

# BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email [info.bmjopen@bmj.com](mailto:info.bmjopen@bmj.com)

# BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023487
Article Type:	Research
Date Submitted by the Author:	23-Apr-2018
Complete List of Authors:	Lin, Yuan; Chang-Gung Memorial Hospital, Keelung, Taiwan , Department of Emergency Medicine Wu, Hsin-Kuan; Chang-Gung Memorial Hospital, Keelung, Taiwan , Department of Emergency Medicine Wang, Te-Hsiung ; Kyoto University Hospital, Integrated Clinical Education Center Chen, Tien-Hsing; Chang-Gung Memorial Hospital, Keelung, Taiwan , Division of Cardiology, Department of Internal Medicine, Lin, Yu-Sheng; Chang-Gung Memorial Hospital, Chiayi, Taiwan, Division of Cardiology, Department of Internal Medicine,
Keywords:	radiofrequency catheter ablation (RFCA), Wolff–Parkinson–White syndrome, supraventricular tachycardia, ventricular tachycardia, complication, recurrence

SCHOLARONE™  
Manuscripts

Only

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

**Yuan Lin MD<sup>1#</sup>, Hsin-Kuan Wu MD<sup>1#</sup>, Te-Hsiung Wang MD<sup>2</sup>, Tien-Hsing Chen MD<sup>3\*</sup>,  
Yu-Sheng Lin MD<sup>4\*</sup>**

- 1. Department of Emergency Medicine, Chang-Gung Memorial Hospital, Keelung, Taiwan**
- 2. Junior resident, Integrated Clinical Education Center, Kyoto University Hospital, Kyoto, Japan**
- 3. Division of Cardiology, Department of Internal Medicine, Chang-Gung Memorial Hospital, Keelung, Taiwan**
- 4. Division of Cardiology, Department of Internal Medicine, Chang-Gung Memorial Hospital, Chiayi, Taiwan**

**#Yuan Lin and Hsin-Kuan Wu contributed equally to this study**

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

**To whom correspondence and reprint requests should be addressed:**

**Dr. Tien-Hsing Chen, Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial Hospital, No. 5, Fu-Shin Street, Kweishan 333, Taoyuan, Taiwan.**

**TEL: +886-3-3281200-8116**

**E-mail: skyheart0826@gmail.com**

## 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)<sup>2-4</sup>. RFCA, which has been widely applied since the 1990s<sup>1</sup>, 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.

1  
2  
3 Although arrhythmias after RFCA are usually not life-threatening, identification and  
4 minimization of the risk of complications are extremely important. The RFCA procedure may  
5 lead to atrioventricular block (AV block) and bradycardia, even requiring permanent  
6 pacemaker implantation. Previous studies were composed of relatively small cohorts or were  
7 single-center studies, and evaluated patients with single arrhythmia. However, there are no  
8 studies comparing RFCA-related complications in patients with five different arrhythmias<sup>5,6</sup>.  
9  
10 The targets for RFCA-related risk minimization are different for different arrhythmias. For  
11 example, when RFCA is used to treat PSVT, the goal is to modify or eliminate AV node or  
12 accessory pathways, and when RFCA is used to treat AF, the goal is to isolate the pulmonary  
13 veins. These RFCA-treated patients share similar complications like AV block, requirement  
14 for permanent pacemaker implantation, pericardial effusion with tamponade requiring  
15 pericardiocentesis, and stroke. However, the complication rates vary in the five different  
16 arrhythmias: paroxysmal supraventricular tachycardia (PSVT), Wolff–Parkinson–White  
17 syndrome (WPW), typical atrial flutter (AFL), atrial fibrillation (AF), and ventricular  
18 tachycardia (VT). It is therefore important to identify the incidence and risk of RFCA-related  
19 complications in these patients.  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36

37 This retrospective study investigated the population trend of patients who received  
38 RFCA for PSVT, WPW, AFL, AF, and VT. We identified the major RFCA-related risk  
39 factors influencing 1) recurrence of arrhythmias, and 2) complications such as AV block,  
40 permanent pacemaker implantation, cardiac tamponade and acute ischemic stroke.  
41  
42  
43  
44  
45  
46  
47  
48  
49

## 50 **Methods**

### 51 **Study design and population**

1  
2  
3 We conducted a nationwide population-based cohort study using data from the  
4 Taiwan NHIRD. In Taiwan, the National Health Insurance (NHI) program has reimbursed  
5 patients who receive RFCA for PSVT, WPW syndrome, AFL, AF and VT since 2001. More  
6 than 99.91% of Taiwan's population is covered by the NHI scheme. The accuracy and  
7 validation of National Health Insurance Research Database (NHIRD) data is based upon  
8 regular auditing by the NHI Bureau<sup>7-9</sup>. The Ethics Institutional Review Board at Chang Gung  
9 Memorial Hospital approved this study.  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19

### 20 **Study cohort, outcome measurement and follow-up**

21  
22 This study accessed NHIRD data for all targeted arrhythmia patients who received  
23 RFCA from 2001 to 2010. The targeted arrhythmias were PSVT (Internal Classification of  
24 Diseases, Ninth Revision, ICD-9, Code 4270), WPW (426.7), AFL (427.32), AF (427.31),  
25 and VT (427.1; Supplemental Table). Patients with arrhythmias other than targeted  
26 arrhythmias (such as premature ventricular beats or atrial tachycardia) and patients with  
27 unidentified arrhythmias who received RFCA were excluded. For patients who received more  
28 than one round of RFCA, we analyzed the data from the first round. The follow-up period  
29 was from the time of hospitalization until death, or until 31st December 2010.  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39

### 40 **Outcome measurement**

41 The primary outcomes included recurrence of arrhythmia, and complications.  
42 Recurrence was defined as either 1) recurrence of original arrhythmias, or 2) receiving  
43 secondary RFCA. Complications included high-grade AV block, high-grade AV block  
44 requiring permanent pacemaker implantation, cardiac tamponade requiring  
45 pericardiocentesis, and new stroke regardless ischemic or hemorrhagic stroke. High-grade  
46 AV block was defined as second or third degree atrioventricular block (AV block) (426.12,  
47 426.13, 426.0). Permanent pacemaker implantation was due to AV block after RFCA.  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 Cardiac tamponade requiring pericardiocentesis was defined as 1) massive pericardial  
4 effusion during RFCA, or 2) patient requiring pericardiocentesis at index admission. New  
5 stroke was defined as stroke (430\*, 431\*, 432\*, 433\*, 434\*, 436\*, 437\*) which occurred  
6 during index admission. In-hospital death was defined as death of the patient due to any cause  
7 during index admission.  
8  
9  
10  
11  
12

### 13 14 15 **Covariate assessment**

16 Comorbidities were assessed according to ICD-9 codes before index admission.  
17  
18 Diabetes mellitus, hypertension (HTN) or chronic diseases were recorded as comorbidities if  
19 there was at least one in-admission diagnosis. All congenital heart disease (CHD) was  
20 reconfirmed by the Catastrophic Illness certification (CIC) which is sub dataset of NHI. A  
21 CIC for congenital heart disease requires imaging proof confirmed by two cardiologists.  
22 Complicated CHD included Tetralogy of Fallot (TOF), transposition of the great vessels,  
23 double outlet right ventricle, total anomalous pulmonary venous connection, tricuspid atresia,  
24 common truncus arteriosus, common ventricle and hypoplastic left heart syndrome. Simple  
25 CHD included ventricular septal defect (VSD), atrial septal defect (ASD), Ebstein's anomaly,  
26 patent ductus arteriosus, congenital pulmonary stenosis, coarctation of aorta, endocardial  
27 cushion defect, and congenital aortic stenosis. Center volume was designed as time-  
28 dependent variety and high center volume was defined as RFCA numbers more than 100  
29 regardless of arrhythmias type.  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

### 48 **Patient and public involvement**

49 This study has no direct relationship with any patient and public involvement during the  
50 development, design and conduct.  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



## 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 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	<i>P</i> 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						0.045
Complicated CHD	7 (0.1)	3 (0.1)	5 (0.3)	1 (0.1)	0 (0.0)	
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

Variable	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%)	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
<b>Age</b>										
0-18 yrs	1.52 (1.02–2.28)	0.041	1.90 (1.27–2.85)		2.17 (0.50–9.41)	0.30	N.A		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)	0.456	0.90 (0.57–1.44)	0.67	1.98 (1.15–3.41)	0.01	1.03 (0.73–1.44)	0.875	0.71 (0.28–1.78)	0.46
55-64 yrs	0.70 (0.47–1.05)	0.084	1.47 (0.87–2.47)	0.14	1.40 (0.78–2.51)	0.26	0.87 (0.61–1.23)	0.430	0.75 (0.24–2.36)	0.62
65-74 yrs	0.68 (0.42–1.11)	0.121	0.95 (0.37–2.41)	0.91	0.93 (0.49–1.77)	0.82	0.54 (0.34–0.86)	0.010	0.19 (0.02–1.56)	0.12

	Above 75 yrs	0.69 (0.35–1.37)	0.289	N.A.		0.28 (0.10–0.76)	0.01 3	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)	0.70 8	1.68 (1.09–2.59)	0.02 0	1.43 (1.05–1.95)	0.023	1.31 (0.66–2.58)	0.43 6
	Diabetes	1.59 (1.01–2.52)	0.047	0.18 (0.03–1.34)	0.09 4	0.80 (0.43–1.49)	0.48 5	0.70 (0.43–1.14)	0.153	0.70 (0.09–5.74)	0.74 1
	Hypertension	1.03 (0.70–1.53)	0.876	1.27 (0.71–2.28)	0.42 4	0.73 (0.46–1.15)	0.17 4	1.29 (0.97–1.72)	0.076	1.49 (0.40–5.49)	0.54 8
	COPD	1.13 (0.50–2.60)	0.765	N.A.		1.08 (0.43–2.72)	0.86 7	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)	0.67 3	0.55 (0.08–4.02)	0.559	4.18 (0.52–33.86)	0.18 0
	CAD	0.85 (0.44–1.64)	0.631	0.53 (0.13–2.17)	0.37 7	0.59 (0.29–1.17)	0.13 1	1.07 (0.73–1.56)	0.743	1.18 (0.26–5.25)	0.83 2
	Heart failure	1.64 (0.40–6.67)	0.493	N.A.		0.91 (0.47–1.75)	0.77 8	0.29 (0.07–1.20)	0.088	2.90 (0.63–13.42)	0.17 3
	TOF	23.00 (4.01–131.81)	<0.001	N.A.		3.32 (1.01–10.96)	0.04 9	N.A.	N.A.	N.A.	
	VSD	N.A.	0.979	2.79 (0.53–14.82)	0.22 8	2.78 (1.29–5.99)	0.00 9	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)	0.44 7	1.46 (0.57–3.71)	0.43 0	1.17 (0.28–4.87)	0.832	3.57 (0.47–27.34)	0.22 1
	Ebstein	1.08 (0.09–12.80)	0.950	4.40 (1.80–10.74)	0.00 1	1.54 (0.21–11.47)	0.67 6	N.A.	N.A.	N.A.	
	High center volume	1.05 (0.82–1.35)	0.679	0.87 (0.63–1.19)	0.38 3	1.78 (1.11–2.85)	0.01 7	3.16 (1.77–5.67)	<0.001	0.49 (0.25–0.97)	0.04 0

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

Variable	Second or third AVB (184 events, 0.89%)		Pacemaker (100 events, 0.48%)		Pericardiocentesis (45 events, 0.22%)		New stroke (23 events, 0.11%)	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
<b>Age</b>								
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	



## 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 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<sup>10</sup>. 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



1  
2  
3 WPW. The number of WPW cases reached a peak in 2005 (N= 377), and had been  
4 decreasing ever since. The number of procedures in the VT group has increased from 57 in  
5 2001 to 123 in 2010, and the average RFCA growth rate over 10 years was 6.81%. This  
6 relatively high growth rate is possibly also due to population aging, and the maturation of 3D  
7 mapping techniques<sup>11</sup>. In summary, the growth models are different for the five arrhythmias.  
8  
9 There has been a rapid increase in RFCA procedures in the AF and AFL groups because of  
10 the population aging. There has been a relatively slow increase in the PSVT group, while the  
11 WPW groups showed stable or decreasing numbers of RFCA.  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21

### 22 **Risk of recurrence**

23  
24 Our results showed that the recurrence rate after RFCA increased in the following  
25 order: PSVT (2%) < WPW (4.9%) < VT (5.7%) < AFL (5.8%) < AF (16.1%) (Figure 2). The  
26 recurrence-free rate was highest for the PSVT group (98.8% for the first year, gradually  
27 decreasing to 97.2% on the 10 years follow-up). However, patients in the PSVT and WPW  
28 groups < 18 years old had a significantly higher chance of recurrence, which agreed with  
29 previous results<sup>12</sup>. This could be because of the smaller cardiac anatomy in children, which  
30 makes it difficult to perform the precise ablation. This could also explain the association of  
31 congenital heart disease and TOF with recurrence of PSVT, possibly because of abnormal  
32 cardiac structure of congenital post-cardiac surgery. Patients with TOF and AF also had a  
33 higher risk of receiving a second RFCA. In contrast, AF and AFL patients had fewer second  
34 RFCA in the age group > 75-years-old<sup>13</sup>.  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

48 Our data showed that patients > 75 years old receiving treatment for AF and AFL  
49 exhibited lower recurrence rates than the same age range in other groups. The reason may be  
50 caused by that cardiologists prefer conservative treatment for senior patients rather than  
51 repeated RFCA in order to avoid complications or mortality after the first procedure due to  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 other comorbidities. Our data suggested that for patients undergoing an elective RFCA,  
4  
5 physicians need to carefully evaluate the risk factors such as younger age and presence of  
6  
7 congenital heart disease (TOF in PSVT, VSD in AFL) which are associated with a high  
8  
9 recurrence rate. Our study also described epidemiologic changes in repeated ablation  
10  
11 procedures for five arrhythmias in Taiwan in the RFCA era.  
12  
13

## 14 15 **Complications**

16  
17 RFCA, which has an approximately 1% complication rate and 0.1% mortality rate<sup>3,14</sup>,  
18  
19 is considered a relatively safe procedure to treat or even cure arrhythmias (Table 4). Our  
20  
21 present study showed different patterns of complications in the five arrhythmia groups.  
22  
23 Patients with PSVT, and WPW had complication rates of 1.04% and 0.61%, respectively,  
24  
25 similar to previous studies. However, in patients with AF and AFL, the complication rate was  
26  
27 2.26%. AFL after RFCA induced second or third degree of AV block (2.26%) compared to  
28  
29 other arrhythmias, and patients with AF RFCA had the highest incidence rate of tamponade  
30  
31 (0.98%). Second or third degree AV block is considered the main complication of ablation  
32  
33 procedures for AFL and PSVT patients because the ablation sites are close to the  
34  
35 atrioventricular node<sup>14</sup>. AFL has been seen combined with sick sinus syndrome.  
36  
37 Bradyarrhythmias appeared when the substance of AF and AFL is eliminated. Patients with  
38  
39 AF RFCA had a relatively higher risk of cardiac tamponade than other arrhythmias, resulting  
40  
41 in a relatively higher complication rate of 0.98%. The major mechanism of RFCA for AF is  
42  
43 to isolate the pulmonary vein and eliminate the substrate in the left atrium. This requires a  
44  
45 longer procedure time and delivers more energy to convert AF to sinus rhythm. RFCA for AF  
46  
47 could therefore cause more cardiac tamponade. RFCA for VT presents same pattern as that  
48  
49 for PSVT and WPW pattern. These data suggested that although RFCA is a common  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 procedure to cure different arrhythmias, different complications should be monitored in  
4  
5 different arrhythmias.  
6

7 Our data also showed that patients with AFL and AF had higher stroke rates (0.43%  
8 and 0.26%, respectively). Anticoagulation therapy is needed in these cases, and it is also  
9 necessary to confirm absence of intracardiac thrombus before RFCA<sup>15</sup>. However,  
10 anticoagulation procedures are sometimes ignored because anti-coagulation is not routinely  
11 used in AFL<sup>16</sup>. Previous studies have shown a high risk of thromboembolic events and a high  
12 incidence of thrombogenic milieu in AFL<sup>17,18</sup>. The inappropriate anticoagulation therapy is  
13 considered a significant risk for thromboembolism in patients with AFL<sup>16</sup>.  
14  
15

16 Age was an important risk factor associated with complications such as second or third  
17 degree AV block, pacemaker implantation, pericardiocentesis and stroke especially in  
18 patients aged > 75-years old (Table 4). These data were consistent with previous studies<sup>19,20</sup>,  
19 and suggested that physicians should be cautious when performing RFCA in patients >75  
20 years old. We also found that diabetes was associated with increased complication rates for  
21 RFCA. A cohort study of 200,000 patients with type II diabetes reported that third degree AV  
22 block was prevalent in subjects with diabetes<sup>21</sup>. Diabetes has been suggested as a risk factor  
23 for autonomic neuropathy, cardiac conduction abnormalities and bradyarrhythmias<sup>22</sup>. When  
24 physicians perform RFCA on diabetic patients, they should monitor for bradyarrhythmia  
25 complications  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45

#### 46 **Limitations**

47  
48 This study had several limitations. Firstly, in this cohort study we did not have access  
49 to laboratory parameters, procedural details, and heart images. Procedure-related parameters,  
50 location of accessory pathway in WPW, PV isolation for AF, and cardiac anomaly, ejection  
51 fraction have been reported as predictors for arrhythmia recurrence and RFCA complication  
52  
53  
54  
55  
56  
57  
58  
59  
60

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.

