The association between *SCN5A*, *KCNQ1* and *KCNE1* gene polymorphisms and complex ventricular arrhythmias in survivors of myocardial infarction

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Abstract

Background: Post-MI patients are highly susceptible to sudden cardiac arrest (SCA) and sudden cardiac death (SCD) resulting from ventricular arrhythmia (VA). The search for new clinical predictors to identify those patients who are at the highest risk of these events is therefore essential. Numerous data indicate that the presence of polymorphisms and mutations in the cardiac ion channel genes *SCN5A*, *KCNQ1* and *KCNE1* might serve as such a predictor. Since genetic alterations in these genes underlie congenital long QT syndrome (LQTS), which is associated with an increased occurrence of arrhythmic complications and SCD, we decided to verify how alterations in these genes contribute to QT interval abnormalities and consequently to VA, SCA and SCD in post-MI patients.

Aim: To detect single nucleotide polymorphisms (SNP) in *SCN5A*, *KCNQ1* and *KCNE1* of post-MI patients, and to assess whether they are related to electrophysiological markers of cardiac arrhythmia (QT interval) and the clinical course.

Method: The study group consisted of 100 patients (27 females, mean age 69 years) with documented MI ≥3 months before enrolment. All patients underwent baseline and (after 12 months) control examinations encompassing history, physical examination, basic laboratory analysis, resting 12-lead ECG, 24-hour 12-lead Holter ECG monitoring and echocardiography. Genetic tests were performed during baseline examination.

Results: In post-MI patients two exonic polymorphisms, H558R in *SCN5A* and *S38G* in *KCNE1*, and two intronic ones, in *KCNQ1*, were detected. H558R was associated with an increase in QT dispersion (QTd) at minimum and maximum heart rate and QT interval prolongation before premature ventricular beats (PVB), whereas S38G and intronic polymorphisms were related to an increase in QTd before PVB. None of the above polymorphisms was related to complex VA, SCA or SCD.

Conclusion: The above polymorphisms were associated with abnormal repolarisation phase patterns in post-MI patients, which manifested in QT interval prolongation and QTd increase. There was no relationship between these polymorphisms and complex VA, SCA or SCD. The results show that not only exonic alterations but also intronic ones may affect the phenotype.

Key words: myocardial infarction, single nucleotide polymorphisms, QT interval, ventricular arrhythmia

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Introduction

Cardiovascular disease accounts for approximately 50% of all deaths in Poland, 43% in men and 54% in women. The leading cause in both gender groups is coronary artery disease, particularly myocardial infarction (MI) [1].

An issue of clinical importance in this group of patients is sudden cardiac death (SCD). Risk factors of SCD are generally similar to those of atherosclerotic disease. However, accumulating data indicate that in prediction of SCD, independently from other clinical variables, specific changes in genotype are relevant. They include either polymorphisms or mutations of single nucleotides of sodium *SCN5A* and potassium *KCNE1* and *KCNQ1* genes encoding cardiac ion channel proteins.

Proper function of cardiac ion channels and resulting normal ion currents are responsible for cardiac electric performance. Both mutations and polymorphisms of genes encoding proteins may affect electrophysiological cardiac

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function and lead to shortening or prolongation of cardiomyocyte action potential and thus to QT interval abnormalities and increased risk of arrhythmic adverse events. The majority of published data on *SCN5A*, *KCNE1* and *KCNQ1* gene abnormalities link them to congenital monogenic arrhythmogenic diseases, including long QT syndrome [2-5].

In post-MI patients, arrhythmic events occur more frequently than in the healthy population [6]. Thus it is of paramount importance to identify such patients, a subset of individuals at the highest risk of life-threatening ventricular tachyarrhythmias. Both mutations and polymorphisms in *SCN5A*, *KCNE1* and *KCNQ1* genes are likely to become markers of high arrhythmic risk. Disturbances found in these patients may explain the mechanisms leading to SCD and may be used as indicators of the highest SCD risk in post-MI patients. Thus we aimed to find SNP in *SCN5A*, *KCNE1* and *KCNQ1* genes in this group of patients. We also intended to verify whether genetic abnormalities were associated with changes of QT interval duration, known to reflect arrhythmogenicity. Finally we tested associations between genotype and clinical course of the disease, including complex ventricular arrhythmias (CVA), cardiac arrest (CA) and SCD. Additionally, we tried to find out if the changes in the gene introns might have any impact on the clinical course of disease.

