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Evaluation of the Relationship of P-Wave Duration in the Development of Atrial Fibrillation in the MASHAD Cohort Study Between 2010 to 2020

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Abstract

Background: Atrial fibrillation is the most common clinical arrhythmia. Early detection of AF can prevent further complications. The present study was designed to find the relationship between P-wave duration and AF-incidence.

Methods: The study included baseline data collected in 2010 through 2020 on 9,704 person's age 35 to 65 years from the MASHAD cohort study. P-wave duration was analyzed by the study cardiologists using lead II ECG recordings in the recruitment phase of the study for all participants.

Results: During the 10 year period, 27 persons developed AF. The results did not show any association between P-wave duration and AF. Also other ECG factors that we measured (QRS duration, QT Min, QT Max) did not show a relationship with AF incidence. In this study age showed a significant relationship (P<0.001). Also, systolic blood pressure (P=0.022) and diastolic blood pressure (P=0.025) demonstrated significant relationship with AF. In a logistic regression age (P=0.001 OR: 1.08 95% CI=1.03-1.13), HTN (P=0.02 OR: 2.36; 95% CI=1.11-5.04), SBP (P=0.02 OR: 1.01 95% CI=1.00-1.02) and platelets count (P=0.002 OR: 0.98 95% CI=0.98-0.99) showed statically relation with AF.

Conclusion: The results of this study suggest that the incidence of AF was related to blood pressure and platelet count, but no relationship was found between the P-wave duration and the incidence of AF.

Keywords: Atrial fibrillation; Electrocardiography; P-wave; P-wave duration

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Introduction

Atrial fibrillation is the most common clinical cardiac Arrhythmia (AF) [1-3]. AF is a supraventricular tachyarrhythmia caused by mechanical insufficiency of the atrium, which occurs as a result of uncoordinated atrial function. Heart failure, stroke, and other cardiovascular illnesses have been linked to an increased risk of death in people with AF [4-8]. The most essential risk factor for AF is ageing. Other causes of AF include the presence of disorders, e.g., cardiovascular diseases (heart failure, mitral valve stenosis, cardiac hypertrophy, and coronary artery disease), diabetes, hypertension, hyperthyroidism, pulmonary embolism, and excessive alcohol use. AF can sometimes be an independent condition that is not accompanied by any other illnesses.

Palpitation, chest pain, shortness of breath, fatigue, and vertigo are all common symptoms of AF [9-11]. AF is not always symptomatic (symptoms are uncommon in people under the age of 40), but when symptoms do occur, they can cause disability in patients [11,12]. Identifying those who at the risk for AF is important to prevent AF-related complications and improve community health [9,10,12].

Atrial fibrillation can be diagnosed and treated for three reasons: To reduce symptoms, or for the prevention of cardiomyopathy and thromboembolism. Tachycardia needs to be treated since it can lead to cardiomyopathy. Thromboembolism prophylaxis is also crucial since it can lead to stroke. Finding an irregular rapid pulse (more than 150 beats per minute) during a clinical examination might lead to suspicion of AF, especially if the patient is not taking any medications. An electrocardiogram is a noninvasive, simple, and low-cost test that is commonly used to confirm a clinical diagnosis of atrial fibrillation [9,13-16].

