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Prophylactic Catheter Ablation of Ventricular Tachycardia in Ischemic Cardiomyopathy: a systematic review and meta-analysis of randomized controlled trials.

Electrophysiology Collaborative Consortium for Metaanalysis – ELECTRAM Investigators

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Abstract

Aims: Catheter ablation is an effective strategy for drug-refractory ventricular tachycardia (VT) in ischemic cardiomyopathy. We aimed to perform a systematic review and meta-analysis of outcomes of prophylactic catheter ablation (PCA) of Ventricular Tachycardia (VT) in ischemic cardiomyopathy patients

Methods We performed a comprehensive literature search through February 10, 2020, for all eligible randomized controlled trials that compared "PCA" versus "No PCA" for VT. Primary efficacy outcomes included - appropriate ICD therapy (composite of anti-tachycardia pacing and ICD shock), appropriate ICD shocks, electrical storm, cardiac mortality, and all-cause mortality. The primary safety outcome was any adverse events.

Results. Four randomized controlled trials (N = 505) met inclusion criteria. Prophylactic catheter ablation was associated significant reduction in appropriate ICD therapies (RR 0.70; 95% CI 0.55 - 0.89, p = 0.004), appropriate ICD shocks (RR 0.57 95% CI 0.40 - 0.80, p = 0.001) with a trend towards reduced risk of electrical storm (RR 0.64; CI 0.39 - 1.05; p = 0.075) compared to "No PCA". There was no significant difference in cardiac mortality (RR 0.66, 95% CI 0.31 – 1.43, p = 0.29) and all-cause mortality (RR 0.98, 95% CI 0.52 – 1.82, p = 0.94) with similar adverse events (RR 1.46, 95% CI 0.73 – 2.95, p = 0.29) between two groups.

Conclusion. Prophylactic catheter ablation in ischemic cardiomyopathy patients was associated with a lower risk of ICD therapies, including ICD shocks and VT storm with no difference in cardiac and all-cause mortality.

Introduction

Patients with ischemic cardiomyopathy who survive a spontaneous episode of ventricular arrhythmias are at an increased risk for recurrent ventricular tachycardia (VT) or ventricular fibrillation (VF). Implantable cardioverter-defibrillators (ICDs) reduce the risk of sudden cardiac death (SCD) in these patients and have, therefore, become the standard of care in the management of ventricular arrhythmias [1]. However, patients who experience ICD shocks have a decreased quality of life and increased mortality compared to patients who do not receive shocks, even if the shocks are considered inappropriate [2,3]. Additionally, ICDs do not provide absolute protection from SCD in about 3-7 % of patients [4]. Thus, modalities that can effectively reduce recurrent ventricular arrhythmias and ICD therapies (both shocks and anti-tachycardia pacing) are of great importance. Drug treatment, especially amiodarone in combination with beta-blockers reduces ICD interventions, but are associated with serious adverse events on long-term treatment [5]. Catheter ablation for VT in the past was infrequently used because VT episodes were often hemodynamically unstable, rendering the mapping of clinical VT difficult [6]. Recent advances in mapping and ablation strategies have enabled electrophysiologists to perform both activation mapping/ablation during VT and substrate mapping/ablation during sinus rhythm targeting late/fractionated

Key Words

Ventricular Tachycardia, Prophylactic Catheter Ablation, Ischemic Cardiomyopathy.

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potentials, thereby resulting in higher acute procedure success and long-term clinical outcomes. Several trials have also demonstrated that catheter ablation of scar related VT significantly reduces ICD therapies, including shocks and overall VT burden [7-10]. Despite encouraging data from randomized controlled trials, the optimal timing of catheter ablation for VT remains unclear. The current guidelines recommend referral for catheter ablation in patients who failed antiarrhythmic treatment [11]. Prophylactic catheter ablation ("PCA") has also been evaluated as an adjunct treatment option in patients eligible for ICD implantation (with documented life threatening ventricular arrhythmias), with conflicting results [12-15]. Given the lack of data, we aimed to perform a systematic review and meta-analysis of outcomes of prophylactic catheter ablation for VT in ischemic cardiomyopathy patients.

Methods

Search strategy

The reporting of this systematic review and meta-analysis complies with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [16] (Supplement Table 1).

The initial search strategy was developed by two authors (K.S. and M.T). We performed a systematic search, without language restriction, using PubMed, EMBASE, SCOPUS, Google Scholar, and ClinicalTrials.gov from inception to February 10th, 2020, for studies comparing clinical outcomes between "PCA" versus "No PCA"—only in eligible patients with VT and ischemic cardiomyopathy. We used the following keywords and medical subject heading: "ventricular tachycardia," "ventricular fibrillation," "catheter ablation," "implantable cardioverter-defibrillator."

