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Research

The Coexistence of Early Repolarization and Atrioventricular Nodal Reentrant Tachycardia: A Case Control Study

Erken Repolarizasyon ve Atriyoventriküler Nodal Reentrant Taşikardinin Birlikte Bulunması: Bir Olgu Kontrol Çalışması

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ABSTRACT

Objective: It has been reported that early repolarization (ER) abnormalities, which have been considered benign for many years, may be associated with many cardiac arrhythmias both malign and benign in the recent period. In our study, we investigated that may be coexisting the atrioventricular nodal reentrant tachycardia (AVNRT), which the most common in paroxysmal tachycardias, with ER abnormalities.

Methods: Our study was designed as a single-centered retrospective descriptive study. The study enrolled 53 patients who underwent ablation due to AVNRT and 50 control group patients. Demographic, clinical, and laboratory data of patients were retrieved from our database. ER, the diagnosis and types of the pattern were determined based on the consensus report published by in 2015. Electrocardiographic measurements were performed semi-automatically by EP caliper application.

Results: Of the patients enrolled in the study, 34 (64.2%) in the AVNRT group and 31 (62%) in the control group were female. The mean age was 47.11±12.79 years in the AVNRT group and the mean age was 44.88±13.02 years in the control group. Although the presence of an ER pattern was numerically higher in the AVNRT group compared with the control group, this difference was not statistically significant. A comparison was made between subgroups, and the slurring with ST elevation type of ER pattern was significantly higher in men [7 people (58.3%) in males 0 in female, p<0.001], the slurring without the ST elevation type of ER pattern was significantly higher [15 people (93.8%) in females and 5 people (41.7%) in males, p<0.002].

Conclusion: In our study, we determined that the pattern of early repolarization, especially the slurring type, was more frequent in patients with AVNRT; however, but this difference was not statistically significant. Additionally, we found that the slurring with ST elevation type of ER is significantly more common in males, whereas the slurring without the ST elevation type of ER is significantly more common in females.

Keywords: Atrioventricular nodal reentrant tachycardia (AVNRT), early repolarization, radiofrequency ablation

ÖZ

Amaç: Uzun yıllar boyunca iyi huylu olarak kabul edilen erken repolarizasyon (ER) bozukluklarının, son dönemde gerek ölümcül gerekse iyi seyirli birçok kardiyak aritmi ile ilişkili olabileceği bildirilmektedir. Biz bu çalışmamızda ER paternleri ile en sık görülen paroksizmal taşikardi olan atriyoventriküler nodal reentran taşikardi (AVNRT) arasındaki ilişkiyi inceledik.

Gereç ve Yöntem: Çalışmamız tek merkezli retrospektif tanımlayıcı çalışma olarak dizayn edildi. Çalışmaya AVNRT tanısı ile ablasyon işlemi yapılan 53 hasta ile 50 kontrol grubu hastası dahil edildi. Hastaların demografik klinik laboratuvar verileri geriye dönük olarak sistemden elde edildi. ER paterni tanısı ve tipleri 2015 yılında tarafından yayınlanan konsensus raporu baz alınarak belirlendi. Elektrokardiyografik ölçümler EP kalipers uygulaması ile yarı otomatik olarak gerçekleştirildi.

Bulgular: Çalışmaya alınan hastaların AVNRT grubunda 34'ü (%64,2), kontrol grubunda 31'i (%62) kadındı. AVNRT grubunda yaş ortalaması 47,11±12,79 yıl, kontrol grubunda yaş ortalaması 44,88±13,02 yıl idi. ER patern varlığı AVNRT grubunda kontrol grubuna kıyasla sayısal olarak fazla olsa da bu fark istatistiksel olarak anlamlı değildi. Alt gruplar arasında karşılaştırma yapıldığına ise ST yükselmeli slurring tip ER paterni

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erkeklerde [7 kişi (%58,3) erkeklerde, kadınlarda 0, p<0,001), ST yükselmesiz slurring tip ER paterni kadınlarda anlamlı olarak daha yüksek saptandı [kadınlarda 15 kişi (%93,8), erkeklerde 5 kişi (%41,7) p<0.002].

