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Prevalence and associated factors of ECG abnormality patterns indicative of cardiac channelopathies among adult general population of Tehran, Iran: a report from the Tehran Cohort Study (TeCS)

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Abstract

Background The characteristics of electrocardiogram (ECG) abnormalities related to cardiac channelopathies potentially linked to sudden cardiac death (SCD) are not widely recognized in Iran. We examined the prevalence of such ECG patterns and their related factors among adult residents of Tehran, Iran.

Methods The clinical characteristics and 12-lead ECGs of Tehran Cohort Study participants were examined. Long QT intervals, short QT intervals, Brugada syndrome (BrS) patterns, and early repolarization (ER) were evaluated using computer-based assessment software validated by cardiologists. Logistic regression models were employed to identify the factors associated with the prevalence of different ECG patterns.

Results Out of 7678 available ECGs, 7350 were included in this analysis. Long QT interval, ER pattern, BrS patterns, and short QT interval were found in 3.08%, 1.43%, 0.31%, and 0.03% of participants, respectively. The prevalence of long QT interval increased with age, opium consumption, and presence of hypertension. Younger age, lower body mass index (BMI), alcohol use and male sex were independently linked to an elevated prevalence of ER pattern. Most individuals with BrS patterns were men (95%) and had lower BMI, high- and low-density lipoprotein, and total cholesterol compared to those without the BrS pattern. At a mean follow-up of 30.2 ± 5.5 months, all-cause mortality

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in the group exhibiting abnormal ECG patterns (6.3%) was approximately twice as high as that in the group without such patterns (2.96%).

Conclusion Abnormal ECG patterns corresponding to channelopathies were relatively rare among adult residents of the Tehran population, and their prevalence was influenced by various factors.

Clinical trial number Not applicable.

Keywords Electrocardiography, Heart conduction system, Long QT syndrome, Brugada syndrome, Population surveillance, Cross-sectional studies

Introduction

Several cardiac channelopathies have been recognized to date, with the most common being long QT syndrome (LQTS), short QT syndrome (SQTS), Brugada syndrome (BrS), and early repolarization (ER). LQTS and SQTS are characterized by the prolongation and shortening of the QT interval on the electrocardiogram (ECG), respectively. These conditions are typically accompanied by syncopal events, cardiac dysrhythmias, and sudden cardiac death (SCD) [1, 2]. BrS is defined by an elevation of the ST-segment in the right precordial leads, occurring in the absence of ischemia, electrolyte imbalances, or structural heart disease. This syndrome can be associated with ventricular fibrillation (VF) and SCD [3]. The ER pattern, another ECG marker for channelopathies, was previously considered benign but has recently been linked to idiopathic VF and SCD [4].

Cardiac channelopathies leading to SCD are commonly observed in infants, children, and young individuals who lack significant cardiac structural disease or cardiovascular risk factors. Nevertheless, ECG patterns suggestive of these disorders, even without clinical symptoms, can also be present in adulthood, indicating that there may be abnormalities in repolarization and conduction that could lead to SCD without any identifiable cause. SCD poses a challenge for physicians as it might be the only manifestation of a cardiac issue. As such, determining the prevalence of such ECG abnormalities and associated factors in local populations is crucial. This information can help develop cost-effective strategies for prevention, timely detection, and treatment [5].

The frequency of long and short QTc intervals in the general population greatly varies across countries. This variation depends on population characteristics and the established cut-off for interval prolongation and shortening, ranging from 0.17 to 31.6% [6–11] and 0.02–9% [8, 11–15], respectively. A recent meta-analysis reveals that the prevalence of ER patterns also varies by population, ranging from 1.3 to 45.8%, with a pooled prevalence of 11.6% [16]. There is also a significant variation in the prevalence of BrS-type ECG across different populations, ranging from 0.07 to 6% [17–23]. Prior research has also identified links between the aforementioned ECG patterns and various demographic and clinical characteristics; while some of these associations are consistent between studies, the majority vary across populations [6, 7, 12, 24–26].

This study aimed to ascertain the frequency of long QT intervals, short QT intervals, BrS-type ECG patterns, and ER patterns in a random sample of apparently healthy adult residents of Tehran. Additionally, it sought to identify the factors significantly associated with these ECG patterns.

Materials and methods

Study design and participants

This research was a cross-sectional analysis with a short-term follow-up, conducted on participants from the initial phase of the Tehran Cohort Study (TeCS) who had a digital ECG. Each subject provided written consent before participating in the study. The TeCS is primarily focused on investigating the prevalence, incidence, and trends of cardiovascular diseases, psychological symptoms, injuries, and risk factors within the Tehran population. More details about the TeCS protocol can be found in a previously published paper [27].