Study selection and data extraction

Only randomized controlled trials that compared "PCA" versus "No PCA" were included in the analysis. The data from included studies were extracted using a standardized protocol and a data extraction form. Any discrepancies between the two investigators were resolved with a consultation with the senior investigators (D.L and J.G). Studies comparing prophylactic catheter ablation versus antiarrhythmic drugs, review articles, editorials were excluded from our analysis. The following data were extracted: title, study date, sample size, comorbid conditions, ejection fraction, mapping and ablation technique, antiarrhythmic drugs, ICD type (single, dual, or cardiac resynchronization therapy), medications, clinical outcomes, and complications. The Cochrane – Risk bias assessment tool was used to appraise the quality of included studies (Supplement Table 2).

Clinical outcomes

The primary efficacy outcome of our study was – (1) appropriate ICD therapy (composite of anti-tachycardia pacing and ICD shock); (2) appropriate ICD shocks; (3) electrical storm, (4) cardiac mortality and (5) all-cause mortality. The definition of the electrical storm was similar across all included trials except BERLIN VT[15] (was not enlisted as clinical outcome). The electrical storm was defined as three or more VT episodes in 24 hours. Deaths secondary to cardiac causes were included under cardiac mortality. The primary safety outcome of our study was any adverse events [acute procedural related adverse events – composite of vascular complications, pericardial effusion (with and without tamponade), heart failure exacerbation secondary to catheter ablation, complete heart block, device and lead dysfunction (requiring replacement), lead dislodgement, stroke/transient ischemic attack, deep vein thrombosis, transient ST-segment elevation, or pneumothorax].

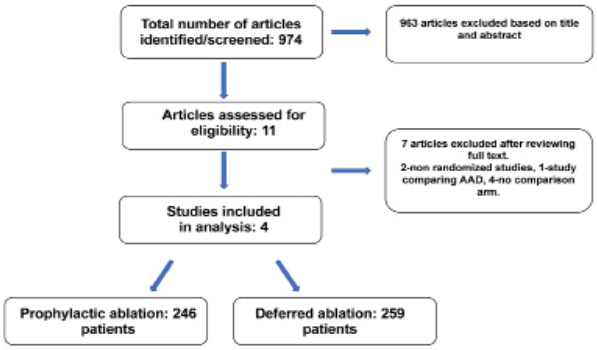


Figure 1: **Flow Diagram illustrating the systematic search of studies**

Statistical analyses

The meta-analysis was performed using a meta-package for R version 4.0 and Rstudio version 1.2. Mantel-Haenszel risk ratio (RR) random-effects model (DerSimonian and Laird method) was used to summarize data across the groups [17]. The heterogeneity of effects among the included studies was assessed by Higgins I-squared (I2) statistic[18]. A value of I2 of 0–25% represented insignificant heterogeneity, 26–50% represented low heterogeneity, 51–75% represented moderate heterogeneity, and more than 75% represented high heterogeneity, as set forth by the Cochrane Collaboration. Publication bias was visually assessed using funnel plots and Egger's linear regression test of funnel plot asymmetry. A two-tailed $p < 0.05$ was considered statistically significant for all analyses.

Results

Search results

A total of 974 citations were identified (Figure 1) during the initial search. Nine hundred sixty-three records were excluded. After a detailed evaluation of these studies, four randomized clinical trial studies ultimately met the inclusion criteria (N=505 patients) [12-15]. The follow-up duration for the studies ranged from 396 days to 40 months. Table 1 summarizes the study characteristics of the included trials.

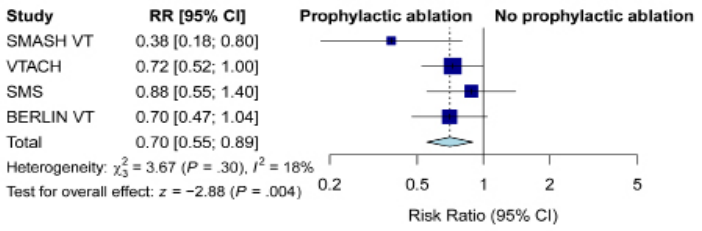
Study characteristics

This meta-analysis of 4 randomized trials includes a total of 505 patients comparing "PCA" (N = 246) versus "No PCA" approach (N = 259). The mean age of the patients included in the trials ranged from 64.4 (±8.2) – 68.4 (±7.7) years. The mean (SD) follow-up duration ranged from 22.5 (5.5) to 27.6 (13.2) months. The mean (%) left ventricular ejection fraction (LVEF) ranged from 30.4±7.3 to 41±6%.

