Article

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The Relationship of *MAPK10P* Gene Polymorphism With P-Wave Peak Time and P-Wave Dispersion in Elderly Patients With Paroxysmal Atrial Fibrillation

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Background: The incidence of atrial fibrillation (AF) presents a markedly increasing trend with advancing age. Thus, with the growing population of elderly individuals, AF has emerged as a significant medical and socioeconomic problem. The objective of this study was to investigate the correlation of mitogen-activated protein kinase 10P (*MAPK10P*) gene polymorphism with P-wave peak time (Pwd) and P-wave dispersion (Pmax) among elderly individuals with paroxysmal AF.

Methods: From January 2021 to October 2022, 125 elderly patients with essential hypertension were recruited for research in our Cardiology Department. According to the European Society of Cardiology (ESC) Atrial Fibrillation Management Guidelines, 53 patients with $\geq$2 documented paroxysmal AF episodes in the previous year were classified as the observation group, while 72 patients without AF formed the control group. Patient data were collected, and a 12-lead electrocardiogram was used to measure Pwd and Pmax. *MAPK10P* genotype was identified using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). The association between *MAPK10P* genotype and AF risk, as well as the impact of different genotypes on Pwd and Pmax parameters, were evaluated.

Results: The baseline characteristics did not show any significant difference between the two groups ($p > 0.05$). The values of Pwd and Pmax in the observation group were significantly greater than those in the control group ($p < 0.05$). The occurrence rate of the *CC* genotype was lower in the observation group than in the control group ($p < 0.05$), while the occurrence rates of the *CG* and *GG* genotypes were higher in the observation group than in the control group ($p < 0.05$). Additionally, the frequency of the *G* allele was higher in the observation group than in the control group ($p < 0.05$). AF patients with the *CG+GG* genotype exhibited higher Pwd and Pmax values compared to those with the *CC* genotype ($p < 0.05$). Patients without AF who had the *CG+GG* genotype had higher Pwd and Pmax values compared to those with the *CC* genotype ($p < 0.05$).

Conclusion: In elderly patients, the presence of the *G* allele in the *MAPK10P* gene polymorphism is linked to an increased risk of AF, as well as Pwd and Pmax. This study provides valuable insights into the potential role of *MAPK10P* gene variations in influencing P-wave characteristics during the development of paroxysmal AF in elderly patients.

Keywords: paroxysmal atrial fibrillation; elderly; *MAPK10P* polymorphism; Pwd; Pmax

Introduction

In the elderly population, paroxysmal atrial fibrillation (AF) is becoming more noticeable as a prevalent and persistent arrhythmia [1]. Population aging is associated with an increasing prevalence of cardiovascular diseases among older individuals, but the occurrence of paroxysmal AF is the actual factor posing a significant challenge to cardiovascular health maintenance. Not only will this irregular heartbeat greatly impact the patients' quality of life, but it will also lead to severe complications like cardiac embolism and stroke, thereby further escalating the medical expenses. Therefore, it is very necessary and of significant clinical importance to delve into the pathogenesis of paroxysmal AF in the elderly and to identify potential targets for intervention. Over the past few years, the investigation of cardiovascular diseases with gene polymorphism has gained significant traction [2].

The mitogen-activated protein kinase 10P (*MAPK10P*) gene, a member of the mitogen-activated protein kinase (MAPK) family, is believed to have a connection with the development of cardiovascular disorders, particularly paroxysmal AF. *MAPK10P* is involved in signaling pathways for a variety of key physiological processes, including apoptosis, differentiation, and proliferation. Apoptosis is associated with elements conducive to the development of AF. *MAPK10P* has been reported to be a key regulator of the development of diabetes-induced AF and may be a target for the prevention and treatment of AF in the future. The variability of the *MAPK10P* gene could

impact the gene's expression and function, consequently controlling the cellular signal transduction pathway and subsequently influencing the heart's electrophysiological traits [3]. We hypothesize that there may be an association between *MAPK10P* gene polymorphism and P-wave peak time and P-wave dispersion in elderly individuals with paroxysmal AF. Additionally, exploring whether this polymorphism could serve as a potential risk indicator for paroxysmal AF is warranted. P-wave is an important waveform in electrocardiogram (ECG), which represents the electrical activity of atrium. Evaluating atrial electrical activity involves assessing two important parameters: P-wave peak time (Pwd) and P-wave dispersion (Pmax) [4,5]. In older individuals experiencing paroxysmal AF, the irregularity of the P-wave could indicate an electrophysiological dysfunction in the atria, potentially playing a significant role in the development and persistence of AF [6,7]. It is worth investigating whether there is a correlation between the polymorphism of the *MAPK10P* gene and cardiac electrophysiology, and if it has any impact on atrial electrical activity.

