# scientific reports

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## OPEN Catheter ablation as first-line treatment for ventricular tachycardia in patients with structural heart disease and preserved left ventricular ejection fraction: a systematic review and meta-analysis

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In this systematic review and meta-analysis, we aim to evaluate the efficacy and safety of catheter ablation as the first-line treatment of ventricular tachycardia (VT) in patients with structural heart disease (SHD) and preserved left ventricular ejection fraction (LVEF). Patients with SHD are particularly susceptible to VT, a condition that increases the risk of sudden cardiac death (SCD). Implantable cardioverter-defibrillators (ICDs) can terminate VT and prevent SCD but do not prevent VT recurrence. The efficacy and safety of CA as a first-line treatment in SHD patients with preserved LVEF remain unclear. We searched PubMed/Medline, EMBASE, Web of Science, and Cochrane CENTRAL for studies reporting the outcomes of CA therapy in patients with VT and preserved LVEF, published up to January 19, 2023. The primary outcome was the incidence of SCD following catheter ablation as the first-line treatment of VT in patients with SHD and preserved LVEF. Secondary outcomes included all-cause mortality, VT recurrence, procedural complications, CA success rate, and ICD implantation after catheter ablation. We included seven studies in the meta-analysis, encompassing a total of 920 patients. The pooled success rate of catheter ablation was 84.6% (95% CI 67.2–93.6). Complications occurred in 6.4% (95% CI 4.0-9.9) of patients, and 13.9% (95% CI 10.1-18.8) required ICD implantation after ablation. VT recurrence was observed in 23.2% (95% CI 14.8-34.6) of patients, while the rate of sudden cardiac death (SCD) was 3.1% (95% CI 1.7-5.6). The overall prevalence of all-cause mortality in this population was 5% (95% Cl 1.8–13). CA appears promising as a first-line VT treatment in patients with SHD and preserved LVEF, especially for monomorphic hemodynamically tolerated VT. However, due to the lack of direct comparisons with ICDs and anti-arrhythmic drugs, further research is needed to confirm these findings.

**Keywords** Ventricular tachycardia, Implantable cardioverter-defibrillators, Catheter ablation, Structural heart disease, Preserved LVEF

<sup>1</sup>Rajaie Cardiovascular Medical and Research Institue, Iran University of Medical Sciences, Tehran, Iran. <sup>2</sup>University Hospital Halle (Saale)Martin-Luther-University, Halle-Wittenberg, Germany. <sup>3</sup>Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran. <sup>4</sup>Tabriz University of Medical Science, Tabriz, Iran. <sup>5</sup>Alborz University of Medical Science, Karaj, Iran. <sup>6</sup>Cardiac Electrophysiology Research Center, Rajaie Cardiovascular Medical and Research Institue, Iran University of Medical Sciences, Tehran, Iran. <sup>⊠</sup>email: majid.haghjoo@gmail.com Electrical abnormalities of the heart, presenting as atrial and ventricular arrhythmias, frequently occur in patients with a diagnosis of structural heart disease (SHD)<sup>1</sup>. Individuals who present with SHD are susceptible to ventricular tachycardia (VT), a heart rhythm disorder that brings about significant clinical difficulties<sup>2</sup>. VT, which is most common in patients with SHD, has been linked to an increased risk of death<sup>3</sup>.

Several options for treatment are currently offered for ventricular arrhythmia management, including antiarrhythmic medications, Implantable Cardioverter Defibrillator (ICD), and catheter ablation. However, no exclusive approach can be implemented with definitive effectiveness, and quite often, a combination of therapies is necessary in order to obtain successful control of ventricular arrhythmias<sup>4</sup>.

Recent multicenter prospective randomized trials indicated the superiority of ICD therapy over antiarrhythmic drug therapy in patients with malignant ventricular arrhythmias and SHD<sup>5-7</sup>. Noteworthy, multiple studies have found a correlation between ICD shocks, increased mortality rates, and reduced quality of life<sup>8,9</sup>. Based on the 2022 ESC and 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias, in the case of hemodynamically well-tolerated sustained VT, ICD remains to be considered the first-line treatment<sup>10,11</sup>. Although ICD is considered the first-line treatment in patients with sustained monomorphic VT, SHD, and preserved left ventricular ejection fraction (LVEF), it does not prevent ventricular arrhythmias and reduces the quality of life of these patients <sup>12,13</sup>.

