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SCIENTIFIC INVESTIGATIONS

Characterization of sleep-disordered breathing in children with Duchenne muscular dystrophy by the American Academy of Sleep Medicine criteria vs disease-specific criteria: what are the differences?

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Study Objectives: Individuals with Duchenne muscular dystrophy (DMD) frequently develop sleep-disordered breathing. Noninvasive ventilation is often prescribed for sleep-disordered breathing treatment based on the American Academy of Sleep Medicine (AASM) criteria. In 2018, DMD disease-specific criteria for sleep-disordered breathing were established. Our study aimed to examine the clinical interpretation differences using these different criteria.

Methods: We performed a multicenter, retrospective chart review of children with DMD followed at The Hospital for Sick Children, Toronto, Canada, and Rady Children's Hospital, San Diego, California, who underwent polysomnography from August 1, 2012, to February 29, 2020. Baseline characteristics and polysomnography data were summarized using descriptive statistics. Agreement for the diagnosis of sleep-disordered breathing evaluated by kappa statistics and sensitivity/specificity analysis was assessed.

Results: One hundred five male children with DMD (mean ± SD age: 12.1 ± 3.8 years; body mass index *z* score: 0.2 ± 2.3) were included. The proportions of children with DMD that met at least 1 AASM criterion and at least 1 DMD criterion were 45.7% and 67.6%, respectively. We found that 32.4% of children met neither AASM nor DMD criteria. Overall agreement between AASM and DMD criteria was moderate (k = 0.57). There was almost perfect agreement in sleep apnea diagnosis (k = 0.90); however, there was only slight agreement in hypoventilation diagnosis (k = 0.12) between AASM and DMD criteria.

Conclusions: There were more children with DMD diagnosed with nocturnal hypoventilation and prescribed noninvasive ventilation using DMD criteria compared with AASM criteria. Future studies should address whether the prescription of noninvasive ventilation for children with DMD based on both criteria is associated with different clinical outcomes.

Keywords: Duchenne muscular dystrophy, hypoventilation, obstructive sleep apnea, sleep-disordered breathing

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BRIEF SUMMARY

Current Knowledge/Study Rationale: The clinical interpretation differences and impact on diagnosis and treatment of sleep-disordered breathing including noninvasive ventilation prescription in children with Duchenne muscular dystrophy (DMD) using American Academy of Sleep Medicine (AASM) criteria vs disease-specific criteria are unknown.

Study Impact: Our study demonstrated that DMD disease-specific criteria led to more individuals with DMD meeting criteria for sleep-disordered breathing diagnosis and noninvasive ventilation prescription compared with the AASM guidelines. These results are beneficial for sleep-disordered breathing diagnosis and noninvasive ventilation prescription in children with DMD, which should be considered as part of standard clinical care for all children with DMD in the future. To our knowledge, this is the first pediatric study to report on the clinical interpretation differences by using AASM criteria vs disease-specific criteria.

INTRODUCTION

Duchenne muscular dystrophy (DMD) is the most common pediatric neuromuscular disease (NMD). It is an X-linked disorder characterized by the production of abnormal dystrophin in muscle.[1] Loss of respiratory muscle strength results in cough impairment, recurrent atelectasis and pneumonia, sleep-disordered breathing (SDB), and chronic respiratory failure.[1–4] Progressive muscle weakness, obesity secondary to the loss of ambulation and use of corticosteroids, as well as scoliosis all contribute to the development of SDB, primarily obstructive sleep apnea (OSA) and hypoventilation.[5] Polysomnography (PSG) is an important component of the respiratory assessment for individuals with DMD in addition to pulmonary function tests.[6,7] Noninvasive ventilation (NIV) is prescribed for the treatment of SDB in individuals with DMD. NIV has been previously shown to prolong survival, improve quality of life and well-being, and slow the rate of pulmonary function decline in patients with DMD.[3,6–9]

The American Academy of Sleep Medicine (AASM) defines specific pediatric rules for scoring respiratory events and

