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Trend of Arrhythmias Burden and Risk factors of Recurrence and Complications after Radiofrequency Catheter Ablation – A Nationwide Observational Study

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Abstract

Objectives: Risk factors for recurrence of arrhythmias and complications after radiofrequency catheter ablation (RFCA) remain unclear. This study is aimed at the recurrence and complications after RFCA among different types of arrhythmias.

Study Design and Setting: In this retrospective study which evaluated data from the Taiwan National Health Insurance Research Database (NHIRD), 19,475 patients who received RFCA were categorized into five groups according to arrhythmia type: paroxysmal supra-ventricular tachycardia (PSVT;N=12,796); Wolff–Parkinson–White syndrome (WPW; N=3,051); atrial flutter (AFL; N=1,854); atrial fibrillation (AF; N=1,162); and ventricular tachycardia (VT; N=612). Primary outcomes included recurrence and complications.

Results:

The most common arrhythmia treated with RFCA was PSVT (N= 12,796), followed by WPW (3,051), AFL (1854), AF (1,162) and VT (612). The recurrence-free rates after RFCA were PSVT (2%), WPW (4.9%), VT (5.7%), AFL (5.8%), and AF (16.1%). Patients > 75 years old had lower recurrence rates than other age groups. The AFL group had more second or third degree atrioventricular block (AV block) (2.26%) compared to other groups. The AF group showed the highest rate of cardiac tamponade requiring pericardiocentesis (0.98 %). Age was significantly associated with second or third degree AV block, pacemaker implantation, cardiac tamponade requiring pericardiocentesis and new stroke. Diabetes was a risk factor of second or third degree AV block.

Conclusions:

There was a rapid increase in RFCA of AF, AFL, and VT from 2001-2010. Recurrence was associated with congenital heart disease in PSVT and WPW groups, and with age in AF and AFL groups. The AFL group had a higher risk of permanent pacemaker implantation, and

new stroke. The AF group had a higher risk of cardiac tamponade requiring pericardiocentesis.

Key words: radiofrequency catheter ablation (RFCA), Wolff–Parkinson–White syndrome, supraventricular tachycardia, ventricular tachycardia, complication, recurrence, risk factors

Strengths and limitations of this study

- This retrospective study is the first nationwide, large-scale study which surveys the burden, recurrence and complication of RFCA. In addition, our observation period is about 10 years so that we recognize the transition of RFCA and the relation between RFCA and population change in Taiwan.
- This article is the first study to compare the recurrence and complications among five different types of arrhythmias integratedly.
- This study did not have access to some detail data such as laboratory parameters, procedural details, and heart images, etc. And some arrhythmias such as premature ventricular beats, and atrial premature beats are not covered by Taiwan National Health Insurance(NHI).

Introduction

Radiofrequency catheter ablation (RFCA) is used to treat patients with supraventricular tachycardia (SVT) or ventricular tachycardia (VT), especially paroxysmal supraventricular tachycardia (PSVT) [2-4] . RFCA, which has been widely applied since the 1990s[1], is an effective therapy that has demonstrated high success, low complications, and low recurrence rates compared to direct current ablation and or surgical ablation. RFCA is superior to conservative treatment such medication or observation for patients with PVST and Wolff–Parkinson–White syndrome (WPW). RFCA was first used to treat atrial fibrillation (AF) in 1998.

Although arrhythmias after RFCA are usually not life-threatening, identification and minimization of the risk of complications are extremely important. The RFCA procedure may lead to atrioventricular block (AV block) and bradycardia, even requiring permanent pacemaker implantation. Previous studies were composed of relatively small cohorts or were single-center studies, and evaluated patients with single arrhythmia. However, there are no studies comparing RFCA-related complications in patients with five different arrhythmias [5,6]. The targets for RFCA-related risk minimization are different for different arrhythmias. For example, when RFCA is used to treat PSVT, the goal is to modify or eliminate AV node or accessory pathways, and when RFCA is used to treat AF, the goal is to isolate the pulmonary veins. These RFCA-treated patients share similar complications like AV block, requirement for permanent pacemaker implantation, pericardial effusion with tamponade requiring pericardiocentesis, and stroke. However, the complication rates vary in the five different arrhythmias: paroxysmal supraventricular tachycardia (PSVT), Wolff–Parkinson–White syndrome (WPW), typical atrial flutter (AFL), atrial fibrillation (AF), and ventricular tachycardia (VT). It is therefore important to identify the incidence and risk of RFCA-related complications in these patients.

This retrospective study investigated the population trend of patients who received RFCA for PSVT, WPW, AFL, AF, and VT. We identified the major RFCA-related risk factors influencing 1) recurrence of arrhythmias, and 2) complications such as AV block, permanent pacemaker implantation, cardiac tamponade and acute ischemic stroke.

Methods

Study design and population

We conducted a nationwide population-based cohort study using data from the Taiwan NHIRD. In Taiwan, the National Health Insurance (NHI) program has reimbursed patients who receive RFCA for PSVT, WPW syndrome, AFL, AF and VT since 2001. More than 99.91% of Taiwan's population is covered by the NHI scheme. The accuracy and validation of National Health Insurance Research Database (NHIRD) data is based upon regular auditing by the NHI Bureau [7-9]. The Ethics Institutional Review Board at Chang Gung Memorial Hospital approved this study.

Study cohort, outcome measurement and follow-up

This study accessed NHIRD data for all targeted arrhythmia patients who received RFCA from 2001 to 2010. The targeted arrhythmias were PSVT (Internal Classification of Diseases, Ninth Revision, ICD-9, Code 4270), WPW (426.7), AFL (427.32), AF (427.31), and VT (427.1; Supplemental Table). Patients with arrhythmias other than targeted arrhythmias (such as premature ventricular beats or atrial tachycardia) and patients with unidentified arrhythmias who received RFCA were excluded. For patients who received more than one round of RFCA, we analyzed the data from the first round. The follow-up period was from the time of hospitalization until death, or until 31st December 2010.

Outcome measurement

The primary outcomes included recurrence of arrhythmia, and complications. Recurrence was defined as either 1) recurrence of original arrhythmias, or 2) receiving secondary RFCA. Complications included high-grade AV block, high-grade AV block requiring permanent pacemaker implantation, cardiac tamponade requiring pericardiocentesis, and new stroke regardless ischemic or hemorrhagic stroke.–High-grade AV block was defined as second or third degree atrioventricular block (AV block) (426.12, 426.13, 426.0). Permanent pacemaker implantation was due to AV block–after RFCA.

Cardiac tamponade requiring pericardiocentesis was defined as 1) massive pericardial effusion during RFCA, or 2) patient requiring pericardiocentesis at index admission. New stroke was defined as stroke (430*, 431*, 432*, 433*, 434*, 436*, 437*) which occurred during index admission. In-hospital death was defined as death of the patient due to any cause during index admission.

Covariate assessment

Comorbidities were assessed according to ICD-9 codes before index admission. Diabetes mellitus, hypertension (HTN) or chronic diseases were recorded as comorbidities if there was at least one in-admission diagnosis. All congenital heart disease (CHD) was reconfirmed by the Catastrophic Illness certification (CIC) which is sub dataset of NHI. A CIC for congenital heart disease requires imaging proof confirmed by two cardiologists. Complicated CHD included Tetralogy of Fallot (TOF), transposition of the great vessels, double outlet right ventricle, total anomalous pulmonary venous connection, tricuspid atresia, common truncus arteriosus, common ventricle and hypoplastic left heart syndrome. Simple CHD included ventricular septal defect (VSD), atrial septal defect (ASD), Ebstein's anomaly, patent ductus arteriosus, congenital pulmonary stenosis, coarctation of aorta, endocardial cushion defect, and congenital aortic stenosis. Center volume was designed as time-dependent variety and high center volume was defined as RFCA numbers more than 100 regardless of arrhythmias type.

Patient and public involvement

This study has no direct relationship with any patient and public involvement during the development, design and conduct.

Statistical analysis

The proportion of categorical variables among different groups was compared using the chi-squared test. Continuous variables were compared using one-way ANOVA. Multivariate Cox regression analysis was used to investigate the association of clinical variables with recurrence and some complications (second or third AV block and pacemaker implantation). Multivariate logistic regression analysis was also used to identify factors clinical variables associated with complications (cardiac tamponade requiring pericardiocentesis and the occurrence of new stroke). Results were presented as the odds ratio (OR) for logistic regression, or hazard ratio (HR) for Cox regression with corresponding 95% confidence intervals (CI). All data analyses were performed using SPSS software version 15 (SPSS Inc, Chicago, Illinois).

Results

There were 24,003 RFCA procedures registered in NHIRD between 1 January, 2001 and 31 December, 2010.–Based on the inclusion and exclusion criteria, a total of 19,475 patients were enrolled, who underwent 20,707 RFCA procedures.

A majority of the study participants were diagnosed with PSVT (N= 12,796), followed by WPW (N= 3,051), AFL (N= 1,854), AF (N= 1,162) and VT (N= 612). The mean age of study participants was 47.6 years (S.D. = 18.3), and the average follow-up period was 4.36 years (S.D. = 2.86). The ratio of changes in individual arrhythmias from 2001 to 2010 is shown in Figure 1a and 1b. The ratio of PSVT decreased from 60% to 51% between 2001 to 2010, while the ratio of AF increased from 2% to 10%. Demographic and baseline clinical characteristics according to arrhythmia types are summarized in Table 1. Patients aged 19-45 years had the highest prevalence of PSVT (38.5%), WPW (58.1%) and VT (47.2%). The prevalence of AF and AFL was 30.5% in patients aged 55–64, and 25.5% in patients aged

65–74 years (25.5%). Patients with AF and AFL had a significantly higher prevalence of diabetes (16.2% and 11.5%) and hypertension (28.9% and 28.1%) compared to patients with other arrhythmias. Simple congenital heart disease was seen in 3.6% of patients with AFL.

Table 1. Baseline data for 19,475 study patients who underwent RFCA procedure

	PSVT	WPW	Atrial flutter	Atrial fibrillation	Paroxysmal ventricular tachycardia	*P* value
Number of patients	12796	3051	1854	1162	612	--
Age	46.2±17.6	37.1±16.6	61.0±15.4	56.3±13.2	43.0±17.8	<0.001
Age group						<0.001
0-18 yrs	863 (6.7)	379 (12.4)	15 (0.8)	0 (0.0)	46 (7.5)	
19-44 yrs	4930 (38.5)	1619 (53.1)	260 (14.0)	216 (18.6)	289 (47.2)	
45-54 yrs	2938 (23.0)	579 (19.0)	329 (17.7)	285 (24.5)	123 (20.1)	
55-64 yrs	2083 (16.3)	308 (10.1)	407 (22.0)	354 (30.5)	75 (12.3)	
65-74 yrs	1344 (10.5)	130 (4.3)	472 (25.5)	222 (19.1)	51 (8.3)	
Above 75 yrs	638 (5.0)	36 (1.2)	371 (20.0)	85 (7.3)	28 (4.6)	
Gender, male	5402 (42.3)	1988 (65.2)	1332 (71.9)	838 (72.2)	327 (53.5)	<0.001
Diabetes	910 (7.1)	113 (3.7)	301 (16.2)	134 (11.5)	32 (5.2)	<0.001
Hypertension	1723 (13.5)	275 (9.0)	535 (28.9)	326 (28.1)	74 (12.1)	<0.001
COPD	286 (2.2)	22 (0.7)	103 (5.6)	28 (2.4)	15 (2.5)	<0.001
CKD	150 (1.2)	12 (0.4)	71 (3.8)	11 (0.9)	5 (0.8)	<0.001
CAD	594 (4.6)	87 (2.9)	288 (15.5)	154 (13.3)	45 (7.4)	<0.001
Heart failure	73 (0.6)	21 (0.7)	205 (11.1)	53 (4.6)	25 (4.1)	<0.001
High center volume ‡	7267 (56.8)	1880 (61.6)	1317 (71.0)	976 (84.0)	317 (51.8)	<0.001
Complicated CHD	10 (0.1)	3 (0.1)	16 (0.9)	2 (0.2)	1 (0.2)	<0.001
TOF	3 (0.0)	0 (0.0)	11 (0.6)	1 (0.1)	1 (0.2)	<0.001
Other Complicated CHD	7 (0.1)	3 (0.1)	5 (0.3)	1 (0.1)	0 (0.0)	0.045
Simple CHD †	69 (0.5)	31 (1.0)	66 (3.6)	9 (0.8)	9 (1.5)	<0.001
VSD	15 (0.1)	6 (0.2)	25 (1.3)	0 (0.0)	4 (0.7)	<0.001
ASDII	50 (0.4)	10 (0.3)	34 (1.8)	9 (0.8)	4 (0.7)	<0.001
Ebstein	4 (0.0)	18 (0.6)	6 (0.3)	0 (0.0)	0 (0.0)	<0.001
Other simple CHD	4 (0.0)	2 (0.1)	6 (0.3)	0 (0.0)	1 (0.2)	<0.001

‡ defined as 100 volume per year;

† There is a discrepancy between the sums of subgroups and the total due to one patient who might have two CHDs;

Risks of recurrence

Multivariate Cox analyses revealed that the major risk factors for recurrence of PSVT after RFCA included: age (0–18 years), male gender, diabetes, and TOF. Younger patients (0–18 *vs.* 19–44 years) and those with Ebstein anomaly were considered at greater risk for recurrence of WPW after RFCA (Table 2). For the AFL group, older individuals (45–54 *vs.* 19–44 years) had a higher risk of recurrence. Male gender, TOF, VSD, and high center volume were also risk factors. In contrast, the incidence of AFL recurrence was low in patients older than 75 years. Patients with AF had a recurrence rate of 16.1% following RFCA, whereas the recurrence rate of PSVT was as low as 2.0%. The recurrence-free rate of AF after RFCA declined with time, while recurrence-free rates for the other 4 groups were greater than 90% (Figure 2). Patients aged 19–44 years had a higher risk of AF recurrence compared with patients older than 65 years; male gender and high center volume were also identified as risk factors. In the VT population, a high center volume was related to decreased risk of recurrence.

Table 2. Risk factors of recurrence

	PSVT (259 events, 2.0%)		WPW (160 events, 4.9%)		Atrial flutter (120 events, 5.8%)		Atrial fibrillation (247 events, 16.1%)		Paroxysmal ventricular tachycardia (38 events, 5.7%)	
Variable	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age										
0-18 yrs	1.52 (1.02–2.28)	0.041	1.90 (1.27–2.85)		2.17 (0.50–9.41)	0.301	N.A		1.19 (0.41–3.48)	0.750
19-44 yrs	Reference		Reference		Reference		Reference		Reference	
45-54 yrs	0.88 (0.64–1.22)	0.456	0.90 (0.57–1.44)	0.670	1.98 (1.15–3.41)	0.014	1.03 (0.73–1.44)	0.875	0.71 (0.28–1.78)	0.460
55-64 yrs	0.70 (0.47–1.05)	0.084	1.47 (0.87–2.47)	0.148	1.40 (0.78–2.51)	0.266	0.87 (0.61–1.23)	0.430	0.75 (0.24–2.36)	0.624
65-74 yrs	0.68 (0.42–1.11)	0.121	0.95 (0.37–2.41)	0.910	0.93 (0.49–1.77)	0.823	0.54 (0.34–0.86)	0.010	0.19 (0.02–1.56)	0.122

Above 75 yrs	0.69 (0.35–1.37)	0.289	N.A.		0.28 (0.10–0.76)	0.013	0.08 (0.02–0.34)	0.001	N.A	
Male gender	1.66 (1.30–2.13)	<0.001	1.06 (0.77–1.48)	0.708	1.68 (1.09–2.59)	0.020	1.43 (1.05–1.95)	0.023	1.31 (0.66–2.58)	0.436
Diabetes	1.59 (1.01–2.52)	0.047	0.18 (0.03–1.34)	0.094	0.80 (0.43–1.49)	0.485	0.70 (0.43–1.14)	0.153	0.70 (0.09–5.74)	0.741
Hypertension	1.03 (0.70–1.53)	0.876	1.27 (0.71–2.28)	0.424	0.73 (0.46–1.15)	0.174	1.29 (0.97–1.72)	0.076	1.49 (0.40–5.49)	0.548
COPD	1.13 (0.50–2.60)	0.765	N.A.		1.08 (0.43–2.72)	0.867	1.45 (0.54–3.94)	0.464	N.A	
CKD	1.61 (0.59–4.36)	0.350	N.A.		0.78 (0.24–2.49)	0.673	0.55 (0.08–4.02)	0.559	4.18 (0.52–33.86)	0.180
CAD	0.85 (0.44–1.64)	0.631	0.53 (0.13–2.17)	0.377	0.59 (0.29–1.17)	0.131	1.07 (0.73–1.56)	0.743	1.18 (0.26–5.25)	0.832
Heart failure	1.64 (0.40–6.67)	0.493	N.A.		0.91 (0.47–1.75)	0.778	0.29 (0.07–1.20)	0.088	2.90 (0.63–13.42)	0.173
TOF	23.00 (4.01–131.81)	<0.001	N.A.		3.32 (1.01–10.96)	0.049	N.A		N.A	
VSD	N.A.	0.979	2.79 (0.53–14.82)	0.228	2.78 (1.29–5.99)	0.009	0.99 (0.13–7.43)	0.993	N.A	
ASD II	2.78 (0.89–8.72)	0.079	0.40 (0.04–4.25)	0.447	1.46 (0.57–3.71)	0.430	1.17 (0.28–4.87)	0.832	3.57 (0.47–27.34)	0.221
Ebstein	1.08 (0.09–12.80)	0.950	4.40 (1.80–10.74)	0.001	1.54 (0.21–11.47)	0.676	N.A		N.A	.
High center volume	1.05 (0.82–1.35)	0.679	0.87 (0.63–1.19)	0.383	1.78 (1.11–2.85)	0.017	3.16 (1.77–5.67)	<0.001	0.49 (0.25–0.97)	0.040

HR = hazard ratio; CI = confidence interval; NA = not applicable

Complications

RFCA-related complications were evaluated for the five different arrhythmia groups (Table 3). The overall prevalence of complications and mortality were less than 1 and 0.1%, respectively. Second or third degree AV block was the most common complication following RFCA in all the arrhythmia groups, except for the AF group. RFCA induced more tamponade requiring pericardiocentesis (0.98%) in the AF group compared to the other arrhythmias. In the AFL group, RFCA caused more second or third AV block (2.26%), permanent pacemaker implantation (1.25%), and new stroke (0.43%)

Table 3 RFCA-related complications according to different types of arrhythmias

	PSVT	WPW	Atrial flutter	Atrial fibrillation	Paroxysmal ventricular tachycardia
Second or third AVB	114 (0.87)	10 (0.31)	47 (2.26)	8 (0.52)	5 (0.75)
Pacemaker implantation	64 (0.49)	5 (0.15)	26 (1.25)	2 (0.13)	3 (0.45)
Tamponade requiring pericardiocentesis	15 (0.11)	8 (0.24)	6 (0.29)	15 (0.98)	1 (0.15)
New stroke	8 (0.06)	2 (0.06)	9 (0.43)	4 (0.26)	0 (0.00)

Risk factors of complications

Risk factors for second or third degree AV block were age > 75 years old, diabetes, and heart failure (Table 4). WPW patients were at a lower risk of developing AV block than PSVT patients. Risk factors of pacemaker implantation were age > 75 years old, diabetes, chronic kidney disease (CKD), and AFL after RFCA (when compared with PSVT). Age > 44

years old, high center volume hospital, and RFCA of WPW or AF (when compared with PSVT) were associated with increased risk of cardiac tamponade requiring pericardiocentesis. Age >55 years old and AFL after RFCA (when compared with PSVT) were associated with a higher risk of stroke following RFCA.

Table 4. Risk factors of complications

	Second or third AVB (184 events, 0.89%)		Pacemaker (100 events, 0.48%)		Pericardiocentesis (45 events, 0.22%)		New stroke (23 events, 0.11%)	
Variable	HR (95% CI)	*P*	HR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Age								
0-18 yrs	0.66 (0.28–1.53)	0.330	0.81 (0.24–2.71)	0.734	N.A		N.A	
19-44 yrs	Reference		Reference		Reference		Reference	
45-54 yrs	1.07 (0.70–1.62)	0.756	1.70 (0.96–3.01)	0.067	11.18 (2.50–50.10)	0.002	4.53 (0.46–44.16)	0.194
55-64 yrs	0.85 (0.52–1.37)	0.499	1.09 (0.55–2.18)	0.803	17.32 (3.87–77.55)	<0.001	19.68 (2.44–158.78)	0.005
65-74 yrs	1.07 (0.65–1.77)	0.793	1.40 (0.69–2.85)	0.355	17.75 (3.68–85.57)	<0.001	9.58 (0.99–91.66)	0.051
Above 75 yrs	2.07 (1.24–3.44)	0.005	3.82 (1.94–7.53)	<0.001	22.70 (4.16–123.95)	<0.001	17.01 (1.73–167.36)	0.015
Male gender	1.14 (0.84–1.54)	0.404	0.74 (0.49–1.12)	0.156	1.12 (0.60–2.12)	0.716	0.84 (0.35–2.00)	0.696
Diabetes	1.77 (1.17–2.70)	0.007	1.95 (1.13–3.37)	0.016	0.33 (0.08–1.39)	0.131	1.22 (0.40–3.70)	0.727
Hypertension	1.08 (0.73–1.59)	0.703	0.94 (0.55–1.59)	0.806	1.01 (0.51–2.01)	0.973	0.52 (0.17–1.59)	0.251
COPD	0.70 (0.28–	0.434	0.77 (0.24–	0.667	N.A		N.A	

	1.72)		2.49)					
CKD	2.10 (0.97–4.54)	0.060	2.69 (1.07–6.76)	0.036	N.A		1.41 (0.18–10.89)	0.743
Heart failure	2.31 (1.28–4.17)	0.006	1.00 (0.35–2.83)	0.994	0.74 (0.10–5.59)	0.769	2.51 (0.68–9.29)	0.169
TOF	N.A.		N.A		N.A		N.A	
VSD	2.20 (0.51–9.47)	0.291	N.A		N.A		N.A	
ASD II	1.55 (0.37–6.47)	0.547	1.94 (0.27–14.10)	0.513	4.10 (0.53–31.84)	0.177	N.A	
Ebstein	3.70 (0.49–27.86)	0.204	N.A		N.A		N.A	
High center volume	0.98 (0.73–1.33)	0.913	0.92 (0.61–1.38)	0.684	3.79 (1.47–9.79)	0.006	1.15 (0.46–2.88)	0.761
Indication								
PSVT	Reference		Reference		Reference		Reference	
WPW	0.37 (0.19–0.71)	0.003	0.41 (0.16–1.04)	0.060	2.98 (1.24–7.15)	0.015	1.63 (0.34–7.85)	0.545
PVT	0.85 (0.35–2.10)	0.728	1.10 (0.34–3.51)	0.874	1.58 (0.21–12.14)	0.658	N.A	
Atrial fibrillation	0.53 (0.25–1.11)	0.093	0.33 (0.08–1.36)	0.125	4.09 (1.90–8.79)	<0.001	2.74 (0.77–9.72)	0.118
Atrial flutter	1.74 (1.17–2.60)	0.006	2.14 (1.27–3.62)	0.004	1.34 (0.49–3.70)	0.566	4.07 (1.39–11.91)	0.010

Discussion

To the best of our knowledge, this is the first observational study to record the impact of RFCA on the treatment of arrhythmias by analyzing the burden, risk factors, recurrence, and complications of patients with five different arrhythmias. There was a rapid increase in the number of RFCAs for the AF, AFL, and VT groups, whereas a gradual increase for the PSVT and WPW groups from 2001-2010 was noticed. Age was a risk factor of recurrence in the different arrhythmia groups, while male gender, diabetes and TOFwere risk factors of recurrence in patients with PSVT after RFCA. Patients in high center volume hospitals had a tendency to receive repeated AF RFCAs. Elderly patients with AF, and AFL had more adverse events during RFCA compared to other subgroups.

Burdens of PSVT, WPW, AFL, AF, and VT

In Taiwan, there has been an increase in the number of AF RFCA over the past ten years, and this group had the greatest growth rate, followed by the VT, AFL, WPW and PSVT groups. Population aging, and advancement of ablation techniques have contributed to this phenomenon especially for AF, and AFL, which are aging-related diseases [10]. From 2001 to 2010, the population of elderly patients (>65 years old) increased from 1,973,357 to 2,487,893. This has resulted in a greater increase in the AF, and AFL RFCA numbers compared to other arrhythmias. The average growth rate of is 9.69% for AF RFCA, and 3.23% for AFL RFCA (Figure 3, Figure 4). In contrast, the average growth rate of PSVT RFCA is just 1.42%. The RFCA growth rate is gradually slowing, but the absolute numbers grew from 1,118 in 2001 to 1,499 in 2010. This pattern is true for PSVT and WPW since 1) PSVT and WPW RFCA are relatively mature than AF. 2) PSVT and WPW require less substrate to be eliminated compared to AF. The crude birth rate of Taiwan during 1980 to 2000 decreased from 23 % to 13 %, reducing the number of patients needing PSVT and

WPW. The number of WPW cases reached a peak in 2005 (N= 377), and had been decreasing ever since. The number of procedures in the VT group has increased from 57 in 2001 to 123 in 2010, and the average RFCA growth rate over 10 years was 6.81%. This relatively high growth rate is possibly also due to population aging, and the maturation of 3D mapping techniques [11]. In summary, the growth models are different for the five arrhythmias. There has been a rapid increase in RFCA procedures in the AF and AFL groups because of the population aging. There has been a relatively slow increase in the PSVT group, while the WPW groups showed stable or decreasing numbers of RFCA.

