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Acute and long-term outcomes of VT radiofrequency catheter ablation in patients with versus without an intramural septal substrate

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A R T I C L E I N F O

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A B S T R A C T

Introduction: Aim of this study was to evaluate efficacy and safety of ventricular tachycardia (VT) catheter ablation in patients with structural heart disease (SHD) in relation to the presence of an intramural septal substrate.
Methods: Consecutive patients undergoing VT ablation between January 2019 and October 2020 were included. All patients were stratified based on the presence of relevant septal substrate and freedom from VT recurrences were analyzed.
Results: In total, 199 consecutive patients (64.2 ± 13.0 years; 89% male; 55% ischemic cardiomyopathy (ICM)) undergoing VT ablation were included. 129/199 patients (65%) showed significant septal substrate (55/90 patients (61%) with non-ischemic cardiomyopathy (NICM) compared to 74/109 patients (68%) with ICM; p = 0.37). Acute procedural success with elimination of all inducible VTs was achieved in 66/70 patients (94%) without and in 103/129 patients (80%) with a septal substrate (p = 0.007). In the cohort including patients with a clinical FU, 15/60 patients (25%) without a septal substrate and 48/123 patients (39%) with a septal substrate experienced VT recurrence during a FU of 8.1 ± 5.9 months (p = 0.069).
Conclusion: Presence of septal VT substrate in patients with a structural heart disease or coronary artery disease is common. Acute success of VT catheter ablation was significantly higher and mid-term success tended to be higher in patients without a septal substrate.

1. Introduction

Catheter ablation is a recommended treatment option in patients with sustained ventricular tachycardia (VT) on the basis of structural heart disease (SHD), in ischemic cardiomyopathy (ICM) and in non-ischemic cardiomyopathy (NICM) patients [1]. Currently, none of the randomized prospective studies evaluating success of VT catheter ablation were able to demonstrate a benefit of catheter ablation compared to antiarrhythmic drug treatment regarding long-term survival. However, catheter ablation in patients with VT and SHD/ICM improves freedom from VT recurrence and adequate ICD shocks compared to pharmacological antiarrhythmic treatment [2–6].

Intramural septal substrate can be a relevant obstacle for catheter ablation of VT in SHD, since identification of septal conducting channels and effective ablation of intramural septal ablation targets are often challenging. Aim of this retrospective study was to evaluate mid- and long-term safety and efficacy of catheter ablation in a cohort of patients with and without septal intramural substrate due to SHD or coronary artery disease. Furthermore, the incidence of a septal substrate in the group of patients with ICM compared to the group of patients with NICM and possible predictors of the presence of a relevant ventricular septal substrate were further issues of interest.

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2. Methods

2.1. Inclusion criteria and study definitions

Patients undergoing VT catheter ablation on the basis of SHD or coronary artery disease from January 2019 to October 2020 at our institution were included consecutively. The data were analyzed retrospectively and the study was approved by the local institutional review board. All patients gave informed consent to the ablation procedure and pre- and post-ablation diagnostics.

SHD is defined as any congenital or acquired cardiac defect affecting the non-coronary components of the heart. ICM is defined as significantly reduced cardiac function resulting from coronary artery disease whereas NICM includes all conditions of decreased cardiac function not associated with coronary artery disease.

2.2. Electroanatomic mapping and catheter ablation strategy

All procedures were performed using a three-dimensional electroanatomical mapping system (CARTO 3, BiosenseWebster, Diamond Bar, CA, USA; or Ensite Precision, Abbott, St. Paul, MN, USA; or Rhythmia, Boston Scientific, Natick, MA, USA) under analgosedation using continuous propofol infusion in addition to morphine derivatives. Catheter ablation was performed using an open-irrigated ablation catheter with or without contact force measurement (ThermoCool SmartTouch SF, BiosenseWebster, Diamond Bar, CA, USA; or Tacticath, Abbott, St. Paul, MN, USA; or Intellanav MIFI XP ablation catheter, Natick, MA, USA). According to our standard approach, a high-density voltage map was acquired using a three-dimensional electro-anatomical mapping system (3DEAM) combined with a high-density multipolar mapping catheter (Pentaray, BiosenseWebster, Diamond Bar, CA, USA; or Advisor HD Grid, Abbott, St. Paul, MN, USA; or Intellamap Orion, Natick, MA, USA). Areas with bipolar voltage values $\leq$ 0.5 mV were defined as scar and of $\leq$ 1.5mv but > 0.5 mV as low voltage areas as initially defined by Marchlinski et al. [7]. This definition was applied uniformly to voltage-maps acquired by single-tip or multipolar high-density mapping catheters. Local abnormal ventricular potentials, late potentials and fractionated low amplitude potentials were additional criteria for identification of abnormal pathological ventricular tissue [8].