Methods

This study involved 100 subjects with documented MI which occurred ≥3 months before enrolment. There were 27 women (at the mean age of 69 years) and 73 men (at the mean age of 67 years) in the study group. The study protocol was approved by the local Ethics Committee. Only patients who expressed written informed consent to participate in the study were enrolled. The exclusion criteria were as follows: acute MI, angina of CCS class IV, electrolyte disturbances and the use of QT interval prolonging agents. All patients underwent baseline and 12-month follow-up examinations. They included taking history, physical examination, basic laboratory tests, resting ECG, 24-hour 12-lead Holter ECG and echocardiography. Genome testing was performed at baseline.

24-hour Holter ECG

Twenty-four-hour Holter ECG was carried out using a 12-lead recorder (H-Scribe 2 Holter System, Mortara Instruments). A recording of ECG from 12 standard leads at 25 mm/s speed was registered. In each patient the following variables were collected: arrhythmic burden, including VA according to Lown classification, myocardial ischaemia, minimal, maximal and mean heart rate, QT interval duration and its dispersion expressed as difference between the longest and the shortest QT interval. QT interval corrected for heart rate was calculated according to Bazzet or Hodges formula. QT interval prolongation (QT max), corrected QT max (QTc max) and QT dispersion (QTd) were measured throughout day and night (from 10 p.m. to 6 a.m.):

- during the period of minimum and maximum heart rate,
- during one second to the last sinus beat prior to sinus beat preceding VA, so-called pre-sinus beat (QT1),
- for the last sinus beat preceding VA, so-called pre-ventricular beat (QT2).

Echocardiography

Echocardiography was performed using a VingMed Sound device – FIDE (GI). Echocardiographic assessment involved M-mode and 2D projections. In this examination, global and regional myocardial contractility, left ventricular ejection fraction (EF) using Simpson method, cardiac valves morphological appearance and function, and finally pericardium were evaluated.

Genetic study

Genetic studies were carried out by Krzysztof Kucharczyk Techniki Elektroforetyczne Sp. z o.o., a Warsaw company. DNA was isolated from 100 patients' blood samples. Using PCR in all samples 28 predefined DNA segments within *SCN5A*, *KCNE1* and *KCNQ1* genes were amplified. DNA segments with known genetic abnormalities (loci found abnormal in previous reports) were analysed. Subsequently, 2800 PCR reaction products were evaluated for polymorphisms using the MSSCP method [7]. Selected PCR products showing electrophoretic variability were sequenced in order to identify genetic changes.

Measured parameters

The following variables were analysed:

- CA or SCD,
- CVA: non-sustained ventricular tachycardia (nsVT), sustained VT (sVT) or ventricular fibrillation (VF),
- QT interval duration (QTmax, QTc max) and QT dispersion (QTd) estimated during 24-hour Holter ECG in association with ventricular arrhythmia as well as with minimal and maximal heart rate.

Statistical analysis

The results are expressed as means ± SD or numbers and percentages. Non-parametric tests were used for statistical analysis since normal data distribution was not confirmed in the Shapiro-Wilk test. The following tests were used to assess correlations:

- Spearman rank test for associations between two quantitative variables,
- Mann-Whitney U test for associations between qualitative and quantitative variables,
- χ^2 test for associations between two qualitative variables.

A value of $p < 0.05$ was considered statistically significant.