Catheter ablation as the first-line treatment of VT in patients with sustained monomorphic ventricular tachycardia (SMVT), SHD, and a preserved left ventricular ejection fraction still remains unclear. Based on our knowledge, no systematic review exists on this specific topic. This systematic review and meta-analysis evaluates the safety and efficacy of catheter ablation of VT as a first-line treatment in SHD patients with preserved LVEF.

#### Methods

This study was conducted according to the Cochrane Handbook's standard methodology<sup>14</sup> and reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement<sup>15</sup> Prior to conducting the review, our protocol, which detailed the search strategy, inclusion criteria, and outcomes of concern, was registered in the International Prospective Register of Systematic Reviews (PROSPERO, registration ID: CRD42023416257).

#### Search strategy

We searched PubMed/Medline, EMBASE, Web of Science, and Cochrane CENTRAL for studies reporting the treatment outcomes of catheter ablation in patients with VT and preserved LVEF, published up to January 19, 2023. Studies written in English were selected. We used the following MeSH terms: "Tachycardia, Ventricular' AND 'Catheter Ablation,' 'Radiofrequency Ablation" (Tables S1–S4). Backward and forward citation searching was performed. To enhance the comprehensiveness of our literature search, we employed backward and forward citation searching techniques. Backward citation searching involves reviewing the reference lists of included studies to find additional relevant studies that might have been missed initially, ensuring foundational and significant prior research is included. Forward citation searching identifies newer studies that have cited the included studies since their publication. Using tools like Google Scholar and Web of Science, this method helps capture the latest research developments and emerging trends. Incorporating these methods ensures a thorough and comprehensive literature search, capturing both seminal and contemporary studies relevant to the efficacy and safety of catheter ablation as a first-line treatment for VT in patients with SHD and preserved LVEF.

#### Study selection

The process of eligibility assessment was performed by A.A. and M.Z., who independently assessed the titles, abstracts, inclusion and exclusion criteria, as well as the full-text. In the event of potential disagreements, a panel discussion was utilized to achieve a settlement, while any unresolved problems were deferred to a third-party reviewer (M.H.).

We did not exclude studies based on sample size. Our inclusion criteria focused on the relevance of the study to our research question, specifically evaluating the efficacy and safety of catheter ablation as the first-line treatment of ventricular tachycardia in patients with structural heart disease and preserved LVEF, regardless of the sample size of the studies.

Any studies that at least evaluated sudden cardiac death as one of their objectives were included. Reviews, editorials, case reports, and case series were excluded. Studies investigating participants with structurally normal hearts or LVEF less than 40% were excluded. mean LVEF of more than 40% was considered as preserved LVEF<sup>11</sup>.

SHD was defined as ischemic and non-ischemic cardiomyopathy arrhythmogenic right ventricular cardiomyopathy (ARVC), congenital heart disease, and hypertrophic cardiomyopathy. Studies that analyzed participants who had prior ICD implantation were excluded. Also, studies that evaluated surgical ablation were excluded.

#### Primary and secondary outcomes

The primary outcome was the incidence of sudden cardiac death (SCD) after CA as the first-line treatment of VT in patients with structural heart disease and preserved left ventricular ejection fraction (LVEF). Secondary outcomes included all-cause mortality, VT recurrence, procedural complications, CA success rate, and ICD implantation after CA.

#### Data extraction

Amir Askarinejad and M.Z. designed a data extraction form. These reviewers extracted data from all studies that met the eligibility criteria and resolved any disagreements through consensus. The subsequent information was extracted: the name of the first author, the year of publication, the type of intervention (endocardial

or endo-epicardial approaches or surgical), the study population, the duration of follow-up, country, mapping system, mean LVEF, SHD categories, start and ending date of the study, the age range of participants, the success rate of the intervention, as well as the incidence of sudden cardiac death, VT recurrence, all-cause mortality, ICD implantation, and procedural complications.

#### Risk of bias assessment

A.A. and M.Z. assess the quality of the studies using the JBI's critical appraisal tools for prevalence studies<sup>14</sup>. A third reviewer (M.H.) was involved in cases of inconsistencies.