According to our standard approach, programmed ventricular stimulation was performed before catheter ablation. Inducible VTs were mapped and the critical isthmus was targeted whenever VT was hemodynamically tolerated. In case of hemodynamically not well tolerated VTs, all identified local abnormal activity and late potentials within scar or low-voltage areas were ablated using 45 Watts and a target ablation index value of 700–1000. Endpoint of catheter ablation was elimination of any inducible VT and ablation of all identified local abnormal activity and late potentials within a reasonable procedure time. Elimination of clinical VT was pursued whenever possible.

The choice of access for endocardial mapping and ablation - i.e. retrograde access through the aortic valve or transseptally through the mitral valve using a large steerable sheath - or both routes - was left to the discretion of the operator. Anterior epicardial access was obtained by the approach first described by Sosa et al. [9]. In case of planned epicardial access, oral anticoagulation using non-vitamin-K oral antagonists (NOACs) were withheld on the day before the procedure, Vitamin-K antagonists (VKAs) were stopped several days before the procedure in order to reach an INR-level below 1.5.

3. Image integration of pre-procedural cardiac MRI or CT

According to our standard approach, a cardiac CT or Late-gadolinium-enhancement Magnetic Resonance Imaging (LGE-MRI) was acquired before the procedure if not contraindicated (i.e. implantable cardiac device with abandoned transvenous leads) and processed using a dedicated software. Processed 3D reconstructions of the ventricles were merged with the 3DEAM using anatomical landmarks intra-procedurally. Abnormal potentials (LAVA - local abnormal ventricular activity, late and fractionated potentials) at sites of imaging defined potential conducting channels were targeted in the first line. Following this focused approach, all remaining abnormal potentials were also targeted.

After completing ablation of all abnormal substrate, a final programmed ventricular stimulation with 2 different S1 cycle lengths and up to 4 extra stimuli from the right and left ventricle was routinely performed. In case of VT induction, the remaining VT was ablated and programmed ventricular stimulation was repeated. Procedural endpoint was effective ablation of clinical VT(s) and of all inducible VTs as far as possible within a reasonable procedure time.

3.1. Post-ablation management

Patients were monitored for at least 24 h after ablation. As needed, antiarrhythmic drugs were prescribed for a limited time in case of unsuccessful or partially successful ablation. In case of successful ablation, antiarrhythmic drugs (Amiodarone) were discontinued before VT ablation without continuation after the procedure. After epicardial mapping and ablation procedures, an epicardial drainage was inserted and left in place for 12 h.

3.2. Study endpoints

Primary endpoint of the study was occurrence of any sustained ventricular arrhythmia (ventricular tachycardia or ventricular fibrillation) documented by ECG or on ICD recordings during follow-up. Secondary endpoints were post-ablation inducibility of clinical and non-clinical VTs and procedural complications.

3.3. Statistical analysis

The data are expressed as mean $\pm$ SD for continuous variables or as frequencies and percentages for categorical variables. To compare continuous and categorical variables between those with and without septal substrate, we used *t*-test or Fisher's exact test whenever appropriate. We performed univariate and multivariate logistic regressions to estimate associations between incidence of VT recurrence and patient characteristics as well as procedural parameters. Multivariate regression included individual parameters, adjusting for clinical parameters reaching significance level P-value <0.1 in the univariate analysis. Two-sided P-values of less than 0.05 were considered statistically significant. All statistical analyses were performed using STATA 15.0 (Chicago, IL, USA).

4. Results

A total of 199 patients with sustained ventricular tachycardia and a structural heart disease receiving a catheter ablation procedure (64.2 $\pm$ 13.0 years; 89% male; 55% ICM) were included in our study. Patient characteristics of the whole cohort and of the patient group with and without a septal substrate are shown in Table 1. In total, 129/199 patients (65%) showed significant septal substrate according to a thoroughly performed electro-anatomical voltage map. In 25 patients, septal substrate was additionally confirmed in preprocedural acquired cardiac imaging (preprocedural cardiac CT n = 22, LGE-MRI = 2 and both modalities n = 1). Of note, 55/90 patients (61%) with NICM compared to 74/109 patients (68%) with an ICM demonstrated significant septal substrate detected by

Table 1
Patient characteristics of the whole patient cohort and of patients with/without a septal substrate.

	Patients without a septal substrate n = 70 (35%)	Patients with a septal substrate n = 129 (65%)	All patients n = 199	P value
Age in years	62.0 ± 15.7	65.4 ± 11.1	64.2 ± 13.0	0.11
Sex: male n (%)	61 (87)	116 (90)	177 (89)	0.47
BMI	29.0 ± 5.0	29.4 ± 5.0	29.3 ± 5.0	0.55
ICM n (%)	35 (50)	74 (57)	109 (55)	0.37
LVEF (%)	36.7 ± 15.0	34.3 ± 12.6	35.2 ± 13.6	0.28
LV septum (mm)	10.9 ± 2.1	10.9 ± 1.9	10.9 ± 2.0	0.91
Hypertension n (%)	54 (77%)	101 (78%)	155 (78%)	0.86
CAD n (%)	36 (51%)	75 (58%)	111 (56%)	0.37
Diabetes n (%)	13 (19%)	38 (29%)	51 (26%)	0.13
Prior Stroke/TIA n (%)	7 (10%)	13 (10%)	20 (10%)	1.0
VT storm on admission n (%)	12 (17%)	11 (9%)	23 (12%)	0.10

voltage mapping using a 3DEAM system or/and by cardiac MRI or CT ($p = 0.37$). Patients with and without a septal substrate did not differ significantly regarding all other patient characteristics. Mean FU after initial VT ablation was 8.1 ± 5.9 months with 16/199 patients lost to FU after discharge from our clinic.

