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İskemik Ventriküler Taşikardi Katater Ablasyonu Yapılan Hastaların Uzun Dönem Sonuçları

Long-Term Outcomes of Catheter Ablation of Ventricular Tachycardia in Patients With Ischemic Cardiomyopathy

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ÖZ

GİRİŞ ve AMAÇ: *İskemik kardiyomiyopatili (ICM) hastalarda ventriküler taşikardinin (VT) ablasyonu için sürekli olarak bir elektroanatomik haritalama (3D EAM) sistemi kullanılmaktadır. Bu çalışmanın amacı, ICM'de ventriküler taşikardide substrat haritalama ve kateter ablasyonunun (CA) uzun dönem sonuçlarını belirlemektir.*

YÖNTEM ve GEREÇLER: *Çalışmaya ICM'li 41 ardışık hasta alındı. 3D EAM kullanan tüm hastalara substrat haritalama ve ablasyon uygulandı. Hastalar akut işlem başarısı, periprosedural komplikasyonlar, mortalite ve VT nüksü açısından takip edildi.*

BULGULAR: *Bu çalışmaya dahil edilen hastalar için yaş ortalaması 61 ± 7 ve hastaların çoğu erkekti (38% 92,6). Ortalama takip süresi 16,5 ± 8,5 aydı ve takip süresinde 6 (% 14,6) hasta kaybedildi ve 10 (% 24,3) VT olgusunda nüks görüldü. Periprosedural komplikasyonlar hastaların 5'inde (% 11.9) meydana geldi.*

TARTIŞMA ve SONUÇ: *Tek merkezli bir retrospektif çalışmada, iskemik kardiyomiyopatili hastalarda için,3D EAM destekli bir yaklaşım ile VT ablasyonu uygulandığında,uzun dönem başarısı yüksek bulundu (% 75.6). Çalışmamızda, sinüs ritmi yada ventriküler pacing altında, substrat haritalama ve ablasyon başarısı gösterilmiştir.*

Anahtar Kelimeler: *Katater ablasyon, Elektroanatomik haritalama, Substrat haritalama, İskemik Kardiyomyopati, Ventriküler taşikardi.*

ABSTRACT

INTRODUCTION: *For ablation of ventricular tachycardia (VT) in patients with ischemic cardiomyopathy (ICM), an electroanatomical mapping (3D EAM) system is constantly used. The goal of this study was to determine the long-term outcomes of substrate mapping and catheter ablation (CA) of Ventricular Tachycardia in ICM.*

METHODS: *The study included 41 consecutive patients with ICM. Substrate mapping and ablation were performed to all patients using 3D EAM. Patients were followed up for acute procedure success, periprosedural complications, mortality and recurrence of VT.*

RESULTS: *For patients that included in this study, mean age was 61 ± 7 and majority of the patients was male (38, 92.6 %). Mean follow-up duration was 16.5 ± 8.5 months and in the follow up duration 6 (14,6%) of study patients were lost and 10 (24,3%) experienced VT recurred. Periprocedural complications occurred in 5 of the patients (11.9 %).*

DISCUSSION AND CONCLUSION: *In a single center retrospective study, when using a 3D EAM guided approach for VT ablation in patients with ischemic cardiomyopathy, the freedom from any ventricular arrhythmia has found high (75.6 %). Substrate mapping and ablation during on sinus rhythm or under pacing shown as successful which we demonstrated in our study.*

Keywords: *Catheter ablation, Electroanatomic mapping, Substrate mapping, Ischemic cardiomyopathy, Ventricular tachycardia.*

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INTRODUCTION

Ischemic ventricular tachycardia, usually occurs from a ventricular scar area which has been form with a myocardial infarction and the mechanism behind the tachycardia is reentry **(Figure 1).** Although implantable cardioverter defibrillators (ICDs) form the basis of sudden cardiac death reduction therapy in patients with ventricular tachycardia (VT) or ventricular fibrillation, ICD shocks are associated with increased morbidity and mortality, although it does not prevent the formation of VT (1).

