Acta Cardiol Sin 2015;31:8–17
Original Article
doi: 10.6515/ACS20140721A

EPS and Arrythmia

Long-Term Follow-Up of Catheter Ablation of Ventricular Arrhythmias: Experiences from a Tertiary Referral Center in Taiwan

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Background: Radiofrequency catheter ablation (RFCA) is an alternative therapeutic management for drug-refractory ventricular arrhythmias (VA). However, long-term follow-up of clinical outcome after RFCA for VAs in Taiwan remains unknown.

Methods: From 1999 to 2013, patients undergoing RFCA for VAs from a single referral center were consecutively enrolled. The annual distribution of cases, clinical characteristics, etiology, disease entity and electrophysiological studies were investigated. The clinical outcomes and recurrences between distinct entities were compared.

Results: A total of 502 patients receiving RFCA of VAs were eligible, including 388 patients for idiopathic VAs and 114 for substrate VAs. The annual distribution displayed a tendency towards a gradual increase in ablation cases within 2009-2013 compared with the prior decade ($p < 0.001$). Acute success was achieved in 453 patients (90.2%), partial success in 3 (0.6%), and failed ablation in 46 (9.2%). During a mean follow-up of 39.77 ± 48.75 months, 126 (25.1%) patients developed recurrences. Kaplan-Meier analysis demonstrated better prognosis after RFCA in patients with idiopathic fascicular VT and RVOT VAs ($p < 0.001$) and attenuation of the occurrences of sustained VT/VF, ICD therapies, and mortality in patients with BrS and ARVD/C ($p = 0.036$), as well as overall ICD interventions in substrate VAs ($p < 0.001$).

Conclusions: RFCA could be an effective and alternative strategy in the elimination of idiopathic VAs and prevention of malignant events in substrate VAs at an experienced referral center in Taiwan. Distinct location of arrhythmogenic trigger and disease entities may result in non-uniform recurrences and prognosis.

Key Words: Idiopathic • Radiofrequency catheter ablation • Recurrence • Substrate • Ventricular arrhythmias

INTRODUCTION

Ventricular arrhythmias (VAs), consisting of ventricular fibrillation (VF), ventricular tachycardia (VT), and frequent premature ventricular complexes (PVC), can be recognized in patients with and without structural heart disease.[1] The clinical manifestations of VAs vary from palpitation, dyspnea, atypical chest pain, syncope, and sudden cardiac death (SCD). The entity of VAs are characterized as "idiopathic" in patients without structural abnormalities or "substrate related" in terms, with the presence of scar or delayed conduction area within the ventricle.[1] Although idiopathic VA is usually considered as "benign", it has been linked to the development of PVC-associated cardiomyopathy[2] and the risk of initiating malignant ventricular fibrillation and

Received: June 27, 2014 Accepted: July 21, 2014
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polymorphic VT by triggers with a very short coupling interval.[3] In addition, ventricular tachyarrhythmias, contributing to the most common cause of SCD in western countries, is of clinical relevance in all forms of structural heart disease.[4] The use of an implantable cardioverter defibrillator (ICD) is warranted for patients who have been resuscitated from ventricular tachyarrhythmias or have an increased risk of SCD due to underlying heart disease.[5,6] However, frequent ICD shocks have been associated with increased mortality and impaired quality of life.[7,8]

Antiarrhythmic drugs play a pivotal role in reducing episodes of ventricular tachyarrhythmias. However, given the disappointing efficacy, potential pro-arrhythmic effects, and variable adverse effects of such antiarrhythmic drugs, radiofrequency catheter ablation (RFCA) has been considered as an important and alternative management to potentially cure or ameliorate the burden of ventricular tachyarrhythmias; this would occur by targeting the arrhythmogenic triggers and eliminating the slow conducted reentrant circuits or abnormal fractionated electrograms within the ventricular scar/low voltage zone or conduction system.[9] With the rapid advancement of mapping and ablation technology, acute procedural success rate of RFCA for idiopathic VAs ablation can be achieved in 80-90% of the cases,[9] whereas RFCA reduced or abolished substrate VT in approximately 70% of the patients.[9-11] The evolution of VA ablation and the associated outcome has not previously been systemically investigated in Taiwan.

Thus, the purpose of this study was to elucidate the advancement of VA ablation, the associated etiology, and ablation outcome by a long-term follow-up from single experienced referral center in recent 15 years in Taiwan.

MATERIALS AND METHODS

Patient selection and clinical evaluation

From 1999 to 2013, consecutive patients were recruited who were referred to our center and underwent an electrophysiological study and RFCA for drug refractory VAs. Baseline characteristics were obtained in substantial detail. Structural heart diseases were assessed by echocardiography, magnetic resonance imaging (MRI) heart study, invasive ventricular angiography, and/or coronary artery angiography before the electrophysiology (EP) study. Both RV and LV ejection fraction were obtained from cardiac MRI and/or echocardiography. The definition of dyslipidemia was based on the third report of the National Cholesterol Education Program (NCEP) expert panel.[12] After the patients were all deemed to be free from anti-arrhythmic drugs, they underwent electrocardiogram (ECG) and 24-hour Holter monitoring prior to ablation. The density of VA was measured, and the clinical manifestations of VA were further categorized into symptomatic PVC (> 20%), nonsustained VT (< 30s), sustained VT (regular tachycardia with a mean cycle length of > 240 ms) and VF [mean tachycardia cycle length (TCL) $\leq$ 240 msec]. The etiology of VA was defined as idiopathic or substrate VA based on the structural assessment and the characteristics of substrates. According to the electrocardiographic, electrophysiological characteristics, electroanatomical mapping and clinical evaluation, the idiopathic VAs consisted of fascicular VTs and VA originating from right ventricular outflow tract (RVOT), left ventricular outflow tract (LVOT), papillary muscle, great cardiac vein/anterior interventricular vein (GCV/AIV), or others. Whereas the substrate VAs were composed of ventricular tachyarrhythmias originating from ischemic substrates, arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C), dilated cardiomyopathy (DCM), Brugada syndrome (BrS), hypertrophic cardiomyopathy (HCM), and others.

