Jordan University of Science and Technology

Titin gene mutations are common in families with both peripartum cardiomyopathy and dilated cardiomyopathy.

Authors: van Spaendonck-Zwarts KY, Posafalvi A, van den Berg MP, Hilfiker-Kleiner D, Bollen IA, Sliwa K, Alders M, **Almomani R**, van Langen IM, van der Meer P, Sinke RJ, van der Velden J, Van Veldhuisen DJ, van Tintelen JP,

Abstract: AIM: Peripartum cardiomyopathy (PPCM) can be an initial manifestation of familial dilated cardiomyopathy (DCM). We aimed to identify mutations in families that could underlie their PPCM and DCM. METHODS AND RESULTS: We collected 18 families with PPCM and DCM cases from various countries. We studied the clinical characteristics of the PPCM patients and affected relatives, and applied a targeted next-generation sequencing (NGS) approach to detect mutations in 48 genes known to be involved in inherited cardiomyopathies. We identified 4 pathogenic mutations in 4 of 18 families (22%): 3 in TTN and 1 in BAG3. In addition, we identified 6 variants of unknown clinical significance that may be pathogenic in 6 other families (33%): 4 in TTN, 1 in TNNC1, and 1 in MYH7. Measurements of passive force in single cardiomyocytes and titin isoform composition potentially support an upgrade of one of the variants of unknown clinical significance in TTN to a pathogenic mutation. Only 2 of 20 PPCM cases in these families showed the recovery of left ventricular function. CONCLUSION: Targeted NGS shows that potentially causal mutations in cardiomyopathy-related genes are common in families with both PPCM and DCM. This supports the earlier finding that PPCM can be part of familial DCM. Our cohort is particularly characterized by a high proportion of TTN mutations and a low recovery rate in PPCM cases.