The NICM patient cohort consisted of patients with dilated cardiomyopathy (n = 51), cardiomyopathy due to myocarditis (n = 18), hypertrophic cardiomyopathy (obstructive n = 3, non-obstructive n = 1), arrhythmogenic cardiomyopathy (n = 6), sarcoidosis (n = 5), myotonic dystrophy (n = 1), valvular cardiomyopathy (n = 1) and non-specified cardiomyopathy (n = 4). Patients with NICM and ICM differed significantly regarding age, left ventricular ejection fraction, LV septum thickness and prevalence of arterial hypertension with NICM patients being significantly younger, having arterial hypertension less often, having a higher LV ejection fraction and a lower LV septum thickness compared to patients with ICM (Table 2).

4.1. Procedural aspects of catheter ablation in VT patients

An important pre-procedural imaging modality was cardiac CT and LGE-MRI for characterization of ventricular substrate before the procedure, to plan initial access (endocardial/epicardial, transseptal or retrograde access) and to guide intraprocedural substrate mapping (Fig. 1). In 60 of 199 patients (30%) a cardiac LGE-MRI and in 38 of 199 patients (19%) a cardiac CT was acquired before VT ablation procedure. In a minority of patients, pre-procedurally acquired cardiac imaging was processed, reconstructed to a 3D model and integrated into the 3DEAM intra-procedurally (n = 16, 8% of patients). As shown in Fig. 2, these reconstructed CT or MRI shells helped focusing on areas of interest for electroanatomic (high-density) mapping (voltage and activation mapping).

In nearly all patients high-density mapping catheters were used to identify ventricular endo- and epicardial substrate in high resolution and with a high reliability (99.5%, 198/199 patients; Fig. 3). Epicardial access was obtained in 21/70 (30%) without and in 23/129 (18%) with a septal substrate ($p = 0.052$) and in 10/109 (9%) patients with ICM and in 34/90 (38%) patients with NICM ($p < 0.001$). Bipolar ablation of septal substrate from an LV and RV septal site was done in one patient with post-myocarditis NICM (Fig. 4). Sequential unipolar ablation from LV and RV was performed in 14/129 (11%) patients with a documented septal substrate. In 40/44 (91%) patients undergoing epicardial mapping, ablation of epicardial substrate was done.

Regarding the whole patient cohort in 152/199 patients (76%), at least one VT was inducible before catheter ablation - 48/70 patients (69%) without a septal substrate vs. 104/129 patients (81%) with a septal substrate, $p = 0.08$.

At least one monomorphic VT with a presumed septal isthmus was inducible in 73/129 patients with a septal substrate (57%) and in 4/70 patients without a septal substrate (6%).

Acute procedural success - i.e. non-inducibility of any VT at the end of procedure - was achieved in 66/70 patients (94%) without and in 103/129 patients (80%) with a septal substrate ($p = 0.007$). Regarding type of cardiomyopathy the difference of acute success between patients with ICM and NICM was not significant (96/109 patients (88%) with ICM vs. 73/90 patients (81%) with NICM; $p = 0.23$). Of note, inducibility of septal VTs before ablation regardless of presence of a septal substrate was significantly associated with a lower acute success rate (non-inducibility of any VT at the end of procedure in 62/77 (80%) patients with septal VTs versus 114/122 (93%) patients without septal VTs; $p = 0.011$). Long-term success was not significantly associated with presence of septal VTs before ablation ((50/77 patients (65%) with septal VTs versus 86/122 patients (71%) without inducible septal VTs before ablation; $p = 0.44$)).

Table 2
Patient characteristics and procedural parameters according to type of CMP.

	Patients with ICM n = 109 (55%)	Patients with NICM n = 90 (45%)	All patients n = 199	P value
Age in years	67.9 ± 10.0	59.7 ± 14.7	64.2 ± 13.0	<0.001
Sex: male n (%)	101 (93)	76 (84)	177 (89)	0.07
BMI	29.3 ± 4.5	29.2 ± 5.5	29.3 ± 5.0	0.93
Septal substrate n (%)	74 (68)	55 (61)	129 (65)	0.37
LVEF (%)	31.7 ± 11.4	39.4 ± 14.8	35.2 ± 13.6	<0.001
LV septum (mm)	11.3 ± 2.0	10.4 ± 1.9	10.9 ± 2.0	0.005
Hypertension n (%)	95 (87%)	60 (67%)	155 (78%)	<0.001
Diabetes n (%)	32 (29%)	19 (21%)	51 (26%)	0.20
Prior Stroke/TIA n (%)	13 (12%)	7 (8%)	20 (10%)	0.36
VT storm on admission n (%)	10 (9%)	13 (14%)	23 (12%)	0.27