Electrophysiological study, mapping, and radiofrequency catheter ablation

After obtaining informed consent from patients, we performed a standardized electrophysiological study on all patients in the fasting state without sedation. Antiarrhythmic drugs were discontinued for a minimum of five half-lives before RFCA (except amiodarone). In the absence of spontaneous VA, rapid ventricular pacing and programmed stimulation up to three extra stimuli were performed with a catheter placed at the right ventricular apex and RVOT sequentially. If VA was still not inducible, intravenous isoprenaline 1-5 μg/min was infused to achieve at least 20% heart rate increment. If spontaneous VAs were not inducible during pharmacological provocation, the induction protocol was repeated. The QRS morphologies of spontaneous and/or induced VAs were compared with that of the documented VAs.

The localization of arrhythmogenic foci or critical isthmus were performed conventionally or by using a 3D mapping system (EnSite NavX™, St Jude Inc., St Paul, MN, USA or CARTO 3, Biosense Webster, Diamond Bar, CA, USA). For idiopathic VAs, activation mapping, defining the earliest local electrograms, and/or pacemapping by comparing the 12-lead QRS morphology of paced PVCs with clinical VAs aiming for at least 11 of 12 leads matching were performed. For hemodynamically stable substrate VTs, activation mapping and entrainment mapping[13] were intended to be performed for localization of the critical isthmus within scar, whereas pacemapping and/or substrate-based modification strategy,[14] targeting the late and fractionated electrograms within scar/low voltage zone during sinus rhythm or ventricular pacing, were used for unstable ventricular tachyarrhythmias.[14] Repeat mapping was performed if suppression and/or elimination of idiopathic VA was not observed. Epicardial approach was performed according to electrocardiographic[15,16] and electroanatomical mapping criteria[17,18] for substrate VAs, BrS,[19] or after failed endocardial ablation for idiopathic VA.

Radiofrequency (RF) energy was delivered in a temperature-controlled mode at 50-60 °C with a pulse duration of 60 seconds; the maximal power was 50 Watts for non-irrigated catheter and 30-35 Watts for irrigated catheter targeting for an impedance drop of 10 Ohms. If the idiopathic VA was suppressed within 30 seconds, RF energy would be maintained for a total of 60 seconds, and additional energy would be applied up to a maximum of 5 burns. For ablation of substrate VAs, we aimed at terminating the hemodynamically stable VT or elimination of all recorded abnormal electrograms from detailed mapping. Procedural success was defined as complete elimination of spontaneous or inducible VAs under the infusion of isoprenaline, following the same induction protocol for 30 minutes to exclude acute recurrences. Partial success included inducible VAs with morphological different from clinical-documented VAs or decreased the burden of idiopathic VAs by 50%, and failed ablation for the remaining. All patients underwent a 24-hour Holter ECG monitoring after ablation.

ICD implantation and clinical follow-up

ICD implantation was performed for prevention of further SCD according to the policies of the National Health Insurance, including previous episodes of resuscitated cardiac arrest, or unexplained syncope with inducible sustained ventricular tachyarrhythmias. Most of the devices had diagnostic memory and the ability to record and store electrocardiographic data, including intracardiac electrograms, for subsequent review. Stored data were reviewed after all discharges, and interrogations were performed routinely every three to six months. Additionally, patients were examined with 12-lead ECGs, 24-hour Holter, and echocardiography after RFCA, and followed-up in a cardiology outpatient clinic every 3 months for the first year, and then every 6 months thereafter. For patients who could not come for outpatient follow up in our institution, they were contacted by telephone for recurrent symptoms and recurrent arrhythmias. We also advised these patients to visit our affiliated institutions to complete follow-up screening. The medical reports were obtained from these affiliated institutions. For idiopathic VAs, the recurrence was composed of the occurrences of sustained VT, nonsustained VT, or greater than 1000 ventricular PVCs[20] during follow-up. For substrate VAs, the overall recurrences, including the presence of nonsustained VT, sustained VT or VF, and the recurrences of unstable ventricular tachyarrhythmias requiring ICD interventions or mortality were investigated individually.

The mortality during follow-up was further confirmed with the National Death Registry database. The cause and date of death were accessible by linking our hospital's database with the National Death Registry through a unique, permanent personal identification number given to every Taiwan citizen. The accuracy of the cause-of-death coding in Taiwan's National Death Registry database has been validated previously.[21] (10817134)

Statistical analysis

Data are expressed as mean ± standard deviation for normally distributed continuous variables and proportions for categorical variables. Continuous variables were analyzed using a two-tailed *t*-test, and discrete variables were compared using a χ^2 test. The Kaplan-Meier cumulative recurrence curves were plotted and survival curves were compared by the log-rank test. All statistical significances were set at $p < 0.05$, and all statistical analyses were carried out using SPSS 17.0 (SPSS, Inc., Chicago, IL, USA).

RESULTS

Patient population

From 1999 to 2013, a total of 502 patients (mean age = 43.75 ± 15.57 yrs, 254 male) who were referred to our institution for RFCA were consecutively reviewed, including 388 patients (77.3%) for idiopathic VAs and 114 (22.7%) for substrate VAs. Compared with idiopathic VAs, patients with substrate VAs were characterized by older age (51.93 ± 17.04 vs. 41.35 ± 14.27, p < 0.001, Table 1), higher prevalence in male (64.9% vs. 46.4%, p < 0.001), more clinical presentation of syncope (49.1% vs. 29.4%, p < 0.001), higher incidence of hypertension (44.7% vs. 29.4%, p < 0.001), heart failure (25.4% vs. 3.4%, p < 0.001), and dyslipidemia (25.4% vs. 9.3%, p < 0.001). Patients with substrate VAs had worse left ventricular systolic function (LVEF; 46.70 ± 12.10% vs. 59.92 ± 5.84%, p < 0.001) and right ventricular systolic function (RVEF; 39.42 ± 10.22% vs. 51.16 ± 7.54%, p < 0.001) than did those with idiopathic VAs.