We examined the demographics, clinical characteristics, and 12-lead standard ECG of individuals aged ≥ 35 years who enrolled between March 2016 and March 2019. A cardiologist reviewed the ECGs and excluded any that fulfilled one or more of the following exclusion criteria: [1] Low ECG quality; [2] Presence of grade 2 or 3 AV blocks; [3] QRS duration of more than 120 ms; [4] Non-sinus rhythms; [5] More than 2 PVCs within 10 s.

We followed individuals identified as high-risk for adverse outcomes based on their ECG through telephone contact to ascertain their survival status. The records of individuals who died during or subsequent to hospitalization were reviewed in person to determine the precise cause of death. SCD was defined as an unexpected mortality due to cardiovascular factors in an individual, regardless of prior cardiac disorders, occurring within one hour following an alteration in clinical state or 24 h of last being seen healthy and alive [28, 29].

Electrocardiogram measurements and interpretation

QT interval measurement

Two M-trace ECG devices (M4Medical, Lublin, Poland) were utilized to record the patients' ECGs. The QT interval measurement was conducted using a custom automated computer software developed by Nabz Hooshmand Co., based in Tehran, Iran. This software interprets digital ECGs and estimates the QT interval by determining the time between the start of the first QRS complex deflection and the point where the T wave returns to the isoelectric line. The accuracy of the software measurement was evaluated by comparing it with expert manual measurement. Two cardiologists used on-screen caliper software to measure the QT interval in a sample of 200 standard ECGs. According to the guidelines established by the International Electrotechnical Commission (IEC), it is considered acceptable for ECG software to have a mean difference of less than 25 ms and a standard deviation (SD) of less than 30 ms compared to observer measurements in terms of accuracy [30]. Three different methods were employed by automated software to measure the QT interval, which were then compared with manual measurements made by experts: (1) The median value of the QT interval across all beats and leads; (2) The mean value of the QT interval across all beats and leads; (3) Initially, the median value of the QT interval for each lead was calculated from beats that fell within the acceptable range ($\pm$SD of the mean). Subsequently, the median QT of all leads was determined for each ECG. Using the last method, the mean difference and SD of differences between the average of experts and software were 9.92 msec and 10.81 msec, respectively, which was acceptable according to IEC standards. The QT interval measurement for the remaining ECGs was performed by the automated software using this third method.

The Bazett formula was utilized to correct the QT measurement based on heart rate (HR). The formula is as follows: Bazett: $QTc = QT / (RR)^{1/2}$ [31]. The heart rate (HR) was calculated using the following formula in lead II:

$$HR = \frac{((\,number\ of\ detected\ R - 1\,)*60)}{(Time\ between\ first\ and\ last\ R)}$$

In accordance with most studies, a long QTc interval was defined as QTc>450 ms in men and QTc>460 ms in women, and a shortened QT interval was defined as QTc<330 ms in men and QTc<340 ms in women [9, 11]. Given the discrepancy of 9.92 msec between expert and machine measurements, a bilateral safety margin of 10 msec was established. This safety margin necessitates that experts recheck any ECGs that are suspicious to prevent potential cases from being overlooked.

An expert cardiologist reviewed all ECGs with suspiciously long (QTc>440 ms in men and >450 ms in women) and short (QTc<340 ms in men and <350 ms in women) QT intervals to verify the accuracy of the QT measurement. Furthermore, if the algorithm reported a QT in fewer than 8 leads, it was considered an unreliable QT report, prompting experts to recheck those ECGs. This rigorous process ensures the accuracy and reliability of the QT measurements.

BrS-type and ER ECG patterns

The ECGs underwent thorough evaluation by two independent cardiologists, who made the diagnosis of BrS-type and ER patterns only after reaching a consensus. In the case of a disagreement between the diagnoses of cardiologists, an experienced electrophysiologist made the ultimate decision.

The BrS-type ECG pattern was identified using the criteria specified by the Heart Rhythm Society and the European Heart Rhythm Association at their 2nd consensus meeting for diagnosing the Brugada pattern [32]. The right precordial leads of the 12-lead standard ECG were analyzed, and the criteria for classifying BrS-type patterns into three types were as follows: [1] Type 1: a coved ST-segment elevation$\geq$2 mm (0.2 mV), followed by a negative T wave; [2] Type 2: a saddle-back ST-segment elevation with a high takeoff ST-segment elevation of $\geq$2 mm (0.2 mV), followed by either a positive or biphasic T wave; [3] Type 3: either a saddle-back or coved appearance with an ST-segment elevation of <1 mm (0.1 mV) [32]. Type 1 BrS ECG pattern has been associated with an increased risk of adverse outcomes, thereby necessitating careful monitoring. Additionally, longitudinal research has indicated that type 2 and 3 BrS patterns may spontaneously evolve into the type 1 BrS pattern. To identify these cases of type 2 and type 3, a challenge test using specific pharmacological agents, such as procainamide or ajmaline, is used to induce the type 1 BrS pattern [32–34]. Given the observational nature of our study in the general population and the impossibility of injecting drugs, we decided to follow up on all BrS-type ECG patterns, as type 2 and type 3 possess the potential to convert into type 1, making them high-risk cases.

