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ORIGINAL RESEARCH

Aldehyde Dehydrogenase 2 rs671 G/A and a/A Genotypes are Associated with the Risk of Acute Myocardial Infarction

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Background: Aldehyde dehydrogenase 2 (ALDH2) is a key catalytic enzyme involved in the aldehyde metabolism that plays an important role in the occurrence and development of acute myocardial infarction (AMI). However, the relationship of *ALDH2* polymorphism and susceptibility to AMI may differ among different regions and populations, and it has not yet been reported in Hakka population. The purpose of the present study was to investigate it in this population.

Methods: Four hundred and nineteen AMI patients and 636 individuals without AMI were included in the present study. The *ALDH2* rs671 polymorphism was genotyped using polymerase chain reaction (PCR)-microarray. Differences in *ALDH2* rs671 genotypes and alleles between patients and controls were compared, and the relationship between *ALDH2* rs671 genotypes and AMI risk was analyzed.

Results: Patients with AMI had a lower frequency of *ALDH2* rs671 G/G genotype (43.2% vs 52.7%, p=0.003), and a higher G/A genotype (45.6% vs 38.5%, p=0.025) than controls. And AMI patients had a lower frequency of *ALDH2* rs671 G allele (66.0% vs 71.9%), and a higher A allele (34.0% vs 28.1%) (p=0.004) than controls. Logistic regression analysis showed that overweight (body mass index (BMI)≥24.0 kg/m^2 vs BMI 18.5–23.9 kg/m^2: odds ratio (OR) 2.046, 95% confidence interval (CI): 1.520–2.754, p<0.001), history of hypertension (yes vs no: OR 3.464, 95% CI: 2.515–4.770, p<0.001), *ALDH2* rs671 G/A genotype (G/A vs G/G: OR 1.476, 95% CI: 1.102–1.976, p=0.009), and A/A genotype (A/A vs G/G: OR 1.656, 95% CI: 1.027–2.668, p=0.038) maybe the independent risk factors for AMI.

Conclusion: Overweight (BMI≥24.0 kg/m^2), a history of hypertension, and *ALDH2* rs671 G/A or A/A genotypes increased the risk of developing AMI in Hakka population.

Keywords: aldehyde dehydrogenase 2, acute myocardial infarction, polymorphism, Hakka

Introduction

Coronary artery disease (CAD) is a heart disease caused by myocardial ischemia or necrosis due to stenosis, blockage and spasm of the coronary artery atherosclerosis.[1,2] Acute myocardial infarction (AMI) is a severe form of CAD, caused by the rupture of coronary atherosclerotic plaques, the acute occlusion of the coronary artery leading to interruption of blood flow, and the myocardial necrosis caused by severe and persistent ischemia and hypoxia.[3,4] AMI is an important disease burden worldwide, with a high fatality rate,[5,6] there are approximately 290 million cardiovascular patients and 2.5 million have AMI in China.[7,8] It is of great significance to identify individuals susceptible to AMI.

The pathological basis of AMI is atherosclerosis. At present, atherosclerosis is regarded as a chronic inflammatory disease characterized by a sequence of immune responses, and inflammation plays an important role in the occurrence and development of atherosclerotic lesions.[9] The formation of atherosclerotic plaque is characterized by lipid accumulation, local vascular inflammation, proliferation of smooth muscle cells (SMCs), apoptosis, and fibrillation, which is

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mainly the activation of inflammatory cells and a series of chronic inflammatory reactions triggered by endothelial cell injury.[10] The anti-inflammatory treatment of AMI is also receiving more research and attention.[11] Some indicators that can reflect the systemic or local inflammation level have potential value in the diagnosis and prognosis assessment of AMI, such as neutrophil-to-lymphocyte ratio (NLR),[12] blood cell ratios associated with immune cells,[13] fibrinogen albumin ratio (FAR),[14] and C-reactive protein (CRP).[15]