Clinical manifestation of idiopathic VA consisted of sustained VT in 130 (33.5%) patients, nonsustained VT in 121 (31.2%) and PVC in 137 (35.3%). In contrast, the manifestation of substrate VA demonstrated higher incidence of sustained VT (71 patients, 62.3%) and less PVC (12 patients, 10.5%, p < 0.001). The clinical manifestations of idiopathic VA and substrate VA regarding the origin and associated disease entity were showed in Figure 1.

Figure 2 showed the annual distribution of total patient numbers and patients with idiopathic VAs/substrate VAs undergoing RFCA for VA (Figure 2A) from 1999-2013. The number of patients receiving RFCA, either for idiopathic or substrate VAs, was significantly increased during the last five years compared with previous two five year periods (1999-2003 vs. 2004-2008 vs. 2009-2013: 47 vs. 51 vs. 290, p < 0.001 for idiopathic VAs and 6 vs. 11 vs. 97, p < 0.001 for substrate VAs, Figure 2B).

Electrophysiological study, mapping, and catheter ablation

Of the 388 idiopathic VA identified during EP study, 242 patients (62.4%; Figure 3A) had idiopathic RVOT VAs, followed by fascicular VT in 84 (21.6%), LVOT VAs in 25 (6.4%), papillary VAs in 20 (5.2%), and VAs originating from the great cardiac vein/anterior interventricular vein in 4 (1.0%). Of the remaining 11 patients, 4 VAs originated from aortomitral continuity, 3 VAs from RV

Table 1. Comparison of characteristics between patients with idiopathic and substrate VA (N = 502)

	Idiopathic VA (N = 388)	Substrate VA (N = 114)	p value
Age	41.35 ± 14.27	51.93 ± 17.04	< 0.001
Gender (male)	180 (46.4%)	74 (64.9%)	0.001
Clinical manifestation			
Syncope/near syncope	114 (29.4%)	56 (49.1%)	< 0.001
Palpitation	341 (87.9%)	82 (71.9%)	< 0.001
Dyspnea	137 (35.3%)	36 (31.6%)	0.50
Underlying disease			
HTN	114 (29.4%)	51 (44.7%)	0.003
DM	24 (6.2%)	11 (9.6%)	0.21
CHF	13 (3.4%)	29 (25.4%)	< 0.001
Dyslipidemia	36 (9.3%)	29 (25.4%)	< 0.001
Structural assessment			
LVEF	59.92 ± 5.84	46.70 ± 12.10	< 0.001
RVEF	51.16 ± 7.54	39.42 ± 10.22	< 0.001
Electrophysiological study and ablation			
Navigation used	267 (68.8%)	100 (87.7%)	< 0.001
Irrigation catheter used	143 (36.9%)	67 (58.8%)	< 0.001
Epicardial approach	5 (1.3%)	20 (17.5%)	< 0.001
ICD implantation	4 (1.0%)	56 (49.1%)	< 0.001

CHF, congestive heart failure; DM, diabetes mellitus; HTN, hypertension; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction; VA, ventricular arrhythmias.

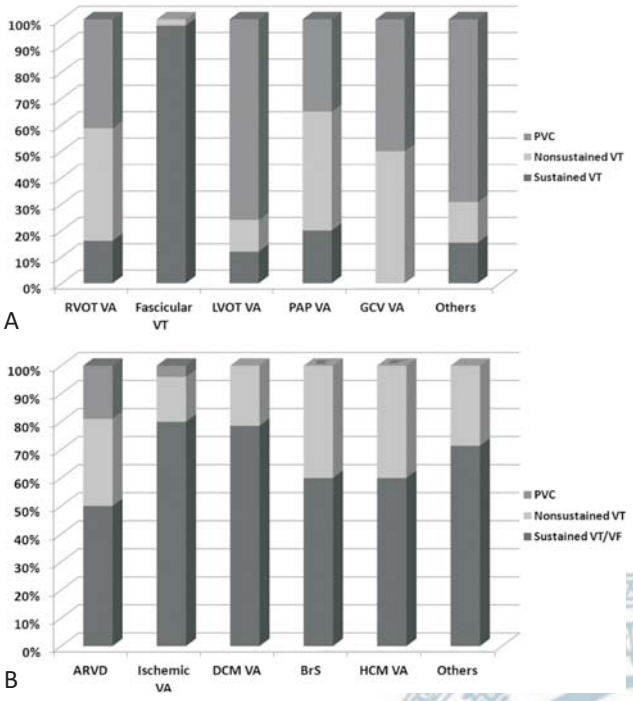


Figure 1. *The clinical manifestations of VAs, including sustained VT/VF, nonsustained VT, and PVC in patients with idiopathic VA (A) and substrate VA (B) with regard to the origin and associated disease entities. ARVD, arrhythmogenic right ventricular dysplasia; BrS, Brugada syndrome; DCM, dilated cardiomyopathy; GCV, great cardiac vein; HCM, hypertrophic cardiomyopathy; LVOT, left ventricular outflow tract; PAP, papillary muscle; PVC, premature ventricular complexes; RVOT, right ventricular outflow tract; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.*