Following the recommendations of the consensus meeting for ERP characterization [35], the ER pattern was defined as an end-QRS notch or slur on the downslope of a prominent R-wave, a J-point elevation of $\geq$0.1 mV in two or more adjacent leads of the 12-lead ECG, excluding leads V1–V3, and a QRS duration<120 ms. The ER patterns were classified based on the region they covered: inferior (leads II, III, aVF), lateral (V4-V6, I, and aVL), or inferolateral [35]. Evidence indicates that inferolateral ER patterns are associated with a greater risk compared to patterns that are confined to inferior or

lateral locations alone [36, 37]. Therefore, we have considered this type of ER pattern as a high-risk population for further follow-up.

Statistical analysis

Continuous variables were shown as mean and standard deviation (SD) or median with 25th and 75th percentiles and compared using the student's t-test or Mann-Whitney test, as appropriate, based on the variable distribution. Categorical variables were shown with frequency and percentage and compared using the chi-square test or Fisher's exact test. We used multivariable logistic regression models to show the adjusted association of covariates with ECG abnormality patterns. The results were reported through odds ratios (ORs) and 95% confidence intervals (CIs). Due to a few cases of Brugada patterns, adjusted model was not conducted. There were just 3 cases of short QT, which were unsuitable for any statistical analyses. Inter-observer agreement for evaluating ECGs was assessed using intraclass correlation coefficients (ICC). Statistical analyses were conducted using SPSS software (version 25).

Results

The database contained 7678 individuals with at least one ECG. Of these, 328 were excluded due to incomplete data, low-quality ECG, non-sinus rhythms, grade 2 or 3 AV blocks, or more than 2 PVCs. The ECGs of 7350 patients (46% men; mean age 53 years) were included in this study's analysis. The mean QTc duration calculated by custom automated computer software and manual method had no significant difference according to IEC standards. A strong agreement was observed between the manual and automatic measure of QT interval (ICC=0.910, 95%CI: 0.868–0.939, $p<0.01$), suggesting the precision of the computer-assessed automated QT interval measurement.

Frequency and characteristics of individuals with long QTc interval

227 individuals (3.08% of the total; 44.9% men) exhibited a long QTc interval in their ECGs based on the established cut-offs. Table 1 presents the demographics and clinical features of individuals with and without long QT interval.

Individuals with a long QT interval were significantly older (58±14 vs. 53±12, $p<0.001$), consumed more opium (9.3% vs. 5.2%, $p=0.007$) and less alcohol (5.3% vs. 9.4%, $p=0.038$), had higher rates of coronary artery diseases (CAD) (12.8% vs. 8.2%, $p=0.014$), and had higher levels of systolic blood pressure (SBP) (128.93±22.56 mmHg vs. 121.1±18.47 mmHg, $p<0.001$), diastolic blood pressure (DBP) (83.53±12.88 mmHg vs. 80.64±10.62 mmHg, $p=0.001$), mean blood pressure (MBP)

(98.64±14.99 mmHg vs. 94.13±12.16 mmHg, $p<0.001$) and fasting blood sugar (FBS) [99 (92–115) mg/dl vs. 97 (90–106) mg/dl, $p=0.013$], compared to those who did not have a long QT interval. Beta-blockers were the only drugs affecting QT interval that a significant number of individuals used on a regular basis; while the frequency of their use was higher in the group with a long QT interval than those with a normal QT interval (19.8% vs. 15.5%), the difference did not reach a significant level ($P=0.077$). Other characteristics were comparable between the groups, as shown in Table 1.

Frequency and characteristics of individuals with ER patterns

Based on the ECGs, 105 individuals (1.43%) exhibited ER patterns. These patterns were classified by their distribution across anatomical regions, as shown in Fig. 1. Table 1 presents the demographics and clinical features of individuals with and without ER patterns.