Risk of recurrence

Our results showed that the recurrence rate after RFCA increased in the following order: PSVT (2%) < WPW (4.9%) < VT (5.7%) < AFL (5.8%) < AF (16.1%) (Figure 2). The recurrence-free rate was highest for the PSVT group (98.8% for the first year, gradually decreasing to 97.2% on the 10 years follow-up). However, patients in the PSVT and WPW groups < 18 years old had a significantly higher chance of recurrence, which agreed with previous results [12]. This could be because of the smaller cardiac anatomy in children, which makes it difficult to perform the precise ablation. This could also explain the association of congenital heart disease and TOF with recurrence of PSVT, possibly because of abnormal cardiac structure of congenital post-cardiac surgery. Patients with TOF and AF also had a higher risk of receiving a second RFCA. In contrast, AF and AFL patients had fewer second RFCA in the age group > 75-years-old [13].

Our data showed that patients > 75 years old receiving treatment for AF and AFL exhibited lower recurrence rates than the same age range in other groups. The reason may be caused by that cardiologists prefer conservative treatment for senior patients rather than repeated RFCA in order to avoid complications or mortality after the first procedure due to

other comorbidities. Our data suggested that for patients undergoing an elective RFCA, physicians need to carefully evaluate the risk factors such as younger age and presence of congenital heart disease (TOF in PSVT, VSD in AFL) which are associated with a high recurrence rate. Our study also described epidemiologic changes in repeated ablation procedures for five arrhythmias in Taiwan in the RFCA era.

Complications

RFCA, which has an approximately 1% complication rate and 0.1% mortality rate [3,14], is considered a relatively safe procedure to treat or even cure arrhythmias (Table 4). Our present study showed different patterns of complications in the five arrhythmia groups. Patients with PSVT, and WPW had complication rates of 1.04% and 0.61%, respectively, similar to previous studies. However, in patients with AF and AFL, the complication rate was 2.26%. AFL after RFCA induced second or third degree of AV block (2.26%) compared to other arrhythmias, and patients with AF RFCA had the highest incidence rate of tamponade (0.98%). Second or third degree AV block is considered the main complication of ablation procedures for AFL and PSVT patients because the ablation sites are close to the atrioventricular node [14]. AFL has been seen combined with sick sinus syndrome. Bradyarrhythmias appeared when the substance of AF and AFL is eliminated. Patients with AF RFCA had a relatively higher risk of cardiac tamponade than other arrhythmias, resulting in a relatively higher complication rate of 0.98%. The major mechanism of RFCA for AF is to isolate the pulmonary vein and eliminate the substrate in the left atrium. This requires a longer procedure time and delivers more energy to convert AF to sinus rhythm. RFCA for AF could therefore cause more cardiac tamponade. RFCA for VT presents same pattern as that for PSVT and WPW pattern. These data suggested that although RFCA is a common

procedure to cure different arrhythmias, different complications should be monitored in different arrhythmias.

Our data also showed that patients with AFL and AF had higher stroke rates (0.43% and 0.26%, respectively). Anticoagulation therapy is needed in these cases, and it is also necessary to confirm absence of intracardiac thrombus before RFCA [15]. However, anticoagulation procedures are sometimes ignored because anti-coagulation is not routinely used in AFL [16]. Previous studies have shown a high risk of thromboembolic events and a high incidence of thrombogenic milieu in AFL [17,18]. The inappropriate anticoagulation therapy is considered a significant risk for thromboembolism in patients with AFL[16].

Age was an important risk factor associated with complications such as second or third degree AV block, pacemaker implantation, pericardiocentesis and stroke especially in patients aged > 75-years old (Table 4). These data were consistent with previous studies [19,20], and suggested that physicians should be cautious when performing RFCA in patients >75 years old. We also found that diabetes was associated with increased complication rates for RFCA. A cohort study of 200,000 patients with type II diabetes reported that third degree AV block was prevalent in subjects with diabetes [21]. Diabetes has been suggested as a risk factor for autonomic neuropathy, cardiac conduction abnormalities and bradyarrhythmias [22]. When physicians perform RFCA on diabetic patients, they should monitor for bradyarrhythmia complications

Limitations

This study had several limitations. Firstly, in this cohort study we did not have access to laboratory parameters, procedural details, and heart images. Procedure-related parameters, location of accessory pathway in WPW, PV isolation for AF, and cardiac anomaly, ejection fraction have been reported as predictors for arrhythmia recurrence and RFCA complication

[12, 23-24, 25]. However, the present study focused on RFCA for five different arrhythmias and each arrhythmia had different surgical parameters. Rather than comparing the same parameter in different arrhythmia ablation procedures, we focused on the effect of comorbidities, gender and age on arrhythmia recurrence, and RFCA-related complications. Our study provided valuable information for cardiologists to help deal with RFCA recurrence and complications. Secondly, some arrhythmias such as premature ventricular beats, and atrial premature beats are not covered by Taiwan NHI. However, excluding these arrhythmias did not influence the study results since they are usually benign. Lastly, recurrence may be misidentified as resulting from ablation of other arrhythmias in this present study. For example, this could happen if the patient had an initial PSVT ablation followed by atrial fibrillation ablation. A single definition of recurrence could consider the second ablation as recurrence of PSVT. Use of double criteria, with repeated ablation combined with the same major principal diagnosis, reduced the coding error in this study.

Conclusions

There was a rapidly increasing trend of RFCA procedures for AF, AFL, and VT during 2001-2010, but a slow increase for PSVT and WPW. The recurrence-free rate of PSVT was higher than other arrhythmias. Elderly patients with AF and AFL RFCA had fewer repeated procedures, while patients in high center volume hospitals had more repeated RFCAs for AF. Congenital heart disease was a risk factor of PSVT recurrence. Aging patients with AF RFCA had more complications. AFL patients had a higher risk of permanent pacemaker implantation, and stroke, while AF patients had a higher risk of cardiac tamponade with pericardiocentesis.

Contributors:

CHEN conceived of the study. Y LIN and WU initiated the study design and WANG helped with implementation. Y LIN, WU and CHEN provided statistical expertise in clinical trial design and WANG and YS LIN are conducting the primary statistical analysis. All authors contributed to refinement of the study protocol and approved the final manuscript.

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Data sharing statement:

Data are available. Please contact corresponding author.

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Figure Legends

Figure 1a. Ratio of PSVT, WPW, AFL, AF and VT in Taiwan during 2001

Figure 1b Ratio of PSVT, WPW, AFL, AF and VT in Taiwan during 2010

Figure 2 Recurrence-free curve for PSVT, WPW, AFL, AF and VT

Figure 3 Number of RFCAs annually in the PSVT, WPW, AFL, AF and VT groups

Figure 4 Annual RFCA growth rate for the PSVT, WPW, AFL, AF and VT groups

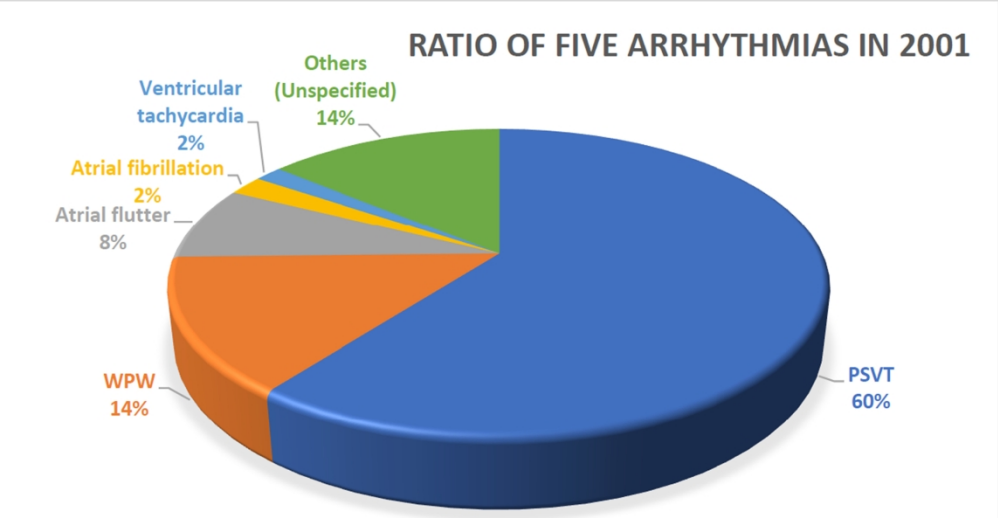

Figure 1a

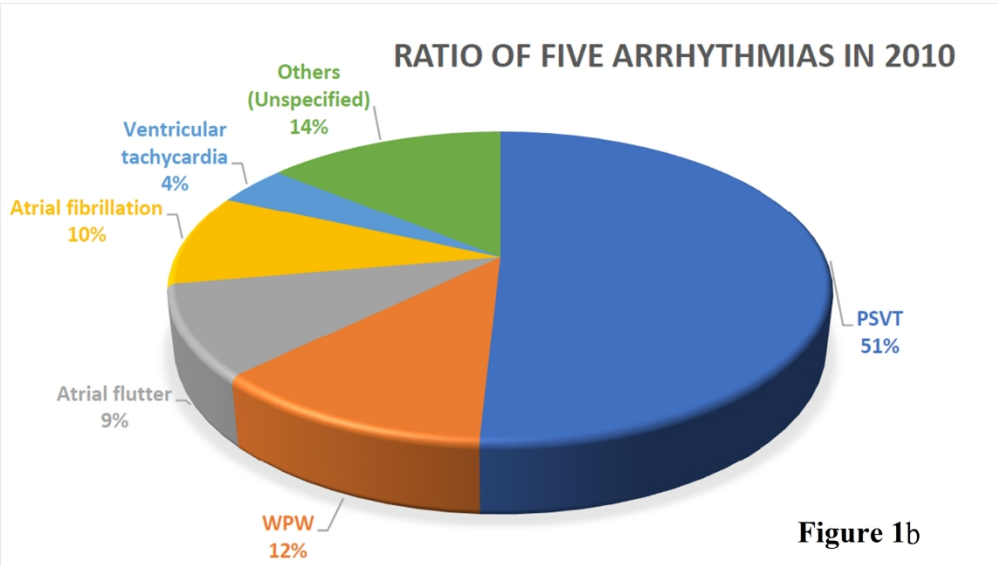

Figure 1b

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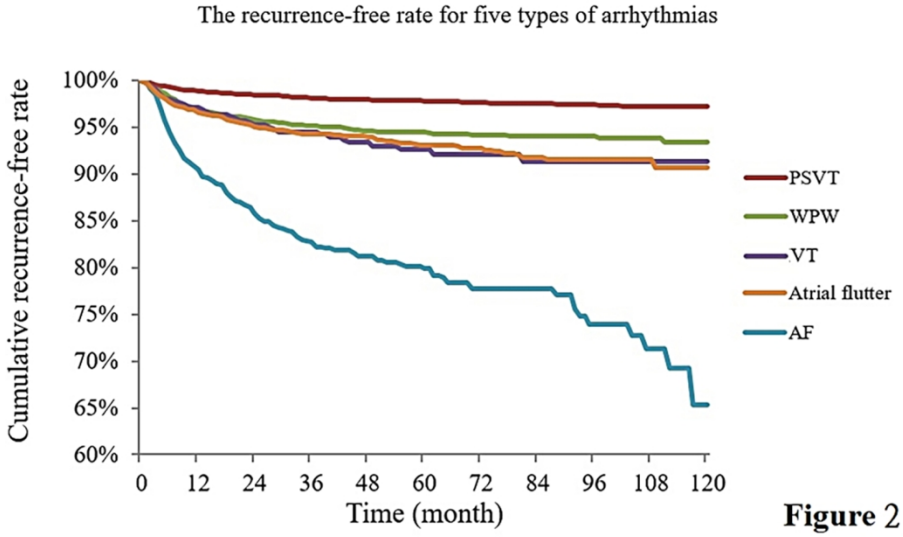

Figure 2

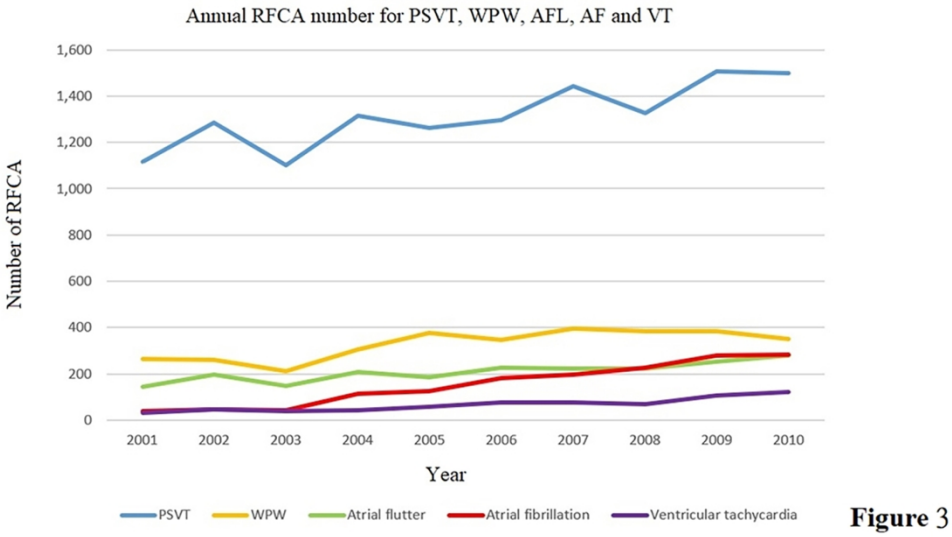

Figure 3 Number of RFCAs annually in the PSVT, WPW, AFL, AF and VT groups

160x90mm (300 x 300 DPI)

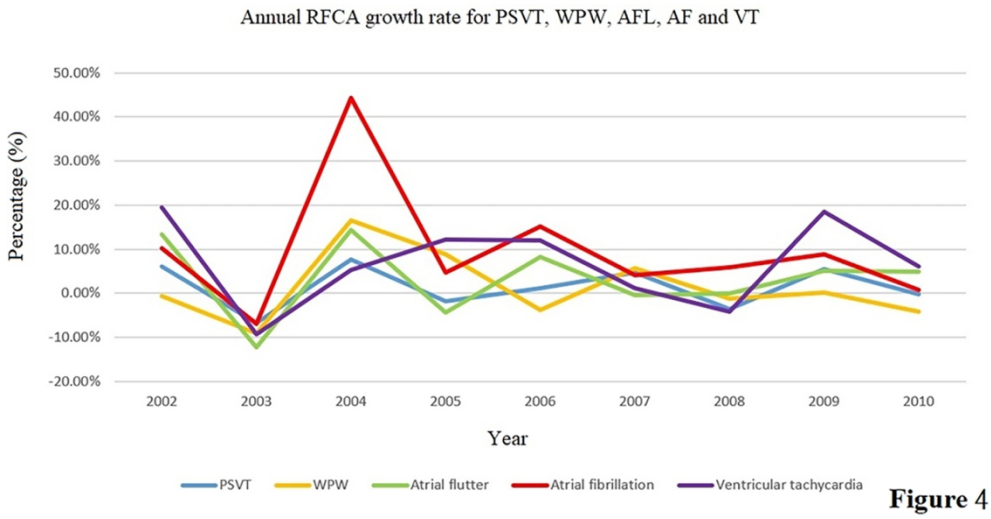

Figure 4 Annual RFCA growth rate for the PSVT, WPW, AFL, AF and VT groups

160x90mm (300 x 300 DPI)

Supplemental Table

Disease	ICD 9 code
PSVT	4270
WPW	426.7
AFL	427.32
AF	427.33
VT	427.1
High grade AVB	426.12, 426.13, 426.0
stroke	430*, 431*, 432*, 433*, 434*, 436*, 437*
DM	250*
hypertension	401*
COPD	490-496
Chronic kidney disease	403, 404, 585
Coronary artery disease	413*, 4140*
Heart failure	428*, 39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493
TOF	745.2
Transposition of the great vessel	745.1
Double outlet right ventricle	745.11
Total anomalous pulmonary venous connection	747.41
Tricuspid atresia	746.1
Common truncus arteriosus	745.0
Common ventricle	745.3
Hypoplastic left heart syndrome	746.7
Ventricular septal defect	745.4
Atrial septal defect	745.5
Ebstein's anomaly	746.2
Patent ductus arteriosus	747.0
Congenital pulmonary stenosis	746.83
Coarctation of aorta	747.1

Endocardial cushion defect	745.6
Congenital aortic stenosis	746.3

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Trend and Risk factors of Recurrence and Complications after Arrhythmias Radiofrequency Catheter Ablation: A Nationwide Observational Study in Taiwan

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Trend and Risk factors of Recurrence and Complications after Arrhythmias Radiofrequency Catheter Ablation: A Nationwide Observational Study in Taiwan

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Abstract

Objectives: Risk factors for recurrence of arrhythmias and complications after radiofrequency catheter ablation (RFCA) remain unclear. This study is aimed at the recurrence and complications after RFCA among different types of arrhythmias.

Study Design and Setting: In this retrospective study which evaluated data from the Taiwan National Health Insurance Research Database (NHIRD), 19,475 patients who received RFCA were categorized into five groups according to arrhythmia type: paroxysmal supra-ventricular tachycardia (PSVT; N=12,796); Wolff–Parkinson–White syndrome (WPW; N=3,051); atrial flutter (AFL; N=1,854); atrial fibrillation (AF; N=1,162); and ventricular tachycardia (VT; N=612). Primary outcomes included recurrence and complications.

Results: The most common arrhythmia treated with RFCA was PSVT, followed by WPW, AFL, AF and VT. During an average follow-up period of 4.36 years, the recurrence rates after RFCA were PSVT (2%), WPW (4.9%), VT (5.7%), AFL (5.8%), and AF (16.1%). Age more than 75 was a protective factor for recurrence in AF and AFL (Adjusted hazard ratio [aHR] 0.28, 95% confidence interval [CI] 0.10–0.76; aHR 0.08, 95% CI 0.02–0.34 respectively. Male sex was associated with higher risk of recurrence in PSVT, AFL and AF (aHR 1.66, 95% CI 1.30–2.13; aHR 1.68, 95% CI 1.09–2.59; aHR 1.43, 95% CI 1.05–1.95 respectively). PSVT patients with Tetralogy of Fallot (TOF), WPW patients with Ebstein anomaly had higher recurrence rates than patient without congenital heart disease. During ablation, AFL patients had more high-grade AV block than other arrhythmias, and AF patients had more life-threatening pericardial effusion. Age more 75 year-old was a risk factor for high grade AV block, pacemaker implantation, life-threatening pericardial effusion and stroke.

Conclusions: There was a rapid increase in RFCA of AF, AFL, and VT from 2001-2010. Recurrence was associated with congenital heart disease in PSVT and WPW groups, and with

age in AF and AFL groups. The AFL group had a higher risk of permanent pacemaker implantation, and new stroke. The AF group had a higher risk of life threatening pericardial effusion.

Key words: radiofrequency catheter ablation (RFCA), Wolff–Parkinson–White syndrome, supraventricular tachycardia, ventricular tachycardia, complication, recurrence, risk factors

Strengths and limitations of this study

- This 10-year longitudinal retrospective study is the first nationwide, large-scale study which surveys the burden, recurrence and complication of RFCA.
- This article is the first study to compare the recurrence and complications among five different types of arrhythmias integratedly.
- Our study provided valuable information about recurrence and complications of arrhythmias RFCA.
- This study did not have access to some detail data such as laboratory parameters, procedural details, and heart images, etc. And some arrhythmias such as premature ventricular beats, and atrial premature beats are not covered by Taiwan National Health Insurance (NHI).
- This study was not able to explore the interactions among the predictive variables because of the limited number of events.

Introduction

Radiofrequency catheter ablation is used to treat patients with supraventricular tachycardia or ventricular tachycardia, especially paroxysmal supraventricular tachycardia [1-3]. RFCA, which has been widely applied since the 1990s[4], is an effective therapy that has demonstrated high success, low complications, and low recurrence rates compared to direct current ablation and or surgical ablation. RFCA is superior to conservative treatments such as

medication or observation for patients with PVST and WPW. RFCA was first used to treat AF in 1998.

Although arrhythmias after RFCA are usually not life-threatening, identification and minimization of the risk of complications are extremely important. The RFCA procedure may lead to atrioventricular block (AV block) and bradycardia, even requiring permanent pacemaker implantation. Previous studies[5] were composed of relatively small cohorts or were single-center studies and evaluated patients with single arrhythmia[5,6]. However, there are no studies comparing RFCA-related complications in patients with five different arrhythmias [7,8]. The targets for RFCA-related risk minimization are different for different arrhythmias. For example, when RFCA is used to treat PSVT, the goal is to modify or eliminate AV node or accessory pathways, and when RFCA is used to treat AF[6], the goal is to isolate the pulmonary veins. High grade AV block, life-threatening pericardial effusion, and stroke are dangerous complications after RFCA procedure. However, the complication rates vary in the five different arrhythmias: PSVT, WPW, AFL, AF, and VT. It is therefore important to identify the incidence and risk of RFCA-related complications in these patients.

This retrospective study investigated the population trend of patients who received RFCA for PSVT, WPW, AFL, AF, and VT. We identified the major RFCA-related risk factors influencing 1) recurrence of arrhythmias, and 2) complications such as AV block, permanent pacemaker implantation, life threatening pericardial effusion and acute ischemic stroke.

Methods

Study design and population

We conducted a nationwide population-based cohort study using data from the Taiwan NHIRD. In Taiwan, the National Health Insurance (NHI) program has reimbursed patients who receive RFCA for PSVT, WPW syndrome, AFL, AF and VT since 2001. More than 99.91%

of Taiwan's population is covered by the NHI scheme. The accuracy and validation of National Health Insurance Research Database (NHIRD) data is based upon regular auditing by the NHI Bureau [9-11]. The Ethics Institutional Review Board at Chang Gung Memorial Hospital approved this study.

Study cohort, outcome measurement and follow-up

This study accessed NHIRD data for all targeted arrhythmia patients who received RFCA from 2001 to 2010. The targeted arrhythmias were PSVT (Internal Classification of Diseases, Ninth Revision, ICD-9, Code 4270), WPW (426.7), AFL (427.32), AF (427.31), and VT (427.1; Supplemental Table). Patients with arrhythmias other than targeted arrhythmias (such as premature ventricular beats or atrial tachycardia) and patients with unidentified arrhythmias who received RFCA were excluded. For patients who received more than one time of RFCA, we enrolled first RFCA. The follow-up period was from the discharge date of index hospitalization until death, loss of follow-up (withdrawal from the NHI program: emigration or put into prison for longer than 6 months) or until 31st December 2010.

Outcome measurement

The primary outcomes included recurrence of arrhythmia, in-hospital complications and long-term complications. Recurrence was defined as either 1) recurrence of original arrhythmias, or 2) receiving secondary RFCA during the follow up. In-hospital complications included life threatening pericardial effusion and new-onset stroke during the admission. Life threatening pericardial effusion was defined as patient requiring pericardiocentesis during RFCA. New stroke was defined as stroke (ICD-9 CM codes: 430-437) which occurred during index admission. Long-term complications included High-grade AV block, high-grade AV block requiring permanent pacemaker implantation after RFCA during the follow up.

Covariate assessment

Comorbidities were assessed according to ICD-9 codes before index admission. Diabetes mellitus, hypertension (HTN) or chronic diseases were recorded as comorbidities if there was at least one in-admission diagnosis. All congenital heart disease (CHD) was reconfirmed by the Catastrophic Illness certification (CIC) which is sub-dataset of NHI. A CIC for congenital heart disease requires imaging proof confirmed by two cardiologists. Complicated CHD included TOF, transposition of the great vessels, double outlet right ventricle, total anomalous pulmonary venous connection, tricuspid atresia, common truncus arteriosus, common ventricle and hypoplastic left heart syndrome. Simple CHD included ventricular septal defect (VSD), atrial septal defect (ASD), Ebstein's anomaly, patent ductus arteriosus, congenital pulmonary stenosis, coarctation of aorta, endocardial cushion defect, and congenital aortic stenosis. Center volume was designed as time-dependent variety and high-activity center was defined as RFCA numbers more than 100 regardless of arrhythmias type.

Patient and public involvement

This study has no direct relationship with any patient and public involvement during the development, design and conduct.

