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Letter to the Editor

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Assessing the effect of non-invasive ventilation on cardiac function in Duchenne muscular dystrophy requires prospective studies

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With interest, we read the article by James et al about a study on the effect of non-invasive positive pressure ventilation on cardiac dysfunction in patients with Duchenne muscular dystrophy, assessed as ejection fraction <55% or fractional shortening <28%.[1] When comparing 140 Duchenne muscular dystrophy patients under full/complete non-invasive positive pressure ventilation (cohort-2) with 403 Duchenne muscular dystrophy patients (cohort-1), non-invasive positive pressure ventilation had no beneficial effect on ejection fraction/fractional shortening.[1] The study has a number of shortcomings.

The main shortcoming is that, according to the abstract, cohort-2 patients were also included in cohort-1. That cohort-1 included non-invasive positive pressure ventilation patients is substantiated by the fact that a mean age at initiation of non-invasive positive pressure ventilation is provided.[1] If the goal was to assess the effect of non-invasive positive pressure ventilation on ejection fraction/fractional shortening, a group under non-invasive positive pressure ventilation needs to be compared with a group without non-invasive positive pressure ventilation.

The second shortcoming is that ejection fraction/fractional shortening and speed of ejection fraction/fractional shortening decline were not correlated with the genetic status of the included patients. Since previous studies suggested that the cardiac phenotype in Duchenne muscular dystrophy may depend on the type and location of a dystrophin mutation,[2] it is crucial to know how many of the patients had deletions, non-sense mutation, or splice site mutations and how many had missense mutations in which locations.

Another shortcoming is that patients taking angiotensin-converting enzyme inhibitors+ beta-blockers with or without steroids were obviously excluded. This issue is crucial as the combination of angiotensin-converting enzyme inhibitors and beta-blockers may be more effective than either drug alone.

A fourth shortcoming is that the 23.5% of cohort-1 patients who were exclusively taking steroids were not compared with those 20% of cohort-1 patients who were not taking steroids at all. This point is relevant to assess if steroids improve ejection fraction/fractional shortening without angiotensin-converting enzyme inhibitors or beta-blockers.

A further shortcoming is that it is unclear upon which criteria the diagnosis was established. We should know in how many of the patients the diagnosis was confirmed genetically and in how many by immune-histology. Diagnosing Duchenne muscular dystrophy solely upon immune-histology may lead to false-positive results.[3]

A sixth shortcoming is that echocardiographies of the included patients were not evaluated for the presence of left ventricular hypertrabeculation. Left ventricular hypertrabeculation has been repeatedly reported in Duchenne muscular dystrophy patients,[4] and it is well-known that left ventricular hypertrabeculation is complicated by heart failure.[5] Thus, it is crucial to know in how many patients left ventricular hypertrabeculation contributed to the deterioration of ejection fraction/fractional shortening.

Missing is an explanation why the rate of patients taking steroids without angiotensin-converting enzyme inhibitors or beta-blockers was highly different between the two cohorts. In cohort-1, 23.5% were taking exclusively steroids, but in cohort-2, 65.7% were exclusively taking steroids. This is another reason why these two cohorts should not be compared.

Unclear remains, if the included patients were taking drugs other than steroids, angiotensin-converting enzyme inhibitors, and beta-blockers, and how many had undergone gene therapy (e.g. exon skipping).

Overall, this interesting study has a number of shortcomings, with regard to design, diagnosis, genetic status, and treatment, which do not allow drawing conclusions as presented. A study with a prospective design including only genetically confirmed patients and comparing patients with and without non-invasive positive pressure ventilation would certainly allow the generation of more reliable results.

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