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ORIGINAL RESEARCH

Catheter Ablation for Ventricular Tachycardia in Patients With Biopsy-Proven Myocarditis

Le Li, MD,[a,*] Ligang Ding, MD,[a,b,*] Shangyu Liu, MD,[a] Lingmin Wu, MD,[a] Lihui Zheng, MD,[a] Yulong Xiong, MD,[a] Zhuxin Zhang, MD,[a] Likun Zhou, MD,[a] Yan Yao, MD[a]

ABSTRACT

BACKGROUND Catheter ablation (CA) is increasingly recognized as an effective treatment for ventricular tachycardia (VT) in myocarditis patients, although current evidence is based on less robust data.

OBJECTIVES The purpose of this study was to confirm CA's efficacy in reducing VT recurrence and to identify arrhythmic risk factors in biopsy-proven myocarditis patients.

METHODS In this dual-center, retrospective study, we included 50 patients with biopsy-proven myocarditis and VT. They were divided into 2 groups: CA (n = 23) and non-CA (n = 27), with the primary endpoint being VT recurrence at 1-year follow-up.

RESULTS The average age of participants was 40.8 ± 14.9 years; 48% were men. Over a median 371-day follow-up, 28 (56%) experienced VT recurrence, with 8 patients (35%) in the CA group and 20 patients (74%) in the non-CA group. Kaplan-Meier analysis showed that the rate of VT recurrence in the CA group was significantly lower than in the non-CA group (log-rank $P = 0.009$). However, this difference was not found in patients with acute myocarditis. Multivariable analysis revealed a significant correlation between the acute stage of myocarditis and VT recurrence in both the general cohort (HR: 3.02; 95% CI: 1.11-8.21; $P = 0.031$) and the subset undergoing CA (HR: 11.4; 95% CI: 1.02-127.5; $P = 0.048$).

CONCLUSIONS CA is significantly associated with reduced VT recurrence in biopsy-proven myocarditis, albeit this association is not observed in cases of acute myocarditis. The acute stage of myocarditis is independently associated with an increased risk of VT recurrence. (JACC Asia. 2024;4:1000–1009) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Myocarditis, an inflammatory condition of the myocardium, is a significant cause of sudden cardiac death (SCD), particularly among younger individuals.[1,2] Current guidelines recommend antiarrhythmic drugs (AADs) and implantable cardioverter-defibrillators (ICDs) for managing ventricular tachyarrhythmias (VTs) associated with myocarditis.[3] However, their application is constrained by insufficient efficacy and merely palliative treatment approaches, respectively.[4] Several studies have demonstrated that catheter ablation (CA) may be a curative method to reduce myocarditis-related VT recurrence.[5-7] Similar to other forms of nonischemic cardiomyopathies,

From the [a]Chinese Academy of Medical Sciences, Peking Union Medical College, National Center for Cardiovascular Diseases, Fuwai Hospital, Beijing, China; and the [b]Fuwai Hospital Chinese Academy of Medical Sciences, Shenzhen, China. *Drs Li and Ding contributed equally to this work.

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myocarditis-related VT often involves specific arrhythmogenic substrates, such as repolarization anomalies, that make it possible to manage these arrhythmic episodes effectively.[8] Moreover, CA is associated with a better outcome in myocarditis compared with other nonischemic cardiomyopathies.[9] In 2020, Peretto et al[10] provided evidence supporting the efficacy of CA in reducing VT recurrence in a larger cohort of patients with myocarditis. However, it is critical to acknowledge that the diagnosis of myocarditis in these studies was not uniformly confirmed through endomyocardial biopsy (EMB), potentially affecting the findings. Given the distinct nature of arrhythmogenic mechanisms in myocarditis, the generalizability of these studies may be limited. Additionally, although cardiac magnetic resonance imaging (CMR) has gained traction as an auxiliary diagnostic tool, its sensitivity for myocarditis is only around 60%.[11]

Despite its invasive nature, EMB remains the gold standard for diagnosing myocarditis.[12] Within the scope of our study, we aimed to shed light on the efficacy of CA in managing VT in patients with histologically verified myocarditis. Recognizing the gaps in current research regarding the identification of risk factors for VT recurrence in myocarditis, our research also embarked on a detailed investigation of potential risk factors for arrhythmic outcomes. This investigation was based on the analysis of more comprehensive and reliable data sets.

METHODS

STUDY POPULATION. This study constituted a retrospective analysis, encompassing a series of consecutive patients diagnosed with myocarditis and VT, who were referred to the electrophysiology departments of 2 tertiary referral centers: Fuwai Hospital (Beijing) and Fuwai Hospital Shenzhen Hospital (Shenzhen). The patient cohort was accrued over a span from January 2017 to December 2023, specifically targeting those presenting with ventricular arrhythmias VAs). In an effort to bolster the reliability of our data, myocarditis was diagnosed exclusively on the basis of EMB, recognized as the gold standard for such diagnoses. The details of indications for EMB in this study could be found in the Supplemental Methods. Before conducting EMB, all participants were subjected to computed tomography angiography or coronary angiography. This was a critical step to evaluate for the presence of coronary artery disease, thereby ensuring a comprehensive assessment of their cardiovascular health.