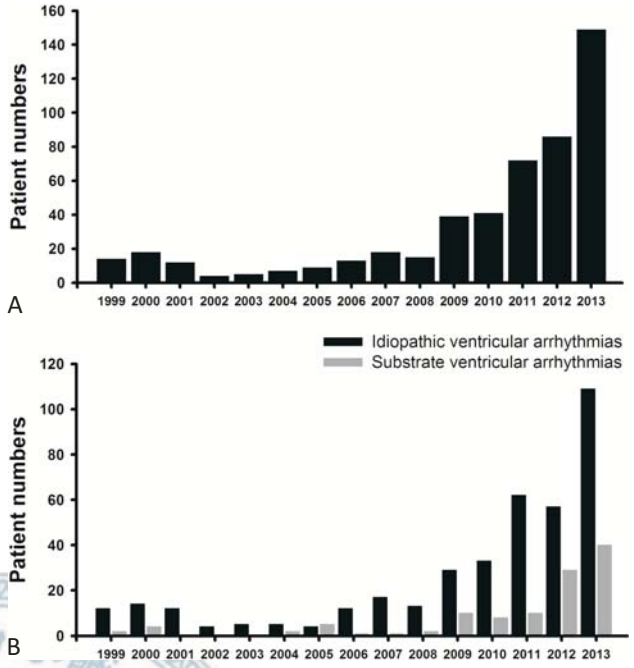


Figure 2. *(A) The annual distribution of total patient numbers undergoing RFCA for VAs during 1999-2013. (B) The annual distribution of patient numbers undergoing RFCA for idiopathic VA and substrate VA during 1999-2013, respectively. RFCA, radiofrequency catheter ablation; VA, ventricular arrhythmia.*

parahisian area, 2 from LV basal septum, 1 from RV basal inferior free wall, and 1 from LV basolateral mitral annulus. Of 114 substrate VAs, 58 patients (50.9%) were attributed to arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) according to modified Task Force Criteria,[22] 25 (21.9%) with ischemic VAs, 14 (12.3%) with dilated cardiomyopathy (DCM), 5 (4.4%) with BrS, and 5 (4.4%) with hypertrophic cardiomyopathy. The remaining 7 patients (6.1%) were categorized as non-ischemic cardiomyopathy with indeterminate etiology. Compared with the procedures performed for idiopathic VAs, RFCA were more frequently achieved by the use of a navigation system (87.7% vs. 68.8%, $p < 0.001$; Table 1), irrigated catheter (58.8% vs. 36.9%, $p < 0.001$), and epicardial procedures (17.5% vs. 1.3%, $p < 0.001$) for substrate VAs.

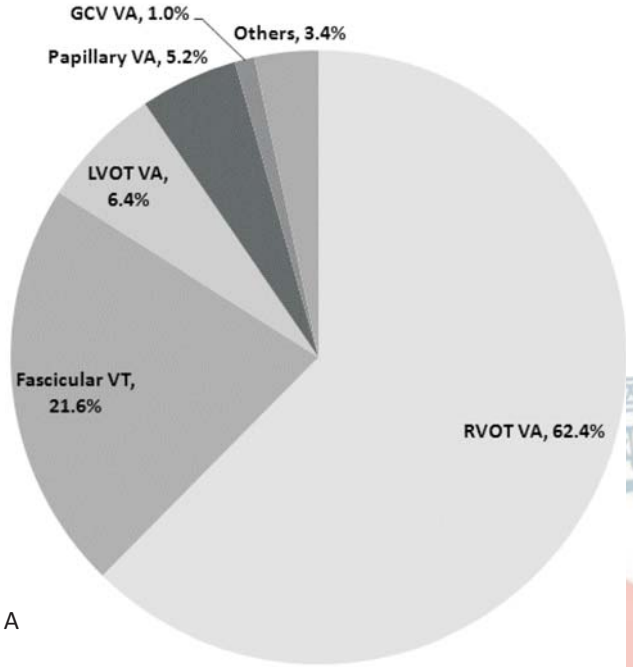
For idiopathic VAs, the arrhythmogenic targets were determined concurrently by both pacemapping and activation mapping in 309 patients (79.6%), activation mapping alone in 34 (8.8%), and pacemapping alone in 45 (11.6%), whereas substrate modification was performed in 88 patients (77.2%) with substrate VAs, activation mapping in 6 (5.3%), pacemapping in 14 (12.3%), and 6 (5.3%) by entrainment. Acute procedural success was achieved in 354 patients (91.2%) with idiopathic VAs and 99 patients with substrate VAs (86.8%); partial success in 3 (2.6%) with substrate VAs, and failed ablation in 34 (8.8%) with idiopathic VAs and 12 (10.5%) with substrate VAs. Peri-procedural complications were identified in 5 patients, including 2 with pericardial effusion, 1 with atrio-ventricular block, 1 with pneumothorax, and 1 with stroke.

Patient follow-up and recurrences

A total of 60 patients (12.0%) received ICD implantation, including 4 with idiopathic VF and 56 with substrate VT/VF episodes. During a mean follow-up period of 39.77 ± 48.75 months (0-184 months), 126 (25.1%) patients developed recurrences, including 80 patients (20.6%) with idiopathic VAs and 46 with substrate VAs (40.4%). Mortality was recognized in 4 patients with substrate VAs, including two patients who died of non-

cardiac diseases (1 stroke and 1 pneumonia), and 2 by severe heart failure. ICD interventions were documented in 13 patients (11.4%) in patients with substrate VAs. Figure 4 demonstrated the Kaplan-Meier results for overall recurrences in patients with idiopathic VAs (4A) and substrate VAs (4B) regarding the origin and disease entity, respectively. For idiopathic VAs, the recurrences rate was significantly lower in patients with fascicular VT, followed by outflow tract (OT)-VAs, whereas VAs originating from papillary muscle and other sites yielded the worst prognosis (log-rank p < 0.001, Figure 4A). In contrast, there were no significant differences of overall VA recurrences in patients with substrate VAs (log-rank p = 0.85; Figure 4B).