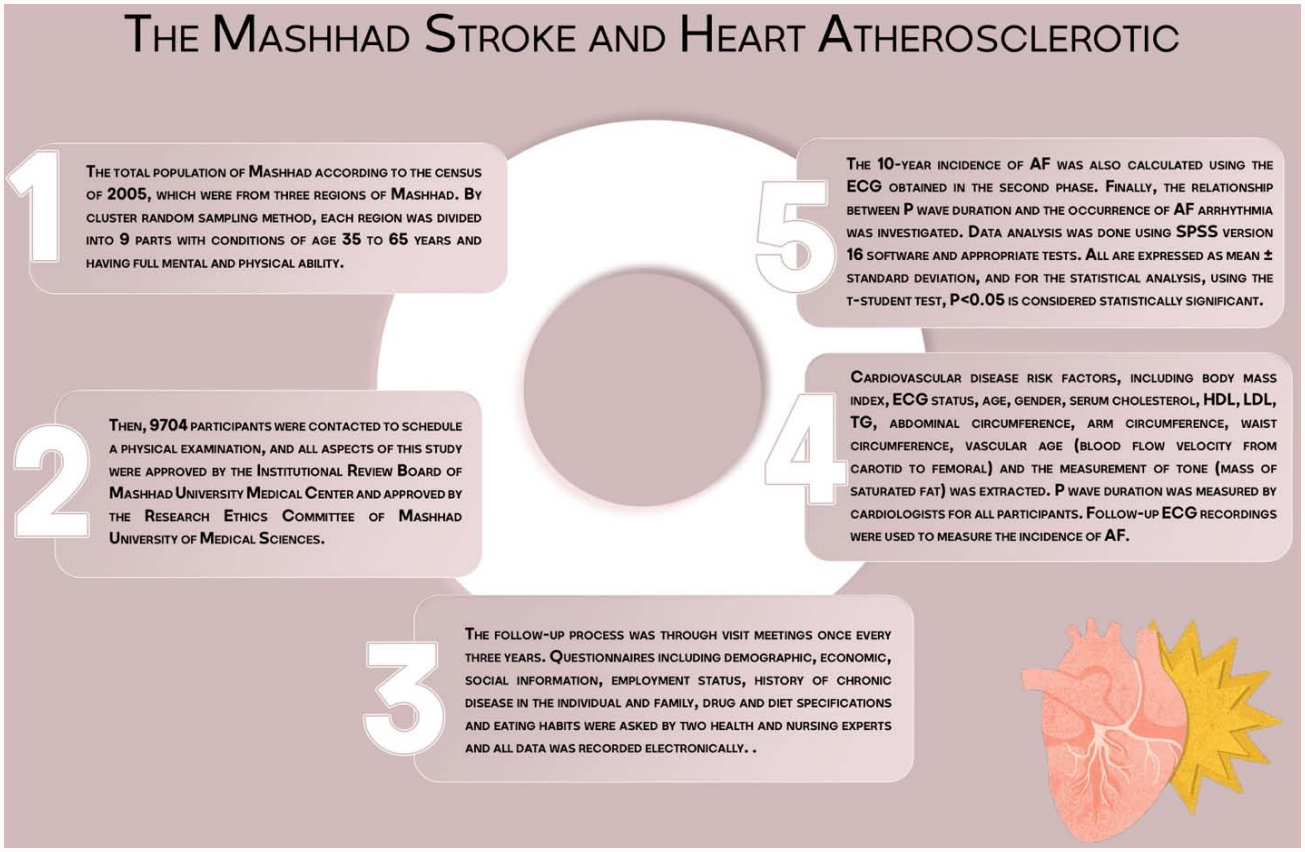

Figure 1: Schematic figure of MASHAD study.

So far, several efforts have been made to establish a predictive factor for the occurrence of AF. Börschel et al. published a study that found a link between blood biomarkers and genetics and the occurrence of AF. In this investigation, NT-proBNP and the PRS were used to predict the risk of AF, and these parameters were found to increase the risk of AF by more than three times.

Although this study yielded valuable results, it is an intrusive and costly method that cannot be used widely in practice. Aeschbacher et al. published another study that found a link between QRS wave and AF. This study found a link between QRS length and the occurrence of AF in women (but not in men), thus it cannot be generalizable to the whole community [17,18].

Atrial depolarization is characterized by the P wave (represent present moving from the sinus node to the atrioventricular node) [19]. There are only a few researches that have looked into the effect of P-wave duration on the risk of AF. One of the most notable of these investigations, the Framingham cardiac study, was in 2011. The researchers looked at the significance of P-wave dispersion and duration in the occurrence of AF and its complications. The study revealed no significant links between P-wave dispersion and the risk of AF, but it did find a link between P-wave duration and an increased risk of AF in elderly patients with P-wave duration in the upper fifth percentile [20].

A study in 2009 analyzed data from participants in ARIC (Atherosclerosis Risk in Communities), which included 15,429 people who were followed for an average of 1 6/7 years. In this study, patients in the top fifth percentile of P wave duration were 2.5 times more likely to develop AF [21].

