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The SNPs rs429358 and rs7412 of APOE gene are association with cerebral infarction but not SNPs rs2306283 and rs4149056 of SLCO1B1 gene in southern Chinese Hakka population

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Abstract

Background: Apolipoprotein E (ApoE) and solute carrier organic anion transporter family member 1B1 (SLCO1B1) regulate lipid metabolism. However, the relationship between genetic polymorphisms of APOE and SLCO1B1 and cerebral infarction (CI) remains unclear.

Methods: A total of 938 CI patients and 1028 control participants were included in the study. The rs429358 and rs7412 single nucleotide polymorphisms (SNPs) in the APOE gene and rs2306283 and rs4149056 SNPs in the SLCO1B1 gene were analyzed by fluorescence polymerase chain reaction (PCR).

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Results: The genotype e3/e3 was the most common APOE genotype, with e3 being the allele with the highest frequency, followed by e4 and e2. Statistically significant differences of genotype e2/e2 (χ² = 3.866, P = 0.049), e2/e3 (χ² = 20.030, P < 0.001), e3/e4 (χ² = 16.960, P < 0.001), and e4/e4 (χ² = 4.786, P = 0.029) between CI patients and controls were detected. The SLCO1B1 genotype *1b/*1b and haplotype *1b showed the highest frequency in the study sample. There was no statistically significant difference in the frequencies of SLCO1B1 genotypes and haplotypes among CI patients comparing with controls. Moreover, e4 carriers had significantly higher low-density lipoprotein-cholesterol (LDL-C) and apolipoprotein B (Apo-B) and lower apolipoprotein A1 (Apo-A1)/Apo-B levels than e2 and e3 carriers, but e2 carriers showed lower LDL-C and Apo-B and higher Apo-A1/Apo-B than e3 and e4 carriers. Further, logistic regression analysis revealed that high LDL-C, high ApoB, smoking, hypertension and the e4 allele were risks for the presence of CI.

Conclusions: This study indicated that the APOE SNPs rs429358 and rs7412 may be associated with susceptibility to cerebral infarction in southern Chinese Hakka population.

Keywords: Apolipoprotein E, Solute carrier organic anion transporter family member 1B1, Gene polymorphism, Cerebral infarction, Relationship, Hakka
Hospital), Guangdong province, China, between September 2016 and December 2018; the sample consisted of 938 ischemic cerebral infarction patients and 1028 individuals with non-cerebral infarction as controls. CI patients’ diagnoses were verified by neurologists according to clinical symptoms and computed tomography (CT)/magnetic resonance imaging (MRI). Patients with transient ischemic attacks, cardiogenic cerebral infarctions, cerebral hemorrhage, or malignant tumors were excluded. Information recorded included age, sex, and cerebrovascular disease risk factors. A flow diagram of the study population recruitment process is illustrated in Fig. 1. Patients were recruited after being diagnosed with CI and with the consent of the patients or their family members. All control subjects were randomly selected from the Physical Examination Center of the Meizhou People’s Hospital during the same period. This retrospective case control study was approved by the Human Ethics Committees of Meizhou People’s Hospital (Clearance No.: 2016-A-29).

Plasma lipid measurements
On the second day of admission, approximately 3 ml of blood was taken from each subject, and plasma was isolated and tested promptly or store at −80 °C for further analysis. Serum samples were evaluated using the Olympus AU5400 system (Olympus Corporation, Tokyo, Japan) for TC, triglyceride (TG), LDL-C, HDL-C, apolipoprotein B (Apo-B) and apolipoprotein A1 (Apo-A1). TC, TG, LDL-C, HDL-C, Apo-A1/Apo-B analyses were carried out using cholesterol esterase/peroxidase (CHOD/PAP) enzymatic method, Glycerophosphate oxidase/peroxidase (GPO-PAP) enzymatic method, direct surfactant removal method, direct immunoinhibition method, and immunoturbidimetry method, respectively.