Statistical analysis

The proportion of categorical variables among different groups was compared using the chi-squared test. Continuous variables were compared using Kruskal-Wallis test due to the lack of normality. Multivariable logistic regression analysis was used to identify clinical features associated with risks of in-hospital complications, including life threatening pericardial effusion and new-onset stroke during the admission. Multivariable Cox regression analysis was

used to investigate the association of clinical variables with time to event outcomes, including recurrence, high-grade AV block and pacemaker implantation during the follow up. In the survival analysis, the time-scale was time since RFCA (the follow up duration). The assumption of proportional hazard was tested by Schoenfeld partial residuals in which the indication was the only explanatory continuous variable. There were 13 pre-specified potential predictive variables which were consisted of two demographics (sex and age), six comorbidities, four types of congenital heart disease, and hospital volume. All these 13 candidate predictive variables were introduced into the multivariable regression models. Multicollinearity among predictors was checked by variance inflation factor which a value less than 10 indicates there was no serious collinearity between the certain variable and other variables. Sensitivity analyses were done by excluding patients with recurrent RCFA during the follow up. A two-sided *P* value lower than 0.05 was considered statistically significant, and no adjustment for multiple testing (multiplicity) was made in this study. Results were presented as the odds ratio (OR) for logistic regression, or hazard ratio (HR) for Cox regression with corresponding 95% confidence intervals (CI). All data analyses were performed using SPSS software version 15 (SPSS Inc, Chicago, Illinois).

Results

There were 24,003 RFCA procedures registered in NHIRD between 1 January 2001 and 31 December 2010. Based on the inclusion and exclusion criteria, a total of 19,475 patients were enrolled, who underwent 20,707 RFCA procedures. But only the first occurrence for each individual was used for analysis

A majority of the study participants were diagnosed with PSVT (N=12,796), followed by WPW (N=3,051), AFL (N=1,854), AF (N=1,162) and VT (N=612). The mean age of study participants when they received RFCA was 47.6 years (SD=18.3), and the average follow-up

period was 4.36 years (SD= 2.86). The ratio of changes in individual arrhythmias from 2001 to 2010 is shown in Figure 1. The ratio of PSVT decreased from 60% to 51% between 2001 to 2010, while the ratio of AF increased from 2% to 10%. Demographic and baseline clinical characteristics according to arrhythmia types are summarized in Table 1. The prevalence of PSVT (38.5%), WPW (58.1%) and VT (47.2%) is highest in the group of age 19-44 years. The prevalence of AF and AFL was 30.5% in patients aged 55–64, and 25.5% in patients aged 65–74 years (25.5%). Patients with AF and AFL had a significantly higher prevalence of diabetes (16.2% and 11.5%) and hypertension (28.9% and 28.1%) compared to patients with other arrhythmias. Simple congenital heart disease was seen in 3.6% of patients with AFL.

Table 1. Baseline data for 19,475 study patients who underwent RFCA procedures stratified by indication

Variable	PSVT	WPW	Atrial flutter	Atrial fibrillation	Ventricular tachycardia	*P* value
Number of patients	12,796	3,051	1,854	1,162	612	–
Age (yrs.), median (IQR)	51.3 (39.2, 64.1)	47.8 (45.7, 61.6)	73.5 (54.7, 77.8)	59.8 (53.4, 66.1)	48.4 (31.7, 60.4)	<0.001
Age group						<0.001
0-18 yrs.	863 (6.7)	379 (12.4)	15 (0.8)	0 (0.0)	46 (7.5)	
19-44 yrs.	4,930 (38.5)	1,619 (53.1)	260 (14.0)	216 (18.6)	289 (47.2)	
45-54 yrs.	2,938 (23.0)	579 (19.0)	329 (17.7)	285 (24.5)	123 (20.1)	
55-64 yrs.	2,083 (16.3)	308 (10.1)	407 (22.0)	354 (30.5)	75 (12.3)	
65-74 yrs.	1,344 (10.5)	130 (4.3)	472 (25.5)	222 (19.1)	51 (8.3)	
Above 75 yrs.	638 (5.0)	36 (1.2)	371 (20.0)	85 (7.3)	28 (4.6)	
Gender, male	5,402 (42.3)	1,988 (65.2)	1,332 (71.9)	838 (72.2)	327 (53.5)	<0.001
Diabetes	910 (7.1)	113 (3.7)	301 (16.2)	134 (11.5)	32 (5.2)	<0.001
Hypertension	1,723 (13.5)	275 (9.0)	535 (28.9)	326 (28.1)	74 (12.1)	<0.001
COPD	286 (2.2)	22 (0.7)	103 (5.6)	28 (2.4)	15 (2.5)	<0.001
CKD	150 (1.2)	12 (0.4)	71 (3.8)	11 (0.9)	5 (0.8)	<0.001
CAD	594 (4.6)	87 (2.9)	288 (15.5)	154 (13.3)	45 (7.4)	<0.001
Heart failure	73 (0.6)	21 (0.7)	205 (11.1)	53 (4.6)	25 (4.1)	<0.001
High-activity center‡	7,267 (56.8)	1,880 (61.6)	1,317 (71.0)	976 (84.0)	317 (51.8)	<0.001
Complicated CHD	10 (0.1)	3 (0.1)	16 (0.9)	2 (0.2)	1 (0.2)	<0.001
TOF	3 (0.0)	0 (0.0)	11 (0.6)	1 (0.1)	1 (0.2)	<0.001
Other Complicated CHD	7 (0.1)	3 (0.1)	5 (0.3)	1 (0.1)	0 (0.0)	0.045
Simple CHD †	69 (0.5)	31 (1.0)	66 (3.6)	9 (0.8)	9 (1.5)	<0.001
VSD	15 (0.1)	6 (0.2)	25 (1.3)	0 (0.0)	4 (0.7)	<0.001
ASDII	50 (0.4)	10 (0.3)	34 (1.8)	9 (0.8)	4 (0.7)	<0.001
Ebstein	4 (0.0)	18 (0.6)	6 (0.3)	0 (0.0)	0 (0.0)	<0.001
Other simple CHD	4 (0.0)	2 (0.1)	6 (0.3)	0 (0.0)	1 (0.2)	<0.001

Abbreviation: RFCA = Radiofrequency catheter ablation; PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome; COPD = Chronic obstructive pulmonary disease; CKD = Chronic kidney disease; CAD = Coronary artery disease; CHD = Congenital heart defect; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; ASD = Atrial septal defect; Ebstein = Ebstein's anomaly;

‡ defined as 100 volume per year;

† There is a discrepancy between the sums of subgroups and the total due to one patient who might have two CHDs.

Risks of recurrence

Multivariable Cox analyses revealed that the major risk factors for recurrence of PSVT after RFCA included: age (0–18 years), male gender, diabetes, and TOF. Younger patients (0–18 *vs.* 19–44 years) and those with Ebstein anomaly were considered at greater risk for recurrence of WPW after RFCA (Table 2). For the AFL group, older individuals (45–54 *vs.* 19–44 years) had a higher risk of recurrence. Male gender, TOF, VSD, and high-activity center were also risk factors. In contrast, the incidence of AFL recurrence was low in patients older than 75 years. Patients with AF had a recurrence rate of 16.1% following RFCA, whereas the recurrence rate of PSVT was as low as 2.0%. The recurrence-free rate of AF after RFCA declined with time, while recurrence-free rates for the other 4 groups did not decline so largely (Figure 2). Patients aged 19–44 years had a higher risk of AF recurrence compared with patients older than 65 years; male gender and high-activity center were also identified as risk factors. In the VT population, a high-activity center was related to decreased risk of recurrence. The results were similar when excluding patients with recurrent RCFA during the follow up (Supplemental Table 2).

Table 2. Risk factors of recurrence by indication

Variable	PSVT (259 events, 2.0%)		WPW (160 events, 4.9%)		Atrial flutter (120 events, 5.8%)		Atrial fibrillation (247 events, 16.1%)		Ventricular tachycardiatachycardia (38 events, 5.7%)	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age										
0-18 yrs.	1.52 (1.02–2.28)	0.041	1.90 (1.27–2.85)	0.004	2.17 (0.50–9.41)	0.30	NA	NA	1.19 (0.41–3.48)	0.75
19-44 yrs.	Reference	—	Reference	—	Reference	—	Reference	—	Reference	—
45-54 yrs.	0.88 (0.64–1.22)	0.46	0.90 (0.57–1.44)	0.67	1.98 (1.15–3.41)	0.014	1.03 (0.73–1.44)	0.88	0.71 (0.28–1.78)	0.46
55-64 yrs.	0.70 (0.47–1.05)	0.08	1.47 (0.87–2.47)	0.15	1.40 (0.78–2.51)	0.27	0.87 (0.61–1.26)	0.43	0.75 (0.24–2.36)	0.62
65-74 yrs.	0.68 (0.42–1.11)	0.12	0.95 (0.37–2.41)	0.91	0.93 (0.49–1.77)	0.82	0.54 (0.34–0.86)	0.01	0.19 (0.02–1.56)	0.12
Above 75 yrs.	0.69 (0.35–1.37)	0.29	NA.	NA	0.28 (0.10–0.76)	0.013	0.08 (0.02–0.31)	0.001	NA	NA
Male gender	1.66 (1.30–2.13)	<0.001	1.06 (0.77–1.48)	0.71	1.68 (1.09–2.59)	0.020	1.43 (1.05–1.95)	0.023	1.31 (0.66–2.58)	0.44
Diabetes	1.59 (1.01–2.52)	0.047	0.18 (0.03–1.34)	0.09	0.80 (0.43–1.49)	0.49	0.70 (0.43–1.14)	0.15	0.70 (0.09–5.74)	0.74
Hypertension	1.03 (0.70–1.53)	0.88	1.27 (0.71–2.28)	0.42	0.73 (0.46–1.15)	0.17	1.29 (0.97–1.72)	0.08	1.49 (0.40–5.49)	0.55
COPD	1.13 (0.50–2.60)	0.77	NA.	NA	1.08 (0.43–2.72)	0.87	1.45 (0.54–3.94)	0.46	NA	NA
CKD	1.61 (0.59–4.36)	0.35	NA.	NA	0.78 (0.24–2.49)	0.67	0.55 (0.08–4.02)	0.56	4.18 (0.52–33.86)	0.18
CAD	0.85 (0.44–1.64)	0.63	0.53 (0.13–2.17)	0.38	0.59 (0.29–1.17)	0.13	1.07 (0.73–1.56)	0.74	1.18 (0.26–5.25)	0.83
Heart failure	1.64 (0.40–6.67)	0.49	NA.	NA	0.91 (0.47–1.75)	0.78	0.29 (0.07–1.20)	0.09	2.90 (0.63–13.42)	0.17
TOF	23.00 (4.0–131.8)	<0.001	NA.	NA	3.32 (1.01–10.96)	0.049	NA	NA	NA	NA
VSD	NA.	NA	2.79 (0.53–14.82)	0.23	2.78 (1.29–5.99)	0.009	0.99 (0.13–7.43)	0.99	NA	NA
ASD II	2.78 (0.89–8.72)	0.08	0.40 (0.04–4.25)	0.45	1.46 (0.57–3.71)	0.43	1.17 (0.28–4.87)	0.83	3.57 (0.47–27.34)	0.22
Ebstein	1.08 (0.09–12.80)	0.95	4.40 (1.80–10.74)	0.001	1.54 (0.21–11.5)	0.68	NA	NA	NA	NA.
High-activity center	1.05 (0.82–1.35)	0.68	0.87 (0.63–1.19)	0.38	1.78 (1.11–2.85)	0.017	3.16 (1.77–5.67)	<0.001	0.49 (0.25–0.97)	0.04

Abbreviation: PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome; COPD = Chronic obstructive pulmonary disease; CKD = Chronic kidney disease; CAD = Coronary artery disease; CHD = Congenital heart defect; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; ASD = Atrial septal defect; Ebstein = Ebstein's anomaly; HR = hazard ratio; CI = confidence interval; NA = not applicable.

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Complications

RFCA-related complications were evaluated for the five different arrhythmia groups (Table 3). The overall prevalence of complications and mortality were less than 1 and 0.1%, respectively. High-grade AV block was the most common complication following RFCA in all the arrhythmia groups, except for the AF group. RFCA induced more life threatening pericardial effusion (1.30%) in the AF group compared to the other arrhythmias. In the AFL group, RFCA caused more High-grade AV block (2.53%), permanent pacemaker implantation (1.40%), and new stroke (0.49%). However, it was noted that the incidence may be confounded by the distribution of year-of-entry in respective groups. For instance, indication of AF increased across years would result in a shorter mean follow up duration and lower incidence. In contrast, indication of PSVT decreased across years would result in a longer mean follow up duration and higher incidence.

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Table 3. RFCA-related complications according to different types of arrhythmias

Complication	PSVT	WPW	Atrial flutter	Atrial fibrillation	Ventricular tachycardia
Number of patients	12,796	3,051	1,854	1,162	612
In-hospital complication					
Life threatening pericardial effusion	15 (0.18)	8 (0.26)	6 (0.32)	15 (1.30)	1 (0.16)
New-onset stroke	8 (0.06)	2 (0.07)	9 (0.49)	4 (0.34)	0 (0.00)
After discharge					
High-grade AVB	114 (0.89)	10 (0.33)	47 (2.53)	8 (0.69)	5 (0.82)
Pacemaker implantation	64 (0.50)	5 (0.16)	26 (1.40)	2 (0.17)	3 (0.50)

Abbreviation: RFCA = Radiofrequency catheter ablation; PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome; AVB = Atrioventricular block.

Risk factors of complications

As to in-hospital complications, multivariable logistic regression revealed that age > 44 years old, high-activity center, and RFCA of WPW or AF (when compared with PSVT) were associated with increased risk of life threatening pericardial effusion. Age >55 years old and AFL after RFCA (when compared with PSVT) were associated with a higher risk of stroke following RFCA (Table 4). As to long-term complications, multivariable Cox regression identified risk factors for high-grade AV block were age > 75 years old, diabetes, and heart failure (Table 4). WPW patients were at a lower risk of developing AV block than PSVT patients. Risk factors of pacemaker implantation were age > 75 years old, diabetes, chronic kidney disease (CKD), and AFL after RFCA (when compared with PSVT). The results were similar when excluding patients with recurrent RCFA during the follow up (Supplemental Table 3).

Testing of Schoenfeld partial residuals revealed insignificant correlation for rank of survival time of AVB and PPM (AVB: number of events = 184, r = 0.084, p = 0.271; PPM: number of events=100, r = 0.149, p = 0.114) which indicated that the assumption of proportional hazard was not violated (data not shown).

Table 4. Risk factors of complications during the index admission or after discharge of the index admission

	During the index admission				After discharge of the index admission			
	Life threatening pericardial effusion (45 events, 0.22%)		New-onset stroke (23 events, 0.11%)		High-grade AVB (184 events, 0.85%)		Pacemaker (100 events, 0.48%)	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age								
0-18 yrs.	NA	NA	NA	NA	0.66 (0.28–1.53)	0.33	0.81 (0.24–2.71)	0.74
19-44 yrs.	Reference	—	Reference	—	Reference	—	Reference	—
45-54 yrs.	11.18 (2.50–50.10)	0.002	4.53 (0.46–44.16)	0.19	1.07 (0.70–1.62)	0.76	1.70 (0.96–3.01)	0.07
55-64 yrs.	17.32 (3.87–77.55)	<0.001	19.68 (2.44–158.78)	0.005	0.85 (0.52–1.37)	0.50	1.09 (0.55–2.18)	0.80
65-74 yrs.	17.75 (3.68–85.57)	<0.001	9.58 (0.99–91.66)	0.05	1.07 (0.65–1.77)	0.79	1.40 (0.69–2.85)	0.36
Above 75 yrs.	22.70 (4.16–123.95)	<0.001	17.01 (1.73–167.36)	0.015	2.07 (1.24–3.44)	0.005	3.82 (1.94–7.53)	<0.001
Male gender	1.12 (0.60–2.12)	0.72	0.84 (0.35–2.00)	0.70	1.14 (0.84–1.54)	0.40	0.74 (0.49–1.12)	0.16
Diabetes	0.33 (0.08–1.39)	0.13	1.22 (0.40–3.70)	0.73	1.77 (1.17–2.70)	0.007	1.95 (1.13–3.37)	0.016
Hypertension	1.01 (0.51–2.01)	0.97	0.52 (0.17–1.59)	0.25	1.08 (0.73–1.59)	0.70	0.94 (0.55–1.59)	0.81
COPD	NA	NA	NA	NA	0.70 (0.28–1.72)	0.43	0.77 (0.24–2.49)	0.67
CKD	NA	NA	1.41 (0.18–10.89)	0.74	2.10 (0.97–4.54)	0.06	2.69 (1.07–6.76)	0.036
Heart failure	0.74 (0.10–5.59)	0.77	2.51 (0.68–9.29)	0.17	2.31 (1.28–4.17)	0.006	1.00 (0.35–2.83)	0.99
TOF	NA	NA	NA	NA	NA.	NA	NA	NA
VSD	NA	NA	NA	NA	2.20 (0.51–9.47)	0.29	NA	NA
ASD II	4.10 (0.53–31.84)	0.18	NA	NA	1.55 (0.37–6.47)	0.55	1.94 (0.27–14.10)	0.51
Ebstein	NA	NA	NA	NA	3.70 (0.49–27.86)	0.20	NA	NA
High-activity center	3.79 (1.47–9.79)	0.006	1.15 (0.46–2.88)	0.76	0.98 (0.73–1.33)	0.91	0.92 (0.61–1.38)	0.68
Indication								
PSVT	Reference	—	Reference	—	Reference	—	Reference	—
WPW	2.98 (1.24–7.15)	0.015	1.63 (0.34–7.85)	0.55	0.37 (0.19–0.71)	0.003	0.41 (0.16–1.04)	0.06
VT	1.58 (0.21–12.14)	0.66	NA	NA	0.85 (0.35–2.10)	0.73	1.10 (0.34–3.51)	0.87
Atrial fibrillation	4.09 (1.90–8.79)	<0.001	2.74 (0.77–9.72)	0.118	0.53 (0.25–1.11)	0.09	0.33 (0.08–1.36)	0.13
Atrial flutter	1.34 (0.49–3.70)	0.57	4.07 (1.39–11.91)	0.010	1.74 (1.17–2.60)	0.006	2.14 (1.27–3.62)	0.004

Abbreviation: AVB = Atrioventricular block; COPD = Chronic obstructive pulmonary disease; CKD = Chronic kidney disease; CAD = Coronary artery disease; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; ASD = Atrial septal defect; Ebstein = Ebstein's anomaly PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome; VT=Ventricular tachycardia; OR = odds ratio; HR =

hazard ratio; CI = confidence interval; NA = not applicable.

Discussion

To the best of our knowledge, this is the first observational study to record the impact of RFCA on the treatment of arrhythmias by analyzing the burden, risk factors, recurrence, and complications of patients with five different arrhythmias. There was a rapid increase in the number of RFCAs for the AF, AFL, and VT groups, whereas a gradual increase for the PSVT and WPW groups from 2001-2010 was noticed. Age was a risk factor of recurrence in the different arrhythmia groups, while male gender, diabetes and TOF were risk factors of recurrence in patients with PSVT after RFCA. Patients in high-activity center had a tendency to receive repeated AF RFCAs. Elderly patients with AF, and AFL, had more adverse events during RFCA compared to other subgroups.

Trend of Arrhythmias

In Taiwan, there has been an increase in the number of AF over the past ten years, and this group had the greatest growth rate, followed by the VT, AFL, WPW and PSVT groups. Population aging, and advancement of ablation techniques have contributed to this phenomenon especially for AF, and AFL, which are age-related diseases [12]. From 2001 to 2010, the population of elderly patients (>65 years old) increased from 1,973,357 to 2,487,893. This has resulted in a greater increase in the AF, and AFL numbers compared to other arrhythmias. The mean growth rate per year between 2001 and 2010 was 9.7% for AF, and 3.2% for AFL (Figure 3- 4). In contrast, the average growth rate of PSVT RFCA is just 1.4%. The PSVT RFCA growth rate is gradually slowing, but the absolute numbers grew from 1,118 in 2001 to 1,499 in 2010. This pattern is true for PSVT since 1) PSVT RFCA is relatively mature ablation than AF ablation. 2) PSVT RFCA had fully covered by Taiwan Health insurance but AF was not. Due to the patients of PSVT and WPW were relatively young age. So, we searched the birth rate from 1980 to 2000. The crude birth rate (births per 1,000 population per

year) of Taiwan during 1980 to 2000 decreased from 23 % to 13 %, reducing the number of patients needing PSVT and WPW. The number of WPW cases reached a peak in 2005 (N= 377), and had been decreasing ever since. The number of procedures in the VT group has increased from 57 in 2001 to 123 in 2010, and the average RFCA growth rate over 10 years was 6.81%. This relatively high growth rate is possibly also due to population aging, and the maturation of 3D mapping techniques [13]. In summary, the growth models are different for the five arrhythmias. There has been a rapid increase in RFCA procedures in the AF and AFL groups because of the population aging. There has been a relatively slow increase in the PSVT group, while the WPW and VT groups showed stable or decreasing numbers of RFCA.

Risk of recurrence

Our results showed that the recurrence rate after RFCA increased in the following order: PSVT (2%) < WPW (4.9%) < VT (5.7%) < AFL (5.8%) < AF (16.1%) (Figure 2). The recurrence-free rate was highest for the PSVT group (98.8% for the first year, gradually decreasing to 97.2% on the 10 years follow-up). However, patients in the PSVT and WPW groups < 18 years old had a significantly higher chance of recurrence, which agreed with previous results [14]. This could be because of the smaller cardiac anatomy in children, which makes it difficult to perform the precise ablation. This could also explain the association of congenital heart disease and TOF with recurrence of PSVT, possibly because of abnormal cardiac structure of congenital post-cardiac surgery. Patients with TOF and AF also had a higher risk of receiving a second RFCA. In contrast, AF and AFL patients had fewer second RFCA in the age group > 75-years-old [15].

Our data showed that patients > 75 years old receiving treatment for AF and AFL exhibited lower recurrence rates than the same age range in other groups. The reason may be caused by that cardiologists prefer conservative treatment for senior patients rather than

repeated RFCA in order to avoid complications or mortality after the first procedure due to other comorbidities. Our data suggested that for patients undergoing an elective RFCA, physicians need to carefully evaluate the risk factors such as younger age and presence of congenital heart disease (TOF in PSVT, VSD in AFL) which are associated with a high recurrence rate. Our study also described epidemiologic changes in repeated ablation procedures for five arrhythmias in Taiwan in the RFCA era.

Complications

RFCA, which has an approximately 1% complication rate and 0.1% mortality rate [3,16], is considered a relatively safe procedure to treat or even cure arrhythmias (Table 3). Our present study showed different patterns of complications in the five arrhythmia groups. Patients with PSVT, and WPW had complication rates of 1.57% and 0.82%, respectively, similar to previous studies. However, in patients with AF and AFL, the complication rate was 2.50% and 4.74%. AFL after RFCA induced more high-grade AV block (2.53%) compared to other arrhythmias, and patients with AF RFCA had the highest incidence rate of life threatening pericardial effusion (1.30%). High-grade AV block is considered the main complication of ablation procedures for AFL and PSVT patients because the ablation sites are close to the atrioventricular node [16]. AFL has been seen combined with sick sinus syndrome. Bradyarrhythmias appeared when the substance of AF and AFL is eliminated. Patients with AF RFCA had a relatively higher risk of life threatening pericardial effusion than other arrhythmias, resulting in a relatively higher complication rate of 1.30%. The major mechanism of RFCA for AF is to isolate the pulmonary vein and eliminate the substrate in the left atrium. This requires a longer procedure time and delivers more energy to convert AF to sinus rhythm. RFCA for AF could therefore cause more life threatening pericardial effusion . RFCA for VT presents same pattern as that for PSVT and WPW pattern. These data suggested that although

RFCA is a common procedure to cure different arrhythmias, different complications should be monitored in different arrhythmias.

Our data also showed that patients with AFL and AF had higher stroke rates (0.49% and 0.34%, respectively). Anticoagulation therapy is needed in these cases, and it is also necessary to confirm absence of intracardiac thrombus before RFCA [17]. However, anticoagulation procedures are sometimes ignored because anti-coagulation is not routinely used in AFL [18]. Previous studies have shown a high risk of thromboembolic events and a high incidence of thrombogenic milieu in AFL [19,20]. The inappropriate anticoagulation therapy is considered a significant risk for thromboembolism in patients with AFL[18].

Age was an important risk factor associated with complications such as High-grade AV block, pacemaker implantation, life threatening pericardial effusion and stroke especially in patients aged > 75-years old (Table 4). These data were consistent with previous studies [21,22], and suggested that physicians should be cautious when performing RFCA in patients >75 years old. We also found that diabetes was associated with increased complication rates for RFCA. A cohort study of 200,000 patients with type II diabetes reported that third degree AV block was prevalent in subjects with diabetes [23]. Diabetes has been suggested as a risk factor for autonomic neuropathy, cardiac conduction abnormalities and bradyarrhythmias [24]. When physicians perform RFCA on diabetic patients, they should monitor for bradyarrhythmia complications

Limitations

This study had several limitations.

