THE NATURAL HISTORY OF BECKER MUSCULAR DYSTROPHY (BMD) – A SYSTEMATIC LITERATURE REVIEW

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BACKGROUND

- Becker muscular dystrophy (BMD) is a dystrophinopathy caused by mutations in the dystrophin gene and is characterized by the progressive degeneration of the smooth, skeletal, and cardiac muscle.[1-3]
- This muscle degeneration may result in loss of muscle function, respiratory and cardiac failure, and premature death.[3]
- The clinical course of BMD is variable across patients, with severe progression in some, while others are nearly asymptomatic, however a thorough synthesis of existing natural history data for BMD was lacking.[2]

OBJECTIVE

- The objective of this study was to characterize the variation in natural history among BMD patients.

METHODS

Data collection

- A comprehensive systematic search of the literature was conducted using MEDLINE and EMBASE to identify available data on the variation in clinical phenotype and disease progression among patients with DMD.
- Only articles published in human BMD patients, in English, from the year 2000 onwards were included.
- Among the patients who did experience the events, data were collected from published individual patient data (IPD) and aggregate means, medians, ranges, and standard deviations (SD) for all natural history outcomes of interest.

Analysis and synthesis of data

Mean age at event

- Mean age at clinical events was calculated as a weighted average from IPD and grouped data for age at occurrence of the event

METHODS CONTINUED

Proportion experiencing the event by age

- The proportion of those experiencing key natural history events, from the ages of 0 to 20, 21 to 40, and 41+ years were summarized.
- To best represent the natural history of BMD, data were only included from studies with a population which was representative of real-world BMD (i.e. not studies focused on patient populations with specific characteristics or clinical symptoms)

RESULTS

- Of 3,915 identified studies, 133 reported data on relevant outcomes; however, four were removed due to redundancy among patient populations, resulting in 129 contributing evidence (**Table 1**).
- 4.3% of included BMD patients were confirmed as corticosteroid treated while the remaining were either not treated, or treatment was not specified.

Table 1. Characteristics of 129 studies contributing evidence

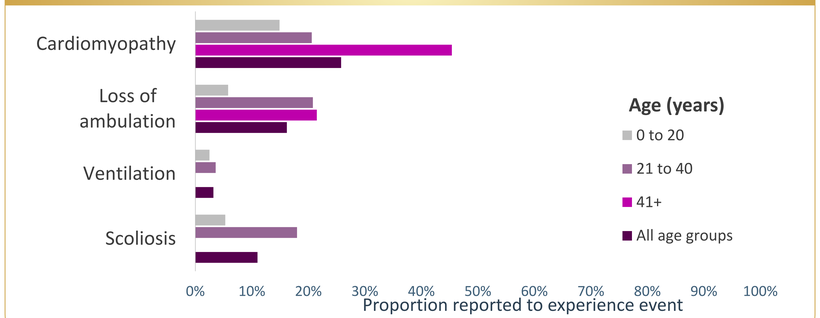
Study characteristic	n studies	% studies
Study design	**129**	**100%**
Cross-sectional	68	53%
Retrospective/prospective cohort*	46	36%
Clinical trial	14	11%
Case series	1	1%
Study Region	**129**	**100%**
Europe	67	52%
Asia	27	21%
USA	17	13%
South America	6	5%
Middle East	6	5%
Global	4	3%
Africa	2	2%

*follow- up ranged from 3 weeks to 23 years

RESULTS CONTINUED

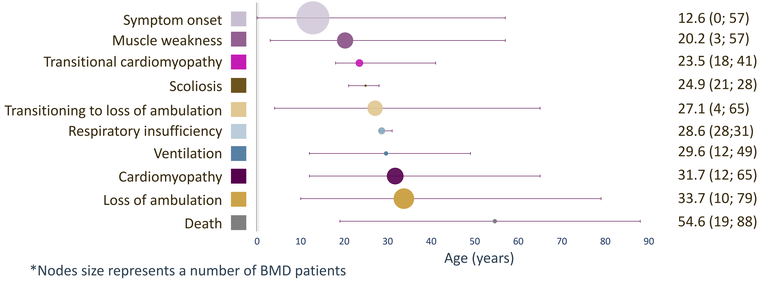
- The proportion of BMD patients experiencing an event was low for the majority of outcomes, ranging from 0% in the cohort of patients where the mean/median age was 41+ years for requiring ventilation and onset of scoliosis, to 45.4% for the cohort aged 41+ years for cardiomyopathy (**Figure 1**).

Figure 1. BMD patients experiencing the event by mean or median age, and overall



- For patients experiencing key natural history outcomes, the mean (SD) of age at the time of event ranged from 12.6 (10.5) years for symptom onset, to 54.6 (21.4) for death **(Figure 2).**
- Wide ranges were observed in reported age at the occurrence of events, for example, symptom onset occurred anywhere from birth to 57 years, and loss of ambulation occurred between the ages of 10 and 79 years.

Figure 2. Mean and range of age at event among BMD patients experiencing the event



*Nodes size represents a number of BMD patients

CONCLUSIONS

- This is the first systematic review of clinical outcomes in BMD. Despite limitations to the available data, key clinical outcomes were consistently reported in studies that include patients across a range of age. In the majority of these patients, key Becker muscular dystrophy-related events such as requiring ventilatory support, loss of ambulation, or scoliosis were not observed, while cardiomyopathy was eventually observed in approximately half. In patients for whom these events were observed, their occurrence varied notably with age.

LIMITATIONS

- This study was limited due to the lack of large-scale longitudinal studies with extensive follow-up that would allow natural-history trajectories to be more clearly characterized.

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