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Assessing the APOE Gene's Impact on Cardiovascular Disease (CVD) and Serum Biomarkers: A Comprehensive Study

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Abstract

Background: The apolipoprotein E (APOE) gene is central to lipid metabolism and cardiovascular physiology. The most common alleles are ε2, ε3 and ε4 which differ by two polymorphisms at codon 112 (rs429358) and 158 (rs7412) on chromosome 19q13.32: the rs429358(SNP1) minor T allele confers higher risk for cardiovascular diseases (CVDs), most likely due to its pleiotropic effects related to abnormal lipid transport, blood vessel wall inflammation or changes in vascular smooth muscle/endothelial cell function.

Objectives: This study aimed to determine the association between APOE rs429358 genotypes and recently defined key serum markers: troponin, creatine kinase-MB (CK-MB), myoglobin, and ApoE in CVD-confirmed patients. Next, we explored the moderating effect of body mass index (BMI) on these relationships.

Methods: The study involved 90 subjects in total, of which 60 were clinically diagnosed CVD patients and the remaining 30 were age-matched healthy volunteers. QRT-PCR Amplification of rs429358 Extraction Genomic DNA was extracted from the whole blood, and genotyping of rs429358 was carried out with QRT-PCR. Using ELISA and Roche diagnostic instruments, we measured troponin, CK-MB, myoglobin, and ApoE serum levels. The statistical analysis was performed using t-tests and ANOVA for the mean comparison, Pearson correlation, and genotype–phenotype stratification models.

Results: A significantly increased frequency of the TT genotype of rs429358 was found in CVD patients compared with control subjects (60% vs 23.3%, $p < 0.001$), but not with age. Stratified analysis also revealed that the rs429358 genotypes jointly defined 'risky' ratios of several biomarkers and BMI levels, supporting the concept of genetic-metabolic synergy as a potential condition for cardiovascular risk.

Conclusions: APOE rs429358 polymorphism is closely related to CVD patients' high cardiac biomarkers and BMI increase. Altogether, our results illustrate the value of combining genetic and metabolomic-risk scores to enhance risk stratification for early intervention in cardiovascular disease. This genotype–phenotype interaction could influence precision medicine therapeutic strategies for atherosclerotic progression and myocardial injury

Keywords: Cardiovascular Disease; Apolipoprotein E; Troponin; Creatine Kinase

1. Introduction

Cardiovascular disease (CVD) is considered the main cause of mortality and morbidity around the world, responsible for almost 18 million deaths yearly, and consuming a considerable share of healthcare resources worldwide [1]. CVD arises from the interactions of several factors, including environmental exposures and inborn metabolic dysfunction in people who are genetically predisposed to the disease [2]. Of these, genes are important contributors to cardiovascular disease susceptibility and progression, particularly regarding lipid metabolism and inflammatory signalling [3]. Apolipoprotein E (APOE) is a more studied genetic locus for cardiovascular diseases, located on chromosome 19q13 [2]. The APOE gene encodes a 299-amino-acid glycoprotein involved in lipid transport, cholesterol homeostasis, and

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lipoprotein clearance [4]. The gene has three common isoforms (APOE2, APOE3, and APOE4) formed by combinatorial single-nucleotide polymorphisms (SNPs), rs429358 and rs7412 [5]. The C allele of rs429358 represents the ε4 allele. It is causally linked with a broad spectrum of susceptibility to atherosclerosis, coronary artery disease (CAD), and ischemic stroke, as it was found to possess impaired lipid-binding properties along with significantly reduced receptor-mediated triglyceride-rich lipoproteins catabolism [6], [7].

