Novel insights on Andersen-Tawil syndrome type 1

A. Mazzanti[1], D. Guz[1], A. Trancuccio[1], E. Pagan[2], T. Chargeishvili[1], E.K. Biernacka[3], L. Sacilotto[4], E. Zorio[5], G. Brugada[6], E. Nof[7], A. Anastasakis[8], V. Sansone[9], J. Jimenez-Jaimez[10], F. Cruz[11], S.G. Priori[1]

[1]ICS Maugeri - IRCCS, Pavia, Italy; [2]University of Milan-Bicocca, Department of Statistics and Quantitative Methods, Milan, Italy; [3]Institute of Cardiology, Department of Congenital Heart Diseases, Warsaw, Poland; [4]Clinical Hospital of the University of Sao Paulo, Department of Cardiology, Sao Paulo, Brazil; [5]University Hospital y Politecnico La Fe, Department of Cardiology, Valencia, Spain; [6]Hospital Sant Joan de Deu, Arrhythmia Inherited Cardiac Diseases and Sudden Death Unit, Barcelona, Spain; [7]Sheba Medical Center, Tel Hashomer, Israel; [8]Onassis Cardiac Surgery Center, Athens, Greece; [9]ASST Great Metropolitan Niguarda, Milan, Italy; [10]University Hospital Virgen de las Nieves, Granada, Spain; [11]National Institute of Cardiology, Rio de Janeiro, Brazil

On behalf of ATS1 International Research Group

Funding Acknowledgement: Type of funding source: Public grant(s) – EU funding. Main funding source(s): ERN Guard-Heart European Reference Network for Rare and Low Prevalence Complex Diseases of the Heart

Background: Andersen-Tawil Syndrome type 1 (ATS1) in a rare arrhythmogenic disease caused by loss-of-function mutations in the KCNJ2 gene and characterized by ventricular arrhythmias, dysmorphic features and episodes of periodic paralysis. Although the prognosis of ATS1 patients is typically considered benign, definitive outcome data are lacking.

Purpose: We aimed to: 1) define the risk of life-threatening arrhythmic events (LAEs); 2) identify risk factors for such events; 3) assess the efficacy of anti-arrhythmic drugs in preventing LAEs.

Methods: We included 118 ATS1 patients from 57 families with confirmed pathogenic or likely pathogenic KCNJ2 mutations. Clinical and genetical data were acquired by investigators from 23 centers in 9 countries.

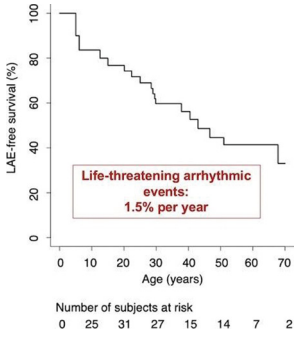
Results: Baseline characteristics of the population are presented in the Table. Over a follow-up of 6.2 years, 17/118 (14%) patients experienced a first LAE, with a 5-year cumulative probability of 7.9% (Figure). Cox multivariable analysis demonstrated that a previous history of syncope (HR 4.5, p=0.02), the documentation of sustained VT (HR 9.3, p=0.001) and the administration of amiodarone (HR 268, p<0.001) were associated with an increased risk of LAE. The baseline rate of LAE was not reduced by beta-blockers alone (1.37 per 100 py; p=1), or in combination with class Ic antiarrhythmic drugs (1.46 per 100 py, p=1).

Conclusions: Our data demonstrate that the clinical course of patients with ATS1 is characterized by a high rate of LAE. A history of unexplained syncope, and documentation of sustained ventricular tachycardia are independently associated with a higher risk of LAE. Amiodarone is proarrhythmic and should be avoided in ATS1 patients.

Baseline characteristics

	Evaluated N (%)	Finding
Female, N (%)	118 (100)	80 (68)
Age (years ± SD)	118 (100)	23±18
Follow-up (years ± SD)	118 (100)	11±12
Syncope, N (%)	118 (100)	19 (16)
Dysmorphic features, N (%)	118 (100)	89 (75)
Muscular weakness, N (%)	118 (100)	41 (35)
QTc (ms ± SD)	86 (73)	424±42
QUc (ms ± SD)	76 (64)	647±61
PVCs/24h (N ± SD)	84 (71)	14,399±17,408
Non sustained VT, N (%)	109 (92)	69 (63)
Sustained VT, N (%)	109 (92)	13 (12)

Characteristics of the study population (n=118) at the time of diagnosis.



ATS1: Diagnosis, Outcome, Risk Factors

Downloaded from https://academic.oup.com/eurheartj/article/41/Supplement_2/ehaa946.0744/6005710 by guest on 10 April 2024