±3.19	24.78±3.67	0.314
Hypertension		81(85.3%)	49(90.7%)	0.446
Coronary artery disease		20(21.1%)	15(27.8%)	0.422
Congestive heart failure		1(1.1%)	0(0%)	1.000
Diabetic retinopathy		23(24.2%)	8(14.8%)	0.211
SBP(mmHg)		140.44±23.67	144.22±22.32	0.340
CBP(mmHg)		76.58±13.46	74.20±11.42	0.277
HbA1C(%)		7.91±1.97	7.27±1.48	0.041
HGB(g/L)		117.97±23.13	105.59±20.01	0.001
HCT(mmol/L)		0.35±0.06	0.31±0.06	0.003
MCV(mmol/L)		87.66±5.94	84.69±9.18	0.018
MCHC(mmol/L)		340.40±14.56	336.41±15.99	0.123
TC(mmol/L)		4.31±1.10	5.23±1.16	0.000
TG(mmol/L)		1.57±1.00	2.92±1.98	0.000
LDL-C(mmol/L)		2.50±0.83	3.01±1.18	0.006
HDL-C(mmol/L)		1.16±0.67	1.17±0.67	0.955
ApoA(mmol/L)		1.30±0.27	1.21±0.29	0.048
ApoB(mmol/L)		0.93±0.0.21	1.28±0.37	0.000
LPa(g/L)		271.31±288.91	253.01±231.51	0.691
Prealbumin (mg/L)		256.76±75.56	243.09±60.66	0.257
Albumin (g/L)		38.49±4.50	36.68±4.97	0.024
K(mmol/L)		4.21±0.53	4.33±0.56	0.215
Na(mmol/L)		140.47±3.58	139.98±3.29	0.403
Cl(mmol/L)		105.58±4.47	105.26±4.61	0.677

Ca(mmol/L)	2.32±0.17	2.26±0.18	0.048
P(mmol/L)	1.22±0.25	1.27±0.23	0.263
CO_2(mmol/L)	22.20±3.57	21.98±3.57	0.710
Fasting blood glucose (mmol/L)	6.92±3.45	6.80±3.91	0.830
Uric acid(μmol/L)	480.42±146.83	480.59±122.07	0.994
Creatinine(μmol/L)	190.29±126.69	250.81±181.31	0.022
BUN(mg/L)	10.44±5.15	13.57±6.53	0.002
CysC(mg/L)	2.08±0.85	2.54±1.23	0.008
CCB	57(60.0%)	37(68.5%)	0.378
ACEI	7(7.4%)	7(13.0%)	0.381
ARB	61(64.2%)	28(51.9%)	0.166
Diuretic	13(13.7%)	17(31.5%)	0.011
Alpha blocker	7(7.4%)	12(22.2%)	0.019
Beta blocker	29(30.5%)	19(35.2%)	0.588
Erythropoiesis stimulating agents	5(5.3%)	5(9.3%)	0.497
Iron preparations	11(11.6%)	8(17.20%)	0.325
Active vitamin D	8(8.4%)	4(7.4%)	1.000
Radionuclide renal dynamic imaging (mL/(min·1.73m^2))	42.22±17.18	35.67±14.98	0.078
eGFR(mL/(min·1.73m^2))	40.96±14.14	36.18±16.84	0.067

Values are expressed as mean ± SD or number (percentage). eGFR: Estimated Glomerular Filtration Rate; BMI: Body Mass Index; ACE inhibitor: Angiotensin-Converting Enzyme Inhibitor; ARB: Angiotensin II Receptor Blocker; CCB: Calcium Channel Blocker. Scr: Serum Creatinine; BUN: Blood Urea Nitrogen; UA: Uric Acid; Cys C: Cystatin C; TC: Total Cholesterol; TG: Triglyceride; HDL: High-Density Lipoprotein; LDL: Low Density Lipoprotein; ApoA: Apolipoprotein A; ApoB: Apolipoprotein B; Lpa: Lipoprotein a; HGB: Hemoglobin; HCT: Hematocrit; MCV: Mean Red Cell Volume; MCHC: Mean Hemoglobin Concentration; ALB: Serum Albumin; HbA1c: Glycosylated Hemoglobin; FPG: Fasting Plasma Glucose; ECT: Emission Computed Tomography.

