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Isovolumic relaxation time is prolonged in fetal long QT syndrome

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Objective:
Long QT syndrome(LQTS) is an inherited channelopathy responsible for unexplained fetal loss and sudden infant death. Prenatal diagnosis is challenging as fetal electrocardiograms are not available. We hypothesized that the left ventricular isovolumic relaxation time (LVIRT), the mechanical correlate of repolarization, is prolonged in LQTS fetuses.
Methods:
This was a retrospective multicenter case series. From fetal pulsed wave Doppler waveforms of mitral inflow and aortic outflow during sinus rhythm, we averaged 3 consecutive measurements of cycle length, LVIRT, ejection time(LVET) and isovolumetric contraction time(LVICT) in LQTS fetuses and controls. We normalized LVIRT, LVET and LVICT for cycle length as we anticipated a lower heart rate in the LQTS fetuses. We compared the measurements between the control and LQTS fetuses, and analyzed trends over time using a linear mixed-effects model.
Results:
Eighty measurements from 29 LQTS fetuses (9-KCNQ1 (1 homozygous), 7-KCNH2, 7-SCN5A, 1-CALM 2 and 5-non-genotyped) were compared with 601 measurements from 466 controls. The LQTS fetal heart rates were significantly lower than the controls from 15 weeks of gestation (Fig.A). There were no significant differences between the N-LVET or N-LVICT between the two groups. The N-LVIRT was significantly longer in the LQTS fetuses after the 25th week of gestation (Fig.B), p<0,001 at 26-30 and 32-36 weeks. The best cutoff point for the diagnosis of LQTS was a N-LVIRT of 11.21msec (95%CI 11.02-12.32) at 32-36 weeks with a 100% sensitivity (95%CI 1-1) and 79% specificity (95%CI 0.68-0.89) [AUC of 0.92 (95%CI 0.84-0.96)].
Conclusion:
The N-LVIRT is prolonged in LQTS fetuses from the 25th week of gestation. We speculate that this prolongation reflects developmental changes in calcium transport and may show genotype specific effects. Together with the findings of sinus bradycardia, an increased fetal N-LVIRT duration may improve prenatal detection of LQTS. Further studies are needed to determine if the fetal LVIRT duration correlates with LQTS mutation type or perinatal ventricular arrhythmia risk.