3rd trimester fetal heart rate discriminates between non-carriers, carriers of single and double *KCNQ1* mutations in Swedish Long QT Syndrome families

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Background

Early diagnosis is of clinical importance in the Long QT Syndrome (LQTS). We investigate 3rd trimester fetal heart rate, routinely recorded within public maternal health care, as a possible marker for LQTS genotype.

Material and Methods

In Swedish LQTS families where cascade screening for *KCNQ1* mutations (LQT1) had been performed in the clinical setting, 3rd trimester fetal heart rates were noted for 124 genotyped fetuses (non-carriers=45, single mutation=67, double mutations=12), see the table below.

The mean fetal heart rate per individual, calculated from all recordings from gestational week 29 and onwards, noted in the maternal health care records, were summarized and compared between genotype groups (no mutation, single mutation, double mutations) using t-tests and non-parametric tests, as appropriate.

Results

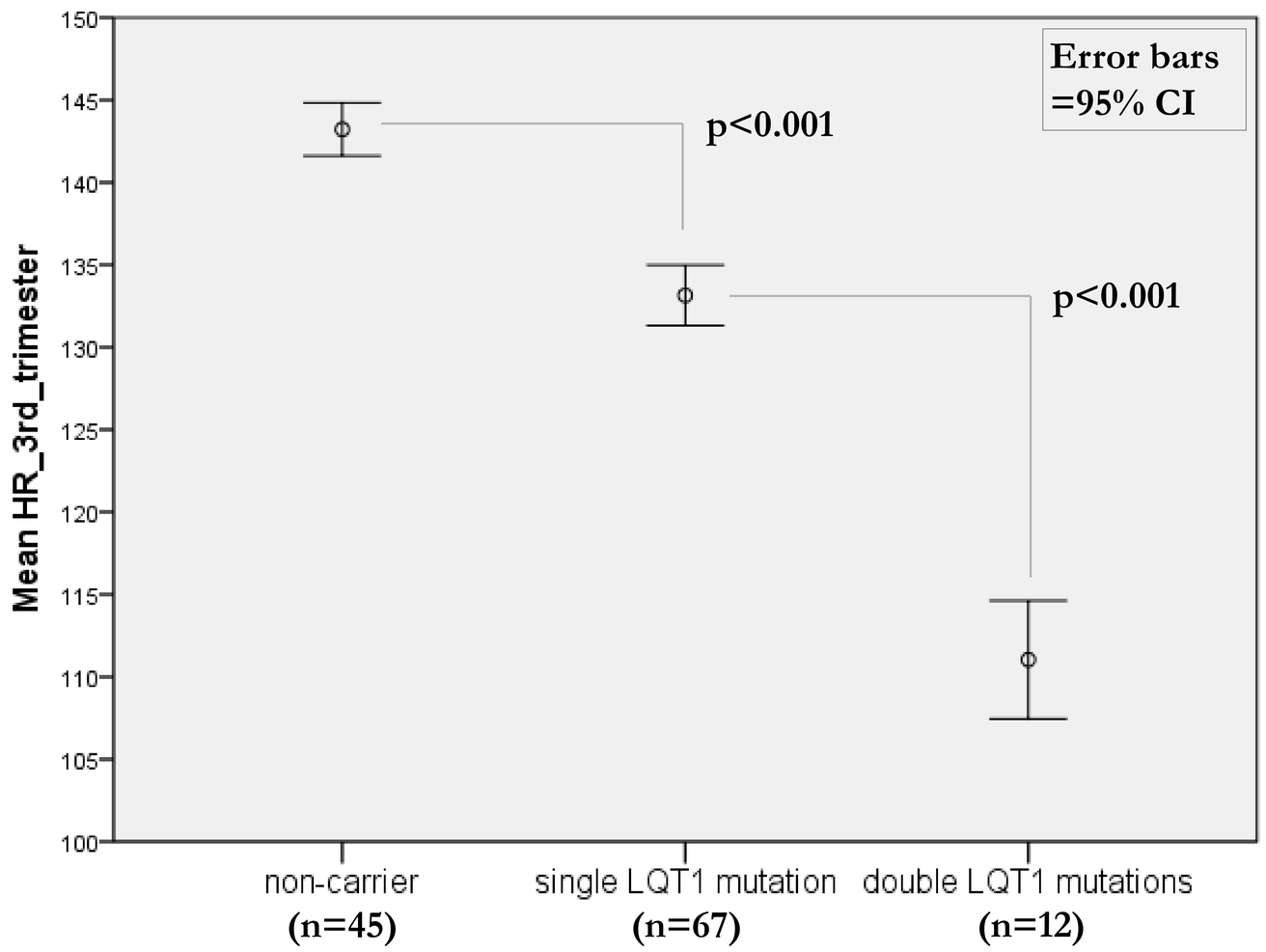
Mean 3rd trimester heart rate correlated with fetal genotype (no mutation 143±5 bpm; one mutation 133±8 bpm; double mutations 111±6 bpm, p<0.001). Mean heart rates were statistically lower per added mutation (no mutation vs. single mutation p<0.001, single mutation vs. double mutation p<0.001), see the Figure below.

Fetal sex did not significantly affect mean 3rd trimester heart rate (p=0.246).

Genotype of included fetuses (n=124)

Non-carriers, n=45 (62% females)	
Single LQT1 mutation, n=67 (46% females)	
Y111C/wild type	63
A525T/wild type	3
R518X/wild type	1
Double LQT1 mutations, n=12 (50% females)	
R518X/R518X	3
R518X/A525T	4
R518X/M159sp	2
R518X/R190W	1
R518X/R539W	1
R518X/349W	1

***LQT1 = KCNQ1 gene mutations**



Conclusion

In this study including 124 fetuses with ascertained genotype from Swedish LQT1 families, 3rd trimester fetal heart rate discriminated between fetal genotypes (no mutation, single mutation and double mutations). This finding strengthens the role of fetal heart rate in the early diagnosis of familial LQTS, and importantly for the identification of fetuses with double mutations, at high risk of early life-threatening arrhythmias.

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