Patients with AAD-refractory VT undergoing EMB were initially included in this study. Study exclusion criteria were as follows: 1) without history of EMB-proved myocarditis (Supplemental Appendix)[1,13]; 2) with giant cell myocarditis or cardiac sarcoidosis; and 3) with definite evidence of coronary artery disease. Myocarditis with a duration of disease <30 days, histologically characterized by the presence of inflammatory cell infiltration and cardiomyocyte injury, is defined as acute myocarditis (AM). Previous myocarditis (PM) refers to a duration of disease 30 days or more, with histological evidence of inflammatory cell infiltration without cardiomyocyte injury (Supplemental Methods).[14,15] All patients with EMB-proven myocarditis and VT were administered optimal AAD, as per current guidelines. Beta-blockers, sotalol, and amiodarone were predominantly employed to manage VAs.[2] Patients who were refractory to AADs were advised to undergo CA to reduce VT events. However, some patients did not underdo this procedure because of financial constraints, poor condition, or personal preferences, forming the non-CA group in this study. ICD therapy was contemplated for those who had survived a cardiac arrest because of VF, or who experienced symptomatic VT, particularly if arrhythmias persisted beyond the acute phase despite pharmacological treatment. The decision to proceed with ICD implantation was tailored to each patient, integrating a spectrum of factors including individual clinical assessments, patient preferences, economic considerations, and specific medical indications. Additionally, immunosuppressive therapy (IST), involving the use of glucocorticoids alone or in conjunction with azathioprine, cyclosporine, or both, was administered to patients diagnosed with virus-negative active myocarditis. The judicious application of IST in myocarditis cases was aligned with the recommendations stipulated in the current position statement of the European Society of Cardiology.[16]

The study was approved by the Ethics Committee of Fuwai Hospital and obeyed the Declaration of Helsinki. Patients had signed written informed consents for catheter ablation and clinical data use before the operations.

EMB PROCEDURE. The indications of EMB were based on the relevant scientific consensus.[12,17] Right ventricular septum was the routine site of EMB. Venous access was obtained via the right femoral approach. In some patients, EMB could be combined with electrophysiological study and/or CA for diagnosis and treatment. The endomyocardial bioptome (Jawz 2. 2 mm Forceps, Maxi-Curved, 105 cm) was passed into the right ventricle through the Swartz

ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drug

CA = catheter ablation

EMB = endomyocardial biopsy

ICD = implantable cardioverter-defibrillator

VT = ventricular tachycardia

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sheath. Under fluoroscopic guidance, sampling was performed at the interventricular septum. A total of 4 to 6 samples of endomyocardial tissue per patient were obtained. After the procedure, fluoroscopic and/or echocardiographic examinations were repeated to exclude EMB-related complications including pericardial effusion. A total of 2 to 4 samples were immediately fixed in 10% buffered formalin at room temperature for performing routine pathological examination. One piece of biopsy specimen was fixed in 2.5% glutaraldehyde at 4 °C refrigerators for electronic microscope, and 1 sample was stored in the RNAlater tubes at room temperature for viral genome detection or mass spectrometry.

MAPPING AND CA PROCEDURE. CA was performed either simultaneously with EMB or within 1 week after EMB. Only patients with drug-refractory VT were considered to perform CA. Conscious sedation was used to perform the procedures. Systemic anticoagulation with intravenous heparin was performed as recommended to reduce the thrombotic risk.[18] All patients underwent substrate mapping at sinus rhythm. Activation mapping was performed in patients with spontaneous or inducible arrhythmias. In cases of left ventricular (LV) VT, transseptal or retrograde access was performed, which depends on the VT location. Endocardial mapping was conducted first. If there were no satisfactory findings from endocardial mapping and ablation, the epicardial approach was conducted through percutaneous subxiphoid puncture. Electroanatomical mapping was performed using a high-intensity mapping catheter.

For substrate-based ablation, the interest area was the sites with late activation or local conduction delay, which could be identified by split, fractionated, or isolated late potentials.[19] VT was induced by standard programmed ventricular stimulation (PVS) with up to 3 ventricular extrastimuli until reaching ventricular refractoriness at 2 sites and burst ventricular pacing (cycle length >200 ms) with or without isoproterenol. For sustained VT, the ablation goal was to block the critical isthmus within the re-entrant circuit, whereas for nonsustained VT and ventricular premature contractions, the aim was to eliminate the abnormal electrical activity at the earliest activation site. Regional ablation strategy, targeting areas that exhibit abnormal electrical potentials, was applied to reinforce the ablation efficacy. Radiofrequency current was delivered using an irrigated-tip catheter with a power setting of between 30 and 40 W and a temperature limit of 43 °C. After ablation, PVS was repeated to evaluate the efficacy. Successful ablation was defined as no inducibility of any VT. Partially successful ablation was defined as inducibility of previously nondocumented VT. When clinical VT was induced, the ablation was regarded as failure. Further details were reported in the Supplemental Appendix.

FOLLOW-UP AND OUTCOMES. Postdischarge, follow-up assessments were conducted at intervals of 3, 6, and 12 months, facilitated through outpatient clinic visits or telephonic consultations. The follow-up duration was calculated commencing from the patient's date of discharge. Mandatory for each follow-up session was the monitoring of arrhythmia through a 24-hour Holter electrocardiogram. In addition, patients who had received ICD therapy were subject to biannual evaluations to extract and analyze the recorded ICD electrogram data. The primary outcome, VT recurrence, for patients with sustained VT was documented sustained VT or appropriate ICD therapy. For nonsustained VT patients, it was any documented VTs or appropriate ICD therapy.