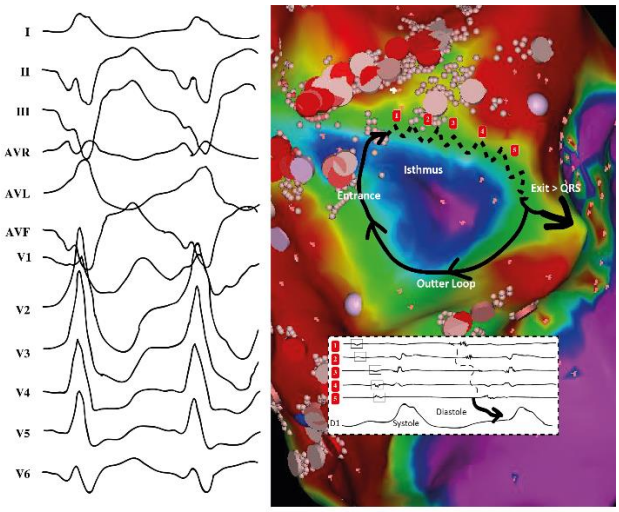

Figure 1. Schematic view of the scar associated reentry.

In large randomized clinical trials, catheter ablation for VT has been shown to be superior to antiarrhythmic therapy in reducing mortality, VT storms and ICD shocks (2). Due to these results, following guide has been written to 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death Guideline: In patients with prior MI and recurrent episodes of symptomatic sustained VT, or who present with VT storm and have failed or are intolerant of amiodarone or other antiarrhythmic medications, catheter ablation is recommended (3,4).

In ischemic ventricular tachycardia catheter ablation, clinical tachycardia-targeted activation and entrainment mapping strategies are used, however they do not have the advantage of targeting for ablation when VT cannot be induced or haemodynamically tolerated(5). Although the Substrate Modification strategy with linear ablation of local abnormal ventricular activities (LAVA) using 3D electroanatomic mapping (3D EAM) eliminates these disadvantages, it also allows to treat potential substrates for current and future VTs (6).

The aim of our study is to report the long-term results of post-myocardial infarction (MI) patients with ventricular tachycardia who underwent catheter ablation and substrate modification in our clinic using 3D EAM.

MATERIAL AND METHODS

Patients population

Of the 41 consecutive patients who underwent a postinfarct sustained VT ablation procedure in Bursa Yuksek Ihtısas Training and Research Hospital our between January 2015 and October 2018. The diagnosis of ischemic cardiomyopathy (ICM) was established according to history of myocardial infarction with focal wall-motion abnormality or fixed perfusion defect correlated with coronary stenosis or previous coronary intervention. One month prior the use of antiarrhythmic medication, patients with recurrent VT or appropriate ICD therapy were also included. Coronary angiography, and transthoracic echocardiography were performed in all patients prior to the ablation. All patients provided written informed consent to participate.

Electrophysiologic study and Electroanatomical mapping

All patients underwent the procedure in the fasting state. Conscious sedation was used for patient comfort at the discretion of the operator. General anesthesia was used during epicardial mapping and ablation procedures. The main aim for RFCA (Radiofrequency catheter ablation) of VT was a substrate-based ablation approach guided by 3D electroanatomic mapping. Left ventricular access was performed via retrograde aortic route or trans-septal puncture and intravenous unfractionated heparin was administered to maintain an activated clotting time between 300-350 seconds. Epicardial mapping and ablation were performed at the discretion of the operator; access to the pericardial space was obtained by using the percutaneous technique described by Sosa et al.(7)

Using fluoroscopic guidance, a decapolar mapping catheter (6F, 110 cm, Inquiry™, St. Jude Medical, St. Paul, Minnesota, USA) was inserted through the right femoral vein and positioned in the coronary sinus. A standard transvenous 6-F quadripolar catheter (6F, 110 cm, Marinr® SC Series, Medtronic, Minneapolis, MN, USA) was placed at the right ventricular apex. Endocardial signal and surface ECG were recorded using the EP Tracer device (Schwarzer Cardiotek, Inc., Germany). ICD's tachycardia therapy settings were programmed to off state during the procedure. Electroanatomical mapping was performed with the EnsiteTM Precision (Abbott, IL, USA) or CARTO (Biosense Webster, USA). The ablation catheter used for mapping and ablation was an 8F quadripolar irrigated ablation catheters Thermocool Smarttouch ST(ContactForce) (Biosense Webster Inc., Diamond Bar, California, USA) and FlexAbility (Endosense/ Abbott, St Paul, Minnesota, USA) with 4-mm-tip and 2-5-2 mm inter-electrode spacing.

