Substrate identification and treatment of right ventricular tachycardia: scar patterns and novel mapping tools

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CHAPTER 6

6

Ablation Compared with Drug Therapy for Recurrent Ventricular Tachycardia in Arrhythmogenic Right Ventricular Cardiomyopathy: Results from a Multicenter Study

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Abstract

Background

The comparative efficacy of antiarrhythmic drug therapy (AAD) versus ventricular tachycardia (VT) ablation in arrhythmogenic right ventricular cardiomyopathy (ARVC) is unknown.

Objectives

We compared outcomes of AAD and/or β-blocker (BB) therapy with those of VT ablation (with AAD/BB) in patients with ARVC who had recurrent VT.

Methods

In a multicenter retrospective study, 110 patients with ARVC (mean age 38 ± 17 years; 91[83%] men) with a minimum of 3 VT episodes were included; 77 (70%) were initially treated with AAD/BB and 32 (29%) underwent ablation. Subsequently, 43 of the 77 patients treated with AAD/BB alone also underwent ablation. Overall, 75 patients underwent ablation.

Results

When comparing initial AAD/BB therapy (n = 77) and VT ablation (n = 32) after ≥3 VT episodes, a single ablation procedure rendered 35% of patients free of VT at 3 years compared with 28% of AAD/BB-only–treated patients (P = .46). Of the 77 AAD/BB-only–treated patients, 43 subsequently underwent ablation. For all 75 patients who underwent ablation, 56% were VT-free at 3 years after the last ablation procedure. Epicardial ablation was used in 40/75 (53%) and was associated with lower VT recurrence after the last ablation procedure (endocardial/epicardial vs endocardial-only; 71% vs 47% 3-year VT-free survival; P = .05). Importantly, there was no difference in survival free of death or transplantation between the ablation- and AAD/BB-only–treated patients (P = .61).

Conclusion

In patients with ARVC and a high VT burden, mortality and transplantation-free survival are not significantly different between drug- and ablation-treated patients. These patients have a high risk of recurrent VT despite drug therapy. Combined endocardial/epicardial ablation is associated with reduced VT recurrence as compared with endocardial-only ablation.

Introduction

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited cardiomyopathy characterized by fibrofatty replacement of myocardial tissue.[1-4] ARVC is associated with an increased risk of ventricular tachycardia (VT) and sudden cardiac death.[5, 6] Implantable cardiac defibrillators (ICDs) have been reported to improve long-term outcome in patients with ARVC and VT.[7] In a subset of patients with ICDs, however, multiple shocks due to recurrent VT result in significant morbidity.[8, 9]

Over the past two decades, a number of studies have reported that VT ablation can reduce arrhythmia burden in ARVC, albeit with significant recurrence rates and a risk of procedural complications.[10-15] Catheter ablation has largely been reserved for patients with a high ICD shock burden despite antiarrhythmic drug (AAD) or β-blocker (BB) therapy, and the impact of adding ablation to AAD therapy relative to continuing or escalating AAD therapy is not well studied. Furthermore, it is now clear that for some patients epicardial ablation is more efficacious than endocardial ablation, but may expose the patient to additional procedural risks. In view of these considerations, the frequency of VT that warrants proceeding to catheter ablation is uncertain. A recent trial in patients with post infarction VT found that patients with ≥3 or more episodes of VT or who had received an ICD shock despite ADD drug therapy had better composite outcomes with ablation rather than escalated AAD drug therapy.[16]

The aim of this multicenter study was to compare outcomes of these treatment strategies in patients with ARVC who had recurrent (≥3 episodes) episodes of VT. All patients were receiving AAD and or BB and we compared three groups: those who continued to receive only drug therapy, those who received adjunctive therapy with endocardial ablation, and those who received combined endocardial/epicardial ablation.

Methods

Patient population

Retrospectively identified patients with ARVC were included from 5 tertiary cardiac centers between January 2000 and May 2015. All patients fulfilled the 2010 Task force criteria for a definite diagnosis of ARVC.[17] The Task Force criteria were evaluated at the time of inclusion into the study. An additional inclusion criterion was that all patients experienced either (1) ≥3 episodes of sustained VT (requiring either external direct current cardioversion, antitachycardia pacing (ATP), ICD shock, or acute chemical cardioversion) resulting in separate presentations at distinct time points or (2) ≥3

cumulative appropriate shocks for VT (either 3 consecutive shocks over the same presentation, that is, VT storm, or 3 cumulative shocks over 2 separate presentations). The study was approved by the institutional review boards at the respective institutions.