STATISTICAL ANALYSIS. The Kolmogorov-Smirnov test was used to evaluate the normal distribution of the data. Continuous variables are expressed as mean ± SD or as median and IQR of 25th to 75th percentiles depending on the distribution of data, and were compared using the Student's *t*-test. Levene's homogeneity of variance test was used to test the assumption of homoscedasticity. If the homoscedasticity was unsatisfied, the Welch's *t*-test was used for comparison between groups. Categorical variables were reported as counts and percentages, and were compared using the chi-square test or the Fisher exact test. Event-free survival was estimated by the Kaplan-Meier method using the log-rank test. Univariable and multivariable analyses by Cox regression model were performed to identify the potential risk factors for VT recurrence. I-VT score was employed to evaluate the VT recurrence risk.[20] Variables with P values <0.05 in the univariate analyses, along with those of clinical importance, were included in the multivariable analyses. Statistical analyses were performed using R software version 4.1.0 (R Foundation for Statistical Computing). All tests were 2-tailed, and a statistical significance was established at a $P < 0.05$.

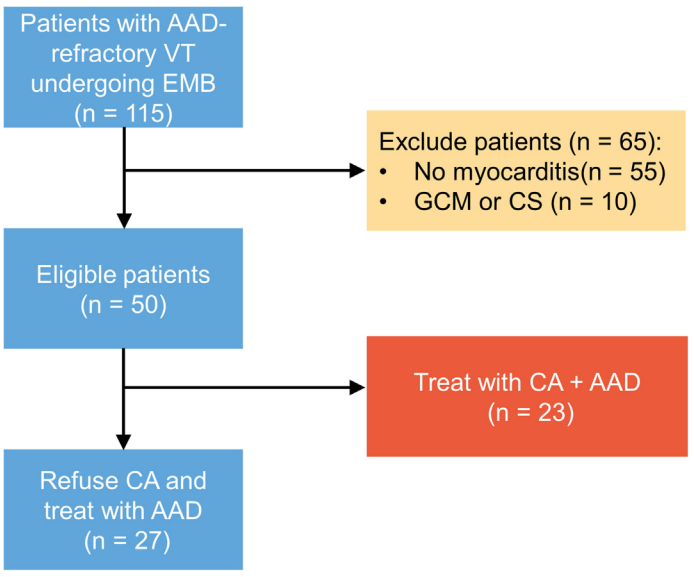
RESULTS

PATIENT CHARACTERISTICS. Overall, 50 patients presenting with myocarditis and VT were ultimately included in the study (Figure 1). All patients presented with drug-resistant VTs. Specifically, the cohort included 37 patients diagnosed with lymphocytic myocarditis and 13 patients with chronic myocarditis (unclassified). An example of the pathological features of myocarditis is depicted in

Supplemental Figure 1. The mean age of these patients was 40.8 ± 14.9 years, with men constituting 48% of the sample. AM was diagnosed in 22 patients (44%). Of the total cohort, 42 patients (84%) presented with sustained VT, and 8 patients had nonsustained VT, with a total of 25 ± 7 VT episodes per day, the longest lasting 16 ± 6 seconds. Additionally, 9 patients (18%) had previously been implanted with an ICD because of VF or symptomatic VT before referral to our institution. CMR was performed on 32 patients (64%), with the results detailed in Supplemental Table 1. Notably, only 20 patients (63%) were diagnosed with myocarditis based on CMR findings, 4 were diagnosed with dilated cardiomyopathy, and 3 had negative findings. Moreover, 27 patients exhibited late gadolinium enhancement, and all 20 patients diagnosed with myocarditis based on CMR had late gadolinium enhancement. In addition, we found that patients with AM had higher CRP, erythrocyte sedimentation rate, cardiac troponin I, and N-terminal forebrain natriuretic peptide compared with PM (Supplemental Table 2). The participants were stratified into 2 groups: the CA group (n = 23) and the non-CA group (n = 27). Among the 27 patients in the non-CA group, 12 were restrained by economic factors, 9 had poor health and could not undergo CA, and 6 were afraid of CA-related complications. At baseline, the average number of AADs administered in both the CA and non-CA groups was comparable (1.63 ± 0.63 vs 1.43 ± 0.84; P = 0.355), as summarized in Supplemental Table 3. Postablation, there was a significant reduction in AAD usage in the ablation group (Supplemental Figure 2). **Table 1** presents a comparison of baseline characteristics between the CA and non-CA groups. Notably, the CA group exhibited a lower incidence of heart failure (44% vs 78%; P = 0.013) compared with the other group.

MAPPING AND ABLATION. Endocardial mapping was systematically conducted in all CA group participants. In 8 patients (35%), endo-epicardial mapping was necessitated when endocardial mapping and ablation failed to yield satisfactory results. An illustrative case of epicardial mapping is depicted in **Figure 2**. Clinical VT was successfully induced in 17 patients (74%), which facilitated the execution of activation-guided ablation. Postablation PVS demonstrated an absence of inducible VT in 15 cases (65%). The residual cohort presented with either nonclinical (n = 4) or clinical (n = 4) inducible VTs. Furthermore, there were 2 CA-related complications (9%), both of which were cases of pericardial effusion necessitating pericardial puncture drainage. Additional details pertaining to the mapping and ablation procedures are outlined in **Table 2**.