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hypoventilation for PSGs.[10] Traditionally, the prescription of NIV for SDB has been based on these scoring rules. In 2018, specific recommendations for the prescription of NIV for individuals with DMD were published.[6] We hypothesized that these new recommendations would lead to more individuals with DMD meeting criteria for SDB diagnosis and to be initiated on NIV as compared with the AASM guidelines. Our aim was to evaluate the clinical interpretation differences resulting from applying the AASM criteria vs the DMD disease-specific criteria to PSGs performed on children and adolescents with DMD clinically referred for evaluation of suspected SDB.

METHODS

Study design and setting

This study was a multicenter, retrospective chart review, which was conducted at The Hospital for Sick Children, Toronto, Ontario, Canada, and Rady Children's Hospital, San Diego, California. This study was approved by the Research Ethics Board at The Hospital for Sick Children (SickKids), University of Toronto, Canada (Research Ethics Board number 1000064481), and University of California San Diego (institutional review board number 190155). Electronic patient charts from the Long-Term Ventilation Clinic at The Hospital for Sick Children, Toronto, Canada, and the Sleep Clinic at Rady Children's Hospital, San Diego, California, were retrospectively reviewed between August 1, 2012, and February 29, 2020.

Study population

The inclusion criteria were as follows: children aged 0–18 years old with confirmed diagnosis of DMD and who underwent a baseline, diagnostic overnight level I PSG at The Hospital for Sick Children or Rady Children's Hospital during the study period.

Data collection methods

Demographics and medical history

We collected study participant information including age, height, weight, body mass index (BMI) *z* score, primary diagnosis, comorbidities, history of adenotonsillectomy, medications including deflazacort, ambulatory status, spirometry and respiratory muscle strength measurements, and date of initiation of NIV.

Polysomnography

All PSGs included 8–10 hours of overnight monitoring. The PSGs were conducted and analyzed in accordance with the AASM guidelines of sleep and associated events with a computer software system.[10] All PSG studies were performed at affiliated hospital sleep laboratories per institutional protocols that have been previously published for Rady Children's Hospital[11] and The Hospital for Sick Children.[12] All PSGs were interpreted by sleep physicians.

AASM criteria

All respiratory events were scored in accordance with the AASM pediatric scoring rules for all children younger than 18 years of age.[10–12] Obstructive apnea-hypopnea index (OAHI) was defined as the number of obstructive apnea, mixed apnea, and hypopnea episodes/hour during sleep. Apnea-hypopnea index (AHI) was defined as the total number of apnea and hypopnea episodes/hour during sleep. The AASM pediatric OSA severity scoring criteria were used: mild OSA = OAHI ≥ 1.5 to < 5 events/h; moderate OSA = OAHI ≥ 5 to < 10 events/h; and severe OSA = OAHI ≥ 10 events/h. Central sleep apnea (CSA) was defined as a central AHI (CAHI) ≥ 5 events/h of sleep. Nocturnal hypoventilation was defined as end-tidal carbon dioxide ($etCO_2$) or transcutaneous carbon dioxide ($tcCO_2$) level > 50 mm Hg for ≥ 25% of total sleep time (TST).[10]

DMD guidelines

According to the 2018 DMD guidelines, there are 4 sleep study criteria indicating the need to initiate NIV: (1) $etCO_2$ or $tcCO_2$ > 50 mm Hg for ≥ 2% of sleep time, (2) a sleep-related increase in $etCO_2$ or $tcCO_2$ of 10 mm Hg above the awake baseline for ≥ 2% of sleep time, (3) oxygen saturation (SpO_2) ≤ 88% for ≥ 2% of sleep time or for at least 5 minutes continuously, or (4) AHI ≥ 5 events/h.[6,7]

PSG studies had all been scored clinically using the AASM pediatric criteria. For the purpose of this study, we rescored all PSGs using the DMD guidelines. **Table 1** summarizes the criteria for respiratory events and gas exchange parameters for both the AASM pediatric criteria and DMD disease-specific criteria.

