Ventricular repolarization intervals in children previously treated with anthracyclines

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Introduction
Anthracyclines used in a wide range of childhood hematologic and solid cancers may cause dose-dependent cardiotoxicity. They inhibit DNA and RNA transcription and replication (blocking topoisomerase II) thereby creating iron-mediated free radicals which damage DNA and cardiac myocytes, mechanism underlying cardiomyopathy. Little is known on the longer term effect of anthracyclines on cardiac repolarization.

We investigated ventricular repolarization indices in children after completing treatment with anthracyclines for neoplastic disease; specifically corrected QT interval (QTc), QT dispersion (QTd), T-wave peak to end (TPE) interval, its dispersion and maximum, TPE/QT, TPE/JT, all these being markers of repolarization heterogeneity and potential for ventricular arrhythmias.

Methods
Twenty patients post-anthracyline treatment for childhood neoplasms were studied. Additionally, 80 healthy age matched subjects served as controls. A 12 lead digital ECG was recorded and stored on a server subsequently retrieved digitally on screen. Intervals measured included RR, QT + dispersion, TPE + dispersion, TPE max/QT and TPE max/JT calculated for heart rate correction. Descriptive and analytical statistics were calculated, significance level set at p<0.05.

Results
Mean patient age 13±4.3 years, time from last anthracycline therapy 5.8±4.6 years. Cumulative anthracycline dose: 185 – 480 mg/m2. Control group mean age 13.4±2.9 years. Repolarization intervals patients versus controls respectively: QTc 423.6 ± 20 vs 408 ± 24 ms; JTc 324 ± 25 vs 315 + 24 ms; TPE dispersion 35 ± 13 vs 16 ± 6 ms; QT dispersion 32 ± 8 vs 12 ± 4 ms, maximum TPE 106 ± 19 vs 92 ± 14 ms; TPE max/QT 0.29 ± 0.04 vs 0.25 ± 0.03; TPE max/JT 0.38 ± 0.06 vs 0.33 + 0.05. All intervals were significantly longer in patients, p< 0.05. Four patients developed a dilated cardiomyopathy, one required heart transplantation, one developed ventricular tachycardia.

Conclusion
These intervals reflect spatial and transmural dispersion in ventricular repolarization and may serve as an arrhythmogenic index. They were prolonged in midterm follow up of some anthracycline receiving patients, signifying potential risk for ventricular arrhythmias. Confounding factors may be responsible in the pathogenesis.