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Long-Term Follow-Up of Idiopathic Ventricular Fibrillation in a Pediatric Population: Clinical Characteristics, Management, and Complications

Antonio Frontera, MD; Konstantinos Vlachos, MD; Takeshi Kitamura, MD; Saagar Mahida, MD, PhD; Xavier Pillois, PhD; Gerard Fahy, MD; Christelle Marquie, MD; Riccardo Cappato, MD; Graham Stuart, MBChB, PGCert, MSc; Pascal Defaye, MD; Juan Pablo Kaski, MD; Joris Ector, MD, PhD; Alice Maltret, MD; Patrice Scanu, MD; Jean-Luc Pasquie, MD; Isabelle Deisenhofer, MD; Ivan Blankoff, MD; Daniel Scherr, MD; Martin Manninger, MD, PhD; Yoshifusa Aizawa, MD; Linda Koutbi, MD; Arnaud Denis, MD; Thomas Pambrun, MD; Philippe Ritter, MD; Frederic Sacher, MD, PhD; Meleze Hocini, MD; Philippe Maury, MD; Pierre Jaïs, MD; Pierre Bordachar, MD, PhD; Michel Haïssaguerre, MD; Nicolas Derval, MD

Background—The natural history and long-term outcome in pediatric patients with idiopathic ventricular fibrillation (IVF) are poorly characterized. We sought to define the clinical characteristics and long-term outcomes of a pediatric cohort with an initial diagnosis of IVF.

Methods and Results—Patients were included from an International Registry of IVF (consisting of 496 patients). Inclusion criteria were: (1) VF with no identifiable cause following comprehensive analysis for ischemic, electrical or structural heart disease and (2) age ≤ 16 years. These included 54 pediatric IVF cases (age 12.7 ± 3.7 years, 59% male) among whom 28 (52%) had a previous history of syncope (median 2 syncopal episodes [interquartile range 1]). Thirty-six (67%) had VF in situations associated with high adrenergic tone. During a median 109 ± 12 months of follow-up, 31 patients (57%) had recurrence of ventricular arrhythmias, mainly VF. Two patients developed phenotypic expression of an inherited arrhythmia syndrome during follow-up (hypertrophic cardiomyopathy and long QT syndrome, respectively). A total of 15 patients had positive genetic testing for inherited arrhythmia syndromes. Ten patients (18%) experienced device-related complications. Three patients (6%) died, 2 due to VF storm.

Conclusions—In pediatric patients with IVF, a minority develop a definite clinical phenotype during long-term follow-up. Recurrent VF is common in this patient group.

Key Words: idiopathic • defibrillator • ventricular fibrillation • complications • ventricular tachycardia • syncope

The majority of cases of arrhythmic sudden cardiac death (SCD) in young patients are attributable to either inherited structural cardiac diseases or primary arrhythmic syndromes.¹ In a subset of patients the cause of ventricular

fibrillation remains undefined despite comprehensive diagnostic evaluation and is referred to as idiopathic ventricular fibrillation (VF). According to contemporary guidelines idiopathic VF is defined as resuscitated cardiac arrest that occurs

From the Electrophysiology Department, Hôpital Haut Lévêque, Bordeaux, France (A.F., K.V., T.K., X.P., A.D., T.P., P.R., F.S., M. Hocini, P.J., P.B., M. Haïssaguerre, N.D.); LIRYC Institute, Bordeaux, France (A.F., X.P., M. Hocini, P.J., P.B., M. Haïssaguerre); Department of Cardiac Electrophysiology and Inherited Cardiac Diseases, Liverpool Heart and Chest Hospital, Liverpool, United Kingdom (S.M.); Cork University Hospital, Cork, Ireland (G.F.); Univ. Lille CHU Lille, F-59000 Lille, France (C.M.); Humanitas Clinical and Research Center, Rozzano, Milan, Italy and Humanitas University, Department of Biomedical Sciences, Milan, Italy (R.C.); Bristol Heart Institute, Bristol, United Kingdom (G.S.); Centre Hospitalier University of Grenoble, France (P.D.); Centre for Inherited Cardiovascular Diseases, Great Ormond Street Hospital, London, United Kingdom (J.P.K.); UCL Institute of Cardiovascular Science, London, United Kingdom (J.P.K.); University Hospital Gasthuisberg, Leuven, Belgium (J.E.); Hôpital Necker Enfants Malades, Service de Cardiologie Pédiatrique et Centre de Référence des Maladies Cardiaques Héritaires, Université Paris Descartes, Paris, France (A.M.); Centre Hospitalier University of Caen, France (P.S.); Centre Hospitalier University of Montpellier, France (J.-L.P.); Herzzentrum München, Munich, Germany (I.D.); Centre Hospitalier University of Charleroi, Belgium (I.B.); Division of Cardiology, Department of Medicine, Medical University of Graz, Austria (D.S., M.M.); Niigata University Graduate School of Medical and Dental Science, Niigata, Japan (Y.A.); Hôpital La Timone, Marseille, France (L.K.); Centre Hospitalier University of Toulouse, France (P.M.).

