

# First-line ablation of ventricular tachycardia in ischemic cardiomyopathy: stratification of outcomes by left ventricular function

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## Abstract

**Purpose** First-line catheter ablation of ventricular tachycardia/ventricular fibrillation (VT/VF) in patients with ischemic cardiomyopathy (ICM) has been associated with improved outcomes; however, most benefit seems to be in patients with moderately depressed left ventricular ejection fraction (LVEF). Herein, outcomes were stratified based on LVEF.

**Methods** A meta-analysis of randomized controlled trials (RCTs) evaluating first-line ablation versus medical therapy in patients with VT and ICM was performed. Risk estimates and 95% confidence intervals (CI) were measured.

**Results** Four RCTs with a total of 505 patients (mean age  $66 \pm 9$  years, 89% male, 80% with previous revascularization) were included. Mean LVEF was  $35 \pm 8\%$ . At a mean follow-up of  $24 \pm 9$  months, a significant benefit in survival-free from appropriate implantable cardioverter-defibrillator (ICD) therapies was observed in all patients undergoing first-line catheter ablation compared with medical management (RR 0.70, 95% CI 0.56–0.86). In patients with moderately depressed LVEF (> 30–50%), first-line VT ablation was associated with a statistically significant reduction in the composite endpoint of survival free from VT/VF and appropriate ICD therapies (HR 0.52, 95% CI 0.36–0.76), whereas there was no difference in patients with severely depressed LVEF ( $\leq 30\%$ ) (HR 0.56, 95% CI 0.24–1.32). Funnel plots did not show asymmetry suggesting lack of bias.

**Conclusions** Patients with ICM and VT undergoing first-line ablation have a significantly lower rate of appropriate ICD therapies without a mortality difference compared with patients receiving an initial approach based on medical therapy. The beneficial effect of a first-line ablation approach was only observed in patients with moderately depressed LVEF (> 30–50%).

Keywords Catheter ablation · Ventricular tachycardia · Ischemic cardiomyopathy · Heart failure

# 1 Introduction

In patients with ischemic cardiomyopathy (ICM), ventricular tachycardia and ventricular fibrillation (VT/VF) typically originate from a relatively discrete portion of the myocardium, within or

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bordering the infarct zone that is amenable to catheter ablation [1]. However, the mainstay of treatment for these patients is typically based on medical therapy and implantable cardioverter defibrillators (ICDs) [2]. Use of anti-arrhythmic drugs (AAD) is typically the first approach as an adjunctive therapy to reduce ICD interventions; yet, success is limited and may be associated with significant drug-related adverse events [3]. Conversely, catheter ablation has emerged as an important therapeutic strategy for VT/VF with the advent of improved mapping technologies and ablation strategies, particularly the success seen with substrate based approaches [4]. As such, randomized controlled trials (RCTs) have shown improved outcomes in patients undergoing first-line catheter ablation for VT in patients with ICM [5, 6]. However, increased early mortality has been reported in patients with severely depressed left ventricular ejection fraction (LVEF), whereas outcomes in moderately depressed LVEF seem different [7]. Herein, we characterized outcomes based on LVEF of patients

with ICM presenting with VT undergoing first-line VT ablation compared with an initial approach based on medical therapy.

# 2 Methods

# 2.1 Search strategy

We searched PubMed, Embase, and Cochrane Central Register of Clinical Trials (Cochrane Library, Issue 5, 2020) to identify studies evaluating the outcomes of patients with prior myocardial infarction that presented with VT were randomized to firstline therapy with catheter ablation or medical therapy. We used the terms ("ventricular tachycardia" OR "VT" OR "ventricular fibrillation" OR "VF" OR "ventricular tachyarrhythmia") AND ("ischemic cardiomyopathy" OR "ICM" OR "myocardial infarction" OR "MI") AND ("catheter ablation" OR "CA" OR "radiofrequency ablation"). Our search was restricted to human studies, published in peer-reviewed journals up to May 2020. No language restriction was applied. The reference lists of identified articles were also reviewed. We also searched clinicaltrials.gov to identify ongoing and unpublished trials.