Results

SCNA polymorphism

In 42 subjects, rs1805124 polymorphism in exon 12 of the *SCN5A* gene was found. It is associated with nucleotide A38620424G exchange that results in replacing histidine with arginine in position 558 of the coded protein. Rs1805124 polymorphism is defined in published data as H558R. In our group, 41 individuals presenting with this polymorphism were heterozygotic (A/G) and one homozygotic (G/G). In the remaining 58 patients no such genotype changes were found. Clinical characteristics of the examined groups are outlined in Table I. No statistically significant differences of incidence of nsVT, sVT, VF, CA or SCD between groups were found.

A significant increase of QTd during the periods of minimal (67.7±23.6 ms vs. 53.6±23.0 ms, p=0.047) and maximal heart rate (68.6±25.7 ms vs. 52.7±18.8 ms, p=0.014), as well as of QT interval (QTmax) in pre-sinus (QT1) and pre-ventricular (QT2) beats preceding single premature ventricular contractions (PVC) during daytime in the group of patients with vs. without H558R polymorphism was found. Data on the means of prolonged QT interval preceding PVC during daytime are presented in Figure 1.

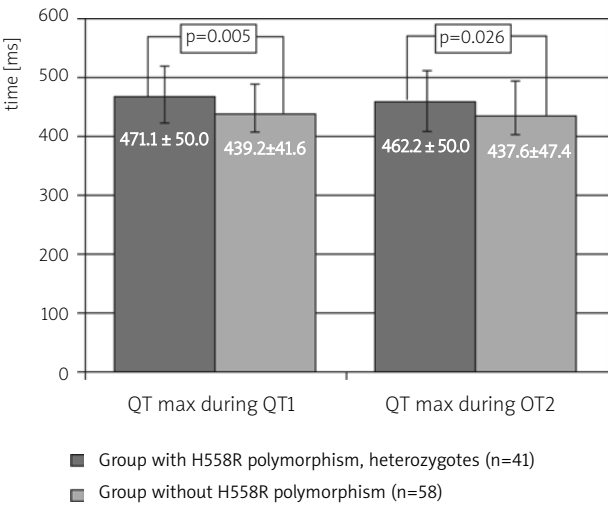

Figure 1. Mean values of QTmax during QT1 and QT2 prior to PVC during daytime

Table I. *SCN5A* gene

Group			With H558R	Without H558R
Number [n]			41 (heterozygotes)	58
Age [years]			68.0±10.7	67.3±10.4
EF [%]	baseline examination		49.0±9.	50.1±11.9
	follow-up examination		50.0±8.3	51.3±12.4
Number of patients with CA episodes			5 (12.5%)	3 (5.2%)
Number of patients with SCD			2 (5%)	3 (5.2%)
Number of patients with CVA in history		nsVT	5 (12.5%)	9 (15.5%)
		sVT	1 (2.5%)	3 (5.2%)
		VF	4 (10%)	2 (3.4%)
Number of patients with ventricular arrhythmia classified according to Lown system (Holter ECG)	baseline test	0	4 (10%)	3 (5.2%)
		I	7 (17.5%)	14 (24.1%)
		II	5 (12.5%)	8 (13.8%)
		III	0 (0%)	0 (0%)
		IVa	10 (25%)	15 (25.9%)
		IVb	14 (35%)	18 (31%)
	follow-up study	0	1 (2.9%)	3 (6%)
		I	10 (29.4%)	9 (18%)
		II	5 (14.7%)	6 (12%)
		III	2 (5.9%)	0 (0%)
		IVa	12 (35.3%)	14 (28%)
		IVb	4 (11.8%)	18 (36%)

Differences between the examined parameters were not significant.
Abbreviations: EF – ejection fraction, CA – cardiac arrest, SCD – sudden cardiac death, CVA – complex ventricular arrhythmias, nsVT – non-sustained ventricular tachycardia, SVT – sustained ventricular tachycardia, VF – ventricular fibrillation