The body will produce a large number of reactive oxygen species (ROS) under stress, which intensifies the peroxidation of mitochondrial polyunsaturated fatty acids, and produces toxic aldehydes.[16] Aldehyde dehydrogenase can metabolize toxic aldehydes into low-toxicity carboxylic acids, thus reducing the damage caused by aldehyde overload on the mitochondria,[17,18] such as aldehyde dehydrogenase 2 (ALDH2).[19] Previous studies have shown that ALDH2 is associated with secondary liver injury, Alzheimer's disease, pulmonary hypertension, and some cancers.[19–22] The relationship between *ALDH2* and atherosclerosis, hypertension, and cardiac insufficiency has been reported.[23,24] ALDH2 activity is influenced by *ALDH2* single nucleotide polymorphism (SNP) rs671 (G>A, Glu504Lys) variants.[25,26] Based on the SNP rs671, the population is composed of three genotypes: wild-type *ALDH2**1/*1 (G/G), heterozygous type *ALDH2**1/*2 (G/A), and homozygous mutant *ALDH2**2/*2 (A/A). The Glu504Lys polymorphism can cause ALDH2 enzyme activity to drop to 30–50% of normal.[27,28]

Several studies found that *ALDH2* variant was associated AMI.[29–31] The susceptibility to AMI may differ among different regions and populations. The Hakka people are an ethnic group formed by the integration of the people from the central plains of China with different ethnic groups during the southward migration, and Meizhou city is one of the main gathering places of Hakka people.[32] The relationship between *ALDH2* gene polymorphisms and the risk of AMI in this region has not yet been reported. The purpose of the present study was to analyze the relationship in this population.

Materials and Methods

Study Participants

As a case-control study, this study included 1055 individuals who received medical treatment or physical examination in Meizhou People's Hospital, Guangdong Province from December 2019 to July 2023 as the study objects, including 419 patients with AMI as the study group and 636 individuals who underwent physical examination as the control group. According to the Fourth Universal Definition of Myocardial Infarction,[33] the diagnostic criteria for AMI were revised to include: increased markers of acute myocardial injury, at least once above the 99th percentile of the upper limit of normal, accompanied by at least one of the following indicators: (1) symptoms of acute myocardial ischemia; (2) new ischemic electrocardiogram changes; (3) new pathological Q wave; (4) imaging evidence of loss of viable myocardium or segmental wall motion abnormalities; or (5) coronary angiography confirmed the presence of coronary thrombosis.

Inclusion criteria for the disease group were as follows: (1) 18 years of age and older; (2) patients diagnosed with AMI; and (3) complete medical records. Controls met the following criteria: (1) age ≥18 years old; (2) absence of a CAD diagnosis; and (3) complete examination and laboratory testing information. Exclusion criteria were as follows: (1) combined with suspected or confirmed other cardiomyopathy, such as dilated cardiomyopathy, myocardial amyloidosis, and hypertrophic obstructive cardiomyopathy; (2) other malignant or severe diseases; and (3) pregnancy or tumor.

This study was performed in accordance with the ethical standards of the Declaration of Helsinki and approved by the Human Ethics Committee of Meizhou People's Hospital. Sample size calculation was performed using Clinical Research Sample Size Calculator (CRESS version 1.3): odds ratio was set at 1.4, *ALDH2* variant allele frequency was 28% in Hakka population,[34] statistical power was 90%, type I error rate (α) at 0.05, two-sided significance tests, resulting in a sample of 278 patients with AMI and 278 controls.

Data Collection

Information such as age, sex, body mass index (BMI), history of smoking, history of alcohol consumption, history of diabetes mellitus, and history of hypertension was collected from the patient's medical record information system. BMI was divided into three subgroups based on the Chinese criteria:[35,36] <18.5 kg/m^2, 18.5–23.9 kg/m^2, and ≥24.0 kg/m^2. Early morning fasting blood collection and serum separation. Criteria for the diagnosis of hypertension:[37] systolic

≥140mmHg and/or diastolic ≥90 mmHg from 2 blood pressure measurements taken on different days without anti-hypertensive medication. Diagnostic criteria for diabetes mellitus:[38] have symptoms of diabetes and plasma glucose ≥11.1mmol/L at any one time, fasting plasma glucose (FPG)≥7.0mmol/L, or 2h 75-g oral glucose tolerance test (OGTT) ≥11.1mmol/L.