Firstly, the major limitation of this study is that we were not able to explore the interactions among the predictive variables because of the limited number of events. For instance, the number of high-grade AVB was 184 events and may allow a maximum of 18-19

predictive variables due to the "ten-one rule" [25-27]. However, there were 13 predictors so that 78 two-way potential interaction effect might exist. Therefore, it seems not feasible to perform a regression analysis (logistic or Cox regressions) with so many explanatory variables in the equation which would induce a statistical problem of overfitting. Secondly, in this cohort study we did not have access to laboratory parameters, procedural details, heart images, and smoking status, obesity, alcoholism, and the costs. Procedure-related parameters, location of accessory pathway in WPW, PV isolation for AF, and cardiac anomaly, ejection fraction have been reported as predictors for arrhythmia recurrence and RFCA complication[14, 28-30]. The lack of these information could induce residual confounding, especially with the results of age. However, the present study focused on RFCA for five different arrhythmias and each arrhythmia had different surgical parameters. Rather than comparing the same parameter in different arrhythmia ablation procedures, we focused on the effect of comorbidities, gender and age on arrhythmia recurrence, and RFCA-related complications. Our study provided valuable information for cardiologists to help deal with RFCA recurrence and complications. Thirdly, some arrhythmias such as premature ventricular beats, and atrial premature beats are not covered by Taiwan NHI. However, excluding these arrhythmias did not influence the study results since they are usually benign. Lastly, recurrence may be misidentified as resulting from ablation of other arrhythmias in this present study. For example, this could happen if the patient had an initial PSVT ablation followed by atrial fibrillation ablation. A single definition of recurrence could consider the second ablation as recurrence of PSVT. Use of double criteria, with repeated ablation combined with the same major principal diagnosis, reduced the coding error in this study.

Conclusions

There was a rapidly increasing trend of RFCA procedures for AF, AFL, and VT during 2001-2010, but a slow increase for PSVT and WPW. The recurrence-free rate of PSVT was higher than other arrhythmias. Elderly patients with AF and AFL RFCA had fewer repeated procedures and AF patient in high-activity center hospitals had more repeated RFCA. Congenital heart disease was a risk factor of PSVT recurrence. AF RFCA patients had more life-threatening pericardial effusion especially age more than 65, and patients receiving AFL RFCA suffered from bradycardia requiring permanent pacemaker implantation.

Contributors:

CHEN conceived of the study. Y LIN and WU initiated the study design and WANG helped with implementation. Y LIN, WU and CHEN provided statistical expertise in clinical trial design and WANG and YS LIN are conducting the primary statistical analysis. All authors contributed to refinement of the study protocol and approved the final manuscript.

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Disclaimer:

The leading author confirms that the content of this manuscript is honest and transparent.

Competing interests:

None declared.

Patient consent:

Not required.

Ethics approval:

The Ethics Institutional Review Board at Chang Gung Memorial Hospital approved this study.

Data sharing statement:

Data are available. Please contact corresponding author.

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Figure Legends

Figure 1. Proportion of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia in Taiwan during 2001 and 2010

Figure 2. Recurrence-free survival curves for Paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia

Figure 3. Number of radiofrequency catheter ablation annually in the paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia groups

Figure 4. Annual radiofrequency catheter ablation growth rate for the paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia groups

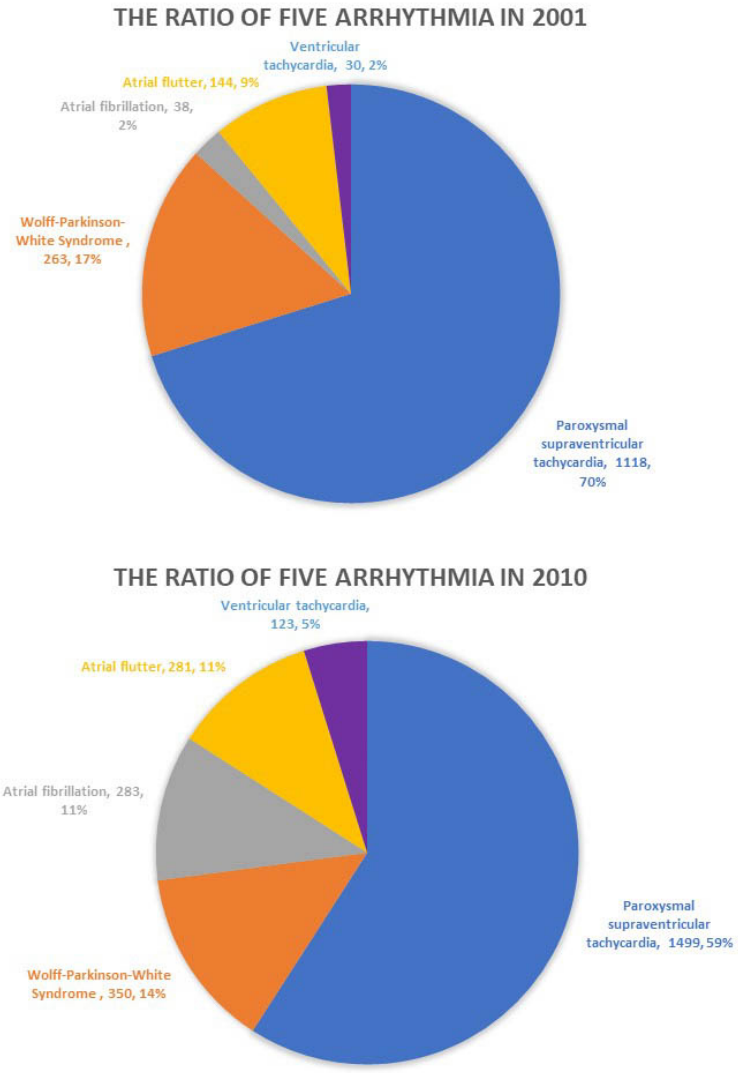

figure 1

60x88mm (300 x 300 DPI)

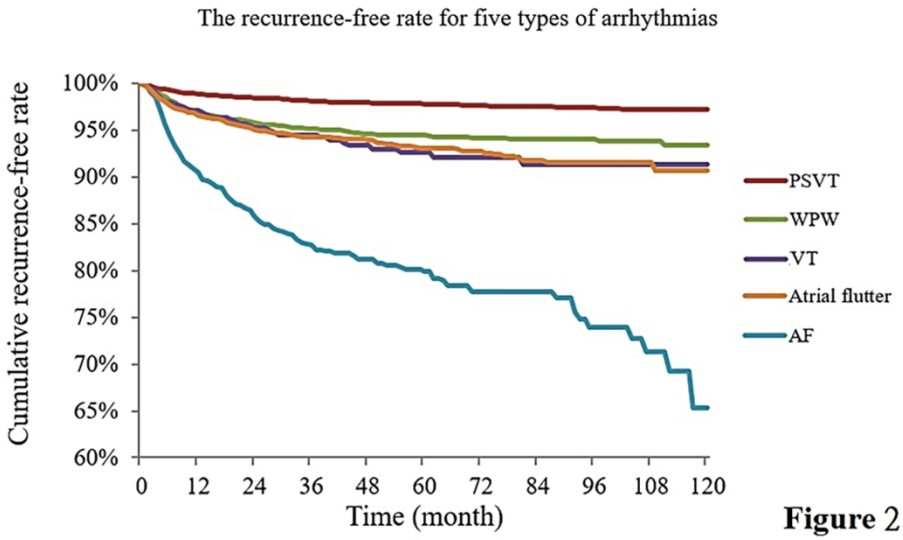

Figure 2

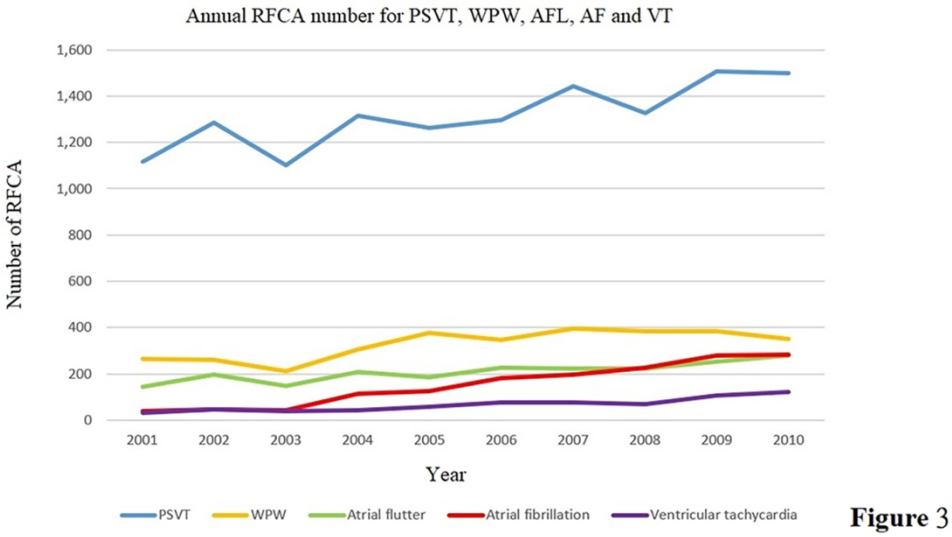

Figure 3 Number of RFCAs annually in the PSVT, WPW, AFL, AF and VT groups

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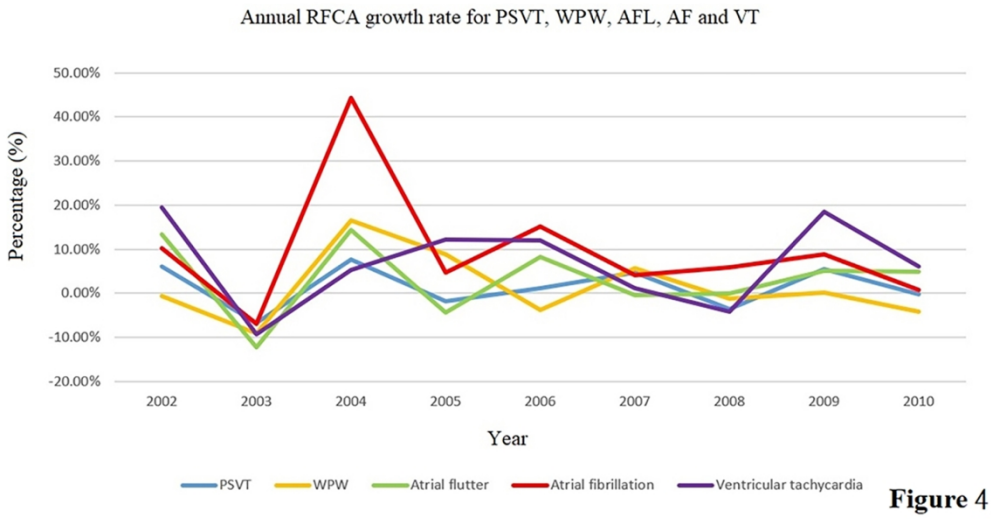

Figure 4 Annual RFCA growth rate for the PSVT, WPW, AFL, AF and VT groups

160x90mm (300 x 300 DPI)

Supplemental table 1

Disease	ICD 9 code
PSVT	4270
WPW	426.7
AFL	427.32
AF	427.33
VT	427.1
High-grade AVB	426.12, 426.13, 426.0
stroke	430*, 431*, 432*, 433*, 434*, 436*, 437*
DM	250*
hypertension	401*
COPD	490-496
Chronic kidney disease	403, 404, 585
Coronary artery disease	413*, 4140*
Heart failure	428*, 39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493
TOF	745.2
Transposition of the great vessel	745.1
Double outlet right ventricle	745.11
Total anomalous pulmonary venous connection	747.41
Tricuspid atresia	746.1
Common truncus arteriosus	745.0
Common ventricle	745.3
Hypoplastic left heart syndrome	746.7
Ventricular septal defect	745.4
Atrial septal defect	745.5
Ebstein's anomaly	746.2
Patent ductus arteriosus	747.0
Congenital pulmonary stenosis	746.83

Coarctation of aorta	747.1
Endocardial cushion defect	745.6
Congenital aortic stenosis	746.3

PSVT: paroxysmal supra-ventricular tachycardia, WPW: Wolff–Parkinson–White syndrome, AFL: atrial flutter, AF: atrial fibrillation, VT: ventricular tachycardia, High-grade AV block: High-grade atrioventricular block, DM: diabetes mellitus, COPD: Chronic Obstructive Pulmonary Disease, TOF: Tetralogy of Fallot

Supplemental Table 2. RFCA-related complications according to recurrence or not during the follow up (*N* = 20707 RFCAs)

Complication	Recurrence (*n*=988)	Non-recurrence (*n*=19,719)	*P*[a]
In-hospital complication			
Life-threatening pericardial effusion	3 (0.3)	42 (0.21)	0.48
New-onset stroke	0 (0)	23 (0.12)	0.63
After discharge			
High-grade AVB	3 (0.3)	181 (0.92)	0.05
Pacemaker implantation	0 (0)	100 (0.51)	0.016

Abbreviation: RFCA = Radiofrequency catheter ablation; AVB = Atrioventricular block; a, Fisher's exact test.

Supplemental Table 3. RFCA-related complications according to different types of arrhythmias for the patients without recurrence during the follow up

Complication	PSVT	WPW	Atrial flutter	Atrial fibrillation	Paroxysmal ventricular tachycardia
Number of patients	12,519	2,895	1,710	949	578
In-hospital complication					
Life-threatening pericardial effusion	15 (0.12)	6 (0.21)	5 (0.29)	12 (1.26)	1 (0.17)
New-onset stroke	8 (0.06)	2 (0.07)	8 (0.47)	4 (0.42)	0 (0)
After discharge					
High-grade AVB	109 (0.87)	8 (0.28)	42 (2.46)	7 (0.74)	5 (0.87)
Pacemaker implantation	62 (0.50)	5 (0.17)	24 (1.40)	2 (0.21)	3 (0.52)

Abbreviation: RFCA = Radiofrequency catheter ablation; PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome; AVB = Atrioventricular block.

Supplemental Table 4. Risk factors of complications for the patients without recurrence during the follow up

	During the index admission				After discharge of the index admission			
	Life-threatening pericardial effusion (39 events, 0.21%)		New-onset stroke (22 events, 0.12%)		High-grade AVB (171 events, 0.92%)		Pacemaker (96 events, 0.51%)	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age								
0-18 yrs.	NA	NA	NA	NA	0.70 (0.29–1.69)	0.424	0.92 (0.28–3.01)	0.887
19-44 yrs.	Reference	—	Reference	—	Reference	—	Reference	—
45-54 yrs.	17.46 (2.22–137.60)	0.007	4.69 (0.48–45.74)	0.184	1.17 (0.76–1.81)	0.472	1.93 (1.08–3.45)	0.026
55-64 yrs.	33.05 (4.26–256.70)	0.001	18.46 (2.26–150.86)	0.007	0.91 (0.55–1.52)	0.731	1.17 (0.57–2.40)	0.672
65-74 yrs.	28.85 (3.47–240.16)	0.002	9.21 (0.95–89.41)	0.056	1.22 (0.73–2.05)	0.452	1.65 (0.80–3.41)	0.178
Above 75 yrs.	35.53 (3.90–323.63)	0.002	15.43 (1.54–154.54)	0.020	2.16 (1.26–3.70)	0.005	4.24 (2.09–8.62)	<0.001
Male gender	1.20 (0.61–2.37)	0.596	1.01 (0.41–2.45)	0.991	1.19 (0.87–1.63)	0.278	0.79 (0.52–1.19)	0.259
Diabetes	0.16 (0.02–1.20)	0.074	1.26 (0.41–3.87)	0.683	1.62 (1.05–2.51)	0.031	1.94 (1.10–3.40)	0.021
Hypertension	1.12 (0.54–2.31)	0.757	0.56 (0.18–1.73)	0.316	1.16 (0.78–1.73)	0.454	0.93 (0.54–1.60)	0.784
COPD	NA	NA	NA	NA	0.72 (0.29–1.80)	0.487	0.81 (0.25–2.62)	0.719
CKD	NA	NA	1.48 (0.19–11.54)	0.708	2.21 (1.02–4.81)	0.045	2.95 (1.18–7.40)	0.021
Heart failure	0.80 (0.10–6.11)	0.828	2.67 (0.71–10.06)	0.145	2.30 (1.24–4.24)	0.008	0.77 (0.23–2.54)	0.667
TOF	NA	NA	NA	NA	NA	NA	NA	NA
VSD	NA	NA	NA	NA	NA	NA	NA	NA
ASD II	5.65 (0.71–45.04)	0.102	NA	NA	1.22 (0.17–8.64)	0.844	2.21 (0.31–15.64)	0.426
Ebstein	NA	NA	NA	NA	NA	NA	NA	NA
High-activity center	3.64 (1.40–9.45)	0.008	1.17 (0.46–2.93)	0.742	0.96 (0.70–1.31)	0.788	0.90 (0.59–1.35)	0.599
Indication								
PSVT	Reference	—	Reference	—	Reference	—	Reference	—
WPW	2.45 (0.93–6.43)	0.068	1.68 (0.35–8.11)	0.520	0.42 (0.22–0.82)	0.011	0.52 (0.22–1.24)	0.141
PVT	1.68 (0.22–12.91)	0.619	NA	NA	1.02 (0.41–2.51)	0.973	1.26 (0.39–4.04)	0.694
Atrial fibrillation	4.57 (2.03–10.33)	<0.001	3.86 (1.09–13.65)	0.036	0.77 (0.35–1.68)	0.507	0.52 (0.13–2.06)	0.351
Atrial flutter	1.21 (0.41–3.59)	0.729	3.88 (1.27–11.84)	0.017	1.95 (1.28–2.97)	0.002	2.34 (1.36–4.02)	0.002

Abbreviation: AVB = Atrioventricular block; COPD = Chronic obstructive pulmonary disease; CKD = Chronic kidney disease; CAD = Coronary artery disease; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; ASD = Atrial septal defect; Ebstein = Ebstein's anomaly

PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome; OR = odds ratio; HR = hazard ratio; CI = confidence interval; NA = not applicable.

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6,7
		(*b*) Describe any methods used to examine subgroups and interactions	6,7
		(*c*) Explain how missing data were addressed	7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10, 11, 13
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-12
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20,21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	18,19
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Trend and Risk Factors of Recurrence and Complications after Arrhythmias Radiofrequency Catheter Ablation: A Nationwide Observational Study in Taiwan

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Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Health services research, Public health, Medical management, Epidemiology
Keywords:	radiofrequency catheter ablation (RFCA), Wolff–Parkinson–White syndrome, supraventricular tachycardia, ventricular tachycardia, complication, recurrence

Trend and Risk Factors of Recurrence and Complications after Arrhythmias Radiofrequency Catheter Ablation: A Nationwide Observational Study in Taiwan

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*** Tien-Hsing Chen and Yu-Sheng Lin contributed equally to this study**

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Abstract

Objectives: This study determined the recurrence and complication rates after radiofrequency catheter ablation (RFCA) for those with paroxysmal supra-ventricular tachycardia (PSVT), Wolff–Parkinson–White Syndrome (WPW), atrial flutter (AFL), atrial fibrillation (AF) and ventricular tachycardia (VT).

Study Design and Setting: This retrospective study included RFCAs for 2001-2010 in the Taiwan National Health Insurance Research Database. Primary outcomes included perioperative complications (pericardial effusion and new-onset stroke), RFCA recurrence and long-term outcomes (high-grade atrioventricular block [AVB] and pacemaker implantation).

Results: Of 19,475 RFCA patients, prevalence rates were 56.7% for PSVT, 13.5% for WPW, 9.5% for AFL, 5.1% for AF and 2.7% for VT. Prevalence rates increased in AF, AFL and VT over the study years. During an average follow-up period of 4.36 years (standard deviation: 2.86 years), recurrence rates for PSVT, WPW, VT, AFL and AF were 2%, 4.9%, 5.7%, 5.8% and 16.1%, respectively. Compared to the PSVT group, the WPW and AF groups had significantly higher risk of pericardial effusion during admission (adjusted odds ratio [aOR] 2.98, 95% confidence interval [CI] 1.24–7.15; aOR 4.09, 95%CI 1.90–8.79, respectively); the AFL group had a higher risk of new-onset stroke during admission (aOR 4.07, 95%CI 1.39–11.91); the WPW group had a lower risk of high-grade AVB during follow up (adjusted hazard ratio [aHR] 0.37, 95% CI 0.19–0.71) while the AFL group had a greater risk (aHR 1.74, 95%CI 1.17–2.60); and the AFL group had a higher risk of permanent pacemaker (aHR 2.14, 95%CI 1.27–3.62).

Conclusions: The RFCA rate increased rapidly during 2001-2010 for AF, AFL and VT. Recurrence was associated with congenital heart disease in PSVT and WPW, and with age in AF and AFL. AFL had a higher risk of permanent pacemaker implantation and new stroke. AF had a higher risk of life-threatening pericardial effusion.

Key words: radiofrequency catheter ablation (RFCA), Wolff–Parkinson–White Syndrome, supraventricular tachycardia, ventricular tachycardia, complication, recurrence, risk factors

Strengths and limitations of this study

- This 10-year longitudinal retrospective study is the first nationwide, large-scale study of the trend, recurrence and complications of radiofrequency catheter ablation (RFCA).
- This article is the first study to compare recurrence and complications among five different types of arrhythmias after RFCA.
- Our study provides risks of arrhythmia recurrence and complications after RFCA.
- This study did not have access to certain data such as laboratory parameters, procedural details, and heart images. Also, some arrhythmias such as premature ventricular beats and atrial premature beats are not covered by Taiwan National Health Insurance (NHI).
- This study was not able to explore the interactions among the predictive variables because of the limited number of events.

Introduction

Radiofrequency catheter ablation (RFCA) is used to treat patients with supraventricular tachycardia or ventricular tachycardia (VT), especially paroxysmal supraventricular tachycardia (PSVT).[1-3] Widely applied since the 1990s,[4] RFCA is an effective therapy with demonstrated high success, low complications and low recurrence rates compared to direct current ablation or surgical ablation. RFCA is superior to conservative treatments such as medication or observation for patients with PSVT and WPW. RFCA was first used to treat atrial fibrillation (AF) in 1998.

Although arrhythmias after RFCA are usually not life-threatening, identification and minimization of the risk of complications are extremely important. The RFCA procedure may lead to atrioventricular (AV) block and bradycardia, even requiring permanent pacemaker implantation. Previous studies[5] were composed of relatively small cohorts or were single-center studies and evaluated patients with a single arrhythmia.[5,6] However, there are no studies comparing RFCA-related complications in patients with five different arrhythmias.[7,8] The targets for RFCA-related risk minimization differ by type of arrhythmia. For example, when RFCA is used to treat PSVT, the goal is to modify or eliminate AV node or accessory pathways; when used to treat AF,[6] the goal is to isolate the pulmonary veins. High grade AV block, life-threatening pericardial effusion, and stroke are dangerous complications after an RFCA procedure. However, the complication rates vary by type of arrhythmia: PSVT, Wolff-Parkinson-White Syndrome (WPW), atrial flutter (AFL), AF and VT. It is therefore important to identify the incidence and risk factors of RFCA-related complications in these patients.

This retrospective study investigated the population trend of patients who received RFCA for PSVT, WPW, AFL, AF and VT. We identified the major RFCA-related risk factors influencing 1) recurrence of arrhythmias and 2) complications such as AV block, permanent pacemaker implantation, life-threatening pericardial effusion and acute ischemic stroke.

Methods

Study design and population

We conducted a nationwide population-based cohort study using data from the Taiwan National Health Insurance Research Database (NHIRD). In Taiwan, the National Health Insurance (NHI) program has reimbursed patients who receive RFCA for PSVT, WPW, AFL, AF and VT since 2001. More than 99.91% of Taiwan's population is covered by NHI benefits.

The accuracy and validation of NHIRD data is based upon regular auditing by the NHI Bureau.[9-11] The Institutional Review Board of Chang Gung Memorial Hospital approved this study.

Study cohort, outcome measurement and follow-up

This study accessed NHIRD data for all targeted arrhythmia patients who received RFCA from 2001 to 2010. The targeted arrhythmias were PSVT (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9 CM] Code 4270), WPW (426.7), AFL (427.32), AF (427.31) and VT (427.1; Supplemental Table 1). Patients with arrhythmias other than those targeted (such as premature ventricular beats or atrial tachycardia) and patients with unidentified arrhythmias who received RFCA were excluded. We enrolled only the patient's first RFCA. The follow-up period was calculated from the discharge date of the index hospitalization until death, loss to follow up (withdrawal from the NHI program: emigration or prison incarceration for longer than six months) or until the study end date (31 December 2010).

Outcomes measurement

The primary outcomes included recurrence of arrhythmia, in-hospital complications and long-term complications. Recurrence was defined as either 1) recurrence of original arrhythmia or 2) receipt of a second RFCA during the follow up period. In-hospital complications included life-threatening pericardial effusion and new-onset stroke during the admission. Life-threatening pericardial effusion was defined as the patient requiring pericardiocentesis during RFCA. New stroke was defined as stroke (ICD-9 CM codes 430-437) which occurred during the index admission. Other complications included high-grade AV block and permanent pacemaker implantation.