Electrophysiology study and catheter ablation

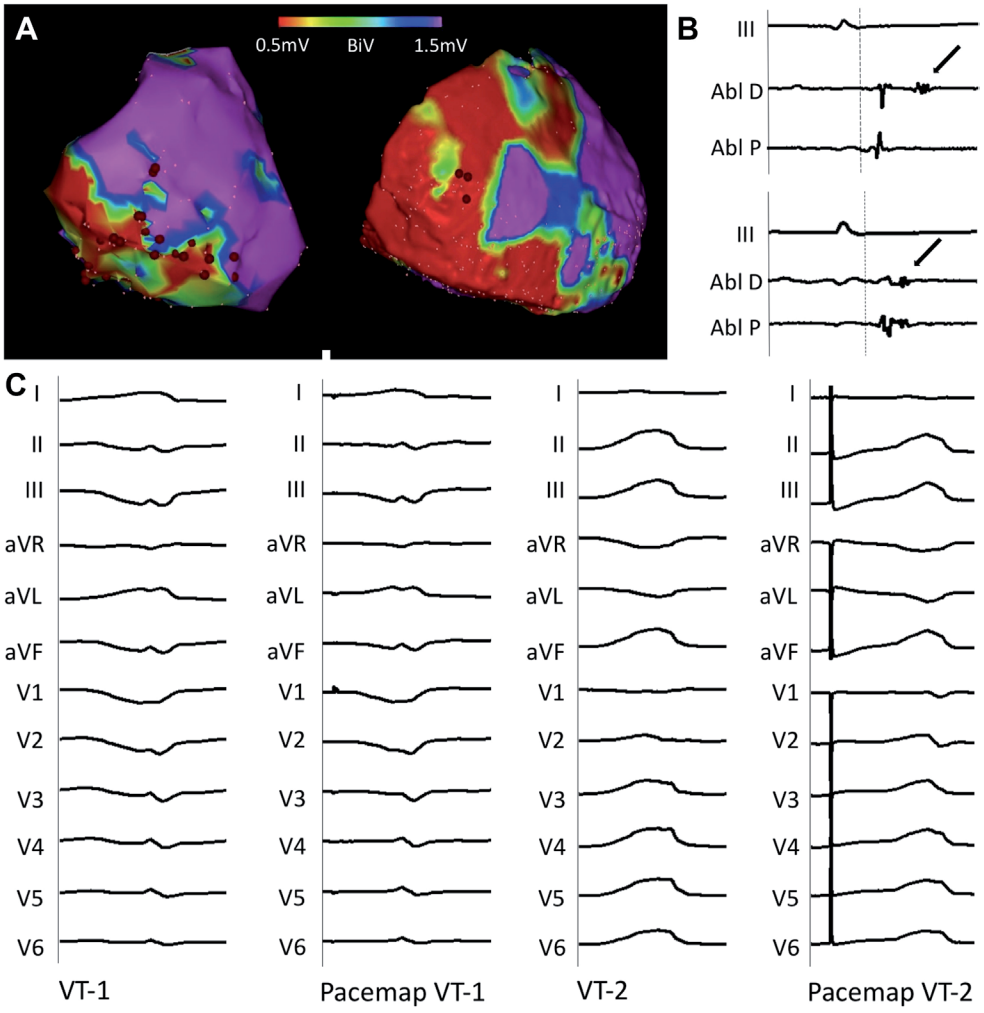
The decision to treat with AAD/BB or to perform VT ablation was at the treating physician's discretion. In the subset of patients that underwent VT ablation, endocardial mapping was performed in all patients. Epicardial mapping and ablation was performed in selected patients, also at the physicians' discretion. A percutaneous subxyphoid approach was used to gain epicardial access.[18] Three-dimensional electroanatomical substrate maps were created using either the Carto (Biosense Webster, Diamond Bar, CA) or NavX (St. Jude Medical, St Paul, MN) mapping system. *Normal bipolar voltage* was defined as >1.5 mV; scar was defined as <0.5 mV; and scar border zones were defined as 0.5-1.5 mV.[19]

All monomorphic VTs that the treating physician thought were clinically relevant (on the basis of cycle length/morphology matching the clinically documented VT) were targeted during ablation, including all mappable VTs. Conventional entrainment and activation mapping techniques were used to identify critical target sites for mappable VTs. A substrate-based approach was used in patients with unmappable VTs. Substrate ablation targeted sites with low-amplitude electrograms with wide fractionation (usually multicomponent electrograms <0.5 mV; >133 ms), sites with late (usually >10 ms after the end of QRS complex) and split (usually an isoelectric period of >30–50 ms between spikes) potentials, and sites with a paced QRS morphology matching a VT (usually with a stimulus to QRS interval of >40 ms).[20, 21] An example of a voltage map and potential targets for substrate ablation are illustrated in Figure 1. VT inducibility was assessed post-ablation with programmed stimulation using 3 extrastimuli (until refractoriness or a minimum cycle length of 200 ms was reached).

Follow-up

The follow-up period for the comparison between AAD/BB therapy and VT ablation began after the third VT episode/third shock. The follow-up period for the comparison between endocardial-only ablation and combined endocardial/epicardial ablation began after the last VT ablation procedure. In patients with ICDs, data from sequential ICD interrogations was documented. Failure of VT ablation or AAD/BB therapy was defined as a recurrence of sustained VT, including episodes terminated by ICD shocks, episodes treated with ATP, and monitored sustained VT episodes requiring direct current cardioversion or chemical cardioversion.

Figure 1. Representative data from a substrate based VT ablation in a patient with ARVC



A: Three-dimensional endocardial and epicardial bipolar voltage maps (right anterior oblique projection) demonstrating a predominantly inferior right ventricular endocardial scar and a more extensive epicardial scar extending to the free wall and outflow tract. Ablation lesions (red circles) were delivered in the mid and inferior right ventricle. **B:** An example of late potentials recorded from ablation sites (arrows indicate late potentials, and dashed line indicates end of QRS complex). **C:** The left panel demonstrates the 12-lead electrocardiogram of the first clinical VT (VT-1), which had a left bundle branch block morphology and superior axis. The pace map at the ablation site in the inferior right ventricle matched VT-1. The right panel demonstrates the 12-lead electrocardiogram for the second clinical VT (VT-2). The pace map at the ablation site in the mid right ventricular free wall matched VT-2. BiV = bipolar voltage; VT = ventricular tachycardia.