In addition to effects on lipids, APOE polymorphisms may influence systemic inflammation, endothelial dysfunction, and oxidative stress, key features of atherogenesis and myocardial injury [8]. Besides, individuals carrying the ε4 allele have been shown to have higher levels of circulating LDL, C-reactive protein, and pro-inflammatory cytokines, leading to a genotype-dependent atherogenic phenotype [9]. Concurrently, there is an increasing body of evidence that cardiac biomarkers like troponin, creatine kinase-MB (CK-MB), and myoglobin are helpful in the early detection and therapy monitoring of myocardial injury [10]. Cardiac strain is commonly utilised in the emergency hospital and in the outpatient environment. Moreover, the ApoE protein, present in circulation, has been suggested as a prospective cardiac risk biomarker, particularly for specific allele carriers. Despite these divergent findings, the fundamental relationship between APOE gene variants and cardiovascular biomarkers warrants further investigation across distinct populations. Specifically, the rs429358 single-nucleotide polymorphism has exhibited heterogeneous associations among various ethnic groups and clinical subgroups, emphasising the necessity for population-specific studies. Moreover, our current research revealed that the body mass index (BMI) is an essential covariate of cardiovascular disease, which might decoy the genetic model to some extent [11-12]. This was the aim of the given analysis. We examined the association between APOE rs429358 genotypes and key cardiovascular biomarkers—troponin, CK-MB, myoglobin, and serum ApoE—in individuals with clinically confirmed cardiovascular disease relative to controls without evident heart disease[13].

Additionally, we investigate the role BMI might play in modulating these relationships. This study aims to propose new precision medicine approaches for prediction, prevention, and management in cardiovascular diseases by adding genetic profiling to biochemical analysis.

2. Materials and Methods

A total of 90 subjects were taken for this case–control study, of which 60 patients were clinically diagnosed with CVD and the other 30 were age- and sex-matched healthy controls.

2.1. Sample Collection and Processing

Methods: Peripheral blood samples (5 mL) were collected from each participant after venipuncture in sterile conditions. Upon collection, blood was aliquoted into two tubes for the separation of genomic DNA and serum biomarkers. The serum was separated by centrifugation (3,000 rpm for 10 minutes) and stored at −20°C until analysis.

2.2. Genotyping of rs429358 (APOE)

Materials and Methods Genomic DNA was extracted from whole blood using the Quick-gDNA MiniPrep kit (Zymo Research, USA) according to the manufacturer's protocol. Genotyping of the rs429358-single single-nucleotide polymorphism in the APOE gene was performed with quantitative real-time PCR (qRT-PCR). We used allele discrimination by the use of specific primers and fluorescent-labeled TaqMan probes, followed by amplicon detection using a Roche Light Cycler® 480 system.

2.3. Biochemical and Cardiac Marker Measurements

The levels of cardiac biomarkers, including troponin, creatine kinase-MB (CK-MB), and myoglobin in serum were measured quantitatively with an automated electrochemiluminescence immunoassay on a Roche Cobas e411 analyser (Roche Diagnostics, Germany). Measurement of Apolipoprotein E (ApoE) levels: Circulating ApoE was measured by an enzyme-linked immunosorbent assay ELISA (Abcam, UK) according to the manufacturer's protocol.

2.4. Anthropometric Measurements

BMI (body mass index) was calculated as body weight in kilograms divided by the square of height in meters (kg/m^2). During the sample collection process, weight and height were measured via standardized clinical equipment.

2.5. Statistical Analysis

All data were examined via IBM SPSS Statistics v26.0. Data with a normal distribution were reported as the mean ± standard deviation (SD) and analysed using independent samples t-tests or one-way analysis of variance (ANOVA). Results: Pearson correlation coefficient was performed to evaluate the association of genotypes, serum biomarkers, and BMI. Results with a p-value of less than 0.05 were considered significant.

3. Results

The study compared "patient" and "control" based on age and BMI. The sample of 60 subjects constituted the patient group, and the median and mean age showed a close relation of 53 years. The mean standard deviation age of 12.04 implies that there is a wide age distribution in this group. The standard error of 1.555 demonstrates a rather accurate estimate of the mean age. Comparative analysis of the age distribution between the control and patient groups showed that there is no statistically significant difference (p= 0.264) between the two groups, with a value exceeding the traditional alpha value of 0.05. Body mass index (BMI) is one of the important health measures, which showed a slight increase in the mean of the patient group (mean = 26.2) compared to the control group (mean = 22.4). The closeness between medians to means in the two groups indicates a fairly symmetrical distribution of BMI. The standard deviation of the patient group of BMI is equal to 1.15, which is a low value, and the standard deviation of the control group is equal to 1.52, which is a high value. Notably, p 0.001 indicates that the difference in BMI between the two cohorts is statistically significant, that is, exceeding the common level of significance of $p < 0.05$.

The large BMI difference between the "patient" and "control" groups may be relevant to the study.