# 2.2 Selection criteria

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for reporting systematic reviews and meta-analyses was applied to the methods of this study. Studies with the following characteristics were considered eligible for this analysis: (a) had a randomized controlled design, (b) included patients with prior myocardial infarction and VT, (c) reported outcomes stratified by LVEF, (d) included patients that were randomized to first-line VT ablation or a control group based on medical therapy as an initial therapy, (e) patients were followed for an average duration of at least 12 months, and (f) reported survival-free from VT/VF and/or rates of appropriate ICD therapies as their endpoints.

## 2.3 Study outcomes

#### 2.3.1 Primary outcome

The primary outcomes were (1) all-cause mortality, (2) appropriate ICD therapies, and (3) adverse events in all the patients included.

#### 2.3.2 Secondary outcomes

The secondary outcomes were (1) composite of survival-free from VT/VF and appropriate ICD therapies in patients with moderately depressed LVEF (> 30-50%) and (2) composite of survival-free from VT/VF and appropriate ICD therapies in patients with severely depressed LVEF ( $\leq 30\%$ ).

#### 2.4 Sensitivity analysis

Sensitivity analyses were performed for the secondary endpoints, considering the composite nature of the outcomes, using the leave-one-study-out method in order to address the influence of each study by testing whether deleting each individually would significantly change the pooled results of the meta-analysis. Additionally, chronological cumulative analyses were used to test whether the effect size and precision would shift based on technical advancement of mapping technology and ablation strategies.

#### 2.5 Data extraction and quality assessment

Two investigators (D.F.B and J.R) independently screened all titles and abstracts and manually searched the full text versions of all pertinent studies that fulfilled the inclusion criteria. References of the relevant studies were independently reviewed for potential identification of further studies. Two investigators (D.F.B and J.R) independently assessed the quality items. Disagreements were resolved by consensus. Quality assessment of all included studies was done by using the 6 domains of the Cochrane tool for assessing risk for bias of RCTs.

## 2.6 Statistical analysis

Hazard ratios (HR) or Mantel–Haenszel (MH) risk ratio (RR) models and 95% confidence intervals (CI) were used to summarize data across treatment arms. The Cochran *Q*-test and the Higgins *I*-squared ( $I^2$ ) statistic were used for heterogeneity testing; in cases of heterogeneity (defined as  $I^2 > 25\%$ ), random effects models of DerSimonian and Laird were used; otherwise ( $I^2 < 25\%$ ) fixed effects models were used. To address publication bias, we used the funnel plots. If any bias was observed, further bias quantification was measured using the Begg-Mazumdar test, Egger test, and the Duval and Tweedie's trim and fill test.

Descriptive statistics are presented as means and standard deviations (SD) for continuous variables or number of cases (n) and percentages (%) for dichotomous and categorical variables. Number needed to treat (NNT) was calculated. Statistical analysis was performed in line with recommendations from the Cochrane Collaboration and the PRISMA guidelines, using Review Manager (RevMan) (Computer program) Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014, and the Comprehensive Meta-Analysis Software version 2.0 (Biostat, Inc).

# **3 Results**

### 3.1 Qualitative analysis

#### 3.1.1 Study selection

We screened 455 abstracts, out of which 12 full-text articles were retrieved and reviewed for possible inclusion based on inclusion criteria. Ultimately, four studies fulfilled the inclusion criteria and were analyzed. Flow chart of the literature review is illustrated in Fig. 1.

