



Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care

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Associations of Apolipoprotein ApoA and the ApoB/ApoA Ratio with the Risk of Chronic Kidney Disease

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Objectives : Apolipoprotein A (ApoA) and apolipoprotein B (ApoB) are well-established markers in cardiovascular disease, but their roles in chronic kidney disease (CKD) are not well known. Given their opposing functions in lipid metabolism, this study investigated the associations of ApoA, ApoB, and the ApoB/ApoA ratio with incident CKD to assess their clinical relevance.

Methods : This study included 373,043 UK Biobank participants without baseline CKD (median age, 58 years; 47% women). ApoA, ApoB, and the ApoB/ApoA ratio were categorized into quartiles. The primary outcome was incident CKD diagnosed with ICD-10 and OPCS-4 codes. Incident CKD, defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m², was also assessed in a sub-cohort with creatinine follow-up data.

Results : During a median follow-up of 13.7 years, 14,329 (3.84%) participants developed incident CKD. In multivariable-adjusted Cox proportional hazards models, higher quartiles of ApoA were significantly associated with a lower risk of incident CKD relative to Q1 (adjusted HR [95% CI]: Q2, 0.92 [0.86–0.99]; Q3, 0.85 [0.79–0.91]; Q4, 0.79 [0.74–0.86]; P-for-trend <0.001). In contrast, higher quartiles of the ApoB/ApoA ratios were significantly associated with an increased risk of incident CKD compared with Q1 (adjusted HR [95% CI]: Q2, 1.07 [1.00–1.14]; Q3, 1.12 [1.05–1.21]; Q4, 1.31 [1.22–1.41]; P-for-trend <0.001). Similar results were observed with the eGFR-defined CKD outcome. Mediation analysis revealed that the associations of ApoA and the ApoB/A ratio with incident CKD were mediated by HDL cholesterol and VLDL cholesterol lipid components.

Conclusions : Higher ApoA levels were associated with a decreased risk of CKD. In contrast, higher ApoB/ApoA ratios were associated with an increased risk, suggesting that apolipoprotein imbalance may serve as a clinically relevant marker for CKD risk stratification, partly through HDL- and VLDL-related lipid pathways.