The aim was to determine the regions of triggerred activity in substrate mapping and the critical isthmus for VT in patients with ICM. The bipolar voltage map in the left ventricle during sinus rhythm or with pacing from right ventricle was performed. Based on previously published data; "normal" myocardium was defined as a bipolar voltage of> 1.5 mV. "Dense scar" was defined as a bipolar voltage of <0.5 mV, and "abnormal" myocardium was voltage between 0.5 and 1.5 mV. The region of "local abnormal ventricular activities (LAVA)" on myocardium, most commonly found surrounding the scar, defined the scar border zone(8). Epicardial approach decision were made when 12-lead electrocardiography of the VT suggested an epicardial origin or endocardial ablation unsuccessful. Somewhat different parameters are used during epicardial mapping, with the low-voltage area defined as a bipolar signal amplitude, 1.0 mV(9). **(Figure 2)**

Substrate ablation and prosedural endpoints

The main goal of RFCA was to eliminate the clinical VTs and all mappable nonclinical VTs. For hemodynamically tolerated VTs, entrainment mapping was performed within the low voltage area at sites exhibiting diastolic activity to identify critical

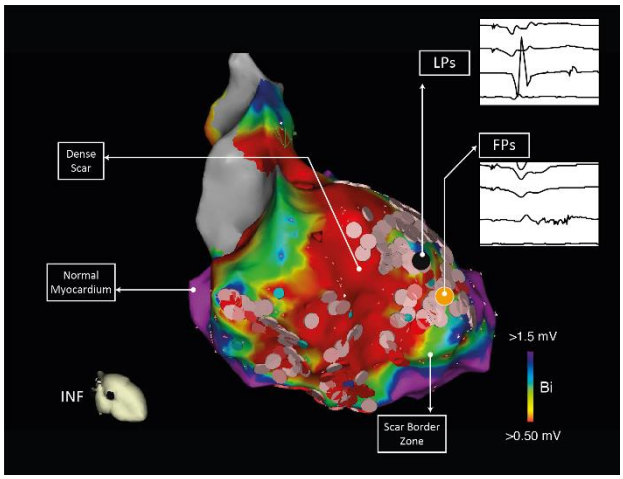

Figure 2. Electroanatomic substrate mapping and the view of local abnormal ventricular activities

sites of the VT re-entrant circuit. Radiofrequency energy was delivered at these local abnormal ventricular activity sites. For hemodynamically unstable VTs, substrate modification was performed with linear or homogenization lesions targeting sites identified by pace mapping; it included signals withlate potentials or discrete split recorded during sinus rhythm or with right ventricular apical pacing, as previously described (9). Substrate modification was typically extended to target marked as LAVA; there was a specific emphasis on abnormal potentials recorded within a 2-cm to 3-cm radius of the site of origin, defined by entrainment mapping or the best pacemap with clusters of radiofrequency lesions targeting abnormal potentials with the endpoint of signal modification or elimination. Radiofrequency energy was delivered in a power-controlled mode at 30–45 W for the irrigated catheter, targeting for an impedance decrease of 12 to 15 Ω and a temperature limit of 42C to 45C **(Figure 3).**

Acute study endpoints consisted of noninducibility of the clinical or any nonclinical VTs. Long-term study endpoints were mortality and, as a secondary endpoint, recurrence of VT/ventricular fibrillation was reported.

Follow-up

After ablation, patients were monitored for 48 hours by telemetry. Transthoracic echocardiography was performed within 2 days after ablation. After discharged of patients, they were routinely evaluated for 4 to 8 weeks after ablation and then at 3 to 6-

month intervals. When available, the ICD Holter function was permanently activated.