Individuals exhibiting ER ECG patterns had a lower mean age (48.8±12.08 vs. 53.03±12.25, $p=0.001$) and BMI (26.39±4.00 kg/m^2 vs. 27.95±4.79 kg/m^2, $p=0.002$), a higher proportion of males (47.7% vs. 44.2%, $p=0.025$), lower levels of HDL-C [41 (33–49) mg/dl vs. 43 (36–52) mg/dl, $p=0.023$], and a higher prevalence of water-pipe and alcohol usage compared to those without ER ECG patterns.

Frequency and characteristics of individuals with BrS-type ECG pattern

23 individuals (0.31%) had a BrS-type pattern in their ECGs, of whom only 3 had a type 1 pattern, while the others exhibited either type 2 or 3 patterns. Table 1 shows the demographics and clinical features of individuals with and without BrS-type ECG patterns.

Significant differences were observed between individuals with BrS-type patterns and those without. Specifically, individuals with BrS-type patterns were predominantly male (95% vs. 45.9%, $p<0.001$). They also had lower levels of BMI, HDL-C, LDL-C, and total cholesterol (TC) compared to those without BrS-type patterns. In terms of physical activity, both low and high levels were more prevalent among individuals with BrS-type patterns (22.7% vs. 16.1% and 45.5% vs. 24.9%, respectively), while intermediate levels of physical activity were less prevalent ($p=0.021$). Other clinical characteristics were similar between the two groups.

Frequency and characteristics of individuals with short QTc interval

Three (0.03%) people exhibited a short QTc interval in their ECGs based on the established cut-offs. Supplementary Table 1 describes the demographics and clinical characteristics of these cases.

Table 1 Characteristics of individuals with and without ECG abnormalities

Variables	Total sample	Long QT interval (n)			BrS-type pattern			ER pattern		
		+ (227)	- (7123)	P	+ (23)	− (7327)	P	+ (105)	− (7263)	P
Age, y	53 ± 12	58 ± 14	53 ± 12	**< 0.001**	55 ± 14	53 ± 12	0.559	48.8 ± 12.08	53.03 ± 12.25	**0.001**
Male, n (%)	3381 (46%)	102 (44.9)	3253 (45.7)	0.827	22 (95)	3358 (45.9)	**< 0.001**	42 (47.7)	3256 (44.2)	**0.025**
Ethnicity, n(%) Fars Azari Others	3572 (48.6) 2190 (29.8) 1588 (21.6)	102 (44.9) 73 (32.2) 52 (22.9)	34.81 (48.9) 2112 (29.7) 1530 (21.4)	0.522	11 (47.8) 8 (34.8) 4 (17.4)	3651 (47.9) 2296 (30.1) 1675 (22)	0.850	40 (46) 22 (25.3) 25 (28.7)	3721 (49.3) 2251 (29.8) 1586 (20.9)	0.205