Table 1: Baseline Characteristics of Study Population.

Diagnosis and Inclusion Standard: diagnosed by WHO1999 Diabetes Criteria [9], The DKD diagnosis was based on the eGFR and urinary microalbumin quantification as proposed in 'NKF-KDOQI Guidelines' [10]. Exclusion Standard: 1 Type diabetes; acute diabetic complications: diabetic ketosis, hyperosmolar coma etc. patients with possibility of primary or secondary kidney disease; common complications that might affect the urinalysis or renal function, such as urinary calculi infection, fever, heart failure, infection, secondary hypertension etc.; severe hypohepatia.

Data Collection

Data were exported from clinical charts and electronic medical records. Variables collected include demographics (age, sex, and race), longitudinal measures of laboratory measures (hemoglobin, phosphate, potassium, bicarbonate, eGFR, and albumin, et al.), Physiological Parameters (PP)**,** complications and concurrent Disease (Diabetic Retinopathy (DR), Hypertension History, Coronary Heart Disease and Coronary Stenosis (diagnosed by coronary angiogram), history of heart failure.)

Methods

The general clinical data, complications and concurrent diseases, laboratory indexes of the patients that accorded with the inclusion standard were collected, and the data were input, eGFR were calculated by CKD-EPI formula etc., they were divided into RRT group and Non-RRT group on the basis of the entry of RRT, logistic regression model was established, relevant risk factors of entry into RRT were analyzed.

Statistical Analysis

All of the data were treated by SPSS 20.0 software. The measurement data were represented by x±s; enumeration data were represented by percentage; data statistical analysis was done by multi-factor logistic regression. The differences were statistically significant when P<0.05.

Results

There were altogether 149 follow-up cases in this study and were divided into two groups: The Non-RRT group had 95 cases and the RRT group had 54 cases. The baseline information of each observation indexes were seen in Table 1; the differences of gender, family history, smoking history and drinking history of two groups had no statistical significance (P>0.05); the between-group variances of HGB, HCT, MCV, TC, TG, HDL, ApoA, ApoB, ALB, SCr, urea nitrogen, serum cystatin, serum calcium was statistically significant (P<0.05) (Table 1). Logistic regression analysis was conducted to establish the risk analysis model for risk factors of DKD progressing to RRT. As shown in the multi-factors logistic regression analysis, serum creatinine and ApoB (OR=2.745 , P<0.05) were the predictive factors of progressing into RRT in DKD patients in the two-year follow-up. DKD patients of CKD 3-5 stage with increased ApoB had higher risks of progressing into RRT. Every increase 1 of ApoB, the risk of DKD progressing into RRT would increase 2 (Table 2).

		B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
								Lower	Upper
	ApoB	1.010	0.318	10.117	1	0.001	2.745	1.473	5.115
	Cr	0.002	0.001	7.614	1	0.006	1.002	1.001	1.004
	Constant	-2.248	0.438	26.337	1	0.000	0.106		

Table 2: Logstic Regression Analysis Risk Factor of Progressing into RRT of the DKD Patients for Following Up Two Years.

Discussion

Diabetic kidney disease is the chronic microangiopathy of diabetes, the main cause is the renal arteriosclerosis, glomerular sclerosis caused by ANS arteriolonephrosclerosis and renal microvascular lesion. It is reported that the impairment of renal function caused by dyslipidemia associated with the effect of lipid on vascular mesangial cells and renal tubular cells [11]. ApoB is composed by ApoB 100 and ApoB 48 sub-units, ApoB can directly involve into the transport metabolism and transformation of plasma lipids, ApoB is correlated with T2DM kidney disease, ApoB can preferably predict the occurrence of T2DM kidney disease than LDL-C. Tabas, et al. [12] study that a long-term disturbance of carbohydrate metabolism produces the increased blood lipid, redundant ApoB retains and sedimentates in the sub-endothelial arteries, this kind of sedimentation process is an unceasing progression; necrosis will occur to the sedimentary location when it reaches to a certain level, the necrosis shall activate the cytokines such as interleukin, PDGF, IFG-1 etc. The ApoB increases in patients with chronic kidney disease [13]. The lipid-lowering therapy can postpone the progression of kidney disease and retard the descent velocity of renal function in DN patients. Colhoun et al study results prompted that, the lipid-lowering therapy with statins had remarkably protected the renal function of patients with diabetes and proteinuria, and retarded the descending level of eGFR [14].

