TDI-Echocardiography: A New Screening Tool for Long QT Syndrome?

Please see page 209 for the article by Savoye et al. (doi: 10.1016/S1525-2167(03)00011-8) to which this editorial pertains.

The long QT syndrome (LQTS) is characterized by an abnormally prolonged repolarization phase noted on the EKG as a prolonged corrected QT interval (QTc). The syndrome can both be acquired as well as congenital. LQTS is known as an autosomal dominant trait with normal hearing, i.e. Romano–Ward syndrome, and as an autosomal recessive trait with congenital deafness, i.e. Jervell and Lange-Nielsen syndrome. The prolonged repolarization results in increased QT dispersion, which could favour a reentry mechanism. Also, early after-depolarization have been identified as a plausible mechanism for arrhythmia induction. The characteristic arrhythmia is the so-called Torsades de Pointes resulting in syncope or even sudden death. Untreated patients are at considerable risk of developing syncope or dying suddenly. The prognosis in untreated cases depends on several factors like history of syncope or aborted sudden death, severity of QTc prolongation and female gender. However, even 6% of affected patients with a normal QTc (<440 ms) had a history of syncope or cardiac arrest[1]. Treatment is highly effective in preventing sudden cardiac death and consists of anti-adrenergic therapies (especially beta-blockers) and sometimes implantation of a cardiac pacemaker or ICD. Therefore, identification of both symptomatic as well as asymptomatic patients is crucial in preventing sudden cardiac death.

In the past 10 years, enormous progress has been made in the molecular biology of the LQTS. Currently seven genes have been identified, six of them encoding for part of ion channels, including the slow and rapid components of the delayed rectifier (KCNQ1 and KCNH2 for LQTS1 and LQTS2, respectively) and the sodium channel (SCN5A for LQTS3). The different types can be recognized on the basis of several clinical characteristics[2]. LQTS mutations have a variable phenotypic penetrance, including normal or virtually normal QT intervals in known mutation carriers. This causes considerable overlap of the QTc between carriers and non-carriers. Therefore, additional clinical parameters for making the diagnosis of the LQTS would be welcome.

In this issue of the journal, Savoye et al.[3] present new echocardiographic data using tissue Doppler imaging (TDI). They obtained TDI information as well as conventional echocardiographic data from 10 LQTS patients with only mildly prolonged QTc (mean 454 ms). Four patients had almost normal QTc values (<440 ms). They confirmed previously described regional systolic wall motion abnormalities of the left ventricle. They added new TDI findings of an abnormal increase in regional isovolumic relaxation time and of diastolic velocities in all patients. Of potential importance is the fact that the found echographic differences were also found in patients with QTc < 440 ms, although it is not indicated whether the abnormalities are present to a similar extent in these patients as observed in LQTS patients with prolonged repolarization. They also found clear regional differences in these parameters, but did not attempt to provide a satisfactory explanation. Indeed, these differences are not easily explained, since the abnormal ion channels are equally distributed over the left and right ventricle. Hence, why are there differences in the echo parameters between the septal regions and the lateral regions? Even more sophisticated and probably more sensitive TDI-echocardiographic measurements, like strain and strain-rate imaging and indices of contractility like Tei-index, could provide additional insight into the spatio-temporal distribution of the observed systolic and diastolic abnormalities in LQTS, and elucidate if global myocardial performance is altered. The proposed mechanism for the late systolic plateau is an altered calcium handling which in turn will also influence...
diastolic parameters. Indeed, verapamil has been shown to abolish the wall motion abnormalities in LQTS patients\[4\].

It is unclear from the presented data whether overlap exists between the TDI-measurements in the LQTS group and the control group, and the influence of the QTc on the found differences. It could be anticipated that the abnormalities increase with further increase of the QTc. Therefore, larger groups of patients and controls have to be analyzed to develop cut-off values which are needed to separate affected individuals with normal to minimally prolonged QTc intervals from normal controls with adequately high sensitivity and specificity, to warrant prophylactic treatment in these patients. Of interest would be to study the ability of TDI in differentiating between genotypes. Indeed, it might be anticipated that action potential morphology is different in various LQTS genotypes with different effects on TDI parameters. Furthermore, the influence of age and common conditions like LVH or mild valvular abnormalities on the presented parameters have to be evaluated, since these conditions will be encountered when screening larger groups of individuals.

TDI seems to be promising as a new diagnostic tool in a variety of disorders to identify subclinical patients. In a study comparable to Savoye et al.\[3\], Ho et al.\[5\] reported on the ability of TDI to identify genotype-positive subjects in preclinical hypertrophic cardiomyopathy. In the coming years, TDI will give us the opportunity to characterize the myocardial tissue and possibly perform echocardiographic genotyping in some disease entities.

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References