Statistical analysis

Data analysis was performed with SPSS version 23.0 (IBM SPSS, Armonk, NY). Continuous variables were expressed as mean ± SD or median and interquartile range (IQR). Continuous variables were compared using the Student's t- Test or Mann-Whitney *U* test. Categorical variables were compared using the $\chi 2$ test. The endpoints of freedom from sustained VT and freedom from death/heart transplantation were determined using Kaplan-Meier analysis. Only interventions after 3 VT episodes/shocks were included in the analysis (failure of VT ablation procedures or AAD/BB therapies before 3 VT episodes were 'blanked').

Results

Patient population

The patient cohort comprised of 110 ARVC patients (specific numbers from each contributing center are included in Supplemental table 1). Patient characteristics are summarized in Table 1. The mean age at first presentation with a ventricular arrhythmia was 38 ± 17 years. Patients were predominantly male (91[83%]) and of Caucasian descent (105 [95%]). An ICD had been implanted in 109 (99%) patients.

Antiarrhythmic drug therapy and VT ablation

After 3 VT episodes/3 shocks, 109 of 110 patients were treated with AAD/BB while 1 patient had no therapeutic interventions. Of these 109 patients, 32 (29%) underwent an adjunctive ablation procedure (including epicardial ablation in 11 patients) after the third VT episode/third shock. Numbers of patients undergoing ablation and AAD/BB therapy are summarized in Figure 2. The remaining 77 (71%) were treated with AAD/BB alone (AAD/BB commenced in drug-naïve patients in 19 cases, AAD/BB changed in 20, a second drug added to preexisting therapy in 11, drug dose was increased in 24, and no change in AAD in 3).

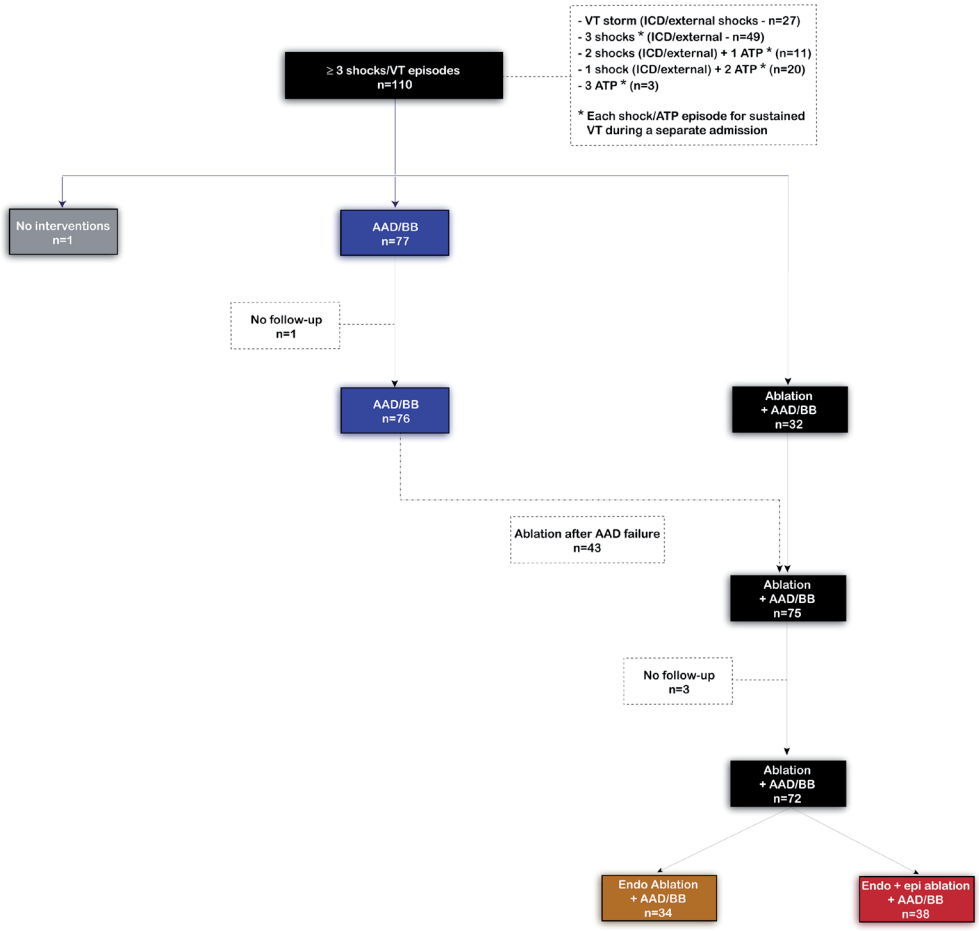
By 3 years, 35% of patients in the ablation group were free of VT after a single ablation procedure while 28% of patients in the AAD/BB-only–treated group were free of VT ($P = 0.46$, Figure 3). When taking individual AAD into account, there were no differences in outcome among patients treated with VT ablation and those treated with amiodarone, sotalol, class 1 drugs, and BBs (Figure 4). Treatment with amiodarone or class 1 drugs was associated with a trend toward improved outcome as compared with sotalol therapy (amiodarone vs sotalol, $P = 0.20$; class 1 vs sotalol, $P = 0.12$). When patients underwent endocardial-only and combined endocardial/epicardial ablation procedures separately, there was a trend toward improved outcome in the combined endocardial/epicardial group (endocardial-only vs endocardial/epicardial ablation, $P = 0.19$; combined endocardial/epicardial group vs AAD, $P = 0.15$) (Supplemental Figure 1).