Correspondence to: Antonio Frontera, Electrophysiology Department, Hôpital Haut Lévêque, 1 Avenue Magellan, Pessac 33600, France. E-mail: a.frontera@gmail.com

Clinical Perspective

What Is New?

- This is the first study to systematically evaluate long-term outcomes among pediatric patients with an initial diagnosis of idiopathic ventricular fibrillation.
- We demonstrate that among pediatric idiopathic ventricular fibrillation patients, arrhythmias commonly occur in the context of high adrenergic tone, and there is a high incidence of recurrent arrhythmic events.
- Only a small minority of patients develop evidence of an underlying cardiac phenotype during long-term follow-up.

What Are the Clinical Implications?

- Over the years, the risk of recurrent arrhythmic events continues to be elevated, and therefore, in addition to implantation of cardiac defibrillators, these patients should be followed up closely.
- The incidence of complications related to implanted cardioverter/defibrillators in this pediatric population is relatively high, which may have important implications in terms of choice of device.

in the absence of cardiac, metabolic, toxicological, and respiratory causes.² Overall, idiopathic VF accounts for up to 8% of arrhythmic sudden cardiac death cases.³

There is a relative paucity of data on the natural history and long-term outcome in patients of pediatric age who present with idiopathic VF (IVF). Available studies have largely focused on adult cohorts with IVF.⁴ The aim of the present study is to define the long-term outcome in pediatric VF patients.

Methods

Data Collection

Patients were included from an International Registry of Idiopathic Ventricular Fibrillation (IVF) that consists of 496 IVF patients⁵ from 45 tertiary cardiac centers worldwide (collected between March 2004 and December 2015). The data are available on request from the authors. Criteria for inclusion in the registry were (1) sudden cardiac arrest with documented VF as the cause of arrest, (2) an absence of an underlying cause following comprehensive analysis for ischemic, electrical, infectious, or structural heart disease, and (3) age ≤ 16 years. The diagnostic criteria for IVF were based on the latest consensus guidelines.¹

Patients were systematically assessed at the referring centers after the index VF episode (before being assigned a diagnosis of IVF). Data on past clinical symptoms, including previous syncopal episodes, were collected. Family history of

SCD was defined as a sudden death that occurred before 55 years of age in the absence of any known underlying pathological conditions.

The clinical workup consisted of a baseline ECG, blood tests (including cardiac enzymes and electrolytes), toxicology screening, and cardiac imaging (echocardiography and/or cardiac magnetic resonance imaging). Ajmaline testing was performed in order to exclude a diagnosis of concealed Brugada syndrome. Isoproterenol or epinephrine testing and exercise stress testing (using a modified Bruce protocol adapted for pediatric patients) were performed to exclude long-QT syndrome and catecholaminergic polymorphic ventricular tachycardia (VT). The aforementioned tests were performed at the investigating physician's discretion at the referring center. Signal-averaged ECG and endomyocardial biopsies were also performed at the investigating physician's discretion. Time of implanted cardioverter/defibrillator (ICD) implantation and device programming were left to the decision of the referring physician (according to latest guidelines in order to reduce the possibility of inappropriate ICD shocks). The study was approved by the Institutional Review Board at CHU Bordeaux (inclusion in the IVF registry was approved by the institutional review boards at the respective institutions).

