Results of the clinical genetic testing pilot study for cardiomyopathies conducted in Dubrava University Hospital

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Background: Cardiomyopathies represent an important cause of heart failure and genetic testing for cardiomyopathies has become an established care pathway in contemporary cardiology practice[1,2].

Patients and Methods: In this pilot study we have conducted genetic testing for cardiomyopathies in selected patients with clear non-ischemic cardiomyopathy phenotypes. Genetic testing was performed in Dubrava University Hospital genetic laboratory using standard next-generation sequencing (NGS) Illumina cardiomyopathy gene panel covering 174 genes most associated with cardiomyopathies, arrhythmias and aortopathies. The results were uploaded and analyzed using Variant Interpreter Illumina, a cloud-based interpretation and reporting platform for genomic data.

Results: From June 2020 to March 2021 16 patients underwent genetic testing (10 males, 33.6±18.7 years), as a part of a pilot testing. Of these patients, 7 had previously undergone heart transplantation (HTx), while one was on the waiting list for HTx, 7 were in a regular follow up and one analysis was postmortem. Clinically, 12 patients were classified as having dilated cardiomyopathy (DCM), two had hypertrophic cardiomyopathy (HCM) and two arrhythmogenic cardiomyopathy (ACM). Diagnostic yield of the performed genetic testing was relatively high, in only two patients out of 16 we did not identify any mutations **(Table 1).** This testing led to the detection of Danon's disease in one family, and to change of clinical treatment in one patient. The results were discussed with the clinical geneticist; in seven cases the patients were referred to genetic counseling, while further family screening was initiated in five cases.

Conclusion: Genetic testing provides insight into diagnosis, treatment, and prognosis of patients with non-ischemic cardiomyopathies, and directs screening which allows the identification of relatives at risk and initiation of appropriate medical and device therapies[1].

TABLE 1. Short summary of the detected variants, classified according to the clinically observed phenotypes.

		DCM	HCM	ACM
	Number (males)	12 (8)	2 (1)	2 (1)
	Average age	27.8±16.9	56.5±10.6	45.5±14.8
	Previous HTx	6	0	1
Variant classification	Pathogenic	5	0	1
	Likely pathogenic	2	1	0
	VUS	4	0	1
	negative	1	1	0

HTx = heart transplantation; VUS = variant of unknown significance; DCM = dilated cardiomyopathy; HCM = hypertrophic cardiomyopathy; ACM = arrhythmogenic cardiomyopathy.

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LITERATURE

1. Yogasundaram H, Alhumaid W, Dzwiniel T, Christian S, Oudit GY. Cardiomyopathies and Genetic Testing in Heart Failure: Role in Defining Phenotype-Targeted Approaches and Management. Can J Cardiol. 2021 Apr;37(4):547-559. https://doi.org/10.1016/j.cjca.2021.01.016
2. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726. https://doi.org/10.1093/eurheartj/ehab368