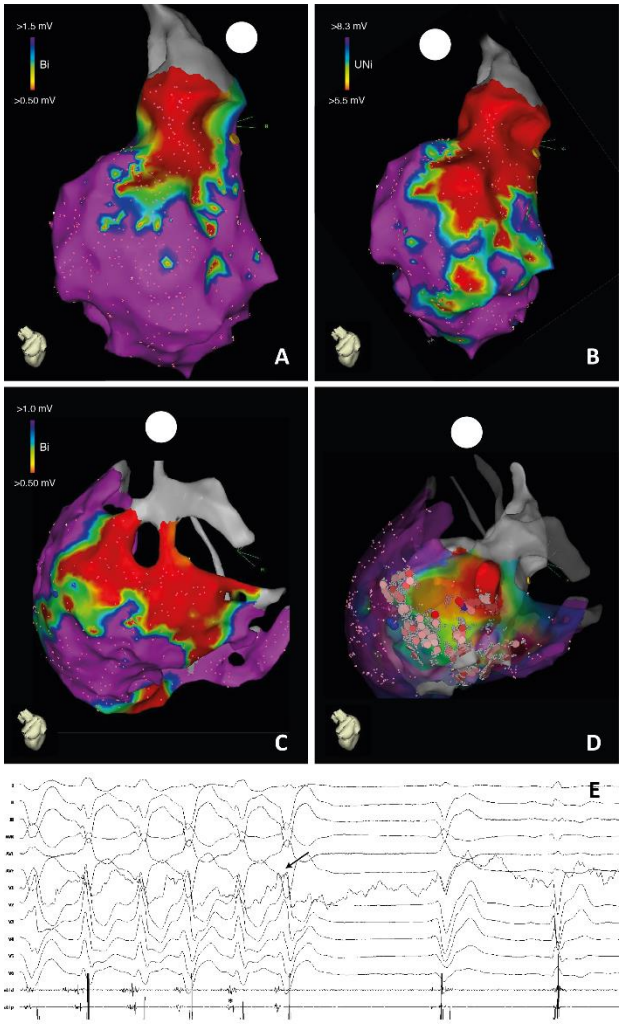

Figure 3. Substrate mapping and endo-epicardial ablation procedure

Statistical Analyses

Statistical analysis was performed with SPSS version 22. Continuous variables were summarized as mean ± standard deviation, or median (minimum, maximum) when normal distribution was not present. Kaplan–Meier curves were used to assess survival and VT recurrence in individual patient groups.

RESULTS

Baseline characteristics of the study population are summarized in **Table 1**. A total number of 41 patients with documented ischemic VT undergone RFCA were enrolled prospectively in this study. Mean age was 61 ± 7 and majority of the patients was male (38, 92.6 %). Fifteen of the patients had type 2 diabetes mellitus (36.6 %), hypertensive patients made up 22 (53.6 %) and 17 (41.5 %) of the patients had dyslipidemia.

Table 1. Baseline Characteristics of the Patients Population (n = 41)

Age, y	61 ± 7
Male sex, n (%)	38 (92,6)
Mean follow up, m	16.5 ± 8.5
Coronary risk factors, n (%)	
Diabetes mellitus	15 (36,6)
Arterial hypertension	22(53,6)
Dyslipidemia	17 (41,5)
Smoking	16(39)
Renal insufficiency n (%)	9(21,4)
Atrial fibrillation or flutter n (%)	10(23,8)
LVEF, %	26.2 ± 9.7
Previous PCI, n (%)	27 (65,9)
Previous CABG, n (%)	7(17,1)
Redo ablation, n (%)	5(12,2)
NYHA functional class, n (%)	
I/II	30(73,2)
III/IV	11(26,8)
Antiarrhythmic drugs, n (%)	
Sotalol/class I	4 (9,5)
Amiodarone	34 (82,9)
Mexiletine	3(7,3)
Two or more drugs	5(12,2)
Other cardiovascular drugs, n (%)	
β-Blocker	39(95,1)
ACEI-ARB	37(92,7)
Statin	30(73,2)
Ivabradine	9(21,9)
MRA	30(73,2)
Digoxin	6(14,6)
Furosemide	31(75,6)
Warfarin /Non-warfarin anticoagulant	8(19)
ICD type, n (%)	
None	10(24,4)
Single or dual chamber	22(53,6)
CRT-D	9(21,9)
Indication for ablation, n (%)	
VT storm/incessant VT	25(61)
Appropriate ICD shock	16(39)

PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft, ACE: angiotensin-converting enzyme inhibitors, ARB: Angiotensin II receptor blockers, MRA:Mineralocorticoid receptor antagonist, ICD: implantable cardioverter defibrillator, CRT: cardiac resynchronization therapy, LVEF: left ventricular ejection fraction, NYHA: New York Heart Association, VT: ventricular tachycardia

Sixteen of the study patients (39%) had tobacco use as an identifiable risk factor. Nine patients (21.4 %) had renal insufficiency in their past medical history. Atrial fibrillation was detected in present medical examination of past medical history in 10 (23.8 %) of the patients. Previous history of coronary artery

disease was identifiable in 27 (65.9 %) as previous PCI and 7 (17.1 %) as CABG. Five patients had a previous history of RFCA for VT (5, 12.2 %).

