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SCN5A mutations in 442 neonates and children: Genotype-phenotype correlation and identification of higher-risk subgroups

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Aims To clarify the clinical characteristics and outcomes of children with SCN5A-mediated disease and to improve their risk stratification.

Methods and results A multicentre, international, retrospective cohort study was conducted in 25 tertiary hospitals in 13 countries between 1990 and 2015. All patients $\leq$16 years of age diagnosed with a genetically confirmed SCN5A mutation were included in the analysis. There was no restriction made based on their clinical diagnosis. A total of 442 children {55.7% boys, 40.3% probands, median age: 8.0 [interquartile range (IQR) 9.5] years} from 350 families were included; 67.9% were asymptomatic at diagnosis. Four main phenotypes were identified: isolated progressive cardiac conduction disorders (25.6%), overlap phenotype (15.6%), isolated long QT syndrome type 3 (10.6%), and isolated Brugada syndrome type 1 (1.8%); 44.3% had a negative electrocardiogram phenotype. During a median follow-up of 5.9 (IQR 5.9) years, 272 cardiac events (CEs) occurred in 139 (31.5%) patients. Patients whose mutation localized in the C-terminus had a lower risk. Compound genotype, both gain- and loss-of-function SCN5A mutation, age $\leq$1 year at diagnosis in probands and age $\leq$1 year at diagnosis in non-probands were independent predictors of CE.

Conclusion In this large paediatric cohort of SCN5A mutation-positive subjects, cardiac conduction disorders were the most prevalent phenotype; CEs occurred in about one-third of genotype-positive children, and several independent risk factors were identified, including age $\leq$1 year at diagnosis, compound mutation, and mutation with both gain- and loss-of-function.

Keywords SCN5A mutation; Sudden death; Inherited arrhythmia; Genotype-phenotype correlation; Risk analysis
Disclosure of interest The authors declare that they have no competing interest.

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Coronary artery aneurysm risk factors for Kawasaki disease patients in North of France

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Objectives Kawasaki Disease (KD) is a child vasculitis. The prognosis is associated with a higher risk of coronary artery aneurysm (CAA). Currently the main goal of treatment consists of preventing CAA. At first the treatment consists on immunoglobulin (IVIG). The last American 2016 guidelines recommends echographical coronary diameter express as z-score. The epidemiology of KD is not well known in France. The aim of this study was to describe the population of the children in a region of North of France and to look for risk factors of CAA.
Methods We included patients with KD who were admitted in hospital centers of the region from 2006 to 2016. We reviewed retrospectively the medical, biological and echographical records and their monitoring data. We compared patients in group with and without CAA at 4 weeks from the diagnosis.
Results We included 240 children from 6 hospital centers. The median age was 28 months (14—50), 20% were less than 1 year old. The male-to-female ratio was 1.8. Diagnosis was done after 7 days of fever at mean. We found 87 children with initial z-score $\geq$ 2DS and 28 with CAA. Patients were treated with IVIG and 35 get more than one cure, 95% get aspirin for anti-inflammatory then 87% as antiplatelet therapy. Five received corticosteroids, 1 an anti-TNFα and 1 an anti-IL1. Risk scores of CAA from Kobayashi, Egami and Sano present low sensitivity and low specificity. Several risk factors were associated with CAA: age < 6 months (OR = 4, $P = 0.05$), IVIG resistance (OR = 3.6, $P = 0.007$), z-score $\geq$ 2DS at diagnosis (OR = 6.7, $P = 0.09\ 10^{-4}$) and platelet count (Pq) $\geq$ 444 G/L ($P = 0.04$). Only the initial z-score $\geq$ 2 DS ($P = 0.02$) and Pq $\geq$ 444 G/l ($P = 0.04$) were significant in multivariate analysis.
Conclusion The Japanese risk scores were not significant in the French population, as previously shown in North American or English populations. The initial z-score $\geq$ 2 DS is a good risk factor of CAA so is the Pq $\geq$ 444 G/l after the day 7th of fever in our population.

Keywords Kawasaki disease; Coronary artery aneurysm; Risk factor
Disclosure of interest The authors declare that they have no competing interest.

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Recent Team experience on Norwood procedure: Conventional palliation techniques are superior

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Hypoplastic left heart syndrome (HLHS) is a severe anomaly. In France prenatal diagnostic is systematically associated with proposal for pregnancy termination. However still many newborns are referred for surgical management. The aim of the present study was to evaluate our recent experience with Norwood type univentricular palliation with particular emphasis to the surgical technique used.
The records of 44 consecutive patients who underwent procedure by Marie-Lannelongue and Jacques-Cartier Hospitals' team between 2010 and 2018 were reviewed. The study group included 28 (64%) HLHS, 6 (14%) hypolplastic left heart complex, 2 (4.5%) unbalanced AV canal.
Norwood-Sano procedure was performed in 29 (66%), conventional Norwood in 7 (16%). A modification of Norwood- procedure using a intravascular Aorta-pulmonaru artery separation patch with hole was performed in 6 and the remaining 2 underwent hybrid-2 stage management. Three patients who underwent conventional Norwood procedure had been managed for biventricular pathway initially however converted in single ventricle pathway. The mortality occurred in 8 (18%, 70% CL 13-25%) patients including all death until stage 2, superior cavopulmonary shunt procedure. The outcome after Norwood-Sano/conventional Norwood procedures were superior to the modified technique ($P = 0.19$). From 36 survivors, 16 had their 2nd stage and 6 their 3rd stage with total cavo-pulmonary shunt procedure. Two patients were converted to biventricular repair. One patient died after 2nd stage.
Despite the lack of conviction for referral, the management of HLHS and similar conditions were managed with favourable outcome. Technical modification that excludes conventional techniques, associated with poorer outcomes, must be avoided.
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