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ELECTROPHYSIOLOGY

Meta-analysis comparing outcomes of catheter ablation for ventricular arrhythmia in ischemic versus nonischemic cardiomyopathy

Indranill Basu-Ray MD[1,2,3,*] | Dibbendhu Khanra MD, DM[4,*] | Sumit K. Shah MD[5] | Anindya Mukherjee MD[6] | Sudhanva V. Char PhD[7] | Bhavna Jain MD[4] | T. Jared Bunch MD[8] | Michael Gold MD[9] | Adedayo A. Adeboye MD[1] | Mohammad Saeed MD[9,10]

[1] Department of Cardiology, Memphis VA Medical Center, 1030 Jefferson Ave, Memphis, TN 38104

[2] School of Public Health, The University of Memphis, Memphis, TN, USA

[3] Dept of Cardiology, All India Institute of Medical Sciences, Rishikesh, UK, India

[4] Department of Cardiology, Heart and Lung Centre, New Cross Hospital, Royal Wolverhampton NHS Trust, Wolverhampton, UK

[5] Department of Cardiology, University of Arkansas for Medical Sciences, Little Rock, Arkansas

[6] Department of Cardiology, NRS Medical College, Kolkata, India

[7] Department of Cardiology, Life University, Marietta, Georgia

[8] Department of Cardiology, University of Utah Hospital, University of Utah School of Medicine, Salt Lake City, Utah

[9] Department of Cardiology, Medical University of South Carolina, Charleston, South Carolina

[10] Department of Cardiology, Baylor College of Medicine, Houston, Texas

Correspondence
Indranill Basu-Ray, MD, Department of Cardiology, Memphis VA Medical Center, 1030

Abstract

Background: Catheter ablation is an effective treatment for ventricular arrhythmia (VA) in ischemic cardiomyopathy (ICM). However, results in non-ICM (NICM) patients are not satisfactory, and studies comparing differences between NICM and ICM are limited. We conducted a meta-analysis of procedural characteristics and long-term outcomes of catheter ablation for VA, comparing results between ICM and NICM.

Methods: Studies in the PubMed, EMBASE, and Cochrane databases were systematically reviewed. Four studies reporting comparison of catheter ablation of VA between ICM and NICM were examined. The Newcastle-Ottawa Scale was used to appraise study quality. A random-effects model with inverse variance method was used for comparisons.

Results: Epicardial approach was significantly more undertaken for the NICM group than in the ICM group (odds ratio [OR]: 0.13; 95% confidence interval [CI]: 0.09-0.18; $P < .00001$). Mean ablation time ($P = .54$), fluoroscopy time ($P = .55$), and procedural time ($P = .18$) did not differ significantly between the ICM and NICM groups. Procedural failure rates (OR: 0.46; 95% CI: 0.24-0.89; $P = .02$) and VA recurrence rates (risk ratio [RR]: 0.68; 95% CI: 0.46-1.01; $P = .06$) were significantly higher in the NICM group than in the ICM group. However, all-cause mortality (RR: 1.37; 95% CI: 0.75-2.49; $P = .31$) did not differ significantly between groups.

Conclusions: Procedural failure and VA recurrence rates were significantly higher in the NICM group, despite significantly more frequent epicardial access. These highlight the limitations of catheter ablation for VA in NICM, given our current knowledge.

Abbreviations: AAD, antiarrhythmic drug; AR, attributable risk; CI, confidence interval; CRT, cardiac resynchronization therapy; ICD, implantable cardiac defibrillator; ICM, ischemic cardiomyopathy; NICM, nonischemic cardiomyopathy; OR, odds ratio; RR, risk ratio; VA, ventricular arrhythmia; VT, ventricular tachycardia.

Jefferson Avenue, Suite G401 A, Memphis, TN 38104.
Email: indranill.basu-ray@va.gov

*Both the authors Indranill Basu-Ray and Dibbendhu Khanra contributed equally to this work and are joint first authors.

KEYWORDS
cardiomyopathy, ischemic heart disease, pacing and electrophysiology

1 | INTRODUCTION

Ventricular arrhythmia (VA) in patients with cardiomyopathy has traditionally been managed with antiarrhythmic drugs (AADs). However, effectiveness of AADs can be limited by patient noncompliance in response to side effects and drug-drug interactions. Implantable cardiac defibrillators (ICDs) are another treatment option for patients with ischemic cardiomyopathy (ICM). Multiple randomized controlled trials have shown improved survival rates in ICM patients who received ICDs for inducible ventricular tachycardia (VT).[1,2] Recently, catheter ablation has become a viable treatment alternative for VAs in patients with ICM in contemporary electrophysiological practices worldwide, thanks to advances in ablation catheter tools, mapping technologies, and ablation strategies.[3,4] Studies have suggested that catheter ablation lowers the risk for VA recurrences, prolongs survival rates, and reduces long-term healthcare costs, compared to AAD therapy.[5–7]

VAs in ICM commonly originate from the relatively fixed, well-defined left ventricular endocardial substrate.[8] Conversely, VAs in non-ICM (NICM) are more likely to originate from the epicardial region or from the right ventricle.[3,4] ICM patients with VA are more likely than NICM patients with VA to be considered appropriate candidates for catheter-based treatment after ICD shock, given that the evidence supporting ICD therapy in NICM is sparse, compared with that for ICM.[9,10] This, along with the limited effectiveness of AADs in NICM patients with VA, makes catheter ablation an option worth exploring.[11] Nonetheless, the success of catheter ablation of VA in NICM patients is limited by the heterogeneous nature of the epicardial substrate, which could lead to higher VA recurrence rates.[8,12] Because of this ambiguity, long-term outcomes for catheter ablation in patients with NICM need further exploration.