Statistical analysis

The study participants' data were summarized using descriptive statistics. Baseline characteristics, sleep architecture, AASM

Table 1—Indications for the prescription of NIV based on AASM criteria vs DMD criteria.

Parameter	AASM Criteria	DMD Criteria
AHI	OAHI ≥ 5 events/h; CAHI ≥ 5 events/h	AHI ≥ 5 events/h
Nocturnal hypoventilation	$etCO_2$ or $tcCO_2$ level > 50 mm Hg for ≥ 25% of TST	$etCO_2$ or $tcCO_2$ > 50 mm Hg for ≥ 2% of sleep time or sleep-related increase in $etCO_2$ or $tcCO_2$ of 10 mm Hg above the awake baseline for ≥ 2% of sleep time
Oxygen saturation	N/A	SpO_2 ≤ 88% for ≥ 2% of sleep time or for at least 5 minutes continuously

AASM = American Academy of Sleep Medicine, AHI = apnea-hypopnea index, CAHI = central apnea-hypopnea index, DMD = Duchenne muscular dystrophy, $etCO_2$ = end-tidal carbon dioxide, N/A = not available, NIV = noninvasive ventilation, OAHI = obstructive apnea-hypopnea index, SpO_2 = oxygen saturation, $tcCO_2$ = transcutaneous carbon dioxide, TST = total sleep time.

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criteria, DMD criteria, and spirometry data were reported as mean (standard deviation [SD]) for normally distributed continuous variables and as median (interquartile range) and frequency (%) for skewed continuous variables and categorical variables, respectively. Normally distributed, continuous variables were compared using Student's *t* tests and categorical variables were compared using the chi-square test. Agreement between AASM and DMD criteria for the diagnosis of SDB was evaluated by kappa statistics, and sensitivity/specificity analysis was performed for each criterion for the prescription of NIV. A *P* value less than .05 indicated statistical significance. Data analysis was carried out using IBM Statistical Package for the Social Sciences (SPSS) for Windows, version 26.0 (IBM Corporation, Armonk, NY).

RESULTS

One hundred five male children with genetically confirmed DMD completed diagnostic PSGs and were included in the final analysis. Mean ± SD for age and BMI *z* score were 12.1 ± 3.8 years and 0.2 ± 2.3, respectively. Only 13 (12%) of children had adenotonsillectomy prior to performing diagnostic PSG. Mean (± SD) total OAHI and CAHI were 6.8 ± 9.1 events/h and 1.6 ± 3.7 events/h with an average SpO_2 nadir of 87.8% ± 5.6% (**Table 2**). Seated percent-predicted forced vital capacity (FVC%) ranged from 15% to 122%, with a mean ± SD FVC of 69.8% ± 26.7%.

The proportion of deflazacort prescriptions was higher in children from The Hospital for Sick Children compared with children from Rady Children's Hospital (80% vs 47%). There were no statistically significant differences between institutions in other demographic factors, such as mean age (*P* = .29), BMI *z* score (*P* = .59), AHI (*P* = .55), or FVC (*P* = .63) (**Table 2**).

The proportion of children with DMD who met at least 1 AASM criterion was 48/105 (45.7%), while the proportion of children who met at least 1 DMD criterion was 71/105 (67.6%). Thirty-four of 105 (32.4%) children met neither AASM nor DMD criteria. Forty-eight (45.7%) children met at least 1 of both AASM and DMD criteria. None of the children met

Table 2—Demographic data and respiratory function (n = 105).