IVF Characteristics

The circumstances during the index VF event were categorized as (1) at rest, (2) daily activity, (3) sleep, (4) emotional stress, or (5) sport/strenuous activity. "At rest" was defined as SCD that occurred during no physical activity. "Daily activity" was defined as SCD that occurred during routine activities with very light physical activity. "Sleep" was defined as SCD occurring during bedtime or while asleep. Emotional stress was defined as intense emotion. Strenuous activity was defined as moderate to severe exercise (including in the setting of sport).

ECG Analysis

All ECGs (during the index hospitalization and at follow-up) were reviewed by 2 independent electrophysiologists (K.T., V.K.). In case of disagreement, the ECG was reviewed by a third electrophysiologist (N.D.). ECGs were analyzed at a paper speed of 25 mm/s and an amplitude of 10 mm/mV. Digital calipers were used to perform measurements (EP Calipers version 1.8 [<http://www.epstudiossoftware.com/>], EP Studios, 2017). P-wave duration and dispersion were calculated from the standard ECG during sinus rhythm where dispersion was defined as the difference between the minimum and maximum P-wave duration. Early repolarization was defined according to the latest consensus guidelines.⁶

Abnormal QRS fragmentation was defined as either ≥ 4 spikes in 1 lead or >1 notches in the nadir of the R or S wave in 2 consecutive leads. Davignon criteria⁷ were used to exclude right and left ventricular hypertrophy. S waves were characterized in terms of amplitude and duration in lead I. T peak–T end interval was measured from the peak to the end of the T wave in the precordial leads.

Invasive Electrophysiology Study

Programmed ventricular stimulation was performed at the investigating physicians' discretion. A consistent stimulation protocol from the right ventricular apex and outflow tract was used (2 drive cycle lengths [600 and 400 ms] and 3 extrastimuli with a minimal coupling up to 180 ms [unless ventricular arrhythmia was induced or the ventricular effective refractory period was reached]). A sustained VT/VF episode, defined as an episode lasting >30 s or VT/VF requiring direct current cardioversion, was considered a positive electrophysiological study. Nonsustained episodes (<30 s) were classified as negative electrophysiological study.

Genetic Testing

When available, genetic testing for variants implicated in heritable cardiomyopathies and/or channelopathies (long QT syndrome, short QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia) was performed per consensus guidelines. When a putative mutation was identified, cascade screening was performed in family members.² The choice of genes targeted during genetic analysis was at the treating physician's discretion. Assignment of pathogenicity of identified variants was based on conventional guidelines.³ Repeat genetic testing with more extensive genetic panels was performed at the treating physician's discretion.

Follow-Up

Patients were followed up with sequential ICD interrogations (at least every 4 months), ECG, and cardiac imaging (echocardiography). Appropriate and inappropriate therapies with an implantable defibrillator were documented. Genotype and phenotype reevaluations during follow-up were performed at the investigating physician's discretion. Phenotypic reevaluation included repeat cardiac imaging, exercise stress testing, and pharmacological stress testing.

Statistical Analyses

Continuous variables were expressed as mean \pm standard deviation. Categorical variables were expressed as percentages. Qualitative variables were compared using the Fisher

exact test, whereas the Mann-Whitney test was used for continuous variables. Kaplan-Meier analysis was also performed for arrhythmia-free survival. A $P < 0.05$ was considered to be statistically significant.

Results

Patient Characteristics

Fifty-four of the 496 patients in the IVF registry fulfilled inclusion criteria. Patient characteristics are summarized in

Table 1. Population Study

Age, y	12.7 \pm 3.7
Male, n (%)	32 (59%)
Ethnicity, n (%)	
White	45 (84%)
Afro-Caribbean	5 (9%)
Asian	4 (7%)
Circumstances of SCD, n (%)	
Sport/strenuous activity	15 (28%)
Daily activity	11 (20%)
Emotional stress	11 (20%)
Rest	12 (22%)
Sleep	5 (10%)
Confirmation of IVF, n (%)	
Coronary angiogram	24 (44%)
Imaging	
Echo	54 (100%)
CMR	38 (70%)
Treadmill test	45 (83%)
Pharmacological tests, n (%)	
Isoproterenol	38 (70%)
Ajmaline	24 (44%)
Flecainide	13 (24%)
Endomyocardial biopsy	7 (13%)
Before the SCD event, n (%)	
Syncope	28 (52%)
Epilepsy	5 (9%)
Palpitations	2 (4%)
Family history of SCD, n (%)	
First degree	10 (67%)
Second degree	3 (20%)
Third degree	2 (13%)

CMR indicates cardiac magnetic resonance; Echo, echocardiogram; IVF, idiopathic ventricular fibrillation; SCD, sudden cardiac death.