Table 1. Baseline characteristics

	Ablation N=32#	AAD/BB N=77#	P value
Age (at first VT)	36±13	39±18	0.35
Male (%)	28 (88%)	63 (81%)	0.37
Caucasian (%)	31 (97%)	74 (96%)	0.80
LVEF (%)	55±13	52±14	0.39
Global/regional dysfunction and structural alterations*			
Major (%)	18 (56%)	48 (62%)	0.72
Minor (%)	5 (16%)		
Tissue characterization of wall*			
Major (%)	2 (7%)	4 (5%)	0.79
Minor (%)	0 (0%)	1 (1%)	
Repolarization abnormalities*			
Major (%)	18 (56%)	49 (64%)	0.06
Minor (%)	4 (13%)	19 (40%)	
Depolarization/conduction abnormalities*			
Major (%)	10 (31%)	29 (38%)	0.14
Minor (%)	6 (19%)	22 (29%)	
Family history*			
Major (%)	15 (47%)	46 (60%)	0.34
Minor (%)	0 (0%)	1 (1%)	
Genotype positive (%)	15/21¶ (71%)	38/52¶ (73%)	
PKP2	9	22	
DSC2	1	2	
DSG2	2	3	
DSP	1	5	
JUP	1		
PLN	1		
TMEM43	2	4	
Drugs at 3rd VT episode			
Beta blockers	6 (19%)	17 (22%)	0.72
Sotalol	13 (40%)	25 (33%)	0.49
Amiodarone	7 (22%)	8 (10%)	0.10
Class I	1 (3%)	11 (14%)	0.09
None	5 (16%)	16 (21%)	0.55
Drugs after 3rd VT episode			
Beta blockers	4 (13%)	12 (16%)	0.69
Sotalol	15 (47%)	35 (45%)	0.85
Amiodarone	3 (9%)	20 (26%)	0.05
Class I	2 (6%)	10 (13%)	0.29
None	8 (25%)	0 (0%)	<0.001

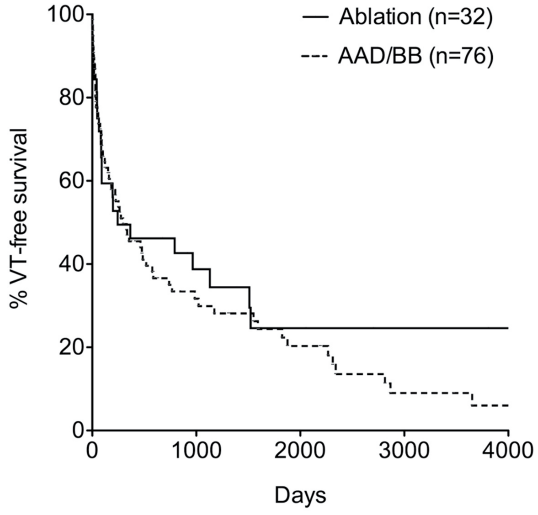
#One of the 110 ARVC patients in the study was not treated with either AAD/BB or VT ablation*Abnormalities as defined by 2010 ARVC taskforce criteria.(17) ¶ No. patients who underwent genotyping. AAD/BB = anti-arrhythmic drug/β-blocker; ARVC = arrhythmogenic right ventricular cardiomyopathy; LVEF = left ventricular ejection fraction; VT = ventricular tachycardia.

Figure 2. Flow diagram demonstrating numbers of patients initially undergoing VT ablation and AAD/BB-only therapy and subsequently all patients who underwent VT ablation



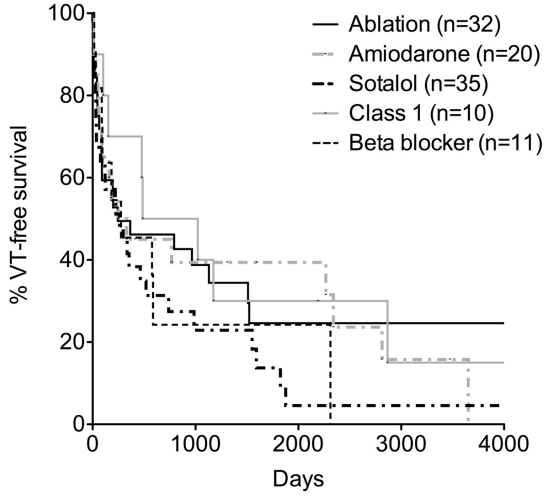
Abbreviations: AAD/BB = antiarrhythmic drug/β-blocker; ATP = antitachycardia pacing; endo = endocardial; epi = epicardial; ICD = implantable cardioverter-defibrillator; VT = ventricular tachycardia.