The primary objective of this retrospective analysis was to examine the association between *MAPK10P* gene polymorphisms and P-wave parameters (peak time and dispersion) in elderly individuals with paroxysmal AF, particularly during episodes of AF. By conducting a comprehensive analysis of this association, our aim was to enhance our comprehension of the development of paroxysmal AF in older individuals and offer a novel insight into safeguarding and monitoring cardiovascular well-being among the elderly.

Materials and Methods

Study Participants

The study included 125 senior individuals diagnosed with essential hypertension, who received treatment at the Cardiology Department of Tianjin First Central Hospital, between January 2021 and October 2022. The age of the included individuals ranged from 65 to 78 years, with a mean age of 68.25 $\pm$ 4.33 years. There were 68 male patients and 57 female patients in this sample, which was divided into two groups. The observation group consisted of 53 patients with paroxysmal AF who had recorded at least two documented AF episodes in the previous year, as per the criteria outlined in the European Society of Cardiology (ESC) Atrial Fibrillation Management Guidelines [8]. On the other hand, the control group comprised 72 patients who did not have AF. The variables of patients including comorbidities, patients' lifestyles, and medication use were collected and used for data analysis. All patients were informed of the protocol and gave their informed consent when they were enrolled in the study. This study has been approved by the Medical Ethics Committee of Tianjin First Central Hospital (Approval No.: 2020N075KY) and obtained written informed consent from all participants in adherence with the Declaration of Helsinki.

Sample Size Calculation

The calculation of sample size is very important in medical research, because the size of sample size will affect the reliability and accuracy of research results. According to the formula for calculating the sample size of continuous variables in experimental research (as follows), α = 0.05 (two-sided), β = 0.10 (one-sided), Z_α = 1.96, Z_β = 1.28, σ = 8.45 (standard deviation of the norm), and d = 1.68 (the difference between the mean values of the two groups after pre-experimental intervention), 106 cases were determined. In the actual study, a total of 125 patients were selected considering a dropout rate of 15% to 20%.

$$N = \frac{2\,(Z_\alpha + Z_\beta)^2\,\sigma^2}{d^2}$$

where σ = the estimated standard deviation; d = the difference between the mean values of two consecutive variables in group i; Z_α = the standard normal deviation corresponding to the level of α; Z_β = the standard normal deviation corresponding to the 1-β level; and N = the calculated sample size of a group.

Inclusion Criteria

Patients who are over the age of 65 and meet the diagnostic criteria for AF were included in this study [8]. The onset of AF was recorded using Holter ECG before the operation. Further inclusion criteria also encompass: (i) patients who have never had prior cardiac surgery; (ii) first-time patients undergoing radiofrequency ablation; (iii) patients who failed to respond to treatment with multiple antiarrhythmic drugs; and (iv) patients who willingly agreed to take part in the research by signing informed consent.

Exclusion Criteria

Individuals suffering from acute coronary syndrome, diabetes, hypertrophic cardiomyopathy, notable valve disorder, impaired left ventricular function (ejection fraction less than 50%), tumor, kidney, liver, thyroid ailment, or any other significant non-cardiac systemic ailment were excluded. Patients with atrioventricular block, bundle branch block, ventricular preexcitation or pacemaker implantation who had coagulation system diseases or hemorrhagic diseases were also excluded. Patients who refused to participate in the study or could not provide informed consent were also excluded.

Methods

Biochemical Analysis

Venous blood samples were obtained from patients after fasting overnight for at least 10 hours, then cen-

Table 1. Baseline characteristics between control and observation groups.

Variable	Control group (n = 72)	Observation group (n = 53)	T value/χ^2 value	*p*-value
Gender (male: female)	40:32	29:24	0.009	0.926
Age (years)	67.91 ± 3.21	68.75 ± 4.19	1.127	0.262
BMI (kg/m^2)	23.35 ± 1.76	23.17 ± 2.11	0.519	0.605
TC (mmol/L)	4.33 ± 0.26	4.29 ± 0.33	0.788	0.432
LDL-C (mmol/L)	2.43 ± 0.35	2.44 ± 0.31	0.198	0.844
HDL-C (mmol/L)	1.47 ± 0.33	1.42 ± 0.35	0.816	0.416
SBP (mmHg)	144.57 ± 16.04	141.39 ± 20.51	0.973	0.333
DBP (mmHg)	82.36 ± 14.57	83.29 ± 11.44	0.385	0.701

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, Total cholesterol.

trifuged at 2500 rpm for 30 minutes at 4 °C and immediately stored at –80 °C for further analysis. Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured using TC Colorimetric Assay Kit (Catalog number: EEA026, Thermo Fisher Scientific, Waltham, MA, USA), HDL-C Colorimetric Assay Kit (Catalog number: EEA012, Thermo Fisher Scientific, Waltham, MA, USA), and LDL-C Colorimetric Assay Kit (Catalog number: EEA014, Thermo Fisher Scientific, Waltham, MA, USA), respectively.