Table 1. At the time of the index VF episode, the mean age was 12.7 ± 3.7 years. Thirty-two patients (59%) were male. Patients were predominantly of white descent (45 white [84%]; 5 Afro-Caribbean [9%]; 4 Asian [7%]). Twenty-eight patients (52%) had a prior history of syncope (median 2 syncopal episodes, interquartile range 1). Twenty-four (85%) had effort-induced syncope. The syncopal events occurred 54 ± 10 days before the sudden cardiac arrest. Five patients (9%) had previously been diagnosed with epilepsy. None of the patients had a history of recreational drug use. Specific details of the circumstances of the index episode are included in Table 1. All 54 patients underwent ICD implantation.

Fifteen patients (28%) had a family history of SCD (10 [67%] a first-degree relative; 3 [20%] a second-degree relative; 2 [13%] a third-degree relative). The mean age of sudden cardiac death in the relatives was 35.9 years (SD 19.7). In 1 case, sudden death occurred in 2 siblings.

Investigations

Imaging and Biopsy

Transthoracic echocardiography demonstrated a structurally normal heart in all patients (ejection fraction $61.5 \pm 6.2\%$). Cardiac magnetic resonance imaging was performed in 38 patients (70%) and confirmed the absence of structural heart disease. Coronary angiography was performed in 24 patients (44%) with no cases of anomalous coronary anatomy or significant stenosis identified. Seven patients (13%) underwent endomyocardial biopsy with negative results in all cases.

Table 2. Electrocardiographic Characteristics

Characteristics	Mean Value (SD)
Heart rate, bpm	76.3 (21.2)
P wave duration, ms	96.9 (17.2)
P wave dispersion, ms	36.8 (17.6)
P wave amplitude, mV	0.63 (3.66)
PR duration, ms	159.4 (30.98)
QRS duration, ms	82.9 (14.7)
IVS (Cornell), mm	1.26 (0.79)
QTc (Bazett), ms	416 (48.8)
S wave duration (I), ms	30.3 (12.2)
S wave amplitude (I), mV	0.23 (0.18)
T peak–T end, ms	88.4 (22.2)
QRS fragmentation, N (%)	25 (46.3%)
U wave, N (%)	27 (50%)

IVS indicates interventricular septum thickness (in mm); U wave, evidence of U wave on the 12-lead ECG.

Exercise and Pharmacological Testing

Forty-five patients (83%) underwent exercise stress testing, and 38 patients (70%) had an isoproterenol challenge. There were no QT interval abnormalities or sustained arrhythmias during these tests. In 1 patient the isoproterenol test induced multifocal ventricular ectopic beats. Ajmaline/flecainide challenge was performed in 37 patients (69%) and excluded Brugada syndrome.

ECG

None of the patients presented with left or right ventricular hypertrophy (based on the Davignon criteria). The early repolarization pattern was present in 31 patients (57.4%). Electrocardiographic characteristics are summarized in Table 2. The characteristics of the subset of patients with an early repolarization pattern are included in Table 3.

Invasive Electrophysiology Studies

An electrophysiological study was performed in 34 patients (63%). VF was induced in 3 patients (9%). There were no cases of inducible VT. Three patients (9%) had inducible atrial tachycardia.