Comparing catheter ablation safety and effectiveness outcomes in ICM patients with VA versus NICM patients with VA would undoubtedly shed more light on the effectiveness of the intervention. However, few studies have attempted such comparisons; existing studies are cross-sectional and compromised by relatively small sample sizes, short follow-up periods, various ablation strategies, few reported event outcomes, and conflicting results.[13-22] To address this issue and to systematically assess and synthesize the results of previous studies, we conducted this first meta-analysis comparing outcomes of catheter ablation for VA in ischemic versus NICM.[22]

2 | METHODS

2.1 | Search strategy

We performed a systematic review for literature published till March 2020. Physician-reviewers Dibbendhu Khanra and Sumit K. Shah searched PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) databases for relevant literature using "VT," "VA," "catheter ablation," "radiofrequency ablation," "structural heart disease," "ICM," "NICM," and combinations of these as the search keywords. References of selected articles were searched for additional literature. Discrepancies were resolved by a third reviewer (Indranill Basu-Ray).

2.2 | Study selection

For the meta-analysis, we selected studies that directly compared periprocedural or long-term effectiveness outcomes data for catheter ablation of VA in ICM versus NICM. Studies that involved catheter ablation of VA in structurally abnormal hearts but that did not separately report outcomes data for each cardiomyopathy type were excluded. Single-arm studies, case reports, case series, and cohort studies that had fewer than 10 patients or that did not present adequate safety or effectiveness outcomes data were also excluded (Figure 1).

2.3 | Data extraction

The data isolated from the studies included sample size (numbers of patients in the ICM and NICM groups); baseline demographics such as age and sex; and clinical data such as left ventricular ejection fraction, presence of ICD or cardiac resynchronization therapy (CRT) devices, New York Heart Association functional status, and mean number of failed AADs. Procedural data included ablation details, procedural failures, and complications; clinical outcomes data included VA recurrence and mortality.

2.4 | Primary outcomes

The primary outcomes were long-term results, such as all-cause mortality and VA recurrence, by cardiomyopathy type (ICM versus NICM).