**Funding:**

This article has NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

**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.

## References

1. Joseph JP, Rajappan K. Radiofrequency ablation of cardiac arrhythmias: past, present and future. *QJM : monthly journal of the Association of Physicians* 2012;105:303-14.
2. O'Hara GE, Philippon F, Champagne J, et al. Catheter ablation for cardiac arrhythmias: a 14-year experience with 5330 consecutive patients at the Quebec Heart Institute, Laval Hospital. *The Canadian journal of cardiology* 2007;23 Suppl B:67B-70B.
3. Spector P, Reynolds MR, Calkins H, et al. Meta-analysis of ablation of atrial flutter and supraventricular tachycardia. *The American journal of cardiology* 2009;104:671-677.
4. Bohnen M, Stevenson WG, Tedrow UB, et al. Incidence and predictors of major complications from contemporary catheter ablation to treat cardiac arrhythmias. *Heart rhythm : the official journal of the Heart Rhythm Society* 2011;8:1661-6.
5. Long-Term Outcomes After Catheter Ablation of Cavo-Tricuspid Isthmus Dependent Atrial Flutter: A Meta-Analysis
6. Riccardo Cappato, Hugh Calkins, et al. Worldwide Survey on the Methods, Efficacy, and Safety of Catheter Ablation for Human Atrial Fibrillation
7. Yang YW, Chen YH, Xirasagar S, Lin HC: Increased risk of stroke in patients with bullous pemphigoid: a population-based follow-up study. *Stroke; a journal of cerebral circulation.* 2011;42(2):319-323.
8. Wu CY, Wu MS, Kuo KN, Wang CB, Chen YJ, Lin JT: Effective reduction of gastric cancer risk with regular use of nonsteroidal anti-inflammatory drugs in Helicobacter pylori-infected patients. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2010;28(18):2952-2957.
9. Wu CY, Chen YJ, Ho HJ, Hsu YC, Kuo KN, et al.: Association between nucleoside analogues and risk of hepatitis B virus-related hepatocellular carcinoma recurrence following

1  
2  
3 liver resection. JAMA : the journal of the American Medical Association.  
4  
5 2012;308(18):1906-1914.

6  
7 10. William M. Feinberg, MD; Joseph L. Blackshear, MD; Andreas Laupacis, MD; et al  
8  
9 Prevalence, Age Distribution, and Gender of Patients With Atrial Fibrillation Analysis and  
10  
11 Implications Arch Intern Med. 1995;155(5):469-473.

12  
13 11. Dixit S1, Callans DJ. Mapping for ventricular tachycardia. Card Electrophysiol Rev. 2002  
14  
15 Dec;6(4):436-41.

16  
17 12. Van Hare GF, Javitz H, Carmelli D, Saul JP, Tanel RE, et al.: Prospective assessment  
18  
19 after pediatric cardiac ablation: recurrence at 1 year after initially successful ablation of  
20  
21 supraventricular tachycardia. Heart rhythm : the official journal of the Heart Rhythm Society.  
22  
23 2004;1(2):188-196.

24  
25 13. Tuan TC, Chang SL, Tsao HM, Tai CT, Lin YJ, et al.: The impact of age on the  
26  
27 electroanatomical characteristics and outcome of catheter ablation in patients with atrial  
28  
29 fibrillation. Journal of cardiovascular electrophysiology. 2010;21(9):966-972.

30  
31 14. Walters TE, Kistler PM, Kalman JM: Radiofrequency ablation for atrial tachycardia and  
32  
33 atrial flutter. In: Heart, lung & circulation, p. 386-394 2012.

34  
35 15. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, et al.: 2012 HRS/EHRA/ECAS  
36  
37 expert consensus statement on catheter and surgical ablation of atrial fibrillation:  
38  
39 recommendations for patient selection, procedural techniques, patient management and  
40  
41 follow-up, definitions, endpoints, and research trial design: J Interv Card Electrophysiol  
42  
43 (2012) 33: 171.

44  
45 16. Gronefeld GC, Wegener F, Israel CW, Teupe C, Hohnloser SH: Thromboembolic risk of  
46  
47 patients referred for radiofrequency catheter ablation of typical atrial flutter without prior  
48  
49 appropriate anticoagulation therapy. Pacing and clinical electrophysiology : PACE.  
50  
51 2003;26(1 Pt 2):323-327.

- 1  
2  
3 17. Wood KA, Eisenberg SJ, Kalman JM, Drew BJ, Saxon LA, et al.: Risk of  
4 thromboembolism in chronic atrial flutter. *The American journal of cardiology*.  
5 1997;79(8):1043-1047.  
6  
7  
8  
9 18. Alyeshmerni D, Pirmohamed A, Barac A, Smirniotopoulos J, Xue E, et al.:  
10 Transesophageal Echocardiographic Screening before Atrial Flutter Ablation: Is It Necessary  
11 for Patient Safety? *Journal of the American Society of Echocardiography : official*  
12 *publication of the American Society of Echocardiography*. 2013.  
13  
14  
15  
16  
17 19. Hoffmann BA, Brachmann J, Andresen D, Eckardt L, Hoffmann E, et al.: Ablation of  
18 atrioventricular nodal reentrant tachycardia in the elderly: results from the German Ablation  
19 Registry. *Heart rhythm: the official journal of the Heart Rhythm Society*. 2011;8(7):981-987.  
20  
21  
22  
23 20. Mirza M, Strunets A, Shen WK, Jahangir A: Mechanisms of arrhythmias and conduction  
24 disorders in older adults. *Clinics in geriatric medicine*. 2012;28(4):555-573.  
25  
26  
27  
28 21. Movahed MR, Hashemzadeh M, Jamal MM: Increased prevalence of third-degree  
29 atrioventricular block in patients with type II diabetes mellitus. *Chest*. 2005;128(4):2611-  
30 2614.  
31  
32  
33  
34 22. Movahed MR: Diabetes as a risk factor for cardiac conduction defects: a review.  
35 *Diabetes, obesity & metabolism*. 2007;9(3):276-281.  
36  
37  
38  
39 23. Adao L, Araujo C, Sa AP, Silva P, Oliveira M, et al.: Importance of accessory pathway  
40 location in the efficacy and safety of radiofrequency ablation. *Revista portuguesa de*  
41 *cardiologia : orgao oficial da Sociedade Portuguesa de Cardiologia = Portuguese journal of*  
42 *cardiology : an official journal of the Portuguese Society of Cardiology*. 2011;30(1):35-46.  
43  
44  
45  
46  
47 24. Iturralde P, Guevara-Valdivia M, Rodriguez-Chavez L, Medeiros A, Colin L:  
48 Radiofrequency ablation of multiple accessory pathways. *Europace : European pacing,*  
49 *arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing,*  
50 *arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology*.  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3 2002;4(3):273-280.

4  
5 25. Anselmino M, Grossi S, Scaglione M, Castagno D, Bianchi F, et al.: Long-term results of  
6  
7 transcatheter atrial fibrillation ablation in patients with impaired left ventricular systolic  
8  
9 function. *Journal of cardiovascular electrophysiology*. 2013;24(1):24-32.  
10  
11  
12

### 13 **Figure Legends**

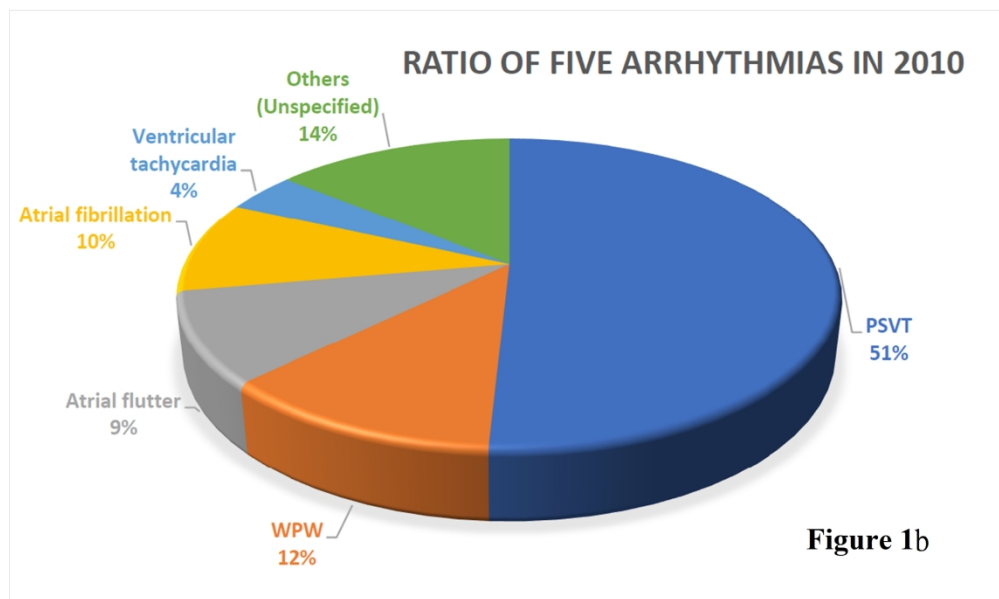
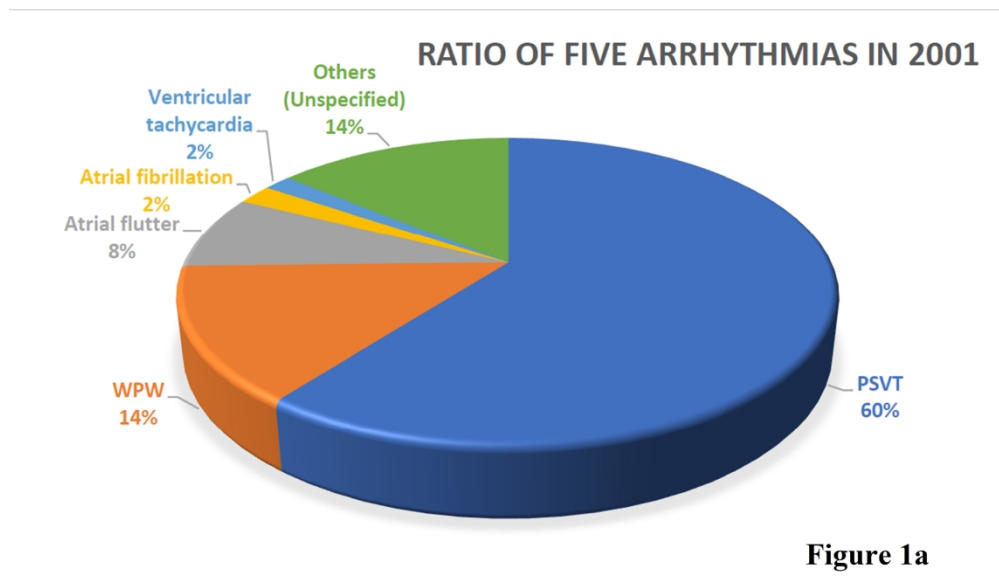
14  
15 Figure 1a. Ratio of PSVT, WPW, AFL, AF and VT in Taiwan during 2001

16  
17 Figure 1b Ratio of PSVT, WPW, AFL, AF and VT in Taiwan during 2010

18  
19 Figure 2 Recurrence-free curve for PSVT, WPW, AFL, AF and VT

20  
21 Figure 3 Number of RFCAs annually in the PSVT, WPW, AFL, AF and VT groups

22  
23 Figure 4 Annual RFCA growth rate for the PSVT, WPW, AFL, AF and VT groups  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



255x299mm (300 x 300 DPI)

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

BMJ Open: first published as 10.1136/bmjopen-2018-023487 on 30 May 2019. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

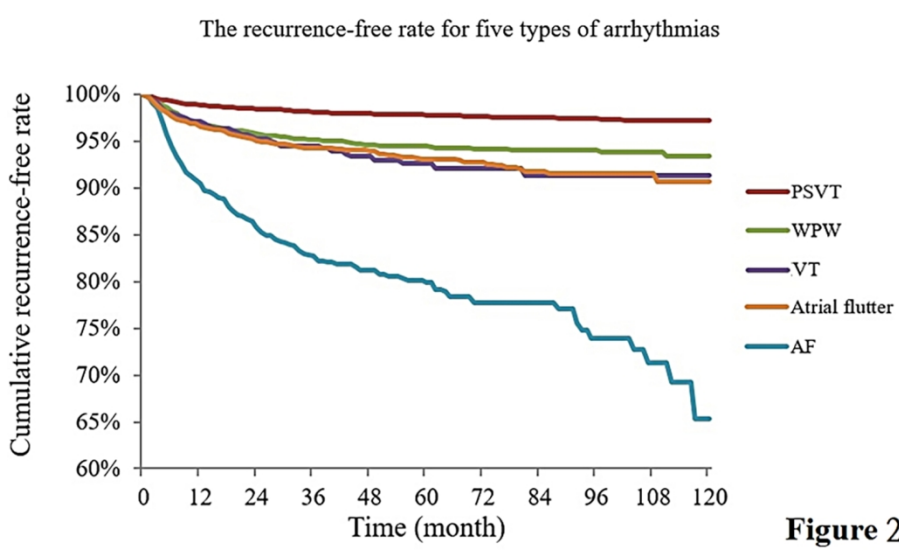
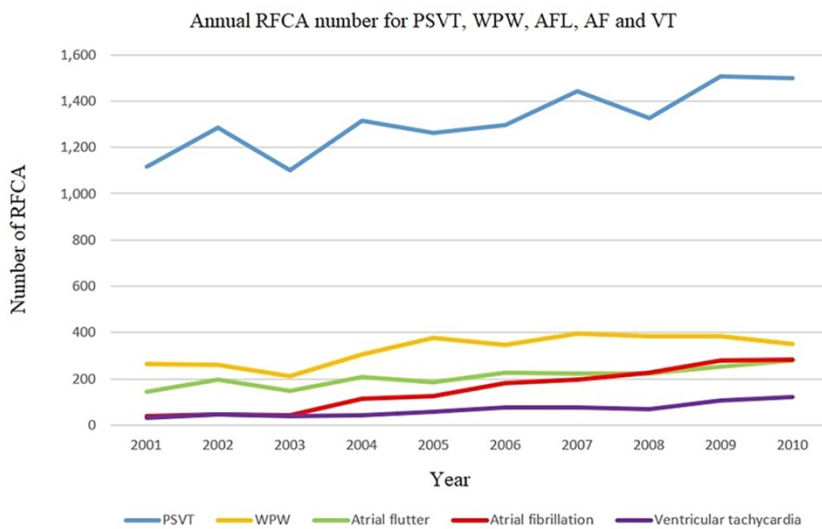


Figure 2



**Figure 3**

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

160x90mm (300 x 300 DPI)

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

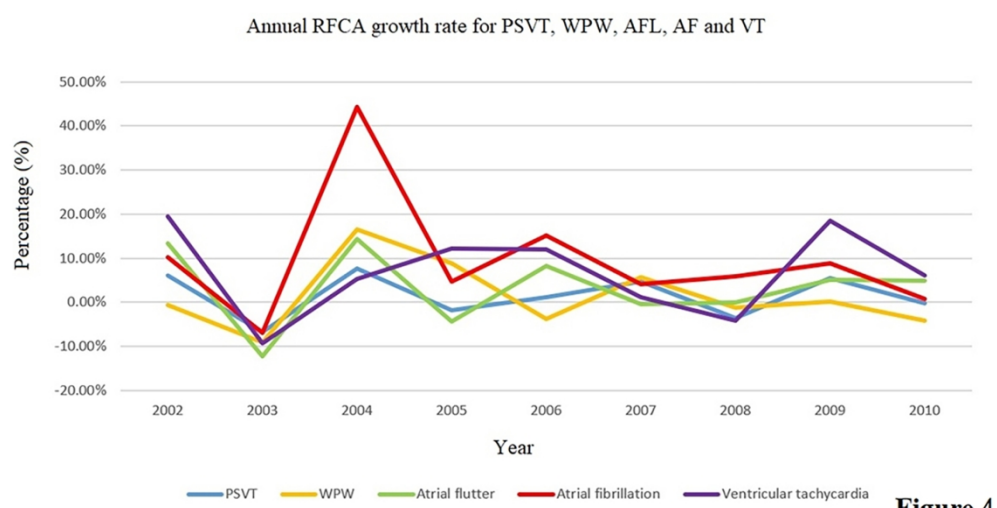


Figure 4

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

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Endocardial cushion defect	745.6
Congenital aortic stenosis	746.3

For peer review only

# BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023487.R1
Article Type:	Research
Date Submitted by the Author:	07-Dec-2018
Complete List of Authors:	Lin, Yuan; Chang-Gung Memorial Hospital, Keelung, Taiwan , Department of Emergency Medicine Wu, Hsin-Kuan; Chang-Gung Memorial Hospital, Keelung, Taiwan , Department of Emergency Medicine Wang, Te-Hsiung ; Kyoto University Hospital, Integrated Clinical Education Center Chen, Tien-Hsing; Chang-Gung Memorial Hospital, Keelung, Taiwan , Division of Cardiology, Department of Internal Medicine, Lin, Yu-Sheng; Chang-Gung Memorial Hospital, Chiayi, Taiwan, Division of Cardiology, Department of Internal Medicine,
<b>Primary Subject Heading</b>:	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

SCHOLARONE™  
Manuscripts



1  
2  
3 **Trend and Risk factors of Recurrence and Complications after Arrhythmias**  
4  
5 **Radiofrequency Catheter Ablation: A Nationwide Observational Study in Taiwan**  
6  
7  
8  
9

10 **Yuan Lin MD<sup>1#</sup>, Hsin-Kuan Wu MD<sup>1#</sup>, Te-Hsiung Wang MD<sup>2</sup>, Tien-Hsing Chen MD<sup>3\*</sup>,**  
11  
12 **Yu-Sheng Lin MD<sup>4\*</sup>**  
13  
14

- 15  
16  
17 **1. Department of Emergency Medicine, Chang-Gung Memorial Hospital, Keelung,**  
18 **Taiwan**  
19  
20 **2. Junior resident, Integrated Clinical Education Center, Kyoto University Hospital,**  
21 **Kyoto, Japan**  
22  
23 **3. Division of Cardiology, Department of Internal Medicine, Chang-Gung Memorial**  
24 **Hospital, Keelung, Taiwan**  
25  
26 **4. Division of Cardiology, Department of Internal Medicine, Chang-Gung Memorial**  
27 **Hospital, Chiayi, Taiwan**  
28  
29  
30  
31  
32  
33  
34