Physical Activity, n (%) Low Intermediate High	1183 (16.1) 4344 (59.1) 1823 (24.8)	43 (18.9) 136 (60) 48 (21.1)	1142 (16) 4218 (59.2) 1763 (24.8)	0.267	5 (22.7) 7 (31.8) 10 (45.5)	1226 (16.1) 4498 (59) 1898 (24.9)	**0.021**	13 (14.9) 45 (51.8) 29 (33.3)	1262 (16.7) 4458 (59) 1838 (24.3)	0.146
Current cigarette smokers, n (%)	956 (13)	33 (14.5)	919 (13)	0.495	4 (18.2)	948 (13)	0.519	934 (12.9)	18 (20.5)	0.054
Opium, n (%)	390 (5.3)	21 (9.3)	367 (5.2)	**0.007**	3 (13.6)	385 (5.3)	0.409	9 (10.2)	379 (5.2)	0.051
Waterpipe, n(%) Never Former Current	6902 (93.9) 37 (0.5) 411 (5.6)	218 (96) 1 (0.5) 8 (3.5)	6628 (93.8) 29 (0.5) 392 (5.7)	0.376	21 (91.4) 1 (4.3) 1 (4.3)	7168 (94) 38 (0.5) 416 (5.5)	0.132	76 (87.4) 2 (2.3) 9 (10.3)	7059 (93.3) 37 (0.5) 462 (6.2)	**0.008**
Alcohol, n (%)	684 (9.3)	12 (5.3)	664 (9.4)	**0.038**	2 (9.1)	674 (9.3)	0.284	22 (25.3)	654 (9.1)	**< 0.001**
History of CAD, n (%)	617 (8.4)	29 (12.8)	584 (8.2)	**0.014**	1 (4.5)	612 (8.4)	0.718	3 (3.4)	610 (8.4)	0.051
Family history of SCD, n (%)	507 (6.9)	12 (9.6)	299 (7.7)	0.527	1 (4.5)	504 (6.9)	0.339	3 (3.4)	502 (6.9)	0.287
Beta Blocker usage, n (%)	1147 (15.6)	45 (19.8)	1104 (15.5)	0.077	3 (13.6)	1146 (15.6)	0.233	12 (13.5)	1137 (15.7)	0.661
BMI, kg/m²	27 ± 4	37.9 ± 4.84	27.93 ± 4.79	0.091	25.82 ± 4.00	27.94 ± 4.79	**0.038**	26.39 ± 4.00	27.95 ± 4.79	**0.002**
SBP, mmHg	121 ± 18	128.93 ± 22.56	121.1 ± 18.47	**< 0.001**	118.63 ± 16.31	121 ± 18	0.243	118.63 ± 16.31	121.37 ± 18.69	0.119
DBP, mmHg	80 ± 10	83.53 ± 12.88	80.64 ± 10.62	**0.001**	79.33 ± 10.80	80 ± 10.71	0.379	79.33 ± 10.80	80.75 ± 10.71	0.212
MBP, mmHg	94 ± 12	98.64 ± 14.99	94.13 ± 12.16	**< 0.001**	92.43 ± 11.85	94 ± 12.29	0.958	92.43 ± 11.85	94.30 ± 12.29	0.153
HDL-C, mg/dl	43 (36–52)	43 (35–53)	43 (36–52)	0.821	36 (31–43)	43 (36–52)	**0.007**	41 (33–49)	43 (36–52)	**0.023**
LDL-C, mg/dl	111 (90–135)	112 (92–139)	111 (90–134)	0.243	89.5 (75–124)	111 (91–135)	**0.013**	116 (99–138)	111 (90–135)	0.433
Total Cholesterol, mg/dl	170 (145–197)	175 (148–202)	170 (145–197)	0.162	145 (125–178)	170 (145–197)	**0.004**	172 (143–198)	170 (145–197)	0.927
TG, mg/dl	125 (88–176)	122 (87–180)	125 (88–197)	0.584	112 (80–194)	125 (88–175)	0.980	125 (88–175)	112 (80–194)	0.457
FBS, mg/dl	97 (90–107)	99 (92–115)	97 (90–106)	**0.013**	94 (89–104)	97 (90–107)	0.505	94 (89–104)	97 (90–107)	0.119
Cr, mg/dl	0.8 (0.7–0.93)	0.8 (0.63–0.97)	0.8 (0.7–0.93)	0.638	0.8 (0.7–0.96)	0.8 (0.7–0.9)	0.162	0.88 (0.78–0.97)	0.8 (0.7–0.93)	**0.002**

