Pediatric Journal Review by Trainees (PJRT) Winter 2022/2023 Edition

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Section #1: Inherited Arrhythmias

- Emmi Helle, MD
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Highly malignant disease in childhood-onset arrhythmogenic right ventricular cardiomyopathy

Marit Kristine Smedsrud, Monica Chivulescu, Marianne Inngjerdingen Forså, Isotta Castrini, Eivind Westrum Aabel, Christine Rootwelt-Norberg, Martin Prøven Bogsrud, Thor Edvardsen, Nina Eide Hasselberg, Andreas Früh, Kristina Hermann Haugaa. *European Heart Journal (2022) ehac485* (Link)

Background: The onset of ARVC is typically observed in the third and fourth decade of life, and there is little research on the clinical characteristics of pediatric ARVC. This study described the phenotype and explored the incidence of severe cardiac events in paediatric (≤18 years) ARVC in a single centre. In addition, the penetrance in paediatric relatives was studied.

Methods: Consecutive paediatric ARVC patients (n=11) and genotype positive relatives ≤18 yrs (n=51) were followed for 6 years with ECG, structural, and arrhythmic characteristics according to the 2010 revised Task Force Criteria. Penetrance of ARVC was defined as fulfilling definite ARVC criteria and severe cardiac events were defined as cardiac death, heart transplantation (HTx) or severe ventricular arrhythmias. Childhood-onset disease was defined as meeting definite ARVC criteria ≤12 years of age.