Figure 3. Outcome of therapy after 3 VT episodes/shocks



Kaplan-Meier curve comparing VT-free survival between patients treated with AAD/BB alone after the third VT episode/shock (*dotted line*) and those treated with an adjunctive VT ablation procedure (single ablation procedure after the third VT episode/shock, *solid line*). There was no significant difference between the 2 initial approaches ($P = .46$). AAD/BB = antiarrhythmic drug/β-blocker; VT = ventricular tachycardia.

Figure 4. Outcome of therapy after 3 VT episodes/shocks



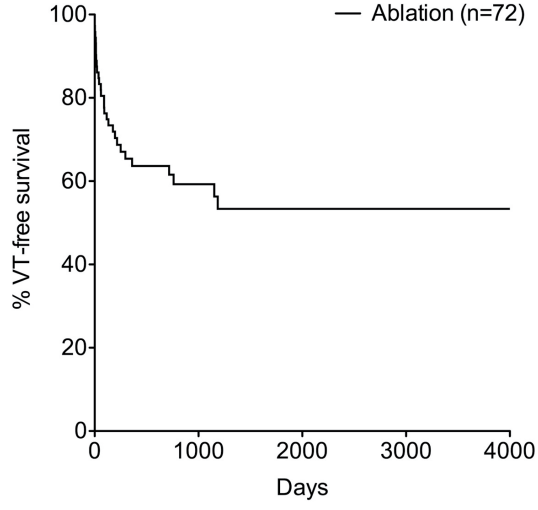
Kaplan-Meier curve comparing VT-free survival between individuals treated with AAD/BB after the third VT episode/shock (amiodarone, *dash-dotted gray*; sotalol, *dash-dotted black*; class 1 drugs, *solid gray*; β-blockers, *dashed black*) and those treated with an adjunctive VT ablation procedure (*solid black*). There were no significant differences in outcome between individuals treated with AAD/BB and those treated with ablation. Amiodarone, class 1 drugs, and ablation were associated with a trend toward improved outcome as compared with sotalol (amiodarone vs sotalol, $P = 0.20$; class 1 vs sotalol, $P = 0.12$; ablation vs sotalol, $P = 0.21$). AAD/BB = antiarrhythmic drug/β-blocker; VT = ventricular tachycardia.

Endocardial and epicardial ablation

Of the 77 patients treated initially with AAD/BB after 3 VT recurrences, 43 underwent ablation after more VT recurrences. Overall, therefore, a total of 75 patients underwent an ablation procedure (Figure 2). These patients had between 1 and 7 procedures (for patients who underwent >1 procedure, VT ablations were performed over a period of 3.0 ± 4.2 years; range 0-17.5 years); a single procedure in 37 [49%] patients; 2 procedures in 22 [29%] patients; 3 procedures in 8 [11%] patients; 4 procedures in 3 [4%] patients; 5 procedures in 3 [4%] patients; 6 procedures in 1 [1%] patient, and 7 procedures in 1 [1%] patient. Forty of the 75 patients who underwent ablation (53%) had at least one combined endocardial/epicardial ablation procedure and 35 (47%) had exclusively endocardial ablations. Two patients had surgical VT ablation procedures. The distribution of endocardial and combined endocardial/epicardial ablation procedures for each contributing center is included in Supplemental Figure 2.

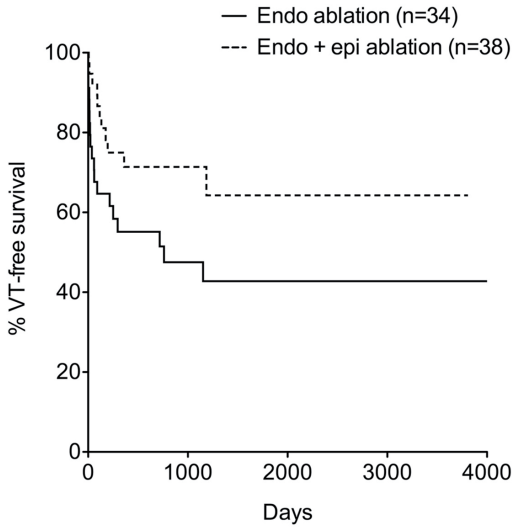
Follow-up data was available in 72 of the above 75 patients. By 3 years after the last ablation procedure, 56% of patients were free of VT (Figure 5). When taking into account combined endocardial/epicardial ablations separately, 71% of patients who had at least 1 combined endocardial/epicardial were free of VT at 3 years as compared to 47% of patients who exclusively underwent endocardial ablation procedures (p=0.05, Figure 6). In patients who experienced post ablation VT recurrences, there was no significant difference in VT burden between the 2 groups (endocardial-only vs. endocardial/epicardial ablation; VT episodes/shocks; median 2 [IQR 2.0; variance 11.1; skewness 2.46] vs. median 1 [IQR 2.5; variance 3.5; skewness 8.80]; p=0.86).

Figure 5. Outcome after the last ablation procedure (after 2 ± 1 ablation procedures)



Kaplan-Meier curve demonstrating VT-free survival for all patients treated with ablation procedures. VT = ventricular tachycardia.