table1.png



Table 1. Baseline characteristics according to apolipoprotein A quartiles

Variables	Total (N=373,043)	Q1 (N=93,159)	Q2 (N=93,035)	Q3 (N=93,461)	Q4 (N=93,388)	P-trend
Demographic data						
Age	58.0 (50.0-63.0)	56.0 (48.0-62.0)	57.0 (49.0-63.0)	58.0 (50.0-63.0)	59.0 (52.0-63.0)	<0.001
Female	176,960 (47.4%)	67,861 (72.8%)	51,730 (55.6%)	36,301 (38.8%)	21,068 (22.6%)	<0.001
Ethnicity						
White	353,015 (94.6%)	86,185 (92.5%)	87,879 (94.5%)	89,180 (95.4%)	89,771 (96.1%)	<0.001
Black	5,611 (1.5%)	1,628 (1.7%)	1,524 (1.6%)	1,338 (1.4%)	1,121 (1.2%)	
Asian/Other	14,417 (3.9%)	5,346 (5.7%)	3,632 (3.9%)	2,943 (3.1%)	2,496 (2.7%)	
Town dep index	-2.2 (-3.7-0.4)	-2.0 (-3.5-1.0)	-2.2 (-3.7-0.4)	-2.3 (-3.7-0.2)	-2.3 (-3.8-0.1)	<0.001
Alcohol drinker status						
Never	15,636 (4.2%)	5,189 (5.6%)	4,090 (4.4%)	3,711 (4.0%)	2,646 (2.8%)	<0.001
Previous	12,730 (3.4%)	5,051 (5.4%)	3,300 (3.6%)	2,647 (2.8%)	1,732 (1.9%)	
Current	344,195 (92.4%)	82,736 (89.0%)	85,536 (92.0%)	87,015 (93.2%)	88,908 (95.3%)	
Smoking status						
Never	204,400 (55.0%)	48,542 (52.3%)	51,208 (55.2%)	52,703 (56.6%)	51,947 (55.8%)	<0.001
Previous	128,516 (34.6%)	31,183 (33.6%)	31,739 (34.2%)	31,940 (34.3%)	33,654 (36.2%)	
Current	38,704 (10.4%)	13,023 (14.0%)	9,743 (10.5%)	8,470 (9.1%)	7,468 (8.0%)	
BMI	26.8 (24.2-29.8)	28.3 (25.8-31.4)	27.3 (24.8-30.3)	26.3 (23.9-29.3)	25.1 (22.9-27.9)	<0.001
Underweight	1,617 (0.4%)	166 (0.2%)	225 (0.2%)	408 (0.4%)	818 (0.9%)	<0.001
Normal	119,948 (32.2%)	17,262 (18.5%)	24,749 (26.6%)	33,254 (35.6%)	44,683 (47.8%)	
Overweight	161,693 (43.3%)	43,384 (46.6%)	42,923 (46.1%)	40,349 (43.2%)	35,037 (37.5%)	
Obesity	89,785 (24.1%)	32,347 (34.7%)	25,138 (27.0%)	19,450 (20.8%)	12,850 (13.8%)	
SBP, mmHg	136.0 (124.5-148.5)	135.5 (125.0-147.5)	136.0 (124.5-148.5)	136.0 (124.0-149.0)	136.5 (124.0-150.0)	<0.001
DBP, mmHg	82.0 (75.0-88.5)	82.5 (76.0-89.0)	82.0 (75.5-89.0)	81.5 (75.0-88.5)	81.0 (74.5-88.0)	<0.001
Comorbidities						
Hypertension	113,032 (30.3%)	33,391 (35.8%)	29,209 (31.4%)	26,548 (28.4%)	23,884 (25.6%)	<0.001
Diabetes	17,563 (4.7%)	7,878 (8.5%)	4,490 (4.8%)	3,167 (3.4%)	2,028 (2.2%)	<0.001
CVD	20,964 (5.6%)	8,476 (9.1%)	5,440 (5.8%)	4,083 (4.4%)	2,965 (3.2%)	<0.001
COPD	13,273 (3.6%)	3,590 (3.9%)	3,224 (3.5%)	3,248 (3.5%)	3,211 (3.4%)	<0.001
Asthma	46,662 (12.5%)	11,336 (12.2%)	11,505 (12.4%)	11,930 (12.8%)	11,891 (12.7%)	<0.001
Depression	25,872 (6.9%)	6,997 (7.5%)	6,359 (6.8%)	6,261 (6.7%)	6,255 (6.7%)	<0.001
Peptic ulcer disease	23,293 (6.2%)	6,885 (7.4%)	5,863 (6.3%)	5,515 (5.9%)	5,030 (5.4%)	<0.001
Laboratory data						
eGFR, ml/min per 1.73m ²	97.3 (87.7-103.7)	97.5 (87.7-104.7)	97.3 (87.6-104.0)	97.3 (87.7-103.5)	97.2 (87.7-103.0)	<0.001
uACR, mg/g	9.04 (5.87-14.38)	7.56 (5.10-12.02)	8.49 (5.61-13.48)	9.51 (6.19-14.93)	10.92 (7.04-16.69)	<0.001
Total cholesterol, mg/dl	218.8 (190.5-248.3)	201.3 (171.8-231.4)	213.6 (186.4-242.9)	222.1 (195.9-250.5)	235.3 (209.7-262.8)	<0.001
LDL-C, mg/dl	136.7 (114.7-159.7)	132.3 (109.0-155.6)	137.2 (114.9-160.3)	138.4 (116.8-161.4)	138.5 (117.8-161.1)	<0.001
HDL-C, mg/dl	53.9 (45.3-64.3)	40.6 (36.7-44.3)	49.8 (46.3-53.4)	58.5 (54.5-62.8)	72.2 (66.0-79.6)	<0.001
Triglyceride, mg/dl	131.5 (92.9-189.7)	164.5 (114.4-236.6)	140.9 (99.8-199.5)	123.7 (89.4-173.6)	107.3 (80.1-148.4)	<0.001
Fasting glucose, mg/dl	88.6 (82.7-95.4)	88.4 (82.1-96.3)	88.5 (82.6-95.3)	88.5 (82.9-94.9)	88.9 (83.2-95.1)	0.001
hsCRP, mg/L	1.31 (0.65-2.71)	1.62 (0.81-3.36)	1.39 (0.70-2.82)	1.22 (0.61-2.50)	1.07 (0.54-2.20)	<0.001
Medication						
Antihypertensive agents	80,634 (21.6%)	24,953 (26.8%)	20,939 (22.5%)	18,509 (19.8%)	16,233 (17.4%)	<0.001
RASBs	48,424 (13.0%)	15,861 (17.0%)	12,818 (13.8%)	10,650 (11.4%)	9,095 (9.7%)	<0.001
Antidiabetic agents	11,838 (3.2%)	5,540 (5.9%)	2,959 (3.2%)	2,024 (2.2%)	1,315 (1.4%)	<0.001
Antiplatelet agents	52,585 (14.1%)	17,608 (18.9%)	13,642 (14.7%)	11,537 (12.3%)	9,798 (10.5%)	<0.001
Lipid lowering agents	63,479 (17.0%)	20,347 (21.8%)	16,698 (17.9%)	14,286 (15.3%)	12,148 (13.0%)	<0.001
NSAIDs	88,981 (23.9%)	21,385 (23.0%)	21,856 (23.5%)	22,499 (24.1%)	23,241 (24.9%)	<0.001
Apolipoproteins						
Apolipoprotein A	1.51 (1.35-1.69)	1.24 (1.17-1.30)	1.43 (1.39-1.47)	1.59 (1.55-1.64)	1.85 (1.76-1.99)	<0.001
Apolipoprotein B	1.02 (0.87-1.18)	1.02 (0.86-1.20)	1.03 (0.88-1.20)	1.02 (0.87-1.18)	1.00 (0.86-1.16)	<0.001
ApoB/ApoA Ratio	0.67 (0.55-0.81)	0.84 (0.70-0.98)	0.72 (0.61-0.84)	0.64 (0.55-0.74)	0.53 (0.45-0.62)	<0.001