Genetic Analysis

Forty-five patients (83%) underwent genetic testing. A putative pathogenic mutation was identified in 15 of the 45 (33%) patients (*RYR2* [n=7]; *TRDN* [n=2]; *CALM1* [n=1]; *CASQ2*

Table 3. ECG Characteristics of Subset of Patients With Early Repolarization

	No ER (n=23)	ER (n=31)	P Value
Female sex, N (%)	9 (40.9%)	11 (35.5%)	0.63
Age, y	12.2	13.1	0.77
HR (bpm) mean	79	74.4	0.45
P wave duration, ms	97.8	96.6	0.78
P wave amplitude, mV	0.16	0.99	0.11
P wave dispersion, ms	38.4	36.06	0.58
PR, ms	152.5	164.6	0.18
QRS duration, ms	83.6	81.7	0.60
QRS fragmentation, n (%)	10 (45.5)	14 (45.2)	0.92
IVS, mm	10.9	13.7	0.22
QTc, ms	426.5	408.8	0.19
S wave duration, ms	26	17	0.82
S wave amplitude, mV	0.156	0.162	0.21
U wave, N (%)	12 (54.5)	15 (50)	0.66
T Peak–T end, ms	94.1	84.5	0.12

ER indicates early repolarization; IVS, interventricular septum thickness (in mm).

Table 4. Pathogenic Mutation Identified in 15 of 45 Patients

Patient	Gene	Identified Variant	Homozygote/ Heterozygote	MAF in gnomAD
1	<i>RYR2</i>	R4608Q	Heterozygote	0
5	<i>SLC22A5</i>	R471H	Heterozygote	0
6	<i>CASQ2</i>	Deletion of Exon1	Heterozygote	0
17	<i>KCNH2</i>	A429P	Heterozygote	0
18	<i>RYR2</i>	D4112N	Heterozygote	0
19	<i>RYR2</i>	D4112N	Heterozygote	0
22	<i>RYR2</i>	R4497C	Heterozygote	0
29	<i>SCN5A</i>	R1644H	Heterozygote	0
37	<i>MYH7</i>	F48L	Heterozygote	0
46	<i>CALM</i>	N98S	Heterozygote	0
47	<i>TRDN</i>	c/53_56delACAG p.(Asp18AlafsTer14)	Compound heterozygote	0
48	<i>TRDN</i>	c.502G>T p.(Glu168Ter)	Compound heterozygote	0
49	<i>RYR2</i>	c.7273T>C	Heterozygote	0
50	<i>RYR2</i>	G3930R	Heterozygote	0
51	<i>RYR2</i>	c.11648A>G	Heterozygote	0

MAF indicates minor allele frequency.

[n=1]; *SCN5A* [n=1]; *KCNH2* [n=1]; *MYH7* [n=1]; *SLC22A5* [n=1]). Two patients did not provide consent for disclosure of their genetic results. Based on the rapidly emerging data on genetic variation in normal populations, we reevaluated the prevalence of the reported genetic variants in the gnomAD database, which spans $\approx 123\ 000$ exomes (<http://gnomad.broadinstitute.org/>). All variants were confirmed to be unique (Table 4).

Pharmacotherapy

Twenty patients (37%) were discharged following the index VF with no drug therapy. Eighteen (33%) were commenced on a selective β -blocker. One patient was discharged with quinidine.

Outcomes

Arrhythmia Recurrences

Patients were followed up for a median time of 109 ± 12 months after the index VF episode. Thirty-one patients (57%), experienced a recurrence of ventricular arrhythmias (23 [74%] had only VF; 8 [26%] had only sustained VT). Four patients (13%) experienced both VT and VF episodes. The patients with recurrences experienced a median of 2 appropriate shocks (interquartile range 5.5). The first recurrence of ventricular arrhythmia occurred after a

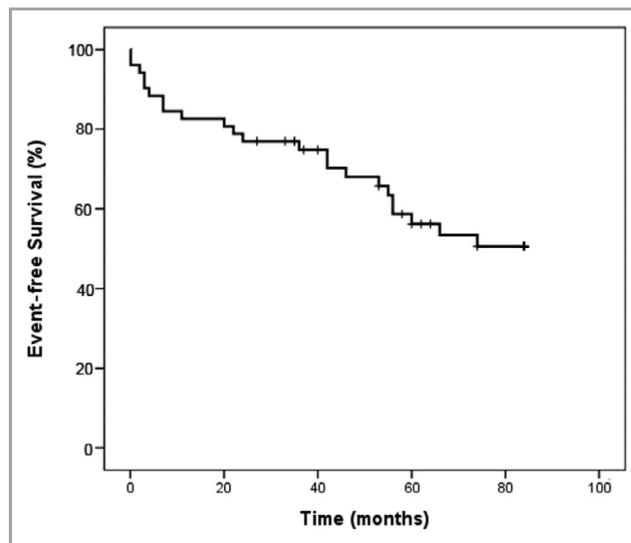


Figure 1. Kaplan–Meier curve demonstrating freedom from ventricular arrhythmias.

mean of 6.4 years after the index VF episode (Kaplan-Meier curve, Figure 1).