FIGURE 1 Flow Chart of Patient Screening



Initially, 115 patients with antiarrhythmic drug (AAD)-refractory ventricular tachycardia (VT) undergoing endomyocardial biopsy (EMB) were included in this study. After applying the exclusion criteria, 65 patients were excluded, resulting in a final study cohort of 50 patients. CA = catheter ablation; CS = cardiac sarcoidosis; GCS = giant cell myocarditis.

PRIMARY OUTCOME. Over a median follow-up duration of 371 days (ranging from 118 to 490 days), VT recurrence was observed in 28 patients (56%), with 8 patients (35%) in the CA group and 20 patients (74%) in the non-CA group. No deaths, heart transplantations, and left ventricular assist device implantations were observed during the follow-up period. Compared with the non-CA group, CA was associated with lower VT recurrence, with a log-rank P value of 0.009 (**Central Illustration**, **Figure 3**). Specifically, in the non-CA group, 20 patients had sustained VT and 3 patients had VT storm. In the CA group, 8 patients had sustained VT and 1 patient had VT storm. During the follow-up period, 6 patients were subjected to the novel implantation of a secondary prevention ICD. Subgroup analysis indicated that, in patients with AM, CA did not significantly diminish the rate of VT recurrence when compared with the non-CA group (63% vs 71%, log-rank P = 0.670), as shown in Supplemental Figure 3. Conversely, in patients with PM, a notably lower VT recurrence rate was observed in the CA group (20% vs 77%, log-rank P = 0.003) (Supplemental Figure 4). Additionally, we compared the ablation outcomes between the AM and PM groups and found a significantly higher VT recurrence rate in the AM group (63% vs 20%, log-rank P = 0.047) (Supplemental Figure 5).

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TABLE 1 Baseline Characteristics

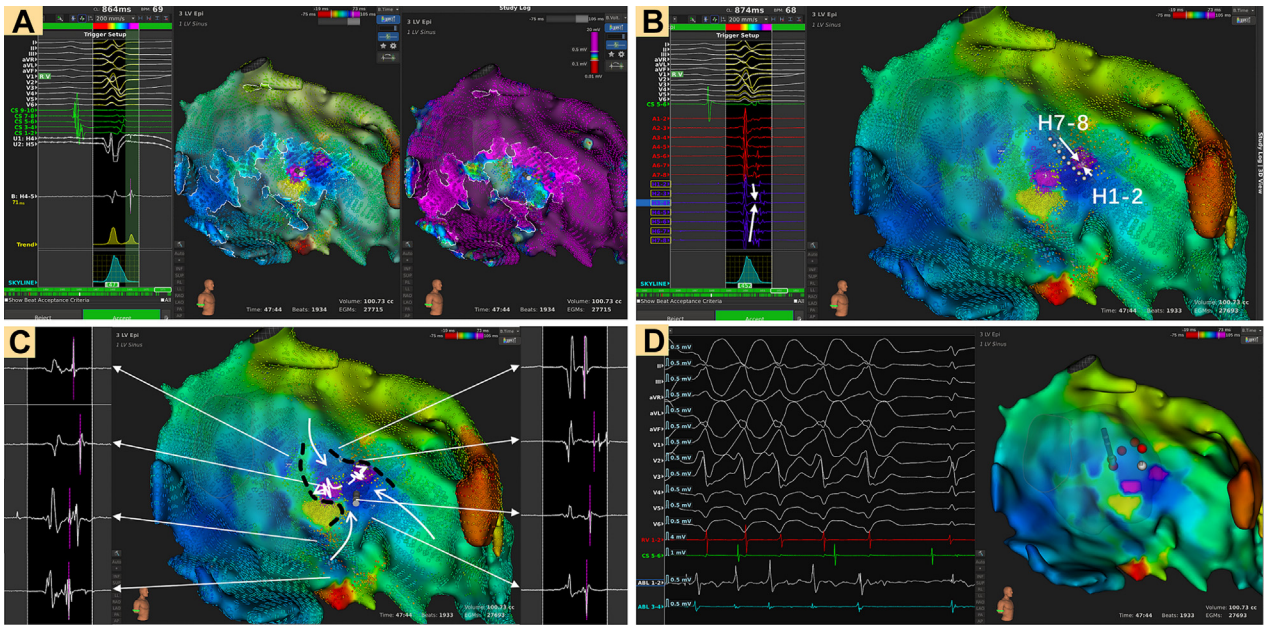
	All (N = 50)	Non-CA (n = 27)	CA (n = 23)	*P* Value
Clinical features				
Age, y	40.8 ± 14.9	38.7 ± 16.3	43.3 ± 13.0	0.274
Male	24 (48)	11 (40)	13 (57)	0.266
AM	22 (44)	14 (52)	8 (35)	0.226
Syncope	9 (18)	4 (15)	5 (22)	0.525
Heart failure	31 (62)	21 (78)	10 (44)	0.013
VT storm	6 (12)	4 (15)	2 (9)	0.507
IST	19 (38)	12 (44)	7 (30)	0.309
Duration from onset to biopsy, m	1.0 (0.4-12.0)	0.7 (0.3-4)	6.0 (1.0-24.0)	0.096
Arrhythmias				
Sustained VT	42 (84)	21 (78)	21 (91)	0.193
Multiple VT morphologies	23 (46)	13 (48)	10 (44)	0.741
AF/AFL	18 (36)	9 (33)	9 (39)	0.670
Intraventricular block	22 (44)	13 (48)	9 (39)	0.522
Prior ICD	9 (18)	5 (19)	4 (17)	0.918
ECG data				
Baseline heart rate, beats/min	76.1 ± 22.5	76.7 ± 18.4	75.3 ± 27.4	0.835
Q-wave abnormal	11 (22)	7 (26)	4 (17)	0.563
PR segment abnormal	6 (12)	2 (7)	4 (17)	0.233
QRS duration, ms	118 ± 30	120 ± 31	116 ± 30	0.614
ST-segment abnormal	20 (40)	12 (44)	8 (35)	0.642
T-wave abnormal	29 (58)	18 (67)	11 (48)	0.310
Low voltage	6 (12)	4 (15)	2 (9)	0.575
UCG data				
LA, mm	37.8 ± 7.2	38.1 ± 7.1	37.3 ± 7.4	0.692
LVEDD, mm	52.2 ± 7.6	52.3 ± 8.2	51.9 ± 6.9	0.867
RV, mm	24.4 ± 3.9	24.5 ± 3.8	24.2 ± 4.1	0.816
LVEF, %	51.9 ± 12.8	49.2 ± 14.1	55.2 ± 10.4	0.106
Valve disease	18 (36)	13 (48)	5 (22)	0.083
CMR data	n = 32	n = 18	n = 14	
CO, L/min	5.1 ± 1.6	5.0 ± 1.4	5.3 ± 1.9	0.670
EDVi, mL/m^2	106 ± 44	109 ± 52	103 ± 32	0.751
LGE+	27 (54)	16 (59)	11 (48)	0.975
Laboratory data				
CRP, mg/dL	2.7 (2.0-6.0)	3.0 (2.4-8.5)	2.2 (1.5-3.7)	0.256
ESR, mm/h	5 (2-14)	7 (2-25)	3 (2-7)	0.134
cTnI, ng/mL	1.49 ± 3.81	2.24 ± 4.68	0.61 ± 2.23	0.134
NT-proBNP, pg/mL	1,640 ± 2,584	2,486 ± 3,271	646 ± 561	0.011
I-VT score				
Risk of VT recurrence score	0.48 (0.48-0.59)	0.48 (0.48-1.20)	0.48 (0.48-0.48)	0.220
Risk of mortality score	0.09 (0.09-0.09)	0.09 (0.09-0.09)	0.09 (0.09-0.45)	0.989