Mapping and ablation techniques varied between the trials – most commonly done using the CARTO electroanatomic system (Biosense Webster, Inc, Diamond Bar, CA). Bipolar electrogram voltage amplitude >1.5 mV was considered as normal myocardium, while <1.5 mV was considered border zone/scarred myocardium.

Table 1: Baseline characteristics of studies included in our meta-analysis

Study ID	SMASH VT[12]	VTACH[13]	SMS[14]	BERLIN VT[15]
Design	Randomized unblinded controlled trial	Randomized unblinded controlled trial	Randomized unblinded controlled trial	Randomized unblinded controlled trial
Study period	2000-2006	2002-2006	2002-2011	2015-2018
Arrhythmic inclusion criteria	Hemodynamically unstable ventricular arrhythmias, or syncope with inducible ventricular tachycardia during invasive electrophysiological testing	Stable clinical ventricular tachycardia defined as a ventricular tachycardia not resulting in cardiac arrest or syncope and during which the systolic blood pressure was higher than 90 mm Hg	Hemodynamically unstable ventricular arrhythmias, or cardiac arrest or syncope with inducible unstable ventricular arrhythmias during electrophysiological study	Sustained stable and unstable ventricular arrhythmia
Follow up	22.5 ± 5.5 months	22.5 ± 9 months	22.5 ± 9 months	396 ± 284 days
Patient age mean ± SD (years)	Prophylactic ablation: 67±9 No Prophylactic ablation: 66±10	Prophylactic ablation: 67.7±8.3 No Prophylactic ablation: 64.4±8.2	Prophylactic ablation: 68.4±7.7 No Prophylactic ablation: 65.9±8.4	Prophylactic ablation: 66±10 No Prophylactic ablation: 66±9
Ejection fraction (%)	Prophylactic ablation: 30.7±9.5 No Prophylactic ablation: 32.9±8.5	Prophylactic ablation: 34±9.6 No Prophylactic ablation: 34.1±8.8	Prophylactic ablation:32±6.9 No Prophylactic ablation: 30.4±7.3	Prophylactic ablation: 41±6 No Prophylactic ablation: 41±6
Interval between last myocardial infarction and enrollment	Prophylactic ablation (years): 8.8 ± 8.5 No Prophylactic ablation (years): 7.9 ± 7.8	Prophylactic ablation (years): 12.6 ± 8.0 No Prophylactic ablation(years):13.3 ± 8.6	Prophylactic ablation (years): 11.1 ± 6.6 No Prophylactic ablation (years): 8.6 ± 7.8	Prophylactic ablation (months): 123 ± 144 No Prophylactic ablation (months): 110 ± 109
Ablation technique	Substrate modification ± entrainment mapping± pace mapping	Endocardial Substrate modification ± entrainment mapping ± pace mapping	Endocardial Substrate modification ± non-inducibility of VT	Substrate modification ± non-inducibility of VT
Epicardial ablation and Late potential ablation	Epicardial ablation not reported but late potentials targeted	No epicardial ablation	No epicardial ablation	Epicardial ablation not reported but late potentials targeted
Ablation endpoints	Non-inducible VT on programmed stimulation	Inducible VT: non-inducible VT on programmed simulation post ablation Non-inducible VT: substrate modification with no evidence of abnormal electrograms in the scar and scar border zone.	Non-inducibility of the clinical tachycardia or lack of adequate endocardial target sites or ineffective lesions despite adequate target sites	Non-inducible VT on programmed stimulation and elimination of abnormal potentials
Mapping	CARTO	CARTO and Non-contact mapping - Ensite	CARTO and Ensite	-
Antiarrhythmic drugs	None	Amiodarone Prophylactic ablation: 35% No Prophylactic ablation: 35%	Amiodarone Prophylactic ablation: 30% No Prophylactic ablation: 35%	Amiodarone Prophylactic ablation: 40.8% No Prophylactic ablation: 26.5%
ICD type				
Single chamber	Prophylactic ablation: 36% No Prophylactic ablation: 48%	Prophylactic ablation: 65% No Prophylactic ablation: 67%	Prophylactic ablation:51.8% No Prophylactic ablation: 57.89%	Prophylactic ablation: 53.94% No Prophylactic ablation: 75.90%
Dual chamber	Prophylactic ablation: 64% No Prophylactic ablation: 52%		Prophylactic ablation: 38.8% No Prophylactic ablation: 31.57%	Prophylactic ablation: 32.9% No Prophylactic ablation: 20.5%
CRT-D			Prophylactic ablation: 9.25% No Prophylactic ablation: 10.52%	Prophylactic ablation: 11% No Prophylactic ablation: 3.6%
Unknown		Prophylactic ablation: 35% No Prophylactic ablation: 33%		
ICD Programming	N/A	VF zone: 200-220 beats/min VT zone: 60 msec above the slowest documented VT, anti-tachycardia pacing and shock	VF zone: 200-220 beats/minute, shock therapy only (detection - 18 out of 24 beats) VT zone: 60 msec above the slowest documented VT, anti-tachycardia pacing and shock (detection - at least 16 consecutive beats)	VF zone: 200-222 beats/minute, one anti-tachycardia pacing, shock (detection 18 out of 24 beats) VT zone: 60 msec above the slowest documented VT, three or more anti-tachycardia pacing and shock
Medications (%)				
Beta-blockers	Prophylactic ablation: 94 % No Prophylactic ablation: 98 %	Prophylactic ablation: 75% No Prophylactic ablation: 75 %	Prophylactic ablation:91% No Prophylactic ablation: 91 %	Prophylactic ablation: 76.3 % No Prophylactic ablation: 71.1 %
ACE inhibitors or angiotensin receptor blockers	Prophylactic ablation: 92 % No Prophylactic ablation: 92 %			Prophylactic ablation: 61.8 % No Prophylactic ablation: 71.1 %
Statins	Prophylactic ablation: 58 % No Prophylactic ablation: 59 %			
Aspirin	Prophylactic ablation: 81 % No Prophylactic ablation: 61 %			