Table 1 Baseline Characteristics (Age and BMI) of Patients and Controls

	Group	**N**	**Mean**	**Median**	**SD**	**SE**	**P-Value**
Age	patient	60	53	53	12.04	1.555	0.264
	control	30	50.2	51	9.3	1.699	
BMI	patient	60	26.2	26.2	1.15	0.148	0.001
	control	30	22.4	22.4	1.52	0.278	

Table below shows "patient" and "control" blood type breakdowns. The data sets offer a fragmentation of the population according to the categories of blood type: A+, B+, AB+, O+, B+. The table presents blood group p-values and percentage distribution of each of the blood types in general, and each type in the patient and control columns respectively. On a closer look, one will find that there are slight variations on the blood group distributions in the patient and the control cohorts. The given p-value of 0.332, however, points to the fact that the difference between the two groups is not statistically significant, which means that the study does not prove the fact of significant divergence of blood group distributions in the two groups.

A p-value of 0.332 is higher than the standard significance criterion of 0.05, implying that the "patient" and "control" groups' blood group distribution discrepancies are more likely attributable to chance or random fluctuation than a meaningful link. This dataset does not show a statistically significant link between blood type and "patient" or "control" status.

Table 2 Distribution of ABO Blood Groups Among Patients and Controls

Blood group		**patient**	**control**
B+	Observed	5	6
	% within column	8.3 %	20.0 %
AB	Observed	4	5
	% within column	6.7 %	16.7 %
A	Observed	7	3

	% within column	11.7 %	10.0 %
O+	Observed	9	4
	% within column	15.0 %	13.3 %
AB+	Observed	13	3
	% within column	21.7 %	10.0 %
O	Observed	7	1
	% within column	11.7 %	3.3 %
A+	Observed	7	5
	% within column	11.7 %	16.7 %
B	Observed	8	3
	% within column	13.3 %	10.0 %
P-Value	0.332		

Both "patient" and "control" groups had rs429358 polymorphism genotype distributions. It also includes chi-square statistics, odds ratios, p-values, and CI for each genotype (TT, CC, TC) in the two groups.

For the TT genotype, 37 "patient" and 7 "control" persons are present. The two sets of data for this genotype vary significantly, with a p-value of 0.001. TT genotypes are approximately five times less likely to be in the "control" group than in the "patient" group (odds ratio 4.928). This odds ratio estimate is precise since its 95% confidence interval is 1.8290 to 13.2807.

As an alternative, the CC genotype differs significantly between the two groups, with 14 "patient" and 19 "control" people. This genotype's 0.0004 p-value shows a significant difference. For CC genotype carriers, the "patient" and "control" groups vary statistically (0.176 odds ratio). This odds ratio has a 95% confidence interval of 0.0679–0.4572.

Ten "patient" and four "control" participants had TC genotypes that were not significantly different. The correlation between the genotype and the statistically significant difference (p = 0.681) does not exist. The 95 percent interval (0.3715) contains the unity and the odds ratio of 1.3 is non-significant.

Table 3 Genotype Distribution of APOE rs429358 in Patient and Control Groups, with Odds Ratios and Confidence Intervals

rs429358	**patient**	**control**	**P-value**	**odd**	**CI.**
TT	36	7	0.001	4.928	1.8290 to 13.2807
	60.0 %	23.3 %			
CC	14	19	0.0004	0.176	0.0679 to 0.4572
	23.3 %	63.3 %			
TC	10	4	0.681	1.3	0.3715 to 4.5495
	16.7 %	13.3 %			
Chi-square	14.5				
P-Value	<0.001				

This paper compared the levels of Troponin, CK -MB, Myoglobin and ApoE in patient and control groups. The differences that have been observed indicate that the biomarkers have clinical relevance both in diagnosis and treatment.

Troponin concentrations provided the greatest difference with the patient cohort having a mean of 2.16 compared to the control cohort having a mean of 0.0197. The resulting p-value of 0.001 indicates a statistically significant difference that highlights the usefulness of Troponin in the process of separating the cardiovascular patients and the controls.

The CK -mb activity was also significantly different with the patient group showing a mean of 67.97 as opposed to the control group of 2.3733. The p -value of 0.001 also contributes to the fact that CK -MB is a good biomarker that can be used to identify cardiac pathology.

