Hitri repetitivni odgovor kot uporaben napovedni dejavnik dolgoročne uspešnosti po radiofrekvenčni ablaciji ventrikularne tahikardije iz iztočnega trakta desnega prekata

Fast repetitive response as a useful predictor of long-term success of radiofrequency ablation of right ventricular outflow tract ventricular tachycardia

Avtor / Author

Damijan Vokac [1,2] Viljemka Nedog[1,2] Vojko Kanic[1,2] Franjo Naji[1,2]

Ustanova / Institute

[1]Univerzitetni klinični center Maribor, Klinika za Interno Medicino, Oddelek za Kardiologijo in Angiologijo, Maribor, Slovenija; [2] Univerza v Mariboru, Medicinska Fakulteta, Katedra za Interno Medicino, Maribor, Slovenija

[1]University Medical Centre Maribor, Clinic for Internal Medicine, Department for Cardiology and Angiology, Maribor, Slovenia; [2] University of Maribor, Faculty of Medicine, Department for Internal Medicine, Maribor, Slovenia

Ključne besede:
Prekatna tahikardija iz iztočnega trakta desnega prekata, ablacija, hitra neobstojna prekatna tahikardija.

Key words:
radiofrequency ablation, right ventricular outflow tract ventricular tachycardia, fast repetitive response

Članek prispel / Received
12. 7. 2018
Članek sprejet / Accepted
11. 9. 2018

Naslov za dopisovanje / Correspondence
Doc. dr. Franjo Naji, dr. med., Univerzitetni klinični center Maribor, Oddelek za kardiologijo in angiologijo, Ljubljanska 5, 2000 Maribor, Slovenija
Telefon +386 23212371
Fax +386 23312393
E-pošta: franjo.naji@yahoo.com

Izvleček

Namen: *Idiopatska tahikardija iz iztočnega trakta desnega prekata je najpogostejša prekatna aritmija pri bolnikih brez strukturne srčne bolezni. Med ablacijo aritmije pogosto opažamo hitro neobstojno prekatno tahikardijo (HNPT) enake morfologije kot je osnovna aritmija. V raziskavi smo poskušali oceniti napovedno vrednost HNPT pri bolnikih po ablaciji omenjene aritmije.*

Metode: *Raziskava je bila prospektivno opazovalna. Primerjali smo skupino bolnikov z zabeleženo HNPT s kontrolno skupino. Vključili smo bolnike po uspešni ablaciji iztočne prekatne tahikardije, ki smo jih razdelili v obe skupini glede na pojavnost HNPT. V obe skupini smo vključili po 33 bolnikov in jih spremljali 24 mesecev. Primerjali smo parametre procedure ter dolgoročni uspeh posegov.*

Rezultati: *Opažali smo statistično pomembno krajši čas posega (120 ± 29 min vs. 70 ± 16 min; P < 0,001) in po-*

Abstract

Purpose: *Idiopathic right ventricular outflow tract ventricular tachycardia (RVOT-VT) is the most frequent type of ventricular arrhythmia in patients without structural heart disease and is frequently treated using radiofrequency ablation (RFA). Fast non-sustained ventricular arrhythmia showing the same morphology as initial arrhythmia, the so-called fast repetitive response (FRR), is sometimes observed during ablation of the desired region. In this study, we evaluated the prognostic impact of FRR in patients after successful RFA of RV-OT-VT.*

Methods: *A prospective observational case-control design was selected for the study. We included patients with successful RFA of previously registered RV-OT-VT. Patients with provoked FRR during RFA were assigned to the FRR group and 33 patients displaying no FRR to the control group. Overall, 33 patients in both groups were monitored for the subsequent 24 months.*

membno manj ablacijskih lezij (21,6 ± 15,6 vs. 13,4 ± 12,5; P = 0,02) v skupini z zabeleženo HNPT. Po 24 mesecih je bilo v skupini z zabeleženo HNPT pomembno manj recidivov (OR 0,19; 95 % CI 0,05–0,83; P = 0,03).