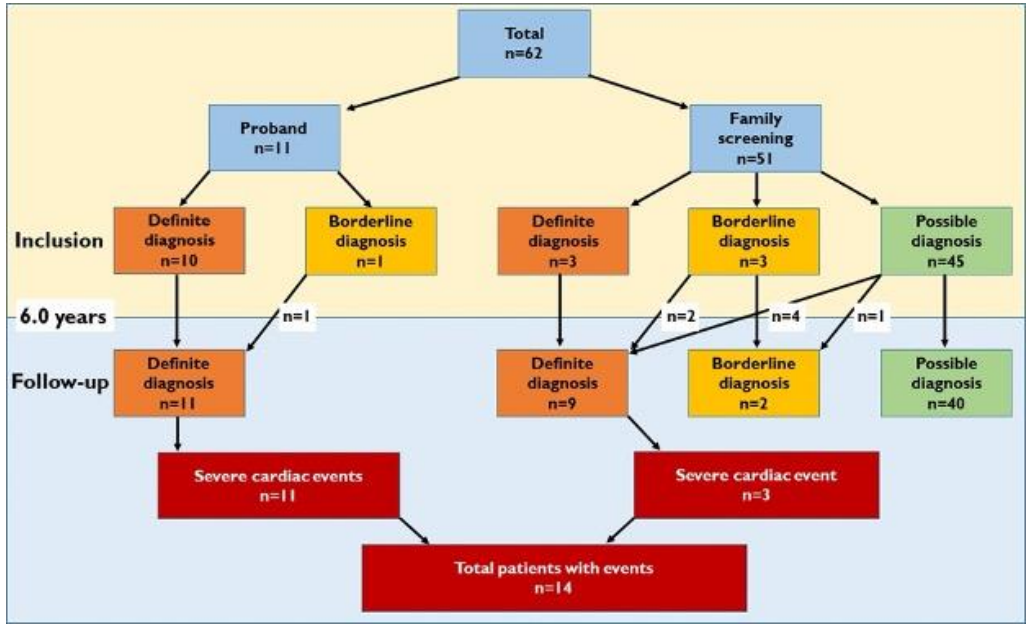

Figure 1: Flowchart of included patients, diagnosis and outcome

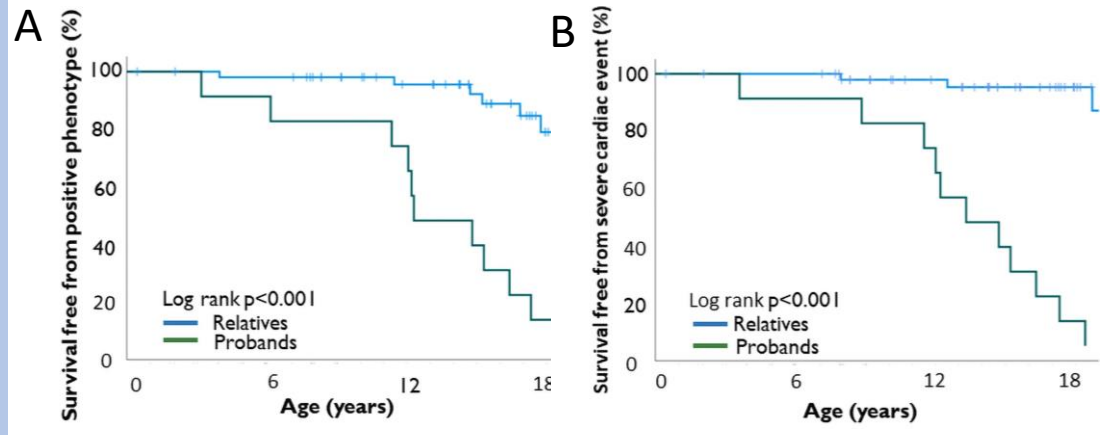

Figure 2: Survival from A) positive phenotype, B) severe cardiac events

Results:

- All (11/11) probands, and 33% (3/9) of relatives with a definitive diagnosis had severe cardiac events during the follow-up period (Figure 1).
- Most (40/51, 78%) relatives did not exhibit symptoms during the follow up (Figure 1).
- In genotype positive paediatric relatives, ARVC penetrance at end of follow-up was 18% (Figure 2A).
- Among the 62 included patients, 6 had a severe cardiac event at inclusion as the first sign of ARVC disease. Eight patients experienced a severe cardiac event during follow-up (Figure 2B).
- The cumulative incidence of severe cardiac events was 23% in paediatric ARVC patients ≤ age 18 (Figure 2B).
- Median age at severe cardiac event was 12.9y (10.9–16.6).

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Results:

- The clinical phenotypes of the study subjects are presented in Table 1.
- 57 (92%) of all study subjects had a disease-causing variant (Table 1).
- The phenotypes identified in the 20 patients with a definite ARVC diagnosis at end of follow-up were right predominant in 11 (55%) and biventricular in 9 (45%) patients.
- In the six patients with a severe cardiac event as a first sign of ARVC disease, all were arrhythmic events (3 ACA, 3 sustained VT) (Table2).
- All five children who underwent HTx had childhood-onset disease and the youngest patient was transplanted at age 3 (Table 2).
- Three (6%) of the relatives experienced severe cardiac events (Table 2).

	Overall (n=62)	Proband (n=11)	Relative (n=51)	p-value
Female sex n(%)	34 (55)	4 (36)	30 (59)	0.18
Age at inclusion, years	9.8 (5.0–14.0)	12.3 (11.4–16.4)	9.0 (4.3–12.9)	0.02
Mutation carrier n(%)	57 (92)	7 (64)	50 (98)	<0.01
Follow-up, years	6.0 (2.9–9.6)	6.6 (1.8–9.9)	5.8 (3.5–9.2)	0.72
Repolarization criteria n(%)	13 (21)	9 (82)	4 (8)	<0.01
Major	0 (0)	0 (0)	0 (0)	1.00
Minor	13 (21)	9 (82)	4 (8)	<0.01
Depolarization criteria n(%)	6 (10)	4 (36)	2 (4)	<0.01
Epsilon wave	0 (0)	0 (0)	0 (0)	1.00
Late potentials	6 (10)	4 (36)	2 (4)	<0.01
Arrhythmia criteria n(%)	16 (26)	9 (82)	7 (14)	<0.01
Major	0 (0)	0 (0)	0 (0)	1.00
>500 PVCs/24 h	16 (26)	9 (82)	7 (14)	<0.01
Abnormal Imaging n(%)	12 (19)	10 (91)	2 (4)	<0.01
Major	12 (19)	10 (91)	2 (4)	<0.01
Minor	0 (0)	0 (0)	0 (0)	1.00

Table 1. Clinical phenotype of probands and relatives

Conclusion:

A high incidence of severe cardiac events were noted with half of them occurring in children ≤12 years of age.

