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Research Article
Effects of Atorvastatin on Carotid Artery Plaques and Blood Lipids in Stroke Patients with Different ApoE Genotypes

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Abstract

Background and Objective: Atorvastatin is a routine drug for treating stroke, reversing plaque formation and reducing cerebrovascular accidents. However, its efficacy varies among different patients. This study aimed to investigate the effects of atorvastatin on carotid artery plaques and blood lipids in stroke patients with different Apolipoprotein E (ApoE) genotypes. **Materials and Methods:** The clinical data of 61 stroke patients admitted to the hospital from January, 2018 to December, 2019 were retrospectively included in the observation group, while another 50 healthy individuals undergoing physical examinations were selected as the control group. All patients were tested for ApoE genotype and treated with atorvastatin and the correlation between genotype and lipid-regulating effect was analyzed. **Results:** After treatment, both ApoE2/2+E3/2 and ApoE3/3 genotype groups showed smaller carotid artery plaque area and lower carotid artery stenosis ratio than before treatment ($p<0.05$). After treatment, the ApoE3/3 genotype group exhibited a higher proportion of plaque stability than the ApoE4/3+E4/4 genotype group ($p<0.05$). After treatment, the ApoE2/2+E3/2 and ApoE3/3 genotype groups showed lower TC, TG and LDL-C levels and higher HDL-C levels than the ApoE4/3+E4/4 genotype group ($p<0.05$). The ApoE3/3 genotype group had a lower incidence of cerebrovascular accidents than the ApoE4/3+E4/4 genotype group ($p<0.05$). **Conclusion:** Atorvastatin shows better lipid-lowering effects in patients with ApoE2/2+E3/2 and ApoE3/3 genotypes compared with those with ApoE4/3+E4/4 genotypes. It effectively reduced plaque area, enhanced plaque stability and reduced cerebrovascular accidents. The efficacy of lipid regulation and plaque treatment in stroke patients may be associated with ApoE gene polymorphism.

Key words: Stroke, apolipoprotein E genotypes, atorvastatin, carotid artery plaques, blood lipid

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Stroke is a common clinical type of cerebro vascular disease, often caused by vascular obstruction and spasms, leading to poor blood flow in the brain and subsequent hypoxic-ischemic necrosis of brain tissues, which can be accompanied by varying degrees of functional loss[1]. Stroke has the characteristics of high disability rate, high recurrence rate and high morbidity and mortality rate and the etiology is complex and diverse, including intracranial arterial stenos is and occlusion, hematological factors, hemodynamic factors, etc., dyslipidemia is an important factor leading to intracranial arterial stenos is and occlusion, hematological abnormality and hemodynamic abnormality, which is closely related to the occurrence and development of stroke[2]. The relevant research reveals that hyperlipidemia is one of the primary risk factors for cardiovascular and cerebrovascular diseases[3]. The lipid levels of the people in China are gradually elevating, while lowering lipid levels can effectively diminish the occurrence of cardiovascular and cerebrovascular events. Therefore, it is of great significance to actively and effectively carry out lipid-regulating therapy to enhance the therapeutic effect of stroke, improve the prognosis of patients and promote an elevation in the quality of life.

Currently, statins are clinically recommended for secondary prevention in stroke patients. Among them, atorvastatin is a commonly used clinical lipid-regulating medication and its lipid-regulating effect has been widely recognized as a standard medication for the treatment of stroke, which can reverse plaque formation and reduce the occurrence of cerebrovascular accidents[4]. However, there is still some variation in the effectiveness of atorvastatin in different patients. A previous study has pointed out that Apolipoprotein E (ApoE) gene polymorphism is one of the important factors affecting lipid-lowering effects and ApoE gene polymorphism can result in variations in the binding capacity between its expressed protein and the low-density lipoprotein receptor, thereby influencing the lipid levels and metabolic conditions[5]. The ApoE is an important component of plasma lipoproteins, present in chylomicrons and intermediate-density lipoproteins, mainly produced by macrophages and the liver as a polymorphic protein classified into three genotypes including ApoE2, ApoE3 and ApoE4 based on allelic differences, which are involved in lipid metabolism processes through the binding of LDL receptors and thus have an impact on lipid regulatory outcomes[6]. To elucidate the difference in lipid-lowering effects of atorvastatin in stroke patients with different ApoE genotypes, this study observed the effect of atorvastatin treatment on lipid levels in stroke patients with different ApoE genotypes, aiming to implement more precise lipid-lowering treatment for stroke patients with different ApoE genotypes.