DNA extraction and genotyping assay
Genomic DNA was extracted from whole blood in EDTA using a QIAamp DNA Blood Mini Kit (Qiagen GmbH, North Rhine-Westphalia, Germany) according to the protocol provided. The DNA concentration was measured using a Nanodrop 2000™ Spectrophotometer (ThermoFisher Scientific, Massachusetts, USA). TaqMan probe fluorescent PCR was used for SLCO1B1 and APOE genotyping, in which different primers and probes combinations were designed for different SNP polymorphisms of the SLCO1B1 and APOE genes, and gene polymorphisms at different loci were detected through different channels in the reaction system. Polymerase chain reaction (PCR) was used to amplify the target fragments ((step 1: 37°C for 10 min; step 2: 95°C for 5 min; step 3 (amplification of 40 cycles): 95°C for 15 s and 60°C for 1 min)). The fluorescence signals, including FAM (SLCO1B1*1b 388A, SLCO1B1*5521 T, ApoE2 526C, ApoE4 388 T), VIC (SLCO1B1*1b 388G, SLCO1B1*5521C, ApoE2 526 T, ApoE4 388C) and ROX (internal standard) (Youzhiyou Medical Technology Co., Ltd., Hubei, China) were collected using a Roche LightCycler 480 II.
Statistical analysis
Data analysis was performed using SPSS statistical software version 21.0 (IBM Inc., State of New York, USA). Continuous variable data are represented by mean ± standard deviation (SD), and categorical variables are represented by percentages. Student’s t test or the Mann-Whitney U test was used for continuous data analysis. Genotype composition ratios and allele frequencies between groups were analyzed by the chi-square test. Logistic regression analysis was applied to assess the interactions between SLC01B1 and APOE polymorphisms and various factors (smoking, alcohol, hypertension, etc.) in cerebral infarction. *P* < 0.05 was considered statistically significant.

Results
Population characteristics
The 1966 individuals in this study, with ages between 20 and 99 years, consisted of 938 CI patients (581 males and 357 females) and 1028 individuals with non-CI (622 males and 406 females) as controls. As shown in Table 1, the CI patients’ average age was 65.6 ± 10.6 years, with 63.9 ± 9.9 years for males and 68.3 ± 11.2 years for females. The average age of the controls was 63.7 ± 12.4 years, with 62.9 ± 12.6 years and 64.8 ± 12.1 years for males and females, respectively. There were statistically significant differences in percentage of smokers (*P* < 0.001), prevalence of hypertension (*P* < 0.001), and prevalence of diabetes (*P* = 0.001) between the patients and controls, though there were no statistically significant differences in age, TC, HDL-C, LDL-C, Apo-A1, Apo-B, Apo-A1/Apo-B or percentage of alcohol cases. The differences in prevalence of hypertension (*P* < 0.001) and TG levels (*P* = 0.003) between female patients and female controls were also statistically significant, and prevalence of hypertension (*P* < 0.001) and TG levels (*P* = 0.009) were significant among males.

Genotype and haplotype frequencies of APOE gene
Among all subjects, the frequencies of genotypes ε3/ε3, ε3/ε4, ε2/ε3, ε2/ε4, and ε2/ε2 were 73.60, 13.33, 9.87, 1.58, 1.07, and 0.56%, respectively. The frequencies of alleles ε3, ε4 and ε2 were 85.20, 8.52, and 6.28% respectively. The genotype distributions in both the CI patients and control participants were consistent with Hardy-Weinberg equilibrium (χ² = 4.495, *P* = 0.488 and χ² = 1.855, *P* = 0.879, respectively). As the results showed, ε3/ε3 was the most common APOE genotype, and ε3 was the allele with the highest frequency, followed by ε4 and ε2 (Table 2).

There were statistically significant differences in genotype ε2/ε2 (χ² = 3.866, *P* = 0.049), ε2/ε3 (χ² = 20.030, *P* < 0.001), ε3/ε4 (χ² = 16.960, *P* < 0.001), and ε4/ε4 (χ² = 4.786, *P* = 0.029) in the patients compared with the controls. The frequencies of genotypes ε2/ε3 (χ² = 14.579, *P* < 0.001) and ε3/ε4 (χ² = 15.177, *P* < 0.001) between male patients and male controls showed statistically significant differences; in contrast, a significant difference only in genotype ε2/ε3 (χ² = 5.744, *P* = 0.017) was detected among females (Patients vs Controls = 6.16% vs

