CARDIOMYOPATHY

LAMP2 cardiomyopathy insights

A study published in the *Journal of the American Medicine Association* has characterized the clinical course of *LAMP2* cardiomyopathy, showing that this disease causes progressive clinical deterioration that leads to cardiac death at an early age. These findings thus highlight the importance of timely genetic testing of young patients presenting with substantial left-ventricular hypertrophy.

Mutations in the X-linked *LAMP2* gene typically cause the multisystem glycogen-storage disease Danon's disease; however, they can also lead to primary cardiomyopathy resembling severe hypertrophic cardiomyopathy. Initial reports of *LAMP2*-related cardiomyopathy revealed clinical features such as early onset, severe hypertrophy, ventricular pre-excitation and asymptomatic elevations of serum proteins; however, the morphological expression and clinical course experienced by patients was not fully established. Maron and colleagues set out to resolve this by re-examining the current clinical status of seven patients previously identified as having *LAMP2* mutations.

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Over the course of the disease (mean follow-up 8.6 years), all seven patients developed marked left-ventricular systolic dysfunction associated with left-ventricular cavity dilatation or enlargement, and five of the patients suffered lethal ventricular tachyarrhythmias despite receiving implantable cardioverter-defibrillators. The time from clinical stability to end-stage heart failure was often brief, which shows that the clinical deterioration caused by *LAMP2* mutations is rapid. Phenotypically, all seven patients showed marked left-ventricular hypertrophy, and postmortem examination of two hearts additionally showed subepicardial necrosis and clusters of myocytes with extensive cytosolic vacuolation.

Documenting the clinical course of these seven patients has shed light on the natural history, pathophysiology and clinical implications of *LAMP2* mutations, and according to the authors of this study, *LAMP2* cardiomyopathies "perhaps represent one of the most lethal cardiomyopathies in young patients". Given the prognosis of these patients and the clinical resemblance of the disease to hypertrophic cardiomyopathy, molecular diagnosis through genetic testing is particularly important to ensure early identification and consideration of heart transplantation.

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Original article Maron, B. M. *et al.* Clinical outcome and phenotypic expression in LAMP2 cardiomyopathy. *JAMA* **301**, 1253–1259 (2009).