Figure 6. Outcome after the last ablation procedure (after 2 ± 1 ablation procedures)



Number at risk					
Endo ablation	34	11	8	3	1
Endo + epi ablation	38	12	4	1	1

Kaplan-Meier curve comparing VT-free survival between patients treated with combined epicardial/endocardial ablation procedures (endo + epi ablation, *dotted line*) and patients treated with endocardial-only ablation (endo ablation, *solid line*). Of the 40 patients in the combined endocardial/epicardial group and 35 patients in the endocardial-only ablation group, follow-up data were available in 38 and 34 patients, respectively. Combined endo + epi ablation was associated with a superior outcome than was endocardial-only ($P = .05$). endo = endocardial; epi = epicardial; VT = ventricular tachycardia.

Complications

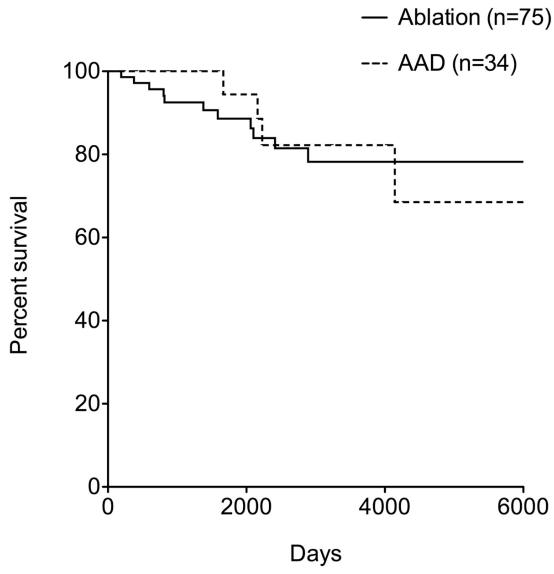
Procedure-related major complications occurred in 3 (4%) patients (1 right ventricular perforation, 1 myocardial infarction [14 days after epicardial ablation],[22] and 1 case of subclavian deep vein thrombosis following surgical ablation). There were no procedure-related deaths.

Survival following VT ablation and antiarrhythmic drug therapy

Patients were followed-up for 6.1 ± 4.5 years after the third VT episode/third shock. During the follow-up period, 10 patients (9%) underwent cardiac transplantation. Mortality from any cause occurred in 9 patients (8%), 3 of whom had previously undergone transplantation. Details of the cause of death were available in 7 of these 9 patients (heart failure [n = 3]; VT storm [n = 1]; VF [n = 1]; stroke [n = 1]; sepsis [n = 1]). As demonstrated in Figure 7, there was no significant difference in survival between

patients who were treated with AAD/BB alone to those who underwent adjunctive VT ablation (p=0.61).

Figure 7.



Number at risk				
Ablation	75	40	12	5
AAD	34	17	7	2

Kaplan-Meier curve comparing the overall survival free of death or cardiac transplantation in patients with arrhythmogenic right ventricular cardiomyopathy treated with AAD/BB alone *(dotted line)* with that in patients who additionally underwent VT ablation *(solid line) (P* = .61). Survival is plotted from the time when patients experienced their third VT episode. AAD/BB = antiarrhythmic drug/β-blocker; VT = ventricular tachycardia.

Early versus late ablation

We compared outcomes of the first-time combined endocardial/epicardial VT ablation in patients who had <10 VT episodes/shocks prior to ablation (median 5 [IQR 3; variance 4.5; skewness 0.87], experienced over median of 3.3 years [IQR 3.8 variance 47.2; skewness 1.35]) to patients who had their first ablation after >10 VT episodes/shocks (median 15, [IQR 16; variance 180.8; skewness 1.05], experienced over a median of 7.7 years [IQR 8.4; variance 28.9; skewness 0.43]). As shown in Supplemental Figure 3, ablation performed in patients with <10 VT episodes/shocks was associated with improved VTfree survival (p=0.04). Of note, there were no differences in AAD/BB therapy between patients with >10 and those with <10 VT episodes/shocks groups (Supplemental table 2).

In contrast, amongst patients undergoing endocardial ablation alone, we did not observe differences in outcome in patients with <10 VT episodes/shocks (median 4,[IQR 2; variance 3.4; skewness 1.38], experienced over a median of 2.5 years [IQR 5.2; variance 32.3; skewness 1.83]) and patients with >10 VT episodes/shocks (median 16 [IQR 5; variance 68.4; skewness 1.43], experienced over a median of 3.1 years [IQR 5.5; variance 21.3; skewness 0.91]). The results are shown in Supplemental Figure 4. Details of AAD/BB therapy between the >10 and <10 VT episodes/shocks groups are included in Supplemental Table 3.

Discussion

In this multicenter study of patients with ARVC, we found that after ≥3 VT episodes, adding a single ablation procedure (endocardial-only ablation in the majority) to AAD therapy was not associated with better VT-free survival as compared with continuing or escalating AAD therapy. Overall, multiple procedures were necessary to maintain freedom from VT. Consistent with previous reports, combined endocardial/epicardial ablation demonstrated superior VT-free survival than did endocardial-only ablation. We also found that early VT intervention with combined endocardial/epicardial ablation may be associated with improved VT-free survival. Finally, VT ablation did not have a significant effect on mortality or the need for cardiac transplantation.