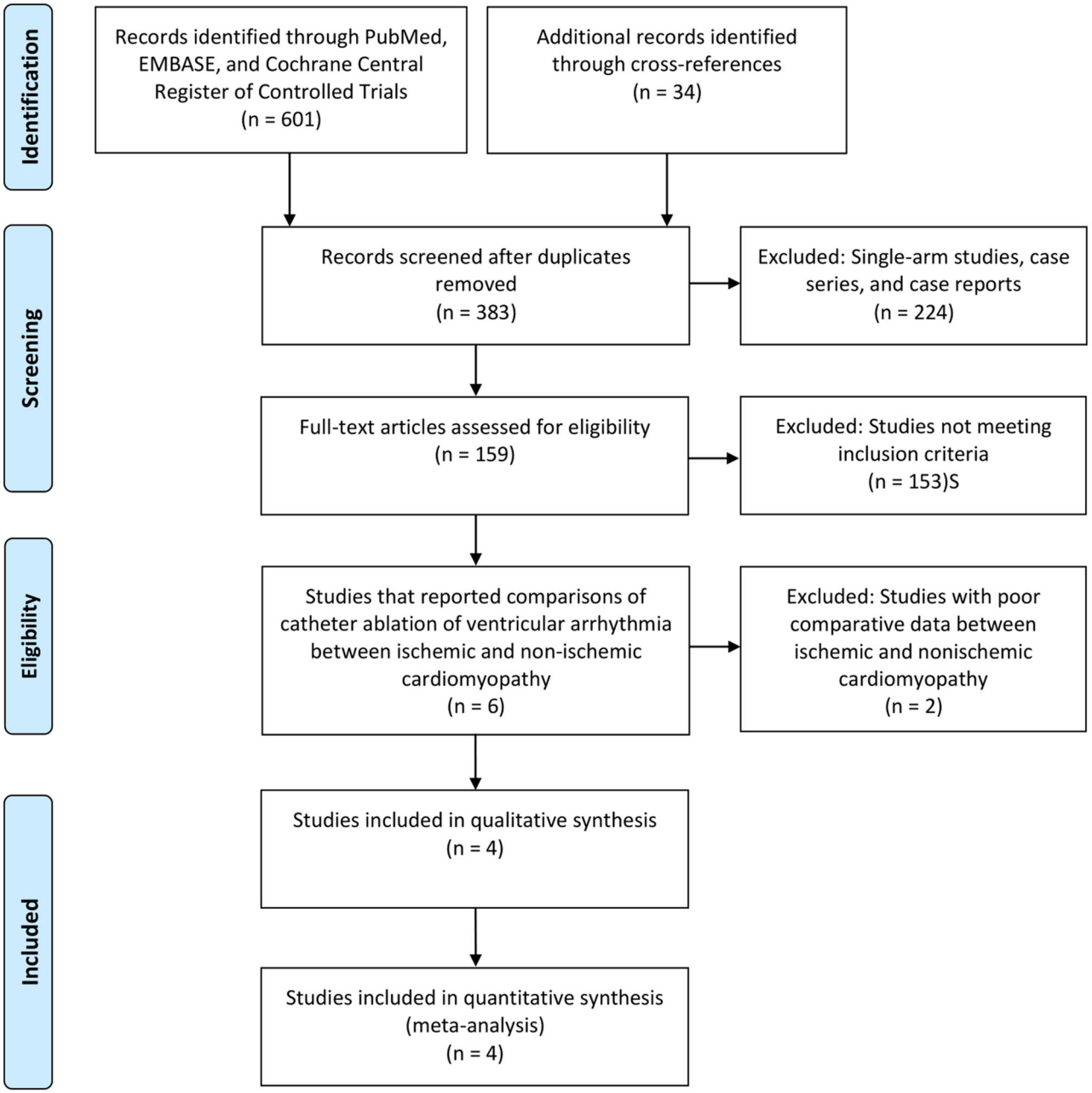

FIGURE 1 PRISMA flow diagram: Schematic of systematic literature search [Color figure can be viewed at wileyonlinelibrary.com]

2.5 | Quality assessment

The Newcastle-Ottawa Scale was used to assess the quality of studies included in the meta-analysis.[23] Good quality is indicated by 3-4 points in the selection domain, 1-2 points in the comparability domain, and 2-3 points in the outcome domain (for an overall rating of 6-9 points). Quality scaling paired with star ratings helps ensure the representative character of the studies as well as the comparability of any nonrandomized studies included in the meta-analysis.

For this study, we used a version of the scale that was customized for assessing comparability in cohort studies.[22] Three benchmark norms were included in the analysis: (a) selection criteria (representativeness of the exposed cohort, selection of the nonexposed cohort, ascertainment of the exposure, demonstration that the outcome of interest was not present at start of study); (b) cohort comparability; and (c) outcomes criteria (assessment of outcome, length and adequacy of follow-up).

2.6 | Data analysis and synthesis

Statistical analyses were performed using Review Manager (RevMan version 5.3, the Cochrane Collaboration, London, United Kingdom, 2014). Odds ratios (ORs) or risk ratios (RRs), as appropriate, were used

TABLE 1 Comparison of study parameters, demographic data, and clinical data included in the meta-analysis

Points	Dinov et al		Goya et al		Kumar et al		Muser et al	
	ICM (n = 164)	NICM (n = 63)	ICM (n = 51)	NICM (n = 19)	ICM (n = 358)	NICM (n = 239)	ICM (n = 196)	NICM (n = 71)
Study parameters								
Design	Cohort		Cohort		Cohort		Cohort	
Follow up, months	27(16-37)	20(16-36)	41 ± 29	35 ± 28	72(36-108)		45(9-71)	
Last planned follow-up, years	3	3	5	5	9	6	6	5
Demographic data								
Age, years	67 ± 10*	59 ± 14*	70 ± 12*	60 ± 16*	67 ± 10*	52 ± 14*	67 ± 11*	60 ± 15*
Male sex	142 (88.4)	52 (82.5)	45 (88)	16 (84)	86* (24)	79* (33.1)	184 (94)	62 (87)
Clinical data								
LVEF percentage	32 ± 11	34 ± 11	33 ± 10	34 ± 10	28 ± 12*	40 ± 17*	28 ± 12*	32 ± 14*
NYHA stage III or IV	91 (63.2)	34 55.7)	NA	NA	56 (15.6)	58 (24.3)	66 (34)	33 (47)
Failed AADs	NA	NA	NA	NA	3 ± 1*	2 ± 1*	2 (1-2)	2 (1-2)
ICD in situ (±CRT)	149 (90.9)	60 (95.2)	43* (84)	19* (100)	110* (30.7)	89* (37.2)	196 (100)	71 (100)

Categorical values are in numbers (n) and (percentage), continuous data, as median (interquartile range), or mean ± standard deviation.
*Between-group differences are statistically significant at $P < .05$.
Abbreviations: CRT, cardiac resynchronization therapy; ICD, implantable cardiac defibrillator; ICM, ischemic cardiomyopathy; LVEF, left ventricular ejection fraction; NA, not available; NICM, nonischemic cardiomyopathy; NYHA, New York Heart Association.

to pool differences in binary events, and mean differences with standard deviations were used to pool differences in continuous outcomes. The random effects model of DerSimonian and Laird was used. To minimize imprecision of the estimate of pooled effects, inverse variance methods were used to calculate effect sizes for both continuous and dichotomous data.[24,25]

Heterogeneity was assessed by I^2 statistics. Funnel plots were drawn to determine publication bias.[26,27] Sensitivity analyses were conducted for variables with high heterogeneity. Bivariate analysis and meta-regression modeling were conducted using R Software (version 3.5.1, package "metabin") to explain the heterogeneity of the primary outcome variable with statistical significance and to construct a bubble plot.[28]

3 | RESULTS

Of the six studies that reported outcomes of catheter ablation for VA in ICM and NICM groups, four cohort studies meeting the inclusion criteria and comprising 769 ICM patients and 410 NICM patients were selected for the meta-analysis (Figure 1).[14–19] Two studies by Tilz et al and Tung et al did not separately report data on ICM and NICM and were therefore excluded.[18,19] The four included studies scored at least 6 points on the customized Newcastle-Ottawa Scale (Table S1), indicating good quality.