MATERIALS AND METHODS

General data: The clinical data of 61 stroke patients admitted to the Affiliated Hospital of Beihua University (Jilin, China) from January, 2018 to December, 2019 were retrospectively analyzed and the patients (n = 61) were included in the observation group, while another 50 healthy individuals undergoing physical examinations were selected as the control group. Inclusion criteria, (1) Patients in the observation group met the diagnostic criteria for stroke and were diagnosed by magnetic resonance imaging or CT scan[7], (2) Patients in the observation group had concomitant primary hyperlipidemia and met any of the following conditions: Total cholesterol (TC) $\geq$5.2 mmol/L, triglycerides (TG) $\geq$2.3 mmol/L, high-density lipoprotein cholesterol (HDL-C) $\leq$1.04 mmol/L, low-density lipoprotein cholesterol (LDL-C) $\geq$4.1 mmol/L, (3) Good compliance, able to follow medication instructions and (4) Complete clinical data. Exclusion criteria: (1) Active liver disease or hepatic insufficiency caused by other factors, (2) Combined thyroid dysfunction, (3) Allergy to statins, (4) Cognitive dysfunction or mental abnormality prior to stroke, (5) Combined systemic acute and chronic infectious diseases, (6) Combined brain tumors, traumatic brain injury and other brain disorders, (7) Lipid-regulating drug therapy prior to enrolment and (8) Combined systemic connective tissue disease, malignant stroma and malignant neoplastic disease.

Ethical consideration: This study was approved by the Ethics Committee of Affiliated Hospital of Beihua University. All the volunteers have signed an informed consent form.

Methods

ApoE genotype detection: Gene sequencing was used to detect the genotypes of the subjects. Polymerase Chain Reaction (PCR) amplification: Upstream primer P1: 5'AGGGTGCTGATGGACGAGAC3', downstream primer P2: 5'GCTCACGGATGGTGCTGAGG3'. Sequencing reaction system: 1 μL Big Dye (2.5×)+1.5 μL Big Dye Seq Buffer (5×) +3 μL primer +1 μL PCR purified product +3.5 μL ddH2O. The sequencing thermal cycling conditions were as follows: 96°C for 10 sec, followed by 25 cycles of (96°C for 10 sec, 50°C for 5 sec, 60°C for 4 min), then a final step at 60°C for 4 min and finally, a hold at 4°C. Sequencing reaction was

followed by purification and the purified product was loaded into the 3100-Avant Genetic Analyzer for electrophoresis. Raw data from sequencing results were automatically analyzed using DNA sequencing analysis 5.1 to obtain sequencing electropherograms and sequences. The sample sequence was compared with the standard sequence using DNA star SeqMan.

Atorvastatin therapy: Patients were given oral atorvastatin (Fujian Dawn rays Pharmaceutical Co., Ltd., No. H20193043, specification: 10 mg/tablet) 20 mg/time, once a day, at the same time, antiplatelet treatment [oral aspirin (ORIGINAL PHARMACOLABO Corporation, No. H20065051, specification: 100 mg/tablet) 100 mg/time, once a day] was given, for consecutive 6 months.

Observation indicators: The general information, including gender, age, body mass index, smoking history and drinking history, were compared between the observation and control groups.

The ApoE genotypes of the observation and control groups were counted, including ApoE2/2+E3/2 genotype, ApoE3/3 genotype and ApoE4/3+E4/4 genotype.

Based on the ApoE genotypes of the observation group, the patients were divided into ApoE2/2+E3/2 genotype group, ApoE3/3 genotype group and ApoE4/3+E4/4 genotype group. Carotid artery plaque area and carotid artery stenos is ratio were compared before and after treatment among the three groups. Carotid artery plaque area was determined using CT angiography before treatment and after 6 months of treatment, respectively and 3 transverse diameters of each plaque were taken to calculate the plaque area comprehensively and the sum of plaque areas was calculated for those with the presence of several plaques and carotid artery stenos was observed.

The stability of carotid artery plaques was compared among the three groups before and after treatment. The CT value range was used to determine the plaque nature. The CT values of 20-39 HU were regarded as thrombotic plaques, which were located on the inner side of the vessel lumen with relatively uniform density, CT values of 40-49 HU were categorized as lipid-rich plaques, CT values of 50-120 HU were classified as fibrous plaques and CT values greater than 120 were regarded as calcified plaques. Among these, calcified plaques were considered stable, while lipid-rich plaques, fibrous plaques and mixed plaques (lipid-rich or fibrous plaques with some calcification) were categorized as unstable plaques.