Table 1 Clinical characteristics of males and females in cerebral infarction patients and control participants

|                     | Total (n = 1966) | Male (n = 1203) | Female (n = 763) |
|---------------------|-----------------|-----------------|-----------------|
| **No. of subjects** | 938             | 1028            | 581             |
| Age, y              | 65.5 ± 10.6     | 63.7 ± 12.4     | 68.3 ± 11.2     |
| Smokers, n(%)       | 258 (27.5%)     | 224 (21.8%)     | 256 (44.1%)     |
| Alcohol, n(%)       | 40 (4.3%)       | 39 (3.8%)       | 40 (6.9%)       |
| Hypertension, n(%)  | 663 (70.7%)     | 505 (49.1%)     | 257 (72.0%)     |
| TG, mmol/L          | 2.145 ± 2.388   | 1.798 ± 1.443   | 2.171 ± 2.101   |
| HDL-C, mmol/L       | 5.114 ± 1.398   | 5.047 ± 1.281   | 5.276 ± 1.299   |
| LDL-C, mmol/L       | 1.279 ± 0.373   | 1.271 ± 0.330   | 1.355 ± 0.368   |
| Apo-A1, g/L         | 2.924 ± 0.902   | 2.864 ± 0.948   | 2.959 ± 0.890   |
| Apo-B, g/L          | 1.142 ± 0.291   | 1.153 ± 0.333   | 1.215 ± 0.322   |
| Apo-A1/Apo-B        | 1.359 ± 0.512   | 1.404 ± 0.611   | 1.429 ± 0.527   |

Values for age expressed as mean ± SD
TG triglycerides
TC total cholesterol
HDL-C high-density lipoprotein-cholesterol
LDL-C low-density lipoprotein-cholesterol
Apo-A1 apolipoprotein A1
Apo-B apolipoprotein B
The frequencies of allele $ɛ_2$ ($\chi^2 = 18.682, P < 0.001$) and $ɛ_4$ ($\chi^2 = 25.516, P < 0.001$) showed statistically significant differences in the patients compared with controls, including between male patients and male controls and between female patients and female controls, respectively (Table 2).

### Genotype and haplotype frequencies of SLCO1B1 gene

The frequencies of genotypes $*1b/*1b$, $*1a/*1b$, $*1b/*15$, $*1a/*15$, $*1a/*1a$, $*15/*15$, and $*1a/*5$ were 41.40, 32.50, 13.48, 5.95, 5.44, 1.17, and 0.05%, respectively, in all subjects. The corresponding frequencies in the CI patient group were 38.70, 33.69, 13.75, 6.72, 5.86, 1.17, and 0% in the control group. The genotype distributions in both the CI patients and control participants were consistent with Hardy-Weinberg equilibrium ($\chi^2 = 1.661, P = 0.962$ and $\chi^2 = 0.514, P = 0.992$, respectively). There was no statistically significant difference in the frequencies of these genotypes in the patients compared with the controls.

Four haplotypes of the two SNPs of SLCO1B1 were analyzed. The $*1b$ (388G-521 T) haplotype (64.39%) presented the highest frequency, followed by haplotype $*1a$ (388A-521 T) (24.69%), $*15$ (388G-521C) (10.89%) and $*5$ (388A-521C) (0.03%) haplotypes. The frequencies of SLCO1B1 haplotypes between male patients and male controls and between female patients and female controls showed no statistically significant differences (Table 3).

### Relationships between serum lipid level and APOE allele and logistic regression analysis of the risk of $ɛ_4$ allele for CI

Relationships between $APOE$ alleles ($ɛ2$, $ɛ3$, and $ɛ4$) and serum lipid levels were analyzed. Subjects with the $APOE$ $ɛ2/ɛ4$ genotype ($n = 31$) were excluded because $ɛ2$ and $ɛ4$ alleles play opposing roles in lipid metabolism.

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**Table 2** Genotypes and allele distribution of $APOE$ gene in cerebral infarction patients and control participants in total and according to gender

| Genotypes | $ɛ2/ɛ2$ | $ɛ2/ɛ3$ | $ɛ2/ɛ4$ | $ɛ3/ɛ3$ | $ɛ3/ɛ4$ | $ɛ4/ɛ4$ |
|-----------|---------|---------|---------|---------|---------|---------|
| All subjects | 11 (0.56%) | 194 (9.87%) | 31 (1.58%) | 1447 (73.60%) | 262 (13.33%) | 21 (1.07%) |
| Patients ($n = 938$) | 2 (0.21%) | 63 (6.72%) | 18 (1.92%) | 684 (72.92%) | 156 (16.63%) | 15 (1.60%) |
| Controls ($n = 1028$) | 9 (0.88%) | 131 (12.74%) | 13 (1.26%) | 763 (74.22%) | 106 (10.31%) | 6 (0.58%) |
| P values (Patients vs controls) | 0.049 | < 0.001 | 0.279 | 0.513 | < 0.001 | 0.029 |