BMI, body mass index; BrS, Brugada syndrome; CAD, coronary artery disease; Cr, creatinine; DBP, diastolic blood pressure; ER, early repolarization; FBS, fasting blood sugar; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MBP, mean blood pressure; SBP, systolic blood pressure; SCD, sudden cardiac death; TG, triglyceride

Factors associated with ECG abnormality patterns

Tables 2 and 3 show the multivariable logistic regression analysis of different variables associated with the long QTc interval and ER pattern, respectively. The frequency of long QT interval increased with age (OR: 1.015, 95%CI: 1.002–1.029, P=0.020), current opium usage (OR: 1.741, 95%CI: 1.016–2.984, P=0.044), and the presence of hypertension (HTN) (OR: 1.788, 95%CI:
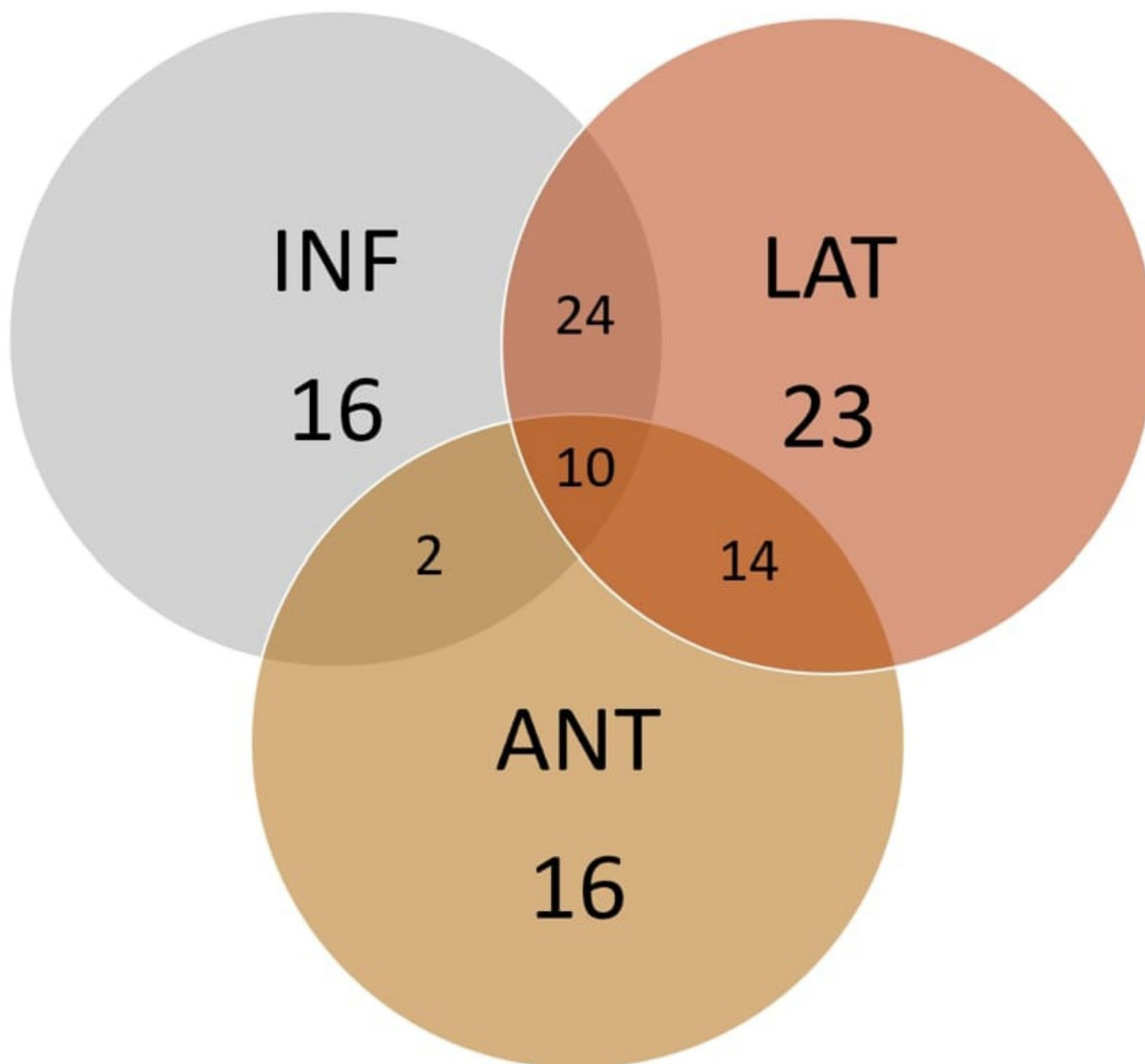
Fig. 1 Distribution of early repolarization patterns based on their anatomical region

1.256–2.545, $P=0.001$). Conversely, the frequency of ER patterns decreased with increasing age (OR: 0.974, 95%CI: 0.953–0.996, $P=0.020$) and BMI (OR: 0.944, 95%CI: 0.896–0.994, $P=0.029$). Males proportion and alcohol consumption were positively and independently associated with an increased frequency of ER pattern (OR: 1.243, 95% CI: 0.896–2.176, $P=0.031$, and OR: 2.462, 95% CI: 1.442–4.203, $P=0.001$, respectively). Other characteristics were not significantly and independently associated with the frequency of long QTc intervals and ER patterns. Due to the small sample sizes, logistic regression analysis was not feasible for estimating variables linked to the frequency of BrS-type patterns and short QT intervals.

Follow-up of high risk cases

A short-term follow-up was conducted on 152 patients identified as high-risk for poor outcomes, including 39 individuals with a very long QT duration (QTc>470 ms), 3 with a very short QT interval (QT<320 ms), 23 with a BrS-type pattern, and 87 with inferolateral ER. 26 patients (17.1%) could not be contacted and were deemed lost to follow-up. The mean duration of follow-up was 30.2 ± 5.5 months. During the follow-up period, there were 5 (12.8%) and 3 (3.4%) total deaths among individuals who had a very long QT interval and inferolateral ER, respectively, of whom one case with a very long QT interval died of SCD. The mortality rate among individuals not classified as high risk for poor outcomes was 2.96%,

Table 2 Multivariable logistic regression analysis of different variables associated with long QTc interval

