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ORIGINAL RESEARCH

Association of Aldehyde Dehydrogenase 2 Gene Polymorphism with Myocardial Infarction

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Objective: This study explored the correlation between myocardial infarction (MI) and the Glu504Lys polymorphism in the aldehyde dehydrogenase 2 (ALDH2) gene in the Qingyuan area.

Methods: The Glu504Lys polymorphism of the ALDH2 gene was analyzed using the polymerase chain reaction and deoxyribonucleic acid microarray analysis for 468 patients diagnosed with MI for the first time and 132 healthy subjects.

Results: There was a significant difference in the distribution of the ALDH2 genotype between the MI group and the control group ($P = 0.0492$), but there was no significant difference in allele frequency between the two groups ($P = 0.1363$). The clinical data showed that there were statistically significant differences ($P < 0.05$) in the two groups' gender and age distributions, rates of diabetes and hypertension, levels of alcohol and tobacco use, serological levels of heart markers, blood lipids and glucose. The subgroup analysis of ALDH2 genotypes found that alcohol consumption, high levels of myoglobin, and low levels of high-density lipoprotein cholesterol were significantly associated with a higher incidence of MI ($P < 0.05$). After adjusting for gender, hypertension, diabetes, and other related influencing factors, logistic regression analysis showed that the ALDH2 genotype GA/AA was an independent risk factor for MI ($P < 0.05$, OR = 1.479, 95% CI = 1.003–2.179).

Conclusion: The presence of risk alleles with the genetic effect (ALDH2 genotype GA/AA) is an independent risk factor for MI.

Keywords: myocardial infarction, aldehyde dehydrogenase 2, polymorphism

Introduction

Coronary arteriosclerosis heart disease (CAD) is induced by many factors, and its morbidity and fatality are increasing worldwide, with a particularly high rate of increase in young people. Morbidity and fatality of myocardial infarction (MI) in patients with heart and cerebrovascular diseases are both high, and the impact of MI on human health is clear.[1] One of the causes of CAD is oxidative damage caused by lipid peroxidation. The most representative of the aldehydes produced in this reaction is 4-hydroxynonenal (4-HNE), which is very stable and can easily spread to other cells, where it causes further tissue damage.[2] The Glu504Lys polymorphism is a very important single-nucleotide polymorphism of mitochondrial acetaldehyde dehydrogenase 2 (ALDH2), and it is a genetic risk marker for acute coronary syndrome.[3] ALDH2 has a higher affinity for acetaldehyde than other ALDH isozymes do, and it is the main enzyme for scavenging 4-HNE. ALDH2 can effectively reduce the cytotoxic effect of aldehydes produced in oxidative stress and protect the myocardium.[4,5] The ALDH2 homozygous genotype AA is

associated with susceptibility to CAD, as demonstrated by the results of a whole genome association study carried out in Japan in 2012.[6] The allele frequency distribution of the ALDH2 Glu504Lys polymorphism is significantly different across different races, nationalities and regions[7]. The purpose of this study is to explore the association of ALDH2 polymorphism with the occurrence of MI in Qingyuan, Guangdong Province, in order to better understand the genetic susceptibility factors for MI and guide the prevention and delay of MI.

Methods

Study Subjects

The MI group in this study comprised 468 patients diagnosed with myocardial infarction for the first time who were treated in the Department of Cardiovascular Medicine of the Sixth Hospital affiliated to the Guangzhou Medical University (Qingyuan City People's Hospital) from 2017 to 2019. The male to female ratio of the MI group was 337:131 and the age range was 25–96 years. Of the 468 patients in the MI group, 347 were diagnosed with acute non–ST-segment elevation cardiac infarction and 121 were diagnosed with acute ST-segment elevation cardiac infarction. The study also included a control group comprising 132 medical examiners who were present at the hospital during the same time period, with a male to female ratio of 27:17 and an age range of 19–95 years. The exclusion criteria for the control group were: (1) hepatic and renal insufficiency and gastrointestinal disease, (2) no ALDH2 gene test, and (3) a definite previous history of MI. Clinical baseline information (sex, age, and personal history) was collected for all study subjects. Three generations of the subjects' ancestors were determined to be Han Chinese who were born or lived in Qingyuan and the surrounding areas. This study was conducted in accordance with the declaration of Helsinki and approved by the Ethics Committee of the Sixth Affiliated Hospital of Guangzhou Medical University. Written informed consent was obtained from all participants.

