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Original Research Article

Long-term outcomes of ventricular tachycardia ablation in ischemic and non-ischemic cardiomyopathy patients: Data from a single center ablation registry

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ABSTRACT

Objective: Catheter ablation is effective in the treatment of ventricular tachycardia (VT). However, long-term outcomes after VT ablation in non-ischemic cardiomyopathy are sparsely described. We aimed to compare the outcomes of VT ablation between patients with ischemic cardiomyopathy (ICMP) and non-ischemic cardiomyopathy (NICMP).

Methods: Acute procedural and long-term outcomes of 212 consecutive patients (ICMP, 135; NICMP, 77) who were ablated for sustained VT and followed for a median of 36 months were gathered and analyzed.

Results: Compared with patients with NICMP, patients with ICM were older, more likely to be men, had lower LVEF, more comorbidities, and had a higher number of inducible VTs. Complete procedure success was higher in patients from the NICMP group (88.3 % in NICMP compared to 79.3 % in ICMP). VT recurrence occurred in 54.8 % of ICMP compared to 38.9 % of NICMP (P value = 0.026). The overall mortality rate was 22 % in the ICMP group, compared to 7 % in the NICMP group (P value = 0.007). Additionally, cardiac mortality occurred significantly more in the ICMP group than in the NICMP group (19 % vs. 6 %) (P value = 0.011).

Conclusion: VT ablation in patients with NICMP was found to be an effective and safe approach, achieving acute procedural success in a noticeable number of patients using the currently available catheter mapping and ablation techniques with acceptable low procedural complications. Overall, procedural failures were significantly more frequent in ICMP patients than in NICMP and were consistent with unhealthier long-term outcomes.

1. Introduction

Ventricular tachycardia (VT) results in significant morbidity and, in patients with structural heart disease, is associated with an increased risk of sudden cardiac death (SCD) [1,2].

Catheter ablation (CA) has shown promising results in reducing VT episodes, improving symptoms, and increasing patients' quality of life. However, there is often confusion regarding indications, outcomes, and patient populations that are most likely to benefit and the success of this procedure depends on various factors, including the underlying cause of VT, specific features of the arrhythmia, and individual patient factors [3,4].

Ischemic and non-ischemic scar-related VT are fundamentally different in the distribution and topography of scar, mapping findings, ablation approaches, and subsequent clinical outcomes in follow-up [5].

Despite the differences between patients with ICMP and NICMP, few studies have directly compared the outcomes of these two groups in follow-up or have been underpowered to detect differences in major endpoints [6,7].

The lack of comprehensive studies specifically focusing on the

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comparison of outcomes after VT ablation between patients with ICMP and NICMP highlights the need for further investigation and analysis to provide a more comprehensive understanding of the differences in procedural success rates, recurrence of VT episodes, and overall patient outcomes between these two patient populations [8].

In this study, we aim to contribute to the existing knowledge by investigating and comparing the results after VT ablation in patients with ICMP and NICMP. Through careful analysis of available data and considering the limitations, our aim is to enhance our understanding of the potential differences in treatment outcomes for patients with two different types of cardiomyopathy.

2. Methods

2.1. Study population

We retrospectively analyzed data from 212 consecutive patients with structural heart disease suffering from recurrent VT, including electrical storm (ES), who underwent CA at Rajaie Cardiovascular Medical & Research Institute, the biggest tertiary cardiovascular center in Iran, between 2018 and February 2021. Patients with ICMP and NICMP, including specific subgroups of patients with NICMP, were enrolled in the study.

NICMP was defined by the criteria of the European Society of Cardiology Working Group for Myocardial and Pericardial Diseases as patients without significant coronary arterial disease approved by coronary angiography.

Patients' baseline data, such as their demographic data, signs and symptoms, and past medical and drug history, were collected from the hospital registry. Recorded ablation data was gathered from the registry of electrophysiology and patients' follow-up data, including VT reoccurrence, arrhythmia occurrence, need for antiarrhythmic drugs, MACE (major advanced cardiovascular event), all-cause mortality, cardiac death, event-free period was obtained from the hospital's database, missing information was conveyed by calling the patients.

ES was defined as $\geq$3 distinct episodes of either sustained VT or VT treated appropriately with ICD interventions (anti-tachycardia pacing and/or shock) within 24 h. In patients without an ICD, ES was defined as continuous sustained VT that recurred despite repeated intervention for termination over several hours.

2.2. Electrophysiological study

This study was approved by our Institute Ethics Committee, and written informed consent was obtained from the patients before the procedure. This study was conducted in accordance with the Declaration of Helsinki.

For non-emergent patients, AADs were cut for five half-lives before the procedure. All ablation procedures were performed under deep sedation and selective ablation procedures were done under general anesthesia when procedural risk was considered high. A 12-lead ECG during VT was used to guide mapping. Clinical VT induction was attempted with programmed electrical stimulation (PES).