35 **#Yuan Lin and Hsin-Kuan Wu contributed equally to this study**  
36

37 **\* Tien-Hsing Chen and Yu-Sheng Lin contributed equally to this study**  
38  
39

40 **To whom correspondence and reprint requests should be addressed:**  
41

42 **Dr. Tien-Hsing Chen, Division of Cardiology, Department of Internal Medicine, Chang**  
43 **Gung Memorial Hospital, No. 5, Fu-Shin Street, Kweishan 333, Taoyuan, Taiwan.**  
44  
45

46 **TEL: +886-3-3281200-8116**  
47

48 **E-mail: skyheart0826@gmail.com**  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## 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<sup>1-3</sup>. RFCA, which has been widely applied since the 1990s<sup>4</sup>, 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

1  
2  
3 medication or observation for patients with PVST and WPW. RFCA was first used to treat AF  
4  
5 in 1998.  
6

7  
8 Although arrhythmias after RFCA are usually not life-threatening, identification and  
9  
10 minimization of the risk of complications are extremely important. The RFCA procedure may  
11  
12 lead to atrioventricular block (AV block) and bradycardia, even requiring permanent  
13  
14 pacemaker implantation. Previous studies<sup>5</sup> were composed of relatively small cohorts or were  
15  
16 single-center studies and evaluated patients with single arrhythmia<sup>5,6</sup>. However, there are no  
17  
18 studies comparing RFCA-related complications in patients with five different arrhythmias<sup>7,8</sup>.  
19  
20 The targets for RFCA-related risk minimization are different for different arrhythmias. For  
21  
22 example, when RFCA is used to treat PSVT, the goal is to modify or eliminate AV node or  
23  
24 accessory pathways, and when RFCA is used to treat AF<sup>6</sup>, the goal is to isolate the pulmonary  
25  
26 veins. High grade AV block, life-threatening pericardial effusion, and stroke are dangerous  
27  
28 complications after RFCA procedure. However, the complication rates vary in the five different  
29  
30 arrhythmias: PSVT, WPW, AFL, AF, and VT. It is therefore important to identify the incidence  
31  
32 and risk of RFCA-related complications in these patients.  
33  
34  
35  
36  
37

38 This retrospective study investigated the population trend of patients who received RFCA  
39  
40 for PSVT, WPW, AFL, AF, and VT. We identified the major RFCA-related risk factors  
41  
42 influencing 1) recurrence of arrhythmias, and 2) complications such as AV block, permanent  
43  
44 pacemaker implantation, life threatening pericardial effusion and acute ischemic stroke.  
45  
46  
47  
48

## 49 **Methods**

### 50 **Study design and population**

51  
52 We conducted a nationwide population-based cohort study using data from the Taiwan  
53  
54 NHIRD. In Taiwan, the National Health Insurance (NHI) program has reimbursed patients who  
55  
56 receive RFCA for PSVT, WPW syndrome, AFL, AF and VT since 2001. More than 99.91%  
57  
58  
59  
60

1  
2  
3 of Taiwan's population is covered by the NHI scheme. The accuracy and validation of National  
4 Health Insurance Research Database (NHIRD) data is based upon regular auditing by the NHI  
5 Bureau<sup>9-11</sup>. The Ethics Institutional Review Board at Chang Gung Memorial Hospital approved  
6 this study.  
7  
8  
9  
10  
11  
12  
13  
14

### 15 **Study cohort, outcome measurement and follow-up**

16  
17 This study accessed NHIRD data for all targeted arrhythmia patients who received  
18 RFCA from 2001 to 2010. The targeted arrhythmias were PSVT (Internal Classification of  
19 Diseases, Ninth Revision, ICD-9, Code 4270), WPW (426.7), AFL (427.32), AF (427.31), and  
20 VT (427.1; Supplemental Table). Patients with arrhythmias other than targeted arrhythmias  
21 (such as premature ventricular beats or atrial tachycardia) and patients with unidentified  
22 arrhythmias who received RFCA were excluded. For patients who received more than one time  
23 of RFCA, we enrolled first RFCA. The follow-up period was from the discharge date of index  
24 hospitalization until death, loss of follow-up (withdrawal from the NHI program: emigration  
25 or put into prison for longer than 6 months) or until 31st December 2010.  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40

### 41 **Outcome measurement**

42  
43 The primary outcomes included recurrence of arrhythmia, in-hospital complications  
44 and long-term complications. Recurrence was defined as either 1) recurrence of original  
45 arrhythmias, or 2) receiving secondary RFCA during the follow up. In-hospital complications  
46 included life threatening pericardial effusion and new-onset stroke during the admission. Life  
47 threatening pericardial effusion was defined as patient requiring pericardiocentesis during  
48 RFCA. New stroke was defined as stroke (ICD-9 CM codes: 430-437) which occurred during  
49 index admission. Long-term complications included High-grade AV block, high-grade AV  
50 block requiring permanent pacemaker implantation after RFCA during the follow up.  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## 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

1  
2  
3 used to investigate the association of clinical variables with time to event outcomes, including  
4 recurrence, high-grade AV block and pacemaker implantation during the follow up. In the  
5 survival analysis, the time-scale was time since RFCA (the follow up duration). The  
6 assumption of proportional hazard was tested by Schoenfeld partial residuals in which the  
7 indication was the only explanatory continuous variable. There were 13 pre-specified potential  
8 predictive variables which were consisted of two demographics (sex and age), six  
9 comorbidities, four types of congenital heart disease, and hospital volume. All these 13  
10 candidate predictive variables were introduced into the multivariable regression models.  
11 Multicollinearity among predictors was checked by variance inflation factor which a value less  
12 than 10 indicates there was no serious collinearity between the certain variable and other  
13 variables. Sensitivity analyses were done by excluding patients with recurrent RCFA during  
14 the follow up. A two-sided *P* value lower than 0.05 was considered statistically significant, and  
15 no adjustment for multiple testing (multiplicity) was made in this study. Results were presented  
16 as the odds ratio (OR) for logistic regression, or hazard ratio (HR) for Cox regression with  
17 corresponding 95% confidence intervals (CI). All data analyses were performed using SPSS  
18 software version 15 (SPSS Inc, Chicago, Illinois).

## 41 42 **Results**

43  
44  
45 There were 24,003 RFCA procedures registered in NHIRD between 1 January 2001  
46 and 31 December 2010. Based on the inclusion and exclusion criteria, a total of 19,475 patients  
47 were enrolled, who underwent 20,707 RFCA procedures. But only the first occurrence for each  
48 individual was used for analysis

49  
50  
51 A majority of the study participants were diagnosed with PSVT (N=12,796), followed by  
52 WPW (N=3,051), AFL (N=1,854), AF (N=1,162) and VT (N=612). The mean age of study  
53 participants when they received RFCA was 47.6 years (SD=18.3), and the average follow-up  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 period was 4.36 years (SD= 2.86). The ratio of changes in individual arrhythmias from 2001  
4 to 2010 is shown in Figure 1. The ratio of PSVT decreased from 60% to 51% between 2001 to  
5  
6  
7  
8 2010, while the ratio of AF increased from 2% to 10%. Demographic and baseline clinical  
9  
10 characteristics according to arrhythmia types are summarized in Table 1. The prevalence of  
11  
12 PSVT (38.5%), WPW (58.1%) and VT (47.2%) is highest in the group of age 19-44 years. The  
13  
14 prevalence of AF and AFL was 30.5% in patients aged 55–64, and 25.5% in patients aged 65–  
15  
16 74 years (25.5%). Patients with AF and AFL had a significantly higher prevalence of diabetes  
17  
18 (16.2% and 11.5%) and hypertension (28.9% and 28.1%) compared to patients with other  
19  
20 arrhythmias. Simple congenital heart disease was seen in 3.6% of patients with AFL.  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



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	<i>P</i> 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 <sup>‡</sup>	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 <sup>†</sup>	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

1  
2  
3 Abbreviation: RFCA = Radiofrequency catheter ablation; PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome;  
4 COPD = Chronic obstructive pulmonary disease; CKD = Chronic kidney disease; CAD = Coronary artery disease; CHD = Congenital heart defect; TOF =  
5 Tetralogy of Fallot; VSD = Ventricular septal defect; ASD = Atrial septal defect; Ebstein = Ebstein’s anomaly;  
6 ‡ defined as 100 volume per year;  
7 † There is a discrepancy between the sums of subgroups and the total due to one patient who might have two CHDs.  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

For peer review only

### 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 tachycardia (38 events, 5.7%)	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
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 (0.61–1.23)	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 (0.34–0.85)	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 (0.02–0.34)	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 (0.13–7.4)	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 (0.28–4.82)	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.

## 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.

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.

**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

Variable	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%)	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
<b>Age</b>								
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
<b>Indication</b>								
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 =

1  
2  
3 hazard ratio; CI = confidence interval; NA = not applicable.  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

For peer review only

6/bmjopen-2018-023487 on 30 May 2019. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.



## 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<sup>12</sup>. 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

1  
2  
3 year) of Taiwan during 1980 to 2000 decreased from 23 % to 13 %, reducing the number of  
4 patients needing PSVT and WPW. The number of WPW cases reached a peak in 2005 (N=  
5 377), and had been decreasing ever since. The number of procedures in the VT group has  
6 increased from 57 in 2001 to 123 in 2010, and the average RFCA growth rate over 10 years  
7 was 6.81%. This relatively high growth rate is possibly also due to population aging, and the  
8 maturation of 3D mapping techniques<sup>13</sup>. In summary, the growth models are different for the  
9 five arrhythmias. There has been a rapid increase in RFCA procedures in the AF and AFL  
10 groups because of the population aging. There has been a relatively slow increase in the PSVT  
11 group, while the WPW and VT groups showed stable or decreasing numbers of RFCA.  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

### 26 **Risk of recurrence**

27  
28 Our results showed that the recurrence rate after RFCA increased in the following order:  
29 PSVT (2%) < WPW (4.9%) < VT (5.7%) < AFL (5.8%) < AF (16.1%) (Figure 2). The  
30 recurrence-free rate was highest for the PSVT group (98.8% for the first year, gradually  
31 decreasing to 97.2% on the 10 years follow-up). However, patients in the PSVT and WPW  
32 groups < 18 years old had a significantly higher chance of recurrence, which agreed with  
33 previous results<sup>14</sup>. This could be because of the smaller cardiac anatomy in children, which  
34 makes it difficult to perform the precise ablation. This could also explain the association of  
35 congenital heart disease and TOF with recurrence of PSVT, possibly because of abnormal  
36 cardiac structure of congenital post-cardiac surgery. Patients with TOF and AF also had a  
37 higher risk of receiving a second RFCA. In contrast, AF and AFL patients had fewer second  
38 RFCA in the age group > 75-years-old<sup>15</sup>.  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53

54 Our data showed that patients > 75 years old receiving treatment for AF and AFL  
55 exhibited lower recurrence rates than the same age range in other groups. The reason may be  
56 caused by that cardiologists prefer conservative treatment for senior patients rather than  
57  
58  
59  
60

1  
2  
3 repeated RFCA in order to avoid complications or mortality after the first procedure due to  
4 other comorbidities. Our data suggested that for patients undergoing an elective RFCA,  
5 physicians need to carefully evaluate the risk factors such as younger age and presence of  
6 congenital heart disease (TOF in PSVT, VSD in AFL) which are associated with a high  
7 recurrence rate. Our study also described epidemiologic changes in repeated ablation  
8 procedures for five arrhythmias in Taiwan in the RFCA era.  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18

### 19 **Complications**

20  
21 RFCA, which has an approximately 1% complication rate and 0.1% mortality rate<sup>3,16</sup>,  
22 is considered a relatively safe procedure to treat or even cure arrhythmias (Table 3). Our present  
23 study showed different patterns of complications in the five arrhythmia groups. Patients with  
24 PSVT, and WPW had complication rates of 1.57% and 0.82%, respectively, similar to previous  
25 studies. However, in patients with AF and AFL, the complication rate was 2.50% and 4.74%.  
26 AFL after RFCA induced more high-grade AV block (2.53%) compared to other arrhythmias,  
27 and patients with AF RFCA had the highest incidence rate of life threatening pericardial  
28 effusion (1.30%). High-grade AV block is considered the main complication of ablation  
29 procedures for AFL and PSVT patients because the ablation sites are close to the  
30 atrioventricular node<sup>16</sup>. AFL has been seen combined with sick sinus syndrome.  
31 Bradyarrhythmias appeared when the substance of AF and AFL is eliminated. Patients with  
32 AF RFCA had a relatively higher risk of life threatening pericardial effusion than other  
33 arrhythmias, resulting in a relatively higher complication rate of 1.30%. The major mechanism  
34 of RFCA for AF is to isolate the pulmonary vein and eliminate the substrate in the left atrium.  
35 This requires a longer procedure time and delivers more energy to convert AF to sinus rhythm.  
36 RFCA for AF could therefore cause more life threatening pericardial effusion. RFCA for VT  
37 presents same pattern as that for PSVT and WPW pattern. These data suggested that although  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 RFCA is a common procedure to cure different arrhythmias, different complications should be  
4  
5 monitored in different arrhythmias.  
6  
7

8 Our data also showed that patients with AFL and AF had higher stroke rates (0.49%  
9 and 0.34%, respectively). Anticoagulation therapy is needed in these cases, and it is also  
10 necessary to confirm absence of intracardiac thrombus before RFCA <sup>17</sup>. However,  
11 anticoagulation procedures are sometimes ignored because anti-coagulation is not routinely  
12 used in AFL <sup>18</sup>. Previous studies have shown a high risk of thromboembolic events and a high  
13 incidence of thrombogenic milieu in AFL <sup>19,20</sup>. The inappropriate anticoagulation therapy is  
14 considered a significant risk for thromboembolism in patients with AFL<sup>18</sup>.  
15  
16  
17  
18  
19  
20  
21  
22  
23

24 Age was an important risk factor associated with complications such as High-grade AV  
25 block, pacemaker implantation, life threatening pericardial effusion and stroke especially in  
26 patients aged > 75-years old (Table 4). These data were consistent with previous studies <sup>21,22</sup>,  
27 and suggested that physicians should be cautious when performing RFCA in patients >75 years  
28 old. We also found that diabetes was associated with increased complication rates for RFCA.  
29 A cohort study of 200,000 patients with type II diabetes reported that third degree AV block  
30 was prevalent in subjects with diabetes <sup>23</sup>. Diabetes has been suggested as a risk factor for  
31 autonomic neuropathy, cardiac conduction abnormalities and bradyarrhythmias <sup>24</sup>. When  
32 physicians perform RFCA on diabetic patients, they should monitor for bradyarrhythmia  
33 complications  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

## 50 **Limitations**

51 This study had several limitations.

52  
53 Firstly, the major limitation of this study is that we were not able to explore the  
54 interactions among the predictive variables because of the limited number of events. For  
55 instance, the number of high-grade AVB was 184 events and may allow a maximum of 18-19  
56  
57  
58  
59  
60

1  
2  
3 predictive variables due to the “ten-one rule”<sup>25-27</sup>. However, there were 13 predictors so that  
4  
5 78 two-way potential interaction effect might exist. Therefore, it seems not feasible to perform  
6  
7 a regression analysis (logistic or Cox regressions) with so many explanatory variables in the  
8  
9 equation which would induce a statistical problem of overfitting. Secondly, in this cohort study  
10  
11 we did not have access to laboratory parameters, procedural details, heart images, and smoking  
12  
13 status, obesity, alcoholism, and the costs. Procedure-related parameters, location of accessory  
14  
15 pathway in WPW, PV isolation for AF, and cardiac anomaly, ejection fraction have been  
16  
17 reported as predictors for arrhythmia recurrence and RFCA complication<sup>14, 28-30</sup>. The lack of  
18  
19 these information could induce residual confounding, especially with the results of age.  
20  
21 However, the present study focused on RFCA for five different arrhythmias and each  
22  
23 arrhythmia had different surgical parameters. Rather than comparing the same parameter in  
24  
25 different arrhythmia ablation procedures, we focused on the effect of comorbidities, gender and  
26  
27 age on arrhythmia recurrence, and RFCA-related complications. Our study provided valuable  
28  
29 information for cardiologists to help deal with RFCA recurrence and complications. Thirdly,  
30  
31 some arrhythmias such as premature ventricular beats, and atrial premature beats are not  
32  
33 covered by Taiwan NHI. However, excluding these arrhythmias did not influence the study  
34  
35 results since they are usually benign. Lastly, recurrence may be misidentified as resulting  
36  
37 from ablation of other arrhythmias in this present study. For example, this could happen if the  
38  
39 patient had an initial PSVT ablation followed by atrial fibrillation ablation. A single definition  
40  
41 of recurrence could consider the second ablation as recurrence of PSVT. Use of double criteria,  
42  
43 with repeated ablation combined with the same major principal diagnosis, reduced the coding  
44  
45 error in this study.  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55

## 56 **Conclusions**

57  
58  
59  
60

1  
2  
3 There was a rapidly increasing trend of RFCA procedures for AF, AFL, and VT during  
4  
5 2001-2010, but a slow increase for PSVT and WPW. The recurrence-free rate of PSVT was  
6  
7 higher than other arrhythmias. Elderly patients with AF and AFL RFCA had fewer repeated  
8  
9 procedures and AF patient in high-activity center hospitals had more repeated RFCA.  
10  
11 Congenital heart disease was a risk factor of PSVT recurrence. AF RFCA patients had more  
12  
13 life-threatening pericardial effusion especially age more than 65, and patients receiving AFL  
14  
15 RFCA suffered from bradycardia requiring permanent pacemaker implantation.  
16  
17  
18  
19  
20  
21

### 22 **Contributors:**

23  
24 CHEN conceived of the study. Y LIN and WU initiated the study design and WANG helped  
25  
26 with implementation. Y LIN, WU and CHEN provided statistical expertise in clinical trial  
27  
28 design and WANG and YS LIN are conducting the primary statistical analysis. All authors  
29  
30 contributed to refinement of the study protocol and approved the final manuscript.  
31  
32