Evaluation of Pwd and Pmax

All patients were placed in a supine position, resting for at least 5 minutes, while recording the standard 12-lead body-surface ECG (25 mm/s, 1 mv/cm, 100 Hz). At 50 mm/s paper speed, sinus heart rhythm, basal line stability, and P-wave clear cardiac cycle were selected. The starting point of P-wave measurement is the intersection of the P-wave starting point and equipotential line, and the end point of measurement is the intersection of the equipotential line and the P-wave measurement endpoint. Each lead measures three P-waves and averages them. The length of the P-wave was manually measured by an experienced researcher using a magnifying glass. The starting and end points of the P-wave were determined as the intersection of the equipotential line and the starting point of P-wave deflection, and the intersection of the endpoint of P-wave deflection and the equipotential line, correspondingly. The average duration of the P-wave was measured for each lead from a 20-second recording, followed by recording the average maximum (Pm) and minimum (Pmin) durations on each ECG. The password was determined by subtracting Pmin from Pm. The heart rate (HR) of both P-wave measurements was corrected by the Bazett formula; the corrected P-wave parameter was equal to the P-wave parameter/(HR)1/2.

Gene Analysis

Genomic DNA was extracted from peripheral blood leukocytes using the salting-out method with minimal modifications [6]. As mentioned earlier, the *MAPK10P* genotype was detected using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) (1861096, Bio-Rad, Hercules, CA, USA). Four microliters of the resulting PCR amplification products were used in a 1.5% gel electrophoresis for 30 min at 80 V (1645050, Bio-Rad, Hercules, CA, USA). The PCR products under electrophoresis were observed with the aid of a gel imager to ensure that their amount was sufficient for restriction enzyme digestion. The amplified products were subjected to enzymatic digestion in a 37 °C water bath for 16 hours. The enzymatic digestion reaction system consisted of 8.0 µL of PCR amplified product, 0.5 µL of restriction enzyme, 2.0 µL of New England (NE) buffer (NEB #B6004, New England Biolabs, Hercules, CA, USA), and 9.5 µL of double-distilled water (ddH_2O). The enzyme digestion products (8 µL) were separated using 2% gel electrophoresis (15 min at 80 V, then 15 min at 120 V) (1645050, Bio-Rad, Hercules, CA, USA), and the enzyme digestion results were observed afterwards.

Statistical Analysis

All continuous variables are expressed as mean ± standard deviation (SD). Student's *t*-test was employed to compare continuous variables between two groups. Genotype and allele frequencies were counted manually. The differences in allele and genotype distribution and Hardy-Weinberg equilibrium deviation between groups were analyzed using a chi-square test. The normality of the distribution is determined by Shapiro-Wilk tests. For the numeric variables that were normally distributed, comparison between two groups was made by independent sample t test, and the Chi-square test was used to analyze the categorical data, and descriptive statistics were presented as frequency (%). All significance tests were double-tailed, with $p < 0.05$ being statistically significant. SPSS version 26.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses.

Table 2. Comparison of Pwd and Pmax in patients of the control and observation groups.

Group	Pwd (ms)	Pmax (ms)
Control group (n = 72)	27.34 ± 2.71	96.25 ± 2.75
Observation group (n = 53)	51.44 ± 3.62	119.34 ± 5.65
T value	42.59	30.21
p-value	<0.001	<0.001

Abbreviations: Pwd, P-wave peak time; Pmax, P-wave dispersion.