Patients were hemodynamically supported with vasopressor drugs if needed, no support devices were used. Electroanatomical substrate and activation mapping was performed using the EnSite NAVX/Velocity/Precision (Abbott Medical, Minneapolis, Minnesota) systems or CARTO 3 (Biosense Webster, Diamond Bar, California).

The primary strategy for VT ablation in our center is substrate-based modification of scar guided by electroanatomical mapping. All cases underwent pace and substrate mapping, and if VT was hemodynamically stable, activation mapping was performed. The clinical VT, followed by non-clinical VTs, were targeted for ablation. The critical isthmus, late potentials, local abnormal ventricular activities (LAVA) potentials, and decrementing early/late potentials were identified. For hemodynamically unstable VTs, substrate modification was performed with lesions targeting sites identified by pace mapping; it also included signals with discrete split or late potentials recorded during sinus rhythm or with right ventricular apical pacing. Pace mapping was used to target potential VT exit sites, where matches with the targeted VT were observed. Substrate ablation was typically extended to target markedly abnormal fractionated split and late potentials, with a set of radiofrequency lesions targeting abnormal potentials with the endpoint of signal modification or elimination.

Acute procedural success was defined as termination of clinical VT with non-inducibility of clinical VT. Ablation failure was defined as the inducibility of the clinical VT at the end of the procedure. Partial success was defined as successful ablation of the clinical VT with the persistence of a nonclinical VT.

2.3. Outcomes

Follow-up was calculated from the first procedure until the last documented clinical follow-up after the VT ablation. Long-term outcomes included all-cause mortality, cardiac mortality, VT recurrence, VT storm, and hospitalization for HF and VT. VT recurrence was defined as any documented episode of sustained ventricular tachycardia (VT) lasting $\geq$30 s or VT requiring appropriate implantable cardioverter-defibrillator (ICD) therapy. Accordingly, VT-free survival was defined as the absence of VT recurrence during follow-up. Long-term outcomes were compared between patients with ischemic and non-ischemic cardiomyopathy who underwent VT ablation.

2.4. Statistical analysis

All statistical analysis was performed using SPSS version 27.0. Continuous variables are demonstrated as mean $\pm$ SD, and categorical data are illustrated as percentages and frequencies. Comparison between 2 groups was done using Students' t-test, chi-square, and Fisher's exact test when applicable. VT recurrence and mortality were estimated using the Kaplan-Meyer model. Univariate and Multivariate Cox Proportional Hazards analyses were employed to assess the impact of baseline covariates on VT recurrence.

3. Results

3.1. Study population

In a cohort of 212 patients who underwent VT ablation, 63.7 % (n = 135) were diagnosed with ICMP, while 36.3 % (n = 77) had NICMP. Of the patients with NICMP, 44.2 % was secondary to dilated cardiomyopathy, 16.9 % to arrhythmogenic right ventricular cardiomyopathy (ARVC), 10.4 % to valvular cardiomyopathy, 9.1 % to myocarditis, 7.8 % to hypertrophic cardiomyopathy, 3.9 % to amyloidosis, 3.9 % to idiopathic VT (non-scar related in patients with DCM), 2.6 % to sarcoidosis, and 1.3 % to postpartum cardiomyopathy. No patients with primary electrical heart disease were included.

A comparative analysis of the baseline clinical characteristics between patients with NICMP and ICMP, as presented in Table 1, revealed several significant differences. Patients with ICMP showed a significantly higher mean age (62 $\pm$ 10 years vs. 48 $\pm$ 16 years; $p < 0.001$) and a higher prevalence of comorbidities, including diabetes mellitus (26.7 % vs. 15.6 %; $p = 0.064$), hypertension (65.9 % vs. 27.3 %; $p < 0.001$), chronic kidney disease or end-stage renal disease (28.1 % vs. 10.4 %; $p = 0.003$), anemia (28.9 % vs. 15.6 %; $p = 0.029$) and hypothyroidism (15.6 % vs. 5.2 %; $p = 0.024$). Furthermore, patients with ICMP exhibited a significantly lower mean left ventricular ejection fraction (LVEF) compared to those with NICMP (20 $\pm$ 9 % vs. 34 $\pm$ 14; $p < 0.001$). Among both groups, atrial fibrillation was found to be the most common concomitant arrhythmia. The most common antiarrhythmic agents included amiodarone, mexiletine, and a combination of them. ICMP group took more beta-blockers than NICMP (p-value = 0.001>).

Table 1
Baseline clinical characteristics.