	RCHSD (n = 17)	SickKids (n = 88)	All Institutions (n = 105)
Demographic data			
Age (y)	13.9 ± 4.0	11.7 ± 3.7	12.1 ± 3.8 (2.2–19.0)
BMI (kg/m^2)	25.5 ± 8.4	21.5 ± 6.7	22.2 ± 7.1 (11.0–49.2)
BMI *z* score	0.6 ± 2.3	–0.1 ± 2.3	0.2 ± 2.3 (11.1–3.1)
Prescribed deflazacort,* n (%)	8 (47)	70 (80)	78 (74)
Snoring present,* n (%)	15 (88)	57 (65)	72 (69)
Adenotonsillectomy prior to PSG,* n (%)	1 (6)	12 (14)	13 (12)
Sleep respiratory data			
Total AHI (events/h)	6.3 ± 4.9	8.8 ± 12.2	8.4 ± 11.4 (0.0–34.3)
Total OAHI (events/h)	5.5 ± 4.7	7.1 ± 9.7	6.8 ± 9.1 (0.0–59.8)
Total CAHI (events/h)	0.7 ± 1.1	1.8 ± 3.9	1.6 ± 3.7 (0.0–32.3)
REM sleep AHI (events/h)	21.5 ± 26.3	18.6 ± 26.1	19.0 ± 26.0 (0.0–120.0)
SpO_2 nadir (%)	88.8 ± 6.0	87.6 ± 5.5	87.8 ± 5.6 (65.0–97.0)
TST SpO_2 < 90% (%)	10.1 ± 2.4	5.0 ± 17.8	6.0 ± 18.9 (0.0–12.8)
TST $etCO_2$ ≥ 50 mm Hg (%)	0.5 ± 1.3	1.6 ± 5.9	1.5 ± 5.4 (0.0–46.2)
TST $tcCO_2$ ≥ 50 mm Hg (%)	1.2 ± 4.5	1.8 ± 9.9	1.7 ± 9.2 (0.0–91.0)
Mean respiratory rate (breaths per minute)	17 ± 3	18 ± 4	18 ± 3 (11–32)
Pulmonary function			
FVC (%)	56.2 ± 20.2	72.7 ± 27.1	69.8 ± 26.7 (15–122)
FEV_1 (%)	58.3 ± 21.0	73.8 ± 27.1	71.1 ± 27.2 (15–122)
PEF (%)	61.3 ± 23.6	81.1 ± 26.8	77.9 ± 27.2 (19–132)
MIP (cm H_2O)	N/A	55.4 ± 14.8	55.4 ± 14.8 (18–80)
MEP (cm H_2O)	N/A	44.7 ± 15.0	44.7 ± 15.0 (20–92)

Data are presented as mean ± SD or mean ± SD (range) unless otherwise indicated. *Represents proportion of total patients who met specified criteria as n (%). AHI = apnea-hypopnea index, BMI = body mass index, CAHI = central apnea-hypopnea index, $etCO_2$ = end-tidal carbon dioxide, FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, MEP = maximal expiratory pressure, MIP = maximal inspiratory pressure, N/A = not available, OAHI = obstructive apnea-hypopnea index, PEF = peak expiratory flow, PSG = polysomnography, RCHSD = Rady Children's Hospital San Diego, REM = rapid eye movement, SD = standard deviation, SickKids = The Hospital for Sick Children, Toronto, Canada, SpO_2 = oxygen saturation, $tcCO_2$ = transcutaneous carbon dioxide, TST = total sleep time.

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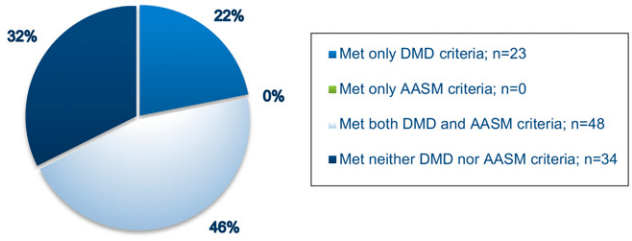
Figure 1—Proportion of patients meeting specific criteria.



AASM = American Academy of Sleep Medicine, DMD = Duchenne muscular dystrophy.

AASM criteria without also meeting 1 or more DMD criteria (**Figure 1**).