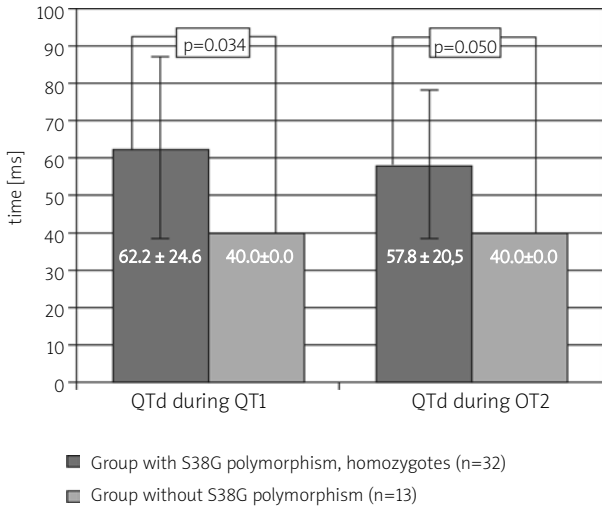

Figure 2. Mean values of QTd during QT1 and QT2 prior to PVC at night

KCNE1 polymorphism

Genetic examinations of *KCNE1* showed rs1805127 polymorphism within the coding gene that resulted in A21483691G nucleotide exchange. It leads to replacement of serine in the 38 protein position (S38G) with glycine. In the literature rs1805127 polymorphism is described as S38G. Thirty-two individuals with this polymorphism were homozygotes (G/G) and 55 heterozygotes (A/G). In the remaining 13 examined subjects, no such genotype change was noted. Clinical characteristics of the examined groups are outlined in Tables II and III. No significant differences between studied groups with respect to prevalence of nsVT, sVT, VF, CA and SCD were seen.

In the group of homozygotes of S38G polymorphism, significantly larger differences of the mean QTd in pre-sinus (QT1) and pre-ventricular beats (QT2) preceding PVC at night were noted when compared to individuals without S38G polymorphism (Figure 2). In the group of S38R polymorphism heterozygotes significantly larger differences were noted only between the mean QTd in the pre-ventricular beats (QT2) prior to PVC at night (Figure 3).

Table II. *KCNE1* gene

Group			With S38G	Without S38G
Number [n]			32 (homozygotes)	13
Age [years]			66.5±10.3	66.5±11.4
EF [%]	baseline examination		49.8±11.9	48.5±10.2
	follow-up examination		49.2±10.5	51.3±7.6
Number of patients with CA episodes			4 (12.9%)	0 (0%)
Number of patients with SCD			1 (3.2%)	0 (0%)
Number of patients with CVA in history		nsVT	3 (9.7%)	3 (32.1%)
		sVT	2 (6.5%)	0 (0%)
		VF	2 (6.5%)	0 (0%)
Number of patients with ventricular arrhythmia classified according to Lown system (Holter ECG)	baseline test	0	1 (3.2%)	1 (7.7%)
		I	7 (22.6%)	2 (15.4%)
		II	5 (16.1%)	3 (23.1%)
		III	0 (0%)	0 (0%)
		IVa	9 (29.0%)	3 (23.1%)
		IVb	9 (29.0%)	4 (30.8%)
	follow-up study	0	2 (7.1%)	0 (0%)
		I	6 (21.4%)	1 (9.1%)
		II	4 (14.3%)	2 (18.2%)
		III	1 (3.6%)	0 (0%)
		IVa	8 (28.6%)	3 (27.3%)
		IVb	7 (25.0%)	5 (45.5%)

Differences between the examined parameters were not significant.
Abbreviations: see Table I