	ICMP (n = 135, 63.6 %)	NICMP (n = 77, 36.3 %)	P Value
Age, y	62 ± 10	48 ± 16	<0.001
Male, n (%)	122 (90.4 %)	53 (68.8)	<0.001
LVEF, %	20 ± 9	34 ± 14	<0.001
Comorbidities, n (%)			
DM	36 (26.7)	12 (15.6)	0.064
HTN	89 (65.9)	21 (27.3)	<0.001
CKD/ESRD	38 (28.1)	8 (10.4)	0.003
Anemia	39 (28.9)	12 (15.6)	0.029
Hypothyroidism	21 (15.6)	4 (5.2)	0.024
Hyperthyroidism	5 (3.7)	1 (1.3)	0.31
AF	12 (52.2)	7 (36.8)	0.96
Smoking, n (%)	58 (43)	15 (19.5)	0.001
FH of CAD/SCD	42 (31.1)	27 (35.1)	0.555
Antiarrhythmic drugs			0.144
Amiodaron	14 (10.4)	6 (7.8)	
Mexilitin	14 (10.4)	3 (3.9)	
Amiodaron + Mexilitin	10 (7.5)	2 (2.6)	
Beta-blocker	122 (90.4)	43 (55.8)	<0.001
Anticoagulant	30 (22.2)	10 [13]	0.098
Type of device, n (%)			<0.001
CRT-D	31 (23)	5 (6.49)	
ICD-VR	60 (44.4)	21 (27.3)	
ICD-DR	26 (19.3)	8 (10.4)	
Device indication, n (%)			<0.001
Primary	70 (51.9)	12 (15.6)	
Secondary	47 (34.8)	22 28.6)	

ICMP: Ischemic cardiomyopathy, NICMP: Non-ischemic cardiomyopathy, LVEF: Left ventricular ejection fraction, DM: Diabetes mellitus, HTN: Hypertension, CKD: Chronic kidney disease, ESRD: End-Stage Renal Disease, AF: Atrial fibrillation, FH of CAD/SCD: Family history of Coronary artery disease or sudden cardiac death, CRT-D: Cardiac resynchronization therapy defibrillator, ICD-VR: Single chamber implantable cardioverter defibrillator, ICD-DR: Dual chamber implantable cardioverter defibrillator.

The most arrhythmic finding in the ICMP group was non-sustained VT (n = 54, 40 %), while among the NICMP group, sustained monomorphic VT (n = 39, 50.6 %) was the most common (Table 2).

A significant proportion of patients in the ICMP group was initially implanted for primary prevention compared to NICMP patients (86.7 % vs. 42.2 %, p < 0.001).

3.2. Baseline clinical presentations

In both ICMP and NICMP groups, palpitations were the most common manifestation and there was no significant difference between the two groups (ICMP = 76.3 %, NICMP = 77.9 %, P Value = 0.787).

Table 2
Comparison of patient presentation in ICMP and NICMP groups.

	ICMP	NICMP	P Value
NYHA class, n (%)			0.002
I	7 (5.2)	15 (19.5)	
II	44 (32.6)	23 (29.9)	
III	50 (37)	15 (19.5)	
IV	34 (25.2)	24 (31.2)	
Device Analysis, n (%)			<0.001
No Device	19 (14.1)	43 (55.8)	
ICD Shock	72 (53.3)	28 (36.4)	
VT in analysis	44 (32.6)	6 (7.8)	
Forms of VT, n (%)			0.053
SMVT	52 (38.5)	39 (50.6)	
SPVT	15 (11.1)	2 (2.6)	
NSVT	54 (40)	32 (41.6)	
VT Storm	14 (10.4)	4 (5.2)	

SMVT: Sustained monomorphic ventricular tachycardia, SPVT: Sustained polymorphic ventricular tachycardia, NSVT: Non-sustained ventricular tachycardia.

However, syncope was the only presentation that showed a significant difference, with a higher incidence among the NICMP group (ICMP = 4.4 %, NICMP = 13 %, P Value = 0.024). Among the ICMP group, a significant proportion of patients presented with ES compared to NICMP patients.

3.3. Procedural characteristics and in-hospital complications

The procedure technique followed the institutional standard of our department. The main procedural data are summarized in Table 3.

The Abbott Velocity/Precision mapping system was used in approximately two-thirds of cases (66 % in ICMP and 70.2 % in NICMP), while CARTO 3 was utilized for the remaining cases. The most common multipolar mapping catheters included HD Grid and Pentaray.

A hemodynamic support using vasopressor drugs was used in nine cases (6.7 %) in the ICMP group and two cases (2.6 %) in the NICMP group (p value 0.16).

Access to the endocardium included both retrograde aortic and antegrade transseptal access to the LV. Ablation was almost exclusively performed via the endocardial route in ICMP patients (99.3 %), and

Table 3
Procedural characteristics and major complications.