To our knowledge, this is the first report comparing outcomes in patients with ARVC undergoing VT ablation with those in patients treated with AAD/BB alone. While patients with ARVC had a high risk of recurrent VT despite AAD therapy or ablation, it is important to consider that a number of factors may have contributed to nonoptimal ablation strategies, which in turn may have influenced outcome. First, only a third of patients had epicardial ablation with their first procedure and only 53% of patients who underwent ablation ever had epicardial ablation. As discussed below, a combined endocardial/epicardial approach is associated with improved VT-free survival. Second, a significant proportion of patients in our cohort underwent late interventions. As outlined above, earlier interventions may be associated with more favorable outcomes. These considerations underscore the importance of optimization of the ablation strategy to improve VT-free survival. Future studies specifically comparing combined early endocardial/epicardial ablation with AAD/BB therapy are necessary to fully define the effect of VT ablation in ARVC.

The outcome of VT ablation in ARVC has been investigated in multiple previous studies. The reported freedom from VT following ablation in these studies is between 45% to 85%, with variable procedure methods and follow-up periods.[10, 13-15, 23, 24]

The outcomes in the present study are comparable, with success rates of 63% at one year. Furthermore, consistent with previous studies, we demonstrate that combined endocardial/epicardial ablation is associated with superior VT-free survival as compared to endocardial ablation alone.[11, 14, 23] It is important to note however, that a number of more recent reports have suggested that in selected patients, endocardial-only ablation is associated with comparable long-term outcomes to the combined endocardial-epicardial approach.[15, 25] Furthermore, endocardial ablation has been reported to be effective for elimination of epicardial VT substrates in ARVC patients.[26] These findings suggest that with evolving VT ablation techniques, the efficacy of endocardial-only ablation may be improving.

The efficacy of different antiarrhythmic drugs in ARVC remains incompletely defined. Marcus and colleagues reported that empirical therapy with amiodarone is associated with superior efficacy compared to sotalol.[27] In contrast, amongst patients undergoing serial testing with programmed stimulation, sotalol has been reported to be more effective than amiodarone in supressing ventricular arrhythmias.[28] Relatively little is known about the efficacy of class 1 antiarrhythmic in ARVC. The addition of flecainide to sotalol/beta blockers has been reported to enhance VT-free survival.[29] In the present study we demonstrate that in patients with a high VT burden, amiodarone and class 1 antiarrhythmic drugs are associated with a trend towards improved VT-free survival as compared to sotalol. Of note, the use of amiodarone in our cohort was relatively limited, which could potentially have influenced overall outcome. However, future prospective studies with larger patient numbers are necessary to more clearly define the relative efficacy of class 1 agents, amiodarone and sotalol.

Study limitations

This study has the inherent limitations of a non-randomized, retrospective observational study. There are also a number of potential sources of bias. Selection of antiarrhythmic drugs and ablation (and ablation techniques) were left to the treating physicians, with some variation among centers. The efficacy of ablation has likely improved over time, which may also have a confounding effect. Acute ablation outcomes were not fully defined. Specifically, while all clinical VTs were targeted in all patients, data on the proportion of patients with elimination of all clinical VTs was not available. Therefore, the relative efficacy of endocardial-only and combined endocardial/epicardial VT ablations in the acute setting was not defined. Finally, non-uniform ICD programming between participating centers is a potential confounding factor that could influence device detection and therapy for recurrent arrhythmias.

Conclusion

Amongst ARVC patients with a high VT burden, mortality and survival free from transplantation is not significantly different between drug- and ablation treated patients These patients have a high risk of recurrent VT despite drug therapy and/or ablation. However, optimization of the ablation strategy, including epicardial ablation, can be expected to improve outcomes.

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Supplemental material

Supplemental table 1. Patient numbers from contributing centers

Center	No. of patients
Brigham and Women's Hospital, Boston	29
Leiden University Medical Center	31
University Heart Center Zurich	21
The Heart Hospital, London	20
Queen Elizabeth II Health Sciences Centre, Halifax	9

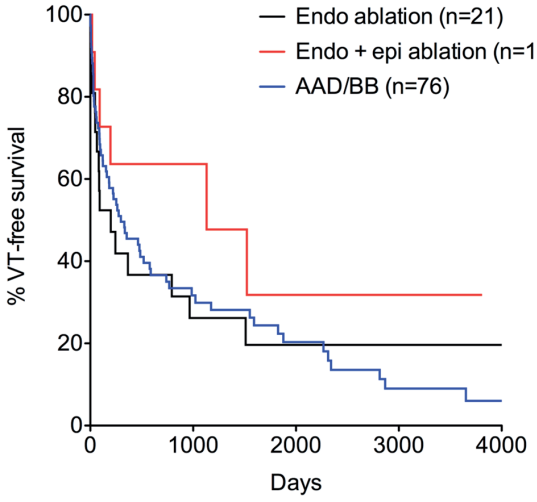
Supplemental table 2. AAD/BB therapy in the combined endocardial/epicardial ablation group based on VT burden

	<10 VT episodes (n=26)	>10 VT episodes (n=10)	P value
Beta blockers only	3 (12%)	2 (20%)	0.51
Sotalol	12 (46%)	3 (30%)	0.34
Amiodarone	3 (12%)	3 (30%)	0.18
Class I	2 (8%)	2 (20%)	0.29
No AAD/BB	6 (23%)	1 (10%)	0.58

Supplemental table 3. AAD/BB therapy in the endocardial ablation group based on VT burden