#### Data synthesis and statistical analysis

Statistical analyses were performed with Comprehensive Meta-Analysis software, version 3.7 (Biostat Inc., Englewood, NJ, USA). Point estimates and 95% confidence intervals (CIs) for the proportion of patients achieving specific treatment outcomes after catheter ablation were calculated. The random-effects model was used because of the estimated heterogeneity of the true effect sizes. The between-study heterogeneity was assessed by Cochran's Q test and the I<sup>2</sup> statistic. Publication bias was evaluated statistically by using Egger's and Begg's tests (p-value <0.05 was considered indicative of statistically significant publication bias) <sup>16</sup>. The funnel plot was not used for publication bias assessment because there were fewer than ten studies in each analysis<sup>17</sup>. A sensitivity analysis was conducted using the one-out approach, where each study was sequentially removed to assess its impact on the overall outcomes. This method helps to determine if any single study disproportionately influences the results.

#### Declaration of generative AI and AI-assisted technologies

In the writing process. During the preparation of this work, the authors used Claude and ChatGPT-4 in order to assist for final language editing. After using these tools/services, the authors reviewed and edited the content as needed and take full responsibility for the publication's content.

#### Results

#### Study selection

Figure 1 displays the flow diagram of study selection. We identified 15,464 papers through databases (PubMed/ Medline, EMBASE, Web of Science, and Cochrane CENTRAL) and screened 10,621 papers after removing duplicates. First, we ruled out 10,542 papers by title and abstract since their subject or outcome were irrelevant to our study. We assessed 79 studies by full-text review. seven articles were selected. Overall, seven studies (one randomized trial <sup>18</sup>, two cohorts<sup>19,20</sup> and four cross-sectional studies<sup>21-24</sup>) met the inclusion criteria.

#### Study characteristics

The characteristics of the included studies are summarized in Table 1. The proportion of male individuals ranges from 68.7 to 96.7%. The mean age of the study population ranges from  $37.2 \pm 13.8$  to  $52.3 \pm 3.6$  years. The mean follow-up duration was between  $32 \pm 27$  and  $72.1 \pm 33.9$  (months). The mean LVEF of the study population ranged from 46.2 to 60.7%. SHD types in the study population included ARVC, ischemic heart disease (IHD), valvular heart disease, post-myocarditis, hypertrophic cardiomyopathy, primary dilated cardiomyopathy, undetermined cardiomyopathy, and isolated ventricular noncompaction. Mapping was done with an electro-anatomical mapping system (CARTO, Biosense Webster Inc., Diamond Bar, CA, or NavX, St. Jude Medical Inc., St. Paul, MN, USA) in most of the studies.

#### Quality of included studies

Based on the JBI checklist for prevalence studies, all of the included studies had a low risk of bias (Table 2). In the study by Maury et al., there were no details provided about the ablation procedures <sup>20</sup>. The JBI checklist for prevalence studies is available in the Supplementary File 1.

#### **Catheter ablation outcomes**

As shown in Table 3, the overall pooled ablation success rate was found to be 84.6% (67.2–93.6) (Fig. 2). Three studies were included in this analysis. Overall, 216 out of 255 patients in these studies had successful ablation.

A total of 6.4% of patients (95% CI 4.0–9.9) experienced complications following ablation, with an event rate of 17 out of 293 patients, as shown in Fig. 3. The analysis of complication rates included four studies. Additionally, 13.9% of patients (95% CI 10.1–18.8) required ICD implantation (Fig. 4). Three studies were included in the ICD implantation analysis, with 67 out of 216 patients needing the device.

VT recurrence was observed in 23.2% of patients (95% CI 14.8–34.6), while the rate of SCD was 3.1% (95% CI 1.7–5.6) (Figs. 5 and 6). The analysis for VT recurrence encompassed three studies, totaling 145 patients, with 23 experiencing VT recurrence. Similarly, the SCD rate analysis included three studies, with 5 out of 145 patients experiencing SCD.

Finally, our meta-analysis showed that the prevalence of all-cause mortality in this population was 5.0% (95% CI 1.8–13.0) (Fig. 7).

#### Publication bias

According to Begg's and Egger's tests, no publication bias was detected for any outcomes based on Begg's test results. However, Egger's test indicated publication bias exclusively for all-cause mortality, with none of the other outcomes showing such bias (Table 3).





#### Sensitivity analysis

Using the one-out approach for sensitivity analysis, no significant differences were observed in any of the outcomes after the removal of each individual study. The figures related to this analysis are provided in Supplementary File 2.