Zaključek: *Pojav HNPT med ablacijo prekatne tahikardije iz iztočnega trakta desnega prekata govori v prid krajšemu času posega in boljši dolgoročni učinkovitosti.*

Parameters of the procedure, such as duration, energy application as well as long-term success, were compared between the two groups.

Results: *We observed significantly shorter duration of procedure performance (120±29 min vs. 70±16 min; P<0.001) with a markedly smaller number of applied lesions [Please note that I am unsure what the author means by 'applied lesions' here.] (21.6±15.6 vs. 13.4±12.5; P=0.02) in the FRR group. After 24 months, the adjusted odds ratio of relapse for patients from the FRR group vs. control group was 0.19 (95% CI 0.05–0.83; P=0.03).*

Conclusion: *In patients with induced FRR during RFA of RVOT-VT, the procedure tended to be drastically shorter and more successful in the long-term.*

INTRODUCTION

Idiopathic right ventricular outflow tract ventricular tachycardia (RVOT-VT) is the most frequent type of ventricular arrhythmia in patients without structural heart disease (1). Its occurrence is generated by so-called triggered activity, a consequence of catecholaminedependence after depolarization and oscillatory release of calcium from the sarcoplasmic reticulum (2-4). Patients can present with different types of arrhythmia, such as single ventricular ectopy, non-sustained tachycardia or sustained tachycardia. Owing to the easily accessible location, radiofrequency ablation (RFA) is the primary treatment mode in symptomatic patients (5). The standard approach consists of precise localization of focal arrhythmia and subsequent application of RFA. In case of inducible tachycardia, electrophysiological tools, such as activation mapping, local activation times and analysis of local electrograms may aid in highlighting the desired regions for implementation of successful RFA. In cases where tachycardia cannot be induced, pace mapping is a helpful tool for ECG tracing, which, in case of multiple leads, match suggest the correct location of the pacing/ablation catheter, and is usually followed by successful ablation of arrhythmia (6-9). The absence of residual ventricular activity is defined as acute procedural success.

While the method is highly successful, due to the focal origin of arrhythmia and modest chance of inducibility, RFA procedures can be prolonged and exhausting for both the patient and the electrophysiologist (8,10-12). Therefore, additional effective markers of correct catheter position and efficient RFA would be beneficial to facilitate precise localization of true arrhythmic loci in the outflow tract region.

Studies in the literature have documented that during RFA of the desired arrhythmogenic substrate, ventricular ectopy with short cycle lengths can be provoked, also known as the socalled fast repetitive or thermal response (FRR) (13,14). Here, we evaluated the utility of this additional response as a marker of correct RFA catheter positioning as well as successful ablation in comparison with the standard approach. Additionally, the long-term success of RFA in cases of provoked FRR was assessed.

MATERIALS AND METHODS

This study was a prospective observational case-control design. Patients scheduled for elective RFA for treatment of RVOT-VT were asked to participate in the study, which was approved by the local ethics

committee. Informed consent was obtained from all participants. The inclusion criteria were as follows: known history of palpitations and registered non-sustained or sustained RVOT-VT with typical ECG tracing of left bundle branch morphology and late R/S transition in precordial leads as well as inferior axis in standard leads. We excluded patients with symptomatic ischemic heart disease, heart failure (NYHA class ≤ II), structural changes in the right ventricle and thyroid disease. After admission, blood tests were performed and twodimensional echocardiograms from standard projection windows recorded. Patients in whom FRR was observed during RF ablation were classified as the FRR group. The control group consisted of patients showing no FRR. The two groups comprised 33 patients in total. After the procedure, patients were followed for 24 months. Patients were monitored during their regular visits at our outpatient clinic and also instructed to visit the emergency department immediately in case of symptoms suggestive of sustained palpitations. In symptomatic patients without documented arrhythmia, additional Holter monitoring was performed. Documented ventricular premature complexes (VPC) with typical morphology, suggestive of RVOT origin or non-sustained/sustained VT, were considered a study endpoint.