	<10 VT episodes (n=41)	>10 VT episodes (n=10)	P value
Beta blockers only	6 (15%)	0 (0%)	0.17
Sotalol	17 (41%)	3 (27%)	0.39
Amiodarone	5 (12%)	7 (64%)	0.0003
Class I	4 (10%)	0 (0%)	0.28
No AAD/BB	9 (22%)	0 (0%)	

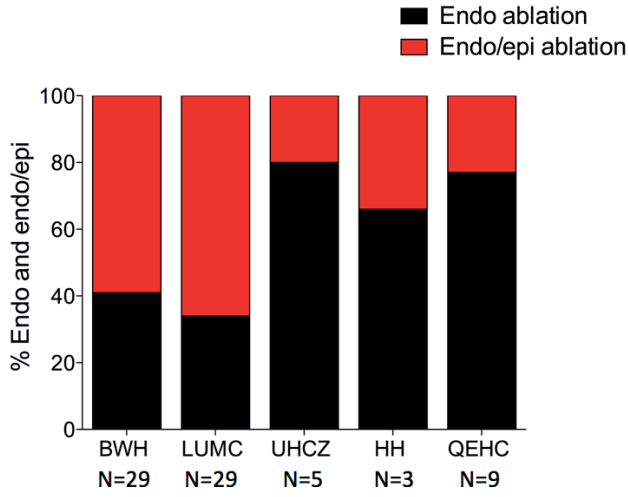
Supplemental figure 1.



Number at risk					
Endo ablation	21	6	3	2	1
Endo + epi ablation	11	5	1	1	1
AAD/BB	76	19	11	5	2

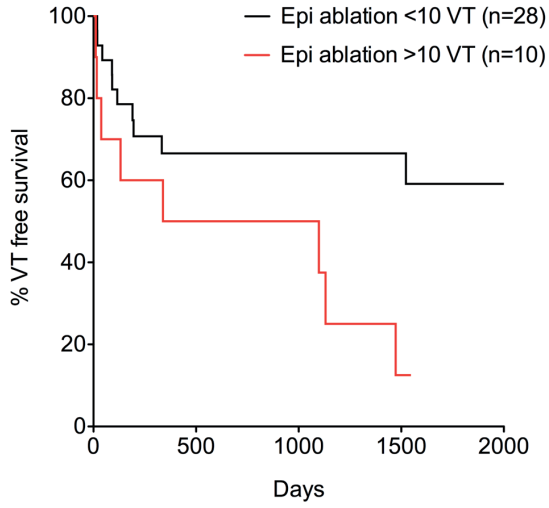
Outcome of therapy after 3 VT episodes/shocks. Kaplan Meier curve comparing VT-free survival between patients treated with AAD/BB-only *(blue)*, adjunctive endocardial-only VT ablation *(black)*, and combined endocardial/epicardial ablation *(red)* after the 3rd VT episode/shock (single ablation procedure after 3rd VT episode/shock). There was a trend towards improved survival in the combined endocardial/epicardial group (endocardial-only vs. endocardial/epicardial ablation, p=0.19; combined endocardial/epicardial group vs. AAD, p=0.15).

Supplemental Figure 2.



Distribution of endocardial-only *(endo ablation)* and combined endocardial/epicardial ablation *(endo/epi ablation)* per contributing center. Abbreviations. BWH, Brigham and Women's Hospital; LUMC, Leiden University Medical Center; UHCZ, University Heart Center Zurich; HH, The Heart Hospital; QEHC, Queen Elizabeth II Health Sciences Centre).

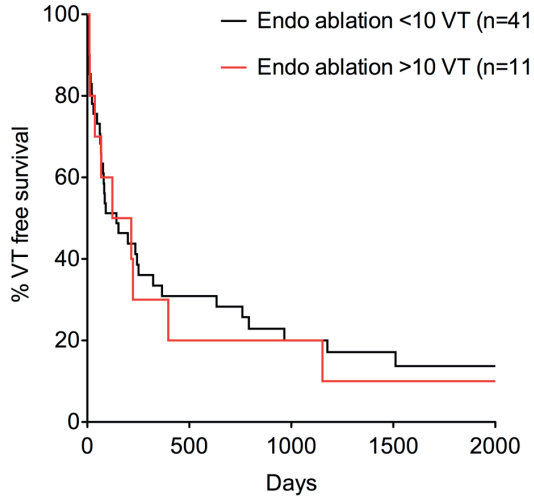
Supplemental figure 3.



Number at risk					
<10 VT episodes	28	14	10	9	4
>10 VT episodes	10	5	4	2	0

Kaplan Meier curve comparing VT-free survival following first-time combined endocardial/epicardial VT ablations in patients who had <10 VT episodes/shocks prior to ablation *(black)* to patients who had >10 VT episodes/shocks *(red)*. Ablations performed in patients with <10 VT episodes/shocks was associated with improved outcome (p=0.04).

Supplemental figure 4.



Number at risk					
<10 VT episodes	41	13	10	9	4
>10 VT episodes	11	6	5	1	1

Kaplan Meier curve comparing VT-free survival following first-time endocardial-only VT ablations in patients who had <10 VT episodes/shocks prior to ablation *(black)* to patients who had >10 VT episodes/shocks *(red)*. There were no significant differences between the two groups (p=0.77).