3.1 | Comparisons of study parameters, demographic data, and clinical data

Comparisons of the study parameters, demographic data, and clinical data from the four studies are summarized in Table 1. The median follow-up duration of the studies ranged from 20 months to 72 months. The ICM cohort was significantly older than the NICM cohort (67.9 years vs 57.7 years, respectively, $P < .001$) and trended toward lower mean left ventricular ejection fraction (mean difference [95% CI] −4.52%, where CI is confidence interval, [−10.64-1.59%], $P = .15$). Despite the higher mean ejection fraction in the NICM group, a greater proportion of these patients had advanced heart failure (New York Heart Association stage III or IV) (190 vs 111, respectively, $P = .26$) and an existing ICD with or without CRT (455 vs 220, respectively, $P = .06$). In both cohorts, most patients had at least two failed attempts of VA management with AADs before catheter ablation was undertaken. The clinical VT cycle length was similar for both the ICM and the NICM cohorts (mean difference [95% CI] 4.16 milliseconds [−39.40-47.71 milliseconds], $P = .85$).

3.2 | Comparisons of procedural data and long-term outcomes

Comparisons of the procedural parameters and long-term outcome data are presented in Table 2 and Figure 2.

TABLE 2 Comparisons of procedural data and long-term outcomes

	Dinov et al		Goya et al		Kumar et al		Muser et al	
Points	ICM(n = 164)	NICM(n = 63)	ICM(n = 51)	NICM(n = 19)	ICM(n = 358)	NICM(n = 239)	ICM(n = 196)	NICM(n = 71)
Procedural data								
Mean fluoroscopy time, minutes	26 ± 19*	39 ± 22*	NA	NA	45 ± 30	43 ± 22	61 ± 31	59 ± 15
Mean ablation time, minutes	NA	NA	NA	NA	33 ± 22*	25 ± 22*	67 ± 36	78 ± 128
Mean procedure time, minutes	155 ± 49*	181 ± 64*	NA	NA	NA	NA	480 ± 120	480 ± 120
Clinical TCL, milliseconds	385 ± 93	364 ± 86	375 ± 80*	431 ± 88*	NA	NA	417 ± 98*	382 ± 94*
Epicardial approach	2* (1.2)	19* (30.2)	4* (7.8)	9* (47.4)	30* (8)	71* (30)	2*	19*
Substrate mapping	147* (89.6)	42* (66.7)	41 (80.4)	13 (68.4)	NA	NA	NA	NA
Procedural failure	8 (4.9)	7 (11.1)	2* (4)	0* (0)	9 (2.5)	13(5.4)	66*	27*
Amiodarone after procedure	69 (42)	21 (33)	NA	NA	NA	NA	69 (35)	21 (30)
Complications	18 (11.1)	7 (11.1)	NA	NA	39 (8.3)	23 (6.7)	7 (3)	4 (3)
Long-term outcomes data								
All-cause mortality	13 (7.9)	8 (12.7)	15	1	186 (52)	62 (26)	57 (29)	19 (27)
VA recurrence	93* (57)	49* (77)	15* (29)	8* (42.1)	165* (46)	110* (62)	54 (27.6)	48 (67.6)

Categorical values are in numbers (n) and percentage, continuous variables as mean ± standard deviation.
*Between-group differences are statistically significant at $P < .05$.
Abbreviations: ICM, ischemic cardiomyopathy; NA, not available; NICM, nonischemic cardiomyopathy; TCL, tachycardia cycle length; VA, ventricular arrhythmia.

An epicardial approach was significantly more likely to be adopted for the NICM group than in the ICM group (OR: 0.13; 95% CI: 0.09-0.18; $P < .00001$), whereas substrate mapping was performed significantly more often in the ICM group than in the NICM group (OR: 3.29; 95% CI: 1.54-7.05; $P < .002$). Among the other procedural parameters, mean ablation time (−4.77 minutes; 95% CI: −20.00-10.46 minutes; $P = .54$), fluoroscopy time (−2.76 minutes; 95% CI:−11.74-6.22 minutes; $P = .55$), and procedural time (−16.78 minutes; 95% CI: −41.16-7.60 minutes; $P = .18$) did not differ significantly between the ICM and NICM groups.

Total procedural complications did not differ significantly between the ICM and NICM cohorts (OR: 1.03; 95% CI: 0.66-1.60; $P = .9$), despite higher rates of epicardial access in the NICM group. The procedural failure rate was significantly higher in the NICM group, approximately double that of the ICM group (OR: 0.46; 95% CI: 0.24-0.89; $P = .02$). The uncorrected failure rates were 3.31% for the ICM group and 6.23% for the NICM group.

Although VA recurrence was significantly more common in the NICM group than in the ICM group (RR: 0.68; 95% CI: 0.46-1.01; $P = .06$), amiodarone use after catheter ablation was similar across groups (OR: 0.93; 95% CI: 0.48-1.79; $P = .82$). Similarly, all-cause mortality was not significantly different between the ICM and NICM groups (RR: 1.37; 95% CI: 0.75-2.49; $P = .31$).