#### Discussion

The results of the present systematic review and meta-analysis support the hypothesis that catheter ablation of VT as the first-line treatment in patients with SHD and preserved LVEF is safe and efficient. There are three key findings of the present research: First, the incidence of SCD and all causes of mortality seems to be considerably low after first-line VT ablation without ICD implantation. Second, the low incidence of significant procedural complications and the high success rate could validate the hypothesis that this procedure seems to be safe. Third, only 14 out of 100 patients needed ICD implantation after the catheter ablation. The overall pooled SCD and all-cause mortality incidence in our study were 3.1% (95% CI 1.7–5.6) and 5.0% (95% CI 1.8–13.0), respectively.

First author, publication year	Wei, 2017	Gandjbakhch, 2021	Santangeli, 2018	Clemens, 2015	Maury, 2014	Yao, 2007	Tung, 2022
Country	China	France	USA	Czech	France	China	China, Japan, South Korea, and Taiwan
Study type	Cross Sectional	Cross Sectional	Cross Sectional	Prospective Cohort	Prospective Cohort	Cross sectional	Randomized clinical trial
Study population (F/M), Male %	48 (15/33), 68.75	65 (14/51), 78.46	32 (9/23), 71.87	31 (1/30), 96.77	544	32 (6/26), 81.25	168 (30/138), 82.14
Age	39.9±12.9	44.5±13.2	45±13	67.0±10	62.0±15	37.2±13.8	52.3±3.6
LVEF (%)	$51.4 \pm 8.0$	$60.7 \pm 4.4$	59.7±7.9	48±6	$50 \pm 10$	55±10	46.2±4.5
VT type	Drug-refractory VTs	Well tolerated mono- morphic VT	Sustained mono- morphic VT	Hemodynamically tolerated VT	Well-tolerated first episode(s) of SMVT	Sustained VT or Fre- quent non-sustained VT	Monomorphic VT
Ablation success definition	The definition of acute procedural success was no induction of clinical VTs and any sus tained VTs (lasting for up to 30 s) by programmed electrical stimulation with intravenous isoprenaline (1–3 µg/ min to increase 20–25% of baseline heart rate) and atropine (1 mg)	Complete procedural success was defined as no sustained VT induced at final EPS including isoproter- enol infusion, partial success as VT still in ducible but clinical VT not inducible, and procedural failure as the ability to induce a sustained clinical VT	VT non-inducibility	A procedure was considered to be completely successful if no VT was induc- ible and par tially successful, if the clinical tachycardia was eliminated, but other morphologies including ventricular fibrillation were still inducible after ablation	Non-inducibility of SMVT after RF procedure	Acute success was defined as nonin- ducibility of any sustained ventricular arrhythmias at the RV apex and the site adjacent to the VT origin despite a complete stim ula- tion protocol for at least three times	Non-inducibility of the targeted clinical VT and elimination of abnormal electro grams within scar
SHD type	ARVC <sup>1</sup> (48)	ARVC <sup>1</sup> (65)	32ARVC <sup>1</sup> (32)	IHD <sup>2</sup> (31)	IHD <sup>2</sup> (91) NICM <sup>5</sup> (31) ARVC <sup>1</sup> (20) VHD <sup>3</sup> (6) CHD <sup>6</sup> (5) Post-myocarditis (5) HCM <sup>5</sup> (2) Undeter- mined (2) Amyloi- dosis (1) Idiopathic left ventricular diverticle (1) Post traumatic/surgery (1) Myxoma(1)	ARVC <sup>1</sup> (32)	ARVC <sup>1</sup> (75) NICM <sup>5</sup> (47) IHD <sup>2</sup> (46)
Mapping*	Three-dimensional electro-anatomical mapping systems (Carto XP)	Three-dimensional electro-anatomical mapping systems (Carto XP)	Three-dimensional electro-anatomical mapping systems (Carto XP)	Three-dimensional electro-anatomical mapping systems (Carto XP)	Not reported	Not reported	High-density map- ping was performed with an impedance- based electroana- tomic mapping system (Ensite Velocity, Abbott)
Combined epicar- dial-endocardial approach	30 (62.5%)	19 (29%)	23 (72%)	None	None	None	31 (55.45%)
Follow-up time (months)	71.4±45.7	72.1±33.9	48.2±11.8	45.6±34.8	32±27	28.6±16	30.6±3.7
Start and ending date of study	2004-2016	2003-2018	2008-2016	2001-2013	2005-2011	2000-2005	2016-2021