The blood lipid levels of the three groups were compared. The 2 mL of fasting venous blood was collected from the three groups before and after treatment and TC, TG, HDL-C and LDL-C levels were measured using a fully automatic biochemical analyzer (Beckman AU5800).

The blood pressure classification was compared among the three groups before and after treatment[8]. The Omron HEM-7121 blood pressure monitor was used to measure patients' blood pressure levels. Normal: Systolic/diastolic blood pressure <140/90 mmHg, Grade 1 hypertension: (140-159)/(90-99) mmHg, Grade 2 hypertension: (160-179)/(100-109) mmHg and Grade 3 hypertension: >180/110 mmHg.

Cognitive function was assessed among the three groups before and after treatment using the Montreal Cognitive Assessment (MoCA)[9] and Clock-Drawing Test (CDT)[10]. The MoCA includes seven dimensions, including naming ability, visuospatial ability, executive function, delayed recall, etc., with a score range of 0-30 points, where a higher score indicates better cognitive function. The CDT: The patient was instructed to draw a clock dial, mark the corresponding numbers and draw the position of the hour and minute hands corresponding to the specified time, with 1 point for drawing the dial, 1 point for partially correct placement of numbers, 1 point for complete correct placement of numbers and 1 point for correct placement of the hour and minute hands. Scoring ranges 0-4 points, with a higher score indicates better cognitive function. The incidence of cerebrovascular accidents (cerebral hemorrhage, subarachnoid hemorrhage, cerebral artery atherosclerosis and cerebral infarction) was compared among the three groups.

Statistical analysis: Data processing was performed using SPSS 23.0 software. Measurement data (carotid artery plaque area, carotid artery stenosis ratio, lipid levels and cognitive function) were expressed as ($\bar{\chi}\pm s$) and analyzed using t-tests. Counting data (ApoE genotype, carotid artery plaque nature, blood pressure classification, cerebrovascular accidents) were presented as n (%) and analyzed using χ^2 tests, with $p<0.05$ indicating statistical significance.

RESULTS

Comparison of general data between the observation and control groups: There was no statistically significant difference between the observation group and the control group in terms of gender, age, body mass index, smoking history and drinking history ($p>0.05$) (Table 1).

Comparison of ApoE genotypes between the observation and control groups: The proportion of ApoE4/3+E4/4 genotype in the observation group was higher than that in the

Table 1: Comparison of general data between the observation and control groups

Indicator		Observation group (n = 61)	Control group (n = 50)	Statistics	p-value
Gender [n (%)]	Male	36 (59.02)	28 (56.00)	$\chi^2 = 0.102$	0.749
	Female	25 (40.98)	22 (44.00)		
Age ($\bar{\chi}\pm$sec, years)		66.49±5.73	65.83±6.18	t = 0.583	0.561
Body mass index ($\bar{\chi}\pm$sec, kg/m^2)		26.03±2.31	25.94±2.24	t = 0.207	0.836
Smoking history [n (%)]	Yes	17 (27.87)	13 (26.00)	$\chi^2 = 0.049$	0.825
	No	44 (72.13)	37 (74.00)		
Drinking history [n (%)]	Yes	22 (36.07)	16 (32.00)	$\chi^2 = 0.202$	0.653
	No	39 (63.93)	34 (68.00)		

Measurement data (age and body mass index) were expressed as ($\bar{\chi}\pm$s) and analyzed using t-tests, Counting data (gender, smoking history, drinking history) were presented as n (%), analyzed using χ^2 tests and p>0.05 for all indicates no statistical significance

Table 2: Comparison of ApoE genotypes between the observation and control groups n (%)

Group	ApoE2/2+E3/2 genotype	ApoE3/3 genotype	ApoE4/3+E4/4 genotype
Observation group (n = 61)	7 (11.48)	38 (62.30)	16 (26.23)
Control group (n = 50)	10 (20.00)	36 (72.00)	4 (8.00)
χ^2	1.540	1.165	6.182
p	0.215	0.281	0.013

Counting data (ApoE genotypes) were presented as n (%), analyzed using χ^2 tests and p<0.05 indicates statistical significance

Table 3: Comparison of carotid artery plaque nature before and after treatment in the three groups

	Stable plaques		Unstable plaques	
Group	Before treatment	After treatment	Before treatment	After treatment
ApoE2/2+E3/2 genotype group (n = 7)	2 (28.57)	5 (71.43)	5 (71.43)	2 (28.57)
ApoE3/3 genotype group (n = 38)	10 (26.32)	29 (76.32)**###	28 (73.68)	9 (23.68)**###
ApoE4/3+E4/4 genotype group (n = 16)	3 (18.75)	6 (37.50)	13 (81.25)	10 (62.50)
χ^2	0.430	7.397	0.430	7.397
p	0.806	0.025	0.806	0.025

Compared with the ApoE4/3+E4/4 genotype group, **p<0.01 and Compared with before treatment, ###p<0.001

control group (p<0.05), there was no statistically significant difference was in the proportion of ApoE2/2+E3/2 genotype and ApoE3/3 genotype between the two groups (p>0.05) (Table 2).