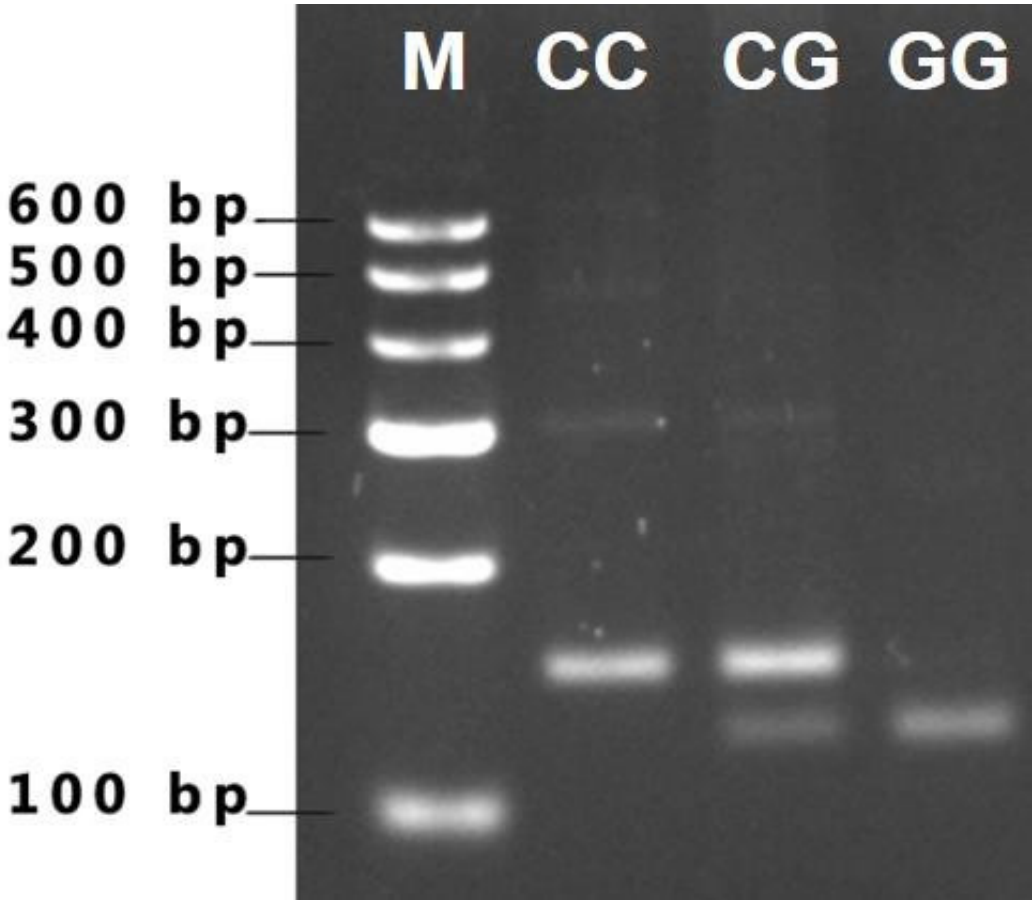

Fig. 1. Detection of *MAPK10P* genotype by PCR-RFLP. PCR-RFLP, polymerase chain reaction-restriction fragment length polymorphism; *MAPK10P*, mitogen-activated protein kinase 10P.

Results

Baseline Characteristics

Based on the overall patient data, the control group exhibited a male-to-female ratio of 40:32, with an average age of 67.91 ± 3.21 years and an average body mass index (BMI) of 23.35 ± 1.76 kg/m^2. The blood lipid analysis for the control group showed TC = 4.33 ± 0.26 mmol/L, LDL-C = 2.43 ± 0.35 mmol/L, and HDL-C = 1.47 ± 0.33 mmol/L. In the observation group, the male-to-female ratio was 29:24, with an average age of 68.75 ± 4.19 years. The subjects in the observation group had an average BMI of 23.17 ± 2.11 kg/m^2. The analysis of blood lipids for the observation group showed TC = 4.29 ± 0.33 mmol/L, LDL-C = 2.44 ± 0.31 mmol/L, and HDL-C = 1.42 ± 0.35 mmol/L. On average, their systolic blood pressure (SBP) was 141.39 ± 20.51 mmHg and diastolic blood pressure (DBP) was 83.29 ± 11.44 mmHg. The baseline characteristics between the two groups showed no significant difference ($p > 0.05$) (Table 1).

Comparison of Pwd and Pmax in Patients

The patients' Pwd and Pmax were measured using a 12-lead body-surface ECG. The Pwd and Pmax of the observation group were significantly higher than those of the control group ($p < 0.05$) (Table 2).

Table 3. Genotype and allele frequencies of *MAPK10P* in the control and observation groups.

Group	*CC*	*CG*	*GG*	*C*	*G*
Control group (n = 72)	47 (65.28%)	18 (25.00%)	7 (9.72%)	(77.78%)	(22.22%)
Observation group (n = 53)	22 (41.51%)	22 (41.51%)	9 (16.98%)	(62.26%)	(37.74%)
χ^2 value		6.981			7.166
p-value		0.030			0.007

Note: The sample sizes for *C*/*G* are n = 144 and n = 106, twice n = 72 and n = 53, for control and observation groups, respectively.

Table 4. Relationship between genotype and Pwd, Pmax parametersin patients with atrial fibrillation.