### 3.1.2 Baseline characteristics

The baseline characteristics of the patients included in this metaanalysis are reported in Table 1. A total of 505 patients (mean age  $66 \pm 9$  years, 89% males) were analyzed. The mean duration of follow-up was  $24 \pm 9$  months. The use of AADs was similar in both groups during the first 12 months of follow-up (mean AAD use was 21% in the first-line ablation group vs. 20% in controls). All the studies evaluated an endocardial-only ablation approach. Previous revascularization with percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass grafting (CABG) was performed in 80% of patients. Mean duration since last MI was  $10 \pm 9$  years. Mean LVEF was  $35 \pm 8\%$ , and 84% of patients were on beta-blockers. Table 2 illustrates a summary of the included studies.

## 3.2 Quantitative analysis

#### 3.2.1 Primary endpoints

A significant benefit was observed with first-line catheter ablation compared with medical management in survival-free from appropriate ICD therapies, with a 30% relative risk reduction and 14% absolute risk reduction when compared with the medical treatment group (RR 0.70, 95% CI 0.56–0.86) (Fig. 2). There was no difference in all-cause mortality (RR 0.98, 95% CI 0.52–1.82) and in adverse events between both treatment strategies (RR 1.51, 95% CI 0.89–2.54) (Supplemental Fig. 1).

#### 3.2.2 Secondary endpoints

In patients with moderately depressed LVEF (>30–50%), survival-free from VT/VF in patients who underwent first-line catheter ablation was 56% vs. 45% in those receiving conservative treatment. A significant benefit of survival-free from VT/VF was observed with first-line catheter ablation, with a 44% relative risk reduction and 11% absolute risk reduction when compared with the medical treatment group (HR 0.56, 95% CI 0.38–0.83) (Fig. 2).

First-line VT ablation was associated with a statistically significant reduction in the composite endpoint of survivalfree VT/VF and appropriate ICD therapies in patients with



Fig. 1 Flow chart of study selection

Study name	First Author, Vear	Type of	Patients (total)	Patients	Mean Follow-	Age (vears)	Male (%)	NTH	DM	Mean LVFF (%)	Time since last	Beta hlockers	Class I or III A A D (%)	ACE/ ARBs
		study		LVEF > 30% n (%)	up (months)						MI (years)	(%)		(%)
SMASH-VT	Reddy, 2007	RCT	128	61 (48)	22.5 ± 5.5	$66.5 \pm 9.5$	86.5	70	44	32 ± 9	$8.4 \pm 8.2$	96	0	92
VTACH	Kuck, 2010	RCT	107	64 (60)	$22.5 \pm 9$	$66.1\pm8.3$	93.5	NR	NR	$34 \pm 9$	$13 \pm 8.3$	74.8	35 (amiodarone)	NR
SMS	Kuck, 2017	RCT	111	62 (44)	$21\pm13$	$67.1\pm8.1$	87	NR	NR	$31.2 \pm 7.1$	$9.8\pm7.3$	91	32 (amiodarone)	NR
BERLIN-VT	Willems, 2020	RCT	159	159 (100)	30	66	87.5	80.6	28.4	41 ± 6	<b>9.7</b> ± 10.5	73.7	36.7	66.5
*Plus-minus v	alues are means =	⊧ standard	deviations (5	SD)										
<i>SMASH-VT</i> p1 heart disease (	ophylactic cathet VTACH): a multi	er ablation centre rand	for the prev lomized cont	ention of defibri trolled trial, SMS	llator therapy, impact of sub	VTACH cath strate modific	neter abla cation by	tion of s catheter	table vei ablation	ntricular tachy on implantab	/cardia before le cardioverte	e defibrillator i r-defibrillator	mplantation in patients interventions in patients	with coronary with unstable

ventricular arrhythmias and coronary artery disease: results from the multicenter randomized controlled SMS (substrate modification study), *BERLIN VT*: Preventive aBlation of vEntricular tachycaRdia in Patients With myocardiaL Infarction; *LVEF*: left ventricular ejection fraction, *RCT* randomized controlled trial, *HTN* hypertension, *DM* diabetes mellitus, *NTHA* New York Heart Association, *MI* myocardial infarction, *PTCA* percutaneous transluminal coronary angioplasty, *CABG* coronary artery bypass grafting, *AAD* anti-arrhythmic drug, *ICD* implantable cardioverter defibrillator, *NR* not reported