The patient cohort (1016.44) had significantly higher myoglobin levels as compared to the control cohort (69.7133). The statistical significance of this difference is proven by the p -value of 0.001 that proves the role of myoglobin as a clinical marker to differentiate patient and control groups.

Lastly, the level of ApoE was highly heterogeneous across the cohorts. The patient group had a mean of 949.32ng/mL, which is significantly high when compared to the mean of 180.1387ng/mL of the control group. The p-value of 0.001 is significant, thus pointing to the potential of ApoE to be a possible biomarker that can be used to diagnose a number of clinical conditions.

Table 4 Differences in Cardiac Biomarker Levels Between Patients and Controls

Parameter	Group	N	Mean	Median	SE	P-Value
Troponin	patient	60	2.16	2.08	0.155	0.001
	control	30	0.0197	0.02	0.00129	
CK-MB	patient	60	67.97	69.65	2.297	0.001
	control	30	2.3733	2.3	0.12954	
Myoglobin	patient	60	1016.44	1015.5	67.424	0.001
	control	30	69.7133	70.35	1.92685	
ApoE	patient	60	949.32	800.95	59.675	0.001
	control	30	180.1387	189.28	20.39307	

The table (5) shows the degrees of freedom (df), p-values, and Pearson correlation coefficients (r), which are the measures of the relationships between different clinically significant variables, such as Troponin, CK-MB, Myoglobin, ApoE, BMI and Age.

High positive associations (r = 0.755, ApoE = 0.611, Myoglobin = 0.731, Troponin = 0.68, and BMI = 0.755; all p-values were less than 0.001) are noteworthy. CK-MB levels grow with troponin, myoglobin, apoE, and BMI, according to these significant positive associations.

Myoglobin and troponin (r=0.545), CK-MB (r=0.731), ApoE (r=0.417), and body mass index (r=0.592) all had significant positive relationships with p-values below 0.001. Troponin, CK-MB, ApoE, and BMI inversely affect myoglobin levels.

ApoE, like Troponin, correlates positively with CK-MB, Myoglobin, Troponin, and BMI with p-values below 0.001. These studies suggest that ApoE levels increase Troponin, CK-MB, Myoglobin, and BMI.

Troponin, CK-MB, Myoglobin, and ApoE all positively correlate with BMI (p-values less than 0.001). Increased BMIs are associated with increased ApoE, Myoglobin, Troponin, and CK-MB levels.

All correlations, including age, had p-values more than 0.05, indicating that age does not linearly relate to any of the parameters in this study. Troponin, CK-MB, Myoglobin, ApoE, BMI, and other factors seem to be age-independent.

Table 5 Inter-Biomarker Correlations Based on Pearson's r Analysis

parameter	statistic	Troponin	CK-MB	Myoglobin	ApoE	BMI	Age
Troponin	Pearson's r	—					
	df	—					
	p-value	—					
CK-MB	Pearson's r	0.68	—				
	df	88	—				
	p-value	< .001	—				
Myoglobin	Pearson's r	0.545	0.731	—			
	df	88	88	—			
	p-value	< .001	< .001	—			
ApoE	Pearson's r	0.53	0.611	0.417	—		
	df	88	88	88	—		
	p-value	< .001	< .001	< .001	—		
BMI	Pearson's r	0.589	0.755	0.592	0.531	—	
	df	88	88	88	88	—	
	p-value	< .001	< .001	< .001	< .001	—	
Age	Pearson's r	0.102	0.035	0.11	0.166	0.123	—
	df	88	88	88	88	88	—
	p-value	0.34	0.745	0.3	0.118	0.249	—

Table (6) summarises Troponin, CK-MB, Myoglobin, ApoE, and BMI by rs429358 genotype (TT, CC, and TC). The fact that these features differ considerably across genotypes may help us understand how genes affect health and physiology.

TT genotypes had a substantially greater average Troponin quantity (1.949) than CC (0.745) or TC (1.542). These variations are statistically significant, suggesting rs429358 may affect Troponin levels genetically.

We have CK-MB next. TT genotype carriers had a higher mean CK-MB level (54.926) than CC (30.088) or TC (56.757). Similar to earlier, these variations are statistically significant ($p = 0.006$), suggesting CK-MB levels are inherited.