The ARVC penetrance in genotype positive paediatric relatives was 18%.

➔These findings may indicate a need for ARVC family screening at younger age than currently recommended.

	Age (y) at Dx	Event	Gene	Sex	Cardiac event
Probands					
1	3.2	3.6	+	M	HTx
2	6.2	8.8	+	F	HTx
3	11.4	11.5	-	F	HTx
4	12.1	12.1	+	M	Sustained VT
5	12.2	12.2	-	M	ACA
6	12.3	13.3	-	M	Sustained VT
7	14.8	14.8	+	F	Sustained VT
8	15.3	15.3	-	F	ACA
9	16.4	16.4	+	M	ACA
10	17.3	17.3	+	M	Sustained VT
11	18.5	18.5	+	M	Sustained VT
Relatives					
12	3.9	7.9	+	F	HTx
13	11.5	12.6	-	F	HTx
14	17.7	18.8	+	M	Sustained VT

Table 2: Severe cardiac events in probands and relatives

Section #2: Ablations

- Claire Newlon, MD
- Vanderbilt University

Multicenter Outcomes of Catheter Ablation for Atrioventricular Reciprocating Tachycardia Mediated by Twin Atrioventricular Nodes

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BACKGROUND

- There is limited data on electrophysiologic properties and ablation outcomes of twin AV node tachycardia (T-AVRT)

METHODS

- International, multicenter retrospective study (PACES, ISACHD)
- Inclusion: EPS with confirmed twin AV nodes
- Exclusion: ablation performed before 1998
- Diagnosis of T-AVRT included the combination of:

1) presence of 2 discrete non–preexcited QRS patterns with intrinsic or paced atrial rhythms

2) evidence of decremental or adenosine-sensitive anterograde and retrograde conduction over 2 separate AV pathways

3) presence of 2 anatomically separate His bundle electrograms, each preceding the QRS pattern and located at the AV annulus, with ≥1 displaying a physiological HV interval while in atrial rhythm and during tachycardia

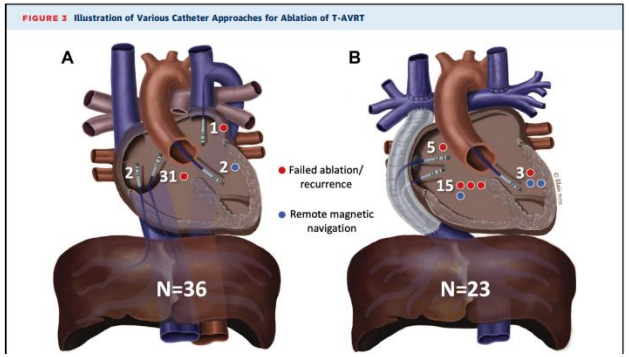
4) QRS complex during tachycardia resembling QRS in atrial rhythm

5) plausibly long VA interval during tachycardia that could account for trans-AV nodal conduction

6) V-A-V response after ventricular overdrive pacing during tachycardia

RESULTS

- N = 59 (median age 8 years [IQR 4.4-17.0 years]; 49% male
- Underlying diagnoses:
  - Heterotaxy in N=55 (93%): RAI N=39, LAI N=8, indeterminate N=8
- Surgical history:
  - Fontan operation N=23 (39%); 12 extracardiac and 11 lateral tunnel
- Atrial access post-Fontan palliation:
  1) conduit or baffle puncture N=15 (65%
  2) fenestration N=5 (22%)
  3) retrograde N=3 (13%)