Comparison of carotid artery plaque area and carotid artery stenosis ratio before and after treatment in the three groups: Before treatment, the carotid artery plaque area in the ApoE2/2+E3/2 genotype group and the ApoE3/3 genotype group was smaller than that in the ApoE4/3+E4/4 genotype group (p<0.05). After treatment, the carotid artery plaque area in the ApoE2/2+E3/2 genotype group and the ApoE3/3 genotype group was smaller than that before treatment and smaller than that in the ApoE4/3+E4/4 genotype group and the carotid artery stenosis ratio in the ApoE2/2+E3/2 genotype group and the ApoE3/3 genotype group was lower than that before treatment and lower than that in the ApoE4/3+E4/4 genotype group (p<0.05). There were no statistically significant differences in carotid artery plaque area and carotid artery stenosis ratio in the ApoE4/3+E4/4 genotype group before and after treatment (p>0.05) (Fig. 1).

Comparison of carotid artery plaque nature before and after treatment in the three groups: After treatment, the proportion of plaque stability was higher in the ApoE3/3 genotype group than in the ApoE4/3+E4/4 genotype group (p<0.05). There were no statistically significant differences in stable plaques and unstable plaques in the ApoE2/2+E3/2 genotype group and the ApoE4/3+E4/4 genotype group before and after treatment (p>0.05) (Table 3).

Comparison of blood lipid levels before and after treatment in the three groups: Before treatment, TC levels in the ApoE2/2+E3/2 genotype group and the ApoE3/3 genotype group were lower than those in the ApoE4/3+E4/4 genotype group (p<0.05). After treatment, both the ApoE2/2+E3/2 genotype and ApoE3/3 genotype groups exhibited lower TC, TG and LDL-C levels than before treatment and the levels of TC, TG and LDL-C in the ApoE2/2+E3/2 genotype and ApoE3/3 genotype groups were lower than those in the ApoE4/3+E4/4 genotype group, whereas the levels of HDL-C in the ApoE2/2+E3/2 genotype and ApoE3/3 genotype groups were higher than those in the ApoE4/3+E4/4 genotype group (p<0.05). There were no statistically significant differences in the levels of TC, TG, HDL-C and LDL-C in the ApoE4/3+E4/4 genotype group before and after treatment (p>0.05) (Fig. 2).

Comparison of blood pressure classification before and after treatment in the three groups: Before treatment, the ApoE2/2+E3/2 genotype group and the ApoE3/3 genotype

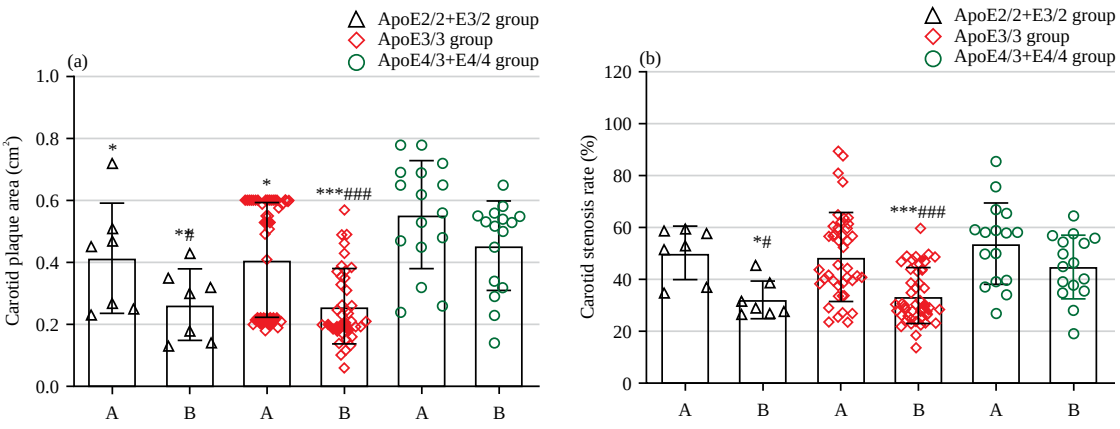

Fig. 1(a-b): Comparison of carotid artery plaque area and carotid artery stenosis ratio before and after treatment in the three groups, (a) Carotid artery plaque area and (b) Carotid artery stenosis ratio

