Letter by Yilmaz et al Regarding Article, “Analysis of Dystrophin Deletion Mutations Predicts Age of Cardiomyopathy Onset in Becker Muscular Dystrophy”

To the Editor:

The study by Kaspar et al1 merits and demands great attention because it nicely demonstrates the importance of integrating protein structure information in genotype–phenotype correlation studies. The authors not only demonstrate that the locus of dystrophin gene mutation is associated with the time of onset (early versus late) of cardiomyopathy but also show that genetic dystrophin mutations that result in the disruption of spectrin repeat phasing (in the rod domain of the dystrophin protein) lead to early onset of cardiomyopathy, despite the absence of any differences in myocardial dystrophin expression compared with those with dystrophin mutations without spectrin repeat phasing disruption.

Unfortunately, there is one essential limitation in this (partly retrospective) study that severely weakens the authors’ conclusions. Assessment of cardiomyopathy was based only on (1) routine clinical echocardiographic results comprising calculation of left ventricular diameters, ejection fraction, and fractional shortening and (2) chest radiograph measuring the heart-to-lung ratio. However, as stated by the authors themselves, cardiomyopathy in patients with muscular dystrophy is often not diagnosed until cardiac symptoms manifest, in particular, when conventional diagnostic methods such as 2D or M-mode echocardiography are used. In this context, recent studies have convincingly demonstrated that initial or subclinical cardiac dysfunction can be diagnosed early and adequately by using tissue Doppler echocardiography or cardiovascular MRI (CMR) before reduction in systolic function does occur. For example, Mertens et al2 have demonstrated that segmental reductions in systolic deformation parameters and in early diastolic myocardial velocities can be detected in patients with Duchenne muscular dystrophy with normal global systolic function, using tissue Doppler echocardiography. Similar results were obtained by Ashford et al3 when CMR tagging was used for myocardial strain analysis. Moreover, recent CMR-based studies have revealed that (sometimes even extensive) myocardial fibrosis can be detected by late gadolinium enhancement CMR even in patients with muscular dystrophy with normal cardiac diameters and systolic function and consequently normal results based on conventional echocardiography.4,5

Therefore, we argue that conventional echocardiographic methods (as applied in this study) are not sufficient to evaluate cardiomyopathy in patients with muscular dystrophy and suggest that intriguing approach of these authors in evaluating the genotype–phenotype correlation with concomitant consideration of changes in dystrophin protein structure in patients with muscular dystrophy should be carefully interpreted as long as verification of their results based on comprehensive CMR data is not achieved.

Disclosures

None.

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References

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