Correspondence

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 al\(^1\) 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 al\(^2\) 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 al\(^3\) when CMR tagging was used for myocardial stain analysis. Moreover, recent CMR-based studies have shown 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.

Ali Yilmaz, MD
Division of Cardiology
Robert-Bosch-Krankenhaus
Stuttgart, Germany

Joseph Suttie, MD
Department of Cardiovascular Medicine
University of Oxford Centre for Clinical Magnetic Resonance Research
University of Oxford
Oxford, United Kingdom

Steffen E. Petersen, MD, DPhil
Centre Lead for Advanced Cardiovascular Imaging
William Harvey Research Institute
Barts and The London NIHR Biomedical Research Unit
The London Chest Hospital
London, United Kingdom

References


Letter by Yilmaz et al Regarding Article, "Analysis of Dystrophin Deletion Mutations Predicts Age of Cardiomyopathy Onset in Becker Muscular Dystrophy"
Ali Yilmaz, Joseph Suttie and Steffen E. Petersen

Circ Cardiovasc Genet. 2010;3:e1
doi: 10.1161/CIRCGENETICS.109.933614
Circulation: Cardiovascular Genetics is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 1942-325X. Online ISSN: 1942-3268

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circgenetics.ahajournals.org/content/3/2/e1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Genetics can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Genetics is online at:
http://circgenetics.ahajournals.org//subscriptions/