Reagents and Instruments

The study used the ALDH2 (Glu504Lys) gene detection kit from Shanghai BaiO Technology Co., Ltd. (Shanghai, China) and the DP318 blood genomic deoxyribonucleic acid (DNA) extraction kit from Tiangen Biotech Co., Ltd. (Beijing, China). The main instruments included the LabAid 824 nucleic acid extraction system (Zeesan Biotech Co., Ltd., Fujian, China), the NanoDrop2000 UV-Vis spectrophotometer (Thermo Fisher Scientific Inc., Waltham, MA, USA), and Life Express nucleic acid amplifiers. Other equipment included the BaiO BR-526-24 fully automated hybridizer, the BaiO BE-2.0 biochip reader, and the BaiO Array Doctor Version 2.0 gene chip image analysis software (Shanghai BaiO Technology Co., Ltd., Shanghai, China).

Research Methodology

(1) Diagnostic Criteria

Myocardial infarction: Coronary angiography examination revealed at least one organic coronary stenosis of more than 50% of the main coronary artery or its main branches. Clinical presentation and electrocardiographic changes met the diagnostic criteria of the fourth universal definition of myocardial infarction.

(2) Blood Collection and Sample DNA Preparation

Samples of 1–2 mL of venous blood from each subject were collected in anticoagulated tubes containing ethylenediaminetetraacetic acid and stored at 4°C for up to one week. The genomic DNA was extracted from the whole blood using the DP318 blood genomic DNA extraction kit, and a 1 μL DNA sample was analyzed for concentration and purity by UV-Vis spectrophotometer. A DNA sample met the detection criteria if the DNA concentration was 10–60 ng/L, a significant absorption peak was exhibited at OD_{260}, and the ratio of OD_{260}/OD_{280} was 1.5–2.0. A TE buffer solution of pH 7.6 was used as a diluent for samples with a higher DNA concentration. DNA samples were stored at 4°C for one week or −20°C for one month, and they were not reused after three repeated freeze–thaw cycles.

(3) PCR Amplification and Hybridization

After the PCR amplification solution had been prepared and the ALDH2 amplification reagent thawed at room temperature, the two were centrifuged at low speed. After centrifugation and mixing at low speed, the PCR amplification reaction system had a volume of 25 μL. The reaction conditions were set for the nucleic acid amplifiers and the product was removed after amplification and stored at 4°C. The immunochromogenic reagent was removed to prepare the antibody solution (stored at −20°C), and the amplification product was added to the hybridization buffer to make the hybridization solution

(stored at 4°C). The hybridization program was set up following the instructions for the automatic hybridization instrument, and the gene chip was removed and labeled. Together with the pre-installed washing solution, the hybridization solution, antibody solution, and chromogenic reagent were placed in their corresponding positions in an octuple hybridization test tube. The hybridization test tube and gene chip were placed in the automatic hybridization instrument. The amplification product and the ALDH2 gene detection probe initiated the biotin-labeled hybridization. Because the enzyme chromatography reaction produced different hybridization signals, gene chip image analysis software was used to scan the chip, analyze the data, and return the results of the genotype test.[8]

(4) Statistical Analysis

Sample analysis calculation was performed using SPSS software (IBM, Armonk, NY, USA). Where counting data were presented as percentages, measurement data that conformed to a normal distribution are presented as mean ± standard deviation; otherwise, data are presented as medians and quartiles [M (Q1, Q3)]. The MI group and the control group were compared using the independent sample *t*-test or the Mann–Whitney non-parametric test. The distributions of ALDH2 genotypes and allele frequencies were tested by the row-list and the association analysis was performed by multifactorial logistic regression. The chi-square test was used to verify whether the ALDH2 genotype distribution in the population complied with the Hardy–Weinberg law. A difference of $P < 0.05$ was considered statistically significant.