Unfortunately, many people have silent AF and they are unaware of their disease, so having a predictor factor for AF is critical. Because no study of this magnitude has been conducted in Iran, we focused on the ECG, particularly the P-wave duration, to assess the association between this parameter and the risk of AF occurrence.

Methods

The Mashhad Stroke and Heart Atherosclerotic Disorder (MASHAD) cohort study provided the data for this study. This prospective study started in 2010 and continued until 2020. The participants that were included in this study were the total population in the city of Mashhad was estimated using the national Iranian census in 2006. Participants were chosen from three regions in Mashhad, located in the north-eastern Iran, using a stratified cluster random sampling technique. Each region was divided into nine sites centered upon Mashhad Healthcare Center divisions. The inclusion criteria were all eligible age between 35 and 65 years who had no definite plans to leave the area that agreed with the informed consent form in the first and second stages of the study and were mentally and physically capable of participating in the clinical examination. Community leaders who were familiar with the community's families also assisted in the selection of potential participants. Participants with a history of AF and those who were not between the ages of 35 and 65 and did not consent to participate in the study were excluded from the present analysis (Figure 1).

After selecting eligible participants, they were contacted to arrange an appointment for the formal physical examination. The study was approved by Mashhad University Medical Center's institutional review board and also received approval from the Research Ethics

Committee of Mashhad University of Medical Science (IR.MUMS.MEDICAL.REC.1399.824). The total number of participants was 9,704 in the end. The follow-up process was once every three years through visit sessions. Questionnaires included data on demographic, economic, social, occupational status, history of chronic illness in the individual and family, medication profile and diet and eating habits were questioned by two certified healthcare professionals and a nurse and all data were recorded electronically. Anthropometry, blood and urine tests, pulse wave volumetric test, electrocardiography, thyroid sonography, dental examination, spirometry test, and orthopedic assessment were all part of the examination procedure.

From the cohort study, cardiovascular disease risk factors, including body mass index, ECG status, age, gender, serum cholesterol, HDL, LDL, TG, abdominal circumference, arm circumference, waist circumference, vascular age (blood flow velocity from carotid to femoral) and tone measurements (saturated fat mass), were extracted. In this study, P-wave duration was measured by study cardiologists using lead II ECG recordings in the entrance phase of the study by all participants. Follow-up ECG recordings were used to measure AF incidence. The diagnosis of AF was based on ECG observations by trained investigators based on the absence of a P wave in lead II and the irregularity of QRS complexes with varying R-R intervals.

The 10-year incidence of AF was also calculated using the ECG obtained in the second phase of the MASHAD cohort. Finally, the relationship between P-wave duration and the occurrence of AF arrhythmia was investigated. Data analysis was performed using SPSS software version 16 (IBM SPSS, Inc., Armonk, NY, USA) and appropriate tests. All data are expressed as mean ± SD and we used student's t-test for statistical analysis also P<0.05 was considered statistically significant.

Result

The baseline characteristics of the study population

The average age of the study population was 48.07 ± 8.25 y. 59.9% of the participants were female (40.1% were male), 68.5% had never smoked, 21.6% were current smokers, and 9.9% were ex-smokers. 14.4% of participants had diabetes and 40.8% had hypertension. During the 10-year period of follow-up, 27 participants developed AF (0.3%). Further information about the study population at baseline is shown in Table 1.

The mean age of participants who developed AF was 53.66 ± 6.45 years (*P*= <0.001) and was significantly higher than the mean age of participants without AF (48.12 ± 8.23). We also measured participants' systolic blood pressure and indicated a significant correlation between SBP in AF patients and those who did not have AF, *P*=0.022 (0.48 ± 0.50 *vs.* 0.28 ± 0.45). Diastolic blood pressure also showed a statistically significant association between those who got AF and other participants *P*=0.025 (0.44 ± 0.5 *vs.* 0.28 ± 0.45). The other parameters we measured were weight, BMI, waist circumference, hip circumference, uric acid, LDL, cholesterol, HDL, TG and high sensitivity C reactive protein, but the results did not show a significant relationship (Table 2).