The lipid levels in the serum samples were assessed using an automated biochemical analysis system (Olympus AU5400 system, Tokyo, Japan). Serum lipid levels included total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), Apolipoprotein A1 (Apo-A1), and Apolipoprotein B (ApoB).

DNA Isolation and ALDH2 Genotyping

Genomic DNA was extracted from venous blood collected from EDTA anticoagulant collection vessels using a blood DNA isolation kit (Qiagen GmbH, Germany). DNA quality and concentration were assessed using a Nano-Drop 2000™ spectrophotometer (ThermoFisher Scientific, Waltham, MA, USA). *ALDH2* genotype was detected using *ALDH2* Gene Detection Kit based on polymerase chain reaction (PCR)-gene chip method (BaiO Technology Co, Ltd., Shanghai, China). Details about *ALDH2* polymorphism detection have been reported in previous articles from our hospital.[39,40]

Statistical Analysis

All statistical analyses were performed using SPSS statistical software (version 26.0; IBM Inc., USA). Continuous variables were expressed as means ± standard deviations and were compared using either Student's *t*-test or the Mann–Whitney *U*-test. The comparison of the genotype composition ratio and allele frequency between the two groups were analyzed using *Chi*-square test. Logistic regression analysis was used to examine the relationship between *ALDH2* polymorphism and AMI. $p<0.05$ was considered to represent statistical significance.

Results

Characteristics of Subjects

Of the 1055 subjects included in this study, 797 (75.5%) were male and 258 (24.5%) were female. There were 146 cases (13.8%) with BMI <18.5 kg/m^2 and 317 cases (30.0%) with BMI≥24.0 kg/m^2. A total of 273 cases (25.9%) patients had a history of smoking, 94 cases (8.9%) had a history of alcohol consumption, 268 cases (25.4%) had hypertension, and 180 cases (17.1%) had diabetes mellitus. The study included 419 patients with AMI and 636 controls. The proportion of overweight subjects in the patient group was higher than that in the control group (185 (44.2%) cases with ≥24.0 kg/m^2 vs 132 (20.8%) controls with ≥24.0 kg/m^2), the difference in BMI distribution among the groups was statistically significant ($p<0.001$). The proportions of history of alcohol consumption, hypertension, and diabetes mellitus in AMI patients and controls were 4.1%, 41.8%, 22.7%, and 12.1%, 14.6%, 13.4% respectively, with the difference being statistically significant (all $p<0.001$). The differences in TC, TG, HDL-C, LDL-C, Apo-A1, and Apo-B levels between groups were statistically significant (all $p<0.001$) (Table 1).

Distribution of the ALDH2 Genotypes and Alleles Between AMI Patients and Controls

The *ALDH2* rs671 genotypes in the AMI patients ($\chi^2=0.102$, $p=0.750$), and controls ($\chi^2=1.344$, $p=0.246$) conformed to the Hardy-Weinberg equilibrium, respectively. A comparison of the frequencies of *ALDH2* genotypes between the two groups showed that AMI patients had a lower frequency of *ALDH2* rs671 G/G genotype (43.2% vs 52.7%, $p=0.003$) and a higher frequency of *ALDH2* rs671 G/A genotype (45.6% vs 38.5%, $p=0.025$). There was no statistically significant difference in *ALDH2* rs671 A/A genotype (11.2% vs 8.8%, $p=0.205$) between the two groups. A comparison of allele frequencies showed that AMI patients had a lower frequency of *ALDH2* rs671 G allele (66.0% vs 71.9%) and a higher A allele (34.0% vs 28.1%) ($p=0.004$) than controls (Table 2).