Covariate assessment

Age was categorized into six groups (0-18, 19-44, 45-54, 55-64, 65-74 and 75 years and above) because previous studies reported different indications for RFCA and different complications between age groups.[1-3] Comorbidities were assessed according to ICD-9 CM codes before the index admission. Diabetes mellitus, hypertension (HTN) or chronic diseases were recorded as comorbidities if there was at least one in-admission diagnosis. All congenital heart disease (CHD) was reconfirmed by the Catastrophic Illness Certification (CIC), which is a sub-dataset of NHI. A CIC for CHD requires imaging proof confirmed by two cardiologists. Complicated CHD included Tetralogy of Fallot (TOF), transposition of the great vessels, double outlet right ventricle, total anomalous pulmonary venous connection, tricuspid atresia, common truncus arteriosus, common ventricle and hypoplastic left heart syndrome. Simple CHD included ventricular septal defect (VSD), atrial septal defect (ASD), Ebstein's anomaly, patent ductus arteriosus, congenital pulmonary stenosis, coarctation of the aorta, endocardial cushion defect and congenital aortic stenosis. Center activity was a time-dependent variable and a high-activity center was defined as more than 100 RFCA surgeries per year, regardless of arrhythmia type.

Patient and public involvement

This study had no direct relationship with any patient and no public involvement during the development, design and conduct.

Statistical analysis

The proportion of categorical variables between groups was compared using the chi-squared test and Fisher's exact test. Continuous variables were compared using Kruskal-Wallis test due to the lack of normality. Multivariable logistic regression analysis was used to identify clinical features associated with the risk of in-hospital complications, including life-threatening

pericardial effusion and new-onset stroke during the admission. Multivariable Cox regression analysis was used to investigate the association of clinical variables with time-to-event outcomes, including recurrence, high-grade AV block and pacemaker implantation during the follow up. In the survival analysis, the time-scale was time since RFCA in days. The assumption of proportional hazard was tested by Schoenfeld partial residuals, in which the indication was the only explanatory categorical variable. The 13 pre-specified potential predictive variables were those clinically relevant to RFCA and its complications: two demographic variables (sex and age), six comorbidities, four types of CHD and hospital volume. All 13 candidate predictive variables were introduced into the multivariable regression models. Multicollinearity among predictors was checked by variance inflation factor, with a value less than 10 indicating no serious collinearity among predictors. Sensitivity analyses were done by excluding patients with recurrent RCFA during the follow up (Supplemental Table 2). A two-sided *P* value lower than 0.05 was considered statistically significant. No adjustment for multiple testing (multiplicity) was made in this study to avoid the low statistical power. Results were presented as the odds ratio (OR) for logistic regression, or hazard ratio (HR) for Cox regression with corresponding 95% confidence intervals (CI). All data analyses were performed using SPSS software version 15 (SPSS Inc., Chicago, IL, USA).

Results

There were 24,003 RFCA procedures registered in NHIRD between 1 January 2001 and 31 December 2010. Based on the inclusion and exclusion criteria, a total of 19,475 enrolled patients underwent 20,707 RFCA procedures. Only the first occurrence for each individual was used for analysis. The proportion of change in rates of RFCA by individual arrhythmias from

2001 to 2010 is shown in Figure 1. The proportion of RFCA for PSVT decreased from 60% to 51% between 2001 to 2010, while the proportion for AF increased from 2% to 10% (Figure 1).

The commonest arrhythmia treated with RFCA was PSVT (n=12796; 56.7%), followed by WPW (n=3051; 13.5%), AFL (n=1854; 9.5%), AF (n=1162; 5.1%) and VT (n=612; 2.7%). The mean age of study participants when they received RFCA was 47.6 years (standard deviation [SD] 18.3). Demographic and baseline clinical characteristics according to arrhythmia type are summarized in Table 1. The prevalence of PSVT (38.5%), WPW (58.1%) and VT (47.2%) was highest in the group aged 19-44 years. Patients were the oldest in the AFL group, followed by the AF group, the PSVT group, the VT group and the WPW group. Patients with AF and AFL had a higher prevalence of diabetes (16.2% and 11.5%, respectively) and hypertension (28.9% and 28.1%, respectively) compared to patients with other arrhythmias. Chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and heart failure were most prevalent in the AFL group since these patients were the oldest (median age 62.9 years). RFCA due to AF was predominantly performed in high-activity centers (84%), followed by AFL (71%). Complicated CHD was more common in the AFL group than in other arrhythmias. Simple CHD was most prevalent in the AFL group (3.6%), followed by the VT group (1.5%).

Table 1. Baseline data for 19,475 study patients who underwent RFCA procedures stratified by indication.

Variable	PSVT	WPW	AFL	AF	VT	*P* value
Number of patients	12,796	3,051	1,854	1,162	612	–
Age (yrs.), median (IQR)	47.0 (33.5, 58.6)	36.3 (22.8, 49.7)	62.9 (51.7, 73.1)	56.9 (48.4, 65.5)	43.1 (28.7, 55.2)	<0.001
Age group						<0.001
0-18 yrs.	863 (6.7)	379 (12.4)	15 (0.8)	0 (0.0)	46 (7.5)	
19-44 yrs.	4,930 (38.5)	1,619 (53.1)	260 (14.0)	216 (18.6)	289 (47.2)	
45-54 yrs.	2,938 (23.0)	579 (19.0)	329 (17.7)	285 (24.5)	123 (20.1)	
55-64 yrs.	2,083 (16.3)	308 (10.1)	407 (22.0)	354 (30.5)	75 (12.3)	
65-74 yrs.	1,344 (10.5)	130 (4.3)	472 (25.5)	222 (19.1)	51 (8.3)	
75+ yrs.	638 (5.0)	36 (1.2)	371 (20.0)	85 (7.3)	28 (4.6)	
Gender, male	5,402 (42.3)	1,988 (65.2)	1,332 (71.9)	838 (72.2)	327 (53.5)	<0.001
Diabetes	910 (7.1)	113 (3.7)	301 (16.2)	134 (11.5)	32 (5.2)	<0.001
Hypertension	1,723 (13.5)	275 (9.0)	535 (28.9)	326 (28.1)	74 (12.1)	<0.001
COPD	286 (2.2)	22 (0.7)	103 (5.6)	28 (2.4)	15 (2.5)	<0.001
CKD	150 (1.2)	12 (0.4)	71 (3.8)	11 (0.9)	5 (0.8)	<0.001
CAD	594 (4.6)	87 (2.9)	288 (15.5)	154 (13.3)	45 (7.4)	<0.001
Heart failure	73 (0.6)	21 (0.7)	205 (11.1)	53 (4.6)	25 (4.1)	<0.001
High-activity center‡	7,267 (56.8)	1,880 (61.6)	1,317 (71.0)	976 (84.0)	317 (51.8)	<0.001
Complicated CHD	10 (0.1)	3 (0.1)	16 (0.9)	2 (0.2)	1 (0.2)	<0.001
TOF	3 (0.0)	0 (0.0)	11 (0.6)	1 (0.1)	1 (0.2)	<0.001
Other Complicated CHD	7 (0.1)	3 (0.1)	5 (0.3)	1 (0.1)	0 (0.0)	0.045
Simple CHD †	69 (0.5)	31 (1.0)	66 (3.6)	9 (0.8)	9 (1.5)	<0.001
VSD	15 (0.1)	6 (0.2)	25 (1.3)	0 (0.0)	4 (0.7)	<0.001
ASDII	50 (0.4)	10 (0.3)	34 (1.8)	9 (0.8)	4 (0.7)	<0.001
Ebstein	4 (0.0)	18 (0.6)	6 (0.3)	0 (0.0)	0 (0.0)	<0.001
Other simple CHD	4 (0.0)	2 (0.1)	6 (0.3)	0 (0.0)	1 (0.2)	<0.001

Abbreviations: RFCA = Radiofrequency catheter ablation; PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White Syndrome; AFL = Atrial flutter; AF = Atrial fibrillation; VT = Ventricular tachycardia; Yrs = years; IQR = Interquartile range; COPD = Chronic obstructive pulmonary disease; CKD = Chronic kidney disease; CAD = Coronary artery disease; CHD = Congenital heart disease; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; ASD = Atrial septal defect; Ebstein = Ebstein's anomaly.

‡ defined as 100 operations per year.

† The discrepancy between the sums of subgroups and the total is due to the possibility that one patient might have two CHDs.

Risks of recurrence

During an average follow-up period of 4.36 years (SD 2.86 years), the recurrence rates after the index RFCA for those with PSVT, WPW, VT, AFL and AF were 2%, 4.9%, 5.7%, 5.8% and 16.1%, respectively. Multivariable Cox analyses revealed that the major risk factors for recurrence of PSVT after RFCA included: age (0-18 years), male gender, diabetes and TOF. Younger patients (0-18 *vs.* 19-44 years) and those with Ebstein's anomaly were considered at greater risk for recurrence of WPW after RFCA (Table 2). For the AFL group, older individuals (45-54 *vs.* 19-44 years) had a higher risk of recurrence. Male gender, TOF, VSD and high-activity center were also risk factors. In contrast, the incidence of AFL recurrence was low in patients 75 years or older. The recurrence rate was 16.1% in patients with AF but 2.0% for those with PSVT. The recurrence-free rate after RFCA declined with time, most sharply for those with AF (Figure 2). Patients aged 19–44 years had a higher risk of AF recurrence compared with patients older than 65 years; male gender and treatment at a high-activity center were also identified as risk factors. In the VT population, treatment at a high-activity center was related to decreased risk of recurrence. The results were similar when excluding patients with recurrent RCFA during the follow up (Supplemental Table 3).

Table 2. Risk factors for recurrence of radiofrequency catheter ablation.

	PSVT (259 events, 2.0%)		WPW (160 events, 5.2%)		AFL (120 events, 5.8%)		AF (247 events, 16.1%)		VT (38 events, 5.7%)	
Variable	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age										
0-18 yrs.	1.52 (1.02–2.28)	0.041	1.90 (1.27–2.85)	0.004	2.17 (0.50–9.41)	0.30	NA	NA	1.19 (0.41–3.48)	0.75
19-44 yrs.	Reference	—	Reference	—	Reference	—	Reference	—	Reference	—
45-54 yrs.	0.88 (0.64–1.22)	0.46	0.90 (0.57–1.44)	0.67	1.98 (1.15–3.41)	0.014	1.03 (0.73–1.44)	0.88	0.71 (0.28–1.78)	0.46
55-64 yrs.	0.70 (0.47–1.05)	0.08	1.47 (0.87–2.47)	0.15	1.40 (0.78–2.51)	0.27	0.87 (0.61–1.25)	0.43	0.75 (0.24–2.36)	0.62
65-74 yrs.	0.68 (0.42–1.11)	0.12	0.95 (0.37–2.41)	0.91	0.93 (0.49–1.77)	0.82	0.54 (0.34–0.86)	0.01	0.19 (0.02–1.56)	0.12
75+ yrs.	0.69 (0.35–1.37)	0.29	NA.	NA	0.28 (0.10–0.76)	0.013	0.08 (0.02–0.34)	0.001	NA	NA
Male gender	1.66 (1.30–2.13)	<0.001	1.06 (0.77–1.48)	0.71	1.68 (1.09–2.59)	0.020	1.43 (1.05–1.95)	0.023	1.31 (0.66–2.58)	0.44
Diabetes	1.59 (1.01–2.52)	0.047	0.18 (0.03–1.34)	0.09	0.80 (0.43–1.49)	0.49	0.70 (0.43–1.14)	0.15	0.70 (0.09–5.74)	0.74
Hypertension	1.03 (0.70–1.53)	0.88	1.27 (0.71–2.28)	0.42	0.73 (0.46–1.15)	0.17	1.29 (0.97–1.72)	0.08	1.49 (0.40–5.49)	0.55
COPD	1.13 (0.50–2.60)	0.77	NA.	NA	1.08 (0.43–2.72)	0.87	1.45 (0.54–3.94)	0.46	NA	NA
CKD	1.61 (0.59–4.36)	0.35	NA.	NA	0.78 (0.24–2.49)	0.67	0.55 (0.08–4.02)	0.56	4.18 (0.52–33.86)	0.18
CAD	0.85 (0.44–1.64)	0.63	0.53 (0.13–2.17)	0.38	0.59 (0.29–1.17)	0.13	1.07 (0.73–1.56)	0.74	1.18 (0.26–5.25)	0.83
Heart failure	1.64 (0.40–6.67)	0.49	NA.	NA	0.91 (0.47–1.75)	0.78	0.29 (0.07–1.20)	0.09	2.90 (0.63–13.42)	0.17
TOF	23.00 (4.0–131.8)	<0.001	NA.	NA	3.32 (1.01–10.96)	0.049	NA	NA	NA	NA
VSD	NA.	NA	2.79 (0.53–14.82)	0.23	2.78 (1.29–5.99)	0.009	0.99 (0.13–7.43)	0.99	NA	NA
ASD II	2.78 (0.89–8.72)	0.08	0.40 (0.04–4.25)	0.45	1.46 (0.57–3.71)	0.43	1.17 (0.28–4.87)	0.83	3.57 (0.47–27.34)	0.22
Ebstein	1.08 (0.09–12.80)	0.95	4.40 (1.80–10.74)	0.001	1.54 (0.21–11.5)	0.68	NA	NA	NA	NA.
High-activity center	1.05 (0.82–1.35)	0.68	0.87 (0.63–1.19)	0.38	1.78 (1.11–2.85)	0.017	3.16 (1.77–5.67)	<0.001	0.49 (0.25–0.97)	0.04

Abbreviations: PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White Syndrome; AFL= Atrial flutter; AF= Atrial fibrillation; VT= Ventricular tachycardia; HR = Hazard ratio; CI = Confidence interval; Yrs = Years; COPD = Chronic obstructive pulmonary disease; NA = not applicable; CKD = Chronic kidney disease; CAD = Coronary artery disease; CHD = Congenital heart disease; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; ASD = Atrial septal defect; Ebstein = Ebstein's anomaly.

Complications

Rates of RFCA-related complications were evaluated for the five arrhythmia groups (Table 3). The overall rates of complications and mortality were less than 1% and 0.1%, respectively. High-grade AV block was the most common complication following RFCA in all groups except the AF group. RFCA was more associated with life-threatening pericardial effusion in the AF group (1.3%) than in the other groups. In the AFL group, RFCA was more associated with high-grade AV block (2.5%), permanent pacemaker implantation (1.4%) and new stroke (0.5%) than in other groups. For instance, indication of AF increased across years would result in a shorter mean follow up duration and lower incidence. In contrast, indication of PSVT decreased across years would result in a longer mean follow up duration and higher incidence of complications.

Table 3. Numbers and Rate of RFCA-related complications according to type of arrhythmias.

Complication	PSVT	WPW	AFL	AF	VT
Number of patients	12,796	3,051	1,854	1,162	612
In-hospital complications (numbers and percent)					
Life-threatening pericardial effusion	15 (0.18)	8 (0.26)	6 (0.32)	15 (1.30)	1 (0.16)
New-onset stroke	8 (0.06)	2 (0.07)	9 (0.49)	4 (0.34)	0 (0.00)
After discharge					
High-grade AVB	114 (0.89)	10 (0.33)	47 (2.53)	8 (0.69)	5 (0.82)
Pacemaker implantation	64 (0.50)	5 (0.16)	26 (1.40)	2 (0.17)	3 (0.50)

Abbreviations: RFCA = Radiofrequency catheter ablation; PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White Syndrome; AFL= Atrial flutter; AF = Atrial fibrillation; VT= Ventricular tachycardia; AVB = Atrioventricular block.

Risk factors for complications

As to in-hospital complications, multivariable logistic regression revealed that age >44 years, high-activity center and RFCA after WPW or AF (when compared with PSVT) were associated with increased risk of life-threatening pericardial effusion. Age >55 years and RFCA after AFL (when compared with PSVT) were associated with a higher risk of stroke following RFCA (Table 4).[3] As to long-term complications, multivariable Cox regression identified the risk factors for high-grade AV block as age ≥75 years, diabetes and heart failure. WPW patients were at a lower risk of developing AV block than PSVT patients. Risk factors for pacemaker implantation were age ≥75 years, diabetes, CKD and RFCA after AFL (when compared with PSVT). The results were similar when excluding patients with recurrent RCFA during the follow up (Supplemental Table 4).

Testing of Schoenfeld partial residuals revealed insignificant correlation for rank of survival time after AV block and permanent pacemaker implantation (AV block: number of events = 184, r = 0.084, p = 0.271; permanent pacemaker implantation: number of events = 100, r = 0.149, p = 0.114), which indicated that the assumption of proportional hazard was not strongly violated (data not shown).

Table 4. Risk factors of complications during the index admission or after discharge of the index admission.

	During the index admission				After discharge of the index admission			
	Life-threatening pericardial effusion (45 events, 0.22%)		New-onset stroke (23 events, 0.11%)		High-grade AVB (184 events, 0.88%)		Pacemaker (100 events, 0.48%)	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age								
0-18 yrs.	NA	NA	NA	NA	0.66 (0.28–1.53)	0.33	0.81 (0.24–2.71)	0.74
19-44 yrs.	Reference	—	Reference	—	Reference	—	Reference	—
45-54 yrs.	11.18 (2.50–50.10)	0.002	4.53 (0.46–44.16)	0.19	1.07 (0.70–1.62)	0.76	1.70 (0.96–3.01)	0.07
55-64 yrs.	17.32 (3.87–77.55)	<0.001	19.68 (2.44–158.78)	0.005	0.85 (0.52–1.37)	0.50	1.09 (0.55–2.18)	0.80
65-74 yrs.	17.75 (3.68–85.57)	<0.001	9.58 (0.99–91.66)	0.05	1.07 (0.65–1.77)	0.79	1.40 (0.69–2.85)	0.36
Above 75 yrs.	22.70 (4.16–123.95)	<0.001	17.01 (1.73–167.36)	0.015	2.07 (1.24–3.44)	0.005	3.82 (1.94–7.53)	<0.001
Male gender	1.12 (0.60–2.12)	0.72	0.84 (0.35–2.00)	0.70	1.14 (0.84–1.54)	0.40	0.74 (0.49–1.12)	0.16
Diabetes	0.33 (0.08–1.39)	0.13	1.22 (0.40–3.70)	0.73	1.77 (1.17–2.70)	0.007	1.95 (1.13–3.37)	0.016
Hypertension	1.01 (0.51–2.01)	0.97	0.52 (0.17–1.59)	0.25	1.08 (0.73–1.59)	0.70	0.94 (0.55–1.59)	0.81
COPD	NA	NA	NA	NA	0.70 (0.28–1.72)	0.43	0.77 (0.24–2.49)	0.67
CKD	NA	NA	1.41 (0.18–10.89)	0.74	2.10 (0.97–4.54)	0.06	2.69 (1.07–6.76)	0.036
Heart failure	0.74 (0.10–5.59)	0.77	2.51 (0.68–9.29)	0.17	2.31 (1.28–4.17)	0.006	1.00 (0.35–2.83)	0.99
TOF	NA	NA	NA	NA	NA.	NA	NA	NA
VSD	NA	NA	NA	NA	2.20 (0.51–9.47)	0.29	NA	NA
ASD II	4.10 (0.53–31.84)	0.18	NA	NA	1.55 (0.37–6.47)	0.55	1.94 (0.27–14.10)	0.51
Ebstein	NA	NA	NA	NA	3.70 (0.49–27.86)	0.20	NA	NA
High-activity center	3.79 (1.47–9.79)	0.006	1.15 (0.46–2.88)	0.76	0.98 (0.73–1.33)	0.91	0.92 (0.61–1.38)	0.68
Indication								
PSVT	Reference	—	Reference	—	Reference	—	Reference	—
WPW	2.98 (1.24–7.15)	0.015	1.63 (0.34–7.85)	0.55	0.37 (0.19–0.71)	0.003	0.41 (0.16–1.04)	0.06
VT	1.58 (0.21–12.14)	0.66	NA	NA	0.85 (0.35–2.10)	0.73	1.10 (0.34–3.51)	0.87
AFL	4.09 (1.90–8.79)	<0.001	2.74 (0.77–9.72)	0.118	0.53 (0.25–1.11)	0.09	0.33 (0.08–1.36)	0.13
AF	1.34 (0.49–3.70)	0.57	4.07 (1.39–11.91)	0.010	1.74 (1.17–2.60)	0.006	2.14 (1.27–3.62)	0.004

Abbreviations: AVB = Atrioventricular block; OR = odds ratio; CI = Confidence interval; HR = Hazard ratio; COPD = Chronic obstructive pulmonary disease; NA = not applicable; CKD = Chronic kidney disease; CAD = Coronary artery disease; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; ASD = Atrial septal defect; Ebstein = Ebstein's anomaly; PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White Syndrome; AFL= Atrial flutter; AF= Atrial fibrillation; VT=Ventricular tachycardia.

Discussion

To the best of our knowledge, this is the first observational study to record the impact of RFCA on the treatment of arrhythmias by analyzing the burden, risk factors, recurrence and complications of patients with five different arrhythmias. From 2001 to 2010, the number of RFCAs increased rapidly for the AF, AFL and VT groups, but decreased gradually for the PSVT and WPW groups. Age was a risk factor for recurrence in all groups, while male gender, diabetes and TOF were risk factors for recurrence in patients with PSVT. AF patients treated in a high-activity center had a tendency to receive repeated RFCAs. Elderly patients with AF and AFL had more adverse events after RFCA compared to other subgroups.

Trend in Types of Arrhythmias

In Taiwan, the number of AF increased the most over the ten years studied, followed by the VT, AFL, WPW and PSVT groups. Population aging and advancements in ablation techniques have contributed to this phenomenon, especially for AF and AFL, which are age-related diseases.[12] From 2001 to 2010, the population of older adult patients (>65 years) increased from 1,973,357 to 2,487,893. This increase has resulted in a greater increase in the incidence of AF and AFL compared to other arrhythmias. The mean growth rate for RFCA per year between 2001 and 2010 was 9.7% for AF and 3.2% for AFL (Figures 3-4). In contrast, the average growth rate of RFCA for PSVT was just 1.4%, which was gradually slowing, although the absolute numbers increased from 1,118 in 2001 to 1,499 in 2010. This pattern is likely present for PSVT since 1) RFCA for PSVT is relatively mature compared to RFCA for AF, and 2) RFCA for PSVT was fully covered by Taiwan NHI but AF was not. Because patients with PSVT and WPW were relatively young, we searched the birth rate from 1980 to 2000. The crude birth rate (births per 1,000 population per year) in Taiwan decreased from 23% in 1980 (413,177 births) to 13% in 2000 (307,200 births), reducing the number of patients needing

PSVT and WPW. The number of WPW cases peaked in 2005 (N= 377) and has since been decreasing. The number of procedures in the VT group increased from 57 in 2001 to 123 in 2010, and the average RFCA growth rate over 10 years was 6.8%. This relatively high growth rate is possibly also due to population aging and the maturation of 3D mapping techniques.[13] In summary, the growth models are different for the five arrhythmias. The AF and AFL groups have increased rapidly in RFCA procedures because of population aging. The PSVT group had a relatively slow increase, while the WPW and VT groups showed stable or decreasing numbers of RFCAs.

Risk of recurrence

Our results showed that the recurrence rate after RFCA increased in the following order: PSVT (2%) < WPW (4.9%) < VT (5.7%) < AFL (5.8%) < AF (16.1%) (Figure 2). The recurrence-free rate was highest for the PSVT group (98.8% for the first year, gradually decreasing to 97.2% for the 10-year follow up). However, patients <18 years in the PSVT and WPW groups had a significantly higher chance of recurrence, a result which agreed with those of Van Hare et al.[14] This recurrence could be a result of the smaller cardiac anatomy in children, which makes the precise ablation difficult to perform. This result could also explain the association of CHD and TOF with recurrence of PSVT, possibly because of the abnormal cardiac structure of the CHD heart post-cardiac surgery. Patients with TOF and AF also had a higher risk of receiving a second RFCA. In contrast, AF and AFL patients aged ≥75 years had fewer second RFCAs than younger patients.[15]

Our data showed that patients ≥75 years receiving treatment for AF and AFL had lower recurrence rates than those the same age in other groups. The reason for this phenomenon may be the conservative treatment preferred by cardiologists for older patients rather than repeated RFCA, in order to avoid complications or mortality after the first procedure due to the presence

of other comorbidities. Our data suggest that, for patients undergoing an elective RFCA, physicians should carefully evaluate the risk factors such as younger age and the presence of CHD (TOF in PSVT, VSD in AFL) which are associated with a high recurrence rate. Our study also described epidemiologic changes in repeated ablation procedures for five arrhythmias in Taiwan in the RFCA era.