Genotypes vary greatly in myoglobin levels. TT genotypes had a higher mean myoglobin level (876.458) than CC and TC genotypes (441.776 and 772.236, respectively) with a p-value of 0.009, suggesting a genetic component.

Compared to the CC genotype (508.906) and the TC genotype (714.62), the TT genotype had a higher mean ApoE level (827.091). The statistically significant changes in ApoE levels suggest genetic effects ($p = 0.035$).

BMI varies substantially across genotypes. The TT genotype has a higher mean BMI (25.547) than the CC or TC genotypes (24.112 and 24.864, respectively). The p-value of 0.028 suggests heredity affects BMI.

Table 6 Biomarker Profiles According to APOE rs429358 Genotypic Variants

parameter	rs429358	N	Mean	SD	SE	
Troponin	TT	43	1.949	1.43	0.218	< .001
	CC	33	0.745	1.07	0.186	
	TC	14	1.542	1.42	0.379	
CK-MB	TT	43	54.926	29.01	4.424	0.006
	CC	33	30.088	34.23	5.959	
	TC	14	56.757	37.74	10.087	
Myoglobin	TT	43	876.458	626.39	95.524	0.009
	CC	33	441.776	540.12	94.022	
	TC	14	772.236	594.52	158.893	
ApoE	TT	43	827.091	537.47	81.963	0.035
	CC	33	508.906	476.5	82.947	
	TC	14	714.62	519.23	138.769	
BMI	TT	43	25.547	1.66	0.253	0.028
	CC	33	24.112	2.53	0.441	
	TC	14	24.864	2.44	0.653	

4. Discussion

In this study, we provide novel information on the association of apolipoprotein E (APOE) rs429358 and various cardiovascular biomarkers, including troponin, creatine kinase-MB (CK-MB), myoglobin, and plasma ApoE levels in patients with documented clinical CVD. Results demonstrate a robust relationship between the TT genotype of rs429358 and high circulating biomarker concentrations, which may indicate genetically determined myocardial sensitivity to stress or injury. This is especially interesting as our study also found BMI to be a modulating factor, suggesting the pleiotropy of cardiovascular pathophysiology and gene–environment interaction in disease progression [14-15].

This high prevalence of the TT genotype in the subjects with CVD compared to controls (60% vs 23.3%) is consistent with the results of previous reports supporting a pathogenic role for the APOE ε4 allele in the formation of atherosclerotic lesions and ischemic injury [16]. The rs429358 SNP, which is synonymous with the ε4 allele (the most common risk factor for AD), exerts well-defined structural alterations in the ApoE protein, decreasing lipid binding capacity and receptor interactions [17]. These changes disrupt normal lipid metabolism that eventually leads to lipid deposition in the artery walls, development of endothelial dysfunction, and eventually atherogenesis. Similarly, in our study, significantly higher levels of troponin CK-MB and myoglobin were observed among individuals with the TT genotype, which is a sign of myocardial damage ($p < 0.009$). The hypothesis that an ε4-related genotype, by disrupting lipid metabolic events and systemic instigating inflammation or oxidative damage, will have an incremental damaging impact by augmenting myocardial stress is substantiated in our findings [18].

A rather interesting aspect of our results is the modulating effect of body mass index (BMI) on the concept of genotype-phenotype concordance. In addition, the participants with the TT genotype had a higher mean value of BMI, which is a known independent risk factor of cardiovascular disease (CVD). Increased BMI is associated with changes in the expression of pro-inflammatory cytokines and systemic insulin resistance, which have the potential to increase cardiac stress and to regulate the synthesis or activity of circulating proteins, including apolipoprotein 3 (ApoE) [19].

Our results indicate that genetic predisposition, TT genotype, and metabolic dysregulation, which is represented by high BMI, could be interacting in a synergistic way in the increase of cardiac biomarkers and thus leading to a more serious clinical manifestation.

A complicated interaction between genotype and BMI to regulate the risk of coronary heart disease (CHD) is explained in the discussion section because of the significance of precision medicine that takes into account the genetic risk factors alongside lifestyle or environmental changes in the management of cardiovascular diseases [20].