Author, year	VT ablation strategy	Inclusion criteria	Study groups	Follow-up	Crossovers	Primary endpoint	Secondary endpoints
Reddy, 2007	Endocardial substrate mapping	Previous MI (> 1 month); recent ICD implantation for VF, hemodynamically unstable VT during EPS; latter: ICD implanted for primary prevention with subsequent appropriate ICD therapy for a single event	ICD implantation+ VT catheter ablation vs. control group: ICD implantation alone	3, 6, 9, 12, 18, and 24 months	Three patients in VT ablation arm -> control group	Survival free from any ICD therapy	Freedom from any appropriate ICD shock, death and ICD storm
Kuck, 2010	Endocardial substrate mapping; Activation mapping; Entrainme- nt mapping; Pace mapping	Previous MI (> 1 month); implanted with secondary prevention ICD following stable clinical VT (not leading to cardiac arrest or syncope, SBP: > 90 mmHg), LVEF: <50%	ICD implantation + VT catheter ablation vs. control group: ICD implantation alone	6, 9, 12, 18, 24, 30 and 36 months	13% from VT ablation arm -> control group; 19% in control group -> VT ablation arm	First recurrence of VT/VF	VT storm, syncope, death
Kuck, 2017	Endocardial substrate mapping; Activation mapping; Entrainme- nt mapping; Pace mapping	Coronary artery disease, LVEF $\leq 40\%$ and clinically unstable spontaneous VT, or cardiac arrest or syncope with unstable VT inducible at the baseline EPS	ICD implantation + VT catheter ablation vs. control group: ICD implantation alone	3, 6, 9, and 12 months during first year, followed by 3- or 6-month intervals until 33 months	One patient in control arm -> ablation group	First recurrence of VT/VF	Appropriate ICD therapies, quality of life, number of hospital readmissions because of a cardiac indication, and severe clinical events (death, number of syncopes, and number of electrical storm episodes, defined as > 3 VT episodes
Willems, 2020	Endocardial substrate mapping	Previous MI; implanted with secondary prevention ICD; history of sustained VT; LVEF: 30–50%	VT ablation at the time of ICD implantation vs. control group: VT ablation following three appropriate shocks	3, 6, 12, 18, and 24 months	9.2% patients in control group did not receive ablation; 12% of deferred group received ablation, but only 9.6% received "premature" ablation before 3 ICD shocks	Time to first event comprising all-cause mortality and unplanned hospitalization for CHF or symptomatic VT/VF	Vitum 2+ ii). Time to first sustained VT/VF, time to first appropriate ICD therapy, time to first inappropriate ICD therapy, time to all-cause mortality, time to cardiac mortality, time to first unplanned all-cause hospitalization, time to first unplanned cardiac hospitalization and change in quality of life up to 12-month follow-up

*VT* ventricular tachycardia, *MI* myocardial infarction, *ICD* implantable cardioverter defibrillator, *VF* ventricular fibrillation, *CHF* congestive heart failure, *EPS* electrophysiologic study, *SBP* systolic blood pressure, *LVEF* left ventricular ejection fraction, *AAD* anti-arrhythmic drug, *DVT* deep vein thrombosis, *NR* not reported

moderately reduced LVEF (HR 0.52, 95% CI 0.36–0.76) (Fig. 3). In patients with severely depressed LVEF ( $\leq$ 30%), first-line VT ablation was not associated with a reduction in the composite endpoint of survival-free VT/VF and appropriate ICD therapies (HR 0.56, 95% CI 0.24–1.32) (Fig. 3).