	ICMP (n = 135)	NICMP (n = 77)	P value
Mapping n (%)			0.03
CRTO 3	46 (34.1)	23 (29.9)	
NAVX	89 (66)	54 (70.2)	
Ablation location n (%)			0.001<
LV	120 (88.9)	33 (42.9)	
RV	9 (6.7)	32 (41.6)	
LV/RV	4 [3]	6 (7.8)	
RCC and LV	0	1 (1.3)	
RCC, LCC commissure	0	2 (2.6)	
Mitral ring	0	1 (1.3)	
NCC	0	1 (1.3)	
LCC	0	1 (1.3)	
Ablation approach, n (%)			0.001<
Endocardial	134 (99.3)	60 (77.9)	
Epicardial	1 (0.7)	17 (22.1)	
Use of hemodynamic support with vasopressor drugs, n (%)	9 (6.7)	2 (2.6)	0.16
Cycle length mean (± SD)	363.59 (66.20)	374.29 (61.24)	0.24
Ablation time (minutes), mean (± SD)	34.21 ± 19.48	28.44 ± 18.6	0.32
Ablation result, n (%)			0.07
Acute procedural success	107 (79.3)	68 (88.3)	
Partial ablation success	21 (15.6)	4 (5.2)	
Unsuccessful ablation	3 (2.2)	4 (5.2)	
Number of VTs induced, n (%)			0.036
One	60 (44.4)	50 (64.9)	
Two	48 (35.6)	19 (24.7)	
3 ≤	23 [17]	7 (9.1)	
In-hospital complications, n (%)			
Pneumothorax	1 (0.7)	0	0.63
AV block	1 (0.7)	1(1.3)	0.59
Infection	0	1(1.3)	0.36
Vascular access-related	6 (4.4)	2 (2.6)	0.39
Stroke, TIA	6 (4.4)	1 (1.3)	0.2
DVT	1 (0.7)	0	0.63
Tamponade	2 (1.5)	3 (3.9)	0.25
Cardiac death	4 [3]	0	0.16
Complications during follow-up, n (%)			
VT recurrence	74 (54.8)	30 (38.9)	0.269
All-cause mortality	30 (22.2)	6 (7.7)	**0.007**
Cardiac mortality	26 (19.2)	5 (6.4)	**0.011**
Time to first Vt recurrence, months mean (± SD)	8.8 (9.6)	10.6 (9.5)	0.26

LV: Left ventricle, RV: Right ventricle, RCC: Right coronary cusp, LCC: Left coronary cusp, NCC: Non-coronary cusp, TIA: Transient ischemic attack, DVT: Deep vein thrombosis.

epicardial access was obtained in 22.1 % of NICMP. A total of 18 epicardial ablation procedures were performed. Of these, 15 were successful based on the elimination of the targeted arrhythmic substrate, 1 procedure was unsuccessful, and 2 procedures achieved only partial success. Regarding the anatomical distribution, epicardial ablation was performed over the left ventricle in 8 cases, the right ventricle in 9 cases, and both LV and RV in 1 case. Among these patients, the underlying structural heart disease included ARVC in 8 cases, HCM in 5, DCMP in 4, cardiac amyloidosis in 2, and a history of myocarditis in 1 case.

The most common mapping strategies included substrate mapping, followed by pace mapping and activation mapping; entrainment mapping was performed if VTs were hemodynamically tolerable. The VT origin was predominantly from the left ventricle (LV) in ICMP patients (88.9 %), whereas in patients with NICMP, a remarkable number of patients had VT originating from the right ventricle (41.6 %).

The majority of patients in the ICMP group had 3 or more induced VTs compared to NICMP. Three or more VT morphologies were induced in 17 % of patients from the ICMP compared with 9.1 % in the NICMP group (p value = 0.036).

The mean tachycardia cycle length of the induced VTs (TCL) wasn't significantly different between the two groups (363.59 ± 66.20 in ICMP vs. 374.29 ± 61.24 in NICMP, p-value = 0.24).

The median RF ablation time was 34.21 ± 19.48 min in ICMP compared to 28.44 ± 18.6 min in the NICMP group with no significant difference between groups (p value = 0.32).

The success rate of ablation was high in both groups, with acute procedural success occurring more frequently in patients from the NICMP group (88.3 % in NICMP compared to 79.3 % in ICMP). Partial ablation success was achieved in 15.6 % of ICMP patients compared to 5.2 % of NICMP patients (p = 0.07). Unsuccessful ablation rates were similar in both groups at 2.2 % vs. 5.2 %.

The major complications and in-hospital mortality are also presented in Table 3. Among the ICMP group, the most frequently reported in-hospital complications were vascular access-related issues (n = 6, 4.4 %); Ischemic stroke, TIA (n = 6, 4.4 %); and cardiac death (n = 4, 3 %). Similarly, in the NICMP group, the most common in-hospital complications were tamponade (n = 3, 3.9 %) and vascular access-related problems (n = 2, 2.6 %). The most peripheral vascular complications were groin hematomas, pseudoaneurysm occurred in one patient with ICMP.

All of them resolved on their own and did not require intervention.

Despite significant differences in baseline characteristics, the acute complication rate between groups did not differ significantly.

3.4. Long-term outcomes

Following a median follow-up period of 36 months (ranging from 8 to 114 months), the cumulative recurrence of VT occurred in 48.1 % of study patients. There was a noticeable trend toward poorer outcomes (VT recurrence, cardiac mortality, all-cause mortality) in the ICMP group as depicted in Fig. 1.