Values are mean ± SD, n (%), or median (Q1, Q3).

AF = atrial fibrillation; AFL = atrial flutter; CA = catheter ablation; CO = cardiac output; CRP = C-reaction protein; cTnI = cardiac troponin I; EDVi = end-diastolic volume index; ESR = erythrocyte sedimentation rate; ICD = implantable cardioverter-defibrillator; IST = immunosuppressive therapy; LA = left atrial; LGE = late gadolinium enhancement; LVEDD = left ventricular end-diastolic dimension; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; RV = right ventricular; VT = ventricular tachycardia.

RISK FACTORS. In this study, a comprehensive array of potential risk factors for VT recurrence was evaluated (Table 1). Among these, AM (HR: 3.02; 95% CI: 1.11-8.21; $P = 0.031$) and multiple VT morphologies (HR: 3.35; 95% CI: 1.11-10.1; $P = 0.032$) were found as independent risk factors of VT recurrence in the entire cohort, as determined through multivariate analysis. Additionally, CA (HR: 0.37; 95% CI: 0.15-0.94; $P = 0.035$) and IST (HR: 0.32, 95% CI: 0.12-0.82; $P = 0.032$) were found to be significantly associated with a reduced risk of VT recurrence. Although factors such as a QRS interval exceeding 120 ms and reduced LVEF were identified as risk indicators in univariate analysis, these associations did not remain significant in multivariate analysis (Table 3). Furthermore, both univariate and multivariate

FIGURE 2 Example of VT Mapping and Ablation



A patient had 6 ventricular tachycardia events in the past year, the histological diagnosis was lymphocytic myocarditis. No target areas containing late potential electrograms were found in left ventricular (LV) endo-myocardium; therefore, the internal surface of the epicardium (epi) was accessed. The depicted area primarily covers the epicardium of the LV inferolateral wall. (A) Activation (left) and voltage mappings (right) during sinus rhythm. The focal areas with low voltage and late potentials were shown. (B) Activation sequence of late potentials was from both ends (H1-2 and H7-8) to center electrode (H3-4) of the mapping catheter (arrows). (C) The recorded late potentials and diagram of the propagation during sinus system. The activation reached the core collection area of late potentials from all directions (arrows); (D) Clinical ventricular tachycardia occurred during ablating in the area with late potentials. After extended ablation, ventricular tachycardia was terminated and cannot be induced.

TABLE 2 Mapping and Ablation Data (n = 23)

Endocardial ablation	23 (100)
Endo-epicardial ablation	8 (35)
Anterograde for LV	9 (39)
Retrograde for LV	8 (35)
Ablation for RV	6 (26)
Substrate mapping	23 (100)
Low voltage in anteroseptal	7 (30)
VT activation mapping	17 (74)
Induced VT cycle, ms	320 (290-350)
Clinical VT	12/17 (71)
Number of induced VT	1 (1-2)
Substrate-guided ablation only	6 (26)
VT- and substrate-guided ablation	17 (74)
Radiofrequency time, mins	23 ± 4
Power, W	38 ± 2
Temperature, °C	43 ± 3
Successful ablation	15 (65)
Partially successful ablation	4 (17)
Unsuccessful ablation	4 (17)