#### 3.3 Sensitivity analysis

Sensitivity analysis for the secondary endpoints involving the removal of each of the studies sequentially demonstrated that if some of the studies were removed from



Fig. 2 Survival-free from VT/VF and from appropriate ICD therapies in patients with ICM presenting with VT undergoing first-line catheter ablation compared with medical management. a Survival-free from appropriate ICD therapies in all patients. b Survival-free from VT/VF



in patients with moderately depressed LVEF (>30-50%). ICD implantable-cardioverter defibrillator, ICM ischemic cardiomyopathy, VF ventricular fibrillation, VT ventricular tachycardia

Fig. 3 Forest plot reporting the hazard ratio illustrating the composite endpoint of survivalfree VT/VF and appropriate ICD therapies in patients with ICM presenting with VT undergoing first-line catheter ablation compared with conservative treatment. a Patients with moderately depressed LVEF (> 30-50%). b Patients with severely depressed LVEF (≤30%). Diamond indicates overall summary estimates for the analysis: width of the diamond represents 95% CI; width of the shaded square represents the size of the population (fixed effects model was used in the analysis). CI confidence interval, ICM ischemic cardiomyopathy, VF ventricular fibrillation, VT ventricular tachycardia



Fixed effects model Heterogeneity: Tau2=0.036; Chi2=2.511; df=2; P = 0.285; I2=20.4% Test for overall effect: Z= -3.380 (P = 0.001)

#### b

Study name	Statistic	s for eac	h study		Hazard r	atio and	<b>1 95% Cl</b>		
	Hazard ratio	Lower limit	Upper limit					Re	elative veight
Reddy 2007	0.49	0.15	1.61		-	■			51.85
Kuck 2010	0.65	0.19	2.23		-				48.15
	0.56	0.24	1.32						
				0.01	0.1	1	10	100	

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Favors Medical Therapy

Fixed effects model Heterogeneity: Tau2=0.000; Chi2=0.105; df=1; P = 0.746; l2=0.0% Test for overall effect: Z= -1.324 (P = 0.185)

the analysis, the summary risk estimates for the composite survival-free VT/VF and appropriate ICD therapies was not influenced making the overall results significant (Fig. 4). The chronologic cumulative analysis for each outcome before inclusion of all studies in the final effect summary did not have a significant impact in the overall final effect (oldest RCT from 2007 and most recent in 2020) (Fig. 4).

### 3.4 Number needed to treat

The absolute difference in event rates yielded an NNT of 10 patients in order to improve survival-free from VT/VF in those with moderately depressed LVEF.

### 3.5 Quality assessment and publication bias

Funnel plots did not show asymmetry, suggesting lack of bias for any outcome (Supplemental Fig. 2). A graph and summary of the tools recommended by the Cochrane Collaboration for the risk of bias (selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias) identified in each individual RCT is shown in Fig. 5.

#### **4** Discussion

In patients with ICM, VT/VF is a major cause of morbidity and mortality. Thus, strategies to minimize arrhythmia burden in these patients is essential. Our study, which included 505 patients enrolled in RCTs, with a mean follow-up duration of  $24 \pm 9$  months, showed that patients with ICM presenting with VT/VF, first-line catheter ablation have a significantly lower rate of recurrent appropriate ICD therapies compared with patients receiving an initial approach based on medical therapy (RR 0.70, 95% CI 0.56-0.86). However, this benefit was only significant in the subgroup of patients with moderately depressed LVEF (>30-50%) (HR 0.52, 95% CI 0.36-0.76) compared with patients with severely depressed LVEF (<30%) (HR 0.56, 95% CI 0.24-1.32). Only RCTs were included in this meta-analysis to minimize bias considering the nature of the research question involving the evaluation of 2 specific interventions in a specific sub-group of patients.

In patients implanted with secondary prevention ICDs, shocks have been reported in up to  $\sim 39\%$  of patients within the first year of implantation [3]. Recurrent ICD shocks may cause deterioration of heart failure, increase hospitalization rates, and have been associated with increased mortality [8]. The SCD-HeFT trial noted that a single appropriate ICD shock increased patient mortality-risk up to five-fold [8].