**Table 1.** Study characteristics. Values are mean ± SD, n (%), or range, unless otherwise indicated. \*A mapping system in catheter ablation for ventricular tachycardia refers to advanced tools that create detailed, threedimensional representations of the heart's electrical activity. These systems enhance the accuracy, safety, and efficiency of procedures, leading to higher success rates and fewer complications. By providing detailed visualizations, they ensure accurate assessment of interventions and contribute to the reliability of our study outcomes. <sup>1</sup>Arrhythmogenic right ventricular cardiomyopathy. <sup>2</sup>Ischemic heart disease. <sup>3</sup>Valvular heart disease. <sup>4</sup>Hypertrophic cardiomyopathy. <sup>5</sup>Non-ischemic cardiomyopathy. <sup>6</sup>Congenital heart disease.

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In the VTACH multicenter randomized controlled trial, 110 patients with VT were randomly allocated to the ablation group (n = 54) and non-ablation group (n = 56) before the ICD implantation. Notably, mortality incidence in the ablation group was 9.25% (n = 5) and 7.14% (n = 4) in the non-ablation group, which did not have a considerable difference (HR = 132 (035–494), p-value = 0677)<sup>25</sup>. In the CALYPSO trial, the use of catheter ablation prior to antiarrhythmic medications for VT management in patients with an ICD was assessed. 27 patients with ICD were enrolled and randomized in two arms, including catheter ablation (n = 13) and antiarrhythmic medication (n = 14). The mortality incidence in catheter ablation plus ICD was 15% (n = 2)<sup>26</sup>. In the SMS trial, 111 individuals with coronary artery disease, unstable ventricular arrhythmia, and an ICD were randomized into two groups: ablation (n = 54) and no-ablation (n = 57). There wasn't a significant difference in mortality between groups. (16.6% in the ablation group and 19.2% in the ICD only group, hazard ratio = 0.82 (CI 0.34–1.97), p-value = 0.65), and only one patient (1.8%) in the ablation group died suddenly 21 days after ICD implantation.

JBI critical appraisal checklist	Wei, 2017	Gandjbakhch, 2021	Santangeli, 2018	Clemens, 2015	Maury, 2014	Yao, 2007	Tung, 2022
Was the sample frame appropriate to address the target population?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were study participants sampled in an appropriate way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the sample size adequate?	No	Yes	Yes	No	Yes	Yes	Yes
Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes	No	Yes	Yes
Was the data analysis conducted with suf- ficient coverage of the identified sample?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were valid methods used for the identifi- cation of the condition?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the condition measured in a stand- ard, reliable way for all participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was there appropriate statistical analysis?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the response rate adequate, and if not, was the low response rate managed appropriately?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Final evaluation	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias

Table 2. Risk of bias assessment of the included studies.

Outcome	No. of study	No. of patients	Point estimate % (95% CI)	Heterogeneity I2 (%)	Begg's/Egger's tests p-value
All-cause mortality	5	340	5.0 (1.8–13.0)	53.94	0.462/0.001
SCD	7	395	3.1 (1.7–5.6)	0.00	0.763/0.235
Recurrent VT	5	318	23.2 (14.8-34.6)	70.0	1.000/0.952
Complications	4	293	6.4 (4.0-9.9)	0.00	0.308/0.124
Ablation success	3	255	84.6 (67.2-93.6)	79.69	1.000/0.685
ICD implantation	3	249	13.9 (10.1–18.8)	0.00	1.000/0.971

**Table 3.** Outcomes of catheter ablation: mortality, complications, and success rates. SCD sudden cardiac death, VT ventricular tachycardia, ICD implantable cardioverter defibrillator.

Ablation success Weight (Random) Event rate and 95% CI Author Year Statistics for each study Event Lower Upper Relative limit limit weight rate 2014 0.867 0.805 0.912 137 / 158 45.90 Maury Santangeli 2018 0.985 0 799 0 999 32 / 32 9 97 Gandjbakhch 2021 0.723 0.603 0.818 47 / 65 44.13 Total 0.846 0.672 0.936 216 / 255 -1.00 -0.50 0.00 0.50 1.00

#### Figure 2. Pooled ablation success rate.

The implementation of the ICD does not entirely prevent the occurrence of sudden cardiac death. The metaanalysis that included all secondary prevention trials revealed that patients with ICD still had a 10% SCD rate after 5 years<sup>27</sup>. According to Della Bella's findings, the population of 121 ischemic patients with tolerated VT, who had a LVEF of  $34 \pm 10\%$  and a majority of whom were not implanted with devices until after ablation failure (11%), exhibited a low rate of sudden death at 2.5% over a period of 40 months<sup>28</sup>. Based on the aforementioned incidence of SCD and mortality in the studies above, it seems that the incidence of SCD and all causes of mortality is considerably low in patients after catheter ablation without ICD implantation.