VT recurrence occurred in 54.8 % of ICMP compared to 38.9 % of NICMP (P value = 0.026), The overall mortality rate was 22.2 % in the ICMP group, compared to 7.7 % in the NICMP group (P value = 0.007). Additionally, cardiac mortality occurred significantly more in the ICMP group than in the NICMP group (19.2 % vs. 6.4 %) (P value = 0.011) (Table 3).

3.5. Predictors of long-term outcomes

We conducted a comprehensive Cox Proportional Hazards Analysis to investigate the relationship between baseline covariates and the risk of VT recurrence at follow-up in all patients, as shown in Table 4. In the univariate model, several factors including age, LVEF, CKD/ESRD, history of AF, NYHA functional class, VT cycle length, hemodynamic support using inotropic agents, number of prior ablations, repeated RFA and

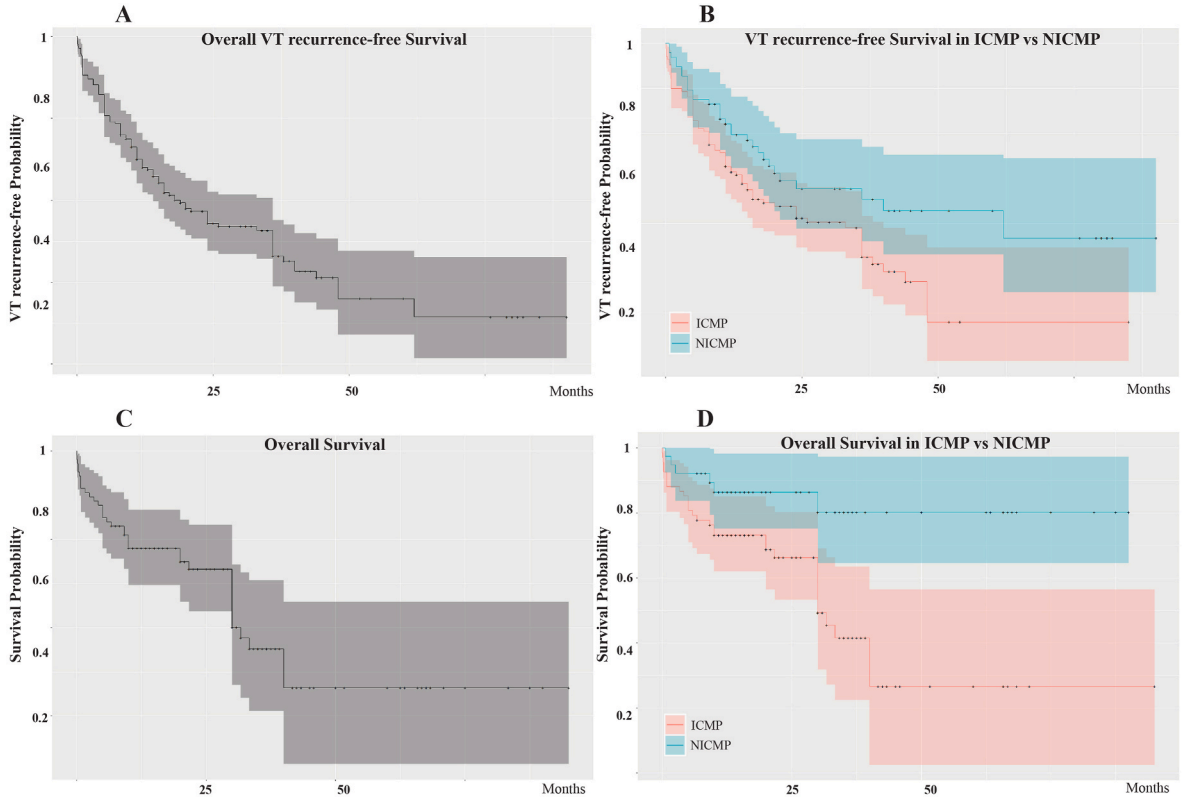

Fig. 1. Displays Kaplan Meier curves illustrating the freedom of ventricular tachycardia (VT) in the overall population (A), a comparison between ICMP and NICMP (B), all-cause mortality in the total population (C), and the ICMP and NICMP groups (D). ICMP, ischemic cardiomyopathy; NICMP, nonischemic cardiomyopathy.

Table 4
Univariate and multivariate cox proportional hazards analysis of baseline covariates concerning VT recurrence at follow-up for all patients.