| Alleles | $ɛ2$ | $ɛ3$ | $ɛ4$ |
|---------|-----|-----|-----|
| All subjects ($n = 3932$) | 247 (6.28%) | 3350 (85.20%) | 335 (8.52%) |
| Patients ($n = 1876$) | 85 (4.53%) | 1587 (84.59%) | 204 (10.87%) |
| Controls ($n = 2056$) | 162 (7.88%) | 1763 (85.75%) | 131 (6.37%) |
| P values (Patients vs controls) | < 0.001 | 0.309 | < 0.001 |

| Numbers in parentheses are percentages |

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The frequencies of SLCO1B1 genotypes between male patients and male controls were not significantly different, nor were those in the female subjects (Table 3).
Table 3 Genotypes and allele distribution of SLCO1B1 gene in cerebral infarction patients and control participants in total and according to gender

| Genotypes   | *15/*15 | *1a/*15 | *1a/*1a | *1a/*1b | *1a/*5 | *1b/*15 | *1b/*1b |
|-------------|---------|---------|---------|---------|--------|---------|---------|
| All subjects| 23 (1.17%) | 117 (5.95%) | 107 (5.44%) | 639 (32.50%) | 1 (0.05%) | 265 (13.48%) | 814 (41.40%) |
| Patients (n= 938) | 11 (1.17%) | 63 (6.72%) | 55 (5.86%) | 316 (33.69%) | 1 (0.11%) | 129 (13.75%) | 363 (38.70%) |
| Controls (n= 1028) | 12 (1.17%) | 54 (5.25%) | 52 (5.06%) | 323 (31.42%) | 0 (0) | 136 (13.23%) | 451 (43.87%) |
| P values (Patients vs controls) | 0.991 | 0.171 | 0.432 | 0.283 | 0.477 | 0.734 | 0.020 |

Males

| Genotypes   | *15 | *5 | *1a | *1b |
|-------------|-----|----|-----|-----|
| All subjects (n= 3932) | 428 (10.89%) | 1 (0.03%) | 971 (24.69%) | 2532 (64.39%) |
| Patients (n= 1876) | 214 (11.41%) | 1 (0.05%) | 490 (26.12%) | 716 (62.42%) |
| Controls (n= 2056) | 214 (10.41%) | 0 (0) | 481 (23.39%) | 1361 (66.20%) |
| P values (Patients vs controls) | 0.315 | 0.477 | 0.048 | 0.014 |

Females

| Genotypes   | *15 | *5 | *1a | *1b |
|-------------|-----|----|-----|-----|
| All subjects (n= 3932) | 428 (10.89%) | 1 (0.03%) | 971 (24.69%) | 2532 (64.39%) |
| Patients (n= 1876) | 135 (11.62%) | 1 (0.09%) | 310 (26.68%) | 716 (62.42%) |
| Controls (n= 2056) | 143 (11.50%) | 0 (0) | 296 (23.79%) | 805 (64.71%) |
| P values (Patients vs controls) | 0.129 | – | 0.267 | 0.051 |

Numbers in parentheses are percentages

this study, ε4 carriers had significantly higher LDL-C and Apo-B and lower Apo-A1/Apo-B levels than ε2 and ε3 carriers, but ε2 carriers showed lower LDL-C and Apo-B and higher Apo-A1/Apo-B than ε3 and ε4 carriers. There were no significant impacts of APOE polymorphism on the TG, TC, HDL-C and Apo-A1 levels (Table 4).

Logistic regression analysis was performed to determine independent predictors for CI (Table 5), and the results indicated significantly higher risks of CI in the

Table 4 Relationships between serum lipid level and APOE allele in cerebral infarction patients and control participants