Compared with the ApoE4/3+E4/4 genotype group, *p<0.05, **p<0.01, ***p<0.001, Compared with before treatment, #p<0.05, ##p<0.01, ###p<0.001, Abscissa: A and B represent before and after treatment, respectively

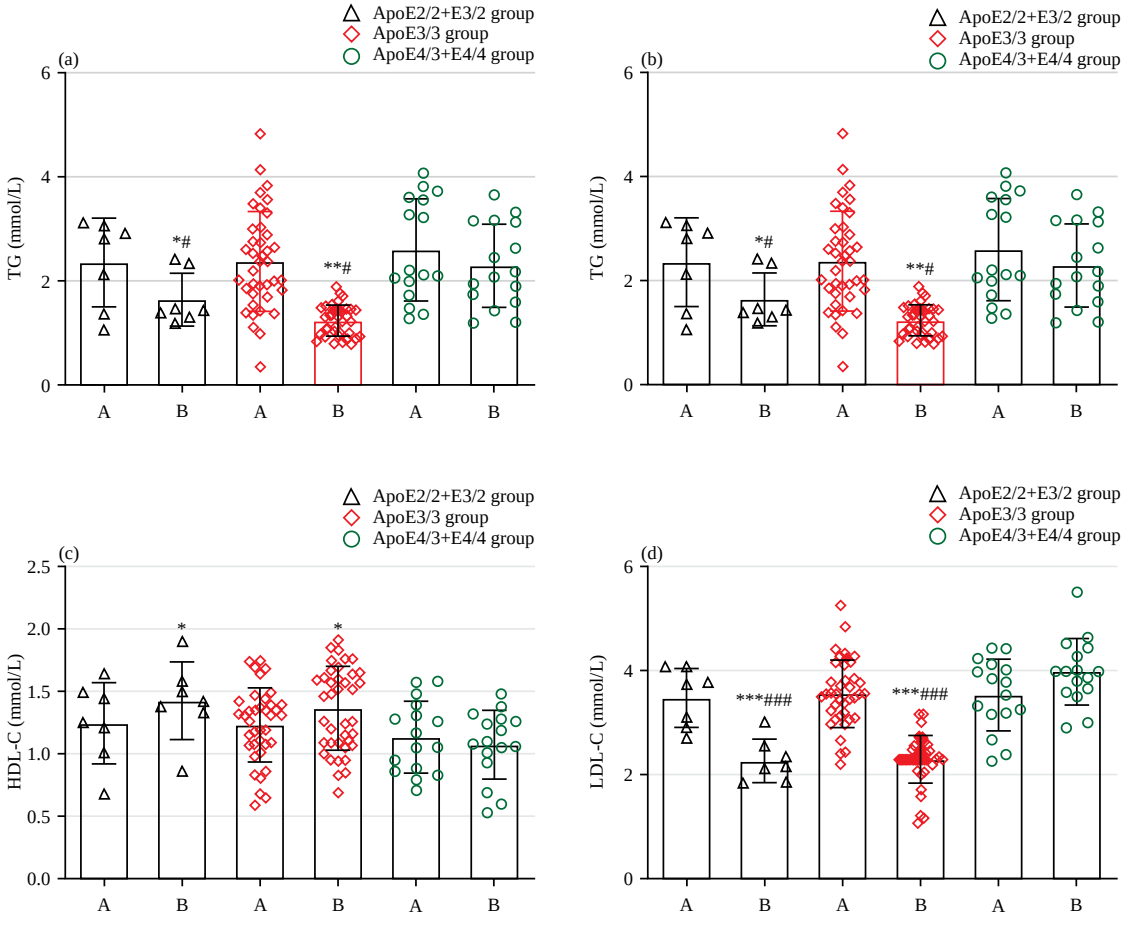

Fig. 2(a-d): Comparison of blood lipid levels before and after treatment in the three groups, (a) TC, (b) TG, (c) HDL-C and (d) LDL-C

Compared with the ApoE4/3+E4/4 genotype group, *p<0.05, **p<0.01, ***p<0.001, Compared with before treatment, #p<0.05, ##p<0.01, ###p<0.001, Abscissa: A and B represent before and after treatment, respectively