### 33 **Funding:**

34  
35 This article has NO affiliations with or involvement in any organization or entity with any  
36  
37 financial interest (such as honoraria; educational grants; participation in speakers' bureaus;  
38  
39 membership, employment, consultancies, stock ownership, or other equity interest; and expert  
40  
41 testimony or patent-licensing arrangements), or non-financial interest (such as personal or  
42  
43 professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials  
44  
45 discussed in this manuscript.  
46  
47  
48

### 49 **Disclaimer:**

50  
51 The leading author confirms that the content of this manuscript is honest and transparent.  
52  
53

### 54 **Competing interests:**

55  
56 None declared.  
57

### 58 **Patient consent:**

1  
2  
3 Not required.  
4

5 **Ethics approval:**  
6

7 The Ethics Institutional Review Board at Chang Gung Memorial Hospital approved this study.  
8  
9

10 **Data sharing statement:**  
11

12 Data are available. Please contact corresponding author.  
13  
14  
15  
16

17 **References**  
18

- 19 1. O'Hara GE, Philippon F, Champagne J, *et al*. Catheter ablation for cardiac arrhythmias: a  
20 14-year experience with 5330 consecutive patients at the Quebec Heart Institute, Laval  
21 Hospital. *Can J Cardiol* 2009;25:140.  
22  
23 2. Spector P, Reynolds MR, Calkins H, *et al*. Meta-analysis of ablation of atrial flutter and  
24 supraventricular tachycardia. *Am J Cardiol* 2009;104:671-7.  
25  
26 3. Bohnen M, Stevenson WG, Tedrow UB, *et al*. Incidence and predictors of major  
27 complications from contemporary catheter ablation to treat cardiac arrhythmias. *Heart rhythm*  
28 2011;8:1661-6.  
29  
30 4. Joseph JP, Rajappan K. Radiofrequency ablation of cardiac arrhythmias: past, present and  
31 future. *QJM* 2012;105:303-14.  
32  
33 5. Cosío FG. Atrial flutter, typical and atypical: a review. *Arrhythm Electrophysiol Rev*  
34 2017;6:55-62.  
35  
36 6. Nyong J, Amit G, Adler AJ, *et al*. Efficacy and safety of ablation for people with non-  
37 paroxysmal atrial fibrillation. *Cochrane Database Syst Rev* 2016;11:CD012088.  
38  
39 7. Pérez FJ, Schubert CM, Parvez B, *et al*. Long-term outcomes after catheter ablation of cavo-  
40 tricuspid isthmus dependent atrial flutter: a meta-analysis. *Circ Arrhythm Electrophysiol*  
41 2009;2:393-401.  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 8. Cappato R, Calkins H, Chen SA, *et al.* Updated worldwide survey on the methods, efficacy,  
4 and safety of catheter ablation for human atrial fibrillation. *Circulation* 2010;3:32-8.  
5  
6
- 7 9. Yang YW, Chen YH, Xirasagar S, *et al.* Increased risk of stroke in patients with bullous  
8 pemphigoid: a population-based follow-up study. *Stroke* 2011;42:319-23.  
9  
10
- 11 10. Wu CY, Wu MS, Kuo KN, *et al.* Effective reduction of gastric cancer risk with regular use  
12 of nonsteroidal anti-inflammatory drugs in Helicobacter pylori-infected patients. *J Clin Oncol*  
13 2010;28:2952-7.  
14  
15
- 16 11. Wu CY, Chen YJ, Ho HJ, *et al.* Association between nucleoside analogues and risk of  
17 hepatitis B virus-related hepatocellular carcinoma recurrence following liver resection. *JAMA*  
18 2012;308:1906-14.  
19  
20
- 21 12. Feinberg WM, Blackshear JL, Laupacis A, *et al.* Prevalence, age distribution, and gender  
22 of patients with atrial fibrillation Analysis and implications. *Arch Intern Med* 1995;155:469-  
23 73.  
24  
25
- 26 13. Dixit S, Callans DJ. Mapping for ventricular tachycardia. *Card Electrophysiol Rev*  
27 2002;6:436-41.  
28  
29
- 30 14. Van Hare GF, Javitz H, Carmelli D, *et al.* Prospective assessment after pediatric cardiac  
31 ablation: recurrence at 1 year after initially successful ablation of supraventricular tachycardia.  
32 *Heart rhythm* 2004;1:188-96.  
33  
34
- 35 15. Tuan TC, Chang SL, Tsao HM, *et al.* The impact of age on the electroanatomical  
36 characteristics and outcome of catheter ablation in patients with atrial fibrillation. *J Cardiovasc*  
37 *Electrophysiol* 2010;21:966-72.  
38  
39
- 40 16. Walters TE, Kistler PM, Kalman JM. Radiofrequency ablation for atrial tachycardia and  
41 atrial flutter. *Heart Lung Circ* 2012;21:386-94.  
42  
43
- 44 17. Calkins H, Kuck KH, Cappato R, *et al.* 2012 HRS/EHRA/ECAS expert consensus  
45 statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3 selection, procedural techniques, patient management and follow-up, definitions, endpoints,  
4 and research trial design. *J Interv Card Electrophysiol* 2012;33:171-257.

5  
6  
7  
8 18. Grönefeld GC, Wegener F, Israel CW, *et al*. Thromboembolic risk of patients referred for  
9 radiofrequency catheter ablation of typical atrial flutter without prior appropriate  
10 anticoagulation therapy. *Pacing Clin Electrophysiol* 2003;26:323-7.

11  
12  
13  
14 19. Wood KA, Eisenberg SJ, Kalman JM, *et al*. Risk of thromboembolism in chronic atrial  
15 flutter. *Am J Cardiol* 1997;79:1043-7.

16  
17  
18  
19 20. Alyeshmerni D, Pirmohamed A, Barac A, *et al*. Transesophageal echocardiographic  
20 screening before atrial flutter ablation: is it necessary for patient safety? *J Am Soc Echocardiogr*  
21 2013;26:1099-105.

22  
23  
24  
25 21. Hoffmann BA, Brachmann J, Andresen D, *et al*. Ablation of atrioventricular nodal  
26 reentrant tachycardia in the elderly: results from the German Ablation Registry. *Heart rhythm*  
27 2011;8:981-7.

28  
29  
30  
31 22. Mirza M, Strunets A, Shen WK, *et al*. Mechanisms of arrhythmias and conduction  
32 disorders in older adults. *Clin Geriatr Med* 2012;28:555-73.

33  
34  
35  
36 23. Movahed MR, Hashemzadeh M, Jamal MM. Increased prevalence of third-degree  
37 atrioventricular block in patients with type II diabetes mellitus. *Chest* 2005;128:2611-4.

38  
39  
40  
41 24. Movahed MR. Diabetes as a risk factor for cardiac conduction defects: a review. *Diabetes*  
42 *Obes Metab* 2007;9:276-81.

43  
44  
45  
46 25. Peduzzi P, Concato J, Kemper E, *et al*. A simulation study of the number of events per  
47 variable in logistic regression analysis. *J Clin Epidemiol* 1996;49:1373-9.

48  
49  
50  
51 26. Concato J, Peduzzi P, Holford TR, *et al*. Importance of events per independent variable in  
52 proportional hazards analysis I. Background, goals, and general strategy. *J Clin Epidemiol*  
53 1995;48:1495-501.

- 1  
2  
3 27. Peduzzi P, Concato J, Feinstein AR, *et al.* Importance of events per independent variable  
4 in proportional hazards regression analysis II. Accuracy and precision of regression  
5 estimates. *J Clin Epidemiol* 1995;48:1503-10.  
6  
7  
8  
9  
10 28. Adao L, Araujo C, Sa AP, *et al.* Importancia da posicao anatomica da via acessoria na  
11 eficacia e na seguranca da ablacao por radiofrequencia. *Rev Port Cardiol* 2011;30:35-46.  
12  
13 29. Iturralde P, Guevara-Valdivia M, Rodríguez-Chávez L, *et al.* Radiofrequency ablation of  
14 multiple accessory pathways. *Europace* 2002;4:273-80.  
15  
16  
17 30. Anselmino M, Grossi S, Scaglione M, *et al.* Long-term results of transcatheter atrial  
18 fibrillation ablation in patients with impaired left ventricular systolic function. *J Cardiovasc*  
19 *Electrophysiol* 2013;24:24-32.  
20  
21  
22  
23  
24  
25  
26  
27

## 28 **Figure Legends**

29  
30  
31 Figure 1. Proportion of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White  
32 Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia in Taiwan during 2001  
33 and 2010  
34  
35

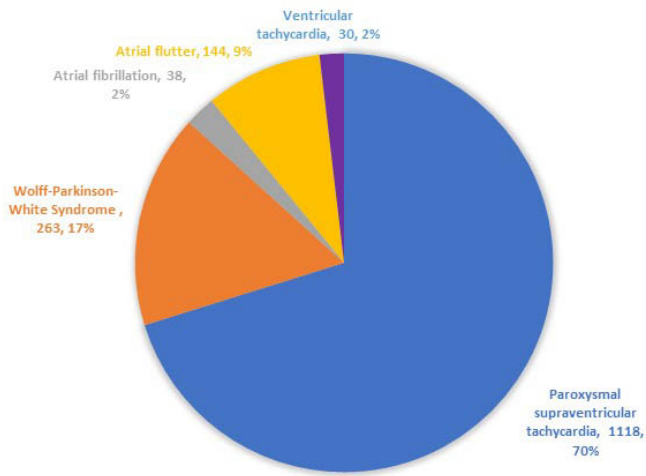
36  
37  
38 Figure 2. Recurrence-free survival curves for Paroxysmal supraventricular tachycardia, Wolff-  
39 Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia  
40

41  
42 Figure 3. Number of radiofrequency catheter ablation annually in the paroxysmal  
43 supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation  
44 and ventricular tachycardia groups  
45  
46  
47

48  
49 Figure 4. Annual radiofrequency catheter ablation growth rate for the paroxysmal  
50 supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation  
51 and ventricular tachycardia groups  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

THE RATIO OF FIVE ARRHYTHMIA IN 2001



THE RATIO OF FIVE ARRHYTHMIA IN 2010

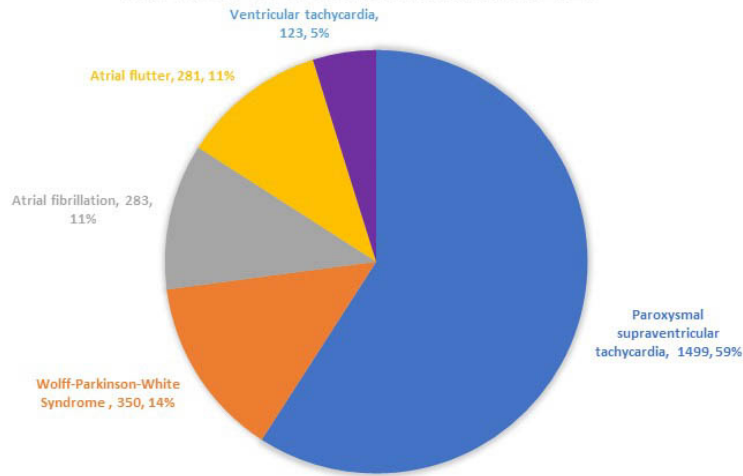


figure 1

60x88mm (300 x 300 DPI)

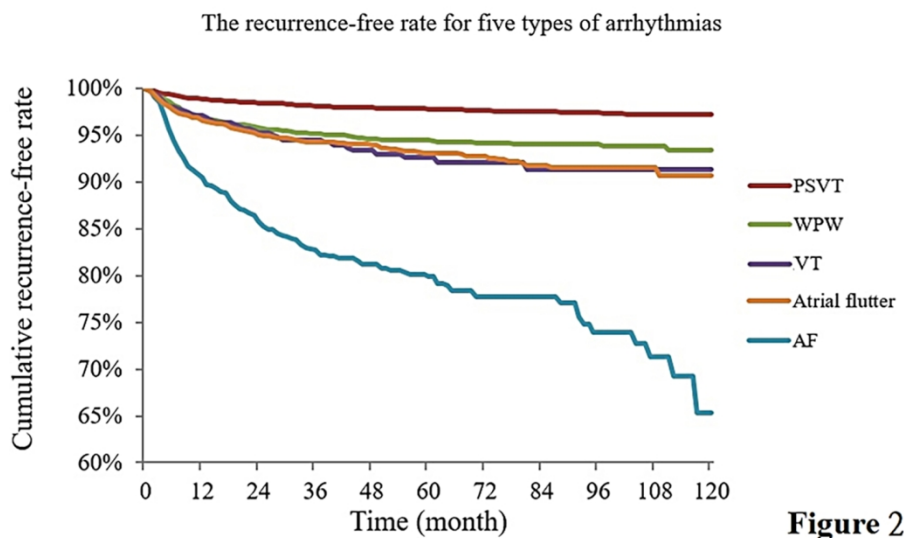


Figure 2

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

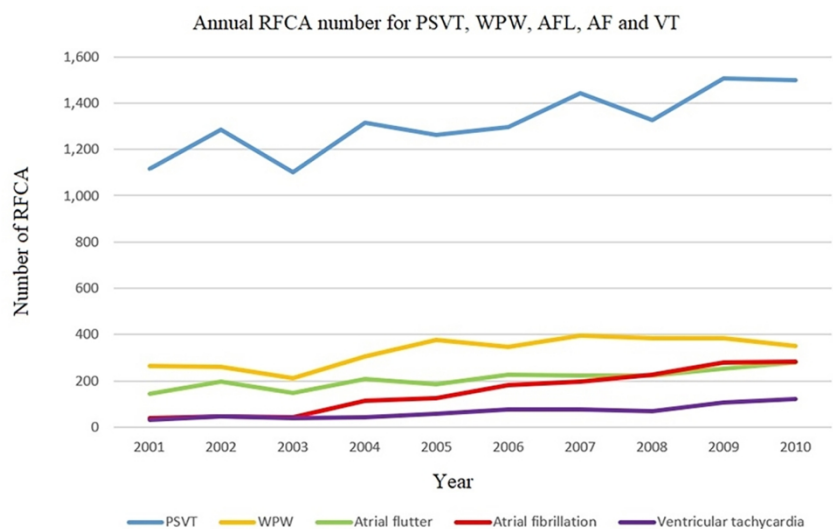
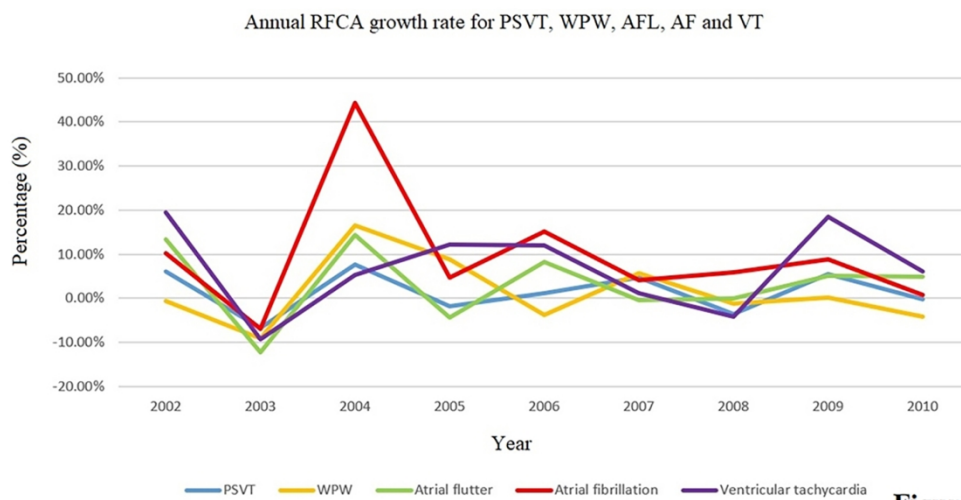


Figure 3

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

160x90mm (300 x 300 DPI)



**Figure 4**

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

Variable	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%)	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
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

1  
2  
3 PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White syndrome; OR = odds ratio; HR = hazard ratio; CI =  
4 confidence interval; NA = not applicable.  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

For peer review only

## STROBE Statement

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

Section/Topic	Item No	Recommendation	Reported on Page No
<b>Title and abstract</b>	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
<b>Introduction</b>			
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
<b>Methods</b>			
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
		(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
		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
		(a) Describe all statistical methods, including those used to control for confounding	6,7
Statistical methods	12	(b) Describe any methods used to examine subgroups and interactions	6,7
		(c) Explain how missing data were addressed	7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —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
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, excluded 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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	10, 11, 13
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —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	
<b>Discussion</b>			
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
<b>Other Information</b>			
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](http://www.strobe-statement.org).

For peer review only

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

# BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023487.R2
Article Type:	Research
Date Submitted by the Author:	21-Feb-2019
Complete List of Authors:	Lin, Yuan; Chang Gung Memorial Hospital Keelung Branch, Emergency Medicine department Wu, Hsin-Kuan; Chang Gung Memorial Hospital Keelung Branch, Emergency Medicine department Wang, Te-Hsiung ; Kyoto University Hospital, Integrated Clinical Education Center Chen, Tien-Hsing; Chang Gung Memorial Hospital Keelung Branch, Division of Cardiology, Department of Internal Medicine Lin, Yu-Sheng; Chiayi Chang Gung Memorial Hospital, Division of Cardiology, Department of Internal Medicine
<b>Primary Subject Heading</b>:	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

SCHOLARONE™  
Manuscripts

1  
2  
3 **Trend and Risk Factors of Recurrence and Complications after Arrhythmias**  
4 **Radiofrequency Catheter Ablation: A Nationwide Observational Study in Taiwan**  
5  
6  
7  
8  
9

10 **Yuan Lin MD<sup>1#</sup>, Hsin-Kuan Wu MD<sup>1#</sup>, Te-Hsiung Wang MD<sup>2</sup>, Tien-Hsing Chen MD<sup>3\*</sup>,**  
11 **Yu-Sheng Lin MD<sup>4\*</sup>**  
12  
13  
14

- 15  
16  
17 **1. Department of Emergency Medicine, Chang-Gung Memorial Hospital, Keelung,**  
18 **Taiwan**  
19  
20 **2. Junior resident, Integrated Clinical Education Center, Kyoto University Hospital,**  
21 **Kyoto, Japan**  
22  
23 **3. Division of Cardiology, Department of Internal Medicine, Chang-Gung Memorial**  
24 **Hospital, Keelung, Taiwan**  
25  
26 **4. Division of Cardiology, Department of Internal Medicine, Chang-Gung Memorial**  
27 **Hospital, Chiayi, Taiwan**  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**#Yuan Lin and Hsin-Kuan Wu contributed equally to this study**

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

**To whom correspondence and reprint requests should be addressed:**

**Dr. Tien-Hsing Chen,**

**Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial  
Hospital, No. 5, Fu-Shin Street, Kweishan 333, Taoyuan, Taiwan.**

**TEL: +886-3-3281200-8116**

**E-mail: skyheart0826@gmail.com**

## 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).<sup>1-3</sup> Widely applied since the 1990s,<sup>4</sup> 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.