This study had conducted multi-factors logistic regression analysis, it was concluded that ApoB was a risk factor of DKD progression, the increase of serum creatinine and ApoB, were the independently risk factors of progressing into renal replacement therapy in DKD patients within 2 years following up(P<0.05). So we prompt that the increase of ApoB may be considered as the predictive factor of progressing into RRT.

In conclusion, multiple previous researches indicated that the increase of ApoB had no direct correlation with CKD progression. However, our study found that ApoB was an independent risk factor of progressing into RRT for DKD patients of the CKD 3-5 stage; the increase of ApoB prompts unfavorable prognosis, lipid-lowering therapy may postpone the decrease of eGFR in diabetic patients complicated with proteinuria; However, this study had fewer patients included, large-scale clinical verifications were still in need.

References

1. Kaysen GA (2011) New insights into lipidmetabolism in chronic kidney disease. J Ren Nutr 21: 120-123.
2. Bobulescu IA (2010) Renal lipid metabolism and lipotoxicity, Curr. Opin. Nephrol Hypertens 19: 393e402.
3. Ruan XZ, Varghese Z, Moorhead JF (2009) An update on the lipid nephrotoxicity hypothesis. Nat Rev Nephrol 5: 713e721.

4. Vaziri ND (2014) Role of dyslipidemia in impairment of energy metabolism, oxidative stress, inflammation and cardiovascular disease in chronic kidney disease. Clin Exp Nephrol 18: 265-268.

5. Florens N, Calzada C, Lyasko E, Juillard L, Soulage CO (2016) Modified Lipids and Lipoproteins in Chronic Kidney Disease: A New Class of Uremic Toxins. Toxins (Basel) 8.

6. Samuelsson O, Mulec H, Knight-Gibson C, Attman PO, Kron B, et al. (1997) Lipoprotein abnor-malities are associated with increased rate of progression of hu-man chronic renal insufficiency. Nephrol Dial Transplant 12: 1908-1915.

7. Schaeffner ES, Kurth T, Curhan GC, Glynn RJ, Rexrode KM, et al. (2003) Cholesterol and the risk ofrenal dysfunction in apparently healthy men. J Am Soc Nephrol 14: 2084-2091.

8. Dalrymple LS, Kaysen GA (2008) The effect of lipoproteins on the development and progression of renal disease. Am J Nephrol 28: 723-731.

9. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (2003) Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1: S5-20.

10. KDOQI (2007) KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. Am J Kidney Dis 49: S12-154.

11. Athyms VG, Papageorgiou AA, Elisaf M, Mikhailidis DP; GREACE Study Collaborative Group (2003) Statins and renal function in patients with diabetes mellitus. Curt Med Res 19: 615-617.

12. Tabas I, Williams KJ, Borén J (2007) Subendothelial lipoprotein re-tention as the initiating process in atherosclerosis:update and therapeutic implications. Circulation 116: 1832-1844

13. Yamamoto T, Hirano T, Mori Y, Tokuno A, Nagashima M, et al. (2008) Significant increase of apolipoprotein B48 levels by a standard test meal in type 2 diabetic patients with nephropathy. J Atheroscler Thromb 15: 199-205.

14. Colhounhm, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, et al. (2009) Effects of atorvastatin on kidney out-comes and cardiovascular disease in patients with diabetes: an analysis from the Collaborative Atorvastatin Diabetes Study(CARDS). Am J Kidney Dis 54: 810-819.