Table III. *KCNE1* gene

Group			With S38G	Without S38G
Number [n]			55 (heterozygotes)	13
Age [years]			68.1±9.6	66.5±11.4
EF [%]	baseline examination		49.9±10.9	48.5±10.2
	follow-up examination		50.7±9.4	51.3±7.6
Number of patients with CA episodes			4 (7.3%)	0 (0%)
Number of patients with SCD			4 (7.3%)	0 (0%)
Number of patients with CVA in history		nsVT	8 (14.5%)	3 (23.1%)
		sVT	2 (3.6%)	0 (0%)
		VF	4 (7.3%)	0 (0%)
Number of patients with ventricular arrhythmia classified according to Lown system (Holter ECG)	baseline test	0	5 (9.1%)	1 (7.7%)
		I	12 (21.8%)	2 (15.4%)
		II	5 (9.1%)	3 (23.1%)
		III	0 (0%)	0 (0%)
		IVa	14 (25.5%)	3 (23.1%)
		IVb	19 (34.5%)	4 (30.8%)
	follow-up study	0	2 (4.3%)	0 (0%)
		I	13 (28.3%)	1 (9.1%)
		II	5 (10.9%)	2 (18.2%)
		III	1 (2.2%)	0 (0%)
		IVa	15 (32.6%)	3 (27.3%)
		IVb	10 (21.7%)	5 (45.5%)

Differences between the examined parameters were not significant.
Abbreviations: see Table I

KCNQ1 polymorphism

In 4 examined patients, rs17221882 polymorphism in the *KCNQ1* gene was found and exchanged nucleotides involved T2746739C. Individuals with this polymorphism are heterozygotic (T/C). The locus of genetic mutation is located in intron 11 of the gene. The second polymorphism of the *KCNQ1* gene, also revealed in 4 other subjects, was rs163150, which was found in intron 12 with changed G2753896A nucleotides. Two patients were heterozygotes (G/A) and another 2 heterozygotes (A/A). In the remaining 92 patients a detailed genetic study of DNA did not confirm any polymorphisms of analysed genes. Clinical characteristics of patients with intron polymorphisms and without genetic changes are outlined in Table IV. In two patients clinical data were lost due to unresolved technical problems.

No significant differences in the prevalence of nsVT, CA or SCD between patients with and without polymorphisms were noted. However, in the group of patients with polymorphisms, increased QTd in pre-ventricular beats (QT2) preceding PVC at night were shown. Comparison of mean QTd prior to PVC during daytime between groups with and without intron polymorphisms is presented in Figure 4.

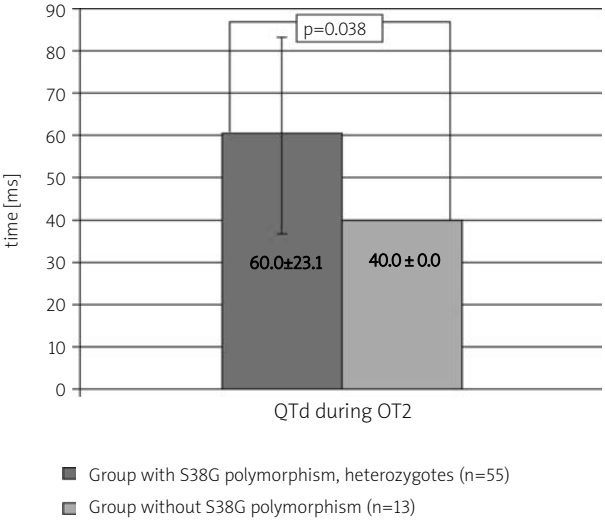

Figure 3. Mean values of QTd during QT2 prior to PVC at night

Table IV. *KCNQ1* gene

Group			With intron polymorphisms	Without intron polymorphisms
Number [n]			8	90
Age [years]			64±8.4	67.7±10.2
EF [%]	baseline examination		52.9±13.4	49.2±10.9
	follow-up examination		46.3±13.4	50.9±10.7
Number of patients with CA episodes			1 (12.5%)	7 (7.9%)
Number of patients with SCD			0 (0%)	5 (5.6%)
Number of patients with CVA in history		nsVT	3 (37.5%)	11 (12.4%)
		sVT	1 (12.5%)	3 (3.4%)
		VF	0 (0%)	6 (6.7%)
Number of patients with ventricular arrhythmia classified according to Lown system (Holter ECG)	baseline test	0	0 (0%)	6 (6.7%)
		I	1 (12.5%)	18 (20.2%)
		II	0 (0%)	13 (14.6%)
		III	0 (0%)	0 (0%)
		IVa	3 (37.5%)	23 (25.8%)
		IVb	4 (50%)	29 (32.6%)
	follow-up study	0	0 (0%)	3 (4%)
		I	1 (14.3%)	17 (22.7%)
		II	2 (28.6%)	9 (12%)
		III	0 (0%)	2 (2.7%)
		IVa	1 (14.3%)	25 (33.3%)
		IVb	3 (42.9%)	19 (25.3%)