In addition, analyzing the recurrences of sustained VT/VF, ICD therapies and overall mortality, the Kaplan-Meier curve demonstrated that use of ablation in patients with BrS could yield the best outcome, followed



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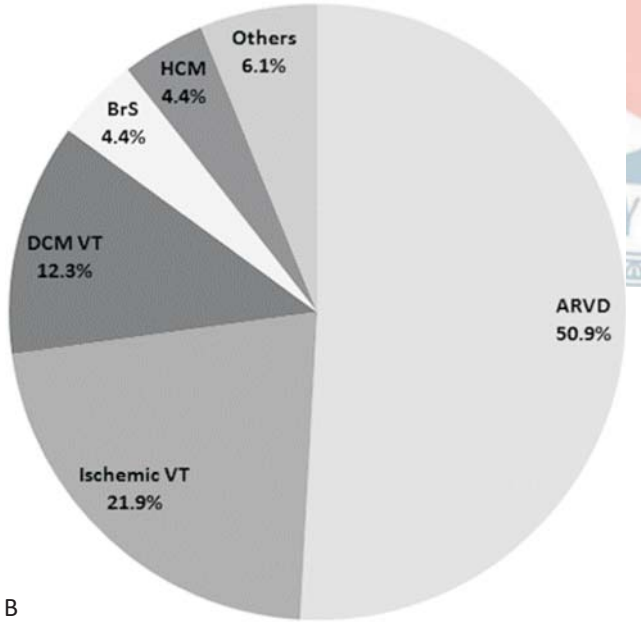
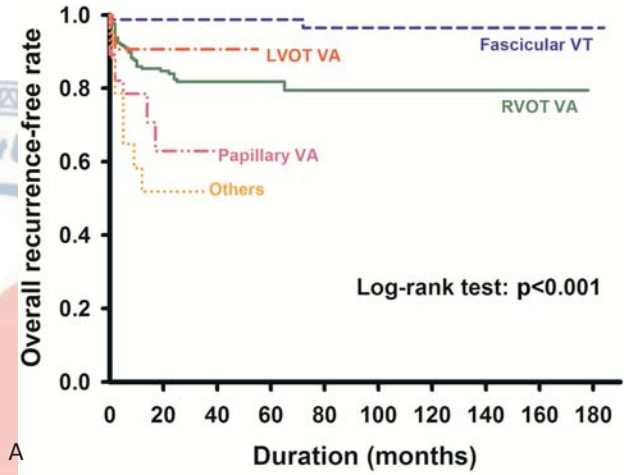


B

Figure 3. *The etiology and disease entities of patients undergoing RFCA for idiopathic VAs (A) and substrate VAs (B). Idiopathic RVOT VAs were the most common etiology for idiopathic VAs (p < 0.001), whereas ARVD/C contributed to the most common disease entity for substrate VAs (p < 0.001). Abbreviations as Figure 1.*



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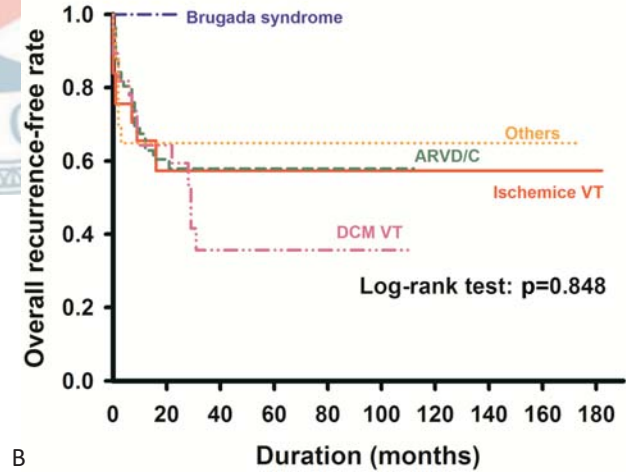

B

Figure 4. *Overall recurrences of VAs including nonsustained/sustained VT/VF or PVCs after successful RFCA for idiopathic VAs (A) and substrate VAs (B). (A) showed better ablation outcome for idiopathic VAs for fascicular VT and idiopathic OT-VAs (p < 0.001). In contrast, there was no statistical significance of overall recurrence with regard to different disease entities in patients with substrate VAs (p = 0.848). Abbreviations as Figure 1.*

by ARVD/C, whereas DCM VAs was associated with the worst prognosis (log-rank p = 0.04; Figure 5). Of the 56 patients who received an ICD implantation for substrate VAs, RFCA significantly attenuated ICD therapies and mortality comparing those before RFCA (log-rank p < 0.001; Figure 6).

DISCUSSION

Major findings

The present study demonstrates several important findings. First, we reported the current status of RFCA for VAs from one experienced referral center in Taiwan during a long-term follow-up. The number of subjects undergoing RFCA of either idiopathic VAs or substrate VAs revealed a gradual increase in the most recent 5 years compared with the prior decade. Second, most of the substrate VAs were composited by patients with ARVD/C, which reflected a distinct patient population compared to reports from western countries. Third, RFCA of idiopathic VAs could be achieved and be an effective strategy for drug refractory cases with a high acute success rate, especially for idiopathic RVOT VAs and fascicular VT. Fourth, despite having similar VA recurrences in patients with abnormal substrates, RFCA by substrate modification could yield better outcomes in preventing the occurrence of sustained VT/VF, ICD therapies and mortality in patients with ARVD/C and BrS, compared with other disease entities. Finally, RFCA could significantly reduce the recurrent episodes of ICD interventions for patients with sustained substrate VT/VF.