Sonuç: Çalışmamızda AVNRT'li hastalarda ER paterninin, özellikle slurring tipinin daha sık olduğunu belirledik, fakat bu fark istatistiksel olarak anlamlı değildi. Ayrıca, ER'nin ST yükselmeli slurring tipi erkeklerde anlamlı olarak daha yaygın olduğunu, ST yükselmesiz slurring'in kadınlarda anlamlı olarak daha yaygın olduğunu saptadık.

Anahtar Kelimeler: Atriyoventriküler nodal reentrant taşikardi (AVNRT), erken repolarizasyon, radyofrekans ablasyonu

INTRODUCTION

The term early repolarization (ER) is often used to describe morphological changes called notch or slurring, where the end of the QRS junction the ST segment (with or without ST elevation) and its prevalence is reported from 2% to 31% (1). Previously, ER was mostly considered a benign electrocardiographic sign. In 2008, Haïssaguerre et al. (2) published their study, in which they reported that there may be a relationship between ER and idiopathic ventricular fibrillation. In subsequent studies, it has been reported that there is a relationship between ER and both atrial tachycardias and arrhythmic death (3,4). Furthermore, similarities in responses to physiological changes and pharmacological agents between Brugada syndrome (BrS) and ER have been demonstrated (5).

Atrioventricular nodal reentrant tachycardia (AVNRT) is a regular supraventricular tachycardia caused by dual pathways (usually slow/fast) within the atrioventricular node and in occasionally the peripheral atrial tissue. It has been reported by the study published by Hasdemir et al. (6) that BrS, which has close similarities with ER, may have co-existence with AVNRT. In our study, we investigated the relationship between the morphological changes (the ER patterns) observed in the junction region (J point) between complete depolarization and repolarization of the action potential curve with AVNRT.

METHODS

The present study was conducted as a single-centered retrospective and descriptive study. Seventy six patients who were underwent ablation therapy due to AVNRT in the electrophysiology laboratory of University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Hospital between 2019-2022 were included in the current study. All AVNRT patients underwent successful ablation after the diagnosis was confirmed with differential maneuvers. Of these 76 patients, 12 patients had fascicular block, branch block, or fragmented QRS on basal electrocardiogram, 2 patients had ejection fraction below 50%, 2 patients had left ventricular hypertrophy, 2 patients had frequent ventricular extra beats after the procedure and were excluded from the study. The data of the remaining 53 patients without uncontrolled hypertension, chronic kidney disease, or stenosis of any coronary artery above 50%, which are our other criteria for exclusion, were analyzed and these patients were determined as the AVNRT group. Fifty healthy volunteers, who were similar to the AVNRT group in terms of their demographic and clinical characteristics and did not have any arrhythmic complaints, were identified as a control group.

ER morphologies were defined based on a consensus report published by Macfarlane et al. (7) in 2015. Accordingly, if there was a positive deflection of at least 0.1 mV above the isoelectric line after the onset of the J point, it was defined as a notch, if there was an angulation of more than 10% in the last half of the descent of the R wave, it was defined as slurring. If there is at least 0.1 mV ST segment above the isoelectric line after 100 ms from the beginning of the J point, was defined as the ST elevation (excluding leads V1 to V3).

This study was approved by the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (decision no: 2022-16-06, date: 15.08.2022) and conducted in accordance with the principles of the Helsinki Declaration. Written informed consent was obtained from all the participants.

Statistical Analysis

Demographic characteristics of patients and collected data were entered into IBM® SPSS® (the Statistical Package for the Social Sciences) Statistics version 23. Variables were characterized using mean and percentage values were used for qualitative variables. Categorical variables were expressed using frequency and percentage, and numerical variables expressed using mean ± standard deviation. The normality of the distribution of quantitative variables was evaluated using the Kolmogorov-Smirnov test. To compare the two independent groups, the Student t-test for parametric numerical variables and the Mann-Whitney U test for nonparametric variables were used. Categorical variables were compared with the Pearson chi-square test. Statistical significance was considered $p<0.05$.

RESULTS

The mean age of the 103 patients included in the study was 47.11±12.79 years in the AVNRT group and the mean age of the control group was 44.88±13.02 years. There were 34 (64.2%) female individuals in the AVNRT group and 31 (62%) female individuals in the control group. No statistically significant difference was found between the two groups in terms of demographic, clinical, echocardiographic, and laboratory parameters (Table 1).