3.3 | Study heterogeneity

Outcomes of epicardial approach and VA recurrences had high heterogeneity, as evidenced by $I^2 > 50\%$. We therefore prepared funnel plots for these outcomes to examine publication bias (Figure S1). However, because fewer than 10 studies were included in the meta-analysis, the test's power may have been too low to detect true asymmetry from chance, and thus no definitive inference can be drawn.[28] Although a random effects model was used, and sensitivity analyses were performed for these two outcome variables, none of the studies included in the analyses contributed to major heterogeneity.

For VA recurrence, heterogeneity was denoted by $I^2 > 90\%$. However, tau^2, which is a direct estimation of inconsistency, was low (0.14).[29] Because of the variable length of follow-up and a high chi-square value (28.2), we constructed a bubble plot of VA recurrences with respect to maximum duration of follow-up (Figure S2). Follow-up duration did not affect the VA recurrence rate in the meta-regression model.

4 | DISCUSSION

To our knowledge, this is the first meta-analysis comparing procedural characteristics and long-term outcomes of catheter ablation for

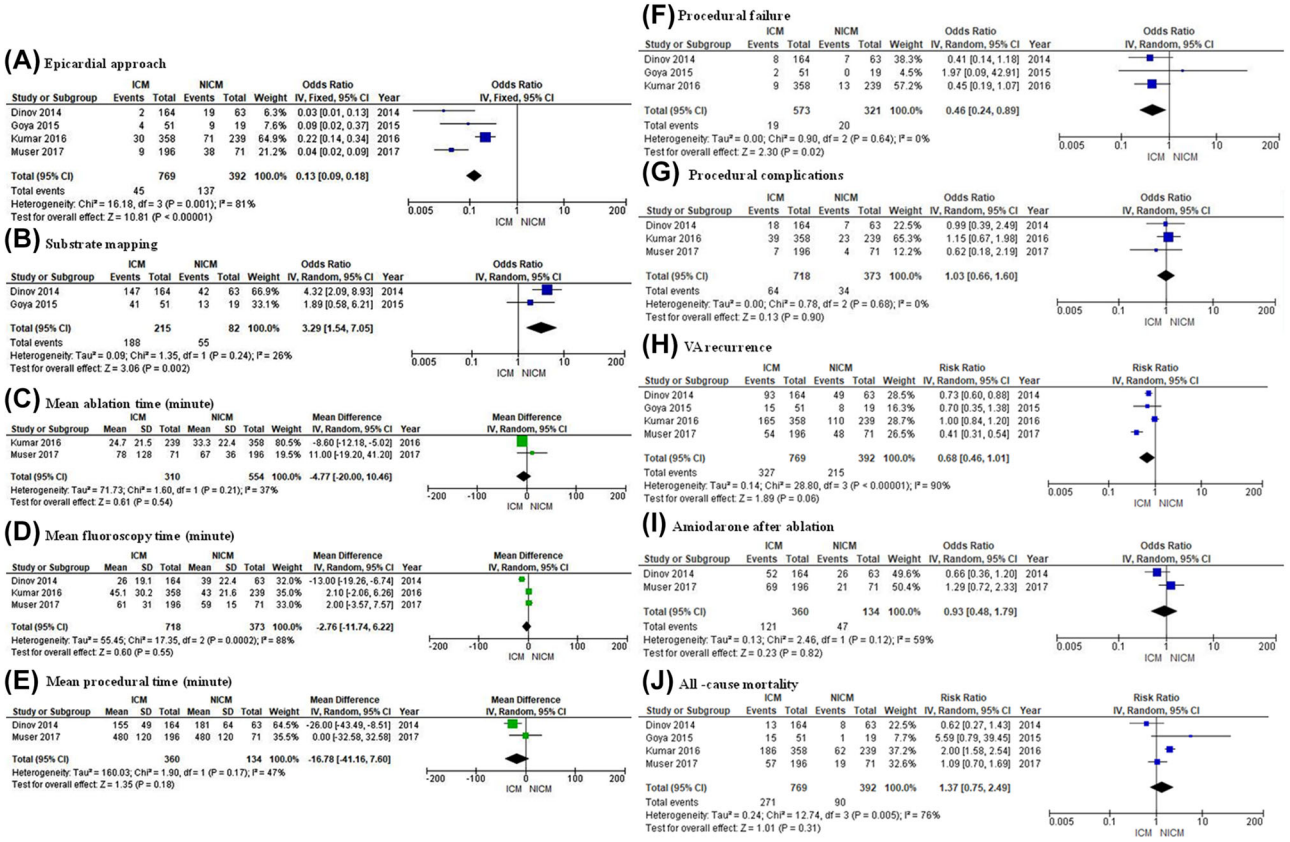

FIGURE 2 Forest plots comparing characteristics of the studies included in the meta-analysis and long-term clinical outcomes
Abbreviations: CI, confidence interval; ICM, ischemic cardiomyopathy; IV, inverse variance method; NICM, nonischemic cardiomyopathy; SD, standard deviation
[Color figure can be viewed at wileyonlinelibrary.com]

VA in both ICM and NICM patients. The main findings of the analysis are that NICM had lower acute and long-term success rates compared with ICM. In addition, procedural aspects of catheter ablation vary by substrate, with epicardial access more commonly employed in NICM patients and substrate mapping more commonly performed in ICM patients.