Variable	Long QT		
	OR	95%CI	P value
Age, y	1.015	1.002–1.029	**0.020**
BMI, kg/m^2	0.987	0.957–1.018	0.399
Cr, mg/dl	1.245	0.829–1.869	0.291
Ethnicity	1.208	0.880–1.658	0.243
Current cigarette smoking	1.025	0.654–1.607	0.913
Waterpipe use	0.915	0.439–1.905	0.812
Opium use	1.741	1.016–2.984	**0.044**
Physical activity	0.991	0.627–1.566	0.968
Alcohol use	0.556	0.294–1.052	0.071
History of CAD	1.039	0.652–1.655	0.872
Beta Blocker usage	0.860	0.583–1.269	0.448
Family history of SCD	0.988	0.586–1.664	0.963
HTN (SBP ≥ 140 and/or DBP ≥ 90)	1.788	1.256–2.545	**0.001**
DM (FBS ≥ 126)	1.022	0.728–1.436	0.898

BMI, body mass index; CAD, coronary artery diseases; CI, confidence interval; Cr, creatinine; DBP, diastolic blood pressure; DM, diabetes mellitus; FBS, fasting blood sugar; OR, odds ratio; SBP, systolic blood pressure; SCD, sudden cardiac death

Table 3 Multivariable logistic regression analysis of different variables associated with ER pattern

Variable	Early repolarization pattern		
	OR	95% CI	P value
Age, y	0.974	0.953–0.996	**0.020**
BMI, kg/m^2	0.944	0.896–0.994	**0.029**
Cr, mg/dl	1.406	0.911–2.17	0.12
Waterpipe use	3.03	0.669–13.717	0.15
Opium use	1.742	0.839–3.614	0.136
Alcohol use	2.462	1.442–4.203	**0.001**
History of CAD	0.553	0.116–1.843	0.335
HTN(SBP ≥ 140 and/or DBP ≥ 90)	1.090	0.644–1.845	0.748
HLP (Total Cholesterol ≥ 200 and/or TG ≥ 150)	0.822	0.477–1.416	0.479
Gender (male)	1.243	0.896–2.176	**0.031**

BMI, body mass index; CAD, coronary artery diseases; CI, confidence interval; Cr, creatinine; DBP, diastolic blood pressure; DM, diabetes mellitus; HLP, hyperlipidemia; OR, odds ratio; SBP, systolic blood pressure

much lower than that of high-risk individuals. None of the patients reported experiencing syncope.

Discussion

In this study, we provided detailed characteristics of individuals with ECG abnormalities suggestive of cardiac channelopathies, including long QT intervals, short QT intervals, BrS-type ECG patterns, and ER ECG patterns among the adult general population of Tehran, the capital city of Iran. In line with previous findings, the frequency of these ECG patterns was infrequent, with a male preponderance observed in those with BrS-type ECG patterns. As individuals got older, there was a noticeable rise in the frequency of long QT intervals, whereas the

frequency of ER patterns tended to decline. Current opium use and the presence of hypertension were independently associated with an increased frequency of long QT intervals. The frequency of ER pattern was positively influenced by male proportion and alcohol consumption, while BMI exhibited a reverse relationship with the frequency of ER pattern. During the short-term follow-up, it was observed that individuals who had an ECG abnormality indicating high risk for poor outcomes had a mortality rate that was approximately twice as high as those who were not at high risk.

The frequency of a long QT interval in our study, characterized as QTc > 450 ms in males and QTc > 460 ms in females, was 3.08%. This estimate was at least three and ten times lower than that reported by Magodoro et al. [6] in Uganda adults aged 38.4 years, with a QTc cut-off point of 470 ms in females and 450 ms in males, and Ma et al. [7] in a Chinese population aged 56 years, with a cut-off point of 440 ms for both genders, respectively. The high prevalence rate seen in the Ma et al. study is most likely owing to the low and non-specific cut-off used to define QT prolongation in both genders. There were also some reports in which their estimate of long QT interval frequency was significantly lower than ours (≤1%) [10, 11], which could be attributed to the different population characteristics they considered, as their sample was primarily made up of young male individuals, whereas ours was middle-aged with the same gender distribution. The frequency our study observed was close to that in middle-aged Finnish people with a similar sex distribution to our sample, wherein the frequency of the long QT interval was 2.6% [9].

Our study found that age and hypertension are correlates of long QTc interval frequency, which is supported by prior research [6, 7, 38]. We also identified a correlation between current opium use and a long QTc interval; however, more research is needed to validate this association. Obesity, diabetes, and female sex have all been linked to longer QTc intervals in prior studies [6, 7, 38]; however, we failed to detect any evidence of a significant association between these factors and long QTc intervals.