Patients before biventricular repair or Fontan operation (A) and after the Fontan operation (B). Numbers refer to the sum of the various approaches used in the study population and the solid red circles indicate failed catheter ablation or recurrent tachycardia during follow-up. Solid blue circles indicate procedures using remote magnetic navigation

RESULTS

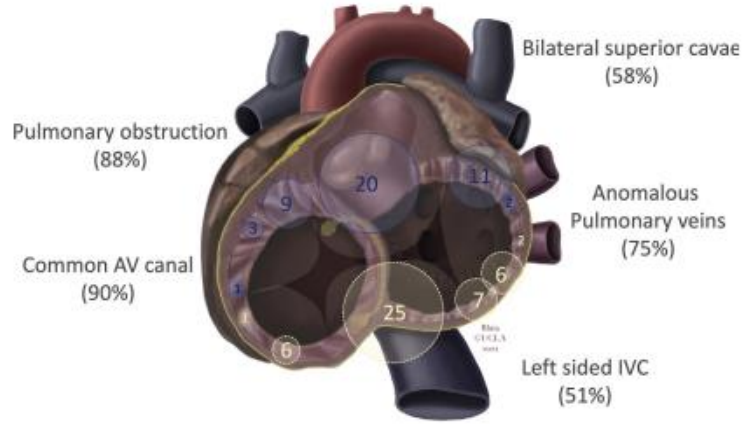
EP study characteristics:

- Similar EP properties of the anterior and posterior AV nodes
- Both anterior and posterior AV nodes could serve as the antegrade limb of T-AVRT
- T-AVRT could operate in either direction in a minority of patients
- Indirect evidence of continuous conduction sling in 75% of the T-AVRT patients

Outcomes:

- Acute success: N=43 (91%) of 47 attempts (targeting an anterior node in 23 and posterior node in 24)
- Complications: No high-grade AV block or change in QRS duration.
- Recurrences: N=3 recurrences over median 3.8 yrs follow-up.
- Of 7 patients with failed index procedure or recurrent T-AVRT, 6 (86%) were associated with anatomical hurdles such as prior Fontan or catheter course through an interrupted inferior vena cava–to–azygous vein continuation

CENTRAL ILLUSTRATION Anatomical Substrates and Locations of Atrioventricular Nodes



Moore JP, et al. J Am Coll Cardiol EP. 2022;8(3):322-330.

Schematic summarizing anatomical substrates and locations of anterior and posterior atrioventricular (AV) nodes in the study population. **Blue numbers** correspond to the documented locations of anterior AV nodes and **yellow numbers** to posterior AV nodes. No patient simultaneously displayed >1 anterior or posterior AV node. IVC = inferior vena cava.

TABLE 2 Results of Electrophysiology Testing

Baseline, N = 59	
2 separate HBEs identified	41 (69)
2 QRS morphologies, differential atrial pacing	39 (66)
Retrograde decremental VA	47 (80)
Antegrade decremental	56 (95)
Wenckebach cycle length	
Anterior node, ms	300 (247-372)
Posterior node, ms	275 (252-315)
Adenosine administered	25 (42)
Adenosine response[a]	
Ventriculo-atrial block	12
AV block	4
Bidirectional block	9
Isoproterenol administered	9 (15)
Tachycardia, N = 44	
Tachycardia induced	44 (75)
Tachycardia cycle length, ms	343 (308-380)
Retrograde limb	
Anterior AVN	22 (50)
Posterior AVN	14 (32)
Either posterior or anterior AVN	8 (18)
VOP during tachycardia	10 (23)
VAV response[b]	7
PPI-TCL, ms	115 (90-146)
His refractory VPD delivered	24 (55)
Pre-excite atrium	6

Values are n (%) or median (interquartile range), unless otherwise indicated.
[a]Unidirectional block tested in 16. [b]Response unavailable in 3.
AV = atrioventricular; AVN = atrioventricular node; HBE = His bundle electrogram; H = His; PPI = post-pacing interval; TCL = tachycardia cycle length; VAV = ventricle-atrium-ventricle; VOP = ventricular overdrive pacing; VPD = ventricular premature depolarization.