Results

(1) Hardy–Weinberg Equilibrium

Based on the analysis of the collected ALDH2 genotypes of the Han population in Qingyuan, the actual frequencies of GG, GA, and AA in the MI group were 203, 215, and 50, respectively, while the frequencies of GG, GA, and AA in the control group were 70, 48, and 14, respectively. The actual frequency in each group was compared with the theoretical frequency using the Hardy–Weinberg equilibrium (HWE) test. The analysis of the MI group found $\chi^2 = 0.194$ and $P = 0.907$, and the analysis of the control group found $\chi^2 = 0.779$ and $P = 0.678$. The actual and theoretical frequencies of the two groups' ALDH2 genotypes matched well, and the genotypic distributions were in accordance with HWE ($P > 0.05$), indicating that the subjects in both groups were regionally representative. (Table 1).

(2) Distribution of ALDH2 Genotype and Allele Frequencies

The distribution of the ALDH2 genotypes and the allele frequencies in the MI group and the control group were analyzed by DNA microarray; the results are shown in Table 2. The proportions of GG, GA and AA genotypes were 43.4%, 45.9%, and 10.7%, respectively, in the MI group, and they were 53.0%, 36.4%, and 10.6%, respectively, in the control group. The G and A allele frequencies were 66.3% and 33.7%, respectively, in the MI group, and 71.2% and 28.8%, respectively, in the control group. The A allele was mainly expressed as the GA genotype of the ALDH2 gene in both the MI and control groups, which suggests that the A allele is mainly present in the GA heterozygous type in the Qingyuan population. Because the chi-square test showed no significant difference between GA and AA genotypes ($\chi^2 = 0.4400$, $P = 0.5071$), the ALDH2 genotypes were divided into GG and GA/AA genotypes. When the MI and control groups were compared, there was found to be a statistically significant difference in the distribution of the GG and GA/AA genotypes of ALDH2 ($\chi^2 = 3.8699$, $P = 0.0492$).

(3) Comparison of Clinical Baseline Data

According to the results of the analysis, the MI group and the control group differed significantly ($P < 0.05$) in terms of their gender and age distributions, rates of hypertension and diabetes, levels of tobacco and alcohol use, and serum levels of glucose; myocardial injury markers (cardiac troponin I and myoglobin); myocardial enzymes (lactate dehydrogenase, creatine kinase, and

Table 1 Equilibrium Test of ALDH2 Genotype Polymorphisms

Group	n	Actual Frequency			Theoretical Frequency			χ^2	*P*
		GG	GA	AA	GG	GA	AA		
MI	468	203	215	50	206	209	53	0.194	0.907
Control	132	70	48	14	67	54	11	0.779	0.678

Table 2 Distribution of ALDH2 Genotype and Allele Frequencies

ALDH2	MI	Control	χ^2	*p* value
Genotype				
GG	203 (43.4)	70 (53.0)	3.8699	0.0492
GA/AA	265 (56.6)	62 (47.0)		
Allele				
G	621 (66.3)	188 (71.2)	2.2196	0.1363
A	315 (33.7)	76 (28.8)		

creatine kinase-MB); and blood lipids (total cholesterol), triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol). All of the risk factors—the percentage of men; rates of hypertension and diabetes; levels of tobacco and alcohol use; and levels of myocardial damage indicators, myocardial enzymes, TC, LDL-C, and glucose—were significantly higher in the MI group than in the control group ($P < 0.05$), while the age distribution was significantly lower in the MI group than in the control group ($P < 0.01$) There was no statistically significant difference in the TG and HDL-C levels of the MI and control groups ($P > 0.05$). (Table 3).