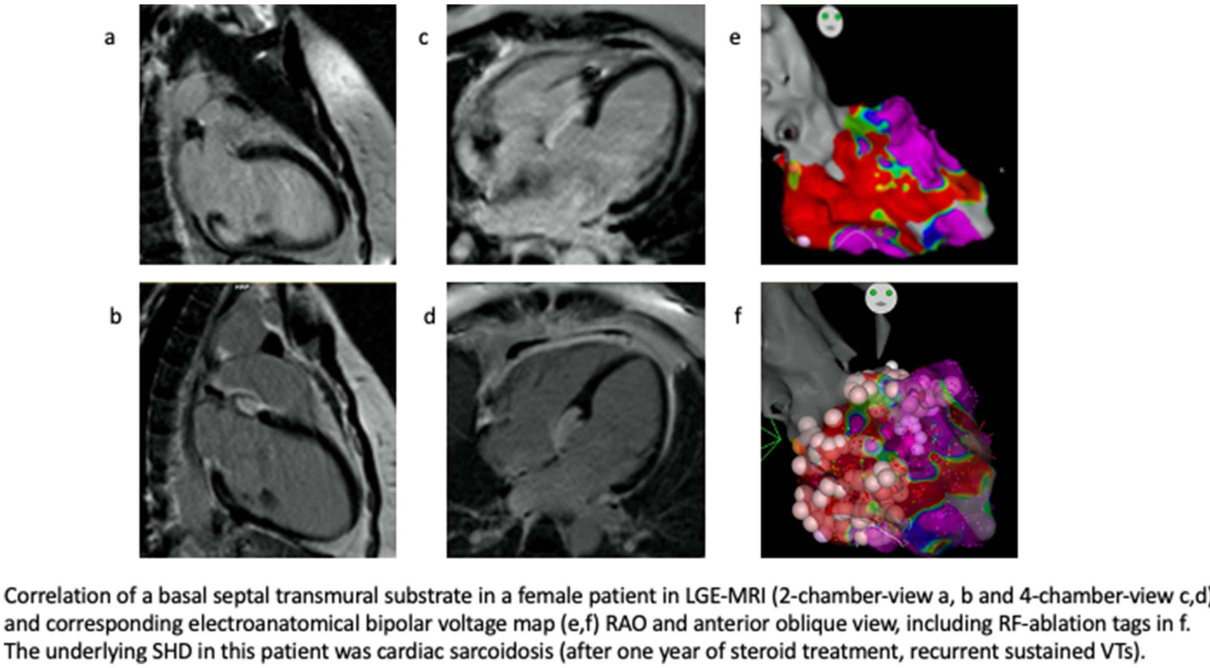

Fig. 1. Correlation of a basal septal transmural substrate in a female patient in LGE-MRI (2-chamber-view a, b and 4-chamber-view c,d) and corresponding electroanatomical bipolar voltage map (e,f) RAO and anterior oblique view, including RF-ablation tags in f. The underlying SHD in this patient was cardiac sarcoidosis (after one year of steroid treatment, recurrent sustained VTs).