CONCLUSIONS

T-AVRT can be targeted successfully with low risk for recurrence (6.9%). Complications were rare in this population. Anatomical challenges were common among patients with reduced short and long-term efficacy, representing opportunities for improvement in procedural timing and planning.

Section #3: Clinical Electrophysiology

- Jonathan Uniat, MD
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Spectrum and prevalence of side effects and complications with guideline-directed therapies for congenital long QT syndrome

Katherine Martinez, Sahej Bains, BS, John R. Giudicessi, MD, PhD, J. Martijn Bos, MD, PhD, Raquel Neves, MD, Michael J. Ackerman, MD, PhD (Link)

BACKGROUND

- Beta-blockers (BBs), sodium channel blockers (SCBs), left cardiac sympathetic denervation (LCSD), and implantable cardioverter-defibrillators (ICDs) are used to prevent or counter long QT syndrome (LQTS)-triggered syncope, seizures, and sudden cardiac death.
- The spectrum and extent of the side effects/ complications associated with these guideline-directed therapies (GDT) remain unknown.

OBJECTIVES

- Identify the types/prevalence of treatment-associated side effects/complications for patients with the most common LQTS subtypes after GDT.

Methods

- Retrospective analysis performed on 1310 patients with type 1, 2, or 3 LQTS evaluated in single center (Mayo Clinic)
- Must have been treated with one or more GDTs (BBs, SCBs, LCSD, ICDs)
- Patients only included if they had pathogenic or likely pathogenic variants in *KCNQ1*, *KCNH2*, or *SCN5A*
- Patients evaluated by single physician (M.J.A.)
- Electronic health records queried for patient information and reported treatment-related side effects.

RESULTS

Characteristic	Entire cohort
Cohort totals	1310 (100)
Female	758 (58)
Age at the time of diagnosis (y)	22 ± 18
Average QTc interval (ms)	469 ± 39
Treatment totals	
BBs	1102 (84)
SCBs	104 (8)
LCSD	197 (15)
ICD	251 (19)

BBs*

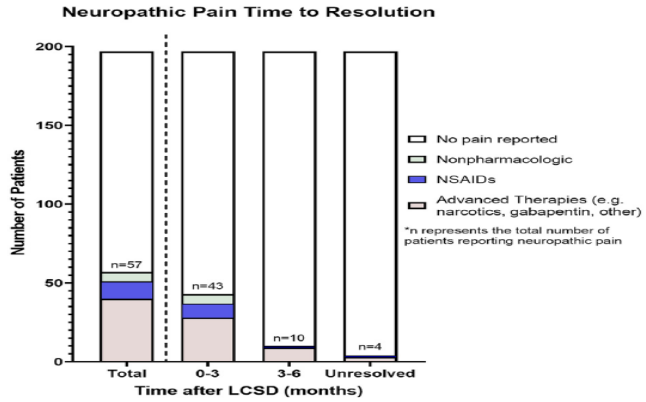
- 490 (44%) reported complications:
  - Fatigue (35%)
  - Lightheadedness (6%)
  - Weight gain (4%)
  - Depression (4%)

SCBs*

- 28 (27%) reported complications:
  - GI distress/vomiting (17%)
  - Lightheadedness (7%)
  - Fatigue (6%)

LCSD*

- 80 (41%) reported complications:
  - Neuropathic pain (29%)
  - Lightheadedness (7%)
  - Fatigue (6%)



ICD*

- 129 (51%) reported complications:
  - Inappropriate shocks >1 (18%)
  - Lead fracture (15%)
  - Posttraumatic stress disorder (7%)

*Top 3 most frequent complications listed

CONCLUSIONS

- With BB therapy, fatigue was common (35%). Symptoms improved after adjusting treatment to entirely exclude or lower the dosage of BBs
- Neuropathic pain was common status post LCSD but 93% had symptom resolution with available therapy
- Complications were common with ICD implantation (51%)