| Serum lipid level | Cerebral infarction patients (n = 920) | Controls (n = 1015) |
|-------------------|----------------------------------------|---------------------|
|                   | ε2(n = 65) | ε3(n = 684) | ε4(n = 171) | P values | ε2(n = 140) | ε3(n = 763) | ε4(n = 112) | P values |
| TG, mmol/L         | 2.064 ± 1.986 | 1.787 ± 1.434 | 1.773 ± 1.285 | 0.324 | 2.449 ± 2.917 | 2.069 ± 2.208 | 2.310 ± 2.879 | 0.170 |
| TC, mmol/L         | 4.893 ± 1.245 | 5.048 ± 1.272 | 5.093 ± 1.320 | 0.560 | 5.170 ± 1.476 | 5.096 ± 1.351 | 5.242 ± 1.558 | 0.534 |
| HDL-C, mmol/L      | 1.302 ± 0.336 | 1.277 ± 0.326 | 1.234 ± 0.336 | 0.225 | 1.281 ± 0.393 | 1.284 ± 0.367 | 1.256 ± 0.407 | 0.762 |
| LDL-C, mmol/L      | 2.584 ± 0.766 | 2.925 ± 0.894 | 3.031 ± 0.922 | 0.003 | 2.734 ± 0.971 | 2.866 ± 0.917 | 3.061 ± 1.064 | 0.023 |
| Apo-A1, g/L        | 1.179 ± 0.327 | 1.150 ± 0.284 | 1.098 ± 0.307 | 0.064 | 1.174 ± 0.315 | 1.161 ± 0.344 | 1.082 ± 0.282 | 0.050 |
| Apo-B, g/L         | 0.802 ± 0.222 | 0.905 ± 0.263 | 0.934 ± 0.276 | 0.002 | 0.858 ± 0.312 | 0.904 ± 0.286 | 0.955 ± 0.347 | 0.035 |
| Apo-A1/Apo-B       | 1.605 ± 0.739 | 1.366 ± 0.501 | 1.244 ± 0.409 | < 0.001 | 1.529 ± 0.643 | 1.401 ± 0.616 | 1.260 ± 0.506 | 0.002 |

P value shows the differences compared between groups (ε2, ε3, ε4)

*P < 0.05 versus corresponding ε3 group

1P < 0.05 versus corresponding ε4 group
presence of high LDL-C (OR 1.524, 95% CI 1.092–2.100, \( P = 0.013 \)), and high ApoB (OR 3.046, 95% CI 1.188–7.809, \( P = 0.020 \)), smoking (OR 1.459, 95% CI 1.166–1.825, \( P = 0.001 \)), hypertension (OR 2.599, 95% CI 2.136–3.164, \( P < 0.001 \)), and the \( \varepsilon 4 \) allele (OR 1.822, 95% CI 1.390–2.388, \( P < 0.001 \)).

Discussion

Stroke is one of the most common causes of death and long-term disability worldwide [20]. Moreover, the stroke burden in China is expected to increase further due to an aging population and a continuing high prevalence of risk factors such as hyperlipidemia [21]. Cerebral infarction, the most common type of stroke, is known as localized brain tissue necrosis or cerebral ischemia caused by cerebral blood disorders, resulting from a blockage of the blood vessels that supply blood to the brain [22–25]. Many studies have shown that the etiology of cerebral infarction is complex, including genetic and environmental factors [26, 27]. The relationship between genetic polymorphisms of APOE and SLCO1B1 and CI were analyzed in this study.

The APOE gene encodes a major lipid-binding protein that serves as a cholesterol carrier [28]. Atherosclerosis is an important pathophysiological basis of CI. APOE gene polymorphisms have been shown to be associated with atherosclerosis [29, 30]. However, the results of previous studies on the relationship between APOE gene polymorphisms and CI are not very consistent. For example, Yan et al. [31] indicated that the \( \varepsilon 4 \) allele was associated with TC and LDL-C and believed that \( \varepsilon 4 \) was a genetic marker of CI. Liu et al. [32] confirmed by MRI scanning that brain injury was aggravated in \( \varepsilon 4 \) allele carriers CI patients after stroke. However, Wang et al. [33] proposed that APOE gene polymorphism did not correlate significantly with CI. Based on the results of the present study, there were statistically significant differences in genotypes \( \varepsilon 2/\varepsilon 2 \), \( \varepsilon 2/\varepsilon 3 \), \( \varepsilon 3/\varepsilon 4 \), and \( \varepsilon 4/\varepsilon 4 \) among CI patients compared with controls. \( \varepsilon 4 \) carriers had significantly higher LDL-C and Apo-B and lower Apo-A1/Apo-B levels than the other groups, while \( \varepsilon 2 \) carriers showed lower LDL-C and Apo-B and higher Apo-A1/Apo-B. Logistic regression analysis indicated that participants with \( \varepsilon 4 \) allele had a significantly higher risk of CI.

APOE gene polymorphisms are important determinants of blood lipid levels, and it may be the reason for the correlation between APOE gene polymorphisms and CI [34]. The APOE \( \varepsilon 4 \) allele is associated with higher serum lipid levels, whereas the \( \varepsilon 2 \) allele is associated with the lower levels [35]. In addition, the presence of \( \varepsilon 2 \) has been associated with lower LDL-C level but with no influence on HDL-C level [34]. Another study showed that the C allele of SNP rs2910164 of the miR-146a gene is a risk factor for atherosclerotic cerebral infarction (ACI) and that APOE \( \varepsilon 4 \) may enhance ACI susceptibility by reducing miR-146a expression [36].