(4) Subgroup Analysis of ALDH2 Genotypes

All subjects were classified into the mutant group (GA and AA type) or the GG group based on the presence of the A allele. Subgroup analysis was then used to analyze the relevant risk factors, which included male gender, age, hypertension, diabetes, tobacco use, alcohol use, serum levels of myocardial injury markers and glucose, and dyslipidemia index. The subgroup analysis found that the distribution of ALDH2 genotype was statistically significant ($P < 0.05$) among subjects who drank alcohol, had evidence of myocardial injury (Mb >140 μg/L), or had low levels of HDL-cholesterol (HDL-C ≤1.74 mmol/L); in these groups, the incidence of MI was significantly different between those with ALDH2 genotype GA+AA and those with GG, suggesting that alcohol consumption, elevated Mb levels and reduced HDL-C levels can cause an increased risk of MI; this may indicate that alcohol consumption, high Mb levels, and low HDL-C levels can increase the risk of MI. There was no statistical significance in the ALDH2 genotype distribution among the subjects when grouped by the other factors ($P > 0.05$). (Table 4).

(5) Multifactorial Logistic Regression Analysis

According to the study of Bellia et al, metabolic syndrome is related to cardiovascular disease, and blood glucose, blood pressure and blood lipids are important influencing factors of metabolic syndrome. Therefore, history of hypertension, history of diabetes, TC, TG, HDL-C, LDL-C and GLU and other common risk factors were included

Table 3 Comparison of Clinical Baseline Data in MI and Control Groups

	MI (n=468)	Control (n=132)	*p* value
Male (%)	337 (72.0)	81 (61.4)	0.019
Age (year)	63.98±12.33	67.31±14.52	0.008
Hypertension (%)	234 (50.0)	43 (32.6)	0.000
Diabetes (%)	98 (20.9)	14 (10.6)	0.007
Smoking (%)	243 (51.9)	45 (34.1)	0.000
Drinking (%)	78 (16.7)	35 (26.5)	0.011
cTnI (μg/L)	30.78 (1.35,50.00)	0.10 (0.01,0.85)	0.000
Mb (μg/L)	293.40 (63.50, 1200.0)	55.60 (34.65,93.30)	0.000
LDH (U/L)	431.50 (241.25, 808.75)	228.50 (182.50, 291.00)	0.000
CK (U/L)	786.00 (161.00, 2527.00)	95.00 (60.00, 175.75)	0.000
CK-MB (U/L)	96.50 (25.00, 220.50)	19.50 (14.00,25.00)	0.000
TC (mmol/L)	4.56 (3.81,5.27)	4.19 (3.29,5.21)	0.008
TG (mmol/L)	1.33 (0.99,1.84)	1.18 (0.87,1.88)	0.104
HDL-C (mmol/L)	1.04 (0.88,1.29)	1.07 (0.83,1.31)	0.830
LDL-C (mmol/L)	3.08 (2.32,3.75)	2.64 (1.93,3.42)	0.000
GLU (mmol/L)	6.36 (5.50,8.05)	5.90 (5.27,6.76)	0.000

Abbreviations: cTnI, cardiac troponin I; Mb, myoglobin; LDL-C, low-density lipoprotein cholesterol; CK, creatine kinase; CK-MB, Creatine Kinase Isoenzyme-MB; TC, total cholesterol; TG, Triglyceride; HDL-C, high-density lipoprotein cholesterol; GLU, glucose.

Table 4 Subgroup Analysis of ALDH2 Genotypes in Two Groups [n (%)]