Table 1 Clinical Characteristics of the Subjects of This Study

Variables	Total (n=1055)	Controls (n=636)	AMI Patients (n=419)	*p* values
Gender				
Male, n(%)	797(75.5%)	468(73.6%)	329(78.5%)	0.079
Female, n(%)	258(24.5%)	168(26.4%)	90(21.5%)	
BMI (kg/m^2)				
<18.5	146(13.8%)	127(20.0%)	19(4.5%)	<0.001
18.5–23.9	592(56.1%)	377(59.3%)	215(51.3%)	
≥24.0	317(30.0%)	132(20.8%)	185(44.2%)	
History of smoking				
No	782(74.1%)	476(74.8%)	306(73.0%)	0.519
Yes	273(25.9%)	160(25.2%)	113(27.0%)	
History of alcohol consumption				
No	961(91.1%)	559(87.9%)	402(95.9%)	<0.001
Yes	94(8.9%)	77(12.1%)	17(4.1%)	
Hypertension				
No	787(74.6%)	543(85.4%)	244(58.2%)	<0.001
Yes	268(25.4%)	93(14.6%)	175(41.8%)	
Diabetes mellitus				
No	875(82.9%)	551(86.6%)	324(77.3%)	<0.001
Yes	180(17.1%)	85(13.4%)	95(22.7%)	
Serum lipid-lipoprotein levels				
TC, mmol/L	4.48±1.23	4.18±1.12	4.94±1.26	<0.001
TG, mmol/L	1.62±1.07	1.46±0.96	1.86±1.18	<0.001
HDL-C, mmol/L	1.14±0.40	1.09±0.44	1.23±0.33	<0.001
LDL-C, mmol/L	2.58±0.88	2.37±0.77	2.90±0.94	<0.001
Apo-A1, g/L	1.00±0.31	0.94±0.33	1.10±0.26	<0.001
Apo-B, g/L	0.84±0.27	0.79±0.25	0.91±0.28	<0.001

Abbreviations: AMI, Acute myocardial infarction; BMI, body mass index; Values for age expressed as mean±SD; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; Apo-A1, apolipoprotein A1; Apo-B, apolipoprotein B.

Table 2 Distribution Frequencies of ALDH2 rs671 Genotype and Allele in AMI Patients and Controls

Variable	Genotypes/Alleles	Total (n=1055)	Controls (n=636)	AMI Patients (n=419)	χ^2	*p* values
ALDH2 rs671 genotypes						
	G/G	516(48.9%)	335(52.7%)	181(43.2%)	9.075	0.003
	G/A	436(41.3%)	245(38.5%)	191(45.6%)	5.196	0.025
	A/A	103(9.8%)	56(8.8%)	47(11.2%)	1.668	0.205
ALDH2 rs671 alleles						
	G	1468(69.6%)	915(71.9%)	553(66.0%)	8.430	0.004
	A	642(30.4%)	357(28.1%)	285(34.0%)		
	HWE (χ^2, *P*)	χ^2=0.601, *p*=0.438	χ^2=1.344, *p*=0.246	χ^2=0.102, *p*=0.750		

Abbreviation: HWE, Hardy Weinberg Equilibrium.

Clinical Characteristics and Serum Lipid-Lipoprotein Levels of Subjects Stratified by ALDH2 rs671 Genotypes

There was a statistically significant difference in the proportion of patients with a history of alcohol consumption among the *ALDH2* rs671 G/G, G/A, and A/A genotypes ($p<0.001$). The individuals with A/A genotype had lower TG levels (1.34±0.82 mmol/L vs 1.68±1.09 mmol/L and 1.61±1.08 mmol/L, $p<0.001$) than individuals with G/G genotype and G/A genotype, respectively. There were no statistically significant differences in the BMI distribution, history of smoking, and levels of other serum lipid lipoproteins among *ALDH2* rs671 G/G, G/A, and A/A genotype groups (all $p>0.05$) (Table 3).