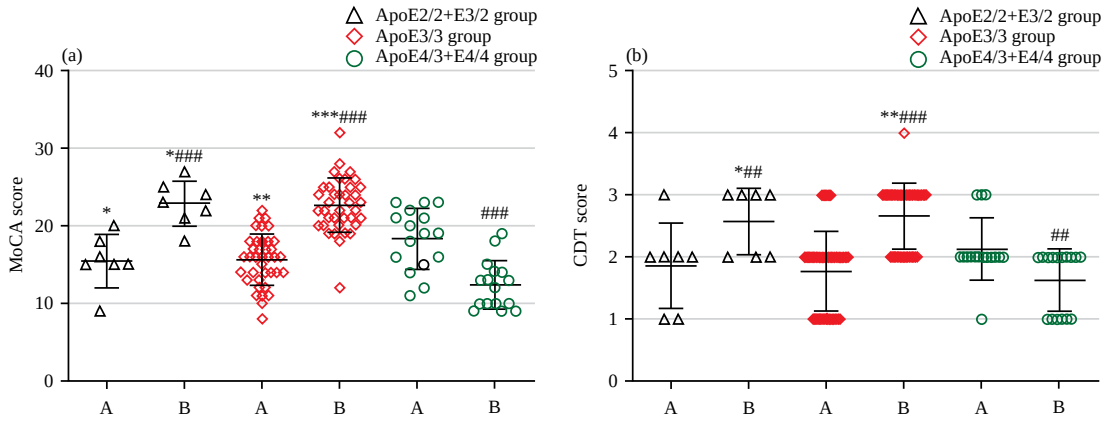

Fig. 3(a-b): Comparison of cognitive function before and after treatment in the three groups, (a) MoCA score and (b) CDT score
Compared with the ApoE4/3+E4/4 genotype group, *p<0.05, **p<0.01, ***p<0.001, Compared with before treatment, ##p<0.01, ###p<0.001, Abscissa: A and B represent before and after treatment, respectively

Table 4: Comparison of blood pressure classification before and after treatment in the three groups

Time	Group	Normal	Grade 1	Grade 2	Grade 3
Before treatment	ApoE2/2+E3/2 genotype group (n = 7)**	2 (28.57)	3 (42.86)	2 (28.57)	0
	ApoE3/3 genotype group (n = 38)**	9 (23.68)	12 (31.58)	14 (36.84)	3 (7.89)
	ApoE4/3+E4/4 genotype group (n = 16)	0	2 (12.50)	8 (50.00)	6 (37.50)
	Z	17.280			
	P	0.008			
After treatment	ApoE2/2+E3/2 genotype group (n = 7)*	5 (71.43)	2 (28.57)	0	0
	ApoE3/3 genotype group (n = 38)**##	22 (57.89)	11 (28.95)	5 (13.16)	0
	ApoE4/3+E4/4 genotype group (n = 16)#	2 (12.50)	8 (50.00)	5 (31.25)	1 (6.25)
	Z	15.739			
	P	0.015			

Compared with the ApoE4/3+E4/4 genotype group, *p<0.05, **p<0.01, Compared with before treatment, #p<0.05, ##p<0.01, Rank data were represented by n (%) and rank sum test was used and p<0.05 indicates statistical significance

Table 5 Comparison of cerebrovascular accidents in the three group's n (%)

Group	Cerebral hemorrhage	Subarachnoid hemorrhage	Cerebral artery atherosclerosis	Cerebral infarction	Total
ApoE2/2+E3/2 genotype group (n = 7)	0	0	1 (14.29)	0	1 (14.29)
ApoE3/3 genotype group (n = 38)*	1 (2.63)	0	1 (2.63)	1 (2.63)	3 (7.89)
ApoE4/3+E4/4 genotype group (n = 16)	2 (6.25)	1 (12.50)	2 (6.25)	1 (12.50)	6 (37.50)
χ^2	6.527				
P	0.038				

Compared with the ApoE4/3+E4/4 genotype group, *p<0.05, The total incidence of cerebrovascular accidents among the three groups was compared by χ^2 test and p<0.05 indicates statistical significance

group had a lower blood pressure classification than the ApoE4/3+E4/4 genotype group (p<0.05). After treatment, the blood pressure classification in the ApoE3/3 genotype group and the ApoE4/3+E4/4 genotype group was lower than before treatment, with the ApoE2/2+E3/2 genotype group being lower than the ApoE3/3 genotype group and ApoE4/3+E4/4 genotype group (p<0.05) (Table 4).