4.1 | Baseline characteristics

Critical baseline characteristics at the time of catheter ablation differed by cardiomyopathy type. Patients with NICM had worse functional status, despite being younger and having better left ventricular systolic function, compared with the ICM group. Higher rates of ICD with or without CRT in the NICM group may reflect more advanced disease and worse functional status. All of these factors influence presentation, referral patterns for move advanced therapies, and as a consequence response to both AADs and catheter ablation.

NICM patients commonly have less cardiovascular comorbidity. This was shown in the study by Muser et al, in which patients with NICM had significantly less hypertension, diabetes, hyperlipidemia, and atrial fibrillation or flutter.[17] Patients with VA included in our analysis had already been on two or more AADs before catheter ablation was performed. In a study by Frankel et al, approximately two-thirds of NICM patients were referred late for catheter ablation, after amiodarone escalation and multiple VA episodes.[30] In the present study, NICM patients were younger than ICM patients, and this may reflect a need for earlier referral due to cardiomyopathy progression and decline in functional status.

4.2 | Procedural characteristics

Most studies have used standard programmed electrical stimulation of the left ventricle from the right ventricle to induce faster VT, with up to triple extra stimuli having at least two drive cycle lengths for arrhythmia induction. In our analysis, we observed some variance in induction approaches: Goya et al used just two extra stimuli; in the study by Muser et al, 52% of patients underwent a repeat noninvasive programmed stimulation 2-4 days after catheter ablation to induce residual VA.[15,17]

For patients with NICM, the endocardial substrate can be limited and may not reflect disease severity or arrhythmia risk. In the study by Dinov et al, activation and entrainment mapping were performed in patients with hemodynamically stable VA.[14] Goya et al also mapped and ablated stable VA during arrhythmia; unstable VA was

mapped during sinus rhythm or by substrate modification.[15] Muser et al did voltage-based substrate mapping in their sample of patients with electrical storm, due to the instability of arrhythmia-based mapping.[17] Similar substrate mapping was also used by Kumar et al, but key data were not presented in that manuscript.[16] Ablation strategies based on substrate delineation, late-potential ablation, and scar modification are not always applicable in NICM, given the heterogeneity of the disease and the lack of endocardial substrate. Kumar et al reported that 25% (91/358) of ICM patients and 27% (78/289) of NICM patients underwent more than one VA ablation procedure.

Procedural time was longer for the NICM group than for the ICM group, but the difference was not statistically significant. Overall, the longer procedure times in the NICM group might be explained by more frequent utilization of an epicardial approach and the presence of heterogeneous substrate. Mean procedure time in Muser et al was greater than that in Dinov et al, probably because all patients of Muser et al underwent substrate mapping as a consequence of having presented in electrical storm.[14,17] General anesthesia was used in one-third of those patients, and ablation time was longer.

The standard access to the left ventricle was retrograde across the aortic valve in the study by Goya et al and antegrade via a transseptal puncture in Dinov et al.[14,15] Fluoroscopy time was significantly higher in the NICM group than in the ICM group in Dinov et al.[14] However, overall fluoroscopy time was not significantly different among both the groups in our meta-analysis, with a mean difference of −2.76 minutes.

Ablation time was significantly longer in the ICM group than the NICM group in the study by Kumar et al, as radiofrequency applications were repeated in target areas until they were rendered electrically unexcitable, with unipolar pacing at 10 milliamps and a 2-millisecond pulse width.[16] Ablation time was longer in the study by Muser et al, as all patients presented with electrical storm, and ablation time was increased to >3 minutes at sites associated with transient VT suppression.[17]

In a recent meta-analysis by Romero et al, a combination approach comprising endocardial and epicardial mapping and ablation was associated with a lower risk for VA recurrence, compared with endocardial approaches alone.[31] In that meta-analysis, sensitivity analysis suggested a lower risk when a combination approach was used in patients with ICM (RR: 0.43) and in patients with arrhythmogenic right ventricular cardiomyopathy (RR: 0.59), compared with NICM patients (RR: 0.87). The combination approach also significantly increased procedural risk (RR: 2.62).[31] However, our current aggregate data did not show that a combination approach improved outcomes in NICM patients to the degree that they would be similar to ICM patients. Although the complication rate did not increase, procedural time was lengthened.

Kumar et al related procedural failure to long-term VA recurrence risk and all-cause mortality in the ICM and NICM groups.[16] In the study by Goya et al, acute success was achieved in all NICM patients.[15] Muser et al reported that at least one VT with cycle length >250 milliseconds was inducible in 26% of patients with ICM and in 32% of patients with NICM.[17] In multivariable analysis, inducibility of any VT with a cycle length >250 milliseconds at the end of the procedure was the only variable independently associated with VT recurrence during follow-up. In Dinov et al, procedural failure or partial success was associated with VA recurrence in both the ICM and NICM groups.[14] Overall, procedural failures were significantly more frequent in NICM patients than in ICM patients and were consistent with unhealthier long-term outcomes. Tau^2 and I^2 were 0, and chi-square was 0.90, which was relatively low given the large sample size (769 NICM patients and 410 ICM patients). Thus, the heterogeneity factor is likely not of importance.

The HELP VT trial found no significant differences in procedure-related complications between the two groups.[15] In ICM subjects the most common major complication was access-related (4.8%), followed by worsening of heart failure (1.8%), third degree atrio-ventricular block (1.2%) and pneumonia or acute respiratory distress syndrome (3.2%). Muser et al reported pericardial effusion (2.6%) as the commonest complication among ICM subjects and coronary artery occlusion (2.8%) as the most frequent complication in NICM group.[16] Kumar et al also did not find any significant difference in complications between the two groups.[17] Overall, our meta-analysis also did not report any significant difference in complications between the two groups.