A comparison between both genders in terms of ER and its subtypes is shown in Table 2. Of the 65 female individuals included in the study, 16 (24.6%) and 12 (31.6%) of the 38 male individuals had any type of ER morphological changing; however, this difference between both genders was not statistically significant (p=0.495). When the subgroup analysis of the detected ER types was performed, it was found that slurring with ST elevation was statistically significantly higher in males than in females (p<0.001). The slurring without ST elevation type ER was determined to be significantly higher in female individuals compared with male individuals (p=0.002). Individuals were divided into two groups by accepting the cut-off value of 40 years, and no significant difference was found between the two groups in terms of the presence of ER and its subtypes (Table 3).

While 16 (30%) patients in the AVNRT group had any type of change in ER morphology, 12 (24%) individuals in the control group had any type of change in ER morphology. Although ER patterns were numerically more frequent in the AVNRT group compared with the control group, this difference was not statistically significant (p=0.480). Notch -type ER was observed in only 1 patient in the AVNRT group. All types of ER -detected individuals in the control group was the slurring type ER. ER with ST elevation was determined in 3 patients in the AVNRT group and in 4 volunteers in the control group. There was no significant difference the ER patterns with ST elevation between the groups. In Table 4, the AVNRT and control groups were compared in terms of electrocardiographic characteristics.

Additionally, no morphological changes were observed in the ER patterns after the procedure compared to before the procedure in patients who underwent successful ablation due to AVNRT.

DISCUSSION

After the studies published by Tikkanen et al. (3,8) showing an increased frequency of cardiac arrhythmias with ER patterns, the idea has arisen that ER patterns, contrary to popular belief, may not be innocent. In addition to their clinical importance, there is still no complete consensus on the terminology and definition of ER patterns. This study aimed to investigate the coexistence of AVNRT, the most

Table 1. Comparison of demographic, echocardiographic and laboratory parameters of the AVNRT group and the control group

	AVNRT group (n=53)	Control group (n=50)	p-value
Age	47.11±12.79	44.88±13.02	0.382
Sex (female, %)	34 (64.2%)	31 (62%)	0.821
HT	6 (11.3)	6 (12)	0.914
DM	2 (3.8)	2 (4.1)	0.936
CAD	1 (1.9)	1 (2.1)	0.944
EF	58.7 (60-60)	61.1 (60-60)	0.918
IVS	9.2 (10-10)	8.7	0.843
PW	8.6 (10-10)	8.4	0.952
LA	36 (35-37)	35 (34-37)	0.256
Na	138 (137-141)	139 (138-140)	0.441
K	4.36±0.29	4.24±0.32	0.156
Ca	9.30±0.28	9.33±0.50	0.571
CL	103 (101-104)	102 (100.25-104)	0.680
Hgb	13.57±1.47	13.67±1.41	0.776
Hct	40.74±4.07	40.85±3.89	0.915

AVNRT: Atrioventricular nodal reentrant tachycardia, HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary artery disease, EF: Ejection fraction, IVS: Interventricular septum, PW: Posterior wall, LA: Left atrium, Na: Sodium, K: Potassium, Ca: Calcium, Cl: Chlorine, Hgb: Hemoglobin, Hct: Hematocrit

common form of paroxysmal supraventricular tachycardia, with ER patterns (9).

ER syndromes and BrS, which have pathophysiologically similar features to it, are the main components of J wave syndromes (10). It is considered that J wave abnormalities are caused by mutations that develop in a way that disrupts the inward flow functions of the Ito ion channels, especially in the inferior region of the left ventricle (11). Furthermore, several publications are associated with J-point elevations in the inferior and lateral leads, increased frequency of idiopathic VF, and cardiovascular death (2,12,13). Defects of cardiac ion channels that lead to repolarization dysfunction are not limited to the ventricular myocardium but are also likely to affect the atrial tissue. It has been reported in previously studies that there may be a coexisting between BrS and atrial fibrillation and AVNRT (6,14).