Differences between the examined parameters were not significant.
Abbreviations: see Table I

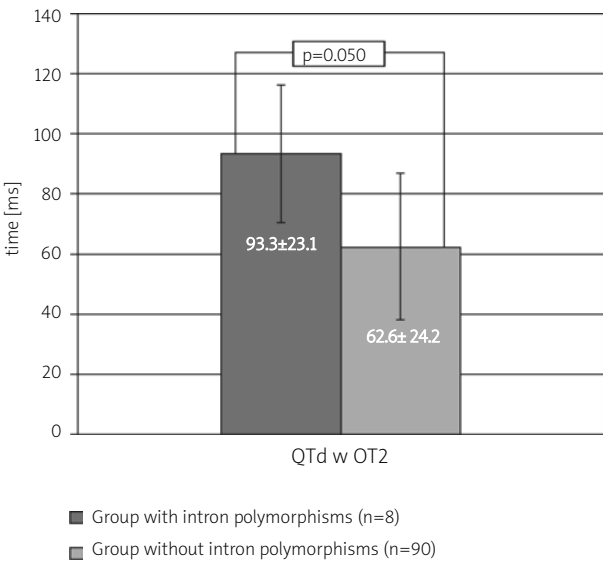

Figure 4. Mean values of QTd during QT2 prior to PVC during day

Discussion

Patients with a history of MI represent a heterogeneous group of patients with an increased risk of serious adverse events such as CVA and SCD. It seems necessary to search for new risk predictors of such events in this particular group of patients. Accumulating data indicate a significant role of mutations or SNP in the genes coding cardiac ion channels such as *SCN5A*, *KCNE1*, *KCNE2* and KCNQ1, that might become risk factors of CVA and SCD. The majority of reports dealing with this issue have involved congenital monogenic pro-arrhythmic diseases such as LQTS. Small studies on genetic predisposition to acquired long QT syndrome have been published. Their authors provided evidence that even mild, genetically 'silent' disorders in standard conditions, might become clinically relevant when combined with other abnormalities such as myocardial ischaemia, drug interactions or electrolyte imbalance. Such 'hidden' genetic changes may act as an additional factor facilitating malignant ventricular arrhythmias. An example may be the report of Seti et al., who found SNP in the *KCNE2* gene among individuals with prolonged QT related to sulfamethoxazole administration [8]. Kubota et al. showed

sense-type mutation of the *KCNQ1* gene resulting in hypokalaemia-induced QT prolongation and torsade de pointes [9]. Similarly, Napolitano et al. revealed mutation in the *KCNQ1* gene in a patient with CA induced by cisapride [10].

In our study we searched for any abnormalities in the *SCN5A*, *KCNQ1* and *KCNE1* genes of SNP type in order to identify a group of patients with the highest risk for CVA, CA or SCD. Our genetic study revealed H558R polymorphism of the *SCN5A* gene, S38G in exons of the *KCNE1* gene and two *KCNQ1* gene polymorphisms in introns such as rs17221882 and rs163150. Using the NCBI database we found that these polymorphisms are known genotype variants, but only H558R polymorphism has been described earlier in patients with acute MI [11].

Another aim of our study was to assess whether the aforementioned genetic changes were associated with electrophysiological predictors of arrhythmia, such as QT interval changes, that could be used as novel clinical markers to identify MI patients at a higher combined risk of PVC and SCD.