Amiodarone was the most commonly utilized antiarrhythmic drug in the study patients (34 patients, 82.9%) while other commonly used antiarrhythmic drugs were only used in a few of the patients (Sotalol in 4 patients, 9. 5 % and mexiletine in 3 patients, 7.3 %). Only 5 patients were on combination antiarrhythmic therapy (12.2 %). Use of other important classes of cardiovascular drugs were as follows: β-Blockers in 39 (95.1 %), any renin-angiotensin system blocker in 37 (92.7%), statin in 30 (73.2 %), mineralocorticoid receptor antagonist in 30 (73.2 %), furosemide in 31 (75.6 %) patients. Nine of the patients were on ivabradine (21.9 %) and 6 were on digoxin (14.6%). Eight of the patients (19 %) were on any type of oral anticoagulant by the time of initial evaluation. While approximately a quarter of the patients were not receiving any type of device therapy for their arrhythmia (10 patients, 24.4 %), about half of the patients were receiving ICD (22, 53.6 %) and 9 patients were on combination therapy with cardiac resynchronization therapy and ICD (21.9 %).

Almost 3/4 of the patients were in lower functional classes (NYHA I/II), (30,73.2 %) while the remaining were in higher functional classes (NYHA III/IV) (11, 26.8 %). Mean LVEF was 26.2 ± 9.7 %. Indication for RFCA was identified as VT storm or incessant VT in 25 of the patients (61 %) while appropriate ICD shocks confirmed by device interrogation was the indication in 16 of the patients (39 %).

Arrhythmic substrate was identified and ablated in all patients. Left ventricle cavity was accessed by transaortic access in majority of the patients (35, 85.3%) while 9 (4 %) in whom the procedure started with transaortic access, transseptal route was also required. In 2 of the patients (4.9 %) transseptal route was preferred. Mapping and ablation of the substrate necessitated epicardial access in 4 of the patients (18.9 %). CARTO was the 3D electroanatomical mapping system used the most in more than half of the study participants (53.6 %), EnSite Precision system was used in 15 (36.6 %) and Columbus system was used in 4 patients (9.7 %). Additional non-clinical VTs were detected during electroanatomical mapping in 34 patients (82.9 %). Although substrate ablation was performed successfully in all patients, procedural success defined as the "non-inducibility of the clinical VT and any inducible VT" in post-procedural stimulation procedures was achieved in 35 (85.3 %). Total RF energy application time was 39.9 ± 18.4 minutes, procedure time was 167.9 ± 58.2 minutes and fluoroscopy time was 29.2 ± 18.7. Periprocedural complications occurred in 5 of the patients (11.9 %). Preprocedural complications were tamponade in a patient, cerebrovascular accident in 1 patient which resolved with complete recovery and entry-site hematoma in 2 patients and peripheral embolism in 1 patient peripheral embolism. None of the hematoma cases needed blood transfusion or further intervention. Procedural characteristics are summarized in **Table 2.**

Table 2. Procedural Characteristics of ventricular tachycardia ablation in patients with ischemic VT

Procedural Characteristics	n=41
Mapping and ablation	
3D-Electroanatomic mapping system	
CARTO, n (%)	22 (53,6)
EnSite Precision, n (%)	15(36,6)
Columbus, n (%)	4 (9,7)
Irrigated ablation catheter, n (%)	41 (100)
LV access	
Transseptal, n (%)	35(85,3))
Transaortic retrograde, n (%)	2(4,9)
Both, n (%)	4(9,7)
Scar localization, n (%)	
Anterior wall	15 (36,6)
Infero-posterior wall	21 (51,2)
Septal wall	5 (12,2)
Substrate ablation	41(100)
Mapping during sinus rhythm	35(85,3)
Mapping during RV pacing	6 (14,6)
Epicardial Access	4 (9.7)
Additional induced VTs (non-clinical)	34 (82.9 %)
Procedural outcomes	
Non-inducible, n (%)	35(85,3)
Partial/failure, n (%)	6(14,6)
Procedural parameters	
Radiofrequency time, min	39.9±18.4
Total procedure time, min	167.9±58.2
Fluoroscopy time, min	29.2±18.7
Procedural complications, n (%)	5(11.9)