Table 3 Clinical Characteristics and Serum Lipid-Lipoprotein Levels of Subjects Stratified by ALDH2 rs671 Genotypes

Variables	G/G (n=516)	G/A (n=413)	A/A (n=103)	*p* values
Gender				
Male, n(%)	379(63.5%)	337(63.9%)	81(64.1%)	0.287
Female, n(%)	137(36.5%)	99(36.1%)	22(35.9%)	
BMI (kg/m^2)				
<18.5	71(22.6%)	57(18.5%)	18(20.5%)	0.537
18.5–23.9	291(49.0%)	251(49.6%)	50(48.7%)	
≥24.0	154(28.5%)	128(31.9%)	35(30.8%)	
History of smoking				
No	379(12.5%)	320(4.6%)	83(4.6%)	0.293
Yes	137(12.5%)	116(4.6%)	20(4.6%)	
History of alcohol consumption				
No	442(12.5%)	416(4.6%)	103(4.6%)	<0.001
Yes	74(12.5%)	20(4.6%)	0(0)	
Hypertension				
No	371(12.5%)	334(4.6%)	82(4.6%)	0.117
Yes	145(12.5%)	102(4.6%)	21(4.6%)	
Diabetes mellitus				
No	423(12.5%)	361(4.6%)	91(4.6%)	0.293
Yes	93(12.5%)	75(4.6%)	12(4.6%)	
Serum lipid-lipoprotein levels				
TC, mmol/L	4.47±1.23	4.49±1.24	4.45±1.21	0.935
TG, mmol/L	1.68±1.09$^{\$}$	1.61±1.08$^{\$}$	1.34±0.82$^{\#,*}$	0.011
HDL-C, mmol/L	1.15±0.42	1.13±0.38	1.16±0.41	0.825
LDL-C, mmol/L	2.54±0.86	2.62±0.91	2.61±0.83	0.326
Apo-A1, g/L	1.02±0.34	1.00±0.28	0.99±0.30	0.528
Apo-B, g/L	0.84±0.27	0.84±0.27	0.81±0.25	0.605

Notes: $^{\#}$Compared with G/G, $p<0.05$; *Compared with G/A, $p<0.05$; $^{\$}$Compared with A/A, $p<0.05$.
Abbreviations: AMI, Acute myocardial infarction; BMI, body mass index; Values for age expressed as mean±SD. TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; Apo-A1, apolipoprotein A1; Apo-B, apolipoprotein B.

Logistic Regression Analysis of Risk Factors Associated with AMI

Univariate logistic regression showed that overweight (BMI≥24.0 kg/m^2 vs BMI 18.5–23.9 kg/m^2: odds ratio (OR) 2.458, 95% confidence interval (CI): 1.859–3.249, $p<0.001$), history of hypertension (yes vs no: OR 4.188, 95% CI: 3.123–5.615, $p<0.001$), history of diabetes mellitus (yes vs no: OR 1.901, 95% CI: 1.376–2.626, $p<0.001$), *ALDH2* rs671 G/A genotype (G/A vs G/G: OR 1.443, 95% CI: 1.111–1.874, $p=0.006$), A/A genotype (A/A vs G/G: OR 1.553, 95% CI: 1.013–2.383, $p=0.044$) maybe the risk factors of AMI. And history of alcoholism (yes vs no: OR 0.307, 95% CI: 0.179–0.527, $p<0.001$) was a protective factor for AMI. Multivariate logistic regression showed that overweight (BMI≥24.0 kg/m^2 vs BMI 18.5–23.9 kg/m^2: OR 2.046, 95% CI: 1.520–2.754, $p<0.001$), history of hypertension (yes vs no: OR 3.464, 95% CI: 2.515–4.770, $p<0.001$), *ALDH2* rs671 G/A genotype (G/A vs G/G: OR 1.476, 95% CI: 1.102–1.976, $p=0.009$), A/A genotype (A/A vs G/G: OR 1.656, 95% CI: 1.027–2.668, $p=0.038$) maybe the independent risk factors for AMI, and history of alcoholism (yes vs no: OR 0.277, 95% CI: 0.150–0.512, $p<0.001$) was a protective factor (Table 4).