	GA+AA type		GG Type		*P* value
	MI	Control	MI	Control	
Gender					
Male	190 (56.4)	40 (49.4)	147 (43.6)	41 (50.6)	0.2557
Female	75 (57.3)	22 (43.1)	56 (42.7)	29 (56.9)	0.0865
Age (year)					
≤55	67 (54.5)	14 (43.8)	56 (45.5)	18 (56.2)	0.2794
>55	198 (57.4)	48 (48.0)	147 (42.6)	52 (52.0)	0.0963
Hypertension					
YES	133 (56.8)	20 (46.5)	101 (43.2)	23 (53.5)	0.2107
NO	132 (56.4)	42 (47.2)	102 (43.6)	47 (52.8)	0.1375
Diabetes					
YES	64 (65.3)	8 (57.1)	34 (34.7)	6 (42.9)	0.5510
NO	201 (54.3)	54 (45.8)	169 (45.7)	64 (54.2)	0.1050
Smoking					
YES	141 (58.0)	24 (53.3)	102 (42.0)	21 (46.7)	0.5590
NO	124 (55.1)	38 (43.7)	101 (44.9)	49 (56.3)	0.0699
Drinking					
YES	45 (57.7)	13 (37.1)	33 (42.3)	22 (62.9)	0.0433
NO	220 (56.4)	49 (50.5)	170 (43.6)	48 (49.5)	0.2961
cTnI (μg/L)					
≤0.3	46 (44.2)	43 (50.5)	58 (55.8)	43 (50.0)	0.4276
>0.3	219 (60.2)	19 (41.3)	145 (39.8)	27 (58.7)	0.0146
Mb (μg/L)					
≤140	99 (54.7)	53 (47.7)	82 (45.3)	58 (52.3)	0.2486
>140	166 (57.8)	9 (42.9)	121 (42.2)	12 (57.1)	0.0009
LDH (U/L)					
≤250	67 (52.8)	41 (47.1)	60 (47.2)	46 (52.9)	0.4185
>250	198 (58.1)	21 (46.7)	143 (41.9)	24 (53.3)	0.1469
CK (U/L)					
≤310	98 (55.4)	50 (44.2)	79 (44.6)	63 (55.8)	0.0647
>310	170 (57.8)	12 (63.2)	124 (42.2)	7 (36.8)	0.6478
CK-MB (U/L)					
≤24	64 (56.1)	44 (46.8)	50 (43.9)	50 (53.2)	0.1800
>24	201 (56.8)	18 (47.4)	153 (43.2)	20 (52.6)	0.2669
TC (mmol/L)					
≤5.20	189 (55.4)	46 (47.0)	152 (44.6)	52 (53.0)	0.1377
>5.20	76 (60.0)	16 (47.1)	51 (40.0)	18 (52.9)	0.1810
TG (mmol/L)					
≤1.70	180 (54.7)	45 (46.9)	149 (45.3)	51 (53.1)	0.1759
>1.70	85 (61.2)	17 (47.2)	54 (38.2)	19 (52.3)	0.1309
HDL-C (mmol/L)					
≤1.74	251 (56.5)	58 (45.7)	193 (43.5)	67 (54.3)	0.0446
>1.74	14 (60.9)	4 (57.1)	9 (39.1)	3 (42.9)	1.0000

(*Continued*)

Table 4 (Continued).

	GA+AA type		GG Type		*P* value
	MI	Control	MI	Control	
LDL-C (mmol/L)					
≤3.36	154 (52.6)	45 (46.9)	139 (47.4)	51 (53.1)	0.3335
>3.36	111 (63.4)	17 (47.2)	64 (36.6)	19 (52.8)	0.0699
GLU (mmol/L)					
≤6.10	118 (58.7)	38 (48.7)	83 (41.3)	40 (51.3)	0.1315
>6.10	147 (55.1)	24 (44.4)	120 (44.9)	30 (55.6)	0.1540

in Logistic regression analysis.[9] Independent risk factors were screened using multifactorial logistic regression analysis with MI as the dependent variable and the conventional risk factors and ALDH2 genotype as the dependent variables. The results are shown in Table 5. Male gender, age, hypertension, diabetes, tobacco use, and alcohol use were strongly associated with the occurrence of MI. Among subjects with these risk factors, carriers of the A allele of the ALDH2 gene had a higher risk of MI compared to carriers of the GG genotype; this suggests that the GA/AA genotype of ALDH2 is an independent risk factor for MI ($P < 0.05$, OR = 1.479, 95% CI = 1.003–2.179).