Complications

RFCA, which has an approximately 1% complication rate and 0.1% mortality rate,[3,16] is considered a relatively safe procedure to treat or even cure arrhythmias (Table 3). Our present study showed different patterns of complications in the five arrhythmia groups. Patients with PSVT and WPW had complication rates of 1.6% and 0.8%, respectively, similar to previous studies. However, in patients with AF and AFL, the complication rates were 2.5% and 4.7%, respectively. AFL after RFCA induced more high-grade AV block (2.5%) compared to other arrhythmias, and patients with AF after RFCA had the highest incidence rate of life-threatening pericardial effusion (1.3%). High-grade AV block is considered the main complication of ablation procedures for AFL and PSVT patients because the ablation sites are close to the atrioventricular node.[16] AFL has been seen combined with sick sinus syndrome. Bradyarrhythmias appeared when the substance of AF and AFL is eliminated. RFCA patients with AF had a higher risk of life-threatening pericardial effusion relative to patients with other arrhythmias, resulting in a relatively higher complication rate of 1.3%. The major RFCA procedure for AF is to isolate the pulmonary vein and eliminate the substrate in the left atrium. This requires a longer procedure time and delivers more energy to convert AF into sinus rhythm. RFCA for AF could therefore cause more life-threatening pericardial effusion than that for other arrhythmias. RFCA for VT presents same pattern as that for PSVT and WPW. These data

suggest that, although RFCA is a common procedure to treat different arrhythmias, the complications that should be monitored will differ by type of arrhythmia.

Our data also showed that patients with AFL and AF had higher stroke rates (0.49% and 0.34%, respectively) than patients in the other groups. Anticoagulation therapy is needed in these cases, and it is also necessary to confirm the absence of intracardiac thrombus before RFCA.[17] However, anticoagulation procedures are sometimes ignored because anti-coagulation is not routinely used in AFL.[18] Previous studies have shown a high risk of thromboembolic events and a high incidence of thrombogenic milieu in AFL.[19,20] Use of the inappropriate anticoagulation therapy is considered a significant risk factor for thromboembolism in patients with AFL.[18]

Age was an important risk factor associated with complications such as high-grade AV block, pacemaker implantation, life-threatening pericardial effusion and stroke, especially in patients aged ≥75 years (Table 4). These data were consistent with previous studies,[21,22] and suggest that physicians should be cautious when performing RFCA in patients ≥75 years. We also found that diabetes was associated with increased complication rates for RFCA. A cohort study of 200,000 patients with type II diabetes reported that third degree AV block was 3.1 times as prevalent in the diabetic group (95% CI, 3.0-3.3; $p < 0.0001$).[23] Diabetes has been suggested as a risk factor for autonomic neuropathy, cardiac conduction abnormalities and bradyarrhythmias.[24] Physicians performing RFCA in diabetic patients should monitor for bradyarrhythmia complications.

Limitations

Firstly, the major limitation of this study is our inability to explore the interactions among the predictive variables because of the limited number of events. For instance, the 184 high-grade AV blocks allow for a maximum of 18-19 predictive variables, due to the "ten-one

rule."[25-27] However, the 13 predictors indicate that 78 two-way potential interaction effects may exist. Therefore, it seems not feasible to perform a regression analysis (logistic or Cox regressions) because that many explanatory variables in the equation would induce the statistical problem of overfitting. Therefore, further studies with a larger sample size are needed to conduct interaction tests based on clinical knowledge or on exploratory data analysis.

Secondly, in this cohort study we did not have access to laboratory parameters, procedural details, heart images, smoking status, obesity, alcohol use or costs. Procedure-related parameters, the location of the accessory pathway in WPW, PV isolation for AF, cardiac anomaly and ejection fraction have been reported as predictors for arrhythmia recurrence and RFCA complications.[14, 28-30] The lack of this information could induce residual confounding. On the other hand, the different arrhythmia groups had substantial differences in baseline characteristics, especially in terms of age, which may result in potential confounding even if we adjusted for these variables in the multivariable regression models. However, the present study focused on RFCA for five different arrhythmias and each arrhythmia had different surgical parameters. Rather than comparing the same parameter in different arrhythmia ablation procedures, we focused on the effect of comorbidities, gender and age on arrhythmia recurrence and RFCA-related complications. Our study provided valuable information to help cardiologists deal with RFCA recurrence and complications.

Thirdly, some arrhythmias such as premature ventricular beats and atrial premature beats are not covered by Taiwan NHI. However, excluding these arrhythmias did not influence the study results since they are usually benign.

Lastly, recurrence may be misidentified in this present study as resulting from ablation of other arrhythmias. For example, this could happen if the patient had an initial PSVT ablation followed by an AF ablation. A single definition of recurrence could consider the second

ablation as the recurrence of PSVT. Use of double criteria, with repeated ablations combined with the same major principal diagnosis, reduced the coding error in this study.

Conclusions

There was a rapidly increasing trend of RFCA procedures for AF, AFL and VT during 2001-2010, but a slow increase for PSVT and WPW. The recurrence-free rate was higher for PSVT than for other arrhythmias. Older adult patients with AF and AFL had fewer repeat RFCAs and AF patients in high-activity center hospitals had more. CHD was a risk factor for PSVT recurrence. AF patients had more occurrences of life-threatening pericardial effusion, especially those aged more than 65 years, and patients receiving RFCA for AFL suffered more from bradycardia, requiring permanent pacemaker implantation.

Contributors:

CHEN conceived of the study. Y LIN and WU initiated the study design and WANG helped with implementation. Y LIN, WU and CHEN provided statistical expertise in clinical trial design and WANG and YS LIN conducted the primary statistical analysis. All authors contributed to refinement of the study protocol and approved the final manuscript.

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Disclaimer:

The lead author confirms that the content of this manuscript is honest and transparent.

Competing interests:

None declared.

Patient consent:

Not required.

Ethics approval:

The Ethics Institutional Review Board at Chang Gung Memorial Hospital approved this study.

Data sharing statement:

Data are available. Please contact the corresponding author.

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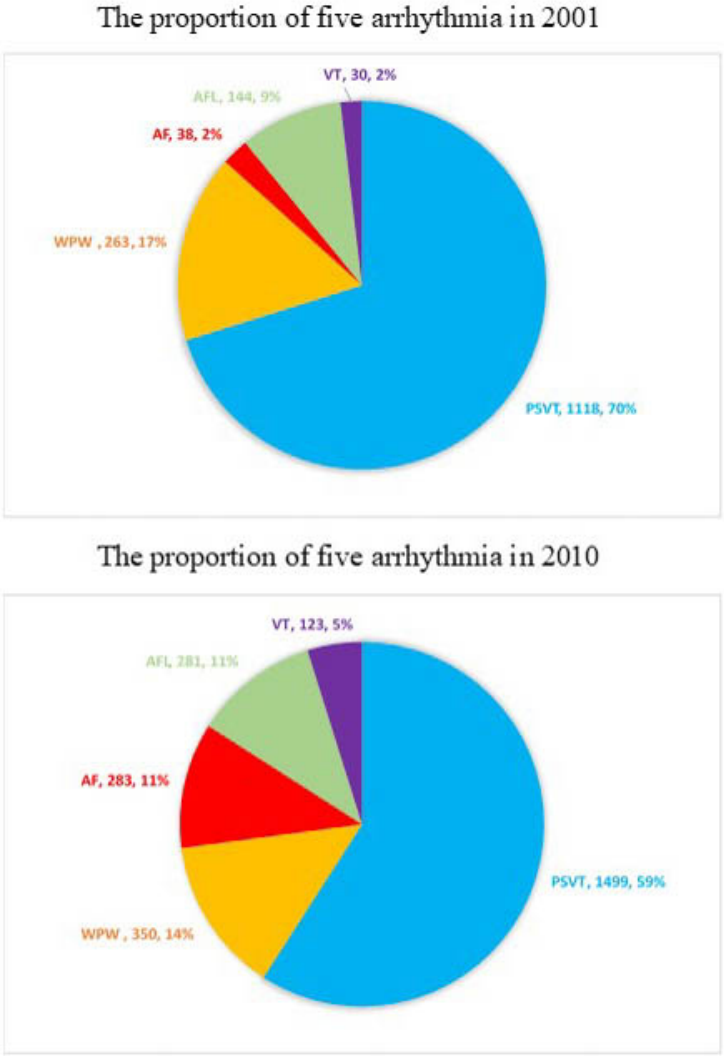
Figure Legends

Figure 1. Proportion of radiofrequency catheter ablation patients diagnosed with paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia in Taiwan during 2001 and 2010.

Figure 2. Recurrence-free survival curves after radiofrequency catheter ablation for groups of patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.

Figure 3. Number of radiofrequency catheter ablations annually in groups of patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.

Figure 4. Annual growth rate in radiofrequency catheter ablations for patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.



Abbreviation: PSVT: paroxysmal supraventricular tachycardia, WPW: Wolff–Parkinson–White syndrome, AFL: atrial flutter, AF: atrial fibrillation, VT: ventricular tachycardia

Figure 1

figure 1

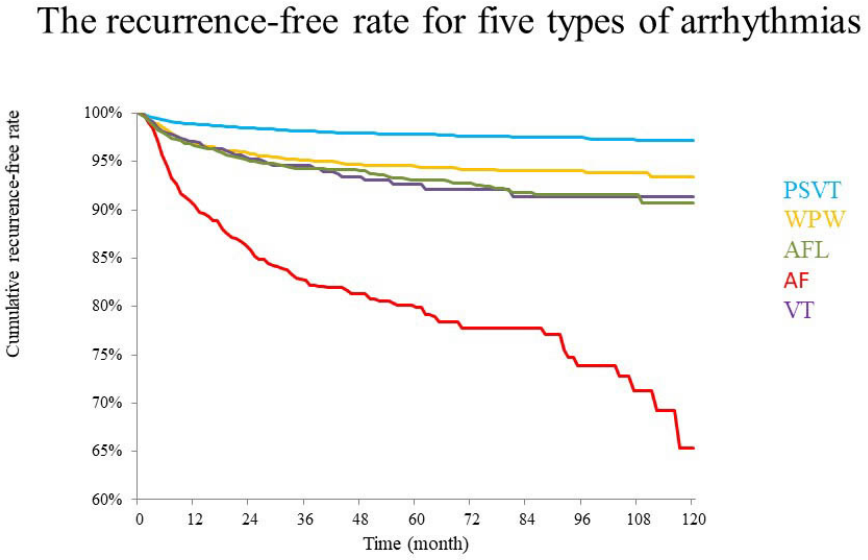


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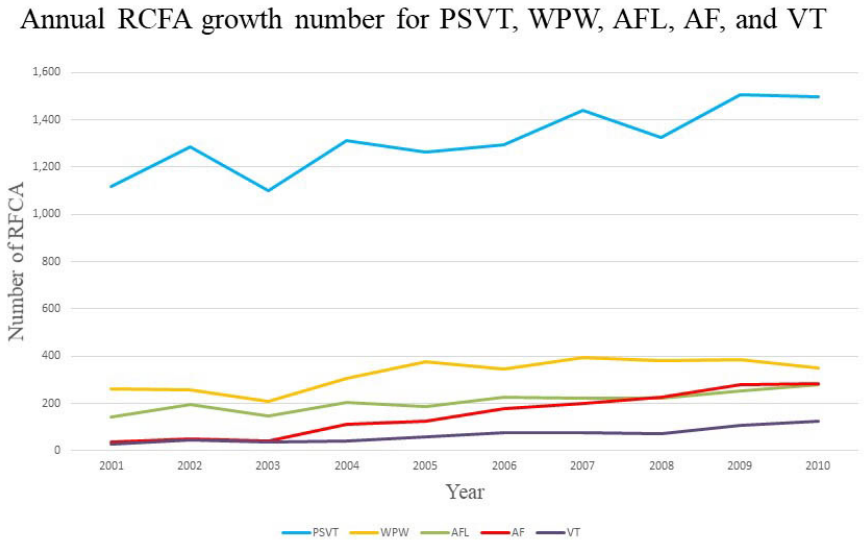
Figure 2

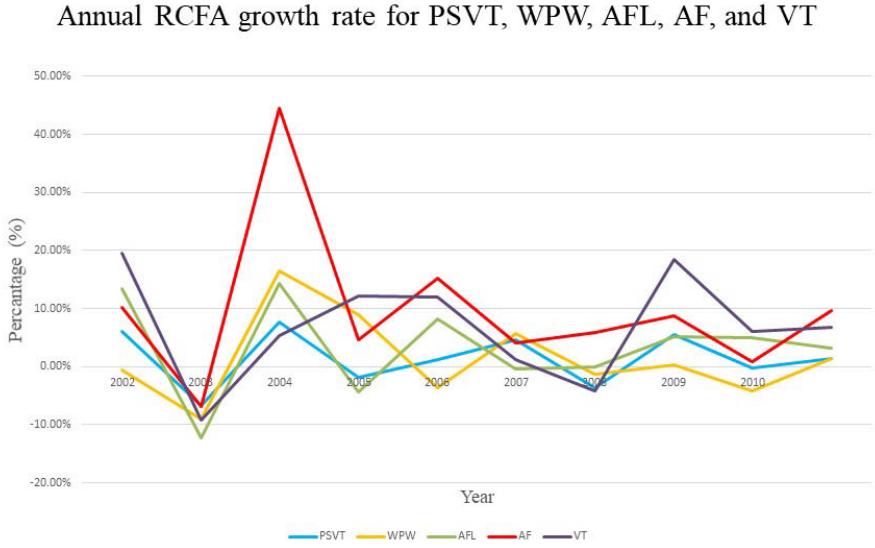
figure 2



Abbreviation: RFCA = Radiofrequency catheter ablation; PSVT: paroxysmal supraventricular tachycardia, WPW: Wolff–Parkinson–White syndrome, AFL: atrial flutter, AF: atrial fibrillation, VT: ventricular tachycardia

Figure 3

figure 3



Abbreviation: RFCA = Radiofrequency catheter ablation; PSVT: paroxysmal supraventricular tachycardia, WPW: Wolff–Parkinson–White syndrome, AFL: atrial flutter, AF: atrial fibrillation, VT: ventricular tachycardia

Figure 4

figure 4

Supplemental Table 1

Disease	ICD 9 code
PSVT	4270
WPW	426.7
AFL	427.32
AF	427.33
VT	427.1
High-grade AVB	426.12, 426.13, 426.0
stroke	430*, 431*, 432*, 433*, 434*, 436*, 437*
DM	250*
hypertension	401*
COPD	490-496
Chronic kidney disease	403, 404, 585
Coronary artery disease	413*, 4140*
Heart failure	428*, 39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493
TOF	745.2
Transposition of the great vessel	745.1
Double outlet right ventricle	745.11
Total anomalous pulmonary venous connection	747.41
Tricuspid atresia	746.1
Common truncus arteriosus	745.0
Common ventricle	745.3
Hypoplastic left heart syndrome	746.7
Ventricular septal defect	745.4
Atrial septal defect	745.5
Ebstein's anomaly	746.2
Patent ductus arteriosus	747.0
Congenital pulmonary stenosis	746.83
Coarctation of aorta	747.1

Endocardial cushion defect	745.6
Congenital aortic stenosis	746.3

PSVT: Paroxysmal supra-ventricular tachycardia; WPW: Wolff–Parkinson–White syndrome; AFL: Atrial flutter; AF: Atrial fibrillation; VT: Ventricular tachycardia; High-grade AV block: High-grade atrioventricular block; DM: Diabetes mellitus; COPD: Chronic obstructive pulmonary disease; TOF: Tetralogy of Fallot

Supplemental Table 2. Risk factors of complications for the patients without recurrence during the follow up

	During the index admission				After discharge of the index admission			
	Life-threatening pericardial effusion (39 events, 0.21%)		New-onset stroke (22 events, 0.12%)		High-grade AVB (171 events, 0.92%)		Pacemaker (96 events, 0.51%)	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age								
0-18 yrs.	NA	NA	NA	NA	0.70 (0.29–1.69)	0.424	0.92 (0.28–3.01)	0.887
19-44 yrs.	Reference	—	Reference	—	Reference	—	Reference	—
45-54 yrs.	17.46 (2.22–137.60)	0.007	4.69 (0.48–45.74)	0.184	1.17 (0.76–1.81)	0.472	1.93 (1.08–3.45)	0.026
55-64 yrs.	33.05 (4.26–256.70)	0.001	18.46 (2.26–150.86)	0.007	0.91 (0.55–1.52)	0.731	1.17 (0.57–2.40)	0.672
65-74 yrs.	28.85 (3.47–240.16)	0.002	9.21 (0.95–89.41)	0.056	1.22 (0.73–2.05)	0.452	1.65 (0.80–3.41)	0.178
Above 75 yrs.	35.53 (3.90–323.63)	0.002	15.43 (1.54–154.54)	0.020	2.16 (1.26–3.70)	0.005	4.24 (2.09–8.62)	<0.001
Male gender	1.20 (0.61–2.37)	0.596	1.01 (0.41–2.45)	0.991	1.19 (0.87–1.63)	0.278	0.79 (0.52–1.19)	0.259
Diabetes	0.16 (0.02–1.20)	0.074	1.26 (0.41–3.87)	0.683	1.62 (1.05–2.51)	0.031	1.94 (1.10–3.40)	0.021
Hypertension	1.12 (0.54–2.31)	0.757	0.56 (0.18–1.73)	0.316	1.16 (0.78–1.73)	0.454	0.93 (0.54–1.60)	0.784
COPD	NA	NA	NA	NA	0.72 (0.29–1.80)	0.487	0.81 (0.25–2.62)	0.719
CKD	NA	NA	1.48 (0.19–11.54)	0.708	2.21 (1.02–4.81)	0.045	2.95 (1.18–7.40)	0.021
Heart failure	0.80 (0.10–6.11)	0.828	2.67 (0.71–10.06)	0.145	2.30 (1.24–4.24)	0.008	0.77 (0.23–2.54)	0.667
TOF	NA	NA	NA	NA	NA	NA	NA	NA
VSD	NA	NA	NA	NA	NA	NA	NA	NA
ASD II	5.65 (0.71–45.04)	0.102	NA	NA	1.22 (0.17–8.64)	0.844	2.21 (0.31–15.64)	0.426
Ebstein	NA	NA	NA	NA	NA	NA	NA	NA
High-activity center	3.64 (1.40–9.45)	0.008	1.17 (0.46–2.93)	0.742	0.96 (0.70–1.31)	0.788	0.90 (0.59–1.35)	0.599
Indication								
PSVT	Reference	—	Reference	—	Reference	—	Reference	—
WPW	2.45 (0.93–6.43)	0.068	1.68 (0.35–8.11)	0.520	0.42 (0.22–0.82)	0.011	0.52 (0.22–1.24)	0.141
VT	1.68 (0.22–12.91)	0.619	NA	NA	1.02 (0.41–2.51)	0.973	1.26 (0.39–4.04)	0.694
AF	4.57 (2.03–10.33)	<0.001	3.86 (1.09–13.65)	0.036	0.77 (0.35–1.68)	0.507	0.52 (0.13–2.06)	0.351
AFL	1.21 (0.41–3.59)	0.729	3.88 (1.27–11.84)	0.017	1.95 (1.28–2.97)	0.002	2.34 (1.36–4.02)	0.002

Abbreviation: AVB = Atrioventricular block; COPD = Chronic obstructive pulmonary disease; CKD = Chronic kidney disease; CAD = Coronary artery disease; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; ASD = Atrial septal defect; Ebstein = Ebstein's anomaly
PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome; VT: Ventricular tachycardia; AFL: Atrial flutter; AF: Atrial fibrillation; OR = odds ratio; HR = hazard ratio; CI = confidence interval; NA = not applicable.

Supplemental Table 3. RFCA-related complications according to recurrence or not during the follow up (N = 20,707 RFCAs)

Complication	Recurrence (n=988)	Non-recurrence (n=19,719)	P[a]
In-hospital complication			
Life-threatening pericardial effusion	3 (0.3)	42 (0.21)	0.48
New-onset stroke	0 (0)	23 (0.12)	0.63
After discharge			
High-grade AVB	3 (0.3)	181 (0.92)	0.05
Pacemaker implantation	0 (0)	100 (0.51)	0.016

Abbreviation: RFCA = Radiofrequency catheter ablation; AVB = Atrioventricular block;
a, Fisher's exact test.

Supplemental Table 4. RFCA-related complications according to different types of arrhythmias for the patients without recurrence during the follow up

Complication	PSVT	WPW	AFL	AF	VT
Number of patients	12,519	2,895	1,710	949	578
In-hospital complication					
Life-threatening pericardial effusion	15 (0.12)	6 (0.21)	5 (0.29)	12 (1.26)	1 (0.17)
New-onset stroke	8 (0.06)	2 (0.07)	8 (0.47)	4 (0.42)	0 (0)
After discharge					
High-grade AVB	109 (0.87)	8 (0.28)	42 (2.46)	7 (0.74)	5 (0.87)
Pacemaker implantation	62 (0.50)	5 (0.17)	24 (1.40)	2 (0.21)	3 (0.52)

Abbreviation: RFCA = Radiofrequency catheter ablation; PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome; AFL: Atrial flutter; AF: Atrial fibrillation; VT: Ventricular tachycardia; AVB = Atrioventricular block;

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6,7
		(*b*) Describe any methods used to examine subgroups and interactions	6,7
		(*c*) Explain how missing data were addressed	7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10, 11, 13
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-12
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20,21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	18,19
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Trend and Risk Factors of Recurrence and Complications after Arrhythmias Radiofrequency Catheter Ablation: A Nationwide Observational Study in Taiwan

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Trend and Risk Factors of Recurrence and Complications after Arrhythmias Radiofrequency Catheter Ablation: A Nationwide Observational Study in Taiwan

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Abstract

Objectives: This study determined the recurrence and complication rates after radiofrequency catheter ablation (RFCA) for those with paroxysmal supraventricular tachycardia (PSVT), Wolff-Parkinson-White syndrome (WPW), atrial flutter (AFL), atrial fibrillation (AF) and ventricular tachycardia (VT).

Study Design and Setting: This retrospective study included RFCAs for 2001-2010 in the Taiwan National Health Insurance Research Database. Primary outcomes included perioperative complications (pericardial effusion and new-onset stroke), RFCA recurrence and long-term outcomes (high-grade atrioventricular block [AVB] and pacemaker implantation).

Results: Of 19,475 RFCA patients, prevalence rates were 56.7% for PSVT, 13.5% for WPW, 9.5% for AFL, 5.1% for AF and 2.7% for VT. Prevalence rates increased in AF, AFL and VT over the study years. During an average follow-up period of 4.3 years (standard deviation: 2.8 years), recurrence rates for PSVT, WPW, VT, AFL and AF were 2.0%, 4.9%, 5.7%, 5.8% and 16.1% respectively. Compared to the PSVT group, the WPW and AF groups had significantly higher risk of pericardial effusion during admission (adjusted odds ratio [aOR] 2.98, 95% confidence interval [CI] 1.24–7.15; aOR 4.09, 95%CI 1.90–8.79, respectively); the AFL group had a higher risk of new-onset stroke during admission (aOR 4.07, 95%CI 1.39–11.91); the WPW group had a lower risk of high-grade AVB during follow up (adjusted hazard ratio [aHR] 0.37, 95% CI 0.19–0.71) while the AFL group had a greater risk (aHR 1.74, 95%CI 1.17–2.60); and the AFL group had a higher risk of permanent pacemaker (aHR 2.14, 95%CI 1.27–3.62).

Conclusions: The RFCA rate increased rapidly during 2001-2010 for AF, AFL and VT. Recurrence was associated with congenital heart disease in PSVT and WPW, and with age in AF and AFL. AFL had a higher risk of permanent pacemaker implantation and new stroke. AF had a higher risk of life-threatening pericardial effusion.

Key words: radiofrequency catheter ablation (RFCA), Wolff-Parkinson-White syndrome, supraventricular tachycardia, ventricular tachycardia, complication, recurrence, risk factors

Strengths and limitations of this study

- This 10-year longitudinal retrospective study is the first nationwide, large-scale study of the trend, recurrence and complications of radiofrequency catheter ablation (RFCA).
- This article is the first study to compare recurrence and complications among five different types of arrhythmias after RFCA.
- Our study provides risks of arrhythmia recurrence and complications after RFCA.
- This study did not have access to certain data such as laboratory parameters, procedural details, and heart images. Also, some arrhythmias such as premature ventricular beats and atrial premature beats are not covered by Taiwan National Health Insurance.
- This study was not able to explore the interactions among the predictive variables because of the limited number of events.

Introduction

Radiofrequency catheter ablation (RFCA) is used to treat patients with supraventricular tachycardia or ventricular tachycardia (VT), especially paroxysmal supraventricular tachycardia (PSVT).[1-3] Widely applied since the 1990s,[4] RFCA is an effective therapy with demonstrated high success, low complications and low recurrence rates compared to direct current ablation or surgical ablation. RFCA is superior to conservative treatments such as medication or observation for patients with PSVT and Wolff-Parkinson-White syndrome (WPW). RFCA was first used to treat atrial fibrillation (AF) in 1998.

