Ventricular arrhythmias after atrial fibrillation electrical cardioversion: A multicenter study

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BACKGROUND Ventricular arrhythmias (VAs) after atrial fibrillation (AF) electrical cardioversion (ECV) have been reported.

OBJECTIVE We sought to assess incidence, timing, and clinical characteristics of patients with post-AF ECV-related VAs.

METHODS Multicenter observational retrospective study including 13 centers, incorporating patients with VAs or sudden cardiac death within 10 days of ECV. The total number of ECVs performed during the collecting period was provided. Patients with pre-ECV VAs were excluded.

RESULTS Twenty-three patients with VAs were identified out of 11,897 AF ECVs performed in 13 centers during a median 2-year period, suggesting post-ECV VA incidence of 0.2%. The patients' mean age was 71 ± 11 years, and 13 (56.5%) were female. AF duration prior to ECV was 71 ± 54 days. Congestive heart failure and hypertension were both found in 17 (74%) patients. QT-prolonging drugs were used by 17 (74%). Index VA occurred 28.5 (interquartile range 5.5–72) hours post-ECV, including torsades de pointes, nonsustained polymorphic ventricular tachycardia, and sudden cardiac death in 17 (74%), 5 (22%), and 1 (4%) patient, respectively. Post-ECV heart rate was slower and QT duration longer compared with pre-ECV (57 ± 11 beats/min vs 113 ± 270 beats/min; $P < .001$; QT duration 482 ± 61 ms vs 390 ± 60 ms; $P < .001$). VAs reoccurred in 9 (39%) patients, 11 (interquartile range 3–13.5) hours post–index VA. Two patients had an arrhythmic death within 72 hours post-ECV.

CONCLUSION VAs post-AF ECV are rare, occur within 3 to 72 hours post-ECV, and are potentially fatal. Our study gives a signal of caution favoring prolonged monitoring in small subset of patients as congestive heart failure patients treated with class III antiarrhythmic drugs, with post-ECV bradycardia, especially (but not exclusively) when QT prolongation noted.

KEYWORDS Atrial fibrillation; Electrical cardioversion; Monitoring; Ventricular arrhythmia

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KEY FINDINGS

- Atrial fibrillation electrical cardioversion (ECV)–related ventricular arrythmias (VAs) are rare (~0.2% of ECVs) but potentially fatal.
- These VAs consist of torsades de pointes and nonsustained polymorphic ventricular tachycardia.
- These VAs occur mostly within 3 to 72 hours after atrial fibrillation ECV.
- Many of these cases had congestive heart failure symptoms, were treated by QT-prolonging medications, and developed bradycardia with QT prolongation post-ECV.
- Overall, a routine same-day discharge post-ECV may not apply for all patients.

Introduction

Electrical cardioversion (ECV) of atrial fibrillation (AF) is commonly performed as part of rhythm control strategy or urgently in cases of AF induced hemodynamic instability. It is considered a safe procedure associated with low complication rates.[1–3]

Postcardioversion, the QT interval may prolong due to multiple factors, including heart rate (HR) slowing, use of antiarrhythmic drugs (AADs), and ventricular repolarization remodeling that occurs mainly in patients with persistent atrial fibrillation (AF).[4–6] Indeed, an increased sensitivity to QT prolongation induced by class III AADs, was documented shortly after AF ECV.[7,8] In addition, electrolyte imbalance and tachycardia-induced cardiomyopathy may further affect the magnitude of QT prolongation.[6,9,10] Few prior studies focusing on the post-ECV QT interval demonstrated QT prolongation, reaching a peak QT duration around 44 hours post-ECV.[4,11]

Post-AF ECV QT prolongation–related ventricular arrhythmias (VAs) were reported by few prior studies and case reports.[12–16] However, the magnitude of the phenomenon and the characteristics of patients at risk are still currently unknown. This may be related to several factors. A rare phenomenon may be ignored unless a large multicenter study, dedicated to this phenomenon, is performed. Also, post-AF ECV short hospitalization duration, which is the common clinical practice, may lead to unawareness of arrhythmic events occurring after discharge. Given the global trend for early discharge during the same day of ECV, there is a crucial need to define the prevalence, timing, and characteristics of patients with post-AF ECV-related VAs, in order to postpone discharge and continue prolonged monitoring for those at risk.

The aim of the current multicenter study was to define the prevalence, timing (post-ECV), and characteristics of patients with post-AF ECV-related VAs who may benefit from longer in hospital monitoring post-ECV.