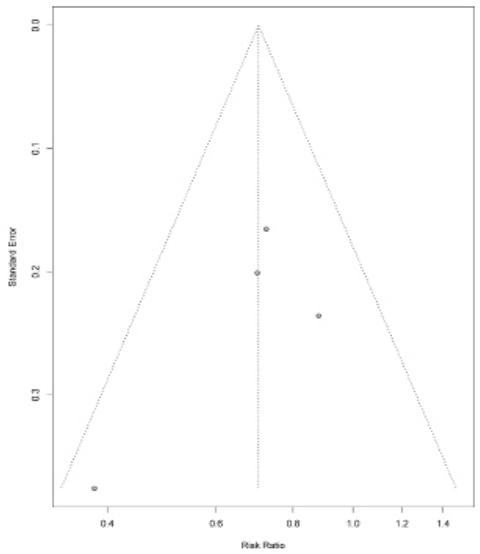
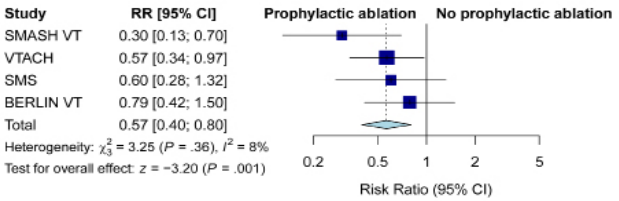


Figure 2a and 2b: Efficacy Outcomes: Appropriate ICD therapy (anti-tachycardia pacing plus shock). The Forest plot shows the outcomes of the individual trials as well as the aggregate. Point estimates to the left favor prophylactic catheter ablation. The Funnel plot demonstrates no publication bias.



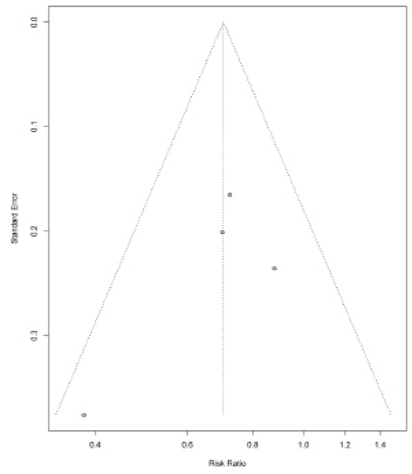


Figure 3a and 3b: Efficacy Outcomes: Appropriate ICD shock. The Forest plot shows the outcomes of the individual trials as well as the aggregate. Point estimates to the left favor prophylactic catheter ablation. The Funnel plot demonstrates no publication bias.

Fractionated and late potentials were identified and tagged along the scar border zone (characterized by multiple high frequency continuous delayed components separated from higher amplitude local ventricular electrograms and recorded within or at the end of QRS complex, respectively. Substrate-based approach ± entrainment mapping ± pace mapping was performed in SMASH-VT[12], VTACH[13], and SMS[14] study, while only substrate-based approach was performed in BERLIN-VT trial[15]. Non-inducibility of VT with programmed stimulation was the endpoint in all studies.