The pooled VT recurrence based on the meta-analysis of our study was 23.2%. Even though the ICD has been shown to be effective in preventing sudden death due to VT in patients with ischemic heart disease, its ability to prevent the recurrence of VT is limited<sup>29–31</sup>. In the BERLIN VT trial, it was indicated that prophylactic ablation before ICD implantation can significantly reduce sustained VT/VF recurrence (from 48.2 to 39.7%)<sup>32</sup>.

Author	Year	Statisti	cs for eac	ch study		Weight (Random)		Event	rate and §	95% CI	
		Event rate	Lower limit	Upper limit		Relative weight					
Yao	2007	0.016	0.001	0.211	0/30	3.01			<u> </u>		
Maury	2014	0.066	0.037	0.116	11 / 166	62.83					
Santangeli	2018	0.031	0.004	0.191	1/32	5.93			Ե		
Gandjbakhch	2021	0.077	0.032	0.172	5 / 65	28.23					
	Total	0.064	0.040	0.099	17 / 293			1	•		
							-1.00	-0.50	0.00	0.50	1.00

#### Complications

Figure 3. Pooled complication rate.

#### Event rate and 95% CI Author Weight (Random) Year Statistics for each study Relative Event Lower Upper limit limit weight rate Maury 2014 0.120 0.079 0.179 20/166 60.34 Clemens 2015 0.111 0.028 0.352 2/18 6.10 Gandjbakhch 2021 0.185 0.108 0.298 12/65 33.56 0.188 34/249 Total 0.139 0.101 1.00 -1.00 -0.50 0.00 0.50

### ICD implantation

#### Figure 4. Pooled ICD implantation.

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					Re	current VT					
Author	Year	Statisti	cs for ea	ch study		Weight (Random)		Event	rate and 95%	CI	
		Event rate	Lower limit	Upper limit		Relative weight					
Maury	2014	0.163	0.114	0.227	27 / 166	26.69	1	1		1	1
Clemens	2015	0.111	0.028	0.352	2/18	9.83					
Wei	2017	0.405	0.261	0.568	15 / 37	21.79				₽	
Santangeli	2018	0.188	0.087	0.359	6/32	17.42				1	
Gandjbakhch	2021	0.292	0.195	0.413	19 / 65	24.27					
	Total	0.232	0.148	0.346	69 / 318				🔶		
							-1.00	-0.50	0.00 0	.50	1.00

#### Figure 5. Pooled recurrent VT rate.

Furthermore, the VTACH study demonstrated that catheter ablation may enhance the survival rate of patients with LVEF > 30% who are free from VT (HR, 10.47; 95% CI 0.24–0.88). However, no significant difference was observed between the two groups of patients with LVEF  $\leq$  30%<sup>25</sup>. Interestingly, in a multicenter registry analyzing more than 2000 ablated patients with lower LVEF than 30%, higher rates of VT recurrences and mortality were indicated <sup>33</sup>.

Based on our results, nearly six patients out of 100 experienced complications from catheter ablation without ICD implantation. A meta-analysis of RCTs reporting ICD implantation complications demonstrated that the pooled complication rate is 9.1%.<sup>34</sup>. Also, it has been indicated that early complications of ICDs (up to 10%) are associated with increased hospital admission days and costs <sup>35</sup>. Moreover, complications of subcutaneous ICDs (SICD) are not lesser than those of ICDs. Recent registries report the early complications of SICDs in the range of 10–15%<sup>36,37</sup>. The lower complication rate of catheter ablation in patients with SHD and preserved LVEF, rather