1  
2  
3 Although arrhythmias after RFCA are usually not life-threatening, identification and  
4 minimization of the risk of complications are extremely important. The RFCA procedure may  
5 lead to atrioventricular (AV) block and bradycardia, even requiring permanent pacemaker  
6 implantation. Previous studies<sup>5</sup> were composed of relatively small cohorts or were single-  
7 center studies and evaluated patients with a single arrhythmia.<sup>5,6</sup> However, there are no studies  
8 comparing RFCA-related complications in patients with five different arrhythmias.<sup>7,8</sup> The  
9 targets for RFCA-related risk minimization differ by type of arrhythmia. For example, when  
10 RFCA is used to treat PSVT, the goal is to modify or eliminate AV node or accessory pathways;  
11 when used to treat AF,<sup>6</sup> the goal is to isolate the pulmonary veins. High grade AV block, life-  
12 threatening pericardial effusion, and stroke are dangerous complications after an RFCA  
13 procedure. However, the complication rates vary by type of arrhythmia: PSVT, Wolff-  
14 Parkinson-White Syndrome (WPW), atrial flutter (AFL), AF and VT. It is therefore important  
15 to identify the incidence and risk factors of RFCA-related complications in these patients.  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32

33 This retrospective study investigated the population trend of patients who received RFCA  
34 for PSVT, WPW, AFL, AF and VT. We identified the major RFCA-related risk factors  
35 influencing 1) recurrence of arrhythmias and 2) complications such as AV block, permanent  
36 pacemaker implantation, life-threatening pericardial effusion and acute ischemic stroke.  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

## 47 **Methods**

### 48 **Study design and population**

49  
50 We conducted a nationwide population-based cohort study using data from the Taiwan  
51 National Health Insurance Research Database (NHIRD). In Taiwan, the National Health  
52 Insurance (NHI) program has reimbursed patients who receive RFCA for PSVT, WPW, AFL,  
53 AF and VT since 2001. More than 99.91% of Taiwan's population is covered by NHI benefits.  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 The accuracy and validation of NHIRD data is based upon regular auditing by the NHI  
4 Bureau.<sup>9-11</sup> The Institutional Review Board of Chang Gung Memorial Hospital approved this  
5  
6 study.  
7  
8  
9

### 10 11 12 **Study cohort, outcome measurement and follow-up**

13  
14 This study accessed NHIRD data for all targeted arrhythmia patients who received  
15 RFCA from 2001 to 2010. The targeted arrhythmias were PSVT (International Classification  
16 of Diseases, Ninth Revision, Clinical Modification [ICD-9 CM] Code 4270), WPW (426.7),  
17 AFL (427.32), AF (427.31) and VT (427.1; Supplemental Table 1). Patients with arrhythmias  
18 other than those targeted (such as premature ventricular beats or atrial tachycardia) and patients  
19 with unidentified arrhythmias who received RFCA were excluded. We enrolled only the  
20 patient's first RFCA. The follow-up period was calculated from the discharge date of the index  
21 hospitalization until death, loss to follow up (withdrawal from the NHI program: emigration or  
22 prison incarceration for longer than six months) or until the study end date (31 December 2010).  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37

### 38 **Outcomes measurement**

39  
40 The primary outcomes included recurrence of arrhythmia, in-hospital complications  
41 and long-term complications. Recurrence was defined as either 1) recurrence of original  
42 arrhythmia or 2) receipt of a second RFCA during the follow up period. In-hospital  
43 complications included life-threatening pericardial effusion and new-onset stroke during the  
44 admission. Life-threatening pericardial effusion was defined as the patient requiring  
45 pericardiocentesis during RFCA. New stroke was defined as stroke (ICD-9 CM codes 430-  
46 437) which occurred during the index admission. Other complications included high-grade AV  
47 block and permanent pacemaker implantation.  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57

### 58 **Covariate assessment**

1  
2  
3 Age was categorized into six groups (0-18, 19-44, 45-54, 55-64, 65-74 and 75 years  
4 and above) because previous studies reported different indications for RFCA and different  
5 complications between age groups.<sup>1-3</sup> Comorbidities were assessed according to ICD-9 CM  
6 codes before the index admission. Diabetes mellitus, hypertension (HTN) or chronic diseases  
7 were recorded as comorbidities if there was at least one in-admission diagnosis. All congenital  
8 heart disease (CHD) was reconfirmed by the Catastrophic Illness Certification (CIC), which is  
9 a sub-dataset of NHI. A CIC for CHD requires imaging proof confirmed by two cardiologists.  
10 Complicated CHD included Tetralogy of Fallot (TOF), transposition of the great vessels,  
11 double outlet right ventricle, total anomalous pulmonary venous connection, tricuspid atresia,  
12 common truncus arteriosus, common ventricle and hypoplastic left heart syndrome. Simple  
13 CHD included ventricular septal defect (VSD), atrial septal defect (ASD), Ebstein's anomaly,  
14 patent ductus arteriosus, congenital pulmonary stenosis, coarctation of the aorta, endocardial  
15 cushion defect and congenital aortic stenosis. Center activity was a time-dependent variable  
16 and a high-activity center was defined as more than 100 RFCA surgeries per year, regardless  
17 of arrhythmia type.  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39

#### 40 **Patient and public involvement**

41  
42 This study had no direct relationship with any patient and no public involvement during  
43 the development, design and conduct.  
44  
45  
46  
47  
48

#### 49 **Statistical analysis**

50  
51 The proportion of categorical variables between groups was compared using the chi-  
52 squared test and Fisher's exact test. Continuous variables were compared using Kruskal-Wallis  
53 test due to the lack of normality. Multivariable logistic regression analysis was used to identify  
54 clinical features associated with the risk of in-hospital complications, including life-threatening  
55  
56  
57  
58  
59  
60

1  
2  
3 pericardial effusion and new-onset stroke during the admission. Multivariable Cox regression  
4 analysis was used to investigate the association of clinical variables with time-to-event  
5 outcomes, including recurrence, high-grade AV block and pacemaker implantation during the  
6 follow up. In the survival analysis, the time-scale was time since RFCA in days. The  
7 assumption of proportional hazard was tested by Schoenfeld partial residuals, in which the  
8 indication was the only explanatory categorical variable. The 13 pre-specified potential  
9 predictive variables were those clinically relevant to RFCA and its complications: two  
10 demographic variables (sex and age), six comorbidities, four types of CHD and hospital volume.  
11 All 13 candidate predictive variables were introduced into the multivariable regression models.  
12 Multicollinearity among predictors was checked by variance inflation factor, with a value less  
13 than 10 indicating no serious collinearity among predictors. Sensitivity analyses were done by  
14 excluding patients with recurrent RCFA during the follow up (Supplemental Table 2). A two-  
15 sided *P* value lower than 0.05 was considered statistically significant. No adjustment for  
16 multiple testing (multiplicity) was made in this study to avoid the low statistical power. Results  
17 were presented as the odds ratio (OR) for logistic regression, or hazard ratio (HR) for Cox  
18 regression with corresponding 95% confidence intervals (CI). All data analyses were  
19 performed using SPSS software version 15 (SPSS Inc., Chicago, IL, USA).  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

## 47 **Results**

48  
49  
50 There were 24,003 RFCA procedures registered in NHIRD between 1 January 2001  
51 and 31 December 2010. Based on the inclusion and exclusion criteria, a total of 19,475 enrolled  
52 patients underwent 20,707 RFCA procedures. Only the first occurrence for each individual was  
53 used for analysis. The proportion of change in rates of RFCA by individual arrhythmias from  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 2001 to 2010 is shown in Figure 1. The proportion of RFCA for PSVT decreased from 60% to  
4 51% between 2001 to 2010, while the proportion for AF increased from 2% to 10% (Figure 1).  
5  
6

7 The commonest arrhythmia treated with RFCA was PSVT (n=12796; 56.7%), followed  
8 by WPW (n=3051; 13.5%), AFL (n=1854; 9.5%), AF (n=1162; 5.1%) and VT (n=612; 2.7%).  
9  
10 The mean age of study participants when they received RFCA was 47.6 years (standard  
11 deviation [SD] 18.3). Demographic and baseline clinical characteristics according to  
12 arrhythmia type are summarized in Table 1. The prevalence of PSVT (38.5%), WPW (58.1%)  
13 and VT (47.2%) was highest in the group aged 19-44 years. Patients were the oldest in the AFL  
14 group, followed by the AF group, the PSVT group, the VT group and the WPW group. Patients  
15 with AF and AFL had a higher prevalence of diabetes (16.2% and 11.5%, respectively) and  
16 hypertension (28.9% and 28.1%, respectively) compared to patients with other arrhythmias.  
17 Chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and heart  
18 failure were most prevalent in the AFL group since these patients were the oldest (median age  
19 62.9 years). RFCA due to AF was predominantly performed in high-activity centers (84%),  
20 followed by AFL (71%). Complicated CHD was more common in the AFL group than in other  
21 arrhythmias. Simple CHD was most prevalent in the AFL group (3.6%), followed by the VT  
22 group (1.5%).  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

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

Variable	PSVT	WPW	AFL	AF	VT	<i>P</i> 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 <sup>‡</sup>	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 <sup>†</sup>	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

1  
2  
3 Abbreviations: RFCA = Radiofrequency catheter ablation; PSVT = Paroxysmal supraventricular tachycardia; WPW = Wolff–Parkinson–White Syndrome;  
4 AFL = Atrial flutter; AF = Atrial fibrillation; VT = Ventricular tachycardia; Yrs = years; IQR = Interquartile range; COPD = Chronic obstructive pulmonary  
5 disease; CKD = Chronic kidney disease; CAD = Coronary artery disease; CHD = Congenital heart disease; TOF = Tetralogy of Fallot; VSD = Ventricular  
6 septal defect; ASD = Atrial septal defect; Ebstein = Ebstein’s anomaly.

7  
8 ‡ defined as 100 operations per year.

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

10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

For peer review only



## 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 RFCA during the follow up (Supplemental Table 3).

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

Variable	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%)	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
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 (0.61–1.23)	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 (0.34–0.85)	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).<sup>3</sup> As to long-term complications, multivariable Cox regression identified the risk factors for high-grade AV block as age  $\geq 75$  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  $\geq 75$  years, diabetes, CKD and RFCA after AFL (when compared with PSVT). The results were similar when excluding patients with recurrent RFCA 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.

Variable	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, 0.8%)		Pacemaker (100 events, 0.48%)	
	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.<sup>12</sup> 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

1  
2  
3 PSVT and WPW. The number of WPW cases peaked in 2005 (N= 377) and has since been  
4 decreasing. The number of procedures in the VT group increased from 57 in 2001 to 123 in  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

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.<sup>13</sup> 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.<sup>14</sup> 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  $\geq 75$  years had fewer second RFCAs than younger patients.<sup>15</sup>

Our data showed that patients  $\geq 75$  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



1  
2  
3 of other comorbidities. Our data suggest that, for patients undergoing an elective RFCA,  
4 physicians should carefully evaluate the risk factors such as younger age and the presence of  
5 CHD (TOF in PSVT, VSD in AFL) which are associated with a high recurrence rate. Our study  
6 also described epidemiologic changes in repeated ablation procedures for five arrhythmias in  
7 Taiwan in the RFCA era.  
8  
9  
10  
11  
12  
13  
14  
15  
16

### 17 **Complications**

18  
19 RFCA, which has an approximately 1% complication rate and 0.1% mortality rate,<sup>3,16</sup>  
20 is considered a relatively safe procedure to treat or even cure arrhythmias (Table 3). Our present  
21 study showed different patterns of complications in the five arrhythmia groups. Patients with  
22 PSVT and WPW had complication rates of 1.6% and 0.8%, respectively, similar to previous  
23 studies. However, in patients with AF and AFL, the complication rates were 2.5% and 4.7%,  
24 respectively. AFL after RFCA induced more high-grade AV block (2.5%) compared to other  
25 arrhythmias, and patients with AF after RFCA had the highest incidence rate of life-threatening  
26 pericardial effusion (1.3%). High-grade AV block is considered the main complication of  
27 ablation procedures for AFL and PSVT patients because the ablation sites are close to the  
28 atrioventricular node.<sup>16</sup> AFL has been seen combined with sick sinus syndrome.  
29 Bradyarrhythmias appeared when the substance of AF and AFL is eliminated. RFCA patients  
30 with AF had a higher risk of life-threatening pericardial effusion relative to patients with other  
31 arrhythmias, resulting in a relatively higher complication rate of 1.3%. The major RFCA  
32 procedure for AF is to isolate the pulmonary vein and eliminate the substrate in the left atrium.  
33 This requires a longer procedure time and delivers more energy to convert AF into sinus rhythm.  
34 RFCA for AF could therefore cause more life-threatening pericardial effusion than that for  
35 other arrhythmias. RFCA for VT presents same pattern as that for PSVT and WPW. These data  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 suggest that, although RFCA is a common procedure to treat different arrhythmias, the  
4 complications that should be monitored will differ by type of arrhythmia.  
5  
6

7  
8 Our data also showed that patients with AFL and AF had higher stroke rates (0.49%  
9 and 0.34%, respectively) than patients in the other groups. Anticoagulation therapy is needed  
10 in these cases, and it is also necessary to confirm the absence of intracardiac thrombus before  
11 RFCA.<sup>17</sup> However, anticoagulation procedures are sometimes ignored because anti-  
12 coagulation is not routinely used in AFL.<sup>18</sup> Previous studies have shown a high risk of  
13 thromboembolic events and a high incidence of thrombogenic milieu in AFL.<sup>19,20</sup> Use of the  
14 inappropriate anticoagulation therapy is considered a significant risk factor for  
15 thromboembolism in patients with AFL.<sup>18</sup>  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

26 Age was an important risk factor associated with complications such as high-grade AV  
27 block, pacemaker implantation, life-threatening pericardial effusion and stroke, especially in  
28 patients aged  $\geq 75$  years (Table 4). These data were consistent with previous studies,<sup>21,22</sup> and  
29 suggest that physicians should be cautious when performing RFCA in patients  $\geq 75$  years. We  
30 also found that diabetes was associated with increased complication rates for RFCA. A cohort  
31 study of 200,000 patients with type II diabetes reported that third degree AV block was 3.1  
32 times as prevalent in the diabetic group (95% CI, 3.0-3.3;  $p < 0.0001$ ).<sup>23</sup> Diabetes has been  
33 suggested as a risk factor for autonomic neuropathy, cardiac conduction abnormalities and  
34 bradyarrhythmias.<sup>24</sup> Physicians performing RFCA in diabetic patients should monitor for  
35 bradyarrhythmia complications.  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50

## 51 **Limitations**

52  
53  
54 Firstly, the major limitation of this study is our inability to explore the interactions  
55 among the predictive variables because of the limited number of events. For instance, the 184  
56 high-grade AV blocks allow for a maximum of 18-19 predictive variables, due to the “ten-one  
57  
58  
59  
60

1  
2  
3 rule.<sup>25-27</sup> However, the 13 predictors indicate that 78 two-way potential interaction effects may  
4 exist. Therefore, it seems not feasible to perform a regression analysis (logistic or Cox  
5 regressions) because that many explanatory variables in the equation would induce the  
6 statistical problem of overfitting. Therefore, further studies with a larger sample size are needed  
7 to conduct interaction tests based on clinical knowledge or on exploratory data analysis.  
8  
9  
10  
11  
12  
13

14 Secondly, in this cohort study we did not have access to laboratory parameters,  
15 procedural details, heart images, smoking status, obesity, alcohol use or costs. Procedure-  
16 related parameters, the location of the accessory pathway in WPW, PV isolation for AF, cardiac  
17 anomaly and ejection fraction have been reported as predictors for arrhythmia recurrence and  
18 RFCA complications.<sup>14, 28-30</sup> The lack of this information could induce residual confounding.  
19 On the other hand, the different arrhythmia groups had substantial differences in baseline  
20 characteristics, especially in terms of age, which may result in potential confounding even if  
21 we adjusted for these variables in the multivariable regression models. However, the present  
22 study focused on RFCA for five different arrhythmias and each arrhythmia had different  
23 surgical parameters. Rather than comparing the same parameter in different arrhythmia  
24 ablation procedures, we focused on the effect of comorbidities, gender and age on arrhythmia  
25 recurrence and RFCA-related complications. Our study provided valuable information to help  
26 cardiologists deal with RFCA recurrence and complications.  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43

44 Thirdly, some arrhythmias such as premature ventricular beats and atrial premature  
45 beats are not covered by Taiwan NHI. However, excluding these arrhythmias did not influence  
46 the study results since they are usually benign.  
47  
48  
49  
50

51 Lastly, recurrence may be misidentified in this present study as resulting from ablation  
52 of other arrhythmias. For example, this could happen if the patient had an initial PSVT ablation  
53 followed by an AF ablation. A single definition of recurrence could consider the second  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 ablation as the recurrence of PSVT. Use of double criteria, with repeated ablations combined  
4  
5 with the same major principal diagnosis, reduced the coding error in this study.  
6  
7  
8  
9