Discussion

The ALDH2 gene is located on chromosome 12, and it has a major single-nucleotide polymorphism site rs671 on exon 12 that can affect enzyme activity. As a result, when the codon that encodes amino acid 504 undergoes the base substitution G→A, the changes in the codon cause an amino acid change, namely the conversion of glutamate (Glu) into lysine (Lys). The result is the Glu504Lys polymorphism of the ALDH2 gene. Based on genetic laws, the ALDH2 genotype can be divided into the GG type, the GA type, and the AA type; among these, GA and AA are mutant types. The dehydrogenase activity of the mutant types is significantly reduced, where the GA type has only 6% of the dehydrogenase activity of the GG type, and dehydrogenase activity is essentially absent in the AA type.[10] Less than 2% of the Chinese Han population has the AA genotype ALDH2, which means that the majority of A alleles in the Chinese Han population are found in the GA genotype.[11] As previously reported, there was no statistically significant difference between the GA and AA genotypes, so they were combined in the statistical analyses of the distribution of ALDH2 genotypes.

The study enrolled 468 patients with MI and 132 healthy people from the Qingyuan area. The analysis found the proportion of the ALDH2 genotype GA/AA to be significantly higher ($P = 0.0492$) in the MI group than it was in the control group. This suggests that the Glu504Lys polymorphism of the ALDH2 gene is closely related to the occurrence of MI in the Qingyuan population.

As mentioned in the previous section, the results of the HWE test confirmed that the genotype distribution was well-represented in both the MI and control groups. The proportion of the AA genotype of ALDH2 was 10.7% in the MI group and 10.6% in the control group respectively, which is higher than the proportion of the wider Chinese Han population previously reported (less than 2%).[11] There was a significant difference in the distribution of ALDH2 genotypes between the MI and control groups

Table 5 Logistic Regression Analysis on Risk Factors of MI

	β	S.E.	OR	95% CI	*p* value
Male	−0.483	0.207	5.432	0.617–0.411	0.020
Age	−0.24	0.008	0.977	0.961–0.992	0.004
Hypertension	0.743	0.209	2.102	1.39–2.167	0.000
Diabetes	0.787	0.302	2.198	1.204–4.013	0.010
Smoking	0.735	0.207	2.086	1.390–3.129	0.000
Drinking	−0.594	0.235	0.552	0.348–0.875	0.011
ALDH2 GA/AA genotype	0.391	0.198	1.479	1.003–2.179	0.048

($P < 0.05$). Subgroup analysis of the ALDH2 genotypes found alcohol use, high levels of Mb, and low levels of HDL-C to be associated with the occurrence of MI. After adjusting for gender, age, hypertension, diabetes, tobacco use, alcohol use, and other factors, logistic regression showed the GA/AA genotype of ALDH2 to be also associated with MI occurrence, where the risk of MI was 1.479 times higher for individuals with the GA/AA genotype than for individuals with the GG genotype. This suggests that the GA/AA genotype of ALDH2 is an independent risk factor for MI.

Preliminary studies conducted in Japan investigated the relationship between ALDH2 gene polymorphism and coronary heart disease, but they did not reach a unified conclusion. One study identified the AA genotype of ALDH2 as a risk factor for the development of MI, suggesting that it may increase the risk of MI by decreasing the concentration of HDL-C,[12] a conclusion which is consistent with the findings of this study. A second study proposed that the AA genotype of ALDH2 has an anti-atherosclerotic effect.[13] The study suggested that ALDH2 gene polymorphism regulates the level of HDL-C, a protective factor for MI, by moderating alcohol consumption,[14] but the exact mechanism of this regulation process has not yet been determined. More recent studies have found that the ALDH2 gene may affect the occurrence and development of cardiovascular diseases caused by oxidative stress, lifestyle factors, and other mechanisms. The results of one study indicate that adrenal phaeochromocytoma (PC12) cells can increase sensitivity to 4-HNE by transfecting the deficient ALDH2 complementary DNA, thereby reducing the incidence of coronary heart disease.[15] Another study observed for rats that the accelerated metabolism of aldehydes can alleviate lung ischemia-reperfusion injury, and the protective effects of accelerated aldehyde metabolism were found to be closely related to high levels of ALDH2 activity.[16] But while the results of these studies suggest that ALDH2 gene polymorphism influences the risk of MI due to genetic, environmental, and metabolic interactions, the key mechanism of this influence is still unknown. More effort should be made in future studies to understand the relationship between the ALDH2 gene and other diseases.