Sleep apnea was diagnosed in 46 of 105 (43.8%) compared with 51 of 105 (48.6%) children based on AASM and DMD criteria, respectively. Nocturnal hypoventilation was diagnosed in only 2 of 105 (1.9%) children based on AASM criteria compared with 32 of 105 (30.5%) children based on DMD criteria. Of the 3 DMD criteria describing nocturnal hypoventilation, the most commonly identified criterion was $etCO_2$/$tcCO_2$ > 50 mm Hg for ≥ 2% TST, which accounted for 24 of 105 (22.8%) of participants (**Table 3** and **Table S1** in the supplemental material).

Table 3—Number of children meeting DMD and AASM criteria.

	Number of Children With DMD (n = 105)
A. AASM criteria	
I. Sleep apnea	
a. OAHI ≥ 5 events/h	43 (40.9%)
b. CAHI ≥ 5 events/h	5 (4.8%)
II. Nocturnal hypoventilation	
a. $etCO_2$ or $tcCO_2$ > 50 mm Hg or 25% TST	2 (1.9%)
B. DMD criteria	
I. Sleep apnea	
a. AHI ≥ 5 events/h	51 (48.6%)
II. Nocturnal hypoventilation	
a. $etCO_2$/$tcCO_2$ > 50 mm Hg for ≥ 2% TST	24 (22.8%)
b. $etCO_2$/$tcCO_2$ during sleep ≥ 10 mm Hg from awake baseline for ≥ 2% TST	20 (19.0%)
c. SpO_2 ≤ 88% for ≥ 2% TST or ≥ 5 minutes continuously	6 (5.7%)

AASM = American Academy of Sleep Medicine, AHI = apnea-hypopnea index, CAHI = central apnea-hypopnea index, DMD = Duchenne muscular dystrophy, $etCO_2$ = end-tidal carbon dioxide, OAHI = obstructive apnea-hypopnea index, SpO_2 = oxygen saturation, $tcCO_2$ = transcutaneous carbon dioxide, TST = total sleep time.

Overall agreement between AASM criteria and DMD criteria was moderate (k = 0.58, $P < .01$). There was almost perfect agreement between the sleep apnea subgroup AASM criteria and the sleep apnea subgroup DMD criteria (k = 0.90, $P < .01$). In contrast, there was only slight agreement between the hypoventilation subgroup criteria (k = 0.12, $P < .01$) (**Table 4**).

Of the 48 children meeting 1 or more AASM criteria, 31 of 48 (64.6%) were initiated on NIV following diagnostic PSG. In comparison, of the 71 children meeting 1 or more DMD criteria, 42 of 71 (59.1%) were initiated on NIV. Interestingly, of the 34 patients meeting neither AASM nor DMD criteria, 9 of 34 (26.5%) were still initiated on NIV following diagnostic PSG (**Figure 2**).

Of the 51 of 105 (48.6%) children with DMD prescribed NIV, 30 of 51 (58.8%) and 32 of 51 (62.7%) were diagnosed with sleep apnea criteria based on AASM criteria and DMD-specific criteria, respectively. In terms of the hypoventilation criteria, 18 of 51 (35.3%) children were prescribed NIV based on DMD-specific criteria compared with 1 of 51 (2.0%) of children who were diagnosed based on AASM criteria. Fourteen children who met hypoventilation criteria based on DMD-specific criteria were not prescribed NIV. There were children who met DMD-specific criteria for sleep apnea and hypoventilation but who did not meet AASM criteria who were initiated on NIV—2 of 51 (3.9%) and 17 of 51 (33.3%), respectively. Finally, 13 of 54 (24.1%) of children who met DMD-specific criteria for hypoventilation but did not meet AASM criteria were not prescribed NIV (**Table S1**).

Compared with the AASM criteria, the DMD criteria had a higher sensitivity of initiating NIV (50.8% vs 82.4%). However, the specificity of NIV initiation based on DMD criteria was lower than the specificity based on AASM criteria (**Table 5** and **Table S2** in the supplemental material).