## 10 **Conclusions**

11  
12  
13 There was a rapidly increasing trend of RFCA procedures for AF, AFL and VT during  
14  
15 2001-2010, but a slow increase for PSVT and WPW. The recurrence-free rate was higher for  
16  
17 PSVT than for other arrhythmias. Older adult patients with AF and AFL had fewer repeat  
18  
19 RFCA and AF patients in high-activity center hospitals had more. CHD was a risk factor for  
20  
21 PSVT recurrence. AF patients had more occurrences of life-threatening pericardial effusion,  
22  
23 especially those aged more than 65 years, and patients receiving RFCA for AFL suffered more  
24  
25 from bradycardia, requiring permanent pacemaker implantation.  
26  
27  
28  
29  
30

### 31 **Contributors:**

32  
33 CHEN conceived of the study. Y LIN and WU initiated the study design and WANG helped  
34  
35 with implementation. Y LIN, WU and CHEN provided statistical expertise in clinical trial  
36  
37 design and WANG and YS LIN conducted the primary statistical analysis. All authors  
38  
39 contributed to refinement of the study protocol and approved the final manuscript.  
40  
41  
42

### 43 **Funding:**

44  
45 This work was supported by grants from the Chang Gung Memorial Hospital, Taiwan  
46  
47 (CGRPG2F0011, CLRPG2C0021, CLRPG2C0022, CLRPG2C0023, CLRPG2C0024,  
48  
49 CLRPG2G0081, and CLRPG2G0082).  
50  
51

### 52 **Disclaimer:**

53  
54 The lead author confirms that the content of this manuscript is honest and transparent.  
55  
56

### 57 **Competing interests:**

58  
59 None declared.  
60

**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.

**References**

1. O'Hara GE, Philippon F, Champagne J, *et al.* Catheter ablation for cardiac arrhythmias: a 14-year experience with 5330 consecutive patients at the Quebec Heart Institute, Laval Hospital. *Can J Cardiol* 2009;25:140.
2. Spector P, Reynolds MR, Calkins H, *et al.* Meta-analysis of ablation of atrial flutter and supraventricular tachycardia. *Am J Cardiol* 2009;104:671-7.
3. Bohnen M, Stevenson WG, Tedrow UB, *et al.* Incidence and predictors of major complications from contemporary catheter ablation to treat cardiac arrhythmias. *Heart rhythm* 2011;8:1661-6.
4. Joseph JP, Rajappan K. Radiofrequency ablation of cardiac arrhythmias: past, present and future. *QJM* 2012;105:303-14.
5. Cosío FG. Atrial flutter, typical and atypical: a review. *Arrhythm Electrophysiol Rev* 2017;6:55-62.
6. Nyong J, Amit G, Adler AJ, *et al.* Efficacy and safety of ablation for people with non-paroxysmal atrial fibrillation. *Cochrane Database Syst Rev* 2016;11:CD012088.
7. Pérez FJ, Schubert CM, Parvez B, *et al.* Long-term outcomes after catheter ablation of cavo-tricuspid isthmus dependent atrial flutter: a meta-analysis. *Circ Arrhythm Electrophysiol* 2009;2:393-401.

- 1  
2  
3 8. Cappato R, Calkins H, Chen SA, *et al.* Updated worldwide survey on the methods, efficacy,  
4 and safety of catheter ablation for human atrial fibrillation. *Circulation* 2010;3:32-8.  
5  
6
- 7 9. Yang YW, Chen YH, Xirasagar S, *et al.* Increased risk of stroke in patients with bullous  
8 pemphigoid: a population-based follow-up study. *Stroke* 2011;42:319-23.  
9  
10
- 11 10. Wu CY, Wu MS, Kuo KN, *et al.* Effective reduction of gastric cancer risk with regular use  
12 of nonsteroidal anti-inflammatory drugs in Helicobacter pylori-infected patients. *J Clin Oncol*  
13 2010;28:2952-7.  
14  
15
- 16 11. Wu CY, Chen YJ, Ho HJ, *et al.* Association between nucleoside analogues and risk of  
17 hepatitis B virus-related hepatocellular carcinoma recurrence following liver resection. *JAMA*  
18 2012;308:1906-14.  
19  
20
- 21 12. Feinberg WM, Blackshear JL, Laupacis A, *et al.* Prevalence, age distribution, and gender  
22 of patients with atrial fibrillation Analysis and implications. *Arch Intern Med* 1995;155:469-  
23 73.  
24  
25
- 26 13. Dixit S, Callans DJ. Mapping for ventricular tachycardia. *Card Electrophysiol Rev*  
27 2002;6:436-41.  
28  
29
- 30 14. Van Hare GF, Javitz H, Carmelli D, *et al.* Prospective assessment after pediatric cardiac  
31 ablation: recurrence at 1 year after initially successful ablation of supraventricular tachycardia.  
32 *Heart rhythm* 2004;1:188-96.  
33  
34
- 35 15. Tuan TC, Chang SL, Tsao HM, *et al.* The impact of age on the electroanatomical  
36 characteristics and outcome of catheter ablation in patients with atrial fibrillation. *J Cardiovasc*  
37 *Electrophysiol* 2010;21:966-72.  
38  
39
- 40 16. Walters TE, Kistler PM, Kalman JM. Radiofrequency ablation for atrial tachycardia and  
41 atrial flutter. *Heart Lung Circ* 2012;21:386-94.  
42  
43
- 44 17. Calkins H, Kuck KH, Cappato R, *et al.* 2012 HRS/EHRA/ECAS expert consensus  
45 statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 selection, procedural techniques, patient management and follow-up, definitions, endpoints,  
4 and research trial design. *J Interv Card Electrophysiol* 2012;33:171-257.

5  
6  
7  
8 18. Grönefeld GC, Wegener F, Israel CW, *et al*. Thromboembolic risk of patients referred for  
9 radiofrequency catheter ablation of typical atrial flutter without prior appropriate  
10 anticoagulation therapy. *Pacing Clin Electrophysiol* 2003;26:323-7.

11  
12  
13  
14 19. Wood KA, Eisenberg SJ, Kalman JM, *et al*. Risk of thromboembolism in chronic atrial  
15 flutter. *Am J Cardiol* 1997;79:1043-7.

16  
17  
18  
19 20. Alyeshmerni D, Pirmohamed A, Barac A, *et al*. Transesophageal echocardiographic  
20 screening before atrial flutter ablation: is it necessary for patient safety? *J Am Soc Echocardiogr*  
21  
22 2013;26:1099-105.

23  
24  
25  
26 21. Hoffmann BA, Brachmann J, Andresen D, *et al*. Ablation of atrioventricular nodal  
27 reentrant tachycardia in the elderly: results from the German Ablation Registry. *Heart rhythm*  
28  
29 2011;8:981-7.

30  
31  
32  
33 22. Mirza M, Strunets A, Shen WK, *et al*. Mechanisms of arrhythmias and conduction  
34 disorders in older adults. *Clin Geriatr Med* 2012;28:555-73.

35  
36  
37  
38 23. Movahed MR, Hashemzadeh M, Jamal MM. Increased prevalence of third-degree  
39 atrioventricular block in patients with type II diabetes mellitus. *Chest* 2005;128:2611-4.

40  
41  
42  
43 24. Movahed MR. Diabetes as a risk factor for cardiac conduction defects: a review. *Diabetes*  
44  
45 *Obes Metab* 2007;9:276-81.

46  
47  
48  
49 25. Peduzzi P, Concato J, Kemper E, *et al*. A simulation study of the number of events per  
50 variable in logistic regression analysis. *J Clin Epidemiol* 1996;49:1373-9.

51  
52  
53  
54 26. Concato J, Peduzzi P, Holford TR, *et al*. Importance of events per independent variable in  
55 proportional hazards analysis I. Background, goals, and general strategy. *J Clin Epidemiol*  
56  
57 1995;48:1495-501.

- 1  
2  
3 27. Peduzzi P, Concato J, Feinstein AR, *et al.* Importance of events per independent variable  
4 in proportional hazards regression analysis II. Accuracy and precision of regression  
5 estimates. *J Clin Epidemiol* 1995;48:1503-10.  
6  
7  
8  
9  
10 28. Adao L, Araujo C, Sa AP, *et al.* Importancia da posicao anatomica da via acessoria na  
11 eficacia e na seguranca da ablacao por radiofrequencia. *Rev Port Cardiol* 2011;30:35-46.  
12  
13  
14 29. Iturralde P, Guevara-Valdivia M, Rodríguez-Chávez L, *et al.* Radiofrequency ablation of  
15 multiple accessory pathways. *Europace* 2002;4:273-80.  
16  
17  
18  
19 30. Anselmino M, Grossi S, Scaglione M, *et al.* Long-term results of transcatheter atrial  
20 fibrillation ablation in patients with impaired left ventricular systolic function. *J Cardiovasc*  
21 *Electrophysiol* 2013;24:24-32.  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



## Figure Legends

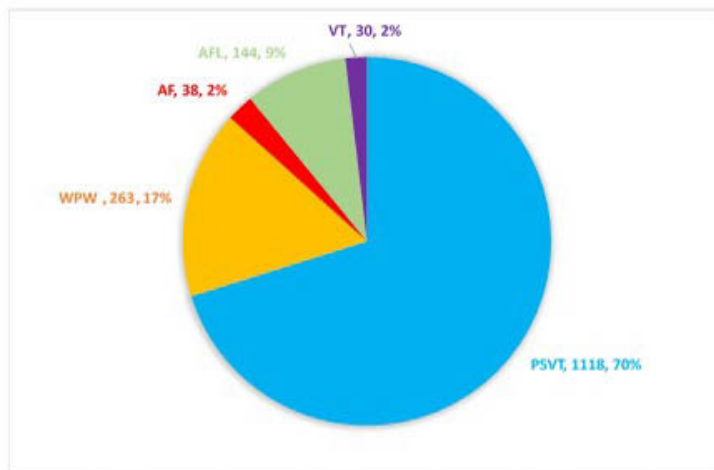
Figure 1. Proportion of radiofrequency catheter ablation patients diagnosed with paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia in Taiwan during 2001 and 2010.

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.

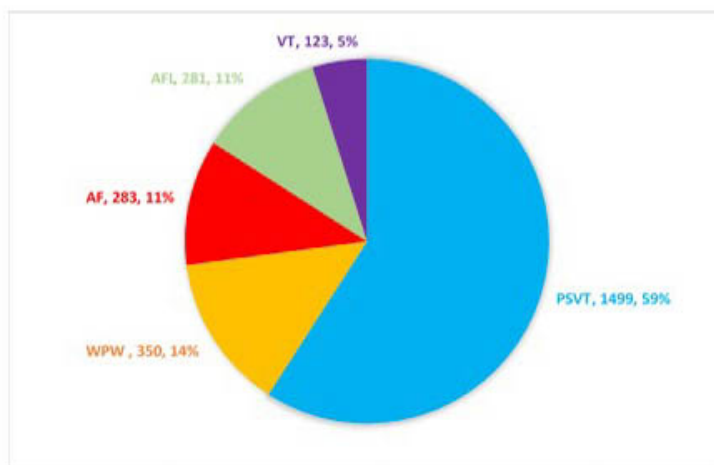
Figure 3. Number of radiofrequency catheter ablations annually in groups of patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White Syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.

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.

The proportion of five arrhythmia in 2001



The proportion of five arrhythmia in 2010



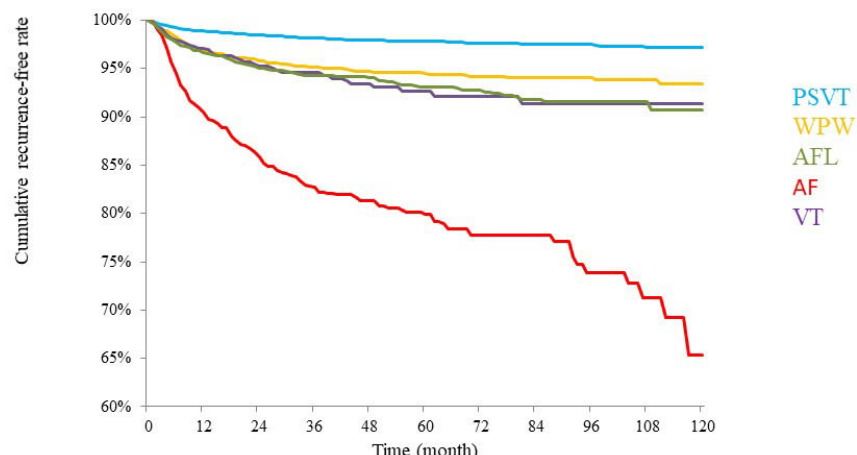
Abbreviation: PSVT: paroxysmal supraventricular tachycardia, WPW: Wolff–Parkinson–White syndrome, AFL: atrial flutter, AF: atrial fibrillation, VT:ventricular tachycardia

Figure 1

figure 1

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

### The recurrence-free rate for five types of arrhythmias

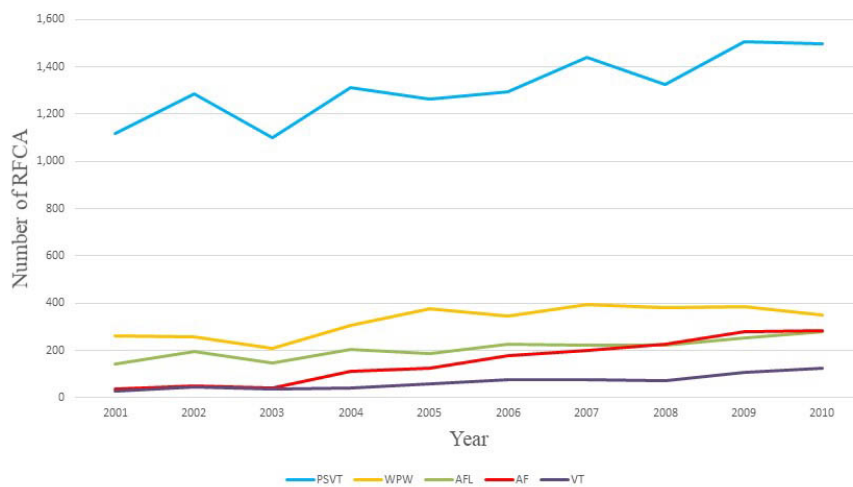


Abbreviation: PSVT: paroxysmal supraventricular tachycardia, WPW: Wolff–Parkinson–White syndrome, AFL: atrial flutter, AF: atrial fibrillation, VT: ventricular tachycardia

Figure 2

figure 2

Annual RCFA growth number for PSVT, WPW, AFL, AF, and VT

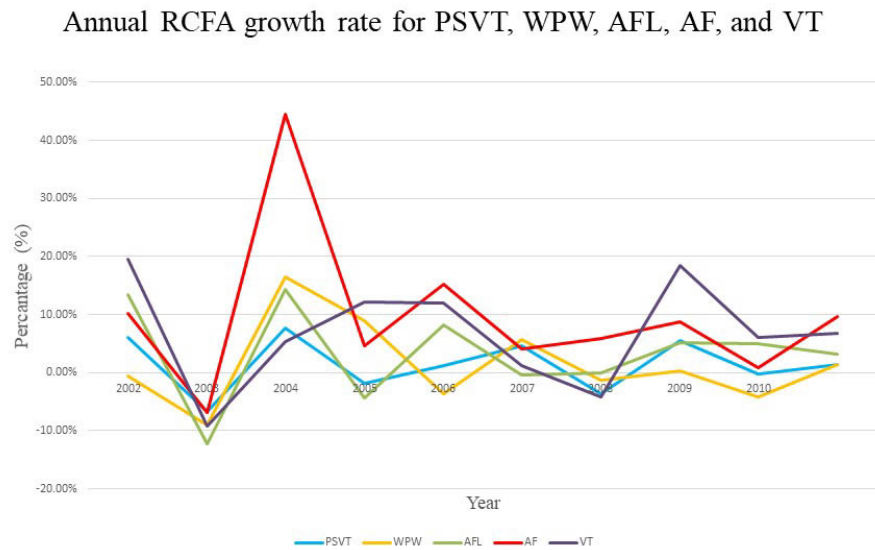


Abbreviation: RFCA = Radiofrequency catheter ablation; PSVT: paroxysmal supraventricular tachycardia, WPW: Wolff–Parkinson–White syndrome, AFL: atrial flutter, AF: atrial fibrillation, VT: ventricular tachycardia

Figure 3

figure 3

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



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

For peer review only

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

Variable	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%)	
	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 ( $n=19,719$ )	$P^a$
<b>In-hospital complication</b>			
Life-threatening pericardial effusion	3 (0.3)	42 (0.21)	0.48
New-onset stroke	0 (0)	23 (0.12)	0.63
<b>After discharge</b>			
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
<b>In-hospital complication</b>					
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)
<b>After discharge</b>					
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
<b>Title and abstract</b>	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
<b>Introduction</b>			
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
<b>Methods</b>			
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
		(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
Participants	6	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —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
		(a) Describe all statistical methods, including those used to control for confounding	6,7
Statistical methods	12	(b) Describe any methods used to examine subgroups and interactions	6,7
		(c) Explain how missing data were addressed	7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	7
		(e) Describe any sensitivity analyses	

1136/bmjopen-2018-023449 on 30 May 2019. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

Section/Topic	Item No	Recommendation	Reported on Page No
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, excluded 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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	10, 11, 13
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —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	
<b>Discussion</b>			
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
<b>Other Information</b>			
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](http://www.strobe-statement.org).