	Univariate			Multivariate		
	HR	95 % CI	P Value	HR	95 % CI	P Value
Age	1.019	1.004–1.034	**0.013**	1	0.983–1.017	0.989
Gender (female)	0.637	0.362–1.120	0.117	–	–	–
LVEF	0.963	0.947–0.980	**0.001>**	0.114	0.017–0.778	**0.027**
Hypertension	1.273	0.864–1.875	0.223	–	–	–
Diabetes	1.055	0.663–1.681	0.82	–	–	–
CKD/ESRD	1.877	1.219–2.892	**0.004**	1.436	0.907–2.273	0.122
History of AF	2.155	1.172–3.961	**0.013**	1.946	1.003–3.776	**0.049**
NYHA functional class	1.379	1.126–1.689	**0.002**	1.206	0.963–1.511	0.103
VT CL	0.997	0.994–1	**0.082**	0.998	0.995–1.001	0.15
Hemodynamic support using inotropic agents	6.027	2.995–12.127	**0.001>**	3.743	1.648–8.503	**0.002**
Number of prior ablations	1.608	1.274–2.030	**0.001>**	1.271	0.964–1.676	0.089
Repeated RFA	2.231	3.562–1.398	**0.001>**	1.381	3.350–0.569	0.476
B-blockers	1.205	0.748–1.941	0.443	–	–	–
Epicardial approach	0.621	0.272–1.416	0.257	–	–	–
Complete ablation success	0.673	0.247–1.831	0.438	–	–	–
Partial ablation success	2.06	1.220–3.479	**0.007**	1.202	0.668–2.160	0.538

VT CL: Ventricular cycle length, RFA: Radiofrequency ablation.

partial ablation success were identified as predictors for VT recurrence during follow-up. Specifically, LVEF (HR = 0.37; 95 % CI, 0.24–0.68; p = 0.002) and VT cycle length had a negative impact on outcomes at the end of the 2-year follow-up period (mean = 36.71 ± 24.28 months).

In the multivariate analysis, we observed that LVEF (HR = 0.11, 95 % CI: 0.01–0.77, p = 0.027), history of AF (HR = 1.94, 95 % CI: 1.003–3.77, p = 0.049), and hemodynamic support using inotropic agents (HR = 3.74, 95 % CI: 1.64–8.50, p = 0.002), remained significant predictors of VT recurrence.

In the separate analysis (Table 5), the findings indicated that hemodynamic support using inotropic agents and B-blocker therapy had a significant impact on the recurrence of VT in the ICMP group. The use of vasopressors for hemodynamic support during ablation was associated with a higher risk of VT recurrence (HR = 7.1; 95 % CI, 2.88–17.44, p < 0.001), while B-blocker therapy was linked to a lower risk of VT recurrence (HR = 0.38; 95 % CI, 0.19–0.76, p = 0.01) in the ICMP group. Furthermore, in the NICMP group, the NYHA functional class was found to be a predictor of VT recurrence, with an increasing risk of VT recurrence (HR = 1.59; 95 % CI, 1.07–2.36, p = 0.021).

4. Discussion

The present study documents the long-term outcomes of CA of VT in a cohort of patients with a median follow-up of 36 months and specifically compares the outcomes in NICMP versus ICMP. The major findings are as follows: 1) CA of VT in patients with NICMP is effective and safe for achieving long-term VT control in most patients. 2) several factors, including age, LVEF, CKD/ESRD, history of AF, NYHA functional class, VT cycle length, hemodynamic intolerable VT, repeated RFA, and partial ablation success were identified as predictors for VT recurrence during follow-up; and 3) the multivariate analysis demonstrated that LVEF, history of AF and hemodynamic support using inotropic agents had the highest impact on VT recurrence.

The use of RFA for VT treatment has steadily increased over the past decade. RFA in NICMP is challenging due to the complexity of the underlying substrate, which tends to be intramural or sub-epicardial in locations.

Shirai et al., delineated VT circuits and demonstrated that among hemodynamically tolerated VT in ICMP, a critical circuit component can almost always be identified in the endocardium. In contrast, among mappable NICMP VTs, although some critical components can usually be identified with the addition of epicardial mapping, the isthmus is uncommonly identified, often due to mid-myocardial location, particularly in those with septal substrates [9].

Clinical trials of NICMP patients who have undergone VT ablation are sparse and may not be generalizable to routine clinical practice, and current data is limited to observational retrospective analysis or prospective non-randomized studies [10].

In a meta-analysis by Ammar A. et al., CA of VT in patients with NICMP was found to be an effective and safe approach achieving acute

Table 5
Univariate and Multivariate Cox Proportional Hazards Analysis of Baseline Covariates about VT Recurrence at Follow-up in ICMP vs. NICMP.

