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Predictive genotype testing in pediatric healthy phenotypes with family history of ARVC-5

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Objectives: Autosomal dominant *TMEM43*-p.S358L mutation encoding for the ER-protein LUMA is a highly malignant fully penetrant missense mutation with a deleterious clinical phenotype causing ARVC5 and unpredictable sudden cardiac death especially in males. Syncopes were reported even in underaged males. In order to understand the disease course and the impact of imaging methods for the identification of the disease onset a close follow up of underaged carriers is of major relevance.

Methods: Three underaged mutation carriers were predictively tested for the Newfoundland mutation TMEM43 p.S358L (12 and 15ys male, 18 ys female) but are currently without clinical phenotype. We repeatedly examined these carriers by ECG, holter-ECG, echocardiography including deformation imaging, tissue Doppler, 3D-echo and cardiac MRI including volumetric data and vitality scan for 6 years follow up.

Results: Predictive testing of the underaged in combination with the family history had psychosocial impact for the kids. Of note, at present there were no significant early changes in morphologic, functional or electric alterations in all 3 adolescents. Task force criteria for ARVC were not fulfilled yet. Patients could be reassured concerning normal physical activities apart from competitive sports. Neither Beta blockade has been established nor ICD´s have been implanted.

Conclusions: The advantage of predictive testing in these upcoming patient group is the possibility of early detection of disease in order to redefine the role of different established new imaging technologies as well as the reassurance of actual healthiness. On the other hand these adolescents have to cope with the problem of upcoming cardiac disease and the timing of medical as well as ICD-therapy has to be redefined. We recommend predictive testing of ARVC5 not before the age of ten years.