For peer review only

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

# BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023487.R3
Article Type:	Research
Date Submitted by the Author:	22-Mar-2019
Complete List of Authors:	Lin, Yuan; Chang Gung Memorial Hospital Keelung Branch, Emergency Medicine department Wu, Hsin-Kuan; Chang Gung Memorial Hospital Keelung Branch, Emergency Medicine department Wang, Te-Hsiung ; Kyoto University Graduate School of Medicine Faculty of Medicine, Department of Primary Care and Emergency Medicine Chen, Tien-Hsing; Chang Gung Memorial Hospital Keelung Branch, Division of Cardiology, Department of Internal Medicine; Chang Gung Memorial Hospital Keelung Branch, Biostatistical Consultation Center Lin, Yu-Sheng; Chiayi Chang Gung Memorial Hospital, Division of Cardiology, Department of Internal Medicine
<b>Primary Subject Heading</b>:	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

SCHOLARONE™  
Manuscripts

1  
2  
3 **Trend and Risk Factors of Recurrence and Complications after Arrhythmias**  
4 **Radiofrequency Catheter Ablation: A Nationwide Observational Study in Taiwan**  
5  
6  
7  
8  
9

10 **Yuan Lin MD<sup>1#</sup>, Hsin-Kuan Wu MD<sup>1#</sup>, Te-Hsiung Wang MD<sup>2</sup>, Tien-Hsing Chen MD<sup>3 4\*</sup>,**  
11  
12 **Yu-Sheng Lin MD<sup>5\*</sup>**  
13  
14

- 15  
16  
17 **1. Department of Emergency Medicine, Chang-Gung Memorial Hospital, Keelung,**  
18 **Taiwan**  
19  
20 **2. Department of Primary Care and Emergency Medicine, Kyoto University Graduate**  
21 **School of Medicine, Kyoto, Japan**  
22  
23 **3. Division of Cardiology, Department of Internal Medicine, Chang-Gung Memorial**  
24 **Hospital, Keelung, Taiwan**  
25  
26 **4. Biostatistical Consultation Center, Chang-Gung Memorial Hospital, Keelung,**  
27 **Taiwan**  
28  
29 **5. Division of Cardiology, Department of Internal Medicine, Chang-Gung Memorial**  
30 **Hospital, Chiayi, Taiwan**  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41

42 **#Yuan Lin and Hsin-Kuan Wu contributed equally to this study**  
43

44 **\* Tien-Hsing Chen and Yu-Sheng Lin contributed equally to this study**  
45

46 **To whom correspondence and reprint requests should be addressed:**  
47

48 **Dr. Tien-Hsing Chen,**  
49

50  
51 **Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial**  
52 **Hospital, No. 5, Fu-Shin Street, Kweishan 333, Taoyuan, Taiwan.**  
53

54 **TEL: +886-3-3281200-8116**  
55

56 **E-mail: skyheart0826@gmail.com**  
57  
58  
59  
60

## 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.

1  
2  
3  
4  
5  
6 **Key words:** radiofrequency catheter ablation (RFCA), Wolff-Parkinson-White syndrome,  
7  
8 supraventricular tachycardia, ventricular tachycardia, complication, recurrence, risk factors  
9  
10

## 11 12 13 **Strengths and limitations of this study** 14 15

- 16 ● This 10-year longitudinal retrospective study is the first nationwide, large-scale study of  
17 the trend, recurrence and complications of radiofrequency catheter ablation (RFCA).  
18
- 19 ● This article is the first study to compare recurrence and complications among five different  
20 types of arrhythmias after RFCA.  
21
- 22 ● Our study provides risks of arrhythmia recurrence and complications after RFCA.  
23
- 24 ● This study did not have access to certain data such as laboratory parameters, procedural  
25 details, and heart images. Also, some arrhythmias such as premature ventricular beats and  
26 atrial premature beats are not covered by Taiwan National Health Insurance.  
27
- 28 ● This study was not able to explore the interactions among the predictive variables because  
29 of the limited number of events.  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40

## 41 **Introduction** 42 43

44  
45 Radiofrequency catheter ablation (RFCA) is used to treat patients with supraventricular  
46 tachycardia or ventricular tachycardia (VT), especially paroxysmal supraventricular  
47 tachycardia (PSVT).<sup>1-3</sup> Widely applied since the 1990s,<sup>4</sup> RFCA is an effective therapy with  
48 demonstrated high success, low complications and low recurrence rates compared to direct  
49 current ablation or surgical ablation. RFCA is superior to conservative treatments such as  
50 medication or observation for patients with PSVT and Wolff-Parkinson-White syndrome  
51 (WPW). RFCA was first used to treat atrial fibrillation (AF) in 1998.  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3 Although arrhythmias after RFCA are usually not life-threatening, identification and  
4 minimization of the risk of complications are extremely important. The RFCA procedure may  
5 lead to atrioventricular (AV) block and bradycardia, even requiring permanent pacemaker  
6 implantation. Previous studies<sup>5</sup> were composed of relatively small cohorts or were single-  
7 center studies and evaluated patients with a single arrhythmia.<sup>5,6</sup> However, there are no studies  
8 comparing RFCA-related complications in patients with five different arrhythmias.<sup>7,8</sup> The  
9 targets for RFCA-related risk minimization differ by type of arrhythmia. For example, when  
10 RFCA is used to treat PSVT, the goal is to modify or eliminate AV node or accessory pathways;  
11 when used to treat AF,<sup>6</sup> the goal is to isolate the pulmonary veins. High grade AV block, life-  
12 threatening pericardial effusion, and stroke are dangerous complications after an RFCA  
13 procedure. However, the complication rates vary by type of arrhythmia: PSVT, WPW, atrial  
14 flutter (AFL), AF and VT. It is therefore important to identify the incidence and risk factors of  
15 RFCA-related complications in these patients.  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32

33 This retrospective study investigated the population trend of patients who received RFCA  
34 for PSVT, WPW, AFL, AF and VT. We identified the major RFCA-related risk factors  
35 influencing 1) recurrence of arrhythmias and 2) complications such as AV block, permanent  
36 pacemaker implantation, life-threatening pericardial effusion and acute ischemic stroke.  
37  
38  
39  
40  
41  
42  
43  
44

## 45 **Methods**

### 46 **Study design and population**

47  
48 We conducted a nationwide population-based cohort study using data from the Taiwan  
49 National Health Insurance Research Database (NHIRD). In Taiwan, the National Health  
50 Insurance (NHI) program has reimbursed patients who receive RFCA for PSVT, WPW, AFL,  
51 AF and VT since 2001. More than 99.91% of Taiwan's population is covered by NHI benefits.  
52 The accuracy and validation of NHIRD data is based upon regular auditing by the NHI  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 Bureau.<sup>9-11</sup> The Institutional Review Board of Chang Gung Memorial Hospital approved this  
4  
5 study.  
6  
7  
8  
9

### 10 **Study cohort, outcome measurement and follow-up**

12 This study accessed NHIRD data for all targeted arrhythmia patients who received  
13 RFCA from 2001 to 2010. The targeted arrhythmias were PSVT (International Classification  
14 of Diseases, Ninth Revision, Clinical Modification [ICD-9 CM] Code 4270), WPW (426.7),  
15 AFL (427.32), AF (427.31) and VT (427.1; Supplemental Table 1). Patients with arrhythmias  
16 other than those targeted (such as premature ventricular beats or atrial tachycardia) and patients  
17 with unidentified arrhythmias who received RFCA were excluded. We enrolled only the  
18 patient's first RFCA. The follow-up period was calculated from the discharge date of the index  
19 hospitalization until death, loss to follow up (withdrawal from the NHI program: emigration or  
20 prison incarceration for longer than six months) or until the study end date (31 December 2010).  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34

### 35 **Outcomes measurement**

36  
37 The primary outcomes included recurrence of arrhythmia, in-hospital complications  
38 and long-term complications. Recurrence was defined as either 1) recurrence of original  
39 arrhythmia or 2) receipt of a second RFCA during the follow up period. In-hospital  
40 complications included life-threatening pericardial effusion and new-onset stroke during the  
41 admission. Life-threatening pericardial effusion was defined as the patient requiring  
42 pericardiocentesis during RFCA. New stroke was defined as stroke (ICD-9 CM codes 430-  
43 437) which occurred during the index admission. Other complications included high-grade AV  
44 block and permanent pacemaker implantation.  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57

### 58 **Covariate assessment**

1  
2  
3 Age was categorized into six groups (0-18, 19-44, 45-54, 55-64, 65-74 and 75 years  
4 and above) because previous studies reported different indications for RFCA and different  
5 complications between age groups.<sup>1-3</sup> Comorbidities were assessed according to ICD-9 CM  
6 codes before the index admission. Diabetes mellitus, hypertension (HTN) or chronic diseases  
7 were recorded as comorbidities if there was at least one in-admission diagnosis. All congenital  
8 heart disease (CHD) was reconfirmed by the Catastrophic Illness Certification (CIC), which is  
9 a sub-dataset of NHI. A CIC for CHD requires imaging proof confirmed by two cardiologists.  
10 Complicated CHD included Tetralogy of Fallot (TOF), transposition of the great vessels,  
11 double outlet right ventricle, total anomalous pulmonary venous connection, tricuspid atresia,  
12 common truncus arteriosus, common ventricle and hypoplastic left heart syndrome. Simple  
13 CHD included ventricular septal defect (VSD), atrial septal defect (ASD), Ebstein's anomaly,  
14 patent ductus arteriosus, congenital pulmonary stenosis, coarctation of the aorta, endocardial  
15 cushion defect and congenital aortic stenosis. Center activity was a time-dependent variable  
16 and a high-activity center was defined as more than 100 RFCA surgeries per year, regardless  
17 of arrhythmia type.  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39

#### 40 **Patient and public involvement**

41  
42 This study had no direct relationship with any patient and no public involvement during  
43 the development, design and conduct.  
44  
45  
46  
47  
48

#### 49 **Statistical analysis**

50  
51 The proportion of categorical variables between groups was compared using the chi-  
52 squared test and Fisher's exact test. Continuous variables were compared using Kruskal-Wallis  
53 test due to the lack of normality. Multivariable logistic regression analysis was used to identify  
54 clinical features associated with the risk of in-hospital complications, including life-threatening  
55  
56  
57  
58  
59  
60

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 RFCA 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).

1  
2  
3 The commonest arrhythmia treated with RFCA was PSVT (n=12,796; 56.7%),  
4 followed by WPW (n=3,051; 13.5%), AFL (n=1,854; 9.5%), AF (n=1,162; 5.1%) and VT  
5 (n=612; 2.7%). The mean age of study participants when they received RFCA was 47.6 years  
6 (standard deviation [SD] 18.3). Demographic and baseline clinical characteristics according to  
7 arrhythmia type are summarized in Table 1. The prevalence of PSVT (38.5%), WPW (58.1%)  
8 and VT (47.2%) was highest in the group aged 19-44 years. Patients were the oldest in the AFL  
9 group, followed by the AF group, the PSVT group, the VT group and the WPW group. Patients  
10 with AF and AFL had a higher prevalence of diabetes (16.2% and 11.5%, respectively) and  
11 hypertension (28.9% and 28.1%, respectively) compared to patients with other arrhythmias.  
12 Chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and heart  
13 failure were most prevalent in the AFL group since these patients were the oldest (median age  
14 62.9 years). RFCA due to AF was predominantly performed in high-activity centers (84%),  
15 followed by AFL (71%). Complicated CHD was more common in the AFL group than in other  
16 arrhythmias. Simple CHD was most prevalent in the AFL group (3.6%), followed by the VT  
17 group (1.5%).  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

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

Variable	PSVT	WPW	AFL	AF	VT	<i>P</i> 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 <sup>‡</sup>	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 <sup>†</sup>	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

1  
2  
3 Abbreviations: AF = Atrial fibrillation; AFL = Atrial flutter; ASD = Atrial septal defect; CAD = Coronary artery disease; CHD = Congenital heart disease;  
4 CKD = Chronic kidney disease; COPD = Chronic obstructive pulmonary disease; Ebstein = Ebstein's anomaly; IQR = Interquartile range; PSVT =  
5 Paroxysmal supraventricular tachycardia; RFCA = Radiofrequency catheter ablation; TOF = Tetralogy of Fallot; VSD = Ventricular septal defect; VT =  
6 Ventricular tachycardia; WPW = Wolff-Parkinson-White syndrome; Yrs = years.  
7

8  
9 ‡ defined as 100 operations per year.

10 † The discrepancy between the sums of subgroups and the total is due to the possibility that one patient might have two CHDs.  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

### 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.

Variable	PSVT (259 events, 2.0%)		WPW (160 events, 5.2%)		AFL (120 events, 5.8%)		AFL (247 events, 16.1%)		VT (38 events, 5.7%)	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
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 (0.61–1.23)	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 (0.34–0.85)	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: 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  $\geq 75$  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  $\geq 75$  years, diabetes, CKD and RFCA after AFL (when compared with PSVT). The results were similar when excluding patients with recurrent RFCA 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.

Variable	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, 0.84%)		Pacemaker (100 events, 0.48%)	
	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.<sup>12</sup> 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 30<sup>th</sup> June.) in Taiwan decreased from 413,177 births (23 births per

1  
2  
3 1000 population) in 1980 to 307,200 births (13 births per 1000 population) in 2000, reducing  
4 the number of patients needing PSVT and WPW. The number of WPW cases peaked in 2005  
5 (N= 377) and has since been decreasing. The number of procedures in the VT group increased  
6 from 57 in 2001 to 123 in 2010, and the average RFCA growth rate over 10 years was 6.8%.  
7  
8 This relatively high growth rate is possibly also due to population aging and the maturation of  
9 3D mapping techniques.<sup>13</sup> In summary, the growth models are different for the five arrhythmias.  
10  
11 The AF and AFL groups have increased rapidly in RFCA procedures because of population  
12 aging. The PSVT group had a relatively slow increase, while the WPW and VT groups showed  
13 stable or decreasing numbers of RFCAs.  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

### 26 **Risk of recurrence**

27  
28 Our results showed that the recurrence rate after RFCA increased in the following order:  
29 PSVT (2.0%) < WPW (4.9%) < VT (5.7%) < AFL (5.8%) < AF (16.1%) (Figure 2). The  
30 recurrence-free rate was highest for the PSVT group (98.8% for the first year, gradually  
31 decreasing to 97.2% for the 10-year follow up). However, patients <18 years in the PSVT and  
32 WPW groups had a significantly higher chance of recurrence, a result which agreed with those  
33 of Van Hare et al.<sup>14</sup> This recurrence could be a result of the smaller cardiac anatomy in children,  
34 which makes the precise ablation difficult to perform. This result could also explain the  
35 association of CHD and TOF with recurrence of PSVT, possibly because of the abnormal  
36 cardiac structure of the CHD heart post-cardiac surgery. Patients with TOF and AF also had a  
37 higher risk of receiving a second RFCA. In contrast, AF and AFL patients aged  $\geq 75$  years had  
38 fewer second RFCAs than younger patients.<sup>15</sup>  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53

54 Our data showed that patients  $\geq 75$  years receiving treatment for AF and AFL had lower  
55 recurrence rates than those the same age in other groups. The reason for this phenomenon may  
56 be the conservative treatment preferred by cardiologists for older patients rather than repeated  
57  
58  
59  
60

1  
2  
3 RFCA, in order to avoid complications or mortality after the first procedure due to the presence  
4 of other comorbidities. Our data suggest that, for patients undergoing an elective RFCA,  
5 physicians should carefully evaluate the risk factors such as younger age and the presence of  
6 CHD (TOF in PSVT, VSD in AFL) which are associated with a high recurrence rate. Our study  
7 also described epidemiologic changes in repeated ablation procedures for five arrhythmias in  
8 Taiwan in the RFCA era.  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18

### 19 **Complications**

20  
21 RFCA, which has an approximately 1% complication rate and 0.1% mortality rate,<sup>3,16</sup>  
22 is considered a relatively safe procedure to treat or even cure arrhythmias (Table 3). Our present  
23 study showed different patterns of complications in the five arrhythmia groups. Patients with  
24 PSVT and WPW had complication rates of 1.6% and 0.8%, respectively, similar to previous  
25 studies. However, in patients with AF and AFL, the complication rates were 2.5% and 4.7%,  
26 respectively. AFL after RFCA induced more high-grade AV block (2.5%) compared to other  
27 arrhythmias, and patients with AF after RFCA had the highest incidence rate of life-threatening  
28 pericardial effusion (1.3%). High-grade AV block is considered the main complication of  
29 ablation procedures for AFL and PSVT patients because the ablation sites are close to the  
30 atrioventricular node.<sup>16</sup> AFL has been seen combined with sick sinus syndrome.  
31 Bradyarrhythmias appeared when the substrate of AF and AFL is eliminated. RFCA patients  
32 with AF had a higher risk of life-threatening pericardial effusion relative to patients with other  
33 arrhythmias, resulting in a relatively higher complication rate of 1.3%. The major RFCA  
34 procedure for AF is to isolate the pulmonary vein and eliminate the substrate in the left atrium.  
35 This requires a longer procedure time and delivers more energy to convert AF into sinus rhythm.  
36 RFCA for AF could therefore cause more life-threatening pericardial effusion than that for  
37 other arrhythmias. RFCA for VT presents same pattern as that for PSVT and WPW. These data  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3 suggest that, although RFCA is a common procedure to treat different arrhythmias, the  
4 complications that should be monitored will differ by type of arrhythmia.  
5  
6

7  
8 Our data also showed that patients with AFL and AF had higher stroke rates (0.49%  
9 and 0.34%, respectively) than patients in the other groups. Anticoagulation therapy is needed  
10 in these cases, and it is also necessary to confirm the absence of intracardiac thrombus before  
11 RFCA.<sup>17</sup> However, anticoagulation procedures are sometimes ignored because anti-  
12 coagulation is not routinely used in AFL.<sup>18</sup> Previous studies have shown a high risk of  
13 thromboembolic events and a high incidence of thrombogenic milieu in AFL.<sup>19,20</sup> Use of the  
14 inappropriate anticoagulation therapy is considered a significant risk factor for  
15 thromboembolism in patients with AFL.<sup>18</sup>  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