Ablation was performed before ICD implantation in all patients in BERLIN-VT, 92% in VTACH, 88.9% in SMS, and 13% in the SMASH-VT trial. None of the patients in SMASH-VT received antiarrhythmic medications (until any ICD event). This is in contrast to the VTACH trial, where 35% of patients were on amiodarone, 32% in SMS trial, and 33% in the BERLIN VT study.

Table 2: Adverse Events Related to Catheter Ablation and Implanted Device reported in the individual studies

Study	Complications Prophylactic ablation versus No Prophylactic ablation	Complication type	
		Prophylactic ablation	No Prophylactic ablation
SMASH VT[12]	3 (4.68%) vs 0	Ablation related: 3 1 = pericardial effusion without tamponade 1 = heart failure exacerbation 1 = deep vein thrombosis requiring Anticoagulation	None
VTACH[13]	4 (7.69%) vs 8 (14.54%)	Ablation related: 2 1 = stroke with aphasia 1 = transient ischemic ST segment Elevation Device related: 2 2 = lead dislodgement	Device related: 9 2 = lead dislodgement 2 = dislodged ICD lead requiring repositions 1 = T wave oversensing 1 = lead insulation damage 1 = Twiddler's syndrome 1 = ICD system infection needing extraction
SMS[14]	14 (25.92%) vs 8 (14.03%)	2 = stroke 2 = complete heart block 2 = pericardial effusion requiring pericardiocentesis 1 = heart transplant 4 = lead dislodgement 2 = lead dysfunction 1 = lead perforation	3 = lead dislodgement or / repositioning 3 = lead dysfunction 1 = pneumothorax 1 = heart transplant
BERLIN VT[15]	12 (15.78%) vs 7 (8.43%)	Ablation related:7 1 = cardiac perforation requiring surgery 1 = Cardiac tamponade 1 = pericardial effusion 2 = major groin bleed 1 = major nasopharyngeal bleed 1 = complete heart block Device related:6* 3 = right atrial lead dislodgement 3 = right ventricular lead dislodgement * 1 patient had both RA and RV lead dislodgement	Deferred ablation: 2 1 = complete heart block 1 = thrombophlebitis Device related: 6* 1 = right atrial lead d dislodgment 4 = right ventricular lead dislodgement 1 = inappropriate retention of ICD therapies for VT * 1 patient had both RA and RV leaddislodgement

Clinical outcomes

Efficacy outcomes

Appropriate ICD therapy (anti-tachycardia pacing plus shock) and ICD shock

The data for any ICD therapy or ICD shock was available in all four studies. There was a significant reduction in appropriate ICD therapy (32.1% vs. 47.1% respectively; RR 0.70; 95% CI 0.55 – 0.89, p = 0.004) in "PCA" versus "No PCA" approach. No heterogeneity was observed (I2 =18%) (Figures 2a and 2b). The number needed to prevent any appropriate ICD therapy was 7.

Similarly, the "PCA" approach was associated with reduced risk of appropriate ICD shocks (16.66% vs. 30.11% respectively; RR 0.57 95% CI 0.40 – 0.80, p=0.001) as compared to "No PCA" approach. No significant heterogeneity was observed (I2 = 8%). No publication bias was observed for either outcome (Figures 3a and 3b). The number needed to prevent appropriate ICD shock was 7.

Electrical Storm

The data on the electrical storm was not reported in the BERLIN VT study. Prophylactic catheter ablation demonstrated trend towards reduced risk of electrical storm compared to "No PCA" approach (12.35% vs 20.45%; RR 0.64; CI 0.39 – 1.05; p = 0.08). No significant heterogeneity was observed. (I2 =1%). No publication bias was observed (Figures 4a and 4b).

All-cause mortality

The data for all-cause mortality was available in all four trials. Prophylactic catheter ablation was not associated with decreased all-cause mortality (RR 0.98, 95% CI 0.52 – 1.82, p = 0.94). Mild heterogeneity was observed between trials (I2 =27%). No publication bias was observed (Figures 5a and 5b).

Cardiac mortality

The data for cardiac mortality was available in all four trials. Prophylactic catheter ablation was not associated with decreased cardiac mortality (RR 0.66, 95% CI 0.31 – 1.43, p = 0.29). No significant heterogeneity was observed between trials (I2 =0%). No publication bias was observed (Figures 6a and 6b).

Safety outcome

Adverse events

The adverse event rates were reported in all clinical trials (Table 2). The overall rate of adverse effects was similar in the "PCA" and "No PCA" group (13.41% versus 8.88%, respectively; RR 1.46, 95% CI 0.73 – 2.95, p=0.29]. Mild heterogeneity was observed (I2 =37%). No publication bias was observed (Figures 7a and 7b).