Electrophysiological studies were performed after obtaining informed consent. In all patients, one electrophysiological quadripolar and one decapolar catheter with 5 mm inter-electrode spacing were introduced through the right femoral vein and positioned in the high right atrial region and His-bundle area. Through a 7 French sheath previously inserted in the right femoral vein, a steerable radiofrequency ablation catheter with a 4 mm tip was introduced and advanced to the outflow tract region of the right ventricle. Surface ECG electrodes were placed in standard positions to obtain continuous surface ECG traces. All recordings were filtered between 30 and 1000 Hz and stored on an optical disc for post-hoc analysis. We employed the electrophysiology software, Prucka, provided by General Electric [USA]. An Osypka ablation generator [Osypka AG, Germany] was used for RFA purposes.

The ablation regions in all patients were determined with the aid of activation mapping and local activation times. The region within RVOT with earliest depolarization was considered an ablation target. In the case of non-inducibility, we enhanced induction with continuous infusion of isoproterenol. If the induction method failed, the desired region was pinpointed based on analysis of local intracardiac electrograms and pace mapping methods. A 12/12 match between VT ECG and paced ECG established the accurate position of the ablation catheter. In addition to the 12/12 ECG match, we used so-called FRR, which was provoked during ablation of the target region, as a marker for proper positioning of the ablation catheter as well as the desired focus. FRR has been described in earlier reports (13,14). In brief, the thermic effect during ablation is thought to induce depolarization of the resting membrane potential and early afterdepolarization and consequently enhance automaticity. During RFA, ventricular complexes with identical QRS morphology to VT and very short cycle length are provoked but usually not sustained, and gradually slowed down during RFA. Ablation was performed with a 4 mm tip catheter adjusted to ensure energy delivery of 45 J at a temperature range up to 60°C. At a typical site of successful ablation, FRR was initially induced, and during energy delivery, the cycle length was gradually prolonged. Abolishment of arrhythmia and FRR was considered an RFA endpoint (Figure 1). Patients were divided into two groups according to inducibility of FRR. Comparative data between the groups are presented in Table 1. Continuous data are presented as means ±SD and categorical variables expressed as percentages. The differences between continuous variables were evaluated using the Student's t-test and chi-square test applied for categorical variables. Simple logistic regression was employed to assess the correlation between recurrence of RVOTVT after 2 years and the treatment method. Multivariable logistic regression was used to adjust the results for potential confounders. Statistical analyses were performed using the SPSS statistical package (SPSS; Chicago, IL).

RESULTS

Only patients with successfully accomplished procedures were included for analysis. At the beginning