Continuous variables are expressed as medians and interquartile ranges. Frequency variables are expressed as absolute numbers and percentages. Abbreviations: Townsend deprivation index; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; SBP, systolic BP; DBP, diastolic BP; uACR, urine albumin-to-creatinine ratio; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; hsCRP, high-sensitivity C-reactive protein; NSAIDs, nonsteroidal anti-inflammatory drugs; RASB, renin-angiotensin blocker.

table1.png



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Table 2. Incidence rates and hazard ratio of CKD outcomes according to apolipoprotein index quartiles

Apolipoproteins	ICD outcome				eGFR outcome			
	Univariable HR	P value	Multivariable HR*	P value	Univariable HR	P value	Multivariable HR*	P value
Apolipoprotein A								
Q1	Reference		Reference		Reference		Reference	
Q2	0.81 (0.78-0.85)	< 0.001	0.90 (0.86-0.95)	< 0.001	0.86 (0.81-0.92)	< 0.001	0.92 (0.86-0.99)	0.016
Q3	0.72 (0.69-0.75)	< 0.001	0.86 (0.82-0.90)	< 0.001	0.78 (0.73-0.83)	< 0.001	0.85 (0.79-0.91)	< 0.001
Q4	0.63 (0.60-0.66)	< 0.001	0.80 (0.76-0.85)	< 0.001	0.72 (0.67-0.77)	< 0.001	0.79 (0.74-0.86)	< 0.001
Total	0.83 (0.82-0.84)	< 0.001	0.91 (0.90-0.93)	< 0.001	0.88 (0.86-0.90)	< 0.001	0.92 (0.90-0.95)	< 0.001
	P-for-trend	< 0.001	P-for-trend	< 0.001	P-for-trend	< 0.001	P-for-trend	< 0.001
Apolipoprotein B								
Q1	Reference		Reference		Reference		Reference	
Q2	0.69 (0.66-0.73)	< 0.001	0.97 (0.92-1.01)	0.164	0.65 (0.61-0.70)	< 0.001	0.96 (0.89-1.02)	0.199
Q3	0.65 (0.62-0.68)	< 0.001	1.01 (0.96-1.07)	0.622	0.65 (0.61-0.70)	< 0.001	1.13 (1.05-1.22)	0.001
Q4	0.64 (0.61-0.67)	< 0.001	1.02 (0.97-1.08)	0.362	0.68 (0.64-0.73)	< 0.001	1.20 (1.12-1.30)	< 0.001
Total	0.83 (0.82-0.84)	< 0.001	1.01 (0.99-1.03)	0.303	0.86 (0.84-0.88)	< 0.001	1.09 (1.06-1.12)	< 0.001
	P-for-trend	< 0.001	P-for-trend	0.170	P-for-trend	< 0.001	P-for-trend	< 0.001
ApoB/ApoA ratio								
Q1	Reference		Reference		Reference		Reference	
Q2	0.94 (0.90-0.98)	0.005	1.03 (0.98-1.08)	0.193	0.92 (0.86-0.98)	0.014	1.07 (1.00-1.14)	0.057
Q3	0.90 (0.86-0.95)	< 0.001	1.06 (1.01-1.11)	0.019	0.87 (0.81-0.93)	< 0.001	1.12 (1.05-1.21)	0.001
Q4	0.88 (0.84-0.92)	< 0.001	1.18 (1.12-1.24)	< 0.001	0.84 (0.79-0.90)	< 0.001	1.31 (1.22-1.41)	< 0.001
Total	0.95 (0.93-0.97)	< 0.001	1.06 (1.04-1.08)	< 0.001	0.95 (0.92-0.97)	< 0.001	1.12 (1.09-1.15)	< 0.001
	P-for-trend	< 0.001	P-for-trend	< 0.001	P-for-trend	< 0.001	P-for-trend	< 0.001

* Adjusted for age, sex, ethnicity, body mass index, hypertension, diabetes, cardiovascular disease, eGFR, urine albumin-to-creatinine ratio, high-sensitivity C-reactive protein, renin-angiotensin system blockers, statin.

Abbreviations; ApoA, apolipoprotein A; ApoB, apolipoprotein B.