Table 4 Logistic Regression Analysis of Risk Factors for AMI

Variables	Univariate OR (95% CI)	*p* values	Multivariate OR (95% CI)	*p* values
Gender (Male/Female)	0.762(0.569–1.021)	0.068	0.761(0.543–1.067)	0.113
BMI (kg/m^2)				
18.5–23.9	1.000(reference)	–	1.000(reference)	–
<18.5	0.262(0.157–0.437)	<0.001	0.290(0.172–0.491)	<0.001
≥24.0	2.458(1.859–3.249)	<0.001	2.046(1.520–2.754)	<0.001
History of smoking (Yes/No)	1.099(0.830–1.454)	0.511	1.396(0.983–1.983)	0.062
History of alcoholism (Yes/No)	0.307(0.179–0.527)	<0.001	0.277(0.150–0.512)	<0.001
Hypertension (Yes/No)	4.188(3.123–5.615)	<0.001	3.464(2.515–4.770)	<0.001
Diabetes mellitus (Yes/No)	1.901(1.376–2.626)	<0.001	1.176(0.818–1.691)	0.382
ALDH2 rs671 genotypes				
G/G	1.000(reference)	–	1.000(reference)	–
G/A	1.443(1.111–1.874)	0.006	1.476(1.102–1.976)	0.009
A/A	1.553(1.013–2.383)	0.044	1.656(1.027–2.668)	0.038

Discussion

The pathological features of AMI include myocardial hypertrophy, decreased myocardial contractile function, myocardial fibrosis, and cardiomyocyte apoptosis.[41,42] ROS produced by cells can cause membrane lipid peroxidation by attacking polyunsaturated fatty acids to produce the acetaldehyde derivative, 4-hydroxynonenal (4-HNE). 4-HNE is a strong electrophilic agent that causes apoptosis or necrosis by absorbing intracellular proteins, binding glutathione, and inhibiting the phosphorylation activity of sodium-potassium-ATPase.[43] ALDH2 is an important aldehyde oxidase in the mitochondria.[44] ALDH2 plays an important role in the formation of foam cells, which are involved in the occurrence and development of atherosclerosis via the 4-HNE/PPARγ/CD36 pathway.[45] In addition, ALDH2 is involved in the migration of coronary endothelial cells,[46] endoplasmic reticulum stress and smooth muscle cell apoptosis.[47] These biological processes may be the mechanisms by which ALDH2 plays an important role in the occurrence and development of AMI.

Regard to *ALDH2*, a meta-analysis suggested that the A allele of the *ALDH2* rs671 polymorphism may increase the risk of CAD and AMI.[48–50] Jiang et al found that *ALDH2* variant may be an independent risk factor for AMI.[29] *ALDH2* rs671 A allele is prevalent among Japanese patients with acute ST-segment elevation myocardial infarction (STEMI) patients.[30] *ALDH2* rs671 A allele additively increases the risk of AMI in the Japanese population.[31] Zhu et al found that *ALDH2* GA and AA genotypes were independent risk factors for myocardial infarction.[51] *ALDH2* rs671 A/A genotype is a risk factor for myocardial infarction in Japanese men.[52] *ALDH2* rs671 G/A and A/A genotypes were independent risk factors for myocardial infarction in elderly Korean men.[53] In this study, *ALDH2* rs671 G/A and A/A genotypes were independent risk factors for AMI. Our results are consistent with these findings.

In this study, individuals with A/A genotype had lower TG levels than those with G/G genotype and G/A genotype, respectively. A genome-wide association study (GWAS) showed that *ALDH2* rs671 was associated with TG levels.[54] Han et al found that individuals with *ALDH2* G/G genotype had higher lipid levels and a higher proportion of TC disorders.[55] In Japanese males, the *ALDH2* rs671 variant was associated with lower HDL-C levels,[56] another study from Japan showed that individuals carried *ALDH2* G/G genotype had high TG levels.[57] A recent meta-analysis showed that the rs671 A allele was associated with higher levels of LDL-C and lower TG and HDL-C.[58] The relationship between *ALDH2* polymorphism and blood lipid may be related to the process of ALDH2 participating in the metabolism of lipid aldehydes generated by lipid peroxidation to carboxylic acids. However, more researches are needed to uncover the exact mechanism.