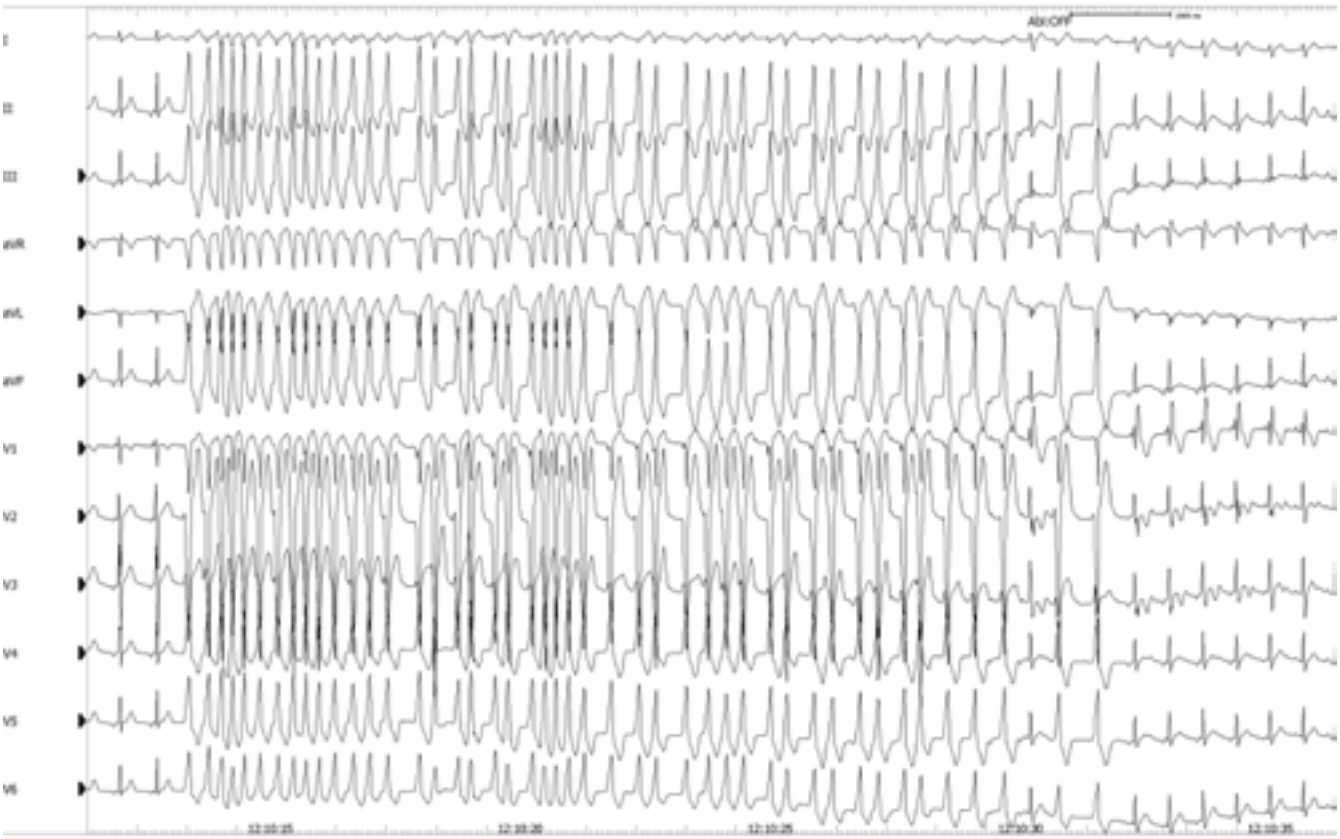

Figure 1. *FRR at the site of successful application of RF energy characterized by acceleration and subsequent termination of ventricular ectopic activity with RVOT-VT morphology.*

of follow-up, both groups consisted of a total of 33 patients. No patients were lost during follow-up and no significant differences in baseline parameters between the groups were evident (Table 1). However, we observed a significant shorter duration of procedure time (120±29 min vs. 70±16 min; P<0.001) in cases where FRR was observed. Patients in the FRR group also received significantly less radiofrequency (RF) applications (21.6±15.6 vs. 13.4±12.5; P=0.02). After a 24-month observation period, composite relapse (clinically significant VPC or VT) occurred in 12 (46%) patients in the control group and five (16%) patients in the FRR group. In the control group, we observed nine cases (35%) of recurring ventricular premature contractions (VPC) and three cases of VT recurrence (11.5%) while in the FRR group, VPCs occurred in four cases (12%) and VT in one case (3.2%). No significant differences regarding VT recurrence were observed between the two groups. However, in case of composite relapse, the unadjusted odds ratio for arrhythmia recurrence in patients with observed FRR was 0.22 (95% CI 0.06–0.74; P=0.01). After adjustment for several confounders, such as sex, age, left ventricular ejection fraction, RVOT-VT cycle length, number of RF applications and cumulative RF energy, adjusted odds ratio retained statistical significance (OR, 0.19; 95% CI, 0.05–0.83; P=0.03).

DISCUSSION

To our knowledge, this is the first study to demonstrate that provoked FRR translated to better long-term outcome and the largest in this regard. Moreover, in patients with FRR, the procedure time was significantly shorter and smaller doses of RF were required to generate lesions.