	ICMP				NICMP			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95 % CI)	P Value	HR (95 % CI)	P Value	HR (95 % CI)	P Value	HR (95 % CI)	P Value
Age	0.996 (0.971–1.021)	0.74	–	–	1.029 (1.004–1.053)	**0.021**	1.001(0.974–1.029)	0.941
Gender (female)	0.696 (0.301–1.610)	0.397	–	–	0.723 (0.321–1.631)	0.435	–	–
LVEF	0.030 (0.001–0.595)	**0.021**	0.103(0.005–2.286)	0.151	0.020 (0.001–0.268)	**0.003**	0.108(0.005–2.353)	0.157
Hypertension	1.018 (0.630–1.643)	0.943	–	–	1.229 (0.562–2.691)	0.606	–	–
Diabetes	0.798 (0.463–1.376)	0.417	–	–	1.935 (0.769–4.873)	0.161	–	–
CKD/ESRD	1.615 (0.996–2.618)	**0.052**	1.186(0.701–2.006)	0.524	2.161 (0.740–6.305)	0.159	–	–
AF	1.761 (0.841–3.690)	0.134	–	–	3.330 (1.121–9.890)	**0.03**	2.233(0.677–7.353)	0.187
NYHA functional class	1.248 (0.956–1.630)	0.103	–	–	1.556 (1.104–2.194)	**0.012**	1.595(1.074–2.369)	**0.021**
VT CL	0.998 (0.994–1.001)	0.251	–	–	0.997 (0.991–1.003)	0.366	–	–
Use of hemodynamic support	9.433 (4.262–20.876)	**0.001>**	7.1(2.889_17.448)	**0.001>**	1.57 (0.213–11.595)	0.658	–	–
B blockers	0.419(0.218–0.805)	**0.009**	0.384(0.193–0.765)	**0.006**	1.751(0.820–3.739)	0.148	–	–
Epicardial approach	0.986(0.733–1.328)	0.929	–	–	0.724(0.276–1.897)	0.511	–	–
Complete ablation success	0.291(0.091–0.932)	**0.038**	0.352(0.098–1.269)	0.111	1.423(0.193–10.489)	0.729	–	–
Partial ablation success	2.390(1.364–4.187)	**0.002**	1.545(0.824–2.894)	0.175	0.531(0.072–3.912)	0.534	–	–

HR: Hazard ratio, CI: Confidence interval.

complete procedural success in more than half of the patients using the currently available catheter mapping and ablation techniques with acceptable relatively low procedural complications. The epicardial approach is usually needed in VT ablation of patients with NICMP and should be considered as part of the initial strategy, especially in the presence of ECG and CMR findings suggestive of the epicardial substrate [9]. This meta-analysis highlights the need for a multicenter randomized trial to look at the short- and long-term outcomes of VT ablation in patients with NICMP and predictors of success.

In a large single-center series, Kumar et al. reported the long-term outcomes of VT ablation in patients with and without structural heart disease. NICMP patients compared to ICMP patients were younger and had less left ventricle (LV) dysfunction. Patients with NICMP had more ablation procedures and more epicardial ablation than patients with idiopathic or ICMP, suggestive of the intra-mural substrate. No significant differences in complications between groups were observed. During the median follow-up of 6 years from the last ablation procedure, VA-free survival was greater in patients with ICMP than NICMP ($p = 0.03$), though ICMP patients were poorer in overall survival than NICMP patients ($p \leq 0.001$) [10].

Pooled data from 7,473 patients over two decades of published data comparing patients with ICMP and NICMP shows fundamental differences in their clinical characteristics, ablation approaches, acute procedural outcomes, and likelihood of VT recurrence.

Whilst ICMP patients are a cohort with generally more advanced disease, their acute procedural success is higher, and arrhythmic outcomes are more favorable in follow-up compared to NICMP patients. VT ablation in NICMP has a lower likelihood of procedural success with an increased risk of VT recurrence, consistent with known challenging arrhythmia substrate [11].

The cumulative available evidence would suggest a higher risk of VT recurrence and mortality in patients with NICMP compared with those with ICMP.

Our findings are in contrast with this concept; we found a noticeable trend toward poorer outcomes in terms of VT recurrence, cardiac mortality, and all-cause mortality in the ICMP group as depicted in Fig. 1. VT recurrence occurred in 54.8 % of compared to 38.9 % of NICMP (P value = 0.026). Additionally, cardiac mortality occurred significantly more in the ICMP group than in the NICMP group (19 % vs. 6 %) (P value = 0.011) (Table 3).

Overall, 51.9 % of patients were free from recurrent VT at a median follow-up of 36 months.

This difference may be related to the fact that a very selected group of ICMP patients with a high baseline arrhythmic burden were referred to our center for CA. On the other hand, the poorer outcome observed in the ICMP group in our study might be a reflection of a rather late ablative strategy. Patients might have a more advanced disease which is a marker of a worse outcome. This was an issue, since in majority of ICMP patients, CA has not been pursued by referring physicians as a primary treatment strategy.

The mortality trend we observed in ICMP patients probably reflected their older age and more advanced left ventricular systolic dysfunction. Owing to the retrospective nature of our study, there were clear differences in baseline characteristics in the ICMP group, compared with the NICMP group.

Similar to our study, Kumar et al. reported that patients with ICMP are typically older, have a lower LVEF, and are affected by more comorbidities compared with patients with NICMP. However, contrary to our study, patients with ICMP in the study by Kumar et al. had better long-term VT-free survival compared with patients with NICMP [10].