4.3 | Long-term outcomes

Mortality data were extracted either from reported study results or from Kaplan-Meier survival curves. Overall, mortality trended higher in the ICM group compared with the NICM group but did not reach statistical significance. Although the 1.37 relative risk indicates a 37% greater risk in the ICM group, this needs to be considered cautiously, as the *P*-value for the overall effect was .31. This may be explained in part by the relatively older age and the more-severe left ventricular dysfunction in the ICM cohort and the higher use of ICD with or without CRT in the NICM group. Other factors that may provide insight into the higher ICM mortality rate are race or ethnic composition, economic status, genetic make-up, and lifestyle, which at times may be factored into Kaplan-Meier estimations of survival. Further, the morphological substrate for ICM is often fixed, whereas in NICM there are multiple factors that lead to the progression and modification of the arrhythmia substrate over time.[8,15] Although VT ablation can successfully modify the existing substrate at the time of the procedure, it generally will not impede disease progression or the formation of new substrates or new triggers.

Calculating the attributable risk (AR) is another approach to evaluating mortality rates. AR is the difference in the probabilities of mortality between two groups. The RR of 1.37 for all-cause mortality takes into account the weights attached to each one of the four studies. If RR were computed using the raw data for all-cause mortality, the probability of mortality would be .3524 in ICM and .2295 in NICM. The difference between these two probabilities is .1229; the other variables were considered to be equal, and factors modifying arrhythmia substrates were ignored. This means that 12.29% of the reduction in mortality could be attributed to the intervention factor in the NICM group.

AR can also be measured by the etiological fraction, according to the following formula: etiological fraction = ($Mortality_{ICM}$

– $Mortality_{NICM}$)/$Mortality_{ICM}$. By this formula, the etiological fraction is 34.88%, somewhat conspicuous if the observer does not keep in mind the confounding factors touched on above. The AR point could be a muddling influence in decision making about VA in NICM vis-à-vis ICM, unless eliminated by alluding to the considerable heterogeneity features.

Long-term VA recurrences can reflect not only procedural effectiveness, but also the disease state.[13,32] In this analysis, amiodarone was prescribed similarly after catheter ablation of VA in both the ICM and NICM groups, such that the arrhythmia-related outcomes are comparable. To improve catheter ablation approaches for those with NICM, patients will need to be further categorized by specific type of NICM, because the underlying mechanisms vary greatly; analysis results can then be compared. Of note, exercised abundant caution in interpreting the outcomes data is presented in Table 2, so as to avoid Type I (α) or Type II (β) errors.

4.4 | Study limitations

This study should be interpreted in light of certain methodological limitations. The number of studies is small, and the study of Kumar et al contributed the lion share of patients. This is particularly problematic since it seems that ablation was the primary treatment strategy in Kumar et al, because most of the patients in that series did not have an ICD. This issue is particularly important since, in majority of cases, ablation is not pursued as a primary treatment strategy except in patients with VT and otherwise normal hearts. Baseline characteristics of the ICM and NICM cohorts were not similar in the meta-analysis. No uniform mapping or ablation protocol was followed across the studies, and follow-up periods were variable. The I^2 value was 90% in the analysis of VA recurrence data. Subgroup analysis or meta-regression analysis could not be completed due to lack of data; similarly, funnel plots could not be interpreted formally due to the small number of studies.

5 | CONCLUSIONS

Despite significantly longer procedural times for catheter ablation in NICM, procedural failures and VA recurrences were significantly more common in that group which may be attributed to heterogeneous substrate, unpredictable disease progression, and widely varying underlying mechanisms. These aggregate procedural characteristics and their associated outcomes highlight the limitations of catheter ablation for NICM, given our current knowledge and tools. The mortality trend we observed in ICM patients probably reflected their older age, more-advanced left ventricular systolic dysfunction, and less-frequent use of ICD or CRT. Prospective studies are needed to address short- and long-term outcomes of catheter ablation of VA in NICM patients, with further definition of their cardiomyopathy subtype and adequate follow-up duration.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