Of the clinical factors examined, older age was associated with NIV initiation in both patients who met DMD criteria (12.9 ± 2.8 years vs 10.5 ± 4.1 years; $P = .005$) and patients who met AASM criteria (13.2 ± 3.9 vs 12.6 ± 4.4 years; $P = .004$). Neither AHI (11.3 ± 8.4 events/h vs 11.4 ± 17.6 events/h; $P = .97$) nor OAHI (10.4 ± 8.2 events/h vs 7.8 ± 12.4 events/h; $P = .29$) were significant determinants of NIV initiation in children meeting DMD criteria. However, awake baseline SpO_2 was significantly lower in patients who initiated NIV based on DMD criteria (96.3% ± 1.3% vs 97.1% ± 1.0%; $P = .004$) and AASM criteria (96.2% ± 1.4% vs 97.2% ± 1.1%; $P = .02$). The SpO_2 sleep nadir was lower in patients who initiated NIV based on DMD criteria (85.0% ± 6.4% vs 88.6% ± 4.1%; $P = .008$), but this was not statistically significant for AASM criteria (83.8% ± 6.8% vs 87.0% ± 4.4%; $P = .09$). Similarly, maximum $tcCO_2$ was higher in children initiating NIV based on DMD criteria (41.1 ± 16.4 mm Hg vs 47.7 ± 4.7 mm Hg; $P = .04$) but not significant in children meeting AASM criteria (41.8 ± 15.0 mm Hg vs 42.7 ± 11.5 mm Hg; $P = .82$).

Other clinical factors, such as BMI z score ($P = .92$, $P = .09$), average heart rate ($P = .24$, $P = .56$), average respiratory rate ($P = .61$, $P = .38$), and FVC% predicted ($P = .23$, $P = .23$) were not statistically significant predictors of NIV initiation in children meeting either DMD or AASM criteria, respectively (**Table S1**). Similarly, there was not a statistically significant difference in

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Table 4—Measure of agreement (kappa) between AASM and DMD criteria.

	n (%)	k	95% CI
Overall criteria agreement			
Met ≥ 1 AASM criteria	48 (45.7%)	0.575	0.44–0.71
Met ≥ 1 DMD criteria	71 (67.6%)		
Sleep apnea criteria agreement			
Met AASM criteria: OAHI and/or CAHI ≥ 5 events/h	46 (43.8%)	0.904	0.82–0.98
Met DMD criteria: AHI ≥ 5 events/h	51 (48.6%)		
Hypoventilation criteria agreement			
Met AASM criteria: $etCO_2/tcCO_2$ > 50 mm Hg for > 25% TST	2 (1.9%)	0.123	−0.03 to 0.28
Met DMD criteria: $etCO_2/tcCO_2$ > 50 mm Hg for ≥ 2% TST and/or $etCO_2/tcCO_2$ during sleep ≥ 10 mm Hg from awake baseline for ≥ 2% TST and/or SpO_2 ≤ 88% for ≥ 2% TST or ≥ 5 minutes continuously	32 (30.5%)		

AASM = American Academy of Sleep Medicine, AHI = apnea-hypopnea index, CAHI = central apnea-hypopnea index, CI = confidence interval, DMD = Duchenne muscular dystrophy, $etCO_2$ = end-tidal carbon dioxide, OAHI = obstructive apnea-hypopnea index, SpO_2 = oxygen saturation, $tcCO_2$ = transcutaneous carbon dioxide, TST = total sleep time.