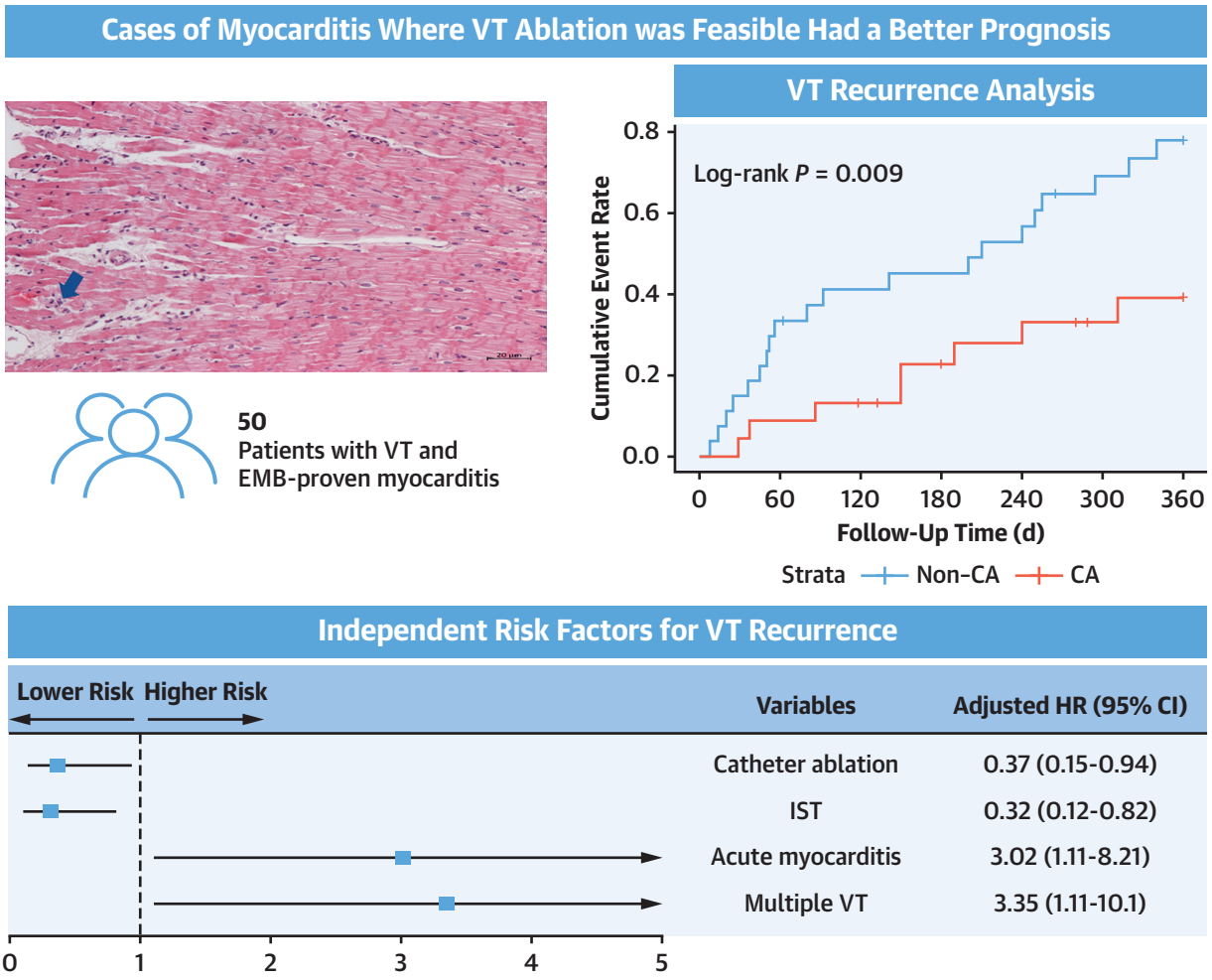
Values are n (%), median (Q1, Q3), or mean ± SD.
LV = left ventricular; other abbreviations as in Table 1.

analyses were conducted specifically within the subset of patients who underwent CA to pinpoint risk factors of VT recurrence postablation. Notably, as detailed in Supplemental Table 4, only AM (HR: 11.4; 95% CI: 1.02-127.5; $P = 0.048$) was found to be strongly correlated with an increased risk of arrhythmic recurrence following ablation.

DISCUSSION

This investigation sought to assess the comparative efficacy of CA plus AAD vs AAD alone in managing VT in patients with biopsy-proven myocarditis. The robustness of this study is underpinned by the fact that myocarditis diagnosis in all cases was validated through EMB. Our study suggests that CA is associated with a reduction in VT recurrence in patients with PM, although this association was not as clear in AM cases. Additionally, we observed that the stage of myocarditis was highly associated with an increased risk of arrhythmic recurrence following CA. Furthermore, our findings indicate