In our study, it was found that 1.43% of the participants exhibited ER patterns in their ECGs. This result was in line with that reported by Sun et al. in their study on a Chinese middle-aged general rural population (1.3%) [24] and Uberoi et al. in their study on Caucasian-American middle-aged subjects (1.7%) [39]. Nevertheless, a recent meta-analysis found a wide range of prevalence rates for ERP across different regions, ranging from as low as 1.3% to as high as 45.8%. The pooled frequency in the general population was found to be 11.6%, with certain groups such as blacks, men, and physically active individuals showing a tendency towards higher rates [16]. In our study, younger age and male gender were

independent correlates of ER pattern, which was in line with the results of the Framingham Heart Study and the Health 2000 Survey [40]. Moreover, Sun et al. [24], whose sample comprised individuals of comparable age and sex distribution to ours, identified independent associations of ER patterns with male gender and younger ages, which is consistent with our findings. Moreover, our research demonstrated a significant relationship between a lower BMI and the presence of ER patterns. This finding supports the results of the Matta et al. study [25], which examined the adult general population of Latin America and similarly identified this inverse connection. Our study also discovered an independent relationship between alcohol use and the presence of ER patterns; however, this result has not been examined in prior research. In a case series involving 19 patients diagnosed with BrS or ER syndrome with an average follow-up of about 6 years, four of them experienced syncope or aborted SCD after consuming alcoholic beverage [41]. It has been suggested that alcohol consumption may induce repolarization abnormalities and subsequent lethal events by affecting sympathovagal tone and disrupting the balance between outward K^+ currents and inward Na^+ and Ca^{2+} currents [42–44].

In our study, the frequency of BrS-type patterns was 0.31%, which was close to a meta-analysis in which the pooled frequency of BrS-type patterns was estimated to be 0.4%, with Asians having a greater rate (0.9%) than those in Europe (0.3%) and North America (0.2%) [45]. Moreover, consistent with the results of this meta-analysis, the frequency of BrS-type patterns in our study was higher in males.

In our population, only three participants (0.03%) had a short QT interval (QTc < 330 ms in males and < 340 ms in females). This was comparable to the study by Kobza et al. [11] that examined QT intervals < 320 ms in Swiss young male citizens and reported a prevalence of 0.02%. A higher prevalence of short QT interval was found in a Finnish middle-aged (0.1% and 0.4% based on 320 ms and 340 ms cut-off points, respectively) [13], a young United Kingdom (UK) (0.1% based on 320 ms cut-off point [14] and a Japanese middle-aged (0.4% based on 362 ms and 369 ms cut-off points for men and women, respectively) population [12]. In another Japanese study, the prevalence of short QTc was 1.25% in males and 1.63% in females, based on a cut-off point that was 2 SDs lower than the mean QTc in males (354 ms) and females (364 ms) [15]. Chandra et al. [8] examined QT interval < 380 ms among young UK subjects, a higher cut-off compared to prior research, and reported a prevalence of 6.9% for non-athletes and 13% for athletes. Overall, these studies indicate a large variance in the frequency estimates of the short QT interval, with the frequency being less than 1% at the 320–340 ms QTc cutoff point and increasing dramatically as the cutoff point climbed to 360–380 ms. Regional and racial disparities may also play a role in the varying results.

The strength of our study was that we for the first time provided an epidemiologic description of ECG abnormalities associated with cardiac channelopathies and SCD in a large adult general population from Iran, highlighting the importance of demographics and clinical factors associated with these ECG patterns. Understanding the range and frequency of ECG abnormalities and the factors that contribute to them is crucial for developing tailored screening programs.

The study had important limitations. First, it had a cross-sectional design, so it could only describe the clinical correlations of ECG abnormalities and not their predictive significance for cardiovascular outcomes. Although we conducted a short-term follow-up on subjects with a high-risk ECG for SCD and discovered higher rates of mortality than those without a high-risk ECG, longitudinal research with long-term follow-up is necessitated to better understand the link between these ECG abnormalities and cardiovascular outcomes in the adult general population. This will help establish whether adding ECG to the present cardiovascular screening program improves its precision. Second, the low frequency of BrS-type patterns and short QT intervals in our sample prevented us from running regression models due to a lack of statistical power. Finally, we excluded individuals under the age of 35, which may have resulted in an underestimation of our results.

Conclusions

Overall, this study found that ECG abnormalities linked to cardiac channelopathies and SCD are not common among the adult general population of Iran. Older age, opium use, and the presence of hypertension were factors independently linked to the frequency of the long QT interval. Younger age, male gender, alcohol consumption, and low BMI were independent correlates of ER pattern frequency. This research would aid in estimating the range of apparently healthy individuals who are at high risk for cardiovascular events by analyzing ECG abnormalities, ultimately providing data for health care decision-makers to optimize screening strategies for the Iranian general population.

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