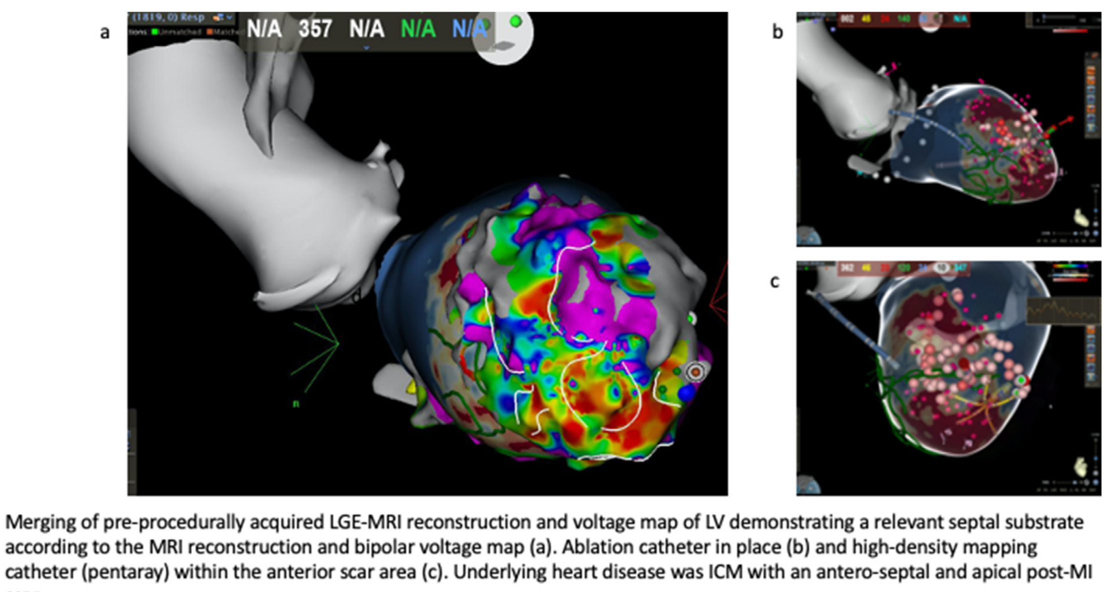

Fig. 2. Merging of pre-procedurally acquired LGE-MRI reconstruction and voltage map of LV demonstrating a relevant septal substrate according to the MRI reconstruction and bipolar voltage map (a). Ablation catheter in place (b) and high-density mapping catheter (pentaray) within the anterior scar area (c). Underlying heart disease was ICM with an antero-septal and apical post-MI scar.

4.2. Incidence of VT or VF during FU in relation to presence of a septal substrate and to type of underlying CMP

In the whole cohort including only patients with a clinical FU, 15/60 patients (25%) without a septal substrate and 48/123 patients (39%) demonstrating a significant septal substrate experienced recurrence of sustained VT or VF with or without ICD therapy during FU ($p = 0.069$). In ICM patients with available FU results, 6/33 (18%) without a septal substrate and 23/70 patients (33%) with a septal substrate experienced a VT/VF recurrence during FU ($p = 0.16$) compared to 9/27 NICM patients (33%) without a septal substrate and 25/53 NICM patients (47%) with a septal substrate ($p = 0.34$).

The group of patients with versus without VT/VF recurrences differed significantly regarding VT inducibility at the end of the procedure and prevalence of arterial hypertension according to univariate and multivariate analysis (Table 3). Of note, VT inducibility seemed to be a predictor of VT/VF recurrence, whereas

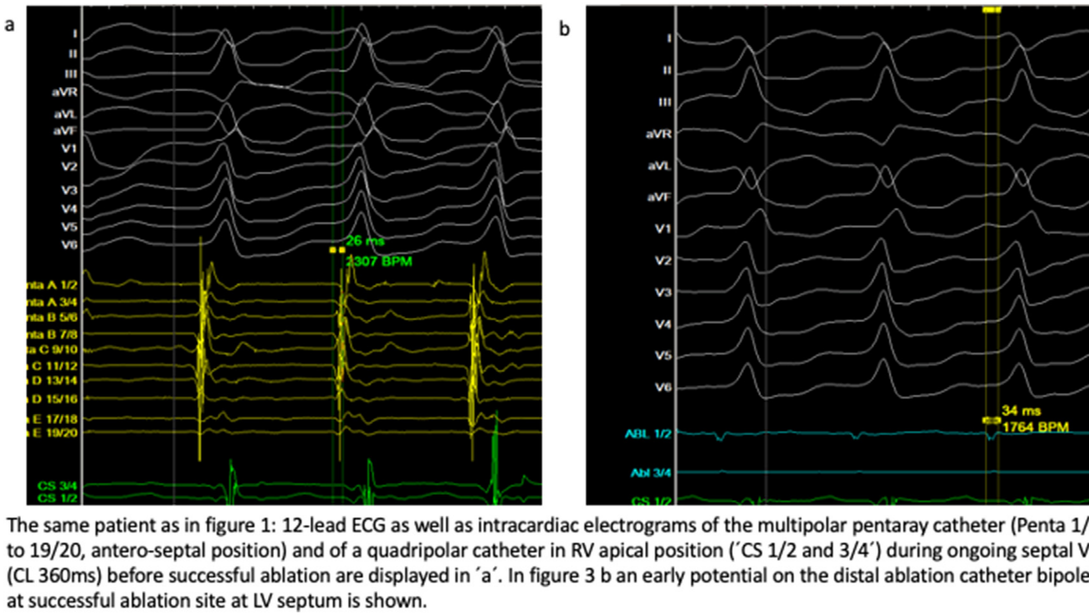

Fig. 3. The same patient as in Fig. 1: 12-lead ECG as well as intracardiac electrograms of the multipolar pentaray catheter (Penta 1/2 to 19/20, antero-septal position) and of a quadripolar catheter in RV apical position ('CS 1/2 and 3/4') during ongoing septal VT (CL 360 ms) before successful ablation are displayed in 'a'. In Fig. 3 b an early potential on the distal ablation catheter bipole at successful ablation site at LV septum is shown.