Genotype	Pwd (ms)	Pmax (ms)
CC (n = 22)	48.52 ± 2.46	102.44 ± 3.69
CG+*GG* (n = 31)	57.33 ± 2.79	116.35 ± 2.92
T value	11.885	15.31
p-value	<0.001	<0.001

Table 5. Relationship of *MAPK10P* genotype with Pwd and Pmax parameters in patients without atrial fibrillation.

Genotype	Pwd (ms)	Pmax (ms)
CC (n = 47)	43.33 ± 2.88	89.21 ± 3.84
CG+*GG* (n = 25)	52.41 ± 2.96	101.35 ± 4.10
T value	12.62	12.48
p-value	<0.001	<0.001

Frequencies of MAPK10P Genotype and Allele in Patients

In the control group, the frequencies of *CC*, *CG*, and *GG* genotypes of this *MAPK10P* polymorphism were 65.28%, 25.0%, and 9.72%, respectively, while in the observation group, the frequencies were 41.51%, 41.51%, and 16.98%, for the genotypes in the same order. In the control group, the *C* allele had a frequency of 77.78%, while the *G* allele had a frequency of 22.22%. In the observation group, the *C* allele had a frequency of 62.26%, and the *G* allele had a frequency of 37.74%. The frequencies of *CC*, *CG*, and *GG* genotypes in the observation group were significantly different from those in the control group ($p < 0.05$). Additionally, the frequency of the *G* allele in the observation group was significantly higher than that in the control group ($p < 0.05$) (Fig. 1, Table 3).

Relationship Between Different Genotypes and Clinical Features of Pwd and Pmax in Patients With Atrial Fibrillation

An evaluation was conducted on how various genotypes impact the parameters of Pwd and Pmax in individuals diagnosed with AF. The findings indicated that individuals with AF and the *CG*+*GG* genotype had elevated levels of Pwd and Pmax compared to AF patients with the *CC* genotype ($p < 0.05$) (Table 4).

Relationship Between Different Genotypes and Clinical Features of Pwd and Pmax in Patients Without AF

An analysis was conducted on the impact of various genotypes on the Pwd and Pmax in individuals without AF. The findings indicated that non-AF individuals with *CG*+*GG* genotype exhibited higher Pwd and Pmax values compared to non-AF individuals with *CC* genotype ($p < 0.05$) (Table 5).

Discussion

As the elderly population continues to grow, there is a corresponding increase in the prevalence of cardiovascular disorders. Atrial fibrillation is an increasingly common pathological condition among elderly patients, posing a significant health concern. This condition is frequently seen as an irregular heartbeat caused by abnormal electrical activity in the atria, resulting in irregular contractions and an elevated risk of developing blood clots and blockages in the heart [9–11]. Managing and treating AF in older individuals necessitates a comprehensive evaluation of patients' conditions and physiological events. Elderly patients with AF commonly experience a range of chronic illnesses, including but not limited to hypertension, diabetes, and heart failure, which contribute to its characteristics and risks [12,13]. Elderly patients may exhibit less apparent symptoms of AF in comparison to younger patients, yet they face a greater risk. AF may result in atrial blood clot formation and raise the likelihood of stroke and other events caused by embolism. The elderly are usually accompanied by cardiovascular and metabolic changes, which may affect the choice and tolerance of drug treatment.

MAPK10P gene belongs to the mitogen-activated protein kinase family; specifically, it is a copy of the *MAPK10* (also known as *JNK3*) gene [14]. This gene polymorphism refers to the existence of many different alleles or variants of the same gene in different individuals, which may

lead to different genotypes, thus affecting the physiological status and disease susceptibility of individuals. In recent years, there has been significant interest in the association between the genetic variation of the *MAPK10P* gene and cardiovascular disorders, particularly AF. These polymorphisms may affect gene expression, protein function and interaction with related signal transduction pathways. Therefore, the study of *MAPK10P* gene polymorphism can help to understand its role in cardiovascular health and disease development. Several research studies have attempted to investigate the correlation between genetic variation in the *MAPK10P* gene and cardiovascular disorders, particularly AF [15–18]. The focus of these studies was to determine if there is a correlation between various genotypes and the vulnerability to AF, as well as their association with ECG parameters and cardiac electrophysiological traits in patients diagnosed with AF. By conducting these studies, scientists can gain a deeper comprehension of how genetic diversity impacts the electrical function of the heart on the cellular and molecular scale, so as to gauge patients' susceptibility to AF [16–18].