Methods

Study design

This was a retrospective observational study. Seventy-seven centers were approached. Centers were invited to retrieve all AF patients with VAs, occurring within 10 days post-AF ECV, and the corresponding number of total AF ECVs performed during the period in which the VA cases occurred. The study was approved by hospital Institutional Review Board.

Inclusion criteria

Patients with documented sustained or nonsustained monomorphic or polymorphic ventricular tachycardia (VT), torsades de pointes (TdP), or ventricular fibrillation (VF) occurring within 10 days post-AF ECV were included. Nonsustained monomorphic or polymorphic VT was defined by >3 consecutive ventricular beats. In addition, patients in whom sudden cardiac death (SCD) occurred within 10 days post-AF ECV (whether resuscitated successfully or not), were included as well.

Exclusion criteria

Patients with prior evidence of sustained VA, who have been previously resuscitated from SCD, and those diagnosed with long QT syndrome or other channelopathies were all excluded.

Data collected

Post-ECV–related VA cases were identified in each center by a computerized search of the electronic medical records of patients undergoing AF ECV, looking for a diagnosis or remark of VAs, occurring during the same hospitalization period of the ECV itself.

In each case of post-AF ECV-related VA (defined as index VA) we obtained the following data, including total number of AF ECVs performed in the years in which post-AF ECV-related VAs occurred (for example, if the index VA events occurred during a 2-year period, we collected the total number of AF ECVs performed in the specific center during these 2 years); baseline patients characteristics including duration of AF before ECV, medical therapy including AAD therapy used for ECV and other QT-prolonging medications used; baseline 12-lead electrocardiography (ECG) prior to and post-ECV; and documentation of VA initiation. The pre- and post-ECV ECGs used for this analysis were those performed at the closest time to the ECV. Transthoracic echocardiography (TTE) results were based on TTE performed at the closest time to ECV and not more than 6 months prior to ECV, and laboratory test results were taken from ECV hospitalization.

Long-term therapy and follow-up involved the device implanted (if any), either permanent pacemaker (PPM) or implantable cardioverter-defibrillator (ICD), and recurrence of VAs after the index VA event. The date of last follow-up was defined as last clinical visit or documented medical

study (ECG/Holter/TTE examination). Death from any cause was assessed and SCD noted.

AF ECV was divided into elective or urgent. Urgent ECV was defined by an ECV performed without any delay, usually in cases of hemodynamic instability or pulmonary edema.

Statistical analysis

Characteristics were described by mean ± SD or median (interquartile range) for continuous variables and as number and percentage for categorical variables. Relations between categorical variables was evaluated by chi-square and Fisher's exact tests. The effect of categorical variables on continuous measurements was tested by Student *t* and Mann-Whitney tests or by 1-way analysis of variance and Kruskal-Wallis tests. The choice of a parametric or nonparametric test depended on the distribution of a continuous variable. All tests were 2-sided. $P < .05$ was considered statistically significant.

The research reported in this article was approved by the ethical committee (Helsinki) in each of the participating hospitals. Notably, patient consent was waived due to the retrospective nature of the study, which was based on de-identified data collection.

Results

Incidence

Thirteen centers provided data, of which 9 reported cases and 4 reported no cases of VAs post-AF ECV (index VA). Our study included 23 cases of post-AF ECV-related VAs obtained from 9 large European medical centers during a median period of 24 (interquartile range 12–60) months (Table 1). These included 6 of 5400 AF ECVs performed during the collecting period in 4 Italian centers, 10 of 750 AF ECVs from 2 Israeli centers, 5 of 1830 AF ECVs from a single Czech center, 1 of 327 ECVs from 1 Spanish center, and 1 of 300 ECVs from 1 center in the Netherlands. There were 0 cases out of 3290 ECVs performed in 4 other centers, resulting in overall prevalence of post-AF ECV-related VAs of 23 out of 11,897 ECVs (0.2%), ranging between 0% and 1.3% in different centers. Hospitalization duration post-ECV in centers with no VAs post-AF ECV was significantly shorter than in other centers in which VAs were found (9 ± 7 hours vs 21 ± 9 hours; $P = .04$).