ORCID

Indranill Basu-Ray MD https://orcid.org/0000-0003-0961-0588

REFERENCES

1. Buxton A, Lee KL, Fisher JD, et al. A randomized study of the prevention of sudden death in patients with coronary artery disease. *N Engl J Med*. 1999;341:1882-1890.
2. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002;346:877-883.
3. Turagam MK, Atkins D, Tung R, et al. A meta-analysis of manual versus remote magnetic navigation for ventricular tachycardia ablation. *J Interv Card Electrophysiol*. 2017;49:227-235.
4. Turagam M, Iskandar S, Lavu M, et al. A meta-analysis of substrate modification versus clinical ventricular tachycardia ablation in structural heart disease. *Circulation*. 2016;134(suppl_1):A15975.
5. Atti V, Vuddanda V, Turagam MK, et al. Prophylactic catheter ablation of ventricular tachycardia in ischemic cardiomyopathy: a systematic review and meta-analysis of randomized controlled trials. *J Interv Card Electrophysiol*. 2018;53:207-215.
6. Sapp JL, Wells GA, Parkash R, et al. Ventricular tachycardia ablation versus escalation of antiarrhythmic drugs. *N Engl J Med*. 2016;375:111-121.
7. Coyle K, Coyle D, Nault I, et al. Cost effectiveness of ventricular tachycardia ablation versus escalation of antiarrhythmic drug therapy: the VANISH trial. *JACC Clin Electrophysiol*. 2018;4:660-668.
8. Liang JJ, Santangeli P, Callans DJ. Long-term outcomes of ventricular tachycardia ablation in different types of structural heart disease. *Arrhythm Electrophysiol Rev*. 2015;4:177-183.
9. Kadish A, Dyer A, Daubert JP, et al. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. *N Engl J Med*. 2004;350:2151-2158.
10. Køber L, Thune JJ, Nielsen JC, et al. Defibrillator implantation in patients with nonischemic systolic heart failure. *N Engl J Med*. 2016;375:1221-1230.
11. Thompson N, Frontera A, Takigawa M, et al. Catheter ablation for ventricular tachycardia in patients with nonischemic cardiomyopathy. *Card Electrophysiol Clin*. 2017;9:47-54.
12. Deyell MW, Callans DJ. How we ablate ventricular tachycardia in nonischemic, left ventricular cardiomyopathy. *J Innov Card Rhythm Manag*. 2011;2:558-565.
13. Vaseghi M, Hu TY, Tung R, et al. Outcomes of catheter ablation of ventricular tachycardia based on etiology in nonischemic heart disease: an international ventricular tachycardia ablation center collaborative study. *J Am Coll Cardiol EP*. 2018;4:1141-1150.
14. Dinov B, Fiedler L, Schönbauer R, et al. Outcomes in catheter ablation of ventricular tachycardia in dilated nonischemic cardiomyopathy compared with ischemic cardiomyopathy: results from the Prospective Heart Centre of Leipzig VT (HELP-VT) study. *Circulation*. 2014;129:728-736.
15. Goya M, Fukunaga M, Hiroshima K, et al. Long-term outcomes of catheter ablation of ventricular tachycardia in patients with structural heart disease. *J Arrhythm*. 2015;31:22-28.

16. Kumar S, Romero J, Mehta NK, et al. Long-term outcomes after catheter ablation of ventricular tachycardia in patients with and without structural heart disease. *Heart Rhythm*. 2016;13:1957-1963.
17. Muser D, Liang JJ, Pathak RK, et al. Long-term outcomes of catheter ablation of electrical storm in nonischemic dilated cardiomyopathy compared with ischemic cardiomyopathy. *JACC Clin Electrophysiol*. 2017;3:767-778.
18. Tilz RR, Lin T, Eckardt L, et al. Ablation outcomes and predictors of mortality following catheter ablation for ventricular tachycardia: data from the German multicenter ablation registry. *J Am Heart Assoc*. 2018;7:07045.
19. Tung R, Vaseghi M, Frankel DS, et al. Freedom from recurrent ventricular tachycardia after catheter ablation is associated with improved survival in patients with structural heart disease: an International VT Ablation Center Collaborative Group study. *Heart Rhythm*. 2015;12:1997-2007.
20. Della Bella P, Brugada J, Zeppenfeld K, et al. Epicardial ablation for ventricular tachycardia: a European multicenter study. *Circ Arrhythm Electrophysiol*. 2011;4:653-659.
21. Wissner E, Stevenson WG, Kuck KH. Catheter ablation of ventricular tachycardia in ischaemic and non-ischaemic cardiomyopathy: where are we today? A clinical review. *Eur Heart J*. 2012;33:1440-1450.
22. Basu Ray I, Khanra D, Duggal B, et al. Abstract S-PO06-082: a comparison of outcomes of catheter ablation (CA) for ventricular arrhythmias (VA) in ischemic cardiomyopathy (ICMP) vs non-ischemic cardiomyopathy (NICMP): a meta-analysis of cohort studies (abstr). Heart Rhythm Society 40th Scientific Sessions; May 8–11, 2019; San Francisco CA. *Heart Rhythm*. 2019;16:S555-S556.
23. Wells GA, Shea B, O'Connell D, et al. *The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses*. 2019. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed November 21, 2019.
24. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177-188.
25. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339:b2535.
26. Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw*. 2010;36:1-48.
27. Rücker G, Schwarzer G, Carpenter J. Arcsine test for publication bias in meta-analyses with binary outcomes. *Stat Med*. 2008;27:746-763.
28. Knapp G, Hartung J. Improved tests for a random effects meta-regression with a single covariate. *Stat Med*. 2003;22:2693-2710.
29. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557-560.
30. Frankel DS, Tung R, Santangeli P, et al. Sex and catheter ablation for ventricular tachycardia: an International Ventricular Tachycardia Ablation Center Collaborative Group study. *JAMA Cardiol*. 2016;1:938-944.
31. Romero J, Cerrud-Rodriguez RC, Di Biase L, et al. Combined endocardial-epicardial versus endocardial catheter ablation alone for ventricular tachycardia in structural heart disease: a systematic review and meta-analysis. *JACC Clin Electrophysiol*. 2019;5:13-24.
32. Okubo K, Gigli L, Della Bella P. Catheter ablation of ventricular tachycardia in nonischemic cardiomyopathy. *J Arrhythm*. 2018;34:347-355.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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