CENTRAL ILLUSTRATION Overview of This Study



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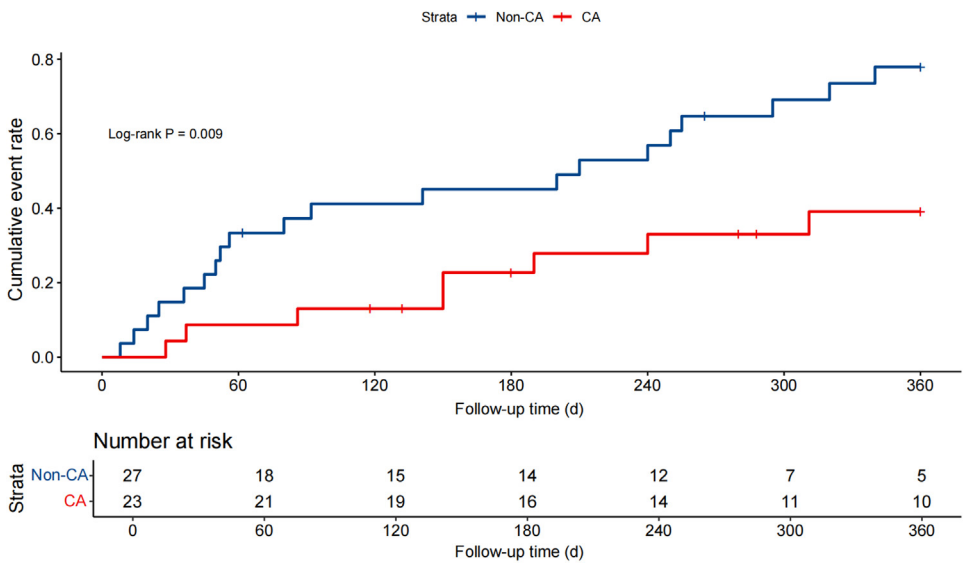
50 patients with VT and biopsy-proven myocarditis from 2 centers are included. VT recurrences of ablation and drug groups by 1-year follow-up are shown. AAD = antiarrhythmic drug; CA = catheter ablation; VT = ventricular tachycardia.

that CA can be effective in managing arrhythmias, potentially reducing the reliance on AADs. These observations contribute to our understanding of CA's role in managing VT in myocarditis patients. The heterogeneity of clinical manifestations in myocarditis poses a significant challenge for its timely diagnosis.

Although EMB stands as the gold standard for diagnosing myocarditis, its utilization is often constrained by its invasive nature.[21] As an alternative, CMR has gained prominence as a noninvasive diagnostic modality, capable of detecting myocardial inflammation indicators such as edema, fibrosis, and hyperemia.[22,23] However, the diagnostic sensitivity of CMR for myocarditis remains less than ideal, reported to vary between 30% and 80%.[22,24] In our study, CMR exhibited a sensitivity of merely 63%. The potential for both missed and incorrect diagnoses via CMR suggests that a significant subset of myocarditis patients might be deprived of optimal treatment strategies. A critical limitation in prior studies has been the inconsistent verification of myocarditis through EMB.[6,10] In contrast, our study ensured the reliability of its findings by adhering strictly to EMB criteria for diagnosing all cases of myocarditis.

VAs are a predominant clinical manifestation of myocarditis. According to earlier guidelines on managing VAs, AAD and ICD have been recommended for addressing arrhythmic complications in myocarditis.[25,26] However, these guidelines have not

FIGURE 3 **Kaplan-Meier Survival Curve of Ventricular Tachycardia Recurrences by 1-Year Follow-Up**



The noncatheter ablation (CA) group exhibited a higher rate of ventricular tachycardia recurrence compared with the CA group.

specifically delved into the role of VA ablation in myocarditis cases. Recent studies have highlighted the effectiveness of CA in both sarcoidosis and myocarditis, demonstrating its association with reduced ICD shocks and VT recurrence.[6,10,27,28] Based on these positive outcomes, the 2022 ESC guidelines for the management of VA have advocated considering CA in postmyocarditis patients experiencing recurrent VT (Class IIa).[3] In our study, the 1-year VT-free survival rate in the CA group was approximately 65%, which is lower compared with the findings of Casella et al[6] (87%) and Dello Russo et al[5] (90%). This discrepancy may be attributable to the inclusion of both AM and PM patients in our study, with AM identified as an independent risk factor for VT recurrence.[10] Moreover, in AM patients, VT primarily arises from disruptions in myocardial cell electrophysiology driven by persistent inflammation. Conversely, in PM patients, VT is frequently linked to myocardial scarring, a sequelae of inflammation resolution. Accordingly, patients with AM more often present with polymorphic and irregular VAs, whereas PM patients more often present with monomorphic and regular VAs. This fundamental difference in pathophysiological mechanisms underpins the observed variance in ablation outcomes between the cohorts.

Given the unpredictable nature of arrhythmic outcomes following optimal treatment in myocarditis, our study employed univariate and multivariate Cox regression analyses to pinpoint potential risk factors. We identified that AM was an independent risk factor for VT recurrence among myocarditis patients, including those who underwent CA. Previous research has underscored that AM, because of its active inflammatory status, is an effective risk factor of VT recurrence.[10] In the acute phase of myocarditis, VT may stem from the instability in myocardial cell electrical activity caused by direct cell damage and membrane dissolution.[29] Thus, it is advisable to avoid ablation in patients during this acute phase when selecting candidates for the procedure. Furthermore, Peretto et al[30] suggested that IST may be an effective protection factor for malignant VA in myocarditis, with an HR of 0.30 (95% CI: 0.2-0.7; $P = 0.01$). However, the early myocarditis treatment trial demonstrated no benefit from IST in myocarditis patients.[31] In our study, we found that the usage of IST was independently associated with a reduced risk of VT recurrence. Although there is a rationale for IST to suppress overactivated immune inflammatory response then to improve outcomes in virus-negative myocarditis, the prospective trials are needed to confirm the efficacy.

