Introduction: Fetal sinus bradycardia combined with 2:1 atrioventricular block (AVB) or intermittent ventricular tachycardia (VT) are important clues to the diagnosis of congenital long QT syndrome (LQTS). LQTS patients with 2:1 AVB usually manifest in fetal or neonatal period, and tend to show severe clinical course, leading to a poor prognosis. However, long-term outcome of these particular patients remain unclear. The purpose of this study is to evaluate the clinical course, genotype, medication, device therapy, and prognosis of fetal and neonatal LQTS with 2:1 AVB.

Methods: Fetuses and neonates diagnosed with congenital LQTS were registered from 44 institutions/hospitals in Japan using questionnaire. Clinical course, genotypes, treatment, and prognosis were compared between (1) patients with 2:1 AVB (AVB group; n = 35) and (2) patients without AVB (non-AVB group; n = 53).

Result: Eighty-eight patients were registered. (1) Age at diagnosis: 43% and 57% of the cases were diagnosed during fetal and neonatal period in AVB group, respectively, compared to 19% and 81% in non-AVB group. (2) Family history of LQTS or sudden cardiac death (SCD) was positive in 20% in AVB group and 51% in non-AVB group. (3) The proportion of LQTS genotypes: LQT1 0%, LQT2 17%, LQT3 23%, LQT8 14%, unknown/untested 46% in AVB group, whereas LQT1 30%, LQT2 15%, LQT3 13%, unknown/untested 42% in non AVB group. (4) ECG findings: the mean QTc values were 579ms and 523ms; VT/ torsade de pointes (TdP) occurred in 32% and 17% in AVB and non-AVB groups, respectively. (5) Medication: 86% and 57% of the patients received medication in AVB and non AVB groups. Mexiletine was used most frequently (74%) in AVB group, while propranolol was chosen as the first line drug (57%) in non-AVB group. (6) Device therapy: 40% and 6% of the patients received device therapy in AVB and non AVB group. (7) Prognosis: mortality rate was 23% and 4% in AVB and non-AVB group (median follow-up period of 4 years and 3 months). Kaplan-Meier analysis revealed lower survival probability in AVB group (figure). There was only one death noted among patients who received device therapy in neonatal period.

Conclusion: Fetal and neonatal LQTS with 2:1 AVB tend to develop VT/TdP, leading to poor prognosis. Frequently identified genotypes in these patients were LQT2 and LQT3, and none of the
patients with LQT1 (KCNQ1 mutation) showed this phenotype. Device therapies were required in many patients, and were considered effective. However, the percentage of patients who received device therapy was still low in Japan compared to that reported from other countries. Aggressive device therapy in addition to medication should be considered in fetal and neonatal LQTS with AVB.