Fig. 4 Forest plots reporting the sensitivity analysis for the secondary endpoint: a leave-one-study-out method for moderately depressed LVEF; b leave-one-study-out method for severely depressed LVEF; c chronological cumulative analysis for moderately depressed LVEF; d chronological cumulative analysis for severely depressed LVEF.

Diamond indicates overall summary estimate for the analysis (width of the diamond represents the 95% CI); width of the shaded square, size of the population. CI confidence interval, ICD implantable-cardioverter defibrillator, ICM ischemic cardiomyopathy, LVEF left ventricular ejection fraction, VF ventricular fibrillation, VT ventricular tachycardia **Fig. 5** a Methodological quality graph and **b** methodological quality summary for the risk of bias from the included randomized controlled trials using the 6 domains of the Cochrane tool



Shocks with their potential to worsen HF also tend to alter mode of mortality in the direction of non-arrhythmic death, thereby, offsetting the arrhythmic mortality advantage offered by ICDs [9]. Moreover, they do not alter the underlying pathological substrate and do not prevent VT. Therefore, it is important to adopt a strategy that reduces the absolute incidence of VT/VF, and as such, subsequent ICD shocks. Utilization of AADs and ICD reprogramming has been employed with moderate degrees of success [3]. Accordingly, the VANISH trial demonstrated that there was a significantly lower rate of the composite primary outcome of death, VT storm, or appropriate ICD shock among patients undergoing catheter ablation than among those receiving an escalation in AAD (HR 0.72, 95% CI 0.53 to 0.98; p = 0.04) [10].

In patients with ICM, VT usually arises from a fairly distinct region of the myocardium, within or neighboring the scar tissue. This scar tissue is comprised of non-excitable fibrous material, with islands of surviving myocytes composing the substrate for VT. A general physiology seems to be common in patients with ICM and sustained monomorphic VT, characterized by larger endocardial lower voltage zones, more frequent fractionated, very late voltage potentials as compared with patients with a similar profile without VT [11]. Nonetheless, scars are not homogenous considering tissue characteristics can be variable in each patient depending largely on the infarct type (i.e., size, location, revascularization time) posing a challenge for the treatment of VT/VF. Therefore, is not surprising that ablation studies have shown variable results reflecting conservative guideline recommendations. Guidelines recommend VT ablation as a Class I indication in patients with prior MI, only with recurrent episodes of symptomatic sustained VT, or VT storm, and have failed or are intolerant to AADs [2]. However, this recommendation may not apply to every patient, as there seems to be a significant benefit in different subgroups of patients including those undergoing early ablation and preserved LVEF [12]. In general, a lower threshold to consider catheter ablation of VT (whether it is determined by failure of 1 AAD or immediately

after a VT episode) could be associated with a favorable outcome [12]. Furthermore, data from the International VT Ablation Center Collaborative Group reported higher rates of both VT recurrence and mortality in patients with lower EF and higher NYHA status [13]. In contrast, ICM and higher EF (> 30%) were associated with lower probability of VT recurrence that was reflected in improved transplant-free survival compared with those with VT recurrence (93% vs. 89%, adjusted HR 3.190 (1.517–6.707); p = 0.002) [13].