Advancement of VA ablation

Given the up-to-date revision of the indications, techniques, and improvements seen in clinical outcomes, RFCA of VAs is increasingly performed in western countries.[9,23] However, the current situation in Asia regarding the potential of RFCA for Vas has been rarely reported. To the best our knowledge, this study is the first to demonstrate detailed patient characteristics, electrophysiological properties, and the efficacy of RFCA from one experienced referral center in Taiwan in a long-term follow-up. Similar to reports from western countries, the number of patients undergoing RFCA for VAs, either idiopathic VAs or substrate VAs, has displayed a gradual and significant increase in the last 5 years, reflecting the popularization of the management of drug-refractory VAs, the improvement of ablation techniques, and the advancement of the navigation system in Taiwan.

Furthermore, Sacher et al. has reported about the evolution of VT ablation and showed an increase in substrate VT rather than idiopathic VT, especially for non-

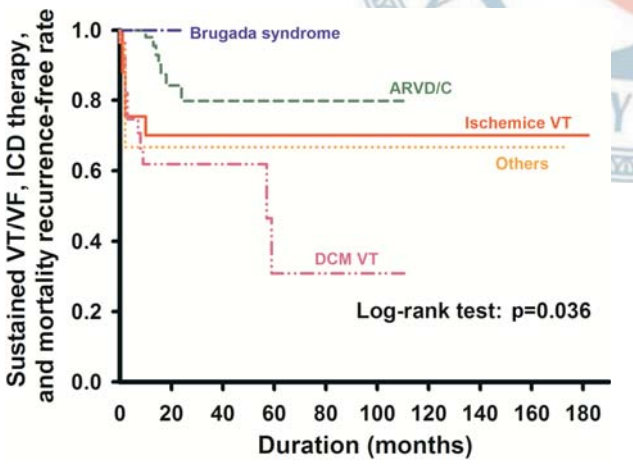

Figure 5. *Recurrences of sustained VT/VF, ICD therapies and mortalities after RFCA for substrate VAs. RFCA for VAs in patients with BrS and ARVD/C could yield better outcome compared with those in other disease entities (p = 0.036). ARVD/C, arrhythmogenic right ventricular dysplasia/cardiomyopathy; BrS, Brugada syndrome; DCM, dilated cardiomyopathy; ICD, implantable cardioverter-defibrillator; VA, ventricular arrhythmia; VF, ventricular fibrillation; VT, ventricular tachycardia.*

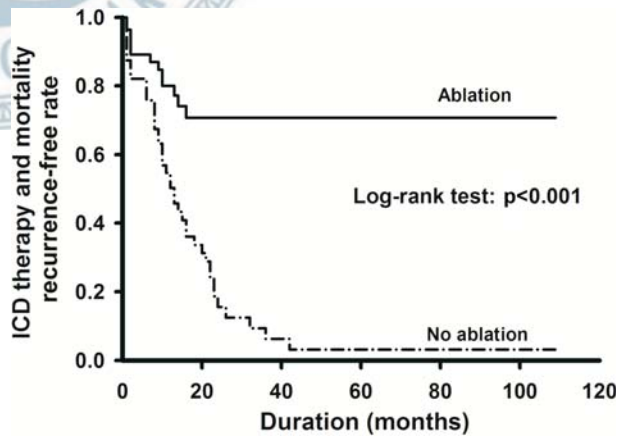

Figure 6. *Recurrences of ICD therapies and mortalities in patients with substrate VAs receiving an ICD implantation. RFCA significantly reduced the recurrent episodes of ICD interventions and mortalities in patients with substrate VAs (p < 0.001). ICD, implantable cardioverter-defibrillator; RFCA, radiofrequency catheter ablation; VA, ventricular arrhythmia.*

ischemic cardiomyopathy.[23] Ischemic cardiomyopathy composited the main proportion of RFCA for substrate VT. Contrary to the present finding, a significant growth of VA ablation resulted from either idiopathic or substrate VA, and ARVD/C serves the most common disease, reflecting distinct pattern in the evolution of VA ablation and non-uniform characteristics between different ethnicities.

RFCA of idiopathic VAs: characteristics and recurrences

RFCA of idiopathic VAs has been considered as an effective strategy for drug refractory cases with a high acute success rate. Except for fascicular VT, most cases of idiopathic VAs were related to focal triggered activity. Accurate identification and abolition of the foci could lead to high acute success rate of 82-100% with a variable recurrence rate ranging from 5 to 52% during non-uniform follow-up period.[24-26] Consistent with earlier reports, the acute elimination of arrhythmogenic foci could be achieved in 354 patients (91.2%) with VA recurrence rate of 20.6%, indicating that RFCA was an effective strategy for patients with idiopathic VA who failed to respond to medical therapy. Moreover, in the present study, 4 patients presented with idiopathic VF caused by frequent PVCs before ablation. However, none of them died from cardiac disease nor developed structural heart disease during follow-up. It therefore supported the fact that idiopathic VA is a benign entity and is generally associated with a more favorable outcome.

The recurrence of idiopathic VAs can be attributed to several reasons, including inaccurate mapping during ablation, arrhythmogenic foci located intramurally or epicardially that was not penetrable by endocardial ablation energy, and the development of new arrhythmogenic triggers.[27] This would support the present findings of a higher recurrence rate in patients with VAs originating from papillary muscle and other sites. Additionally, given the complexity of OT anatomical structure, the OT-VAs exhibited a higher recurrence rate compared with fascicular VT. However, further studies are required to explore the underlying mechanism for the development of new arrhythmogeninc foci in contributing to the recurrence of idiopathic VAs.