Clinical characteristics

Among index cases, there were 13 (56.5%) females, the mean age was 71 ± 11 years, and 22 (96%) were Caucasians. The vast majority (n = 22 of 23 [96%]) of cases had no prior VAs (patients with prior sustained VAs were excluded according to the study's exclusion criteria, and 22 of 23 had no prior nonsustained VAs, as well). There was a single patient who had 2 nonsustained polymorphic VT events few hours after prior pulmonary vein isolation ablation for AF, with marked QT prolongation on ECG postablation. The patients' medical history is shown in Table 2. Noteworthy, 17 patients had hypertension (HTN) and 17 had CHF symptoms (74% for both). Patients' mean left ventricular (LV) ejection fraction was 45 ± 9%, and 15 (65%) patients had LV dysfunction (LV ejection fraction <50%).

Twenty (87%) patients had persistent AF lasting ≥7 days, and the mean AF duration prior to ECV was 71 ± 54 days. AADs used prior to ECV included amiodarone, sotalol, Ic (as propafenone and flecainide), beta-blockers, and digoxin in 11 (48%), 4 (17%), 3 (13%), 19 (83%), and 4 (17%) patients, respectively (Table 2). Five (22%) patients received QT-prolonging drugs other than AADs including ranolazine, ciprofloxacin, and escitalopram. Overall, 17 (74%) cases were taking QT-prolonging medications at the time of ECV. Baseline hypokalemia <3.5 mmol/L was seen in 3 (13%) patients (range 2.9–3.4 mmol/L). High creatinine levels (≥1.5 mg%) pre-ECV were seen in 8 (61%) patients, with an average creatinine of 1.6 ± 1.2 mg/dL. The AF ECV was elective and urgent in 10 (43%) and 13 (57%) patients, respectively.

Comparing the pre- and post-ECV ECG data revealed significant HR slowing and QT prolongation post-ECV (Table 3). The HR slowed from 113 ± 27 beats/min pre-ECV to 57 ± 11 beats/min post-ECV ($P < .001$); QT duration prolonged from 390 ± 60 ms pre-ECV to 482 ± 61 ms post-ECV ($P < .001$). Notably, HR slowing and QT prolongation post-ECV were noticed in 22 (96%) and 21 (91%) patients, respectively. The pre- and post-ECV QTc was 523 ± 66 ms and 460 ± 59 ms, respectively ($P = .003$). There was no change in QRS duration pre- and post-ECV (111 ± 29 ms and 111.5 ± 28 ms; $P = .9$).

Arrhythmia characteristics

Post-ECV VA (index VA) included TdP in 17 (74%), nonsustained polymorphic VT in 5 (22%), and SCD in 1 (4%) patient. VA documentation was available in 20 (87%) patients. The 3 cases without VA documentation include a case of SCD that occurred at home after discharge and 2 cases with VAs during hospitalization in which VAs were seen and recorded in patients' records but in which the VAs monitor tracings were lost. Index VA occurred 45 ± 54 hours post-ECV or median 28.5 (interquartile range 5.5–72) hours post-ECV. Notably, VAs occurred within 3–72 hours post-ECV in 19 (82.6%) cases, within <1 hour in 3 (13%) cases, and 10 days post-ECV in a single case. Figure 1 demonstrates an example of serial ECG changes, revealing marked HR slowing and a dynamic QT prolongation post-ECV, resulting in TdP occurrence. A VA storm (defined as >3 VA episodes within 24 hours) occurred in 11 (48%) patients. VAs reoccurred after the index VA event in 9 (39%) patients, at 13 ± 15 (range 0.5–48) hours after the index VA. The VAs which reoccurred were TdP in 5 (22%), VF in 2 (9%), sustained monomorphic VT, in 1 (4%), and nonsustained polymorphic VT in 1 (4%) patient.

Arrhythmia therapy

The index VA was terminated acutely via ECV in 10 (43%) patients. Class III AADs and QT-prolonging medications were discontinued in all patients. Intravenous electrolytes