However, because FRR could not be induced in all

our patients, further research is warranted to clarify whether induction of FRR is a consequence of better or more precise positioning of the ablation catheter with regard to arrhythmogenic focus or additional tissue or cellular properties in certain patients could facilitate thermal induction of arrhythmia.

The concept of FRR was introduced in a landmark study by Chinushi et al. (14), where the authors showed that in patients with RVOT-VT, inducible FRR frequently occurred during successful RFA. QRS morphology in FRR was almost identical to baseline tachycardia, which led to the conclusion that thermal injury underlies this response. The group additionally hypothesized that occurrence of FRR is more frequent if a wider anatomical region is responsible for RVOT-VT.

In a study by Clyne et al. (13), thermal mapping was conducted in patients with RVOT-VT when tachycardia could not be induced. The group applied short bursts of energy at the target regions and continued with ablation upon induction of FRR. A high rate of acute as well as long-term success was achieved, suggesting that thermal response could present a valuable additional tool in cases where activation mapping is unsuccessful. However, the study sample was small, including only 13 patients. Moreover, no control group was included for comparison of data (13). To date, limited studies have attempted to address this issue, which may be attributable to the implementation of novel electroanatomic mapping methods. However, electrophysiological testing and understanding of arrhythmia remain the basis for developing an optimal approach. In cases of RVOT-VT, simple fluoroscopy may be as effective as advanced electroanatomic systems, along with the added advantage of lower costs (10).

Table 1: *Baseline parameters and results (see text for the relevant explanations)*

	FRR group	Control group	P value
Number of patients	33	33	ns
Age (years)	51.4 ± 15.0	50.2 ± 14.2	0.73
Sex (female)	13 (39.4%)	5 (15.2%)	0.05
Ejection fraction (%)	55.1 ± 5.9	52.3 ± 5.7	0.05
VT cycle length (msec)	335.0 ± 81.2	357.0 ± 73.8	0.26
Duration of procedure (min)	70.0 ± 16.5	120.5 ± 29.6	0.00
N of RFA applications	13.4 ± 12.5	21.6 ± 15.6	0.02
Power (J)	42.7 ± 3.3	42.9 ± 2.5	0.83
Temperature (°C)	60.9 ± 5.8	61.5 ± 4.9	0.64
Mean FRR cycle length (msec)	292.7 ± 60.9		
Mean FRR duration (sec)	16.0 ± 12.1		
AH (msec)	95.7 ± 19.6	106.6 ± 25.9	0.06
HV (msec)	41.9 ± 6.0	44.5 ± 5.6	0.08
QRS (msec)	99.0 ± 9.6	106.2 ± 17.5	0.06
VT recurrence (N)	1 (3.1%)	3 (11.5%)	0.32
VPC recurrence (N)	4 (12%)	9 (35%)	0.06
Composite recurrence (N)	5 (15.6%)	12 (46%)	0.02

LIMITATIONS

Comparison of data from the two experimental groups revealed a slightly lower ejection fraction of the left ventricle as well as prolonged conduction intervals in the control group, suggesting the possibility of a higher rate of unrecognized or underdeveloped cardiomyopathy in these patients. However, the measurements obtained were still within a normal range, which allowed exclusion of developed structural heart disease. Because magnetic resonance imaging was not performed in this study, we were unable to exclude possible morphologic changes in the right ventricle and thus eliminate patients with unrecognized right ventricular dysplasia from our analysis. A relatively small long-term success rate in the control group was additionally noted, which was mainly attributable to the observation of recurrent VPCs along with a low rate of VT recurrence, consistent with earlier results.

CONCLUSION

In conclusion, induction of thermal response or FRR with identical morphology to VT ECG was a valuable tool in the ablation procedure in patients with RVOT-VT and may serve as a useful additional parameter, aiding in pinpointing the focal origin of tachycardia more accurately and successful accomplishment of the procedure. FRR induction appeared to be associated with significant shortening of the procedure and improved outcomes in the long term. However, the predilection factors triggering FRR in certain patients remain to be established.