Given these findings, we suggest that CA may offer a beneficial strategy for managing drug-refractory VT in myocarditis. Optimal patient selection emerges as a crucial factor in the success of VT ablation in myocarditis contexts. Notably, CA does not appear to further reduce VT recurrence risk in AM cases, suggesting that CA procedures should be cautiously

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TABLE 3 Risk Factor Analysis for VT Recurrence in the Overall Population

	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Clinical features				
Age >40 y	0.88 (0.41-1.85)	0.727	0.96 (0.35-2.65)	0.936
Male	0.46 (0.21-1.01)	0.054	0.69 (0.24-1.98)	0.487
Active myocarditis	2.51 (1.13-5.56)	0.023	3.02 (1.11-8.21)	0.031
Syncope	1.09 (0.42-2.86)	0.866		
Heart failure	1.12 (0.52-2.43)	0.773		
VT storm	1.80 (0.68-4.74)	0.237		
Catheter ablation	0.35 (0.15-0.80)	0.012	0.37 (0.15-0.94)	0.035
IST	0.58 (0.26-1.30)	0.186	0.32 (0.12-0.82)	0.032
Arrhythmias				
Sustained VT	1.45 (0.59-3.59)	0.417		
Multiple VT morphologies	3.75 (1.67-8.43)	0.001	3.35 (1.11-10.1)	0.032
AF/AFL	0.93 (0.43-2.01)	0.846		
Severe bradycardia	1.39 (0.66-2.94)	0.387		
IVB	1.22 (0.58-2.56)	0.603		
Prior ICD	1.63 (0.56-4.70)	0.370		
ECG data				
Heart rate >100 beats/min	1.60 (0.48-5.34)	0.443		
Heart rate <50 beats/min	0.90 (0.12-6.56)	0.916		
Q-wave abnormal	1.62 (0.71-3.68)	0.250		
PR abnormal	0.47 (0.11-2.00)	0.310		
QRS >120ms	2.17 (1.03-4.61)	0.043	0.70 (0.25-1.97)	0.502
ST abnormal	1.07 (0.50-2.26)	0.863		
T-wave abnormal	0.74 (0.35-1.57)	0.435		
Low voltage	2.07 (0.71-6.02)	0.180		
UCG data				
LA >40	1.09 (0.50-2.37)	0.819		
LVEDD >55	1.22 (0.54-2.77)	0.638		
RV >25	1.00 (0.45-2.20)	0.990		
LVEF <35%	3.06 (1.37-6.88)	0.007	1.50 (0.41-5.54)	0.540
Valve disease	2.19 (1.04-4.63)	0.039	1.84 (0.72-4.67)	0.200
Laboratory data				
CRP >10 mg/dL	0.92 (0.34-2.46)	0.869		
ESR >20 mm/h	0.88 (0.41-1.87)	0.740		
cTnI >0.04 ng/mL	1.25 (0.58-2.70)	0.576		
NT-proBNP >450 pg/mL	1.04 (0.46-2.34)	0.973		

Abbreviations as in Table 1.

considered in the acute stage of myocarditis. Additionally, the early identification of high-risk patients should be prioritized, potentially enhancing treatment outcomes.

STUDY LIMITATIONS. First, our work was based on the data retrospectively collected from 2 referral centers; therefore, the results of comparison between the 2 management strategies (CA and AAD) may be affected by the selection bias. Although endo-epicardial ablation may surpass endocardial ablation in efficacy, it was performed in only approximately 35% of patients because of the demanding expertise required and the higher risk of complications. Second, the sample size was small. Only patients who underwent EMB were included, which guaranteed reliable findings but limited the target population. In addition, the paucity of events may reduce the reliability of the risk factor analysis. Third, not all patients underwent ICD implantation, leading to heterogeneity in the follow-up methods for VT recurrence. Therefore, our study acknowledges the potential impact of this variability in rhythm monitoring intensity. Fourth, we acknowledge significant baseline differences between the non-CA and CA groups, including variations in heart failure proportions and acute myocarditis prevalence, which may introduce bias and affect VT recurrence rates. Fifth, despite the high sensitivity of EMB, it may not capture all cases of myocarditis, particularly if the disease is focal or the biopsy location does not adequately represent the affected myocardium, which may lead to some patients being excluded. Accordingly, the results of this study should be interpreted with caution. Larger and prospective studies are needed to confirm our findings.

CONCLUSIONS

For patients with biopsy-proven myocarditis and VT, the combination of CA and AAD is significantly associated with decreased VT recurrence compared with AAD alone. This benefit, however, is not evident in acute myocarditis cases. This finding suggests a potentially limited role for CA in AM, highlighting the necessity for discerning patient selection based on the stage of myocarditis.

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ADDRESS FOR CORRESPONDENCE: Dr Yan Yao, Chinese Academy of Medical Sciences, Fuwai Hospital, Beilishi Road 167#, Xicheng District, Beijing 100037, China. E-mail: ianyao@263.net.cn.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: CA could further reduce VT recurrence in patients with previous biopsy-proven myocarditis based on AADs. Acute myocarditis may be the relatively contraindication for catheter ablation.

TRANSLATIONAL OUTLOOK: Future prospective randomized controlled trials are needed to clarify the efficacy of CA on patients with myocarditis-related VT.

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KEY WORDS antiarrhythmic drug, catheter ablation, myocarditis, outcomes, ventricular tachycardia

APPENDIX For an expanded Methods section as well as supplemental tables and figures, please see the online version of this paper.