Table 1 Post-AF ECV-related index VA cases

Patient	Country	Age (y)	Sex	CAD	CHF	EF (%)	Valvular*	Pre-ECV AF duration (d)	Pre-ECV heart rate (beats/min)	Pre-ECV QT (ms)	Pre-ECV AAD	Elective/urgent ECV	Post-ECV index VA	Index VA timing post ECV (h)	DCCV needed for index VA	Post ECV heart rate (beats/min)	Post-ECV QT (ms)	VA recurrence post–index VA
1	Italy	76	F	Yes	Yes	40	No	90	79	450	Amio, BB, O	Elective	TdP	72	No	81	414	No
2	Italy	64	M	No	Yes	45	No	60	74	464	Amio, BB	Elective	TdP	0.5	No	50	470	No
3	Italy	51	M	Yes	No	55	No	45	81	458	Sotalol	Elective	NSPVT	0.2	No	48	452	Yes
4	Italy	58	M	No	Yes	39	No	70	64	470	Amio, BB	Elective	TdP	0.1	Yes	44	473	Yes
5	Italy	78	M	No	Yes	40	No	15	138	372	Amio, BB	Urgent	TdP	72	Yes	57	487	No
6	Italy	82	F	No	Yes	35	No	180	142	450	Amio, BB, Dig, O	Urgent	TdP	72	Yes	70	500	No
7	Netherlands	72	F	Yes	No	50	No	9	75	425	Sotalol	Elective	TdP	24	Yes	45	600	Yes
8	Spain	80	F	No	No	45	No	1	130	383	BB, Dig, O	Urgent	TdP	5	Yes	80	425	Yes
9	Czechia	72	M	Yes	Yes	55	No	180	119	352	BB	Elective	SCD	12	No	46	436	No
10	Czechia	69	M	Yes	Yes	30	No	25	113	380	Amio, BB	Elective	TdP	1	No	55	440	No
11	Czechia	71	M	Yes	Yes	47	No	1	132	344	BB, Ic	Urgent	NSPVT	4	Yes	68	445	No
12	Czechia	78	M	Yes	Yes	60	No	100	94	428	BB	Elective	NSPVT	3	No	63	466	No
13	Czechia	61	M	No	No	58	No	135	92	402	Amio, BB	Elective	NSPVT	6	No	61	432	No
14	Israel	80	F	No	No	52	No	60	115	470	Sotalol, BB	Elective	TdP	7	Yes	53	510	Yes
15	Israel	78	F	No	No	60	No	2	126	340	BB, Ic, O	Urgent	TdP	240	No	75	394	Yes
16	Israel	70	M	No	Yes	30	No	36	82	430	Amio, BB, O	Urgent	TdP	33	Yes	44	590	Yes
17	Israel	41	F	No	Yes	37	No	90	150	400	BB, Dig	Urgent	TdP	24	Yes	52	480	Yes
18	Israel	86	F	Yes	Yes	52	Yes	30	117	340	BB, Dig	Urgent	TdP	72	Yes	44	520	No
19	Israel	66	F	No	Yes	37	Yes	180	130	340	BB, Ic, Dig	Urgent	TdP	5	No	52	520	Yes
20	Israel	84	F	No	Yes	42	No	60	150	360	BB	Urgent	TdP	72	No	62	640	No
21	Israel	62	F	Yes	Yes	42	Yes	210	120	340	Amio, BB	Urgent	TdP	72	Yes	51	440	No
22	Israel	66	F	No	Yes	40	Yes	60	120	400	Amio	Urgent	TdP	48	No	60	480	No
23	Israel	88	F	No	Yes	52	No	7	158	280	Sotalol	Urgent	NSPVT	48	No	50	480	No

AF = atrial fibrillation; Amio = amiodarone; BB = beta-blocker; CAD = coronary artery disease; Dig = digoxin; DCCV = direct-current cardioversion; ECV = electrical cardioversion; EF = ejection fraction; F = female; Ic = class Ic antiarrhythmic drug; M = male; O = other QT-prolonging medication; SCD = sudden cardiac death; TdP = torsades de pointes; VA = ventricular arrythmia; NSPVT = nonsustained polymorphic ventricular tachycardia.

*Moderate-severe or severe valvular stenosis/regurgitation.

Table 2 AF ECV-related VA patients' clinical background

Parameter	Prevalence (n = 23)
Age, y	71 ± 11.6
Female	13 (56.5%)
Hypertension	17 (74%)
Diabetes mellitus	6 (26%)
Ischemic heart disease	9 (39%)
Congestive heart failure	17 (74%)
Chronic renal failure	7 (30.5%)
Chronic obstructive lung disease	4 (17.5%)
TTE	
LVEF	45 ± 9%
AS (moderate/severe)	5 (22%)
MR (moderate/severe)	15 (65%)
TR (moderate/severe)	11 (48%)
Medication prior to AF ECV	
Beta-blockers	19 (83%)
Digoxin	4 (17.5%)
Amiodarone (PO/IV)	9 P.O + 2 I.V = 11 (48%)
Sotalol (PO)	4 (17.5%)
Ic	3 (13%)
QT-prolonging drugs (not AADs)	5 (22%)
AF duration prior to ECV, d	71 ± 54

Values are AAD = antiarrhythmic drug; AF = atrial fibrillation; AS = aortic stenosis; ECV = electrical cardioversion; Ic = class Ic AAD; IV = intravenous; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; PO = orally; TR = tricuspid regurgitation; TTE = transthoracic echocardiography; VA = ventricular arrythmia.

