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Top Stories: Clinical Electrophysiology

Top stories on congenital long QT syndrome

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This is a one-eyed, understandably skewed selection of recent articles on long QT syndrome (LQTS) all sharing very practical clinical implications.

Exercise-induced QT prolongation or exercise-induced LQTS?

The 2 capital sins in LQTS are to not recognize that a patient is affected and to diagnose as affected someone who is not. The first may engender a life, and the second may ruin it. This study was triggered by the serendipitous observation that after detraining, some patients diagnosed with LQTS by expert clinicians were showing complete normalization of repolarization.[1] This observation calls attention to the fact that in the many youngsters who engage in exercise training many hours per week, a small fraction develops T-wave abnormalities and QT prolongation perfectly mimicking LQTS. Of the 310 consecutive young athletes suspected of having LQTS, 33 showed a complete normalization after detraining (corrected QT interval [QTc] shortened from 492 ± 37 to 423 ± 25 ms; $P < .001$) while those who resumed exercise showed the reappearance of repolarization abnormalities. All these individuals are genotype negative and have a negative family history. They should not be regarded as affected by LQTS, but they appear to have a sort of mildly acquired LQTS. They should be told to reduce their workload and to monitor their QTc because QT prolongation, when excessive, is arrhythmogenic, independently of its origin. Before diagnosing LQTS in genotype-negative athletes, a period of detraining could help avoiding errors.

Left cardiac sympathetic denervation for LQTS: 50 Years' experience

This is a report of a single-center experience with left cardiac sympathetic denervation (LCSD) in 125 patients with LQTS over a 50-year period, with an average follow-up of 13 years.[2] There was an 86% reduction in arrhythmic events. The QTc shortening effect of LCSD was confirmed: a QTc of <500 ms measured 6 months post-LCSD predicted an excellent outcome, and patients with a baseline QTc of >500 ms had a 50% chance of shortening it by an average of 60 ms. LCSD results were not affected by common genotypes. Conceptually, a significant novelty of this study is to have realized that the probability of success of LCSD is not the same for all patients with LQTS. Specifically, the authors identified a "very high risk" group comprising patients with cardiac events in the first year of life or with highly malignant mutations (calmodulin, *CACNA1C*, or mutations causing Jervell and Lange-Nielsen syndrome) with recurrences despite β-blockade. Most of these patients require LCSD and implantable cardioverter-defibrillator (ICD) implantation.[2]

Cardiac sympathetic denervation in channelopathies

This is an unabashed, highly provocative review by the 2 cardiologists with the largest experience with LCSD in the world.[3] They are not coy (they go as far as proposing their own guidelines), and when discussing the extent of denervation, they do not hesitate in defining operations that leave intact the stellate ganglion as "experimental surgery" that should not be allowed by ethical committees. Equally strongly, they state that "*most patients with LQTS and catecholaminergic polymorphic ventricular tachycardia (CPVT) do not need and should not receive an ICD*" [p 2102]. Finally, they don't hide their dismay to note how so many cardiologists, even in referral centers, are ready to implant ICDs in a large number of LQTS/CPVT patients but seem unable to offer them the alternative of LCSD. This is disturbing also because of a previous study looking at the quality of life after LCSD in 109 patients.[4] The side effects of surgery were mainly modest and of no consequence. For pediatric patients, the majority of their parents reported that life was