Maury       2014       0.024       0.009       0.062       4 / 166       40.64         Clemens       2015       0.026       0.002       0.310       0 / 18       5.07         Wei       2017       0.081       0.026       0.223       3 / 37       28.70	Author	Year	Statistic	cs for ead	ch study		Weight (Random)	Event	rate and §	95% CI	
Maury       2014       0.002       0.009       0.062       4 / 166       40.64         Clemens       2015       0.026       0.002       0.310       0 / 18       5.07         Wei       2017       0.081       0.026       0.223       3 / 37       28.70											
Clemens       2015       0.026       0.002       0.310       0 / 18       5.07         Wei       2017       0.081       0.026       0.223       3 / 37       28.70	Yao	2007	0.016	0.001	0.211	0 / 30	5.12		ф—		
Wei       2017       0.081       0.026       0.223       3/37       28.70         Santangeli       2018       0.015       0.001       0/32       5.13         Gandjbakhch       2021       0.008       0.000       0.110       0/65       5.17         Tung       2022       0.021       0.003       0.136       1/47       10.19	Maury	2014	0.024	0.009	0.062	4 / 166	40.64				
Santangeli         2018         0.015         0.001         0.201         0 / 32         5.13           Gandjbakhch         2021         0.008         0.000         0.110         0 / 65         5.17	Clemens	2015	0.026	0.002	0.310	0 / 18	5.07		- F	-	
Gandjbakhch 2021 0.008 0.000 0.110 0/65 5.17	Wei	2017	0.081	0.026	0.223	3/37	28.70		<b>D-</b>		
Tung 2022 0.021 0.003 0.136 1/47 10.19	Santangeli	2018	0.015	0.001	0.201	0/32	5.13				
	Gandjbakhch	2021	0.008	0.000	0.110	0 / 65	5.17		ф-		
Total 0.031 0.017 0.056 8 / 395	Tung	2022	0.021	0.003	0.136	1 / 47	10.19		ф-		
		Total	0.031	0.017	0.056	8 / 395					

#### SCD

Figure 6. Pooled SCD rate.

Author	Year	Statistic	cs for eac	h study		Weight (Random)		Event	rate and 9	5% CI	
		Event rate	Lower limit	Upper limit		Relative weight					
Yao	2007	0.016	0.001	0.211	0/30	10.49			<b>þ</b> —		
Maury	2014	0.120	0.079	0.179	20 / 166	40.30					
Santangeli	2018	0.015	0.001	0.201	0/32	10.49			φ <del>π</del>		
Gandjbakhch	2021	0.008	0.000	0.110	0 / 65	10.55			ф <b>-</b>		
Tung	2022	0.064	0.021	0.180	3/47	28.17					
	Total	0.050	0.018	0.130	23 / 340						
							-1.00	-0.50	0.00	0.50	1.00

#### All-cause mortality

#### Figure 7. Pooled all-cause mortality rate.

than ICD implantation complication rates, may lead to the catheter ablation being considered as the first-line treatment in these patients.

In the current study, the pooled rate of successful catheter ablation was 84.6%. Recent studies have shown that successful ablation is associated with better outcomes in patients with VT<sup>25,38,39</sup>. In the study of Tung et al., it was indicated that catheter ablation success is independently associated with lower mortality in patients after scar-related VT catheter ablation <sup>33</sup>. Notably, there are studies indicating successful catheter ablation is associated with reduced VT recurrence and mortality<sup>40</sup>. Altogether, the high rate of successful catheter ablation in patients with SHD and preserved LVEF is an advantage in VT management of these patients with catheter ablation as the first line.

After catheter ablation as the first line in patients with SHD and preserved LVEF, only 13.9% needed ICD implantation after the catheter ablation procedure. The reasons for ICD implantation after the catheter ablation were SMVT recurrence, arrhythmogenic cardiomyopathy, decreased LVEF associated with signs of heart failure, and unsuccessful catheter ablation<sup>19,20,22,41</sup>. Based on this result and considering the high complication rates and cost of ICD implantation, it can be concluded that first-line catheter ablation of VT in patients with preserved LVEF is a proper therapeutic approach.

First of all, our study is not without limitations. Due to a lack of studies comparing the outcomes between patients managed with VT ablation only vs. ICD, we could not conduct the meta-analysis comparing these two therapeutic options. Therefore, this systematic review and meta-analysis points out the efficacy, safety, and complications of catheter ablation as the first line in this group using the best evidence that is currently available. On the other hand, although we did a comprehensive search in four major data bases but all non-English articles were excluded that can lead to bias in the results. Including a heterogeneous SHD population in our meta-analysis broadens the applicability of our findings but requires careful interpretation.