(magnesium and potassium) were effective in arrhythmia control in 16 (89%) of 18 patients, intravenous isoproterenol was effective in 1 (20%) of 5 patients, and temporary pacing was effective for arrhythmia control in 3 (60%) of 5 patients in whom it was used. An ICD and PPM were implanted in 7 and 4 patients, respectively. Notably, recurrence of VAs after the index VA event did not seem to be related with the decision on device implantation, as 5 of 9 patients with VAs recurrence were eventually implanted an ICD/PPM vs 6 of 14 patients without VAs recurrence who were implanted with an ICD/PPM ($P = .7$).

Patient outcome

Two (8.7%) patients expired shortly after the ECV. The first (patient 5, Table 1) was a 78-year-old male with HTN, CHF symptoms (NYHA functional class III), with mildly reduced LV function, moderate mitral regurgitation, and moderate aortic stenosis, who developed an acute HF exacerbation and fatal TdP, unresponsive to cardiopulmonary resuscitation attempts including multiple external defibrillator shocks, 72 hours post-ECV, which was done urgent due to worsening HF symptoms. The other (patient 9, Table 1) was a 72-year-old man with HTN, chronic renal failure (creatinine 2.4 mg%), ischemic heart disease, and CHF symptoms (NYHA functional class II), with preserved LV function, who died suddenly at home 12 hours after an elective ECV, without prior neurological complains (we attribute his sudden death to represent a fatal index VA). During mean follow-up of 28 ± 40 months, there was 1 more death occurring 18 months after the index VA, in a patient implanted with an ICD, and its cause was unknown.

Table 3 Medical background, post-ECV ECG data, and index VA treatment among patients with and without VA recurrence post–index VA event

	VA recurrence (n = 9)	No VA recurrence (n = 14)	*P*
Age, y	70.1 ± 13.3	74 ± 9	.4
Female	6 (66.7%)	7 (50%)	.43
Hypertension	6 (66.7%)	11 (78.6%)	.52
Diabetes mellitus	3 (33.3%)	3 (21.4%)	.52
Chronic renal failure	3 (33.3%)	4 (28.6%)	.8
COPD	1 (11.1%)	3 (21.4%)	.55
Ischemic heart disease	2 (22.2%)	7 (50%)	.18
TTE data			
LVEF	43.9 ± 9.5	46.1 ± 9.4	.59
Moderate/severe MR	5 (55.6%)	8 (57.1%)	.94
Moderate/severe TR	3 (33.3%)	8 (57.1%)	.26
Moderate/severe AS	2 (22.2%)	3 (21.4%)	.97
AAD during ECV			
Class III AAD or other QT-prolonging drugs	7 (77.8%)	9 (64.3%)	.5
Post-ECV ECG data			
Post-ECV HR, beats/min	54.8 ± 13.4	59.2 ± 10.3	.38
Post-ECV HR <60 beats/min	7 (77.8%)	6 (42.8%)	.09
Post-ECV QT	491.5 ± 73.2	463.8 ± 62.6	.34
Post-ECV QT >500 ms	4 (44.4%)	2 (14.3%)	.1
Post-ECV QTc	461.5 ± 44	458.4 ± 69.4	.9
Treatment for index VA			
ECV	6 (66.7%)	5 (35.7%)	.14
IV isoproterenol	5 (55.6%)	0 (0%)	.01*
AAD discontinuation	7 (77.8%)	10 (71.4%)	.73
Temporary pacing	3 (33.3%)	2 (14.3%)	.25

Values are mean ± SD or n (%).

AAD = antiarrhythmic drug; AS = aortic stenosis; COPD = chronic obstructive pulmonary disease; ECG = electrocardiography; ECV = electrical cardioversion; HR = heart rate; IV = intravenous; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; TR = tricuspid regurgitation; TTE = transthoracic echocardiography; VA = ventricular arrythmia.

*Statistically significant.