REFERENCES

1. Movsowitz C, Schwartzman D, Callans DJ, Preminger M, Zado E, Gottlieb CD et al. Idiopathic right ventricular outflow tract tachycardia: narrowing the anatomic location for successful ablation. Am Heart J; 1315:930-6.
2. Lerman BB, Belardinelli L, West GA, Berne RM, DiMarco JP. Adenosine sensitive ventricular tachycardia:evidence suggesting cyclic AMP-mediated triggered activity. Circulation 1986; 74: 270-80.
3. Wilber DJ, Baerman J, Olshansky B, Kall J, Kopp D: Adenosine sensitive ventricular tachycardia: clinical characteristics and response to catheter ablation. Circulation 1993; 87:126-34.
4. Lermann BB, Mechanism of outflow tract tachycardia. Heart Rhythm 2007; 4:973–76.
5. Aliot EM, Stevenson WG, Almendral-Garrote JM, Bogun F, Calkins CH, Delacretaz E et al. EHRA/HRS expert consensus on catheter ablation of ventricular arrhythmias: developed in a partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC), and the Heart Rhythm Society (HRS); in collaboration with the American College of Cardiology (ACC) and the American Heart Association (AHA). Europace 2009;11: 771-817.
6. Calvo N, Jongbloed M, Zeppenfeld K. Radiofrequency catheter ablation of idiopathic right ventricular outflow tract arrhythmias. Indian Pacing Electrophysiol J. 2013; 13:14-33.
7. Kamakura S, Shimizu W, Matsuo K, Taguchi A, Suyama K, Kurita T et al. Localization of optimal ablation site of idiopathic ventricular tachycardia from right and left ventricular outflow tract by body surface ECG. Circulation 1998; 98:1525–33.
8. Morady F, Kadish AH, DiCarlo L, Kou WH, Winston S, deBuitlier M et al. Long-term results of catheter ablation of idiopathic right ventricular tachycardia. Circulation 1990; 82:2093–2099.
9. Calkins H, Kalbfleisch SJ, el Atassi R, Langberg JJ, Morady F. Relation between efficacy of radiofrequency catheter ablation and site of origin of idiopathic ventricular tachycardia. Am J Cardiol 1993; 71:827–33.

10. Ito S, Tada H, Naito S, Kurosaki K, Ueda M, Hoshizaki H et al. Development and validation of an ECG algorithm for identifying the optimal ablation site for idiopathic ventricular outflow tract tachycardia. J Cardiovasc Electrophysiol 2003; 14: 1280-6.
11. Wen MS, Taniguchi Y, Yeh SJ, Wang CC, Lin FC, Wu D et al: Determinants of tachycardia recurrences after radiofrequency ablation of idiopathic ventricular tachycardia. Am J Cardiol 81:500, 1998.
12. Vestal M, Wen MS, Yeh SJ, Wang CC, Lin FC, Wu D. Electrocardiographic predictors of failure and recurrence in patients with idiopathic right ventricular outflow tract tachycardia and ectopy who underwent radiofrequency catheter ablation. J Electrocardiol 2003;36: 327-32.
13. Clyne CA, Athar H, Shah A, Kahr R, Rentas A. Thermal mapping of right ventricular outflow tract tachycardia. Pacing Clin Electrophysiol. 2007; 30:343-51.
14. Chinushi M, Aizawa Y, Ohhira K, Fujita S, Shiba M, Niwano S, Furushima H. Repetitive ventricular response induced by radiofrequency ablation for idiopathic ventricular tachycardia originating from the outflow tract of the right ventricle. Pace.1998;21:669-78.
15. Saleem MA, Burkett S, Passman R, Dibs S, Engelstein ED, Kadish AH et al. New simplified technique for 3D mapping and ablation of right ventricular outflow tract tachycardia. Pacing Clin Electrophysiol. 2005; 28:397-403.