Of note, similar to previous reports, despite significant differences in baseline characteristics, the acute complication rate between groups did not differ significantly.

In a large unselected real-world population who underwent VT ablation, the rate of nonfatal major adverse events at 30 days was 7.5 %, and 30-day and 1-year mortality was 4.2 % and 15 %, respectively [12].

The complication rate observed in our study was comparable to the 6 %–15 % complication rate that has been reported in other single- and multi-center studies evaluating VT ablation in patients with structural heart disease. Vascular complications were most frequently observed followed by stroke and pericardial effusion/Tamponade [13,14].

The results of our study provided important insights into long-term outcomes after VT ablation. The overall mortality rate was 22 % in the ICMP group, compared to 7 % in the NICMP group. Additionally, cardiac mortality occurred significantly more in the ICMP group than in the NICMP group (Table 3). Small multicenter studies reported 1-year mortality rates as high as 18 % [4,15].

In a meta-analysis, despite significantly longer procedural times for CA in NICMP, procedural failures, and VA recurrences were significantly more common in that group which may be attributed to heterogeneous substrate, unpredictable disease progression, and varying underlying mechanisms. Prospective studies are needed to address short- and long-term outcomes of CA of VT in NICMP patients, with further definition of their cardiomyopathy subtype and adequate follow-up duration [16].

A previous study has suggested different outcomes for patients with various types of NICMP. Patients with ARVC and myocarditis had better outcomes after CA as compared to DCM patients, however, after adjusting for other confounders, these differences appear to be driven by comorbidities including age and NYHA Class in DCM patients. Patients with sarcoidosis, valvular cardiomyopathy, and HCM were at the highest risk of VT recurrence, even after adjusting for potential comorbidities [17].

The better successful outcome in NICMP patients in our study could be explained by the underlying etiologies of the NICMP group including fewer patients with valvular CMP, HCM, and sarcoidosis. So, in this challenging population, other adjunctive therapies should be considered.

Independent predictors of mortality included higher age, lower LVEF, CKD/ESRD, history of AF, high NYHA functional class, VT cycle length, need for hemodynamic support using inotropic agents, number of prior ablations, repeated RFA, and partial ablation success, which is consistent with prior reports [12].

Of note, LVEF, history of AF, and hemodynamic support using inotropic agents remained significant predictors of VT recurrence in the multivariate analysis.

These results suggest that patients with lower EF likely include a mixture of those with irreversibly advanced or extensive midmyocardial substrate and less treatable VT substrate as demonstrated by a more marked rate of VT recurrence.

Certain factors associated with AF can increase the risk of developing VT. Specifically, a history of AF, particularly in patients with underlying structural heart disease, can be linked to an increased risk of VT recurrence.

More recent studies demonstrated that additional epicardial ablation significantly improved the short-term ablation success in conditions like DCM, arrhythmogenic right ventricular cardiomyopathy, and, more recently, ICMP. In our study, due to the small number of epicardial approaches in the ICMP group, it was not possible to assess the effects of epicardial ablation in the logistic regression model [18,19].

5. Limitations of the study

The inherent potential biases involved in retrospective research must be considered when i nterpreting our results. Owing to the retrospective nature of our study, there were clear differences in baseline characteristics in the ICMP group, compared with the NICMP group.

CMR study was done in a few patients, so the influence of imaging on ablation success was not analyzed. On the other hand, the majority of patients referred to our center and scheduled for VT ablation had an ICD. This issue represents a major limitation affecting image quality with conventional LGE-CMR. In our study, patients without available LGE-CMR, Electroanatomical mapping is considered the gold standard for

invasive scar identification.

6. Conclusion

In this study, VT ablation in patients with NICMP was found to be an effective and safe approach, achieving acute procedural success in a noticeable number of patients using the currently available catheter mapping and ablation techniques with acceptable low procedural complications. Overall, procedural failures were significantly more frequent in ICMP patients than in NICMP and were consistent with unhealthier long-term outcomes.

The result of our study would shed more light on the effectiveness and safety of CA in NICMP.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent to publish

All authors have reviewed and approved the article and have given their consent for its submission and publication.

Ethics approval

The study protocol was approved by the ethics committee of Iran University of Medical Sciences (ethics no: IR.IUMS.FMD.REC.1402.171). This study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author.

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Authors' contribution

R.K. contributed to the study design, data collection, and manuscript writing. F.K. was involved in data collection and interpretation. S.S. contributed to data collection, and manuscript writing. Z.G. played a role in data analysis and manuscript writing and preparation. M.A. contributed to the manuscript writing and preparation. M.H.B. was involved in data collection and interpretation. A.E. contributed to data analysis and manuscript writing. M.H. was involved in study design and data interpretation. A.F.F. contributed to data interpretation and manuscript preparation. S.M. was involved in data collection and interpretation. Z.E. played a role in study design, data interpretation, and manuscript writing.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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