MAPK10P has been reported to be upregulated in mice with AF, and *MAPK10* knockdown reduces structural remodeling and electrical remodeling by inhibiting inflammation, fibrosis, electrical disturbance, and apoptosis, thereby preventing AF from deterioration. However, its expression level in patients and its potential as a biomarker for patients with AF need to be explored. By examining older individuals with essential hypertension, this research first extensively investigated the correlation between genetic variation in *MAPK10P* and the duration of Pwd and the extent of Pmax in cases of paroxysmal AF. By clinically analyzing the detailed ECGs of 125 subjects, we discovered the potential involvement of the *MAPK10P* gene in the development of paroxysmal AF in elderly patients. The observation group showed a significant increase in the Pwd and the Pmax in patients with paroxysmal AF, indicating the presence of atrial electrical activity instability in individuals with AF. P-wave is an important parameter in ECG, which represents the electrical activity of the initial part of the atrium [19]. Under normal circumstances, atrial electrical activity should be stably conducted within a consistent time interval. Nevertheless, the observed rise in P-wave peak duration and P-wave variability suggests that the electrical activity in the atria is erratic and unsteady, potentially impacting the effectiveness of atrial contraction and overall cardiac function. The pathogenesis of AF is closely linked to the instability of electrical activity in the atria. Atrial fibrillation, a type of arrhythmia, features atrium's irregular trembling, resulting in decreased heart pumping ability and heightened embolism risk [20,21]. The recorded rise in P-wave duration and P-wave variability could indicate the disorganized transmission of electrical impulses in the atrium, creating an appropriate electrophysiological setting for the initiation of atrial fibrillation. Simultaneously, the findings from gene analysis additionally reinforced the association between P-wave parameters and AF. For the gene polymorphism under investigation, the *CC* genotype had a low frequency in the observation group, whereas the *CG* and *GG* genotypes had high frequencies, contributing to an increased frequency of the *G* allele. The variation in genotype distribution could potentially be associated with the atrial electrical activity of individuals. Particularly, individuals with the *G* allele (*CG+GG* genotype) exhibited notably higher susceptibility to AF, indicating a definite association between *MAPK10P* gene polymorphism, irregular atrial electrical function, and AF.

According to our study, individuals with the *CG+GG* genotype exhibited a notable rise in the likelihood of experiencing paroxysmal AF. The risk of *CG+GG* genotype carriers increased by approximately 2.68 times compared to individuals with the wild-type *CC* genotype, indicating compelling evidence of the link between the polymorphism of the *MAPK10P* gene and paroxysmal AF, which advocates the significance of the *CG+GG* genotype as a possible risk factor for AF. The heightened susceptibility to AF in individuals with the *CG+GG* genotype may indicate the impact of *MAPK10P* gene variation on the electrical function of the atria. The stability and order of atrial electrical activity are very important for normal cardiac function, and *CG+GG* genotype may lead to uncoordinated conduction and instability of atrial electrical signals, thus providing favorable conditions for the occurrence of AF [22,23]. This instability may lead to the disorder of atrial electrical signals, and eventually trigger the onset of AF. Furthermore, the heightened susceptibility to AF in individuals with the *CG+GG* genotype might be associated with the influence of *MAPK10P* gene variation on cellular signal transmission and the cardiovascular system. The involvement of the *MAPK10P* gene in the regulation of cellular growth, apoptosis, and inflammation may have an impact on cardiovascular well-being [24,25]. The presence of *CG+GG* genotype could potentially result in the aberrant control of genes in the signal transduction pathway, consequently impacting the electrophysiological attributes of the cardiac system. Furthermore, clinical practice and research have also provided evidence for the correlation between instability in atrial electrical activity and the occurrence of AF. Unstable atrial electrical activity may create an environment for electrical chaos in the atrium, which may promote the persistence and attack of AF [26]. Hence, the heightened susceptibility of individuals carrying *CG+GG* genotype could potentially be attributed to a biological foundation of instability in atrial electrical activity. The findings suggest that individuals with the *CG+GG* genotype, which is strongly associated with a higher likelihood of experiencing paroxysmal AF, might have a significant impact on the instability of atrial electrical activity and the heart's electrophysiological regulation, giving us a profound comprehension of the correlation between *MAPK10P* gene variation and AF,

while also indicating the possible influence of genotype on an individual's susceptibility to paroxysmal AF.

The identification of *MAPK10P* gene polymorphism as a risk factor for AF opens up new avenues for personalized medicine approaches. Genotyping *MAPK10P* variants could potentially be used as a screening approach to identifying elderly individuals at higher risk of developing AF, allowing for earlier intervention and possibly improving outcomes. Moreover, understanding the specific biological pathways influenced by *MAPK10P* polymorphisms could aid in the development of targeted therapies. Despite the promising potential, several challenges need to be addressed before *MAPK10P* genotyping can be routinely implemented in clinical practice. The genetic basis of AF is likely multifactorial, with multiple genes and their interactions contributing to disease risk. Therefore, the predictive value of a single gene polymorphism may be limited. Another challenge is the need for larger-scale studies to validate our findings and to determine the exact mechanisms by which *MAPK10P* polymorphisms influence AF risk. Additionally, the clinical applicability of genetic information must be balanced against ethical considerations, including patient privacy and the potential for genetic discrimination.

