The long QT syndrome (LQTS) is a disorder of diverse phenotypic presentations with some genetically affected individuals presenting with significant QTc prolongation and high risk of cardiac events and other carriers of the same genes from the same family might remain asymptomatic, or even might have no QTc prolongation. This diversity of presentations has always raised the questions regarding factors influencing clinical presentation and outcome of LQTS patients. Why LQTS patients with similar QTc prolongation from the same family do not have similar clinical course?

Genotype plays a significant role in modulating risk of cardiac events in LQTS [1], but modifying factors including: age, gender, QTc duration, and beta-blocker use, also play an important role affecting clinical course of patients affected by this disorder [2]. The above mentioned clinical variables could nowadays be utilised by clinicians since the risk stratification based on patient’s age, history of syncope or cardiac arrest, gender, QTc duration, and treatment became feasible based on experience from prior studies [3]. Advances in molecular biology of LQTS lead us to consider other, more sophisticated, factors that might influence phenotypic presentation of LQTS patients. Presence of dual mutations in LQTS individuals, although reported in only about 10–15% of patients, seem to affect clinical presentation and increase risk of cardiac events in particular [4]. Evaluating single nucleotide polymorphisms in LQTS genes (and in other genes that might affect repolarisation response) seem to be of increasing interest. Tomás et al. [5] reported that polymorphisms of NOS1AP gene, that was reported to be associated with QT prolongation in general population, also plays a role in modulating phenotypic presentation of LQTS patients. Location of mutation within a gene (transmembrane, pore locations) also might influence phenotype [6]. Recently Jons et al. [7] demonstrated that studying ion channel kinetics of LQTS gene mutations expressed in vitro might identify subjects who are more symptomatic.

In this issue of Kardiologia Polska, Moric-Janiszewska et al. [8], explored expression of genes (not ion channel kinetics) as possible another important direction regarding diversity of genetic and clinical presentation in LQTS. In this small study, involving 12 LQT1 and 11 LQT2 patients, they evaluated number of mRNA copies of LQT1 (KCNQ1) and LQT2 (KCNH2) genes in blood samples of studied LQTS individuals and in healthy controls. They found that number of mRNA copies of the KCNQ1 gene was higher in LQT1 patients than controls but there was no difference in number of mRNA copies of the KCNQ2 gene between LQT2 patients and controls. Secondly, they reported that symptomatic LQT1 patients had higher number of copies than asymptomatic LQT1 individuals. This was not the case for LQT2 subjects.

The main question which needs to be raised regarding this study is whether peripheral blood should be considered suitable for evaluating gene expression in LQTS. To date, it is accepted that myocardial tissue (taken during biopsy or autopsy) is the only reliable source of information regarding gene expression in myocardium. The same pertains not only to LQTS but also to hypertrophic cardiomyopathy, idiopathic dilated cardiomyopathy, or arrhythmogenic right ventricular cardiomyopathy. Prior literature data supporting use of peripheral blood are very limited and definitely more research is needed to further support this concept. Studies with parallel gene expression evaluated by quantitative analyses in myocardium and in peripheral blood might lead to useful conclusions regarding potential utilisation of peripheral blood for that purposes. The authors’ small pilot study should be considered as a concept triggering further research in this direction with more advanced mechanistic protocols and higher number of subjects to determine whether peripheral blood could reliably be used for the purpose of evaluating gene expression of cardiac disorders.

Conflict of interest: none declared

References