Although arrhythmias after RFCA are usually not life-threatening, identification and minimization of the risk of complications are extremely important. The RFCA procedure may lead to atrioventricular (AV) block and bradycardia, even requiring permanent pacemaker implantation. Previous studies[5] were composed of relatively small cohorts or were single-center studies and evaluated patients with a single arrhythmia.[5,6] However, there are no studies comparing RFCA-related complications in patients with five different arrhythmias.[7,8] The targets for RFCA-related risk minimization differ by type of arrhythmia. For example, when RFCA is used to treat PSVT, the goal is to modify or eliminate AV node or accessory pathways; when used to treat AF,[6] the goal is to isolate the pulmonary veins. High grade AV block, life-threatening pericardial effusion, and stroke are dangerous complications after an RFCA procedure. However, the complication rates vary by type of arrhythmia: PSVT, WPW, atrial flutter (AFL), AF and VT. It is therefore important to identify the incidence and risk factors of RFCA-related complications in these patients.

This retrospective study investigated the population trend of patients who received RFCA for PSVT, WPW, AFL, AF and VT. We identified the major RFCA-related risk factors influencing 1) recurrence of arrhythmias and 2) complications such as AV block, permanent pacemaker implantation, life-threatening pericardial effusion and acute ischemic stroke.

Methods

Study design and population

We conducted a nationwide population-based cohort study using data from the Taiwan National Health Insurance Research Database (NHIRD). In Taiwan, the National Health Insurance (NHI) program has reimbursed patients who receive RFCA for PSVT, WPW, AFL, AF and VT since 2001. More than 99.91% of Taiwan's population is covered by NHI benefits. The accuracy and validation of NHIRD data is based upon regular auditing by the NHI

Bureau.[9-11] The Institutional Review Board of Chang Gung Memorial Hospital approved this study.

Study cohort, outcome measurement and follow-up

This study accessed NHIRD data for all targeted arrhythmia patients who received RFCA from 2001 to 2010. The targeted arrhythmias were PSVT (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9 CM] Code 4270), WPW (426.7), AFL (427.32), AF (427.31) and VT (427.1; Supplemental Table 1). Patients with arrhythmias other than those targeted (such as premature ventricular beats or atrial tachycardia) and patients with unidentified arrhythmias who received RFCA were excluded. We enrolled only the patient's first RFCA. The follow-up period was calculated from the discharge date of the index hospitalization until death, loss to follow up (withdrawal from the NHI program: emigration or prison incarceration for longer than six months) or until the study end date (31 December 2010).

Outcomes measurement

The primary outcomes included recurrence of arrhythmia, in-hospital complications and long-term complications. Recurrence was defined as either 1) recurrence of original arrhythmia or 2) receipt of a second RFCA during the follow up period. In-hospital complications included life-threatening pericardial effusion and new-onset stroke during the admission. Life-threatening pericardial effusion was defined as the patient requiring pericardiocentesis during RFCA. New stroke was defined as stroke (ICD-9 CM codes 430-437) which occurred during the index admission. Other complications included high-grade AV block and permanent pacemaker implantation.

Covariate assessment

Age was categorized into six groups (0-18, 19-44, 45-54, 55-64, 65-74 and 75 years and above) because previous studies reported different indications for RFCA and different complications between age groups.[1-3] Comorbidities were assessed according to ICD-9 CM codes before the index admission. Diabetes mellitus, hypertension (HTN) or chronic diseases were recorded as comorbidities if there was at least one in-admission diagnosis. All congenital heart disease (CHD) was reconfirmed by the Catastrophic Illness Certification (CIC), which is a sub-dataset of NHI. A CIC for CHD requires imaging proof confirmed by two cardiologists. Complicated CHD included Tetralogy of Fallot (TOF), transposition of the great vessels, double outlet right ventricle, total anomalous pulmonary venous connection, tricuspid atresia, common truncus arteriosus, common ventricle and hypoplastic left heart syndrome. Simple CHD included ventricular septal defect (VSD), atrial septal defect (ASD), Ebstein's anomaly, patent ductus arteriosus, congenital pulmonary stenosis, coarctation of the aorta, endocardial cushion defect and congenital aortic stenosis. Center activity was a time-dependent variable and a high-activity center was defined as more than 100 RFCA surgeries per year, regardless of arrhythmia type.

Patient and public involvement

This study had no direct relationship with any patient and no public involvement during the development, design and conduct.

Statistical analysis

The proportion of categorical variables between groups was compared using the chi-squared test and Fisher's exact test. Continuous variables were compared using Kruskal-Wallis test due to the lack of normality. Multivariable logistic regression analysis was used to identify clinical features associated with the risk of in-hospital complications, including life-threatening

pericardial effusion and new-onset stroke during the admission. Multivariable Cox regression analysis was used to investigate the association of clinical variables with time-to-event outcomes, including recurrence, high-grade AV block and pacemaker implantation during the follow up. In the survival analysis, the time-scale was time-since-RFCA in days. The assumption of proportional hazard was tested by Schoenfeld partial residuals, in which the indication was the only explanatory categorical variable. The 13 pre-specified potential predictive variables were those clinically relevant to RFCA and its complications: two demographic variables (sex and age), six comorbidities, four types of CHD and center activity. All 13 candidate predictive variables were introduced into the multivariable regression models. Multicollinearity among predictors was checked by variance inflation factor (VIF), with a value less than 10 indicating no serious collinearity among predictors. Sensitivity analyses were done by excluding patients with recurrent RCFA during the follow up (Supplemental Table 2). A two-sided *P* value lower than 0.05 was considered statistically significant. No adjustment for multiple testing (multiplicity) was made in this study due to the limited size of event number. Results were presented as the odds ratio (OR) for logistic regression, or hazard ratio (HR) for Cox regression with corresponding 95% confidence intervals (CI). All data analyses were performed using SPSS software version 15 (SPSS Inc., Chicago, IL, USA).

Results

There were 24,003 RFCA procedures registered in NHIRD between 1 January 2001 and 31 December 2010. Based on the inclusion and exclusion criteria, a total of 19,475 enrolled patients underwent 20,707 RFCA procedures. Only the first occurrence for each individual was used for analysis. The proportion of change in rates of RFCA by individual arrhythmias from 2001 to 2010 is shown in Figure 1. The proportion of RFCA for PSVT decreased from 60% to 51% between 2001 to 2010, while the proportion for AF increased from 2% to 10% (Figure 1).

The commonest arrhythmia treated with RFCA was PSVT (n=12,796; 56.7%), followed by WPW (n=3,051; 13.5%), AFL (n=1,854; 9.5%), AF (n=1,162; 5.1%) and VT (n=612; 2.7%). The mean age of study participants when they received RFCA was 47.6 years (standard deviation [SD] 18.3). Demographic and baseline clinical characteristics according to arrhythmia type are summarized in Table 1. The prevalence of PSVT (38.5%), WPW (58.1%) and VT (47.2%) was highest in the group aged 19-44 years. Patients were the oldest in the AFL group, followed by the AF group, the PSVT group, the VT group and the WPW group. Patients with AF and AFL had a higher prevalence of diabetes (16.2% and 11.5%, respectively) and hypertension (28.9% and 28.1%, respectively) compared to patients with other arrhythmias. Chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and heart failure were most prevalent in the AFL group since these patients were the oldest (median age 62.9 years). RFCA due to AF was predominantly performed in high-activity centers (84%), followed by AFL (71%). Complicated CHD was more common in the AFL group than in other arrhythmias. Simple CHD was most prevalent in the AFL group (3.6%), followed by the VT group (1.5%).

Table 1. Baseline data for 19,475 study patients who underwent RFCA procedures stratified by indication.

Variable	PSVT	WPW	AFL	AF	VT	*P* value
Number of patients	12,796	3,051	1,854	1,162	612	–
Age (yrs.), median (IQR)	47.0 (33.5, 58.6)	36.3 (22.8, 49.7)	62.9 (51.7, 73.1)	56.9 (48.4, 65.5)	43.1 (28.7, 55.2)	<0.001
Age group						<0.001
0-18 yrs.	863 (6.7)	379 (12.4)	15 (0.8)	0 (0.0)	46 (7.5)	
19-44 yrs.	4,930 (38.5)	1,619 (53.1)	260 (14.0)	216 (18.6)	289 (47.2)	
45-54 yrs.	2,938 (23.0)	579 (19.0)	329 (17.7)	285 (24.5)	123 (20.1)	
55-64 yrs.	2,083 (16.3)	308 (10.1)	407 (22.0)	354 (30.5)	75 (12.3)	
65-74 yrs.	1,344 (10.5)	130 (4.3)	472 (25.5)	222 (19.1)	51 (8.3)	
75+ yrs.	638 (5.0)	36 (1.2)	371 (20.0)	85 (7.3)	28 (4.6)	
Gender, male	5,402 (42.2)	1,988 (65.2)	1,332 (71.8)	838 (72.1)	327 (53.4)	<0.001
Diabetes	910 (7.1)	113 (3.7)	301 (16.2)	134 (11.5)	32 (5.2)	<0.001
Hypertension	1,723 (13.5)	275 (9.0)	535 (28.9)	326 (28.1)	74 (12.1)	<0.001
COPD	286 (2.2)	22 (0.7)	103 (5.6)	28 (2.4)	15 (2.5)	<0.001
CKD	150 (1.2)	12 (0.4)	71 (3.8)	11 (0.9)	5 (0.8)	<0.001
CAD	594 (4.6)	87 (2.9)	288 (15.5)	154 (13.3)	45 (7.4)	<0.001
Heart failure	73 (0.6)	21 (0.7)	205 (11.1)	53 (4.6)	25 (4.1)	<0.001
High-activity center‡	7,267 (56.8)	1,880 (61.6)	1,317 (71.0)	976 (84.0)	317 (51.8)	<0.001
Complicated CHD	10 (0.1)	3 (0.1)	16 (0.9)	2 (0.2)	1 (0.2)	<0.001
TOF	3 (0.0)	0 (0.0)	11 (0.6)	1 (0.1)	1 (0.2)	<0.001
Other complicated CHD	7 (0.1)	3 (0.1)	5 (0.3)	1 (0.1)	0 (0.0)	0.045
Simple CHD †	69 (0.5)	31 (1.0)	66 (3.6)	9 (0.8)	9 (1.5)	<0.001
VSD	15 (0.1)	6 (0.2)	25 (1.3)	0 (0.0)	4 (0.7)	<0.001
ASDII	50 (0.4)	10 (0.3)	34 (1.8)	9 (0.8)	4 (0.7)	<0.001
Ebstein	4 (0.0)	18 (0.6)	6 (0.3)	0 (0.0)	0 (0.0)	<0.001
Other simple CHD	4 (0.0)	2 (0.1)	6 (0.3)	0 (0.0)	1 (0.2)	<0.001

Abbreviations: AF = Atrial fibrillation; AFL = Atrial flutter; ASD = Atrial septal defect; CAD = Coronary artery disease; CHD = Congenital heart disease; CKD = Chronic kidney disease; COPD = Chronic obstructive pulmonary disease; Ebstein = Ebstein's anomaly; IQR = Interquartile range; PSVT = Paroxysmal supraventricular tachycardia; RFCA = Radiofrequency catheter ablation; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; VT = Ventricular tachycardia; WPW = Wolff-Parkinson-White syndrome; Yrs = years.

‡ defined as 100 operations per year.

† The discrepancy between the sums of subgroups and the total is due to the possibility that one patient might have two CHDs.

Risk factors of recurrence

During an average follow-up period of 4.3 years (SD 2.8 years), the recurrence rates after the index RFCA for those with PSVT, WPW, VT, AFL and AF were 2.0%, 4.9%, 5.7%, 5.8% and 16.1%, respectively. All VIF values were less than 4 in the five multivariable models which indicated no apparent multicollinearity problem. Multivariable Cox analyses revealed that the major risk factors for recurrence of PSVT after RFCA included: age (0-18 years), male gender, diabetes and TOF. Younger patients (0-18 *vs.* 19-44 years) and those with Ebstein's anomaly were considered at greater risk for recurrence of WPW after RFCA (Table 2). For the AFL group, older individuals (45-54 *vs.* 19-44 years) had a higher risk of recurrence. Male gender, TOF, VSD and high-activity center were also risk factors. In contrast, the incidence of AFL recurrence was low in patients 75 years or older. The recurrence rate was 16.1% in patients with AF but 2.0% for those with PSVT. The recurrence-free rate after RFCA declined with time, most sharply for those with AF (Figure 2). Patients aged 19–44 years had a higher risk of AF recurrence compared with patients older than 65 years; male gender and treatment at a high-activity center were also identified as risk factors. In the VT population, treatment at a high-activity center was related to decreased risk of recurrence. The results were similar when excluding patients with recurrent RCFA during the follow up (Supplemental Table 3).

Table 2. Risk factors for recurrence of radiofrequency catheter ablation.

	PSVT (259 events, 2.0%)		WPW (160 events, 5.2%)		AFL (120 events, 5.8%)		AF (247 events, 16.1%)		VT (38 events, 5.7%)	
Variable	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age										
0-18 yrs.	1.52 (1.02–2.28)	0.041	1.90 (1.27–2.85)	0.004	2.17 (0.50–9.41)	0.30	NA	NA	1.19 (0.41–3.48)	0.75
19-44 yrs.	Reference	—	Reference	—	Reference	—	Reference	—	Reference	—
45-54 yrs.	0.88 (0.64–1.22)	0.46	0.90 (0.57–1.44)	0.67	1.98 (1.15–3.41)	0.014	1.03 (0.73–1.44)	0.88	0.71 (0.28–1.78)	0.46
55-64 yrs.	0.70 (0.47–1.05)	0.08	1.47 (0.87–2.47)	0.15	1.40 (0.78–2.51)	0.27	0.87 (0.61–1.25)	0.43	0.75 (0.24–2.36)	0.62
65-74 yrs.	0.68 (0.42–1.11)	0.12	0.95 (0.37–2.41)	0.91	0.93 (0.49–1.77)	0.82	0.54 (0.34–0.86)	0.01	0.19 (0.02–1.56)	0.12
75+ yrs.	0.69 (0.35–1.37)	0.29	NA.	NA	0.28 (0.10–0.76)	0.013	0.08 (0.02–0.34)	0.001	NA	NA
Male gender	1.66 (1.30–2.13)	<0.001	1.06 (0.77–1.48)	0.71	1.68 (1.09–2.59)	0.020	1.43 (1.05–1.95)	0.023	1.31 (0.66–2.58)	0.44
Diabetes	1.59 (1.01–2.52)	0.047	0.18 (0.03–1.34)	0.09	0.80 (0.43–1.49)	0.49	0.70 (0.43–1.14)	0.15	0.70 (0.09–5.74)	0.74
Hypertension	1.03 (0.70–1.53)	0.88	1.27 (0.71–2.28)	0.42	0.73 (0.46–1.15)	0.17	1.29 (0.97–1.72)	0.08	1.49 (0.40–5.49)	0.55
COPD	1.13 (0.50–2.60)	0.77	NA.	NA	1.08 (0.43–2.72)	0.87	1.45 (0.54–3.84)	0.46	NA	NA
CKD	1.61 (0.59–4.36)	0.35	NA.	NA	0.78 (0.24–2.49)	0.67	0.55 (0.08–4.02)	0.56	4.18 (0.52–33.86)	0.18
CAD	0.85 (0.44–1.64)	0.63	0.53 (0.13–2.17)	0.38	0.59 (0.29–1.17)	0.13	1.07 (0.73–1.56)	0.74	1.18 (0.26–5.25)	0.83
Heart failure	1.64 (0.40–6.67)	0.49	NA.	NA	0.91 (0.47–1.75)	0.78	0.29 (0.07–1.20)	0.09	2.90 (0.63–13.42)	0.17
TOF	23.00 (4.0–131.8)	<0.001	NA.	NA	3.32 (1.01–10.96)	0.049	NA	NA	NA	NA
VSD	NA.	NA	2.79 (0.53–14.82)	0.23	2.78 (1.29–5.99)	0.009	0.99 (0.13–7.42)	0.99	NA	NA
ASD II	2.78 (0.89–8.72)	0.08	0.40 (0.04–4.25)	0.45	1.46 (0.57–3.71)	0.43	1.17 (0.28–4.87)	0.83	3.57 (0.47–27.34)	0.22
Ebstein	1.08 (0.09–12.80)	0.95	4.40 (1.80–10.74)	0.001	1.54 (0.21–11.5)	0.68	NA	NA	NA	NA.
High-activity center	1.05 (0.82–1.35)	0.68	0.87 (0.63–1.19)	0.38	1.78 (1.11–2.85)	0.017	3.16 (1.77–5.67)	<0.001	0.49 (0.25–0.97)	0.04

Abbreviations: AF = Atrial fibrillation; AFL = Atrial flutter; ASD = Atrial septal defect; CAD = Coronary artery disease; CHD = Congenital heart disease; CI = Confidence interval; CKD = Chronic kidney disease; COPD = Chronic obstructive pulmonary disease; Ebstein = Ebstein's anomaly; HR = Hazard ratio; NA = Not applicable; PSVT = Paroxysmal supraventricular tachycardia; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; VT = Ventricular tachycardia; WPW = Wolff-Parkinson-White syndrome; Yrs = Years.

Complications

Rates of RFCA-related complications were evaluated for the five arrhythmia groups (Table 3). The overall rates of complications and mortality were less than 1% and 0.1%, respectively. High-grade AV block was the most common complication following RFCA in all groups except the AF group. RFCA was more associated with life-threatening pericardial effusion in the AF group (1.3%) than in the other groups. In the AFL group, RFCA was more associated with high-grade AV block (2.5%), permanent pacemaker implantation (1.4%) and new stroke (0.5%) than in other groups.

Table 3. Numbers and rate of RFCA-related complications according to type of arrhythmias.

Complication	PSVT	WPW	AFL	AF	VT
Number of patients	12,796	3,051	1,854	1,162	612
In-hospital complications (numbers and percent)					
Life-threatening pericardial effusion	(15, 0.12%)	(8, 0.26%)	(6, 0.32%)	(15, 1.30%)	(1, 0.16%)
New-onset stroke	(8, 0.06%)	(2, 0.07%)	(9, 0.49%)	(4, 0.34%)	(0, 0.00%)
After discharge					
High-grade AVB	(114, 0.89%)	(10, 0.33%)	(47, 2.53%)	(8, 0.69%)	(5, 0.82%)
Pacemaker implantation	(64, 0.50%)	(5, 0.16%)	(26, 1.40%)	(2, 0.17%)	(3, 0.50%)

Abbreviations: AF = Atrial fibrillation; AFL = Atrial flutter; AVB = Atrioventricular block; PSVT = Paroxysmal supraventricular tachycardia; RFCA = Radiofrequency catheter ablation; VT = Ventricular tachycardia; WPW = Wolff-Parkinson-White syndrome.

Risk factors for complications

All VIF values were less than 4 in the four multivariable models which indicated no apparent multicollinearity problem. As to in-hospital complications, multivariable logistic regression revealed that age >44 years, high-activity center and RFCA after WPW or AFL were associated with increased risk of life-threatening pericardial effusion. Age >55 years and RFCA after AFL were associated with a higher risk of stroke following RFCA (Table 4). As to long-term complications, multivariable Cox regression identified the risk factors for high-grade AV block as age ≥75 years, diabetes and heart failure. WPW patients were at a lower risk of developing AV block than PSVT patients. Risk factors for pacemaker implantation were age ≥75 years, diabetes, CKD and RFCA after AFL (when compared with PSVT). The results were similar when excluding patients with recurrent RCFA during the follow up (Supplemental Table 4).

Testing of Schoenfeld partial residuals revealed insignificant correlation for rank of survival time after AV block and permanent pacemaker implantation (AV block: number of events = 184, r = 0.08, p = 0.27; permanent pacemaker implantation: number of events = 100, r = 0.15, p = 0.11), which indicated that the assumption of proportional hazard was not strongly violated (data not shown).

Table 4. Risk factors of complications during the index admission or after discharge of the index admission.

	During the index admission				After discharge of the index admission			
	Life-threatening pericardial effusion (45 events, 0.22%)		New-onset stroke (23 events, 0.11%)		High-grade AVB (184 events, 0.88%)		Pacemaker (100 events, 0.48%)	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age								
0-18 yrs.	NA	NA	NA	NA	0.66 (0.28–1.53)	0.33	0.81 (0.24–2.71)	0.74
19-44 yrs.	Reference	—	Reference	—	Reference	—	Reference	—
45-54 yrs.	11.18 (2.50–50.10)	0.002	4.53 (0.46–44.16)	0.19	1.07 (0.70–1.62)	0.76	1.70 (0.96–3.01)	0.07
55-64 yrs.	17.32 (3.87–77.55)	<0.001	19.68 (2.44–158.78)	0.005	0.85 (0.52–1.37)	0.50	1.09 (0.55–2.18)	0.80
65-74 yrs.	17.75 (3.68–85.57)	<0.001	9.58 (0.99–91.66)	0.05	1.07 (0.65–1.77)	0.79	1.40 (0.69–2.85)	0.36
Above 75 yrs.	22.70 (4.16–123.95)	<0.001	17.01 (1.73–167.36)	0.015	2.07 (1.24–3.44)	0.005	3.82 (1.94–7.53)	<0.001
Male gender	1.12 (0.60–2.12)	0.72	0.84 (0.35–2.00)	0.70	1.14 (0.84–1.54)	0.40	0.74 (0.49–1.12)	0.16
Diabetes	0.33 (0.08–1.39)	0.13	1.22 (0.40–3.70)	0.73	1.77 (1.17–2.70)	0.007	1.95 (1.13–3.37)	0.016
Hypertension	1.01 (0.51–2.01)	0.97	0.52 (0.17–1.59)	0.25	1.08 (0.73–1.59)	0.70	0.94 (0.55–1.59)	0.81
COPD	NA	NA	NA	NA	0.70 (0.28–1.72)	0.43	0.77 (0.24–2.49)	0.67
CKD	NA	NA	1.41 (0.18–10.89)	0.74	2.10 (0.97–4.54)	0.06	2.69 (1.07–6.76)	0.036
Heart failure	0.74 (0.10–5.59)	0.77	2.51 (0.68–9.29)	0.17	2.31 (1.28–4.17)	0.006	1.00 (0.35–2.83)	0.99
TOF	NA	NA	NA	NA	NA.	NA	NA	NA
VSD	NA	NA	NA	NA	2.20 (0.51–9.47)	0.29	NA	NA
ASD II	4.10 (0.53–31.84)	0.18	NA	NA	1.55 (0.37–6.47)	0.55	1.94 (0.27–14.10)	0.51
Ebstein	NA	NA	NA	NA	3.70 (0.49–27.86)	0.20	NA	NA
High-activity center	3.79 (1.47–9.79)	0.006	1.15 (0.46–2.88)	0.76	0.98 (0.73–1.33)	0.91	0.92 (0.61–1.38)	0.68
Indication								
PSVT	Reference	—	Reference	—	Reference	—	Reference	—
WPW	2.98 (1.24–7.15)	0.015	1.63 (0.34–7.85)	0.55	0.37 (0.19–0.71)	0.003	0.41 (0.16–1.04)	0.06
VT	1.58 (0.21–12.14)	0.66	NA	NA	0.85 (0.35–2.10)	0.73	1.10 (0.34–3.51)	0.87
AFL	4.09 (1.90–8.79)	<0.001	2.74 (0.77–9.72)	0.118	0.53 (0.25–1.11)	0.09	0.33 (0.08–1.36)	0.13
AF	1.34 (0.49–3.70)	0.57	4.07 (1.39–11.91)	0.010	1.74 (1.17–2.60)	0.006	2.14 (1.27–3.62)	0.004

Abbreviations: AF = Atrial fibrillation; AFL = Atrial flutter; ASD = Atrial septal defect; AVB = Atrioventricular block; CAD = Coronary artery disease; CI = Confidence interval; CKD = Chronic kidney disease; COPD = Chronic obstructive pulmonary disease; Ebstein = Ebstein's anomaly; HR = Hazard ratio; NA = Not applicable; OR = Odds ratio; PSVT = Paroxysmal supraventricular tachycardia; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; VT = Ventricular tachycardia; WPW = Wolff-Parkinson-White syndrome.

Discussion

To the best of our knowledge, this is the first observational study to record the impact of RFCA on the treatment of arrhythmias by analyzing the trends, risk factors, recurrence and complications of patients with five different arrhythmias. From 2001 to 2010, the number of RFCAs increased rapidly for the AF, AFL and VT groups, but decreased gradually for the PSVT and WPW groups. Age was a risk factor for recurrence in all groups, while male gender, diabetes and TOF were risk factors for recurrence in patients with PSVT. AF patients treated in a high-activity center had a tendency to receive repeated RFCAs. Elderly patients with AF and AFL had more adverse events after RFCA compared to other subgroups.