Discussion

Ventricular arrhythmias account for approximately 5.6% of total mortality in the United States. Slow and anisotropic conduction via the surviving myocardial fibrils in and around the dense scar (from prior myocardial infarction) accounts for reentrant circuits for ventricular arrhythmias[19]. Also, patients with existing ICD are often referred for VT ablation at later stages (following multiple ICD shocks and

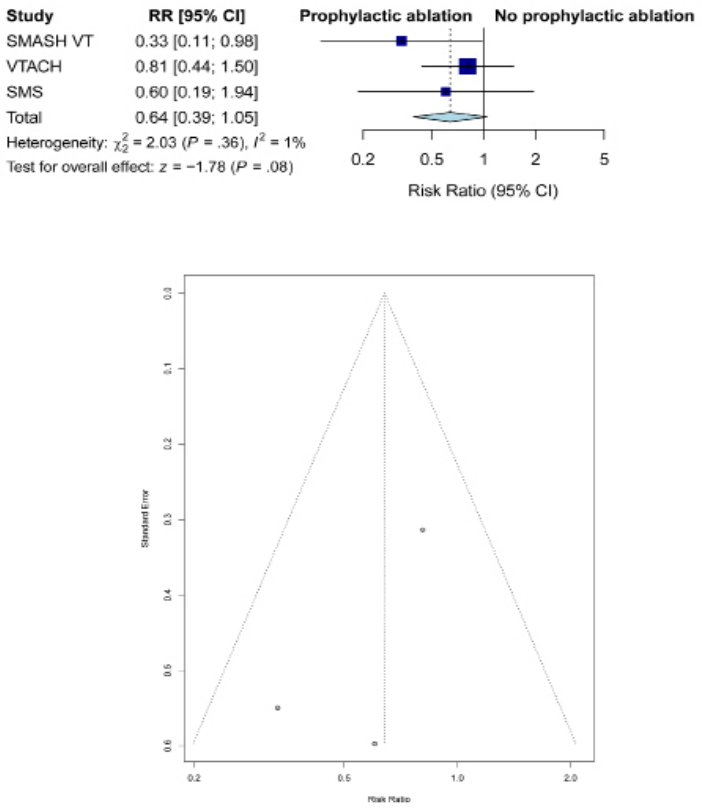


Figure 4a and 4b: **Efficacy Outcomes: Electrical storm. The Forest plot shows the outcomes of the individual trials as well as the aggregate. Point estimates to the left favor prophylactic catheter ablation. The Funnel plot demonstrates no publication bias.**

antiarrhythmic toxicities), resulting in a worse prognosis. Therefore, early referral for prophylactic VT ablation seemed reasonable. In this systematic review and meta-analysis of 4 randomized controlled trials, we demonstrated that prophylactic VT ablation was associated with reduced likelihood of any ICD events and appropriate ICD shocks, with no significant effect on all-cause and cardiac mortality. Studies like SMASH-VT, VTACH, SMS had their primary outcome focused on arrhythmia recurrence and were not statistically powered to look for the difference in all-cause mortality. BERLIN VT, on the other hand, was the only trial that assessed hard clinical outcomes composite of all-cause mortality, hospitalization, and recurrent arrhythmia as their primary outcome of interest. Although the findings in our study are in line with included RCTs, all four trials differed in several ways. VTACH study included patients with only documented stable VT with de novo ICD implantation; SMS included hemodynamically unstable ventricular arrhythmia or syncope with inducible unstable ventricular arrhythmias during electrophysiological study; SMASH VT included hemodynamically unstable ventricular arrhythmias or syncope with inducible ventricular tachycardia during invasive electrophysiological testing while BERLIN VT included patients with both stable and unstable ventricular arrhythmia. Prior to enrollment, amiodarone was used in VTACH (35% of patients), SMS (32%), and BERLIN VT (33%) but not in SMASH VT. Variation in ablation techniques and operator experience, antiarrhythmic use, and differences in ICD programming could have accounted for mild heterogeneity observed in our study (Table 1).