Arrhythmia reoccurrence subgroup analysis

Comparing patient subgroups with and without VAs recurrence after the index VA event did not reveal significant difference in medical background or in post-ECV mean HR, QT, and QTc values (Table 3). Nevertheless, there was a nonsignificant higher prevalence of patients with bradycardia (HR <60 beats/min) and massive QT prolongation (QT >500 ms) among the group with recurrent VA (Table 3). Additionally, significantly more patients were treated with intravenous isoproterenol during the index VA event among the group with subsequent VAs recurrence as compared with the group without VA recurrence (5 of 9 vs 0 of 14; $P = .01$).

Discussion

Our retrospective multicenter study involving 13 large medical centers found 23 cases of post-ECV–related VAs out of 11,897 AF ECVs done in these centers, during a median

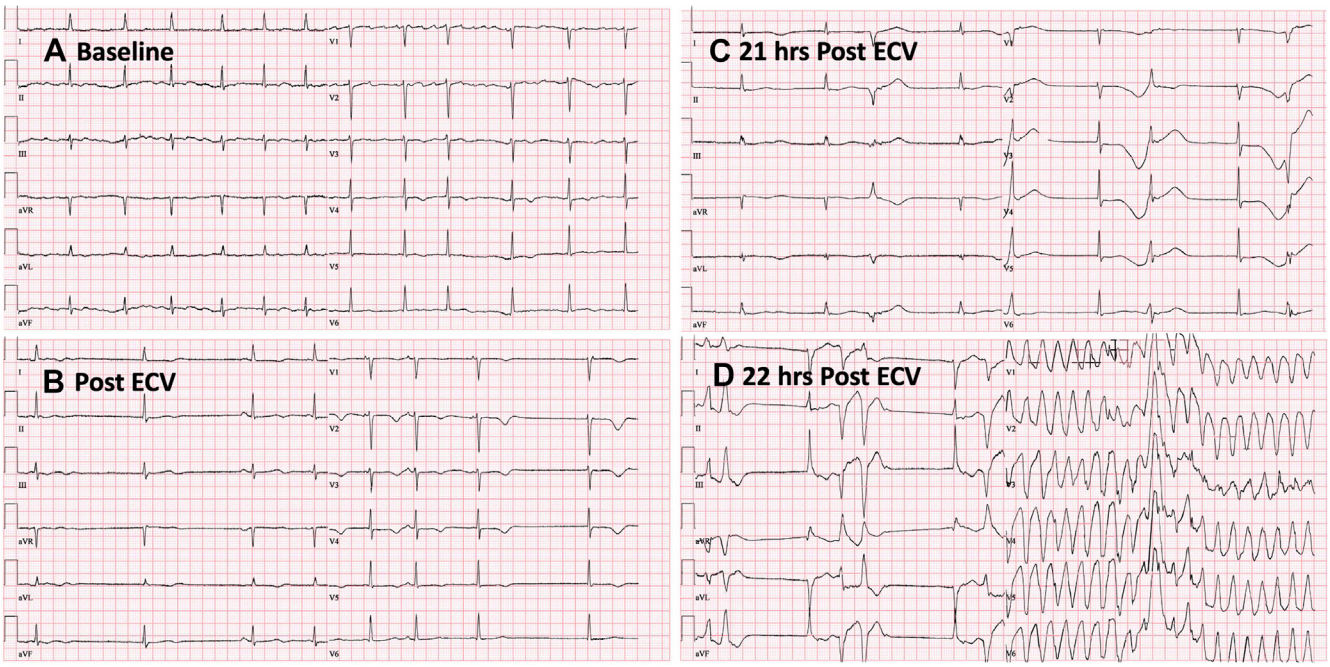

Figure 1 Typical example of post–electrical cardioversion (ECV) QT prolongation resulting in torsades de pointes. A: Baseline electrocardiography (ECG) pre-ECV, atrial fibrillation with ventricular rate 76 beats/min, QT 420 ms. B: ECG immediately post-ECV, sinus bradycardia with intermittent nodal escape is seen, QT 600 ms. C: ECG the next day (21 hours post-ECV) reveals nodal rhythm with premature ventricular contractions, massive QT prolongation of 800 ms. D: ECG 22 hours post-ECV, nodal rhythm with premature ventricular contractions and initiation of torsades de pointes. All images courtesy of Dr Pieter G. Postema.