Four randomized controlled trials have assessed the impact of first-line VT catheter ablation in the setting of ICM [5, 6, 14, 15]. SMASH VT and VTACH trials showed improved outcomes with first-line VT ablation in patients with ICM presenting with VT [5, 6]. However, the SMS and the recently published BERLIN VT trial showed opposite results [14, 15]. As expected, all of these trials had methodological differences but the major approach studied is homogenous, considering the use of first-line VT ablation in each of them and a medication-based approach in the control groups. In terms of the control groups, AADs were used in 31% of patients in the VTACH study, 22% in SMS, and 28% in BERLIN VT at 1-year follow-up, while no AADs were used in SMASH VT [5, 6, 14, 15]. All control groups were medications based except in the BERLIN VT trial, where patients were randomized to receive ablation after the third appropriate ICD shock [15]. Ultimately, 10 patients (12%) received ablation in this group, which is perhaps one of the reasons the trial showed no benefit in the ablation group [15]. They showed that first-line VT ablation did not reduce the combined endpoint of mortality or hospitalization for arrhythmia or worsening heart failure during 1 year of follow-up when compared with the deferred ablation strategy (HR 1.09, 95% CI 0.62–1.92; p = 0.77) [15]. Perhaps the study power, patient cross-over, and endocardial-only ablation strategy were not enough to demonstrate a significant clinical benefit of ablation. VT circuits in ICM are generally thought to have a subendocardial location, easily accessible, and targeted with endocardial mapping and ablation [16]. However, 34-75% of ICM patients may exhibit epicardial substrate, as confirmed by magnetic resonance imaging in post-infarct animal models [17]. This may explain why a combined endocardial-epicardial ablation has been shown to be beneficial in ICM. We recently published a metaanalysis with 17 studies including 975 patients [18]. After a mean follow-up of 27 months, endocardial-epicardial ablation was associated with a 35% reduction in risk of VT recurrence compared with endocardial ablation alone (RR 0.65, 95% CI 0.55 to 0.78; p < 0.001). Sensitivity analysis showed lower risk of VT recurrence in ICM (RR 0.43, 95% CI 0.28 to 0.67; p = 0.0002) with a nonsignificant trend in NICM (RR 0.87, 95% CI 0.70 to 1.08; p = 0.20). More importantly, an endocardial-epicardial approach was associated with reduced all-cause mortality (RR 0.56, 95% CI 0.32 to 0.97; p = 0.04), particularly in patients with ICM [18]. As such, perhaps early ablation using an endocardial-epicardial strategy in patients with LVEF > 30-50% could be the most beneficial therapeutic strategy.

Despite the mixed results from the four RCTs evaluating this concept, our results substantiate the use of VT ablation as a first-line approach in this population to improve survivalfree from VT/VF, which may also have a positive impact from a healthcare resource utilization standpoint [19]. Multiple clinical studies are currently underway aiming to address the best therapeutic approach of these patients: Does Timing of VT ablation Affect Prognosis in Patients with an ICD? (PARTITA) (NCT01547208), Pan-Asia United States PrEvention of Sudden Cardiac Death Catheter Ablation Trial (PAUSE-SCD) (NCT02848781), and The Antiarrhythmics or Ablation for Ventricular Tachycardia 2 (VANISH 2) Study (NCT02830360).

### 4.1 Limitations

Our meta-analysis has several limitations, which should be taken into account while interpreting the results. Only a small number of studies have assessed the impact of first-line VT ablation in patients with ICM, and the data available to stratify outcomes based on LVEF is limited; hence, the necessity to assess a composite endpoint. Also, techniques for VT mapping and ablation differed among the studies. Our results are applicable only to patients with ICM, and should not be generalized to NICM.

# **5** Conclusion

Patients with ICM presenting with VT undergoing first-line VT ablation have a significant lower rate of appropriate ICD therapies without a mortality difference compared with patients receiving an initial approach based on medical therapy. The beneficial effect of a first-line ablation approach in improved survival-free from VT/VF and appropriate ICD therapies was seen only in patients with moderately depressed LVEF. First-line VT ablation should be considered the therapeutic approach of choice in this selected group of patients to improve clinical outcomes.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10840-020-00912-w.

Data availability Available upon request.

#### **Compliance with ethical standards**

**Conflict of interest** Dr. Di Biase is a consultant for Biosense Webster, Boston Scientific, and St. Jude Medical and has received speaker honoraria/travel from Medtronic, Atricure, EPiEP, and Biotronik. Dr. Natale is a consultant for Biosense Webster, Stereotaxis, and St. Jude Medical and has received speaker honoraria/travel from Medtronic, Atricure, EPiEP, Biotronik, and Janssen. The remaining authors report no conflict of interest.

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