In this meta-analysis, we evaluated various outcomes related to cardiac treatments, including all-cause mortality, sudden cardiac death (SCD), recurrent ventricular tachycardia (VT), complications, ablation success, and ICD implantation. Our findings offer valuable insights into the effectiveness and safety of these treatments. The pooled estimate for all-cause mortality was 5.0% (95% CI 1.8–13.0). The heterogeneity for this outcome was moderate ( $I^2$ =53.94%), indicating variability in the effect sizes across the included studies. Begg's test showed

no publication bias (p = 0.462), but Egger's test indicated potential publication bias (p = 0.001). This discrepancy suggests the need for cautious interpretation of the mortality outcome, as Egger's test might be more sensitive in detecting bias. Recurrent VT had a significantly higher point estimate of 23.2% (95% CI 14.8-34.6), with substantial heterogeneity ( $I^2 = 70.0\%$ ). This high level of heterogeneity suggests considerable variability among the studies, potentially due to differences in patient populations, treatment protocols, or study designs. Neither Begg's nor Egger's tests indicated publication bias (p = 1.000 and p = 0.952, respectively). Ablation success was notably high at 84.6% (95% CI 67.2–93.6), but it showed substantial heterogeneity ( $I^2 = 79.69\%$ ), indicating significant variability across studies. The absence of publication bias as indicated by both Begg's and Egger's tests (p = 1.000 and p = 0.685, respectively) suggests that the reported success rates are robust despite the heterogeneity. For outcomes such as SCD, complications, and ICD implantation, there was no observed heterogeneity  $(I^2 = 0.00\%)$ . Detailed statistics for these outcomes, including their point estimates and publication bias tests, are summarized in Table 1. These results indicate consistent findings across studies with no significant publication bias detected. A sensitivity analysis using the one-out approach confirmed the robustness of our results. No significant differences were observed in any of the outcomes after sequentially removing each study, indicating that no single study disproportionately influenced the overall estimates. The detailed figures from this analysis are provided in Supplementary File 2.

Our meta-analysis highlights the varied outcomes and their heterogeneity associated with cardiac treatments. While most outcomes did not show significant publication bias, the presence of substantial heterogeneity in certain outcomes like recurrent VT and ablation success warrants careful consideration. Future research should aim to standardize protocols and include more homogeneous populations to reduce variability and improve the precision of effect estimates.

Our results should be interpreted with caution due to several limitations. The heterogeneity in study cohorts regarding etiologies, treatment protocols, outcome definitions, lower LVEF cut-off inconsistency, monitoring methods, follow-up durations, and endpoint assessments introduces potential biases. Additionally, clinical interventions such as the use of AADs, repeated ablations, and ICD implantation post-ablation were not uniformly accounted for, influencing the outcomes. The lack of detailed data on patients with unsuccessful ablations limits understanding of their prognosis. Future studies should standardize these variables and provide comprehensive data for more accurate conclusions.

The variability in the definition of SCD across primary studies may affect the accuracy and comparability of our pooled results. Standardizing definitions in future research will be crucial for reliable outcomes. Some patients did not have ICDs at baseline but received them post-ablation, potentially influencing outcomes like SCD and overall survival rates. Future studies should account for post-ablation ICD implantation to better assess VT ablation efficacy and safety.

A limitation is the potential insufficient statistical power due to the small number of included studies and their sample sizes. The variability in VT types could influence treatment outcomes and response to catheter ablation. Specifically, patients with drug-refractory VTs or sustained monomorphic VT might have different prognoses and responses compared to those with well-tolerated monomorphic VT or first episodes of SMVT. Additionally, without direct comparisons to other active treatments, our results should be interpreted with caution.

#### Conclusion

Catheter ablation as the first line of VT treatment in patients with SHD and preserved LVEF appears to be a promising therapeutic option. Our findings indicate that VT ablation is viable for patients with SHD and preserved LVEF, especially those with monomorphic hemodynamically tolerated VT. However, due to the lack of direct comparisons with other treatments such as ICDs and anti-arrhythmic medication, further research is needed. These results should be considered preliminary, and additional studies are necessary to establish VT ablation as the definitive first-line treatment in this population.

#### Data availability

Data of the present study is available based on reasonable request to corresponding author.

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#### **Competing interests**

The authors declare no competing interests.

#### Additional information

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