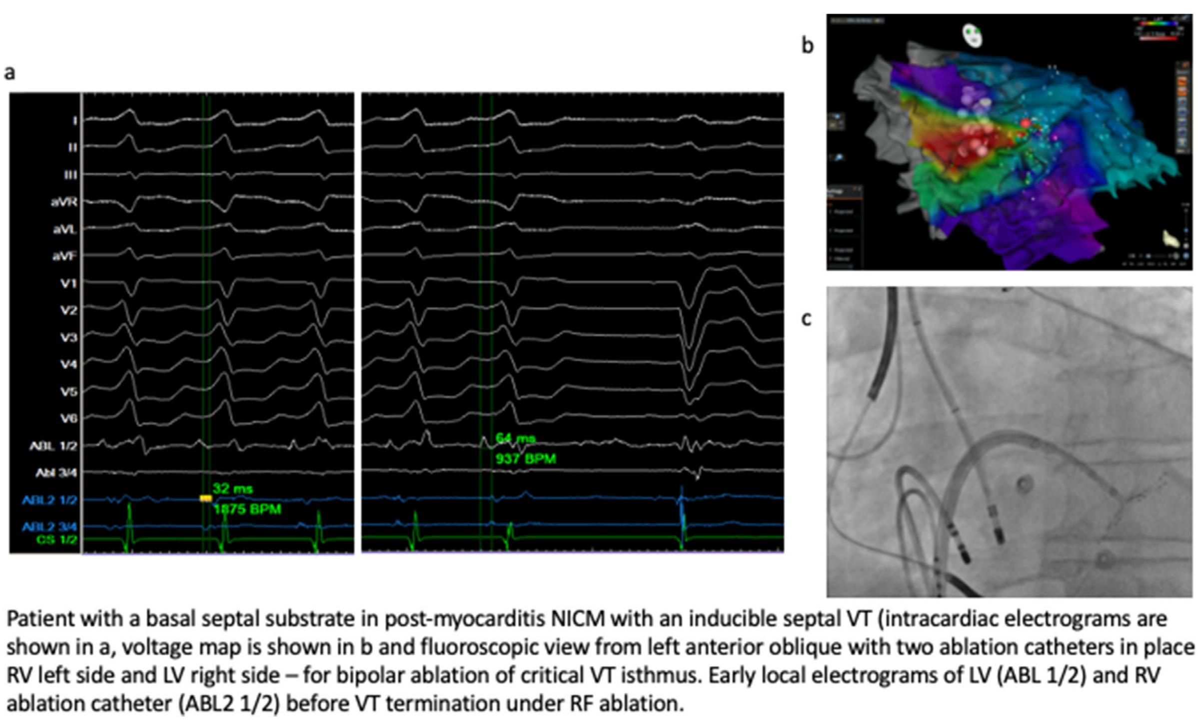

Fig. 4. Patient with a basal septal substrate in post-myocarditis NICM with an inducible septal VT (intracardiac electrograms are shown in a, voltage map is shown in b and fluoroscopic view from left anterior oblique with two ablation catheters in place -RV left side and LV right side - for bipolar ablation of critical VT isthmus. Early local electrograms of LV (ABL 1/2) and RV ablation catheter (ABL2 1/2) before VT termination under RF ablation.

arterial hypertension was associated with a lower rate of VT recurrence.

4.3. Adverse events intra-procedurally and during follow-up

In total, 13 intra- and post-procedural adverse events (6.5%) were reported. Of note, 5 of these complications were minor adverse events without clinical relevance (access site hematoma without relevant blood loss). One patient experienced a cardiogenic shock in a redo-procedure due to VT recurrence and died intra-procedurally (not in the initial procedure). Four patients suffered from high-degree AV-block in the initial procedure. Of note, all of these patients demonstrated significant septal substrate. One Patient experienced a delayed pericardial tamponade, which had to

Table 3
Predictors of VT/VF recurrence according to univariate and multivariate analysis.

	Univariate			Multivariate		
	Odds Ratio	CI 95%	P-value	Odds Ratio	CI 95%	P-value
Male sex	0.86	0.41–1.81	0.69	-	-	-
Age	1.00	0.98–1.02	0.92	-	-	-
Type CMP	1.56	0.95–2.56	0.08	-	-	-
LV EF	0.99	0.97–1.01	0.40	-	-	-
Intraventricular septum	1.05	0.90–1.22	0.53	-	-	-
VT storm on admission	1.67	0.79–3.52	0.18	-	-	-
BMI	1.01	0.95–1.06	0.83	-	-	-
Septal substrate	1.32	0.74–2.35	0.36	-	-	-
VT inducibility at end of procedure	2.59	1.49–4.50	0.001	2.09	1.13–3.84	0.018
Coronary artery disease	0.65	0.39–1.07	0.09	-	-	-
Arterial hypertension	0.47	0.27–0.83	0.009	0.46	0.25–0.84	0.012
Diabetes mellitus	1.14	0.65–1.99	0.66	-	-	-
Number of procedures before index procedure	1.24	0.99–1.54	0.06	0.97	0.75–1.26	0.82

be treated by pericardiocentesis. And finally, in 2 patients, inadvertent puncture of the pleural space occurred during pericardial puncture without any clinically relevant consequence.

During follow-up, a total of 14/199 patients (7%) died (4 patients with a septal substrate; 11 patients with ICM and 3 patients with NICM). Of note, 3/14 patients died of cardiac death (one patient of sudden cardiac death), 2/14 died of a non-cardiac death and in 9/14 patients the cause of death was unknown.