In fact, many potential biomarkers of heart disease and vascular disease at the small molecular level have been found long before the study of genetic associations with heart disease. In the early stage of Acute Myocardial Infarction (AMI), Anello et al showed that H-FABP had a higher positive detection rate than high-sensitivity troponin (hs-TNL),[17] they also proposed that the detection of high-sensitivity troponin (HSTNL) using Single Molecule Counting technique is a candidate strategy for the identification and management of acute coronary syndromes, which can effectively stratify the risk of suspected patients[18] Bivona et al reviewed the limited value of heart-type fatty acid binding protein (HFAPB) in the early diagnosis of acute coronary syndromes and the prediction of mortality after diagnosis.[19] Zinellu et al found that the molecule ADMA in plasma can act as a biomarker and play an important role in suggesting restenosis after endarterectomy.[20] Galectin-3 (Gal-3) serves as an independent predictor of poor prognosis and mortality from heart failure in patients with progression from cardiovascular disease to heart failure.[21] Through in-depth studies at all levels of protein-gene, small molecular biomarkers have increasingly been found to play a crucial role in the diagnosis, treatment and prognosis evaluation of vascular diseases.

Researchers have recently begun to study the distribution of ALDH2 gene polymorphism in the Han populations of different regions of China. Epidemiological studies have shown that the frequency of the rs671 polymorphism in the ALDH2 gene differs according to race and region. It is most common in Asian populations, where 30% to 50% of the population has this polymorphism: the mutation rate is 20–30% in the Chinese Han population, 30% in India, and up to 34.1% in Japan. By contrast, this polymorphism is relatively rare in the White and Black populations of Europe and America.[22,23] Within the Asian countries of India, China, Japan, and Korea, the distribution of ALDH2 gene polymorphism also differs along ethnic and regional lines.[24,25] The frequency of the Glu504Lys polymorphism differs between the southern and northern regions of China and between different ethnic groups.[26–29] Mi et al[30] found that the A allele frequency of the ALDH2 gene was 19.7% in the Shanghai Han population compared to 14.7% in the Han population of Shandong province. Zhang[31] determined that the frequency of the AA genotype in the Han population of the city of Luoyang was lower than in Shanghai or Taiwan but significantly higher than in Japan or China. Li[32] also found that the Beijing Han population had a lower frequency of mutated genes than the Luoyang Han population. The A allele of ALDH2 was identified by Wu as a risk factor

for the development of coronary stenosis in the population of Hainan.[33] Hou suggests that the AA genotype may be a susceptible allele for AMI occurrence.[8] To summarize, while ALDH2 gene polymorphism is common among different groups, the rs671 polymorphism is generally more frequent in northern Han populations than in southern Han populations.

This study has proposed that the Glu504Lys polymorphism in the ALDH2 gene influences the onset of MI in the Qingyuan population and that the GA/AA genotype of the ALDH2 gene may be an independent risk factor for MI. The failure of this study to obtain the same results as previous studies should be considered in light of the following: (1) ALDH2 gene mutations are very common in China. While the study subjects were all from Qingyuan and neighboring regions, our limited information about their geographic origins and genetic background meant that we could not guarantee that they were originally from Qingyuan or of Han ethnicity. (2) There was no uniform standard for the collection of baseline data between the MI group and the control group, such as whether medication was used or an operation performed prior to testing; different times of detection and different frequencies of tests can lead to biased results. (3) The conclusions about the association between the ALDH2 gene and MI are inconsistent and need further exploration. (4) As the main settlement area for ethnic minorities in Guangdong province, Qingyuan has a large ethnic minority population: A study that only considers Han subjects cannot represent the wider Qingyuan population. To better understand ALDH2 gene polymorphism and prevent and treat MI and related diseases, there should be more comprehensive analysis and comparison of the gene polymorphism exhibited by different ethnic groups in Qingyuan. Follow-up studies with large samples are also necessary to provide theoretical support for MI susceptibility screening and individualized control in the Qingyuan region.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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