Trend in Types of Arrhythmias

In Taiwan, the number of AF increased the most over the ten years studied, followed by the VT, AFL, WPW and PSVT groups. Population aging and advancements in ablation techniques have contributed to this phenomenon, especially for AF and AFL, which are age-related diseases.[12] From 2001 to 2010, the population of older adult patients (>65 years) increased from 1,973,357 to 2,487,893. This increase has resulted in a greater increase in the incidence of AF and AFL compared to other arrhythmias. The mean growth rate for RFCA per year between 2001 and 2010 was 9.7% for AF and 3.2% for AFL (Figures 3). In contrast, the average growth rate of RFCA for PSVT was just 1.4%, which was gradually slowing, although the absolute numbers increased from 1,118 in 2001 to 1,499 in 2010. This pattern is likely present for PSVT since 1) RFCA for PSVT is relatively mature compared to RFCA for AF, and 2) RFCA for PSVT was fully covered by Taiwan NHI but AF was not. Because patients with PSVT and WPW were relatively young, we searched the birth rate from 1980 to 2000. The crude birth rate (births per 1,000 mid-year population per year; mid-year population is defined as the population on 30th June.) in Taiwan decreased from 413,177 births (23 births per

1000 population) in 1980 to 307,200 births (13 births per 1000 population) in 2000, reducing the number of patients needing PSVT and WPW. The number of WPW cases peaked in 2005 (N= 377) and has since been decreasing. The number of procedures in the VT group increased from 57 in 2001 to 123 in 2010, and the average RFCA growth rate over 10 years was 6.8%. This relatively high growth rate is possibly also due to population aging and the maturation of 3D mapping techniques.[13] In summary, the growth models are different for the five arrhythmias. The AF and AFL groups have increased rapidly in RFCA procedures because of population aging. The PSVT group had a relatively slow increase, while the WPW and VT groups showed stable or decreasing numbers of RFCAs.

Risk of recurrence

Our results showed that the recurrence rate after RFCA increased in the following order: PSVT (2.0%) < WPW (4.9%) < VT (5.7%) < AFL (5.8%) < AF (16.1%) (Figure 2). The recurrence-free rate was highest for the PSVT group (98.8% for the first year, gradually decreasing to 97.2% for the 10-year follow up). However, patients <18 years in the PSVT and WPW groups had a significantly higher chance of recurrence, a result which agreed with those of Van Hare et al.[14] This recurrence could be a result of the smaller cardiac anatomy in children, which makes the precise ablation difficult to perform. This result could also explain the association of CHD and TOF with recurrence of PSVT, possibly because of the abnormal cardiac structure of the CHD heart post-cardiac surgery. Patients with TOF and AF also had a higher risk of receiving a second RFCA. In contrast, AF and AFL patients aged ≥75 years had fewer second RFCAs than younger patients.[15]

Our data showed that patients ≥75 years receiving treatment for AF and AFL had lower recurrence rates than those the same age in other groups. The reason for this phenomenon may be the conservative treatment preferred by cardiologists for older patients rather than repeated

RFCA, in order to avoid complications or mortality after the first procedure due to the presence of other comorbidities. Our data suggest that, for patients undergoing an elective RFCA, physicians should carefully evaluate the risk factors such as younger age and the presence of CHD (TOF in PSVT, VSD in AFL) which are associated with a high recurrence rate. Our study also described epidemiologic changes in repeated ablation procedures for five arrhythmias in Taiwan in the RFCA era.

Complications

RFCA, which has an approximately 1% complication rate and 0.1% mortality rate,[3,16] is considered a relatively safe procedure to treat or even cure arrhythmias (Table 3). Our present study showed different patterns of complications in the five arrhythmia groups. Patients with PSVT and WPW had complication rates of 1.6% and 0.8%, respectively, similar to previous studies. However, in patients with AF and AFL, the complication rates were 2.5% and 4.7%, respectively. AFL after RFCA induced more high-grade AV block (2.5%) compared to other arrhythmias, and patients with AF after RFCA had the highest incidence rate of life-threatening pericardial effusion (1.3%). High-grade AV block is considered the main complication of ablation procedures for AFL and PSVT patients because the ablation sites are close to the atrioventricular node.[16] AFL has been seen combined with sick sinus syndrome. Bradyarrhythmias appeared when the substance of AF and AFL is eliminated. RFCA patients with AF had a higher risk of life-threatening pericardial effusion relative to patients with other arrhythmias, resulting in a relatively higher complication rate of 1.3%. The major RFCA procedure for AF is to isolate the pulmonary vein and eliminate the substrate in the left atrium. This requires a longer procedure time and delivers more energy to convert AF into sinus rhythm. RFCA for AF could therefore cause more life-threatening pericardial effusion than that for other arrhythmias. RFCA for VT presents same pattern as that for PSVT and WPW. These data

suggest that, although RFCA is a common procedure to treat different arrhythmias, the complications that should be monitored will differ by type of arrhythmia.

Our data also showed that patients with AFL and AF had higher stroke rates (0.49% and 0.34%, respectively) than patients in the other groups. Anticoagulation therapy is needed in these cases, and it is also necessary to confirm the absence of intracardiac thrombus before RFCA.[17] However, anticoagulation procedures are sometimes ignored because anti-coagulation is not routinely used in AFL.[18] Previous studies have shown a high risk of thromboembolic events and a high incidence of thrombogenic milieu in AFL.[19,20] Use of the inappropriate anticoagulation therapy is considered a significant risk factor for thromboembolism in patients with AFL.[18]

Age was an important risk factor associated with complications such as high-grade AV block, pacemaker implantation, life-threatening pericardial effusion and stroke, especially in patients aged ≥75 years (Table 4). These data were consistent with previous studies,[21,22] and suggest that physicians should be cautious when performing RFCA in patients ≥75 years. We also found that diabetes was associated with increased complication rates for RFCA. A cohort study of 200,000 patients with type II diabetes reported that third degree AV block was 3.1 times as prevalent in the diabetic group (95% CI, 3.0-3.3; $p < 0.0001$).[23] Diabetes has been suggested as a risk factor for autonomic neuropathy, cardiac conduction abnormalities and bradyarrhythmias.[24] Physicians performing RFCA in diabetic patients should monitor for bradyarrhythmia complications.

Limitations

Firstly, the major limitation of this study is our inability to explore the interactions among the predictive variables because of the limited number of events. For instance, the 184 high-grade AV blocks allow for a maximum of 18-19 predictive variables, due to the "ten-one

rule."[25-27] However, the 13 predictors indicate that 78 two-way potential interaction effects may exist. Therefore, it seems not feasible to perform a regression analysis (logistic or Cox regressions) because that many explanatory variables in the equation would induce the statistical problem of overfitting. In addition, there is also an issue of multiple testing (five tests in Table 2 and four tests in Table 4) in this study. Many of the results would turn to be statically insignificant if a correction (i.e., Bonferroni adjustment) was done. Therefore, further studies with a larger sample size and more events are needed to conduct interaction tests based on clinical knowledge or on exploratory data analysis along with multiple testing correction.

Secondly, in this cohort study we did not have access to laboratory parameters, procedural details, heart images, smoking status, obesity or alcohol use. Procedure-related parameters, the location of the accessory pathway in WPW, PV isolation for AF, cardiac anomaly and ejection fraction have been reported as predictors for arrhythmia recurrence and RFCA complications.[14, 28-30] The lack of this information could induce residual confounding. On the other hand, the different arrhythmia groups had substantial differences in baseline characteristics, especially in terms of age, which may result in potential confounding even if we adjusted for these variables in the multivariable regression models. However, the present study focused on RFCA for five different arrhythmias and each arrhythmia had different surgical parameters. Rather than comparing the same parameter in different arrhythmia ablation procedures, we focused on the effect of comorbidities, gender and age on arrhythmia recurrence and RFCA-related complications. Our study provided valuable information to help cardiologists deal with RFCA recurrence and complications.

Thirdly, some arrhythmias such as premature ventricular beats and atrial premature beats are not covered by Taiwan NHI. However, excluding these arrhythmias did not influence the study results since they are usually benign.

Lastly, recurrence may be misidentified in this present study as resulting from ablation of other arrhythmias. For example, this could happen if the patient had an initial PSVT ablation followed by an AF ablation. A single definition of recurrence could consider the second ablation as the recurrence of PSVT. Use of double criteria, with repeated ablations combined with the same major principal diagnosis, reduced the coding error in this study.

Conclusions

There was a rapidly increasing trend of RFCA procedures for AF, AFL and VT during 2001-2010, but a slow increase for PSVT and WPW. The recurrence-free rate was higher for PSVT than for other arrhythmias. Older adult patients with AF and AFL had fewer repeat RFCAs and AF patients in high-activity center hospitals had more. CHD was a risk factor for PSVT recurrence. AF patients had more occurrences of life-threatening pericardial effusion, especially those aged more than 65 years, and patients receiving RFCA for AFL suffered more from bradycardia, requiring permanent pacemaker implantation.

Contributors:

CHEN conceived of the study. Y LIN and WU initiated the study design and WANG helped with implementation. Y LIN, WU and CHEN provided statistical expertise in clinical trial design and WANG and YS LIN conducted the primary statistical analysis. All authors contributed to refinement of the study protocol and approved the final manuscript.

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Disclaimer:

The lead author confirms that the content of this manuscript is honest and transparent.

Competing interests:

None declared.

Patient consent:

Not required.

Ethics approval:

The Ethics Institutional Review Board at Chang Gung Memorial Hospital approved this study.

Data sharing statement:

Data are available. Please contact the corresponding author.

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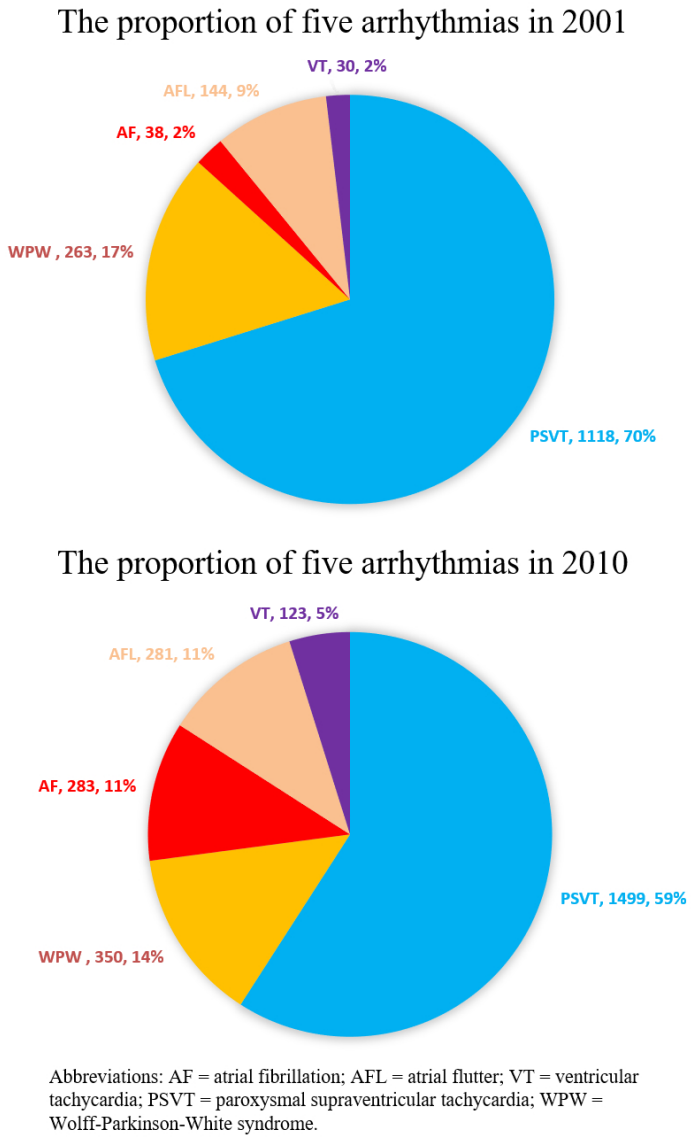
Figure Legends

Figure 1. Proportion of radiofrequency catheter ablation patients diagnosed with paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia in Taiwan during 2001 and 2010.

Figure 2. Recurrence-free survival curves after radiofrequency catheter ablation for groups of patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.

Figure 3. Numbers and growth rate of radiofrequency catheter ablations annually in groups of patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.



Abbreviations: AF = atrial fibrillation; AFL = atrial flutter; VT = ventricular tachycardia; PSVT = paroxysmal supraventricular tachycardia; WPW = Wolff-Parkinson-White syndrome.

Figure 1 Proportion of radiofrequency catheter ablation patients diagnosed with paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia in Taiwan during 2001 and 2010.

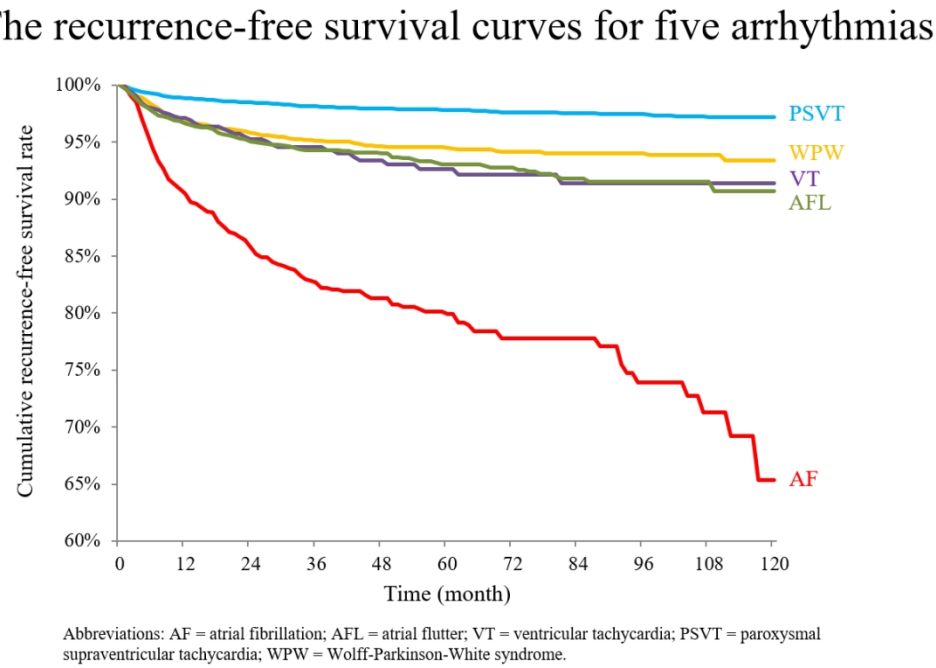
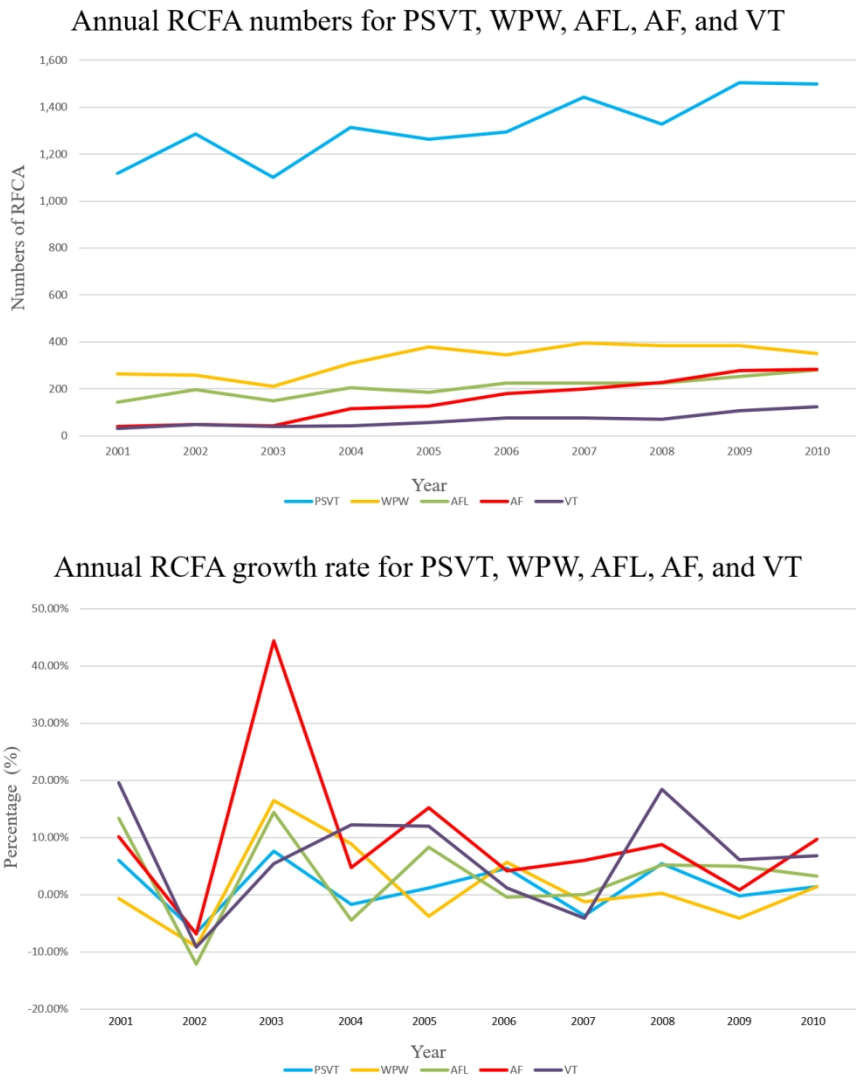


Figure 2 Recurrence-free survival curves after radiofrequency catheter ablation for groups of patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.



Abbreviations: AF = atrial fibrillation; AFL = atrial flutter; VT = ventricular tachycardia; PSVT = paroxysmal supraventricular tachycardia; RFCA = Radiofrequency catheter ablation; WPW = Wolff-Parkinson-White syndrome.

Figure 3 Numbers and growth rate of radiofrequency catheter ablations annually in groups of patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.

Supplemental Table 1

Disease	ICD 9 code
PSVT	4270
WPW	426.7
AFL	427.32
AF	427.33
VT	427.1
High-grade AVB	426.12, 426.13, 426.0
Stroke	430*, 431*, 432*, 433*, 434*, 436*, 437*
DM	250*
Hypertension	401*
COPD	490-496
Chronic kidney disease	403, 404, 585
Coronary artery disease	413*, 4140*
Heart failure	428*, 39891, 40201, 40211, 40291, 40401, 40403, 40411, 40413, 40491, 40493
TOF	745.2
Transposition of the great vessel	745.1
Double outlet right ventricle	745.11
Total anomalous pulmonary venous connection	747.41
Tricuspid atresia	746.1
Common truncus arteriosus	745.0
Common ventricle	745.3
Hypoplastic left heart syndrome	746.7
Ventricular septal defect	745.4
Atrial septal defect	745.5
Ebstein's anomaly	746.2
Patent ductus arteriosus	747.0
Congenital pulmonary stenosis	746.83
Coarctation of aorta	747.1

Endocardial cushion defect	745.6
Congenital aortic stenosis	746.3

Abbreviations: AF = Atrial fibrillation; AFL = Atrial flutter; COPD = Chronic obstructive pulmonary disease; DM = Diabetes mellitus; High-grade AV block = High-grade atrioventricular block; PSVT = Paroxysmal supraventricular tachycardia; TOF = Tetralogy of Fallot; VT = Ventricular tachycardia; WPW = Wolff-Parkinson-White syndrome.

Supplemental Table 2. Risk factors of complications for the patients without recurrence during the follow up

	During the index admission				After discharge of the index admission			
	Life-threatening pericardial effusion (39 events, 0.21%)		New-onset stroke (22 events, 0.12%)		High-grade AVB (171 events, 0.92%)		Pacemaker (96 events, 0.51%)	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age								
0-18 yrs.	NA	NA	NA	NA	0.70 (0.29–1.69)	0.424	0.92 (0.28–3.01)	0.887
19-44 yrs.	Reference	—	Reference	—	Reference	—	Reference	—
45-54 yrs.	17.46 (2.22–137.60)	0.007	4.69 (0.48–45.74)	0.184	1.17 (0.76–1.81)	0.472	1.93 (1.08–3.45)	0.026
55-64 yrs.	33.05 (4.26–256.70)	0.001	18.46 (2.26–150.86)	0.007	0.91 (0.55–1.52)	0.731	1.17 (0.57–2.40)	0.672
65-74 yrs.	28.85 (3.47–240.16)	0.002	9.21 (0.95–89.41)	0.056	1.22 (0.73–2.05)	0.452	1.65 (0.80–3.41)	0.178
Above 75 yrs.	35.53 (3.90–323.63)	0.002	15.43 (1.54–154.54)	0.020	2.16 (1.26–3.70)	0.005	4.24 (2.09–8.62)	<0.001
Male gender	1.20 (0.61–2.37)	0.596	1.01 (0.41–2.45)	0.991	1.19 (0.87–1.63)	0.278	0.79 (0.52–1.19)	0.259
Diabetes	0.16 (0.02–1.20)	0.074	1.26 (0.41–3.87)	0.683	1.62 (1.05–2.51)	0.031	1.94 (1.10–3.40)	0.021
Hypertension	1.12 (0.54–2.31)	0.757	0.56 (0.18–1.73)	0.316	1.16 (0.78–1.73)	0.454	0.93 (0.54–1.60)	0.784
COPD	NA	NA	NA	NA	0.72 (0.29–1.80)	0.487	0.81 (0.25–2.62)	0.719
CKD	NA	NA	1.48 (0.19–11.54)	0.708	2.21 (1.02–4.81)	0.045	2.95 (1.18–7.40)	0.021
Heart failure	0.80 (0.10–6.11)	0.828	2.67 (0.71–10.06)	0.145	2.30 (1.24–4.24)	0.008	0.77 (0.23–2.54)	0.667
TOF	NA	NA	NA	NA	NA	NA	NA	NA
VSD	NA	NA	NA	NA	NA	NA	NA	NA
ASD II	5.65 (0.71–45.04)	0.102	NA	NA	1.22 (0.17–8.64)	0.844	2.21 (0.31–15.64)	0.426
Ebstein	NA	NA	NA	NA	NA	NA	NA	NA
High-activity center	3.64 (1.40–9.45)	0.008	1.17 (0.46–2.93)	0.742	0.96 (0.70–1.31)	0.788	0.90 (0.59–1.35)	0.599
Indication								
PSVT	Reference	—	Reference	—	Reference	—	Reference	—
WPW	2.45 (0.93–6.43)	0.068	1.68 (0.35–8.11)	0.520	0.42 (0.22–0.82)	0.011	0.52 (0.22–1.24)	0.141
VT	1.68 (0.22–12.91)	0.619	NA	NA	1.02 (0.41–2.51)	0.973	1.26 (0.39–4.04)	0.694
AF	4.57 (2.03–10.33)	<0.001	3.86 (1.09–13.65)	0.036	0.77 (0.35–1.68)	0.507	0.52 (0.13–2.06)	0.351
AFL	1.21 (0.41–3.59)	0.729	3.88 (1.27–11.84)	0.017	1.95 (1.28–2.97)	0.002	2.34 (1.36–4.02)	0.002

Abbreviations: AF = Atrial fibrillation; AFL = Atrial flutter; ASD = Atrial septal defect; AVB = Atrioventricular block; CAD = Coronary artery disease; CI = confidence interval; CKD = Chronic kidney disease; COPD = Chronic obstructive pulmonary disease; Ebstein = Ebstein's anomaly; HR = Hazard ratio; NA =

Not applicable; OR = Odds ratio; PSVT = Paroxysmal supraventricular tachycardia; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; VT = Ventricular tachycardia; WPW = Wolff-Parkinson-White syndrome.

Supplemental Table 3. RFCA-related complications according to recurrence or not during the follow up (N = 20,707 RFCAs)

Complication	Recurrence (n=988)	Non-recurrence (n=19,719)	P[a]
In-hospital complication			
Life-threatening pericardial effusion	3 (0.3)	42 (0.21)	0.48
New-onset stroke	0 (0)	23 (0.12)	0.63
After discharge			
High-grade AVB	3 (0.3)	181 (0.92)	0.05
Pacemaker implantation	0 (0)	100 (0.51)	0.016

Abbreviations: AVB = Atrioventricular block; RFCA = Radiofrequency catheter ablation.
a, Fisher's exact test.

Supplemental Table 4. RFCA-related complications according to different types of arrhythmias for the patients without recurrence during the follow up

Complication	PSVT	WPW	AFL	AF	VT
Number of patients	12,519	2,895	1,710	949	578
In-hospital complication					
Life-threatening pericardial effusion	15 (0.12)	6 (0.21)	5 (0.29)	12 (1.26)	1 (0.17)
New-onset stroke	8 (0.06)	2 (0.07)	8 (0.47)	4 (0.42)	0 (0)
After discharge					
High-grade AVB	109 (0.87)	8 (0.28)	42 (2.46)	7 (0.74)	5 (0.87)
Pacemaker implantation	62 (0.50)	5 (0.17)	24 (1.40)	2 (0.21)	3 (0.52)

Abbreviations: AF = Atrial fibrillation; AFL = Atrial flutter; AVB = Atrioventricular block; PSVT = Paroxysmal supraventricular tachycardia; RFCA = Radiofrequency catheter ablation; VT = Ventricular tachycardia; WPW = Wolff-Parkinson-White syndrome.

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6,7
		(*b*) Describe any methods used to examine subgroups and interactions	6,7
		(*c*) Explain how missing data were addressed	7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10, 11, 13
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-12
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20,21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	18,19
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.