Some ECG factors between AF negative and positive subjects

As shown in Table 3, there is no significant correlation between P-duration in those who developed AF during the study and the other participants. We also measured QRS Duration, QT Min, QT Max, and heart rate during the study, and they showed similar results (there was no significant correlation).

Table 1: Baseline characteristics of study population.

		Frequency	Valid Percent%
Age		48.07 ± 8.25	
Sex (9847)	male	3952	40.1
	female	5895	59.9
Smoking status (9837)	non smoker	6739	68.5
	Ex-smoker	976	9.9
	current smoker	2122	21.6
DM (9650)	≥ 126	1386	14.4
	<126	8264	85.6
HTN, mmHg (9736)	no	5761	59.2
	yes	3975	40.8

DM: Diabetes Mellitus; HTN: Hypertension
Values are expressed as No. of participants (%) or mean ± SD

Table 2: Baseline characteristics of study population based on AF.

	AF		
	No (Mean ± SD)	Yes (Mean ± SD)	*P-value**
age/year	48.12 ± 8.23	53.66 ±6.45	<0.001
Weight, kg	71.89 ± 12.87	73.60 ± 13.78	0.49
BMI, kg/m^2	27.91 ± 4.72	28.36 ± 5.44	0.62
Waist circumference, cm	95.18 ± 12.06	98.21 ± 10.92	0.19
Hip circumference, cm	103.74 ± 9.33	105.79 ± 10.11	0.25
SBP, mmHg	0.28 ± 0.45	0.49 ± 0.50	0.022
DBP, mmHg	0.25 ± 0.43	0.44 ± 0.50	0.025
URICACID	4.67 ± 1.40	4.76 ± 1.31	0.73
LDL, mg/dl	116.46 ± 35.38	125.44 ± 32.01	0.19
Cholesterol, mg/dl	191.38 ± 39.19	195.92 ± 38.59	0.55
HDL, mg/dl	42.78 ± 9.95	45.00 ± 10.19	0.25
Triglycerides, mg/dl	142.89 ± 92.46	117.15 ± 56.51	0.15
hs-CRP, mg/dl	4.19 ± 8.95	4.44 ± 9.76	0.89

BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; hs-CRP: high-sensitivity C-Reactive Protein
Values are expressed as mean ± SD
**P*<0.05 was considered statically significant

Relation between ECG and other factors with AF

In a logistic-regression analysis, age was significantly meaningful between the AF positive group and the AF negative group (Sig =0.001 OR: 1.08 95% CI=1.03-1.13) HTN was another factor that showed meaningful association, so clearly the prevalence of HTN was higher in patients who got AF (sig =0.02 OR: 2.36; 95% CI=1.11-5.04) (Table 4).

Also, results of SBP showed a relation in AF patients (sig =0.02 OR: 1.01 95% CI=1.00-1.02). The last factor that showed a significant statistical relation was platelets (sig =0.002 OR: 0.98 95% CI=0.98-0.99). In this logistic regression, none of the ECG characteristics we examined in this study showed a meaningful relation between AF patients and non-AF patients.

Discussion

This study was done in order to find a relationship between p wave duration and AF incidence on the basis of a standard 12-lead in a follow-up period of 10 years. The mean age of participants was 48.07

Table 3: Some ECG factors between AF negative and positive subjects.

	AF				
	No		Yes		
	N	Mean ± SD	N	Mean ± SD	P value*
P Duration, ms	9160	0.08 ± 0.01	27	0.08 ± 0.01	0.71
QRS Duration, ms	9162	0.08 ± 0.01	27	0.07 ± 0.01	0.48
QT Min, ms	9072	0.36 ± 0.03	27	0.35 ± 0.02	0.2
QT Max, ms	9074	0.38 ± 0.04	27	0.38 ± 0.02	0.89
HR, beats/min	9154	71.71 ± 98.15	27	71.71 ± 7.05	0.97

HR: Heart Beat
Values are expressed as mean ± SD
*P<0.05 was considered statically significant

Table 4: Relation between ECG and other factors with AF.

