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

We thank Drs Yilmaz, Suttie, and Petersen for recognizing the novelty and value of our approach that incorporates protein structure information into genotype-phenotype studies.

In their letter, they pointed out the limitations in sensitivity of conventional echocardiography to detect the earliest signs of cardiac involvement in patients with dystrophinopathy. We acknowledge that cardiovascular magnetic resonance (CMR) imaging is more sensitive at localizing the earliest focal posterior left ventricular wall lesions. However, the letter by Yilmaz et al did not explain why our results would have been different if CMR or tissue Doppler data had been available. Indeed, this was a cross-sectional study. Even the most sensitive modalities cannot pinpoint the onset of cardiomyopathy on the basis of a single measurement. Their use could translate into an earlier recognition of cardiac involvement, which would lower the median ages of onset for each patient group in our study. However, the differences among groups would not be affected. As stated in our discussion, our data should be validated in a serial prospective study wherein disease onset can be more precisely captured.

With regard to the criteria and methodology used for the diagnosis of cardiomyopathy, our diagnostic parameters were standard: an ejection fraction $\leq 55\%$ and/or a shortening fraction $\leq 32\%$. We did not use chest radiography as a defining parameter for cardiomyopathy because it is not a reliable diagnostic method, in our opinion. It was used as a secondary parameter to document cardiac dilation together with other echocardiography measurements. We would like to further point out that the study by Yilmaz et al showed that on the basis of both conventional echocardiography and CMR, all patients with an ejection fraction $<60\%$ had subclinical cardiac involvement. We therefore want to clearly state that all patients included in our study had cardiomyopathy and that this diagnosis would not have changed if we had used tissue Doppler or CMR.

Like Drs Yilmaz, Suttie, and Petersen, we believe that there is great value in applying CMR and tissue Doppler to detect the earliest signs of cardiac pathology in Becker muscular dystrophy patients. Future prospective, serial studies are needed to more accurately predict cardiac outcome in Becker muscular dystrophy patients. These should include tissue Doppler and ideally CMR, although the latter is very expensive in the United States and not all Becker muscular dystrophy patients are amenable to such testing. We thank Yilmaz et al for their comments.

Disclosures

None.

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Reference


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