13.2 - Epidemiology, Prognosis, Outcome

Ventricular conduction is a marker for arrhythmic risk in overlap sodium channel disease

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Background: SCN5A-E1784K (c.5350G>A) is the most common variant associated with the LQT3 long QT syndrome (LQTS) and Brugada syndrome (BrS). It exhibits incomplete penetrance and can manifest variably as a mixed clinical phenotype of LQTS, BrS and/or conduction disorders (1-4). This presents a challenge for risk stratification and optimal management. We aimed to describe the clinical characteristics and risk markers in a large, well characterised international cohort of SCN5A-E1784K subjects and identify demographic and/or ECG parameters associated with event free survival.

Methods: Comprehensive clinical data, including initial presentation and follow-up data, were collected from SCN5A-E1784K subjects. Outcome 'events' included sudden death, aborted cardiac arrest, and documented VF or VT or arrhythmic syncope. 'Lethal events' included sudden death, aborted cardiac arrest or documented VF or VT. Associations between clinical characteristics and event free survival were investigated using Cox proportional hazard regression models.

Results: SCN5A-E1784K subjects (n=231) were recruited from 16 centres. Median follow up was 24.9 years (15.2 - 43.3) and 45 individuals (19%) experienced an event. Lethal events were observed in 14 subjects (6%). Figure 1 shows event (A) and lethal event (B) free survival in SCN5A-E1784K subjects. Higher QRS duration (corrected for age) was associated with shorter event-free interval. QRS duration was the only characteristic associated with increased risk with a hazard ratio (HR) of 1.04 or 1.05 per ms for events and lethal events, respectively. The observed survival for events and lethal events for QRS tertiles are shown in Figure 2.

Discussion

Ventricular myocardial conduction, as evidenced by QRS duration, appears to play a role in the risk of arrhythmic events in patients with SCN5A-E1784K. Corrected QT interval and BrS phenotype were, however, not associated with risk. This provides an important opportunity for the personalisation of risk stratification of these patients, whose management can otherwise be very challenging. Figures

Figure 1: Event (A) and lethal event (B) free survival in SCN5A-E1784K subjects. Shaded areas denote the 95% confidence interval.

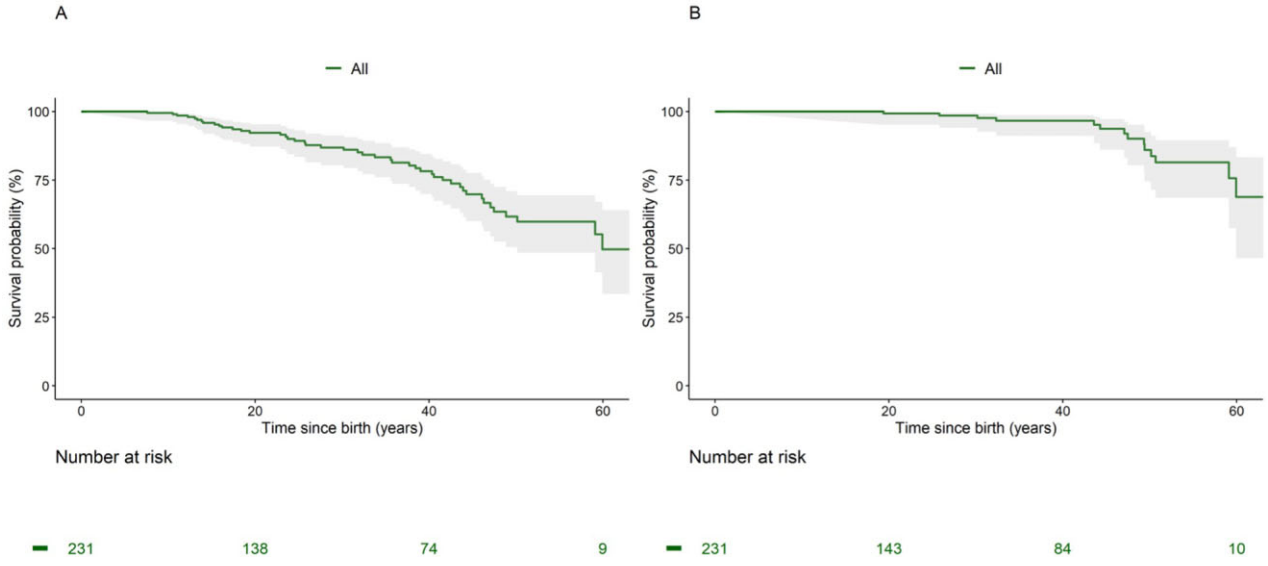

Figure 2: Event (A) and lethal event (B) free survival in SCN5A-E1784K subjects classified based on residual QRS tertiles (i.e. difference between observed and age predicted QRS duration, ranges in ms).