Obesity can lead to the development of cardiovascular disease and can also directly contribute to the development of cardiovascular risk factors, including dyslipidemia, type 2 diabetes, hypertension, and atrial fibrillation.[59–62] Most studies have linked obesity and being overweight to poor outcomes and the risk of death from cardiovascular disease.[60,63,64] However, AMI patients with a low BMI have a worse clinical prognosis than obese patients.[65] It has been suggested that underweight is also

associated with a high risk of cardiac death after AMI.[66] Of course, there was a contrary finding: overweight or obesity was a protective factor for AMI short- and long-term risks of death.[67] Overweight (BMI 25–30 kg/m^2) and obesity (BMI >30 kg/m^2) status are independent risk factors for early onset of AMI.[68] Obesity increased the risk of AMI in patients aged <45 years old.[69] In this study, being overweight (BMI≥24.0 kg/m^2) may be an independent risk factor for AMI.

Canto JG et al found that a history of hypertension is the most common manifestation in patients with myocardial infarction.[70] A history of hypertension is a common risk factor for AMI.[71] According to a clinical study, hypertension, smoking, diabetes, and obesity were the leading risk factors for heart attacks worldwide.[72] In a study from South Korea, age, history of hypertension, diabetes, and smoking were found to be risk factors for AMI in a rural population.[73] Smoking, hypertension, and obesity increased the risk of heart attack in patients aged <45 years.[69] In a Chilean population study, smoking, increased ApoB/ApoAl ratio, and hypertension were found to be risk factors for AMI.[74] Hypertension, smoking, and diabetes are closely associated with the occurrence of early-onset myocardial infarction.[75] In the Bangladeshi population, a history of hypertension was a risk factor for AMI in the elderly population; however, there were no similar results in the younger population.[76]

In addition, most of the individuals with a history of alcohol consumption included in this study had mild to moderate alcohol consumption, and the results showed a history of alcoholism was a protective factor. Several studies found that light to moderate alcohol consumption was beneficial to reduce the incidence of cardiovascular and cerebrovascular diseases. A clinical study (INTERHEART) showed that regular moderate alcohol consumption was associated with a reduced incidence of AMI.[72] A longitudinal study of 11,711 men with hypertension found that one standard unit of alcohol per day reduced the risk of AMI by 30%.[77] Its cardiovascular protection mechanism may be related to the increase of level of serum HDL-C, the increase of fibrinolytic activity, the decrease of platelet aggregation, and the enhancement of insulin sensitivity.[78,79] More clinical and basic researches are needed to uncover the relationship between the type of alcohol consumed and daily alcohol intake and cardiovascular risk.

The present study showed that overweight individuals, a history of hypertension, and *ALDH2* rs671 G/A or A/A genotypes had an increased risk of developing AMI. This study had some limitations. First, the subjects included in this case-control study were all patients who visited the hospital or individuals who underwent physical examination; therefore, the selection of the population may be biased. Second, the study did not consider other possible influencing factors (such as diet, sleep quality, and physical activity). Third, because of the insufficient number of cases included in the present study, patients with AMI were not classified (such as ST-segment elevation myocardial infarction (STEMI), and non-ST-segment elevation myocardial infarction (NSTEMI)) in this study, but this is one of the things we are working on.

Conclusion

In summary, overweight individuals (BMI≥24.0 kg/m^2), those with a history of hypertension, and *ALDH2* rs671 G/A or A/A genotypes had an increased risk of developing AMI. Revealing the characteristics and risks of AMI is of great significance for its prevention and treatment.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval

As this study was a retrospective study, it was not possible for all participants to return to the hospital to sign informed consent. All participants were informed on the study procedures and goals and the informed consent from all the participants was obtained in verbal form through the telephone communication, which was approved by the Ethics Committee of the Meizhou People's Hospital. The study was performed under the guidance of the Declaration of Helsinki and approved by the Ethics Committee of Medicine, Meizhou People's Hospital (Clearance No.: 2021-A-60).

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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 declare that they have no competing interests in this work.

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