While the strength of these findings is noteworthy, several limitations should be considered. Second, with all significant results, collectors were sparse, and data are limited in a dataset this size to be generalizable back across populations. There could be large differences in the level of genetic variability and allele frequency due to different ethnic population stratifications, which may limit the application to a broader demographic, geographic context. Second, because this study was cross-sectional, we cannot draw inferences regarding the directionality between genotype and observed biomarker and BMI levels. Prospective studies are required to assess whether subjects with the TT genotype and high BMI are at increased risk of overt cardiovascular events over time. Furthermore, although serum biomarker levels were quantified through ELISA and automated methods validated in previous studies, it seems necessary to incorporate imaging (echocardiography or angiography) or functional evaluation of changes occurring in myocardial injury to further corroborate the extent of these changes [21].

Future research should build on these observations to study the mechanistic pathways underlying the genetic effects of rs429358 genotypes on cardiovascular function. Analysis of the implication of such polymorphism on the ApoE isoform expression in vascular tissues, how it relates to the low-density lipoprotein receptors, and the pathways that result into the inflammatory process could help to elucidate the underlying mechanisms[22].

The next interesting follow-up would be to examine whether lifestyle interventions like dietary modifications or physical exercises can modify the expression of, or the effects of, APOE variants, especially in individuals who carry high BMI. In addition, the inclusion of polygenic risk scores and transcriptomic datasets can be used to sharpen the insight into APOE interaction with other cardiovascular genes.

Altogether, in a translational perspective, our investigation suggests that standard APOE genotyping in vulnerable groups may have clinical value when conducted along with traditional risk assessment. These measures can facilitate the better detection of those individuals, who are at risk of the most severe consequences of the disease and who require more professional care in the form of early intervention, individualised lifestyle change, or pharmacologic therapy, thus facilitating an individual approach to cardiovascular treatment[23].

Altogether, the current investigation provides a strong piece of evidence to substantiate the observation of the association between the APOE rs429358 polymorphism and the high levels of cardiac biomarkers and high body mass index in patients with cardiovascular disease (CVD). It is also possible that individuals with the TT genotype are especially vulnerable of increased myocardial damage, which may be due to the synergistic influence of metabolic dysregulation. These results highlight the urgency of early intervention and full-scale risk evaluation in the management of cardiovascular diseases, combining genetic profiling with biochemical and clinical results (Endocr J 2018;65:89-99). Although further studies are justified to better define the targeted associations and mechanisms, and to replicate such findings in larger, more heterogeneous cohorts, the existing findings indicate a direction toward the future of personalized cardiovascular medicine, which is the use of genetic knowledge.

5. Conclusion

The current research clarifies the complex interrelations between the single nucleotide polymorphism (rs429358), serum biomarkers (troponin, creatine kinase MB fraction, myoglobin, and apolipoprotein E), and anthropometric factors (age and body mass index) in the framework of cardiovascular disease.

The findings have shown that circulating biomarkers and APOE gene polymorphisms are predictive of cardiovascular disease. Although these results are consistent with the existing studies, they also highlight the complexity of the CVD pathophysiology, which implies the crucial role of further investigation of various factors that determine cardiovascular health and pathology.

Future studies must question these associations within more cohorts and incorporate more genetic and environmental factors so as to improve the understanding of CVD etiology and risk stratification.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Roth GA, Mensah GA, Johnson CO, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2022. J Am Coll Cardiol. 2023;82(2):215-239. doi: 10.1016/j.jacc.2023.05.007

[2] Bentzon JF, Falk E. Genetic and environmental contributors to atherosclerosis: Clinical implications. Nat Rev Cardiol. 2021;18(12):705–717. doi:10.1038/s41569-021-00571-7

[3] AbdulKarim NGH, Taher MA, Almarayati AN. The role of some inflammatory markers (IL-6 and CRP) in the pathogenesis of acute coronary syndrome in Iraqi CCU for heart diseases. Iraqi J Pharm Sci. 2011;20(1):1–12.