Mean follow-up duration was 16.5 ± 8.5 months. Six patients were lost during the follow-up period. Most of the mortality occurred during the first year

(2 patients by the end of the first week due to procedural complications, 1 patient by the end of the 2nd month, 1 patient during the 6th month and 1 patient by the end of the 8th month) following the procedure and one patient was lost while approaching the end of the 2nd year follow-up appointment. Mortality due to periprocedural complications consisted of pericardial tamponade in one of the patients who was treated aggressively with pericardiocentesis and emergency surgical intervention but unfortunately didn't respond to proper management. The other patient experienced a periprocedural peripheral embolic event, was uneventfully discharged home but he was admitted to emergency department with pulseless electrical activity following multiple ICD shocks. One patient with recurrence of VT during 3rd month following the procedure, was offered electrophysiologic study but rejected the procedure. The patient was followed with optimization of antiarrhythmic medications but was lost during the 8th month following his initial procedure. One patient was lost due to noncardiac reasons at the end of the 2nd month post status index procedure. Remaining 2 patients were lost due to worsening heart failure. Overall survival rate in the study group by the end of the follow-up period was 85.6 %. **(Figure 4A)**

Recurrence of arrhythmia was observed in 10 patients and arrhythmia recurrence was associated with mortality in 2 patients. Recurrence-related mortality occurred during the first year of follow-up in these 2 patients. Majority of the recurrences occurred in the first year following the index procedure (8/10) remaining 2 recurrences occurred during the 2nd year. Overall event-free survival rate was 75.6 % in the study population. **(Figure 4B)**

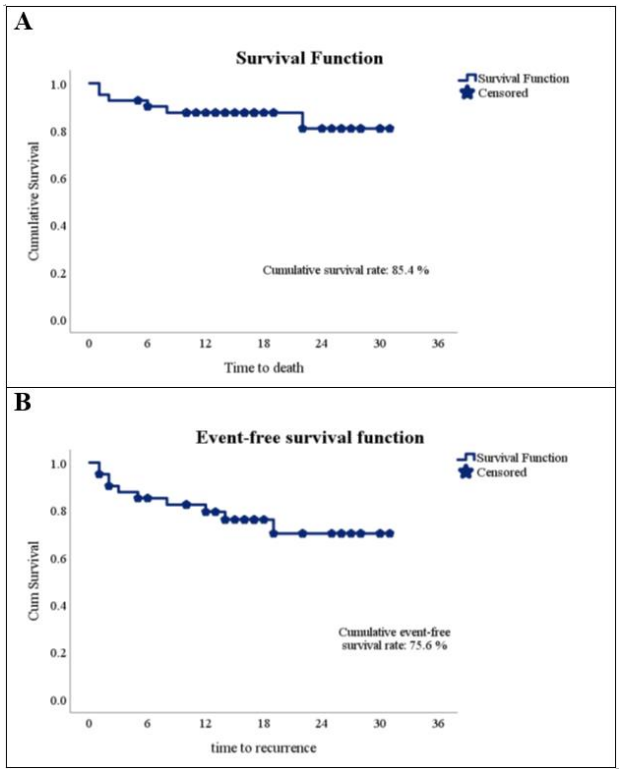

Figure 4. Kaplan-Meier curves for A. Cumulative survival free of all-cause Mortality, B. Cumulative survival free of clinically relevant VTs of ischemic origin

DISCUSSION

Our study shows that the drug refractory ventricular tachycardia in ICM patients's long-term results of RFCA through substrate modification. The major findings are as follows: 1) Substrate ablation method was acute successful for "the non-inducibility of the clinical VT and any inducible VT" in 35 (85.3%) patients. 2) Periprocedural complications were detected in 5 (11,9%) patients. 3) Mean (16.5 ± 8.5 months) follow-up, event-free survival rate was 75.6% in the study population. 4) Overall survival rate in the study group by the end of the follow-up period was 85.6 %.