Comparison of cognitive function before and after treatment in the three groups: Before treatment, the ApoE2/2+E3/2 genotype group and the ApoE3/3 genotype group had higher MoCA and CDT scores than the ApoE4/3+E4/4 genotype group (p<0.05). After treatment, the MoCA and CDT scores in all three groups were higher than before treatment. Among them, the ApoE2/2+E3/2 genotype and ApoE3/3 genotype groups had higher MoCA and CDT scores than the ApoE4/3+E4/4 genotype group (p<0.05) (Fig. 3).

Comparison of cerebrovascular accidents in the three groups: During the treatment period, the incidence of cerebrovascular accidents was lower in the ApoE3/3 genotype

group than in the ApoE4/3+E4/4 genotype group ($p<0.05$). The incidence cerebrovascular accidents in the ApoE2/2+E3/2 genotype group exhibited no statistically significant difference compared to those in the ApoE3/3 genotype and ApoE4/3+E4/4 genotype groups ($p>0.05$) (Table 5).

DISCUSSION

Stroke is a disease influenced by multiple factors and multiple genes, with hyperlipidemia and atherosclerosis being important risk factors leading to stroke[11]. Numerous studies have shown that ApoE gene polymorphism plays a significant role in the occurrence and progression of stroke and can have a significant impact on patient prognosis[12,13]. In this study, the ApoE genotypes of stroke patients and healthy individuals undergoing physical examinations were compared and it was found that the proportion of ApoE4 genotype in the observation group was higher than that in the control group, which indicated that ApoE4 genotype might have a certain association with the occurrence of stroke. This finding is basically consistent with the results of Liping[13]. The ApoE, which contains 299 amino acids, is a glycoprotein encoded by the ApoE gene located on human chromosome 19 and is strongly associated with stroke risk factors such as hypercholesterolemia, diabetes mellitus, hypertension and coronary artery atherosclerosis[14]. In peripheral tissues, the liver is the primary site for the synthesis and secretion of ApoE, playing a crucial role in the metabolism and transport of lipids such as cholesterol and TG in the peripheral circulation, in the central nervous system, ApoE is mainly synthesized and secreted by astrocytes, binds to cell surface ApoE receptors and has a role in transporting TC in the brain and is also involved in the intercellular exchange of metabolites between glial cells and neurons[15,16]. This study compared the ApoE genotypes between stroke patients and healthy individuals undergoing medical examinations and the results showed that the proportion of ApoE4/3+E4/4 genotype in the observation group was higher than that in the control group, indicating a potential association between the ApoE4/3+E4/4 genotype and the occurrence of stroke. The 112th amino acid in the ApoE4/3+E4/4 genotype is arginine, which can selectively bind to Very Low-Density Lipoprotein Cholesterol (VLDL-C) or other lipoproteins in TG. Compared to the other two genotypes, individuals with the ApoE4/3+E4/4 genotype have a faster lipoprotein metabolism, which leads to the transfer of more cholesterol from their blood to the liver through the mediation of the ApoE gene, affecting the body's lipid levels and dyslipidemia is a critical pathological condition in the development of atherosclerosis[17]. The TG causes damage to cerebral vascular smooth muscle cells and endothelial cells through glycation, oxidation and other processes, leading to inflammation in the vascular wall and the formation of atherosclerosis, thereby involving in the pathological process of stroke[18].

Atorvastatin is a hydroxymethylglutaryl coenzyme A reductase inhibitor, which has a significant lipid-regulating effect and can also inhibit the proliferation of vascular smooth muscle cells, promote apoptosis, suppress vascular inflammation, enhance the function of vascular endothelial cells, reduce the level of lipid deposition in the vascular endothelium, reduce the number of foam cells and counteract antiplatelet aggregation, thus leading to a reduction in plaque volume and an improvement in plaque stability[19]. The results of this study showed that after treatment, the levels of TC, TG and LDL-C in the ApoE2/2+E3/2 genotype group and the ApoE3/3 genotype group were lower than those in the ApoE4/3+E4/4 genotype group, the levels of HDL-C were higher than those in the ApoE4/3+E4/4 genotype group, the carotid artery plaque area was smaller than that in the ApoE4/3+E4/4 genotype group and the carotid artery stenosis ratio was lower than that in the ApoE4/3+E4/4 genotype group and the proportion of plaque stability in the ApoE3/3 genotype group was higher than that in the ApoE4/3+E4/4 genotype group. These findings are basically consistent with the results of Chao *et al.*[20]. The results of this study showed that after treatment, the levels of TC, TG and LDL-C in the ApoE2/2+E3/2 genotype group and the ApoE3/3 genotype group were lower than those in the ApoE4/3+E4/4 genotype group and the HDL-C level was higher than that in the ApoE4/3+E4/4 genotype group, the carotid artery plaque area in the ApoE2/2+E3/2 genotype group and the ApoE3/3 genotype group was smaller than that in the ApoE4/3+E4/4 genotype group and the carotid artery stenosis ratio was lower than that in the ApoE4/3+E4/4 genotype group, the ApoE3/3 genotype group had a higher proportion of stable plaques compared to the ApoE4/3+E4/4 genotype group. These suggested that atorvastatin had a better therapeutic effect in stroke patients with ApoE2/2+E3/2 and ApoE3/3 genotypes, while stroke patients with ApoE4/3+E4/4 genotype were relatively less sensitive to atorvastatin. The reason for this may be related to the relatively poor lipid metabolism capacity associated with ApoE4/3+E4/4 genotype, which increases the difficulty of clinical treatment and affects the effectiveness of atorvastatin therapy. Cognitive impairment is a common complication in stroke patients. Due to the damage of the cerebral cortex in stroke patients, the brain remains in a state of ischemia and hypoxia for a prolonged period, leading to the necrosis of brain cells, a

