Mol Cell Biochem. 2017 Aug;432(1-2):169-178. doi: 10.1007/s11010-017-3007-z. Epub 2017 Mar 18.

Loss of dystrophin is associated with increased myocardial stiffness in a model of left ventricular hypertrophy.

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Abstract

Transition from compensated to decompensated **left ventricular hypertrophy** (LVH) is accompanied by functional and structural changes. Here, the aim was to evaluate **dystrophin** expression in murine models and human subjects with LVH by transverse aortic constriction (TAC) and aortic stenosis (AS), respectively. We determined whether doxycycline (Doxy) prevented **dystrophin** expression and **myocardial stiffness** in mice. Additionally, **ventricular** function recovery was evaluated in patients 1 year after surgery. Mice were subjected to TAC and monitored for 3 weeks. A second group received Doxy treatment after TAC. Patients with AS were stratified by normal **left ventricular** end-diastolic wall stress (LVEDWS) and high LVEDWS, and groups were compared. In mice, LVH decreased inotropism and **increased myocardial stiffness associated** with a **dystrophin** breakdown and a decreased mitochondrial O_2 uptake (MitoMVO_2). These alterations were attenuated by Doxy. Patients with high LVEDWS showed similar results to those observed in mice. A correlation between **dystrophin** and **myocardial stiffness** was observed in both mice and humans. Systolic function at 1 year post-surgery was only recovered in the normal-LVEDWS group. In summary, mice and humans present diastolic dysfunction **associated** with **dystrophin** degradation. The recovery of **ventricular** function was observed only in patients with normal LVEDWS and without **dystrophin** degradation. In mice, Doxy improved MitoMVO_2. Based on our results it is concluded that the LVH with high LVEDWS is **associated** to a degradation of **dystrophin** and increase of **myocardial stiffness**. At least in a murine **model** these alterations were attenuated after the administration of a matrix metalloprotease inhibitor.

KEYWORDS: Diastolic function; **Dystrophin**; **Hypertrophy**; **Myocardial stiffness**

PMID: 28316061 DOI: 10.1007/s11010-017-3007-z

[Indexed for MEDLINE]

MeSH terms, Substances

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