26 Age was an important risk factor associated with complications such as high-grade AV  
27 block, pacemaker implantation, life-threatening pericardial effusion and stroke, especially in  
28 patients aged  $\geq 75$  years (Table 4). These data were consistent with previous studies,<sup>21,22</sup> and  
29 suggest that physicians should be cautious when performing RFCA in patients  $\geq 75$  years. We  
30 also found that diabetes was associated with increased complication rates for RFCA. A cohort  
31 study of 200,000 patients with type II diabetes reported that third degree AV block was 3.1  
32 times as prevalent in the diabetic group (95% CI, 3.0-3.3;  $p < 0.0001$ ).<sup>23</sup> Diabetes has been  
33 suggested as a risk factor for autonomic neuropathy, cardiac conduction abnormalities and  
34 bradyarrhythmias.<sup>24</sup> Physicians performing RFCA in diabetic patients should monitor for  
35 bradyarrhythmia complications.  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50

## 51 **Limitations**

52  
53  
54 Firstly, the major limitation of this study is our inability to explore the interactions  
55 among the predictive variables because of the limited number of events. For instance, the 184  
56 high-grade AV blocks allow for a maximum of 18-19 predictive variables, due to the “ten-one  
57  
58  
59  
60

1  
2  
3 rule.<sup>25-27</sup> However, the 13 predictors indicate that 78 two-way potential interaction effects may  
4 exist. Therefore, it seems not feasible to perform a regression analysis (logistic or Cox  
5 regressions) because that many explanatory variables in the equation would induce the  
6 statistical problem of overfitting. In addition, there is also an issue of multiple testing (five tests  
7 in Table 2 and four tests in Table 4) in this study. Many of the results would turn to be statically  
8 insignificant if a correction (i.e., Bonferroni adjustment) was done. Therefore, further studies  
9 with a larger sample size and more events are needed to conduct interaction tests based on  
10 clinical knowledge or on exploratory data analysis along with multiple testing correction.  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21

22 Secondly, in this cohort study we did not have access to laboratory parameters,  
23 procedural details, heart images, smoking status, obesity or alcohol use. Procedure-related  
24 parameters, the location of the accessory pathway in WPW, PV isolation for AF, cardiac  
25 anomaly and ejection fraction have been reported as predictors for arrhythmia recurrence and  
26 RFCA complications.<sup>14, 28-30</sup> The lack of this information could induce residual confounding.  
27 On the other hand, the different arrhythmia groups had substantial differences in baseline  
28 characteristics, especially in terms of age, which may result in potential confounding even if  
29 we adjusted for these variables in the multivariable regression models. However, the present  
30 study focused on RFCA for five different arrhythmias and each arrhythmia had different  
31 surgical parameters. Rather than comparing the same parameter in different arrhythmia  
32 ablation procedures, we focused on the effect of comorbidities, gender and age on arrhythmia  
33 recurrence and RFCA-related complications. Our study provided valuable information to help  
34 cardiologists deal with RFCA recurrence and complications.  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50

51 Thirdly, some arrhythmias such as premature ventricular beats and atrial premature  
52 beats are not covered by Taiwan NHI. However, excluding these arrhythmias did not influence  
53 the study results since they are usually benign.  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

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.

## Funding:

This work was supported by grants from the Chang Gung Memorial Hospital, Taiwan (CGRPG2F0011, CLRPG2C0021, CLRPG2C0022, CLRPG2C0023, CLRPG2C0024, CLRPG2G0081, CLRPG2G0082, and CLRPG2H0041).

## Disclaimer:

1  
2  
3 The lead author confirms that the content of this manuscript is honest and transparent.  
4

5 **Competing interests:**  
6

7  
8 None declared.  
9

10 **Patient consent:**  
11

12 Not required.  
13

14 **Ethics approval:**  
15

16  
17 The Ethics Institutional Review Board at Chang Gung Memorial Hospital approved this study.  
18

19 **Data sharing statement:**  
20

21 Data are available. Please contact the corresponding author.  
22  
23  
24  
25

26 **References**  
27

- 28  
29 1. O'Hara GE, Philippon F, Champagne J, *et al.* Catheter ablation for cardiac arrhythmias: a  
30 14-year experience with 5330 consecutive patients at the Quebec Heart Institute, Laval  
31 Hospital. *Can J Cardiol* 2009;25:140.  
32  
33 2. Spector P, Reynolds MR, Calkins H, *et al.* Meta-analysis of ablation of atrial flutter and  
34 supraventricular tachycardia. *Am J Cardiol* 2009;104:671-7.  
35  
36 3. Bohnen M, Stevenson WG, Tedrow UB, *et al.* Incidence and predictors of major  
37 complications from contemporary catheter ablation to treat cardiac arrhythmias. *Heart rhythm*  
38 2011;8:1661-6.  
39  
40 4. Joseph JP, Rajappan K. Radiofrequency ablation of cardiac arrhythmias: past, present and  
41 future. *QJM* 2012;105:303-14.  
42  
43 5. Cosío FG. Atrial flutter, typical and atypical: a review. *Arrhythm Electrophysiol Rev*  
44 2017;6:55-62.  
45  
46 6. Nyong J, Amit G, Adler AJ, *et al.* Efficacy and safety of ablation for people with non-  
47 paroxysmal atrial fibrillation. *Cochrane Database Syst Rev* 2016;11:CD012088.  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 7. Pérez FJ, Schubert CM, Parvez B, *et al.* Long-term outcomes after catheter ablation of cavo-  
4 tricuspid isthmus dependent atrial flutter: a meta-analysis. *Circ Arrhythm Electrophysiol*  
5 2009;2:393-401.  
6  
7
- 8 8. Cappato R, Calkins H, Chen SA, *et al.* Updated worldwide survey on the methods, efficacy,  
9 and safety of catheter ablation for human atrial fibrillation. *Circulation* 2010;3:32-8.  
10  
11
- 12 9. Yang YW, Chen YH, Xirasagar S, *et al.* Increased risk of stroke in patients with bullous  
13 pemphigoid: a population-based follow-up study. *Stroke* 2011;42:319-23.  
14  
15
- 16 10. Wu CY, Wu MS, Kuo KN, *et al.* Effective reduction of gastric cancer risk with regular use  
17 of nonsteroidal anti-inflammatory drugs in Helicobacter pylori-infected patients. *J Clin Oncol*  
18 2010;28:2952-7.  
19  
20
- 21 11. Wu CY, Chen YJ, Ho HJ, *et al.* Association between nucleoside analogues and risk of  
22 hepatitis B virus-related hepatocellular carcinoma recurrence following liver resection. *JAMA*  
23 2012;308:1906-14.  
24  
25
- 26 12. Feinberg WM, Blackshear JL, Laupacis A, *et al.* Prevalence, age distribution, and gender  
27 of patients with atrial fibrillation Analysis and implications. *Arch Intern Med* 1995;155:469-  
28 73.  
29  
30
- 31 13. Dixit S, Callans DJ. Mapping for ventricular tachycardia. *Card Electrophysiol Rev*  
32 2002;6:436-41.  
33  
34
- 35 14. Van Hare GF, Javitz H, Carmelli D, *et al.* Prospective assessment after pediatric cardiac  
36 ablation: recurrence at 1 year after initially successful ablation of supraventricular tachycardia.  
37 *Heart rhythm* 2004;1:188-96.  
38  
39
- 40 15. Tuan TC, Chang SL, Tsao HM, *et al.* The impact of age on the electroanatomical  
41 characteristics and outcome of catheter ablation in patients with atrial fibrillation. *J Cardiovasc*  
42 *Electrophysiol* 2010;21:966-72.  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

16. Walters TE, Kistler PM, Kalman JM. Radiofrequency ablation for atrial tachycardia and atrial flutter. *Heart Lung Circ* 2012;21:386-94.
17. Calkins H, Kuck KH, Cappato R, *et al.* 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *J Interv Card Electrophysiol* 2012;33:171-257.
18. Grönefeld GC, Wegener F, Israel CW, *et al.* Thromboembolic risk of patients referred for radiofrequency catheter ablation of typical atrial flutter without prior appropriate anticoagulation therapy. *Pacing Clin Electrophysiol* 2003;26:323-7.
19. Wood KA, Eisenberg SJ, Kalman JM, *et al.* Risk of thromboembolism in chronic atrial flutter. *Am J Cardiol* 1997;79:1043-7.
20. Alyeshmerni D, Pirmohamed A, Barac A, *et al.* Transesophageal echocardiographic screening before atrial flutter ablation: is it necessary for patient safety? *J Am Soc Echocardiogr* 2013;26:1099-105.
21. Hoffmann BA, Brachmann J, Andresen D, *et al.* Ablation of atrioventricular nodal reentrant tachycardia in the elderly: results from the German Ablation Registry. *Heart rhythm* 2011;8:981-7.
22. Mirza M, Strunets A, Shen WK, *et al.* Mechanisms of arrhythmias and conduction disorders in older adults. *Clin Geriatr Med* 2012;28:555-73.
23. Movahed MR, Hashemzadeh M, Jamal MM. Increased prevalence of third-degree atrioventricular block in patients with type II diabetes mellitus. *Chest* 2005;128:2611-4.
24. Movahed MR. Diabetes as a risk factor for cardiac conduction defects: a review. *Diabetes Obes Metab* 2007;9:276-81.
25. Peduzzi P, Concato J, Kemper E, *et al.* A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996;49:1373-9.

- 1  
2  
3 26. Concato J, Peduzzi P, Holford TR, *et al.* Importance of events per independent variable in  
4 proportional hazards analysis I. Background, goals, and general strategy. *J Clin Epidemiol*  
5 1995;48:1495-501.  
6  
7  
8  
9  
10 27. Peduzzi P, Concato J, Feinstein AR, *et al.* Importance of events per independent variable  
11 in proportional hazards regression analysis II. Accuracy and precision of regression  
12 estimates. *J Clin Epidemiol* 1995;48:1503-10.  
13  
14  
15  
16  
17 28. Adao L, Araujo C, Sa AP, *et al.* Importancia da posicao anatomica da via acessoria na  
18 eficacia e na seguranca da ablacao por radiofrequencia. *Rev Port Cardiol* 2011;30:35-46.  
19  
20  
21 29. Iturralde P, Guevara-Valdivia M, Rodríguez-Chávez L, *et al.* Radiofrequency ablation of  
22 multiple accessory pathways. *Europace* 2002;4:273-80.  
23  
24  
25  
26 30. Anselmino M, Grossi S, Scaglione M, *et al.* Long-term results of transcatheter atrial  
27 fibrillation ablation in patients with impaired left ventricular systolic function. *J Cardiovasc*  
28 *Electrophysiol* 2013;24:24-32.  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## Figure Legends

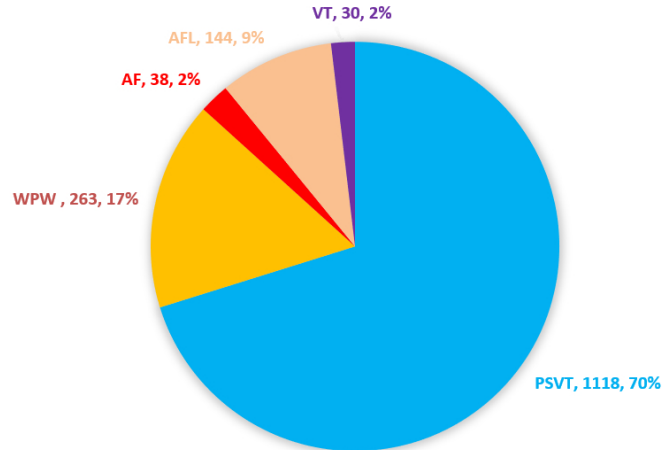
Figure 1. Proportion of radiofrequency catheter ablation patients diagnosed with paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia in Taiwan during 2001 and 2010.

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.

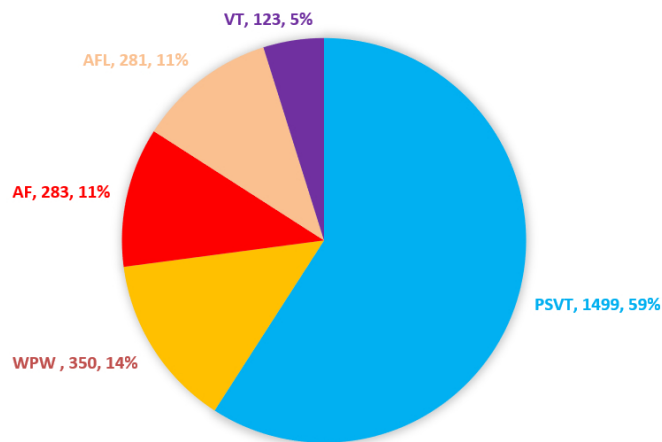
Figure 3. Numbers and growth rate of radiofrequency catheter ablations annually in groups of patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.



The proportion of five arrhythmias in 2001



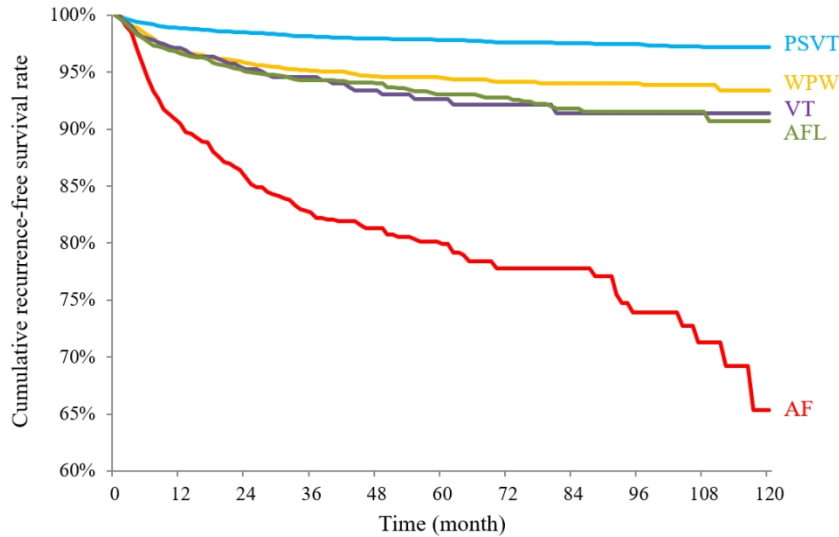
The proportion of five arrhythmias in 2010



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.

## The recurrence-free survival curves for five arrhythmias



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

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.

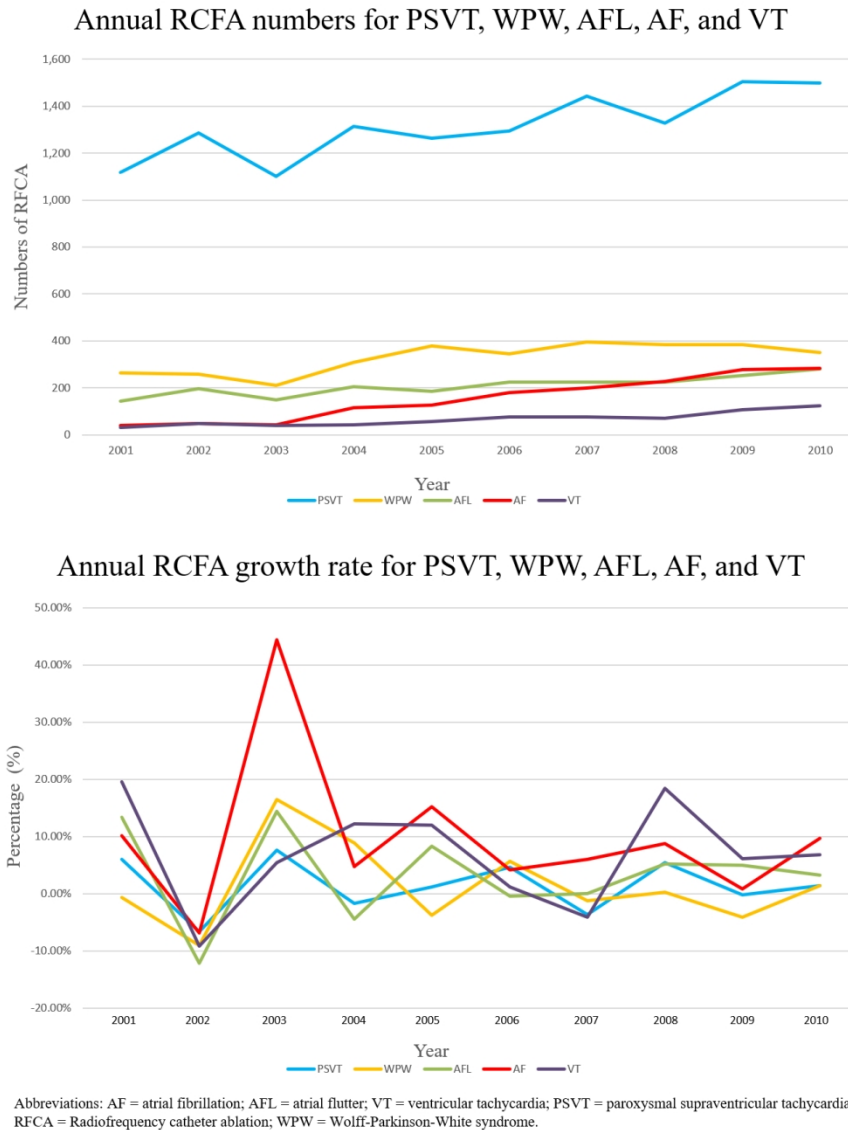


Figure 3 Numbers and growth rate of radiofrequency catheter ablations annually in groups of patients with initial diagnosis of paroxysmal supraventricular tachycardia, Wolff-Parkinson-White syndrome, atrial flutter, atrial fibrillation and ventricular tachycardia.

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.

For peer review only

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

Variable	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%)	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
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
<b>Title and abstract</b>	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
<b>Introduction</b>			
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
<b>Methods</b>			
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
		(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
Participants	6	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
		Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
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
		(a) Describe all statistical methods, including those used to control for confounding	6,7
Statistical methods	12	(b) Describe any methods used to examine subgroups and interactions	6,7
		(c) Explain how missing data were addressed	7
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —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
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, excluded 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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	10, 11, 13
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —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	
<b>Discussion</b>			
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
<b>Other Information</b>			
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](http://www.strobe-statement.org).

For peer review only

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47