RFCA of substrate VAs: disease entities, recurrences

The majority of substrate VAs were due to scar-related reentry in patients with structural heart disease.[9] Recently, targeting the frequent PVC triggers in patients with structural heart disease has been proven to be an alternative strategy to further reduce malignant events.[28-30] Previous reports from other experienced groups demonstrated that the effectiveness or RFCA in abolition or modification of inducible VAs was estimated higher than 75%, whereas elimination of sustained monomorphic VT could be achieved around 70-80%.[9,23] Much like the present results, acute procedural success could be achieved in 86.8% of patients with substrate VAs. Despite the different inclusion criteria from previous studies, most of the patients in the present studies presented sustained or nonsustained ventricular tachyarrhythmias before ablation, indicating the comparable success rate between different groups and mapping strategies.

Noteworthy is the recurrence in patients with substrate VAs. Though there were no significant differences of overall VA recurrences between divergent substrate VAs, the present study demonstrated a novel finding that RFCA in patients with BrS and ARVD/C could have lower recurrences of unfavorable episodes, including sustained VT/VF, ICD interventions, and mortality. Several factors, including intrinsic scar/substrate characteristics, alternations in autonomic tone, non-uniform prescription of anti-arrhythmic medication, and progression of underlying myocardial or coronary disease, might influence the heterogeneous recurrences[9] and explain the current findings. Nonetheless, RFCA significantly reduced further ICD therapies in patients with structural heart disease, supporting the prognostic implication of RFCA in the prevention of recurrences of ventricular tachyarrhythmias after ICD implantation. Despite the recurrences of substrate VAs after RFCA of up to 40.4%, the decrease of ICD therapies has reflected the attenuation and prevention of sustained VT or VF after RFCA for substrate VAs.

Aside from the above, the appropriate timing for the referral to initiate RFCA remains an unresolved question. Chao et al.[31] studied the ICD recipients for secondary preventions in Taiwan from multicenter registry and showed that ischemic cardiomyopathy was the most common etiology, followed by DCM. The discrepancy of patients' characteristics between previous re-

ports and our population implied the gap between ICD implantation and RFCA. Patients in this study were enrolled from a single tertiary referral center, which might reflect a snapshot of the patient population with substrate VAs and contribute to the differences between disease entities from previous reports. Recently, Reddy et al. and Kuck et al. proved the role of prophylactic ablation in prevention of the occurrence of ischemic VT.[10,32] Whether early prophylactic RFCA should be performed in substrates VA with different etiology requires further investigation to clarify these issues.

Limitations

There were several limitations to the present study. First, the assessment of recurrences of idiopathic VAs and substrate VAs without ICD implantation were based on Holter monitoring, which could underestimate of the true recurrence rate. However, all patients in the study underwent regular follow-up. These would reduce the percentage of undetected recurrences. Second, the advancement in navigation system, which could facilitate the identification of the arrhythmogenic foci or substrates, were not applied to every case. Also, both irrigated and non-irrigated ablation catheter were used in this study. These factors might have implication on the ablation outcome. Third, though the prognostic implication on patients with BrS was better than those with other substrate VAs, patients enrolled in this study were limited. Given the rare disease of BrS in entity, the clinical value of application of RFCA in patients with BrS warranted further investigations. Fourth, patients who received RFCA during 2013 were followed less than one year, which might underestimate the recurrences. Finally, advancement in mapping and ablation technique could impact the effectiveness of ablation outcome through a long-term follow-up. The clinical parameters in prediction of the ablation outcome would be the next frontier to break through.

CONCLUSIONS

RFCA of VAs displayed a tendency toward gradual increase in annual distribution within the most recent 5 years. The present results echoed that RFCA serves an effective and alternative strategy in eliminating idiopathic VAs and preventing the recurrences of sustained VT/VF and ICD therapies in patients with substrate VAs in an experienced referral center in Taiwan. The distinct location of arrhythmogenic triggers and disease entities may result in heterogeneous VA recurrences and clinical prognosis.

ACKNOWLEDGEMENTS

This work was supported by National Central University (grant no. CNJRF-99CGH-NCU-A3), the Center for Dynamical Biomarkers and Translational Medicine, Ministry of Science and Technology (102-2314-B-010-056-MY2, NSC 102-2911-I-008-001, NSC 101-2911-I-008-001, NSC 100-2314-B-010-033-MY3, NSC 99-2628-B-075-007-MY3), The Research Foundation of Cardiovascular Medicine (RFCM 96-02-018, 97-02-029, 98-01-020, 98-02-032, 99-01-022, 100-01-004, 100-02-011, 100-02-022, 101-01-001), and Taipei Veterans General Hospital (V102C-128, V103E7-003, VN103-04, V103C-042).

FUNDING SOURCES

None.

DISCLOSURES

None.

REFERENCES

1. Stevenson WG. Current treatment of ventricular arrhythmias: state of the art. *Heart Rhythm*. 2013;10:1919-26.
2. Takemoto M, Yoshimura H, Ohba Y, et al. Radiofrequency catheter ablation of premature ventricular complexes from right ventricular outflow tract improves left ventricular dilation and clinical status in patients without structural heart disease. *J Am Coll Cardiol*. 2005;45:1259-65.
3. Haissaguerre M, Derval N, Sacher F, et al. Sudden cardiac arrest associated with early repolarization. *N Engl J Med* 2008;358: 2016-23.
4. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics -- 2014 update: a report from the American Heart Association. *Circulation* 2014;129:e28-292.
5. Hohnloser SH, Israel CW. Current evidence base for use of the