period of 24 months. None of these patients had sustained VAs prior to ECV. Most patients had persistent AF, lasting 71 ± 54 days prior to ECV. The vast majority of VAs occurred between 3 and 72 hours post-AF ECV (median 28.5 hours, mean 45 hours post-ECV), and consisted of TdP and nonsustained polymorphic VT, associated both with QT prolongation. Most patients (74%) were taking class III AAD or other QT-prolonging medications during the time of ECV, 74% had CHF symptoms and 65% had reduced LV function. Post-ECV–related VAs were terminated by ECV, discontinuation of AADs and other QT-prolonging drugs, correction of QT-related metabolic abnormalities, or use of temporary pacing. Recurrent VAs occurred in 39% of the patients, 13 ± 15 hours after the index VA event. A PPM or ICD was implanted in 48% of the patients. There were 2 (8.7%) patients who died due to VA within 72 hours from the index VA event, both without a PPM/ICD. One other death of unknown cause occurred 18 months after the index VA event, in a patient implanted with an ICD.

Our study found 23 cases of post-EVC-related VAs out of 11,897 AF ECVs, suggesting an overall low incidence of 0.2%, although certain centers had a h higher incidence. Currently, there is a limited and conflicting data regarding the actual prevalence of this AF ECV-related complication.[12–15] While in the 2012 Euro Heart Survey including 712 AF ECVs, post-ECV–related VA occurred in 1.3% of cases,[14] and in another study including 2900 ECVs, post-EVC VF was reported in 0.16% of cases,[13] no VAs needing intervention were found in the Arrhythmic complications after electrical cardioversion of acute atrial fibrillation: the FinCV study, including 7660 AF ECVs,[12] as well as among 543 elective AF ECVs reported by Morani and colleagues.[15] To the best of our knowledge, our retrospective multicenter study involving 11,897 AF ECVs is the largest study evaluating post-AF ECV-related VAs, suggesting that VAs complicating ECV is a real phenomenon, albeit a rare one. Importantly, even in our study there was a marked variability of post-ECV–related VA incidence, ranging from 0% to 1.3% in different centers. We attribute this variability to differing clinical practice in different centers, and specifically to the duration of hospitalization and monitoring post-AF ECV. In accordance with the expectation that a shorter surveillance post-ECV would lead to lower detection of VAs the post-AF ECV hospitalization duration among centers with 0% incidence of VAs was significantly shorter than in other centers in which VAs were found (9 ± 7 hours vs 21 ± 9 hours; $P = .04$). A short observation period post-AF ECV may lead to a falsely low post-ECV–related VA incidence, due to later postdischarge VAs that might occur at home without awareness of the hospital team. Accordingly, we speculate that some ECV-related VAs were not detected even in our study. Thus, we suggest that the true incidence of post-AF ECV-related VAs might be higher than 0.2%.

In our study, vast majority (n = 22 of 23 [95.6%]) of index VA included arrhythmias that are usually related to QT prolongation. Factors contributing to post-ECV QT prolongation in the current cohort included marked and sudden slowing of HR from fast AF to sinus bradycardia in many cases, treatment with class III AADs or other QT-prolonging medications in most cases, and the previously described ventricular repolarization remodeling effect of ECV that may have to do with the prolonged pre-ECV AF duration in our study.[4,5] Indeed, the

period shortly after AF ECV was shown to be specifically susceptible for AAD-induced QT prolongation due to a steeper QT-RR slope during this period, compared with the pre-ECV AF period.[4,7,8,10] Accordingly, the significant HR slowing post-ECV found in our study contributed to marked QT prolongation (due to the steep QT/RR slope) with further prolongation due to class III AAD use. Furthermore, a possibility of genetic susceptibility to drug- and bradycardia-induced prolonged QT could not be ruled out.[17] In a prior study in which all AF patients had a continuous 7-day Holter monitoring starting just before ECV, a significant and dynamic QT prolongation was found in 43% of patients, with peak QT duration occurring on average 44 hours post-ECV.[11] This is consistent with the timing of the index VA in our study, which occurred on average 45 hours post-ECV. Noteworthy, in contrast with the QT prolongation post-ECV found in our study, the QTc had shortened. We attribute this shortening to the marked HR change from rapid AF to sinus bradycardia, resulting in almost twice RR interval increase post-ECV (1082 ± 191 ms vs 561 ± 155 ms; RR ratio of 1.9). Thus, even though the RR interval is taken by square in QTc calculation, its effect dominated the QT prolongation ratio (482 ± 61 ms vs 390 ± 60 ms; QT prolongation ratio 1.2). Overall, it seems that in these cases with significant RR changes induced by ECV, the QT rather than the QTc, might be more clinically relevant.