Several limitations exist in the present study. The sample size included in this study is relatively small, presenting generalizability challenges for other populations; therefore, expanded samples should be considered in future studies. In addition, only univariate analysis was used to evaluate the clinically relevant factors of AF. In future studies, we will continue to validate these results using multivariate analysis.

Conclusion

Our findings indicated that the gene polymorphism of *MAPK10P* is associated with the Pwd and Pmax in elderly patients with AF, with the presence of the *G* allele raising the likelihood of developing AF. The findings of this research offer valuable insights into the correlation between P-wave characteristics and the genetic variation of the *MAPK10P* gene in the development of paroxysmal AF among older individuals.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

(I) Conception and design: WYW and XFW; (II) administrative support: GL; (III) provision of study materials or materials obtained from patients: ALB; (IV) collection and assembly of data: GL, ALB and DL; (V) data analysis and interpretation: GL and LC; (VI) manuscript writing: WYW and XFW; (VII) funding acquisition: XFW; (VIII) final approval of manuscript: All authors contributed significantly to editorial changes of important content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study has been approved by the Medical Ethics Committee of Tianjin First Central Hospital (Approval No.: 2020N075KY) and obtained written informed consent from all participants in adherence with the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Li GHY, Cheung CL, Chung AKK, Cheung BMY, Wong ICK, Fok MLY, *et al*. Evaluation of bi-directional causal association between depression and cardiovascular diseases: a Mendelian randomization study. Psychological Medicine. 2022; 52: 1765–1776.

[2] Chen W, Yao D, Yan H, Wang M, Pan Y. Genetically predicted childhood obesity and adult atrial fibrillation: A mendelian randomization study. Nutrition, Metabolism, and Cardiovascular Diseases. 2022; 32: 1019–1026.

[3] Selvaraj S, Claggett B, Minamisawa M, Windham BG, Chen LY, Inciardi RM, *et al*. Atrial Fibrillation and Ischemic Stroke With the Amyloidogenic V122I Transthyretin Variant Among Black Americans. Journal of the American College of Cardiology. 2021; 78: 89–91.

[4] Cupido AJ, Asselbergs FW, Natarajan P, Ridker PM, Hovingh GK, Schmidt AF, *et al*. Dissecting the IL-6 pathway in cardiometabolic disease: A Mendelian randomization study on both IL6 and IL6R. British Journal of Clinical Pharmacology. 2022; 88: 2875–2884.

[5] Jian Z, Yuan C, Ma Y. Blood Pressure Mediated the Effects of Urinary Uromodulin Levels on Myocardial Infarction: a Mendelian Randomization Study. Hypertension. 2022; 79: 2430–2438.

[6] Ai S, Zhang J, Zhao G, Wang N, Li G, So HC, *et al*. Causal associations of short and long sleep durations with 12 cardiovascular

diseases: linear and nonlinear Mendelian randomization analyses in UK Biobank. European Heart Journal. 2021; 42: 3349–3357.

[7] Nakagawa J, Kinjo T, Iizuka M, Ueno K, Tomita H, Niioka T. Impact of gene polymorphisms in drug-metabolizing enzymes and transporters on trough concentrations of rivaroxaban in patients with atrial fibrillation. Basic & Clinical Pharmacology & Toxicology. 2021; 128: 297–304.

[8] Polidori MC, Alves M, Bahat G, Boureau AS, Ozkok S, Pfister R, *et al*. Atrial fibrillation: a geriatric perspective on the 2020 ESC guidelines. European Geriatric Medicine. 2022; 13: 5–18.

[9] Geurts S, van der Burgh AC, Bos MM, Ikram MA, Stricker BHC, Deckers JW, *et al*. Disentangling the association between kidney function and atrial fibrillation: a bidirectional Mendelian randomization study. International Journal of Cardiology. 2022; 355: 15–22.

[10] Kim EJ, Hoffmann TJ, Nah G, Vittinghoff E, Delling F, Marcus GM. Coffee Consumption and Incident Tachyarrhythmias: Reported Behavior, Mendelian Randomization, and Their Interactions. JAMA Internal Medicine. 2021; 181: 1185–1193.

[11] Peng X, Wang S, Wang J, Ju W, Yang G, Gu K, *et al*. Plasma 8-Hydroxy-2'-Deoxyguanosine, a Potential Valuable Biomarker for Atrial Fibrosis Is Influenced by Polymorphism of DNA Methylation Gene. Circulation Journal. 2023; 87: 964–972.