decrease in the number of brain cells and an impact on the central cognitive center, which results in cognitive impairment such as memory impairment and visuospatial impairment[21]. This study observed the cognitive function of patients and the results showed that, before and after treatment, the ApoE2/2+E3/2 genotype group and ApoE3/3 genotype group had higher MoCA scores, CDT scores and blood pressure classification, compared to the ApoE4/3+E4/4 genotype group. This suggested that the ApoE4/3+E4/4 genotype may have detrimental effects on the cognitive function and blood pressure of stroke patients. The ApoE4/3+E4/4 genotype not only affects patients' cognitive function by causing lipid metabolism abnormalities, but also promotes the deposition of β-amyloid proteins, further exacerbating cognitive impairment in patients[22,23]. The ApoE4/3+E4/4 genotype leads to elevated lipid levels, which can alter vascular structure and function, increase the levels of TC, TC and LDL-C in the blood, damage vascular endothelium, disrupt vascular elasticity and subsequently raise blood pressure levels[24].

The results of this study also indicated that during the treatment period, the incidence of cerebrovascular accidents was lower in the ApoE3/3 genotype group compared to the ApoE4/3+E4/4 genotype group, suggesting that the ApoE4/3+E4/4 genotype may increase the risk of cerebrovascular accidents in stroke patients. The ApoE4/3+E4/4 genotype is involved in the clearance of VLDL-C remnants and the reverse transport of cholesterol, affecting the ability of ApoE to bind to lipid receptors, reducing lipid clearance rates and ultimately increasing the risk of cerebrovascular accidents[25]. In this regard, it is recommended that individuals carrying the ApoE4/3+E4/4 genotype pay close attention to their blood lipids and blood pressure, develop healthy lifestyle and dietary habits, ensure adequate sleep, maintain a balanced diet, engage in appropriate mental and physical activities and actively control the risk factors such as hyperlipidemia, hypertension and atherosclerosis, so as to reduce the risk of cardiovascular and cerebrovascular diseases.

CONCLUSION

Atorvastatin has a more favorable lipid-lowering effect in patients with ApoE2/2+E3/2 and ApoE3/3 genotypes compared with that in stroke patients with ApoE4/3+E4/4 genotype. Moreover, it demonstrates better effect in reducing plaque area, lowering carotid artery stenosis ratio, enhancing plaque stability, reducing blood pressure classification, improving cognitive function and reducing cerebrovascular accidents. The efficacy of lipid regulation and carotid artery plaque treatment in stroke patients may be associated with ApoE gene polymorphism. However, as this study is a retrospective analysis, the sample size was small with single source and the relationship between long-term prognosis in patients and ApoE gene polymorphism was not investigated. Therefore, future large-scale clinical studies should be conducted to further explore this matter.

SIGNIFICANCE STATEMENT

The study observed the influence of atorvastatin on carotid artery plaques and blood lipids in stroke patients with different ApoE (Apolipoprotein E) genotypes. Atorvastatin has a more favorable lipid-lowering effect in patients with ApoE2/2+E3/2 and ApoE3/3 genotypes compared with that in stroke patients with ApoE4/3+E4/4 genotype. Moreover, it demonstrates better effect in reducing plaque area, lowering carotid artery stenosis ratio, enhancing plaque stability, reducing blood pressure classification, improving cognitive function and reducing cerebrovascular accidents. The efficacy of lipid regulation and carotid artery plaque treatment in stroke patients may be associated with ApoE gene polymorphism.

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