In 12 of 31 patients (39%), recurrences of ventricular arrhythmia occurred in the context of high adrenergic tone (exercise or intense stress/emotion), and the remaining recurrences occurred at rest. The arrhythmia recurrences according to clinical characteristics and specific genotypes are represented in Tables S1 and S2. One patient developed paroxysmal atrial fibrillation. The characteristics of individuals with VT/VF-related ICD shocks are included in Table 5. Nine (33%) patients with VF recurrences were drug-naive. Among the 36 patients in whom the index VF episode occurred in the context of high adrenergic tone, 15 (42%) had recurrent ventricular arrhythmias. In the remaining 18 patients (nonadrenergic group), 12 (67%) experienced a recurrence of VF. Recurrence of arrhythmia occurred in 4 patients treated with selective β -blockers and in 1 patient treated with mexiletine. Three patients (6%) died during follow-up. Two died due to an arrhythmic storm. One patient remained in a neurovegetative state following the arrest until death.

Device-Related Complications

Ten patients (18%) experienced device-related complications (ventricular lead fracture [n=5]; lead insulation defect [n=1]; further device procedures due to lead recall [n=2]; late lead dislodgement [n=1]; device infection [n=1]). Eleven patients (20%) experienced inappropriate shocks (sinus tachycardia [n=1]; atrial arrhythmias [n=3]; noise on the ventricular channel [n=3], lead fracture [n=3]; sensing lead insulation defect [n=1]). The mean time from implant to complication was 41 ± 14 months; the mean number of inappropriate shocks was 1.9 ± 1 (Table 6).

Table 5. Recurrences of Ventricular Arrhythmias

	Sex	Past Syncope	Family History	EP Study	Genetic	Death
VF group (n=23)	16 male	12/23 (52%)	8/23 (35%)	Performed in 3/12 Inducible (13%)	18/23 (78%) 1 CALM+ 2 Triadin + 4 RyR2+	2 (9%)
VT group (n=8)	6 male	5/8 (62.5%)	5/8 (62%)	Performed in 6/8 (75%) No inducible ventricular tachycardia	Performed in 7/8 (88%) RyR2+ (2) and Triadin+ (2)	1 (14%)

EP indicates electrophysiological; VF, ventricular fibrillation; VT, ventricular tachycardia.

Repeat Testing

Patients underwent systematic phenotype reevaluation 78±11 months after the index VF episode: all patients underwent repeat ECGs and transthoracic echocardiography. Forty-five percent had a repeat cardiac magnetic resonance; 90% had a repeat stress test (with adult exercise testing protocols); 62% had a repeat isoproterenol challenge. Repeat genetic sequencing with an extended genetic panel was performed in 54% of the population at the discretion of the treating physician. One patient (2%) developed phenotypic evidence of hypertrophic cardiomyopathy during follow-up. Of note, that patient had previously been identified as a *MYH7* variant carrier (patient 37, Table 4). None of the patients who

Table 6. ICD Characteristics and Complications Encountered During the Follow-Up

ICD characteristics	
Endocardial implant, n (%)	47 (87%)
Single-chamber ICD	45 (96%)
Dual-chamber ICD	2 (4%)
Epicardial implant	4 (7%)
Subcutaneous ICD	3 (6%)
ICD complications	
Inappropriate shocks, n (%)	11 (20%)
Sinus tachycardia	1 (9%)
Atrial arrhythmias	3 (27%)
Lead fracture	3 (27%)
Noise on the V channel	3 (27%)
Lead insulation defect	1 (9%)
Device-related complications, n (%)	10 (18%)
Lead fracture	5 (50%)
Lead recall	2 (20%)
Pocket infection	1 (10%)
Sensing lead insulation defect	1 (10%)
Lead dislodgement	1 (10%)

ICD indicates implanted cardioverter/defibrillator.

underwent repeat exercise stress testing or isoproterenol challenge had exercise-induced arrhythmias. Repeat genetic testing did not reveal additional variants. None of the long QT gene carriers had a prolonged QT interval at the time of the index event; 1 of the patients (patient 29 in Table 4) had evidence of QT prolongation during follow-up (*SCN5A* mutation carrier; QT interval 495 ms). The results of phenotypic reevaluation are included in Figure 2.