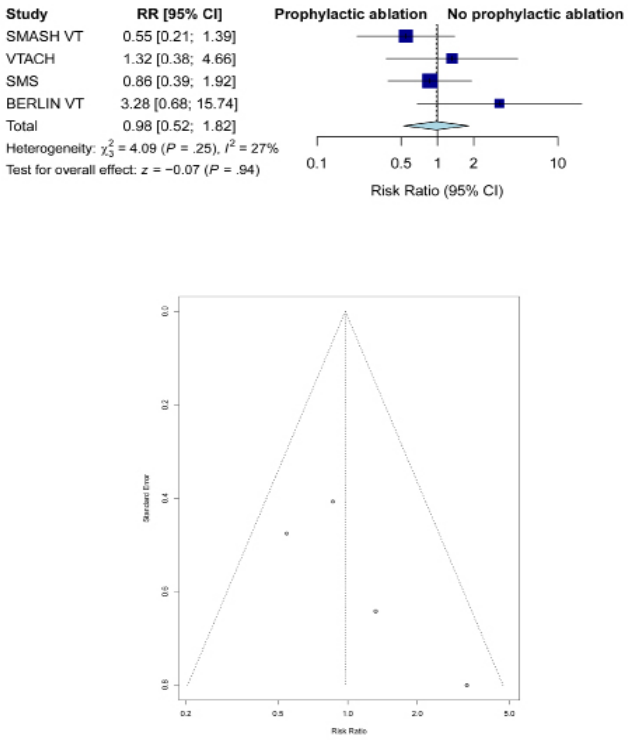


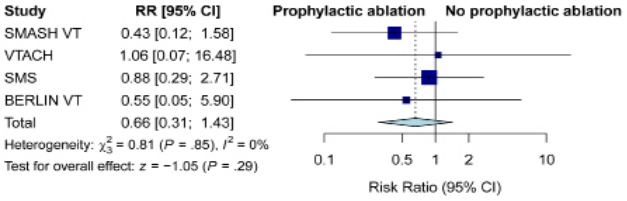
Figure 5a and 5b: **Efficacy Outcomes: All-cause mortality. The Forest plot shows the outcomes of the individual trials as well as the aggregate. Point estimates to the left favor prophylactic catheter ablation. The Funnel plot demonstrates no publication bias.**

VANISH trial (Ventricular Tachycardia Ablation versus Escalation of Antiarrhythmic Drugs) demonstrated that the catheter ablation was associated with reduced risk of primary outcome composite of death at any time or VT storm or appropriate ICD shocks as compared to the control group (escalated antiarrhythmic drug with ICD). However, the study failed to demonstrate a significant reduction in mortality as an individual secondary outcome between the two groups [20]. The significant difference in the primary outcomes was primarily driven by a reduction in appropriate ICD shocks and VT storms in the ablation arm. Studies have shown that recurrent ICD shocks (both appropriate and inappropriate) have been associated with increased mortality [3,21]. Therefore, intuitively prophylactic catheter ablation with an aim to homogenize the myocardial scar (by modifying the channels of slow conduction) may decrease the arrhythmia burden, ICD therapies, and in turn, potentially reduce mortality [7,8]. This has been retrospectively demonstrated by Tung and colleague where 2,061 patients who underwent scar-VT ablation (following ICD shocks), VT free survival was associated with reduced all-cause mortality [22].

Inducible VT's and the number of VT's induced is a significant predictor of recurrent VT[23,24]. Studies have shown that extensive substrate-based ablation strategy [targeting fractionated, late, and local abnormal ventricular activation (LAVA) potentials] is superior to ablation targeting only critical isthmus (for clinical VT) in ischemic cardiomyopathy patients[25-27]. Also, 15% of patients with ischemic cardiomyopathy may have mid myocardial and epicardial substrate requiring adjunct epicardial ablation in addition to the endocardial approach[28,29]. Therefore, a combined epicardial/endocardial ablation approach might be beneficial in VT free survival and, in turn, reduce ICD therapies and all-cause mortality[30,31]. Needless to say, the epicardial mapping and ablation approach was not performed in any of the studies. Also, approximately 10-40% of ischemic cardiomyopathy patients experience VT storm and are at increased mortality risk[32,33]. With the exception of the SMASH-VT trial, no significant difference was observed for VT storm between two groups. One of the possible explanations includes extensive substrate modification of the scar and scar border zone accounting for the reduced burden of ventricular arrhythmias.

As expected with any invasive procedure, the "PCA" group was associated with numerically high complication rates than the "No PCA" group; however, it failed to reach statistical significance (Table 2). The improvement in the quality of life was not significantly different between the two groups in SMS, which is in contrast to the BERLIN-VT trial, where the quality of life score improved in the "PCA" group. This could be secondary to medication compliance and decline in ventricular arrhythmias and ICD therapies, thereby reducing emergency room/physician visits, and subsequent hospitalizations. This could theoretically translate into an overall reduction in healthcare cost utilizations.