Seventy-four percent of our cases had CHF symptoms, raising the possibility that CHF itself may potentiate the risk of post-ECV VA, either due to the use of amiodarone, which is the only AAD suitable for AF maintenance in the presence of reduced LV function in Europe (where dofetilide in not approved for use), or by some other yet unknown mechanisms as well. The incidence of drug-induced TdP among AF patients with CHF was shown to be higher than among AF patients with structurally normal hearts, taking the same drugs, suggesting that CHF itself may serve as a risk factor for drug-induced TdP in AF patients.[7] Our study results support this concept as most of our AF ECV-related VAs cases had CHF symptoms and were taking QT-prolonging medications (74% for both).

Last, there were 9 (39%) cases with recurrent VAs occurring 13 ± 15 hours after the index VA event. We did not find any medical background associated with VA recurrence (Table 3). Post-ECV bradycardia and QT prolongation were more common among patients with recurrent VA, although without statistical significance ($P = .09$ and .1, respectively). A significant association was found between isoproterenol treatment for the index VA event and recurrent VA ($P = .01$). However, because these recurrent VAs occurred on average 13 hours after the index VA event, we find it unlikely that isoproterenol had a direct impact on their reoccurrence, although we cannot rule it out. Nevertheless, we suggest that isoproterenol might have been given during index VA event to patients with more severe bradycardia and QT prolongation, reflecting the potential contribution of bradycardia and QT prolongation to subsequent VA episodes. Thus, the significant association of isoproterenol with recurrent VA may suggest that post-ECV bradycardia and QT prolongation, which were both associated with the index VA event, may still be associated with recurrent VAs as well. Given our small number of cases with VAs, we could not perform multivariable analysis to identify predictors for recurrent VAs occurrence, and this will need to be proven in larger future studies.

Limitations

Our study has several limitations. First, it is an observational retrospective study with all the limitations associated with such trial design. Second, the duration of post-ECV hospitalization as well as postdischarge patient surveillance was different among the participating centers. Therefore, the incidence of post-ECV VAs and SCD might have been underestimated by the current study. Third, the first ECG performed post-ECV was collected in all cases. However, because the post-ECV VAs may have occurred several hours later, we do not always have ECG in proximity to the VA event. Thus, we could not exclude a dynamic QT prolongation with further increase of QT interval occurring just before the index VA episode (as shown in the example in Figure 1), and as was actually shown in a previous study of continuous 7-day Holter post-ECV.[11] The fact that most of the post-ECV index VA types (including TdP and nonsustained polymorphic VT) are usually related to prolonged QT further supports this concept. Fourth, there may be data collection bias, as the cases with post-ECV VAs were identified via a computerized search for VAs occurring after ECV, while the patient was still hospitalized. Nevertheless, as early post-ECV discharge is many times the rule, one could not rule out potential VAs and SCD cases occurring postdischarge, unknown to the medical team and not recorded in the patients' medical records. Moreover, because only 13 out of 77 centers that were approached have participated and sent data, we could not rule out another source of collection bias, in which some centers did not experience such complication and therefore did not think of participating. Last, because there was no control group of patients with AF who underwent ECV without VAs, and given the small number of cases with post-ECV VAs that does not allow performance of multivariate analysis, our presented data should not be overinterpreted in terms of detection of risk factors or predictors for the occurrence of ECV-related VAs. Indeed, we acknowledge this is the main limitation of our study, which could only give a signal of caution for possible high-risk characteristics of patients having post-ECV VAs but not define risk subgroups for post-ECV VAs.

Conclusion

Our multicenter study involving 13 large worldwide centers, showed prolonged QT-related VAs in 0.2% of AF ECVs, occurring mainly within 3 to 72 hours post-ECV. Importantly, in many cases the VAs occurred later than the widespread practice of same-day discharge, implemented in many centers. Most patients with post-ECV VAs had persistent and rapid AF, were taking class III AADs or other QT-prolonging medications, and had CHF symptoms. Some cases had recurrent

VA after the index VA event, and 2 patients died within 72 hours post-ECV. Overall, our study highlights the rare but existing concept of post-ECV VAs and suggests that a routine same-day discharge after AF ECV may not apply for all patients. The current study could not define risk factors for post-ECV VAs, but rather gives a signal of caution favoring prolonged monitoring in a small subset of patients. Further large-scale studies are needed to define predictors for post-ECV–related VAs and patient subgroups at risk, for whom a prolonged post-ECV monitoring may be warranted.

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