Discussion

The main findings of the present study are as follows: (1) the majority of SCD events in pediatric IVF patients occur in the context of high adrenergic tone; (2) close to a fifth of pediatric IVF patients have variants in genes implicated in catecholaminergic polymorphic ventricular tachycardia; (3) pediatric IVF patients have a high risk of recurrent arrhythmic events during long-term follow-up; (4) only a small minority of patients develop evidence of an underlying cardiac phenotype during long-term follow-up. (5) The incidence of ICD-related complications in this pediatric population is relatively high.

The majority of reports on IVF to date have focused on adult populations. There is a relative paucity of data on IVF in pediatric populations. In a large cohort of adult IVF patients, Visser and colleagues reported that, during long-term follow-up, a specific diagnosis was identified in up to a fifth of patients⁴ of whom almost 50% were found to have an underlying cardiomyopathy. In contrast to these findings, during a similar follow-up period specific diagnoses were identified in only 4% of our pediatric cohort. It is important to emphasize, however, that because our cohort was of pediatric age at the index VF event, the initial evaluation was less comprehensive than that routinely performed in adult cohorts. Further, although reevaluation of our cohort during follow-up did not reveal a specific underlying diagnosis, the strategies for reevaluation were variable. Our findings may, however, suggest that the underlying arrhythmogenic substrate in pediatric patients is distinct from that of adult IVF patients and may have a low diagnostic yield.

A potential pathogenic genetic variant was identified in a third of the patients in our cohort. In turn, variants in *RYR2*