implantable cardioverter-defibrillator. *Circulation* 2013;128: 172-83.
6. Al-Khatib SM, Hellkamp A, Bardy GH, et al. Survival of patients receiving a primary prevention implantable cardioverter-defibrillator in clinical practice vs. clinical trials. *JAMA* 2013;309:55-62.
7. Sweeney MO, Sherfesee L, DeGroot PJ, et al. Differences in effects of electrical therapy type for ventricular arrhythmias on mortality in implantable cardioverter-defibrillator patients. *Heart Rhythm* 2010;7:353-60.
8. Sears SF, Hauf JD, Kirian K, et al. Posttraumatic stress and the implantable cardioverter-defibrillator patient: what the electrophysiologist needs to know. *Circ Arrhythm Electrophysiol* 2011; 4:242-50.
9. Aliot EM, Stevenson WG, Almendral-Garrote JM, et al. EHRA/HRS Expert Consensus on Catheter Ablation of Ventricular Arrhythmias: developed in a partnership with the European Heart Rhythm Association (EHRA), a Registered Branch of the European Society of Cardiology (ESC), and the Heart Rhythm Society (HRS); in collaboration with the American College of Cardiology (ACC) and the American Heart Association (AHA). *Heart Rhythm* 2009;6:886-933.
10. Kuck KH, Schaumann A, Eckardt L, et al. Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): a multicentre randomised controlled trial. *Lancet* 2010;375:31-40.
11. Stevenson WG, Wilber DJ, Natale A, et al. Irrigated radiofrequency catheter ablation guided by electroanatomic mapping for recurrent ventricular tachycardia after myocardial infarction: the multicenter thermocool ventricular tachycardia ablation trial. *Circulation* 2008;118:2773-82.
12. NCEP. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106:3143-421.
13. Kocovic DZ, Harada T, Friedman PL, Stevenson WG. Characteristics of electrograms recorded at reentry circuit sites and bystanders during ventricular tachycardia after myocardial infarction. *J Am Coll Cardiol* 1999;34:381-8.
14. Vergara P, Roque C, Oloriz T, et al. Substrate mapping strategies for successful ablation of ventricular tachycardia: a review. *Arch Cardiol Mex* 2013;83:104-11.
15. Valles E, Bazan V, Marchlinski FE. ECG criteria to identify epicardial ventricular tachycardia in nonischemic cardiomyopathy. *Circ Arrhythm Electrophysiol* 2010;3:63-71.
16. Daniels DV, Lu YY, Morton JB, et al. Idiopathic epicardial left ventricular tachycardia originating remote from the sinus of Valsalva: electrophysiological characteristics, catheter ablation, and identification from the 12-lead electrocardiogram. *Circulation* 2006;113:1659-66.
17. Hutchinson MD, Gerstenfeld EP, Desjardins B, et al. Endocardial unipolar voltage mapping to detect epicardial ventricular tachycardia substrate in patients with nonischemic left ventricular cardiomyopathy. *Circ Arrhythm Electrophysiol* 2011;4:49-55.
18. Polin GM, Haqqani H, Tzou W, et al. Endocardial unipolar voltage mapping to identify epicardial substrate in arrhythmogenic right ventricular cardiomyopathy/dysplasia. *Heart Rhythm* 2011;8: 76-83.
19. Nademanee K, Veerakul G, Chandanamattha P, et al. Prevention of ventricular fibrillation episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium. *Circulation* 2011;123:1270-9.
20. Flemming MA, Oral H, Kim MH, et al. Electrocardiographic predictors of successful ablation of tachycardia or bigeminy arising in the right ventricular outflow tract. *Am J Cardiol* 1999;84: 1266-8, A9.
21. Lu TH, Lee MC, Chou MC. Accuracy of cause-of-death coding in Taiwan: types of miscoding and effects on mortality statistics. *Int J Epidemiol* 2000;29:336-43.
22. Marcus FI, McKenna WJ, Sherrill D, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the Task Force Criteria. *Eur Heart J* 2010;31:806-14.
23. Sacher F, Tedrow UB, Field ME, et al. Ventricular tachycardia ablation: evolution of patients and procedures over 8 years. *Circ Arrhythm Electrophysiol* 2008;1:153-61.
24. Joshi S, Wilber DJ. Ablation of idiopathic right ventricular outflow tract tachycardia: current perspectives. *J Cardiovasc Electrophysiol* 2005;16:S52-8.
25. Ribbing M, Wasmer K, Monnig G, et al. Endocardial mapping of right ventricular outflow tract tachycardia using noncontact activation mapping. *J Cardiovasc Electrophysiol* 2003;14:602-8.
26. Ventura R, Steven D, Klemm HU, et al. Decennial follow-up in patients with recurrent tachycardia originating from the right ventricular outflow tract: electrophysiologic characteristics and response to treatment. *Eur Heart J* 2007;28:2338-45.
27. Chung FP, Chong E, Lin YJ, et al. Different characteristics and electrophysiological properties between early and late recurrences after acute successful catheter ablation of idiopathic right ventricular outflow tract arrhythmias during long-term follow-up. *Heart Rhythm* 2014;11:1760-9.
28. Taieb JM, Maury P, Shah D, et al. Reversal of dilated cardiomyopathy by the elimination of frequent left or right premature ventricular contractions. *J Interv Card Electrophysiol* 2007;20:9-13.
29. Philips B, Madhavan S, James C, et al. High prevalence of catecholamine-facilitated focal ventricular tachycardia in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy. *Circ Arrhythm Electrophysiol* 2013;6:160-6.
30. Haissaguerre M, Extramiana F, Hocini M, et al. Mapping and ablation of ventricular fibrillation associated with long-QT and Brugada syndromes. *Circulation* 2003;108:925-8.
31. Chao TF, Lai CH, Tuan TC, et al. Long-term prognosis in recipients of implantable cardioverter-defibrillators for secondary preventions in Taiwan – a multicenter registry study. *Acta Cardiol Sin* 2014;30:22-8.
32. Reddy VY, Reynolds MR, Neuzil P, et al. Prophylactic catheter ablation for the prevention of defibrillator therapy. *N Engl J Med* 2007;357:2657-65.