A report published by Gouas et al. examined the relationship between H558R or S38G polymorphisms and duration of QT interval. The French subpopulation of healthy H558R individuals was more prevalent in the group of subjects with prolonged QT. Polymorphism S38G was not associated with any changes of QT interval duration. It has been suggested that certain polymorphisms of the *KCNQ1*, *KCNE1*, *KCNH2* and *SCN5A* genes, linked to changes of QT interval duration, including H558R, might be risk factors of ventricular arrhythmias and SCD, independently or when accompanied by another cardiovascular disease [12]. Similarly, in the study of Akyol et al., no correlation between QT interval duration and S38G polymorphism with respect to the risk of serious CVA was found in the European Caucasian population. However, such an association was not excluded, especially in subjects with additional risk factors for arrhythmia known from earlier reports on polymorphisms other than S38G [13, 14]. However, the aforementioned studies involved healthy populations, while we enrolled patients with a history of MI. In our group those with H558R polymorphism presented significant prolongation of QT interval within the two last sinus beats (QT1 and QT2) preceding PVC during daytime compared to subjects without such polymorphism. However, no correlation between prolongation of QT interval in patients with either S38G polymorphism of the *KCNE1* gene or polymorphisms in the introns of the *KCNQ1* gene were noted.

The QT interval variability between particular leads in the standard ECG recording called QTd is widely recognised as potentially linked to higher risk of CVA and SCD. However, the clinical relevance of this parameter in patients after MI is not obvious. The majority of retrospective analyses suggest that QTd in post-MI patients is an independent predictor of higher risk of life-threatening ventricular arrhythmias when exceeding 100 ms [15]. However, the only prospective trial, performed by Zabel et al., did not confirm a correlation between QTd and overall mortality, sVT, VF and SCD [16]. In our study we observed increased QTd within pre-sinus (QT1) and pre-ventricular (QT2) beats prior to PVC at night in the group of homozygotic S38G polymorphism in *KCNE1* gene subjects, and only in QT2 in the group of heterozygotes. Meanwhile, patients with polymorphism of the introns of the *KCNQ1* gene presented higher QTd in QT2 prior to PVC during daytime. However, in the group of patients with H558R polymorphism, there was significantly increased QTd during minimal and maximal heart rate compared with patients without. No correlation between H558R, S38G and intron polymorphisms and QT interval duration or CVA was found. No association between these polymorphisms and CA or SCD was observed either.

An explanation of correlations between polymorphisms noted in introns of the *KCNQ1* gene and obtained clinical data would be most interesting. It should be looked for in the latest reports on the mechanism of splicing, a process called 'gene composing' that consists of removing intron sequences and connecting the exons to form pre-mRNA. These studies showed that polymorphisms within introns might play a key role in the abnormal course of this process. They may disturb the process of gene composing and as a result have an adverse impact on the structure and function of the ion channel proteins coded by individual genes and thus on severity of the clinical manifestation of the disease [17-19].

What is important for our analysis is that 10% of patiens enrolled in the study received anti-arrhythmic medications (amiodarone, sotalol) alone or in addition to cardioverter-defibrillator implantation due to previous CVA. The fact that they had a high burden of arrhythmia justified their enrolment in the study, which aimed to evaluate genetic abnormalities that might represent potential risk factors for ventricular arrhythmias. We found after baseline and follow-up examinations that the rate of patients requiring anti-arrhythmic treatment was higher in the group of patients presenting with all detected types of polymorphisms. Medications were initiated due to CVA that occurred during the subsequent episodes of myocardial ischaemia. However, in patients receiving QT-prolonging medications, this parameter was not evaluated, so no conclusions on possible correlations between QT interval and CVA in this group of patients could be drawn.

Conclusions

In patients with a history of MI and presenting with H558R in *SCN5A*, S38G in *KCNE1* and intron polymorphisms in the *KCNQ1* gene, abnormal repolarisation that results in prolongation of QT interval and increase of QTd before PVC

is more often seen. However, no correlations between these genetic changes and CVA, CA or SCD could be documented. Our findings may suggest that not only changes in exons, but also in introns, may be related to particular phenotypes.