5. Discussion

5.1. Salient findings

Major findings of this retrospective single-center study are as follows: firstly, presence of a septal ventricular substrate in a large cohort including ICM and NICM patients undergoing a VT catheter ablation due to sustained VTs is high (65% of the total patient cohort). Of note, the rate of patients with a septal substrate was numerically but not statistically significantly higher in patients with an ICM compared to patients with a NICM.

Secondly, recurrence of VT or VF after VT catheter ablation seemed more frequent but was not statistically significantly higher in patients with a septal substrate compared to patients without a septal substrate during a mean FU of 8 months (25% vs. 39%; $p = 0.069$). However, regarding acute success**,** there was a significantly higher rate of VT non-inducibility at the end of the procedure in the group of patients without a septal substrate.

Pre-ablation inducibility of VTs harbored within the interventricular septum - regardless of presence of a septal substrate - was associated with a lower acute success rate but not with lower long-term success rates.

And thirdly, main predictor of VT/VF recurrence in the whole patient cohort was VT inducibility at the end of the procedure.

5.2. Pre-existing data regarding efficacy and safety of catheter ablation in VT patients with ICM and NICM

Three prospective multi-center trials in patients with ICM analyzed efficacy and safety of VT catheter ablation in comparison to pharmacological antiarrhythmic treatment [4–6]. Regarding efficacy endpoints or combined endpoints including all-cause-mortality and efficacy**,** catheter ablation was more effective regarding freedom from VT recurrence compared to pharmacological antiarrhythmic treatment in patients with ICDs, but none of these studies demonstrated improvement of prognosis by VT catheter ablation.

Catheter ablation of VT turned out to be an effective treatment option not only in patients with ICM but also in patients with NICM [10]. Muser et al. included 267 patients presenting with drug-refractory VT storm (ICM n = 196, NICM n = 71) undergoing catheter ablation with 22% of patients undergoing combined endo-epicardial ablation. In this study**,** catheter ablation was similar**ly** effective in patients with NICM compared to patients with ICM resulting in elimination of VT storm in 95% of cases and long-term VT-free survival of 54%. Interestingly, similar to the results of our study, persisting VT inducibility at the end of the procedure was the only independent predictor of long-term VT recurrence.

In the study published by Dinov et al., all except two patients (1.2%) in the ICM patient cohort were ablated only endocardially, whereas 31% of patients with NICM were ablated epicardially in addition. Non-inducibility of any VT was achieved in 67% of NICM and in 77% of ICM patients in this study [11]. In our study, epicardial access was obtained in 9% of patients with ICM and in 38% of patients with NICM showing a moderately higher proportion of patients with ICM and NICM undergoing epicardial access in the index procedure. Of note, acute success was higher in our study with 81% of NICM patients and 88% of ICM patients demonstrating non-inducibility of any VT at the end of the procedure. As confirmed by the study of Dinov et al., epicardial ablation was an independent predictor of short-term success in the whole cohort as well as in NICM patients. Pre-existing data showed a high rate of epicardial substrate in NICM patients. The study of Bogun et al. demonstrated that only five of 14 patients with NICM and myocardial scar in DE-MRI had purely endocardial scar [12]. Therefore, one explanation of a moderately higher acute success rate in our cohort compared to the results of Dinov et al. could be a higher rate of epicardial access in NICM patients.

5.3. Pre-existing data regarding spontaneous prognosis and catheter ablation outcome of patients with an interventricular septal substrate in SHD

A couple of retrospective clinical trials and registries evaluated the pattern and amount of myocardial substrate in patients with SHD. Halliday et al. analyzed the amount and pattern of myocardial substrate in 874 registry patients with dilated cardiomyopathy excluding patients with coronary artery disease, infiltrative and primary valvular disease and cardiac sarcoidosis [13]. Late-gadolinium enhancement (LGE) was present solely in the septum in 142 patients (16%) and in the septum and other LV locations in 116 patients (13%). Interestingly, presence of a septal LGE turned out to be significantly associated with all-cause-mortality in this study. In a study by Gräni et al. 294 patients with a suspected myocarditis showed LGE on cardiac MRI. Regarding location and pattern of LGE, septal and mid-wall delayed enhancement showed the strongest association with occurrence of major adverse events corresponding to a hazard ratio of 2.55 and 2.39, respectively [14].

Ablating VTs originating from the interventricular septum may be challenging since endocardial conventional unipolar catheter ablation might be insufficient to reach the critical intramural substrate. Alternative ablation strategies include *trans*-coronary alcohol ablation, use of a needle ablation catheter (not commercially available) and bipolar catheter ablation using two RF ablation catheters simultaneously on both sides of the septum. The concept of bipolar ablation and effect on lesion size and depth in vitro was described in 1993 by Chang et al. [15].