Table 2. Comparison of ER and ER subtypes in male and female individuals

	Male (n=38)	Female (n=65)	p-value
Signs of ER of any type	12 (31.6%)	16 (24.6%)	0.495
Type of ER			
Slurring with ST elevation	7 (58.3%)	0	<0.001*
Slurring without ST elevation	5 (41.7%)	15 (93.8%)	
Notch with ST elevation	0	0	0.002**
Notch without ST elevation	0	1 (6.2%)	

ER: Early repolarization, *The result of post hoc analysis conducted between male and female in terms of slurring with ST elevation. **The result of post hoc analysis conducted between male and female in terms of slurring without ST elevation

Table 3. Comparison of ER and ER subtypes by age

	Age <40 years (n=27)	Age ≥40 years (n=76)	p-value
Signs of ER of any type	6 (21.4%)	22 (29.3%)	0.415
Type of ER			
Slurring with ST elevation	2 (33.3%)	5 (22.7%)	0.775
Slurring without ST elevation	4 (66.7)	16 (72.7%)	
Notch with ST elevation	0	0	
Notch without ST elevation	0	1 (4.5%)	

ER: Early repolarization

Table 4. Comparison of electrocardiographic parameters of the AVNRT group and the control group

	AVNRT group (n=53)	Control group n=50	p-value
Heart rate (bpm ± SD)	72.71±11.11	77.00±13.66	0.083
Signs of ER of any type	16 (30.2%)	12 (24%)	0.480
Type of ER			
Slurring with ST elevation	3 (18.8%)	4 (33.3%)	0.497
Slurring without ST elevation	12 (75%)	8 (66.7%)	
Notch with ST elevation	0	0	
Notch without ST elevation	1 (6.3%)	0 (0)	

AVNRT: Atrioventricular nodal reentrant tachycardia, bpm: Beat per minute, ER: Early repolarization, SD: Standard deviation

In our study, more patients in the AVNRT group had ER abnormalities than in the control group; however, this difference was not statistically significant. This may be related to the relatively small size of our sample group. AVNRT is a reentrant tachyarrhythmia that develops mainly in the presence of slow and fast pathways, in which the atrioventricular node is involved. However, some genetic variations (SCN1A, PRKAG2, RYR2, CFTR, NOS1, PIK3CB, GAD2, and HIP1R) and ion channel disorders may be responsible for the formation of pathways with different refractory periods and conduction velocities (15,16). The mutation of SCN5A, which affects INA channel functions, has been previously identified in both ER syndrome and AVNRT cases (6,17). Therefore, it is possible that these two diseases may coexist on a pathophysiological basis.

ER abnormalities are more common in men than in women because of sex hormones, especially testosterone and increased ventricular myocardial mass; on the other hand, AVNRT is more common in females (18,19). In our study, there was no statistically significant difference in the presence of ER abnormalities between male and female individuals. Nevertheless, when the comparison was performed in the subgroups, slurring with ST elevation was statistically more in men, in contrast, slurring without ST elevation was significantly higher in female individuals. Our findings are consistent with the previously reported results. However, new studies are still needed on the differences in the subtypes of ER patterns between the genders.

There are some limitations in our study. First, the study was conducted in a relatively small patient population. Additionally, the relationship between electrophysiological measurements and ER abnormalities in AVNRT patients included in the study was not examined. Finally, genetic test analyses were not available for all patients included in the study, which could be related to ER disorders and AVNRT.

CONCLUSION

To our best knowledge, the present study is the first study in the literature to investigate the co-existence of ER disorders and AVNRT. There have been many publications on the association of ER abnormalities, which have been considered benign for many years, with both ventricular and atrial arrhythmias recently. Although it is not statistically significant, we have found that the ER pattern, particularly the slurring type, is more frequent in patients with AVNRT. Additionally, determined that slurring with ST elevation type of ER is significantly more common in males, while slurring without ST elevation type is significantly more common in females. However, our findings need to be supported by larger-scale studies.

ETHICS

Ethics Committee Approval: Ethical committee approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital (decision no: 2022-16-06, date: 15.08.2022).

Informed Consent: Written informed consent was obtained from all the participants.

Authorship Contributions

Surgical and Medical Practices: O.P., A.S.E., Concept: O.P., Design: O.P., Data Collection or Processing: O.P., A.S.E., Analysis or Interpretation: O.P., A.S.E., Literature Search: O.P., A.S.E., Writing: O.P., A.S.E.

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