Furthermore, this study found \( \varepsilon 3 \) to be the most common allele of the APOE gene, accounting for 85.20%, which was consistent with most previous studies [37, 38]. This indicates that the APOE allele frequencies in the Meizhou area are similar to those of the Chinese-Northeast [39], Chinese-Jiangsu Han [40] and Chinese-Kunming Han [41] areas, though the \( \varepsilon 4 \) allele frequency in Meizhou is lower than that in Shanghai [42].

The frequencies of SLCO1B1 genotypes \( ^{1} b/^{1} b \), \( ^{1} a/^{1} b \), \( ^{1} b/^{1} 5 \), \( ^{1} a/^{1} 5 \), \( ^{1} a/^{1} a \), \( ^{1} 5/^{1} 5 \), and \( ^{1} a/^{5} \) were 41.10, 32.79, 13.03, 5.93, 5.88, 1.22, and 0.05% respectively. The frequency of SLCO1B1 haplotype \( ^{1} b \) revealed its predominance, accounting for 64.01%, followed by \( ^{1} a (25.27\%) , ^{1} 5 (10.69\%) \) and \( ^{5} (0.03\%) \). These results are in agreement with previous studies [43–46]. Greek, German, Indian (North) and Macedonian populations exhibit relatively lower rates of \( ^{1} b \) (less than 50%), whereas Thailand and Chinese populations show higher rates, generally above 60–70%. In contrast, the allele frequency of haplotypes \( ^{1} 5 \) and \( ^{5} \) displayed little difference. In this study, there were no statistically significant differences in the frequencies of SLCO1B1 genotypes and haplotypes between CI patients and control participants. In addition, no information has been published about relationship between cerebral infarction and SLCO1B1 gene polymorphisms in other populations.

Study strengths and limitations

There are several strengths of this study. This is the first study about the relationship of cerebral infarction and SLCO1B1 gene polymorphism. The clinical characteristics, lipid levels and APOE gene polymorphism indicators were included into the analysis to exclude the influence of related confounding factors on the results. There are some limitations to this study that should be noted. First, CI is a kind of multifactorial diseases caused by genetic and environmental factors. As a retrospective case control analysis, the limitations of the original data included in this study constrained assessment of potential gene-environment interactions. Second, the sample

### Table 5 Logistic regression analysis of risks of cerebral infarction in southern Chinese Hakka population

| Variables | \( \beta \) | \( P \) value | Adjusted OR (95% CI) |
|-----------|-----------|-------------|---------------------|
| LDL-C     | 0.415     | 0.013       | 1.092–2.100         |
| ApoB      | 1.114     | 0.020       | 1.188–7.809         |
| Smoking   | 0.378     | 0.001       | 1.166–1.825         |
| Hypertension | 0.955 | < 0.001     | 2.136–3.164         |
| \( \varepsilon 4 \) carrier | 0.600 | < 0.001     | 1.390–2.388         |

OR odds ratio, CI confidence interval, LDL-C low-density lipoprotein-cholesterol
size of this study is not very large, which may lead to some deviations in the results. Therefore, further study with a larger sample size is one of the next tasks. Third, the study was carried out only in Hakka Chinese people, and whether the same is true for other populations needs further investigation.

Conclusions
In conclusion, the present study suggests that the SNPs rs429358 and rs7412 of the APOE gene but not SNPs rs2306283 and rs4149056 of the SLCO1B1 gene are associated with ischemic cerebral infarction in the southern Chinese Hakka population. Therefore, APOE genotyping may be useful to identify individuals at risk of CI and provide guidance for the institution of individualized preventive strategies and therapies for patients.

Abbreviations
APOE: apolipoprotein E; SLCO1B1: solute carrier organic anion transporter family member 1B1; TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; Apo-A1: apolipoprotein A1; Apo-B: apolipoprotein B

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Authors’ contributions
Zhixiong Zhong and Heming Wu designed the study. Heming Wu, Qingyan Huang and Hailing Wu collected clinical data. Heming Wu, Qingyan Huang and Zhikang Yu analyzed the data. Heming Wu prepared the manuscript. All authors were responsible for critical revisions, and all authors read and approved the final version of this work.

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Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate
The study was approved by the Ethics Committee of Medicine, Meizhou People’s Hospital (Huangtang Hospital), Meizhou Academy of Medical Sciences, Meizhou Hospital Affiliated to Sun Yat-sen University.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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