All of these approaches aim at increasing lesion size and depth. Yamada et al. reported their experience in 14 patients with idiopathic LVOT ventricular arrhythmias insufficiently eliminated by endo- or epicardial ablation alone [16]. Ventricular arrhythmias could be eliminated by sequential or simultaneous unipolar (not bipolar) catheter ablation using two ablation catheters and two ablation generators and could be estimated as an alternative approach to bipolar ablation.

Recently, Yang et al. demonstrated successful ablation of mid-myocardial septal substrate in 6 NICM patients refractory to standard unipolar ablation by using simultaneous unipolar ablation from both sides of the ventricular septum [17]. Rationale of this approach is an increase in tissue temperature at mid-myocardial intramural target sites by reducing convective heating at the opposite side and using two sources of resistive heating near the target site.

In our study, we used sequential unipolar ablation from one or both sides of the septum in nearly all cases. Only in one patient we performed bipolar ablation with two irrigated ablation catheters on both sides of the ventricular septum. The clinically relevant septal VT was effectively eliminated using this approach. However, further non-clinical VTs were still inducible at the end of the procedure in this patient. Of note, considering the very low rate of simultaneous bipolar ablation of septal substrate and VTs in our study (in 1/199 patients), acute and long-term success might have been higher in the cohort of patients with an intramural septal substrate if bipolar ablation had been used more frequently in this patient group. Furthermore, the size of the patient cohort and/or duration of follow-up in this study might be too small/too short to demonstrate a significant association between the presence of a septal substrate and VT recurrence during follow-up. Of note, acute procedural success was significantly lower in patients with a septal substrate, which might point to a possible association of septal substrate and a lower long-term success rate. And finally, another relevant limitation of targeting septal VTs is the inability to detect intramural septal substrate by voltage mapping in a statistically relevant number of patients especially in NICM [18].

6. Limitations

A major limitation is the retrospective character of the study. Of course, a sample error due to an inclusion bias could not be completely excluded. However, all patients with SHD or coronary artery disease undergoing VT ablation at our department between January 2019 and October 2020, regardless of the type of underlying cardiac disease, were included in this registry study.

Septal substrate was defined by empiric bipolar voltage cut-off values uniformly for single-tip and multipolar high-density mapping catheters according to conventional criteria [7]. Of note, using the same voltage cut-off values for both single-tip and high-density mapping catheters might be insufficient. However, reliable study data confirming specific unipolar and bipolar voltage values adjusted specifically for each catheter type, identifying scar and low-voltage tissue are still lacking. Tung et al. evaluated performance of electro-anatomical voltage mapping in animal models with induced myocardial infarction using ex vivo MRI as gold standard for detecting infarct borders [19]. Major findings of this study were: Statistically derived voltage thresholds might not be sufficiently sensitive for detection of non-transmural scar defined by ex vivo MRI. And furthermore, in the presence of endocardial scar, unipolar mapping is associated with poor spatial specificity for scar. Therefore, we preferred using widely adopted conventional cut-off values and to rely on bipolar mapping with all limitations associated with this approach.

Despite attempting to acquire a complete follow-up of all patients included in the study, 8% of patients could not be contacted by telephone and information regarding clinical status and occurrence or absence of ventricular arrhythmia recurrences during FU were not available. Remarkably, mean follow-up was 8.1 ± 5.9 months and included device interrogation in 140 patients (70.4%).

7. Conclusion

Presence of an intramural septal substrate in patients with a structural heart disease/coronary artery disease is common. In our cohort, the rate of patients with a septal substrate was numerically but not significantly higher in the group of patients with an ICM. Acute success was significantly higher in patients without a septal substrate, whereas long-term success was not significantly but by tendency higher in patients without a septal substrate before VT ablation. Furthermore, presence of septal VTs before ablation was associated with a lower acute success rate. Non-inducibility of VTs at the end of the procedure as well as preexisting arterial hypertension were associated with a lower VT or VF recurrence rate after VT ablation in this patient cohort. Future studies evaluating VT patients with a relevant septal involvement are needed to better predict catheter ablation success and safety in this specific patient group.

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Data availability statement

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

Ethics approval statement

The study was approved by the local institutional review board.

CRediT authorship contribution statement

Philipp Halbfass: Conceptualization, Methodology, Writing – original draft, Investigation. **Deborah Ludwig:** Methodology, Writing – original draft, Data curation. **Kai Sonne:** Investigation, Validation. **Karin Nentwich:** Investigation, Validation. **Elena Ene:** Investigation, Validation. **Artur Berkovitz:** Investigation, Validation. **Borek Foldyna:** Validation, Formal analysis, Writing – review & editing. **Sebastian Barth:** Writing – review & editing, Validation. **Julian Müller:** Writing – review & editing, Validation. **Lukas Lehmkuhl:** Writing – review & editing, Validation. **Ulrich Lüsebrink:** Writing – review & editing, Validation. **Christian Waechter:** Writing – review & editing, Validation. **Thomas Deneke:** Conceptualization, Methodology, Writing – review & editing, Investigation, Supervision.

Declaration of competing interest

None to declare.

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