	Sig.	Exp(B)	95% CI for EXP(B)	
			Lower	Upper
P Duration, ms	0.71	0.01	0.00	4283156990.84
HR, beats/min	0.97	1.00	0.99	1.00
QT max, ms	0.89	1.87	0.00	21293.39
QT min, ms	0.19	0.00	0.00	29.89
QRS Duration, ms	0.47	0.00	0.00	42280794.44
Sex	0.64	0.83	0.39	1.79
Age/year	0.001	1.08	1.03	1.13
Diabetes	0.34	2.01	0.47	8.54
HTN, mm Hg	0.02	2.36	1.11	5.04
BMI, kg/m^2	0.63	1.01	0.94	1.10
Weight, kg	0.49	1.01	0.98	1.03
WC, cm	0.19	1.02	0.99	1.05
HC, cm	0.25	1.02	0.98	1.06
SBP, mm Hg	0.02	1.01	1.00	1.02
DBP, mm Hg	0.09	1.01	0.99	1.03
PLT	0.002	0.98	0.98	0.99
LDL, mg/dl	0.19	1.00	0.99	1.01
Cholesterol, mg/dl	0.55	1.00	0.99	1.01
HDL, mg/dl	0.26	1.02	0.98	1.05
TG, mg/dl	0.14	0.99	0.98	1.00
hsCRP, mg/dl	0.91	1.00	0.96	1.04
Uric acid	0.75	1.04	0.8	1.34
Glucose	0.72	1.00	0.99	1.01

HR: Heart Beat; HTN: Hypertension; BMI: Body Mass Index; WC: Waist Circumference; HC: Hip Circumference; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; PLT: Platelet; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglyceride; hsCRP: High-Sensitivity C-Reactive Protein; Values are expressed as mean ± SD

± 8.25 y/o. In a study by Go et al. showed an association between age and the incidence of AF that the prevalence of AF increased from 0.1% in people younger than 55 y/o to 9.0% in people older than 80 y/o [5]. Other available studies show that the prevalence of AF increases significantly with aging [22,23]. Our results show a significant correlation between age and AF. The mean age of individuals who developed AF was higher than those who did not develop AF.

We also examined the presence of hypertension in this study, and our results showed both systolic and diastolic blood pressure have a significant relationship with AF. In a study by Benjamin et al. they found a significant relationship between hypertension and AF too Many studies have emphasized the point that hypertension is a risk factor for AF [23-26].

Colkesen et al. concluded that patients with paroxysmal AF have more mean platelets volume (size, function and activation). Increase in mean platelets volume leads to release more thromboxane A2 that involved in progress of thrombosis [27]. We examined the relationship between platelets and AF. Our results showed platelets have a statically meaningful association with AF incidence.

The P wave gives us important information about the atria. It shows electrical depolarization of the atria and we can diagnose some heart diseases (like Wolff-Parkinson-White syndrome, abnormalities in left and right atria, AV and SA node blocks) by measurement of p wave duration and pay attention to its morphology. In this study, P-wave duration did not show any relation with AF. Although we saw a different range of results in other studies but also some studies have reported similar results to ours. For example, Nielsen et al. reported that very short (≤ 89 ms), long (120 ms to 129 ms) and very long (≥ 130 ms) p-wave duration were significantly associated with increased risk of AF [28]. Another study in 2020 had similar results to our study about P-wave duration and they did not find any relationship between p-wave duration and AF [6]. In a study with participants that were older than 60 y/o showed the risk of AF is 2.51 fold in patient with upper 5% of maximum p-wave duration [20]. Further studies in this area are needed to establish a precise relationship between P-wave and AF.

There were some limitations in the present study. One of the important limitations is the low average age of the participants. There is a correlation between the findings of age studies and the likelihood of developing AF. Therefore, it is suggested that in future studies, this study be performed at higher age ranges. Also, since Mashhad is a tourist-medical city, it was not possible to separate the participants based on race and ethnicity, which may cause problems in the study results. Finally, due to the paroxysmal nature of this arrhythmia, not all cases of AF may be recorded.

Conclusion

Overall, the results of this study showed that the incidence of AF has a significant relationship with blood pressure and platelets as a risk factor. On the other hand, no correlation was found between P-wave duration and AF-incidence. Given the importance of early detection of AF, additional studies are needed to find a predictor.

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