[12] Au Yeung SL, Borges MC, Wong THT, Lawlor DA, Schooling CM. Evaluating the role of non-alcoholic fatty liver disease in cardiovascular diseases and type 2 diabetes: a Mendelian randomization study in Europeans and East Asians. International Journal of Epidemiology. 2023; 52: 921–931.

[13] Mohammadi-Shemirani P, Chong M, Narula S, Perrot N, Conen D, Roberts JD, *et al*. Elevated Lipoprotein(a) and Risk of Atrial Fibrillation: An Observational and Mendelian Randomization Study. Journal of the American College of Cardiology. 2022; 79: 1579–1590.

[14] Peng JW, Nfor ON, Ho CC, Hsu SY, Lung CC, Tantoh DM, *et al*. Interactive Association Between CYP2C9 rs2860905 Polymorphism and Atrial Fibrillation on Ischemic Stroke in Taiwan Biobank Participants. Pharmacogenomics and Personalized Medicine. 2021; 14: 1087–1092.

[15] Miyazawa K, Ito K, Ito M, Zou Z, Kubota M, Nomura S, *et al*. Cross-ancestry genome-wide analysis of atrial fibrillation unveils disease biology and enables cardioembolic risk prediction. Nature Genetics. 2023; 55: 187–197.

[16] Costa LBX, Martins GL, Duarte RCF, Rocha PL, Figueiredo EL, Silveira FR, *et al*. Evaluation of serum haptoglobin levels and Hp1-Hp2 polymorphism in the haptoglobin gene in patients with atrial fibrillation. Molecular Biology Reports. 2022; 49: 7359–7365.

[17] Shen Han Y, Ahmed AM, Chao Z, Jun W, Xiaochen Y. Association Between rs2200733 Polymorphism of PITX2 Gene and the Risk of Atrial Fibrillation. Anatolian Journal of Cardiology. 2023; 27: 160–166.

[18] Wang J, Campos AI, Rentería ME, Xu L. Causal associations of sleep apnea, snoring with cardiovascular diseases, and the role of body mass index: a two-sample Mendelian randomization study. European Journal of Preventive Cardiology. 2023; 30: 552–560.

[19] Jameson HS, Hanley A, Hill MC, Xiao L, Ye J, Bapat A, *et al*. Loss of the Atrial Fibrillation-Related Gene, *Zfhx3*, Results in Atrial Dilation and Arrhythmias. Circulation Research. 2023; 133: 313–329.

[20] Okamura S, Ochi H, Onohara Y, Nakashima M, Akiyama R, Tokuyama T, *et al*. GJA1 gene polymorphism is a genetic predictor of recurrence after pulmonary vein isolation in patients with paroxysmal atrial fibrillation. Heart Rhythm. 2022; 19: 2044–2050.

[21] Wang Q, Richardson TG, Sanderson E, Tudball MJ, Ala-Korpela M, Davey Smith G, *et al*. A phenome-wide bidirectional Mendelian randomization analysis of atrial fibrillation. International Journal of Epidemiology. 2022; 51: 1153–1166.

[22] Chen L, Sun X, Wang Z, Lu Y, Chen M, He Y, *et al*. The impact of plasma vitamin C levels on the risk of cardiovascular diseases and Alzheimer's disease: A Mendelian randomization study. Clinical Nutrition. 2021; 40: 5327–5334.

[23] Saez-Maleta R, Merino-Merino A, Gundin-Menendez S, Salgado-Aranda R, AlKassam-Martinez D, Pascual-Tejerina V, *et al*. sST2 and Galectin-3 genotyping in patients with persistent atrial fibrillation. Molecular Biology Reports. 2021; 48: 1601–1606.

[24] Nakagawa J, Kinjo T, Aiuchi N, Ueno K, Tomita H, Niioka T. Impacts of pregnane X receptor and cytochrome P450 oxidoreductase gene polymorphisms on trough concentrations of apixaban in patients with non-valvular atrial fibrillation. European Journal of Clinical Pharmacology. 2023; 79: 127–135.

[25] Sun X, Chen L, Zheng L. A Mendelian randomization study to assess the genetic liability of gastroesophageal reflux disease for cardiovascular diseases and risk factors. Human Molecular Genetics. 2022; 31: 4275–4285.

[26] Fu T, Chen M, Xu L, Gong J, Zheng J, Zhang F, *et al*. Association of the *MYH6* Gene Polymorphism with the Risk of Atrial Fibrillation and Warfarin Anticoagulation Therapy. Genetic Testing and Molecular Biomarkers. 2021; 25: 590–599.