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Związek pomiędzy polimorfizmami w genach *SCN5A*, *KCNQ1* i *KCNE1* a złożonymi komorowymi zaburzeniami rytmu u chorych po zawale serca

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Streszczenie

Wstęp: Wysokie zagrożenie nagłym zatrzymaniem krążenia (NZK) i nagłym zgonem sercowym (NZS), u podłoża którego leżą groźne komorowe zaburzenia rytmu (KZR), u chorych po zawale serca skłania do poszukiwania nowych wskaźników klinicznych, które z dużym prawdopodobieństwem pozwoliłyby na wyodrębnienie spośród nich osób o najwyższym ryzyku tych zdarzeń sercowych. Coraz więcej doniesień wskazuje, że obecność mutacji i polimorfizmów w genach sercowych kanałów jonowych *SCN5A* i *KCNQ1*, KCNE1 może stanowić właśnie taki wskaźnik. Ponieważ zmiany w tych genach mogą powodować wrodzone zespoły wydłużonego odstępu QT, który związany jest ze zwiększoną częstością występowania powikłań arytmicznych i NZS, postanowiono sprawdzić, w jakim stopniu zmiany w tych genach przyczyniają się do nieprawidłowości odstępu QT, a tym samym złożonych KZR, NZK i NZS u chorych po zawale serca.

Cel: Celem badania w tej grupie chorych było poszukiwanie zmian w genotypie w postaci polimorfizmów pojedynczych nukleotydów (ang. *single nucleotide polymorphism*, SNP) w genach *SCN5A*, *KCNQ1* i *KCNE1*. Następnie ocena, czy stwierdzone zaburzenia genetyczne mają związek z elektrofizjologicznym markerem ryzyka zaburzeń rytmu serca, jak odstęp QT, oraz ocena związku pomiędzy stwierdzonymi zmianami w genotypie a klinicznym przebiegiem choroby: złożonymi KZR, NZK i NZS. Dodatkowo sprawdzano, czy zmiany w intronach genów mogą wpływać na przebieg kliniczny.

Metodyka: Badaniem objęto 100 osób z populacji polskiej z udokumentowanym przebytym co najmniej przed 3 mies. zawałem serca. U wszystkich pacjentów przeprowadzono badanie wstępne i po 12 mies. kontrolne. Obejmowały one wywiad, badanie przedmiotowe, podstawowe badania laboratoryjne, spoczynkowe badanie EKG, 24-godzinne monitorowanie EKG metodą Holtera oraz badanie echokardiograficzne. W okresie badań wstępnych wykonano badania genetyczne. W analizie statystycznej korelowano dane genetyczne z danymi klinicznymi.

Wyniki: U chorych po zawale serca w egzonach: genu *SCN5A* wykryto polimorfizm H558R, genu *KCNE1* – S38G, natomiast w intronach genu *KCNQ1* dwa polimorfizmy. Polimorfizm H558R związany był ze zwiększoną dyspersją QT w czasie wolnych i szybkich rytmów serca i z wydłużeniem odstępu QT przed przedwczesnymi pobudzeniami komorowymi, podczas gdy polimorfizmy S38G i intronowe ze zwiększoną dyspersją QT przed przedwczesnymi pobudzeniami komorowymi. Żaden z powyższych polimorfizmów nie był związany ze złożonymi KZR, NZK i NZS.

Wnioski: Powyższe polimorfizmy u chorych po zawale serca związane były z nieprawidłowym przebiegiem fazy repolaryzacji, czego najwyraźniejszym przejawem było wydłużanie się odstępu QT i zwiększenie dyspersji QT. Nie wykazano związku polimorfizmów w tych genach ze złożonymi KZR, NZK ani NZS. Uzyskane wyniki wskazują, że nie tylko zmiany w egzonach, ale i w intronach mogą mieć wpływ na fenotyp.

Słowa kluczowe: zawał serca, polimorfizm pojedynczych nukleotydów, odstęp QT, komorowe zaburzenia rytmu

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