There are several important limitations to our study. 1) The small number of studies and small sample size may still be underpowered to assess net clinical benefit; 2) difference in ICD programming and antiarrhythmic drugs exposure might have led to selection bias and thereby influencing the results; 3) Individual patient-level data, data regarding inappropriate therapies and healthcare cost utilization was not available; 4) there was no uniform standardized definition for



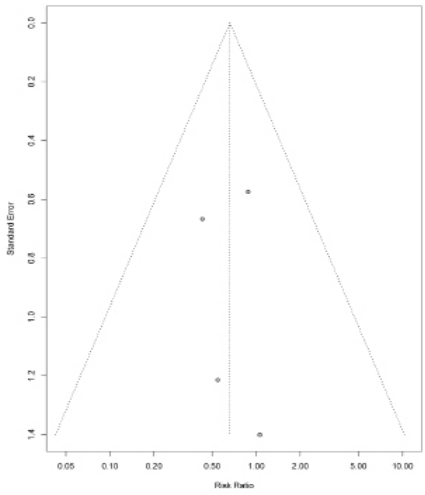


Figure 6a and 6b: **Efficacy Outcomes: Cardiac mortality. The Forest plot shows the outcomes of the individual trials as well as the aggregate. Point estimates to the left favor prophylactic catheter ablation. The Funnel plot demonstrates no publication bias.**

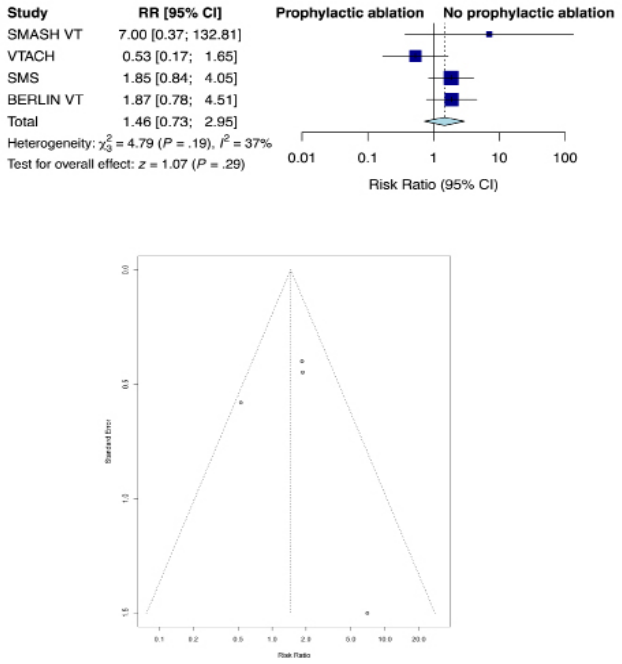


Figure 7a and 7b: **Adverse events. The Forest plot shows the outcomes of the individual trials as well as the aggregate. Point estimates to the left favor prophylactic catheter ablation. The Funnel plot demonstrates no publication bias.**

procedure success that could have impacted clinical outcomes; 5) The BERLIN VT study excluded patients with LVEF ≤ 30%, with a higher mean LVEF of 41% compared to other three trials which could have influenced the outcomes in our analysis (given that these are potentially different patient populations). Finally, there was substantial cross-cover among the trials, which can affect our study results. Further randomized trials on the timing of VT ablation and cost-effectiveness will shed more light on the impact of prophylactic VT ablation versus deferred approach. Despite these limitations, our study provides valuable clinical insights on the role of prophylactic VT ablation without any increased mortality risk.

Despite two decades since the first patient enrollment for prophylactic VT ablation strategy, this has not gained popularity in clinical practice. Current guidelines recommend ablation following the first VT episode regardless of antiarrhythmics [11]. This is conceivably primarily driven by increased susceptibility to procedure-related complications (and nature of complications) with the prophylactic ablation approach. Improved procedure techniques (intracardiac echo, mapping systems), and better catheter design (e.g., force sensing catheters, high power short duration ablation) could potentially circumvent these issues. Nevertheless, in our study, the prophylactic VT ablation approach was associated with reduced ICD therapies and ICD shock, without any increased risk of acute procedural complications and all-cause mortality. However, the decision for prophylactic VT ablation should be equipoised with patient comorbidities and hemodynamics.

Conclusion

Prophylactic catheter ablation in eligible patients with ischemic cardiomyopathy was associated with reduced risk of appropriate ICD therapies, including ICD shocks and VT storm with no difference in all-cause mortality compared with "No PCA" approach. Preventive ablation should not be routinely recommended but can be considered in patients with high-risk of VT burden and ICD therapies.

Click for Supplement Tables

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