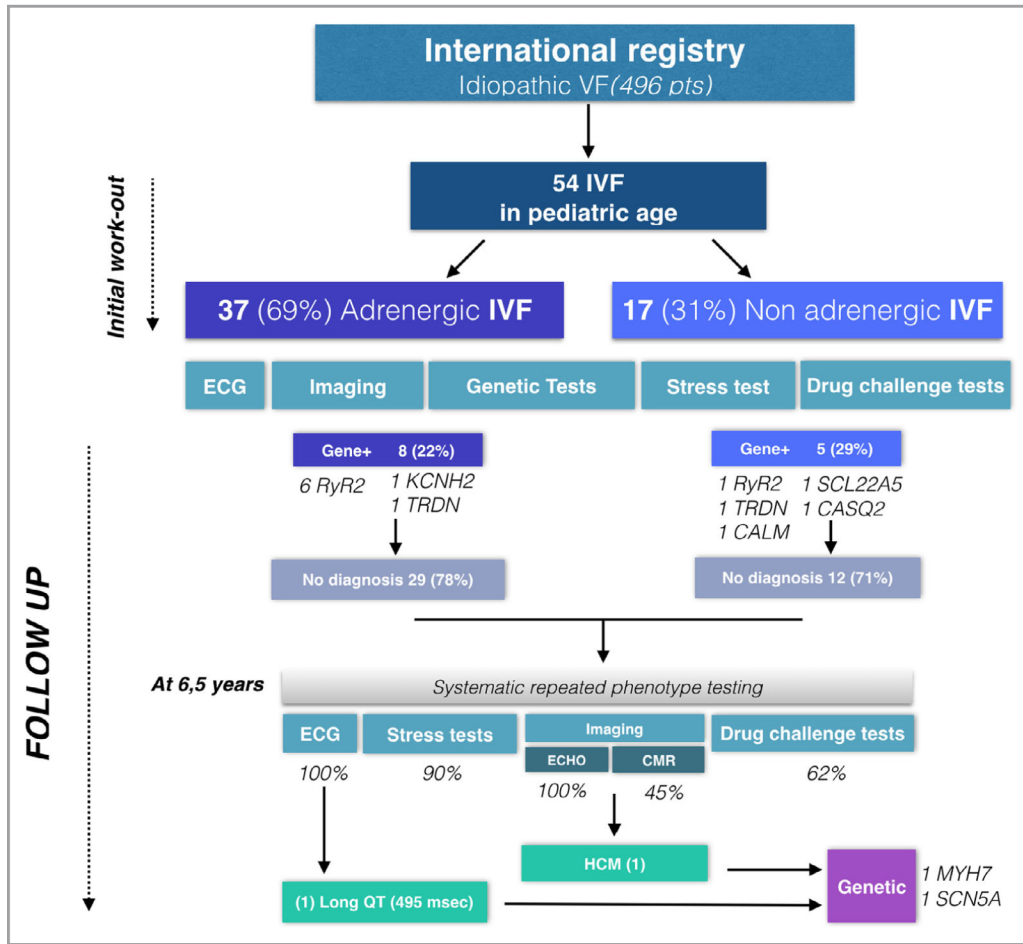


Figure 2. Summary of phenotypic evaluation following index episode and at follow-up (78 ± 11 months). CMR indicates cardiac magnetic resonance; ECHO, echocardiogram; HCM, hypertrophic cardiomyopathy; IVF, idiopathic ventricular fibrillation; VF, ventricular fibrillation.

were identified in close to half of the genotype-positive patients. Consistent with our finding, Lahrouchi et al⁸ reported that in patients with sudden arrhythmic death syndrome, *RYR2* variants were the most commonly identified pathogenic/likely pathogenic variants following postmortem genetic testing (43% of genotype-positive cases). In the study by Visser and colleagues,⁴ on the other hand, the overall yield for genetic testing was lower at 15%, with only a quarter of genotype-positive patients harboring catecholaminergic polymorphic ventricular tachycardia gene variants. Of note, patients included in our study (as in that of Lahrouchi et al) were significantly younger than the patients included by Visser et al. It is important to note, however, that a significant proportion of apparently pathogenic *RYR2* variants may not be disease causing.⁹ Furthermore, although the yield of genetic test may increase with broad multiphenotype genetic testing, this approach may be associated with a higher incidence of variants of uncertain significance.¹⁰

Further, in the study of Visser and colleagues,⁴ a third of adult IVF patients experienced recurrent arrhythmic events.

We observed a higher frequency of recurrent arrhythmic events in our pediatric IVF cohort, with close to half of cases experiencing recurrences. Importantly, despite an overall higher arrhythmic burden, the recurrent arrhythmic events in our cohort occurred at a later stage as compared with those reported in the adult population. These findings suggest that, in pediatric IVF patients, the disease process is associated with a more malignant course, with ongoing arrhythmic risk extending over a more prolonged period of time.

The choice of ICD device is an important consideration in pediatric populations. In recent years increasing evidence has emerged supporting the use of subcutaneous ICD as an alternative to transvenous systems.¹¹ Close to a fifth of patients in our cohort experienced device-related complications, which predominantly consisted of lead-related issues. These findings may support the use of subcutaneous ICD in pediatric populations.

In addition to a family history of SCD, ECG features such as Tpeak-Tend >100 ms with U waves and right bundle branch block were associated with more arrhythmia recurrences in

our cohort. Our findings are in line with similar results in the adult population,¹² and these ECG markers could potentially modulate arrhythmic risk stratification. However, based on the limited size of our cohort, these results should be interpreted with caution.

Limitations

Patients were recruited from a large number of centers over a prolonged period of time (more than a decade) in multiple countries. Therefore, the workup of patients following the VF episode and ICD programming was not standardized. It must be emphasized that guidelines for evaluation of these patients evolved over the time period of the study; therefore, there was some variation in the investigation of patients following episodes of aborted sudden death. During follow-up, close to half of the population did not undergo comprehensive genetic testing. Medications were prescribed at the physician's discretion, and we acknowledge that is also a potential confounding factor. Among patients who did not have a cardiac magnetic image performed (30%), we acknowledge that a diagnosis of myocarditis could have been missed. Genetic testing was performed in the absence of a clear phenotype and on a discretionary basis. Where performed, genetic testing involved a candidate-gene approach that targeted the common genes implicated in cardiac channelopathies and cardiomyopathies.

Conclusion

Our findings suggest that both the clinical course and underlying arrhythmogenic substrate in pediatric patients with IVF are distinct from those previously reported for adult IVF cohorts.

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Disclosures

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