Anti-arrhythmic drugs are constantly used but are frequently ineffective and laden with side effects (10). Catheter ablation of VA's in patients with ischemic cardiomyopathy have shown moderate results at long-term follow-up, even after the introduction of open irrigated ablation(11). Several studies have shown that catheter ablation has a better success rate at follow-up when compared with AADs for the treatment of VA and appropriate ICD shocks. The success rate ranges from 41% to 49% and increases in patients with acute efficacy after ablation (12,13). Nevertheless, patients with VA, recent studies have also shown the superiority of catheter ablation to standard medical therapy (10). However, in more recent studies, the increase in the prevalence of epicardial ablation, increased use of high density mapping catheter, combined analysis of unipolar and bipolar voltage mapping, and new ablation and mapping methods such as Decrement Evoked Potential (DEEP) Mapping have increased

the success of acute and long-term ablation(14,15,16,17).

Current ablation strategies are guided by identification of potential reentry circuit isthmuses and exit sites based on substrate, pace, and entrainment mapping. There are two commonly used ablation methods which are substrate modification and clinical stable VT's ablation. The substrate mapping provides description of the scar based on local abnormal ventricular activity amplitude and abnormal local electrogram configuration. For this reason, nonrandomized and randomized studies have suggested that a substrate-based ablation is superior to ablation of clinical and hemodynamically stable VT (18,19,20). A recent important randomized multicenter study by Luigi Di Biase et all. shown that, substrate-based ablation approach is superior to (VT recurrence rate , all-cause mortality rate, arrhythmia-related rehospitalization) ablation targeting only clinical and stable VTs in patients with ischemic cardiomyopathy presenting with tolerated VT (20). In this study determined that substrate-based ablation was associated with significantly lower VT recurrence rates at 12-month follow-up compared with clinical VT ablation (15.5% vs. 48.3%; log-rank p <0.001). In the study performed by Guler et all. shown that, the demonstration of micro vascular occlusion with cardiac magnetic resonance imaging (CMR) after ablation showed the adequacy of RF lesions and correlated with clinical results.(21) Additionally, The VT recurrence rate was found to be consistent with the results of our study (24,4%), which we followed patients for 16.5 ± 8.5 months.

In our case series, we observed six death cases (14,4%), two of which were post-procedural (4,9%) and four of them were in clinical follow-up. In the present multicenter registry by Pasquale et all. died before hospital discharge occurred in 5% of patients and was associated with clinical and procedural factors indicating poorer clinical status and worse procedural results. These factors include low LVEF, chronic kidney disease, VT storm, unmappable VTs, and postprocedural VT recurrence. With this study, Patients' Risk Profile and Mortality (PAINESD Score) was developed for early mortality after VT ablation prediction(22). Additionally, study present that the occurrence of postprocedural in patients undergoing RFCA of scarrelated VT, and it is essential for understanding the rates of in-hospital and early post-discharge mortality in this complex patient population, allowing for direct comparison with similar indicators developed for other interventional and surgical cardiac procedures. For example, recent estimates of post-procedural associated with PCI and CABG range from 1.5% to 3% respectively (23). However, the post-procedural mortality rate found in our study is in line with what has been shown for interventional and surgical procedures in patients with severe heart disease.(24)

Another important finding of our study is that the rate of periprocedural complications are 5 (11,9%). Preprocedural complications were tamponade in a patient, cerebrovascular accident in 1 patient which resolved with complete recovery and entry-site hematoma in 2 patients and peripheral embolism in 1 patient peripheral embolism. Two large, prospective, multicentre trials reported , major complication rate was occured to be 5-6% (25,26). Additionally, Delacretaz et al. reported complication rates in pooled data from a published series of postinfarction VT ablation. Significant complications occurred in 11% of 393 patients, with 4 (1%) procedure-related deaths and 20 (5%) major complications, the most frequent (>1%) including strokes, transient ischemic attacks, pericardial effusions requiring drainage, and permanent AV block (27). In our case series, most of the complications were related to the peripheral site of intervention. The reason of this difference in the rate of the conversion can be explained by the more frequent use of transaortic retrograde pathways in our study compared to transseptal intervention. Along with Dinov at al. reported that the frequency of complications was similar (11%) (28).

CONCLUSION

Catheter ablation for postinfarction VT has become a treatment option for patients with sustained VT and / or appropriate ICD shocks. In our case series , when using substrate based ablation approach for VT ablation in patients with coronary artery disease, the freedom from any ventricular arrhythmia is high (75,6%). However, post-procedural complication rate found in our study is in

line with what has been shown for coronary surgical procedures in patients with severe heart disease. Therefore, when the difficulties and complication risks of the procedure are evaluated, periprosedural preparation and possible complications should be considered.

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