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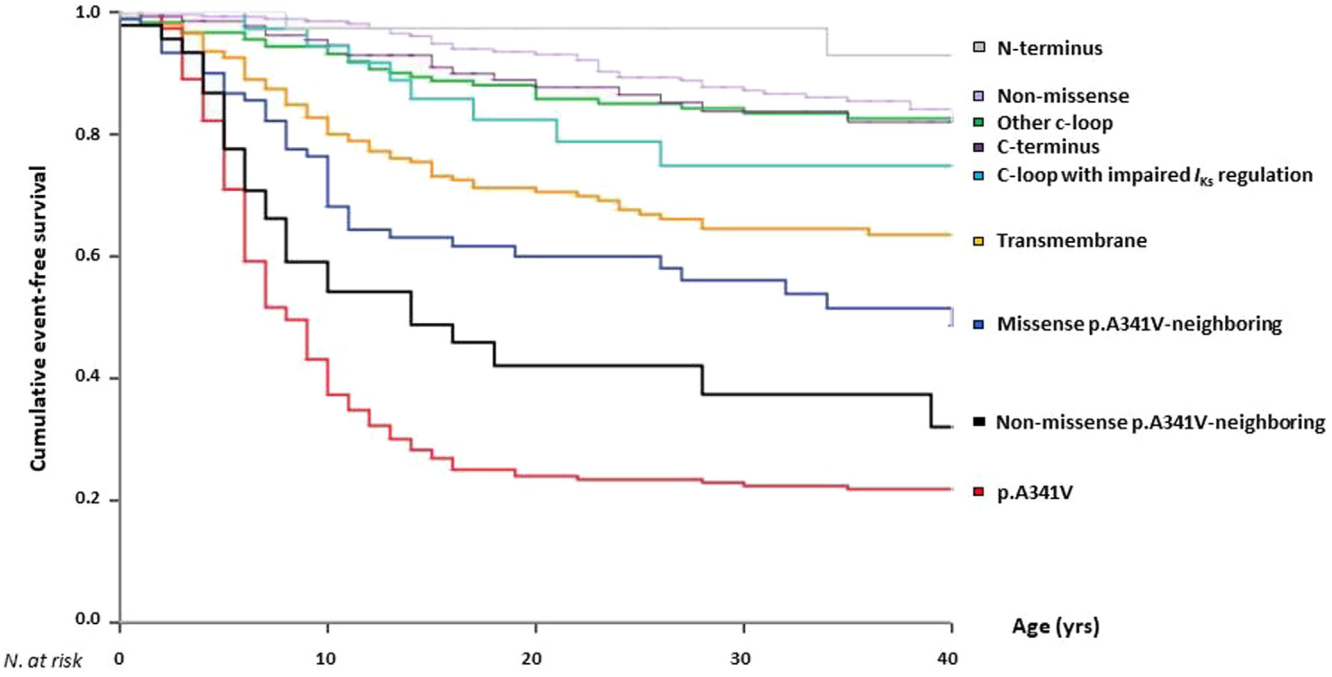

Figure 1
Cumulative event-free survival of patients for all mutations per *KCNQ1* region, that is, p.A341V, p.A341V-neighboring mutations, other membrane-spanning segments (transmembrane), C-loops (S2–S3 and S4–S5), also by protein kinase A–dependent slow delayed rectifier potassium current (I_{Ks}) channel activation, C/N-terminus, and non-missense variants. From Schwartz et al[5] with permission.

better after surgery. Most patients (or their parents) would recommend LCSD to other patients.

Mutation location and I_{Ks} regulation in the arrhythmic risk of LQTS type 1

This study[5] is a reminder that, with channelopathies, clinical art and genetic understanding go together. Clinical and genetic data were obtained from 1316 patients with LQTS type 1 carrying 166 unique *KCNQ1* mutations, including 277 p.A341V-positive subjects, 139 patients with p.A341-neighboring mutations, and 900 other subjects with LQTS type 1. Specific attention was given to the p.A341V variant and to patients carrying mutations neighboring p.A341V in the *KCNQ1* S6 region. Independent of the interesting mechanism underlying the differential arrhythmic risk, a main finding is that mutations in these locations carry a significantly higher clinical severity (Figure 1). Clinical cardiologists should become aware that a proper clinical management of their patients with LQTS can no longer ignore a reasonable level of understanding of the implications of the main characteristics of the disease-causing mutations, including their type and location.

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