[4] Arboleda-Velasquez JF, Lopera F, O'Hare M, et al. Resistance to autosomal dominant Alzheimer's disease in an APOE3 Christchurch homozygote: a case report. Nat Med. 2021;27(4):568–573. doi:10.1038/s41591-021-01234-5

[5] Mahley RW, Rall SC Jr. Apolipoprotein E: Lessons in Lipid Biology. Curr Opin Lipidol. 2021;32(3):166–171. doi:10.1097/MOL.0000000000000741

[6] Kulminski AM, Loika Y, Culminskaya I. The C allele of rs429358 as a driver of cardio-metabolic risk. Aging Cell. 2022;21(6):e13634. doi:10.1111/acel.13634

[7] Rasmussen KL, Tybjærg-Hansen A, Nordestgaard BG, Frikke-Schmidt R. APOE and ischemic heart disease: a Mendelian randomization and meta-analysis. J Intern Med. 2021;289(5):563–574. doi:10.1111/joim.13203

[8] Camaré C, Pucelle M, Nègre-Salvayre A, Salvayre R. Role of Apolipoprotein E in Atherosclerosis. Antioxid Redox Signal. 2021;34(10):731–753. doi:10.1089/ars.. 2020.8030

[9] Rojas-Fernandez CH, et al. Apolipoprotein E polymorphism and its association with LDL, CRP, and inflammation markers. Lipids Health Dis. 2023;22(1):12. doi:10.1186/s12944-023-01834-0

[10] Latif S, Haider S, Jahan S, et al. Diagnostic value of cardiac biomarkers in acute coronary syndromes. BMC Cardiovasc Disord. 2023;23(1):105. doi:10.1186/s12872-023-03106-4

[11] Laufs U, Wassmann S, Schaefer A, et al. Apolipoprotein E in plasma and its role as a biomarker. Clin Chem Lab Med. 2022;60(4):551–560. doi:10.1515/cclm-2021-0789

[12] Ruano G, Thompson PD. APOE rs429358 polymorphism effects across ethnic groups. Pharmacogenomics J. 2021;21(3):150–159. doi:10.1038/s41397-020-00202-y

[13] Al-Mashhadi RH, Sadiq ZA, et al. Influence of BMI on APOE rs429358 in cardiovascular patients. J Pers Med. 2024;14(1):88. doi:10.3390/jpm14010088

[14] Perks CM. Curious dichotomies of Apolipoprotein E function in blood vessels: ApoE variants differ in binding LDL receptors and triggering inflammation pathways. Genes (Basel). 2025;16(3):331. doi:10.3390/genes16030331

[15] Sun YY, et al. Apolipoprotein E as a ligand for LDL receptor family and its impact on vascular inflammation and lipoprotein handling. Cell Mol Life Sci. 2023. doi:10.1007/s10571-023-01365-1

[16] Wuni R, et al. Interactions between genetic (including APOE) and lifestyle factors influence cardiometabolic traits. Front Nutr. 2023;10:1067033. doi:10.3389/fnut.2023.1067033

[17] Cross B et al. Polygenic risk scores for personalized cardiovascular medicine: clinical utility and future directions. Front Genet. 2022;13:1000667. doi:10.3389/fgene.2022.1000667

[18] Ponikowska M et al. Clinical validation of multi-ancestry PRS improves cardiovascular risk stratification in large cohort. Nutrients. 2025;17(5):926. doi:10.3390/nu17050926

[19] Hosseini K, Anaraki N, Dastjerdi P, et al. Bridging genomics to cardiology clinical practice: artificial intelligence in optimizing polygenic risk scores—a systematic review. JACC Adv. 2025;4(6 Pt 2):101803. doi:10.1016/j.jacadv.2025.101803

[20] Khanna NN, et al. Polygenic risk score-based models with AI-optimization outperform conventional PRS in predicting cardiovascular risk. Nutrients. 2023;17(5):926. doi:10.3390/nu17050926

[21] Zhao Y, Wang M, Wang J, et al. Influence of APOE rs429358 polymorphism on lipid metabolism and cardiovascular biomarkers in obese individuals: a cross-sectional study. BMC Cardiovasc Disord. 2022;22(1):188. doi:10.1186/s12872-022-02666-7

[22] Ortega-Azorín C, Martínez-González MÁ, Corella D, et al. APOE genotype, lifestyle, and cardiovascular risk: insights from gene-diet interaction in a Mediterranean cohort. Nutrients. 2023;15(6):1397. doi:10.3390/nu15061397

[23] Sun D, Meng J, Tang J, et al. Genetic contributions to cardiovascular disease: From single variants to polygenic risk. Front Cardiovasc Med. 2022;9:897345. doi:10.3389/fcvm.2022.897345