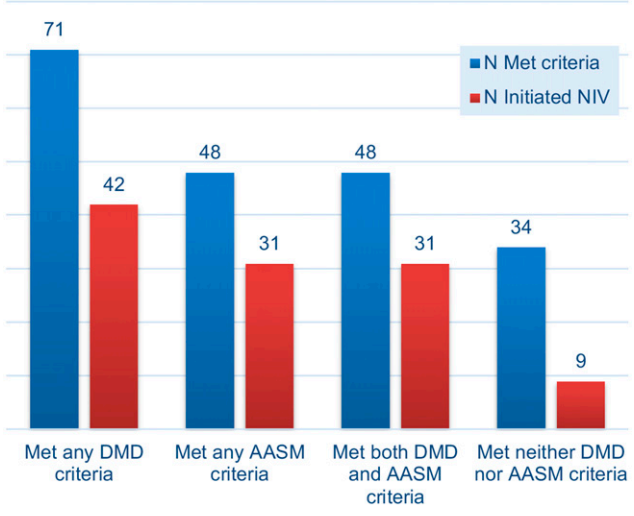
NIV initiation among children prescribed deflazacort compared to those who were not (Fisher's exact test, $P = 1.0$).

DISCUSSION

To the authors' knowledge, this is the first multicenter retrospective study examining the differences between AASM criteria and DMD disease-specific criteria in the characterization of SDB in children as well as their agreement. Traditionally, AASM criteria have been used to define SDB in the absence of disease-specific criteria for children or adults with NMD.[10,13,14] Although virtually all adults with DMD develop hypoventilation, childhood prevalence previously reported based on AASM criteria can vary from 16% to 21%.[5,15,16] A recent prospective study suggested prevalence rates of hypoventilation among children with DMD to be as high as 58%.[17] Our study found that a greater proportion of children met at least 1 DMD disease-specific criterion for the diagnosis of SDB, compared with AASM criteria (68% vs 46%). Furthermore, a greater proportion of patients in our population met nocturnal hypoventilation diagnosis based on DMD criteria compared with AASM criteria (50% vs 2%). However, there are limitations associated with using the AASM criteria for NMD. Individuals with NMD have progressive muscle weakness, resulting in the reduction of airflow and chest and abdominal movement, which are not scored findings unless they are associated with either an arousal or a desaturation.[18,19] In addition, paradoxical breathing may be a consequence of diaphragmatic weakness in patients with NMD and not an obstructive respiratory event.[18–20]

Similarly, consensus statements regarding respiratory management of patients with DMD do not provide specific criteria for the diagnosis of OSA or hypoventilation.[3,4,16] Although the optimal timing and duration of NIV therapy is not well defined for the DMD population, most clinicians agree there is benefit to timely initiation of NIV once hypoventilation is identified.[21,22] NIV therapy can lead to improved survival, fewer hospital days, and preserved lung function.[23,24] There was weak agreement between the hypoventilation subgroup criteria of the AASM and DMD criteria. Weak agreement in the nocturnal hypoventilation subgroup is not surprising given the differences in prevalence of hypoventilation between DMD and AASM criteria (50% vs 2%). Our study suggests that across a multicenter cohort, the DMD criteria may diagnose a larger proportion of children with SDB, specifically nocturnal hypoventilation,

Figure 2—Number of patients meeting criteria who initiated NIV.



After diagnostic PSG, 65% of children meeting 1 or more AASM criteria initiated NIV. In comparison, 59% of children meeting 1 or more DMD criteria initiated NIV. Despite meeting neither AASM nor DMD criteria, 26% were still initiated on NIV after diagnostic PSG. AASM = American Academy of Sleep Medicine, DMD = Duchenne muscular dystrophy, NIV = noninvasive ventilation, PSG = polysomnography.

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Table 5—Sensitivity and specificity of AASM and DMD criteria in NIV initiation.

	Test Criteria	Noninvasive Ventilation Initiation		
		NIV+	NIV–	Predictive Value
A	DMD+, n = 71	42	29	PPV 59.2%
	DMD–, n = 34	9	25	NPV 73.5%
		Sensitivity: 82.4%	Specificity: 46.3%	
B	AASM+, n = 48	31	17	PPV 64.6%
	AASM–, n = 57	20	37	NPV 55.2%
		Sensitivity: 50.8%	Specificity: 68.5%	

(A) Sensitivity/specificity analysis of DMD criteria. **(B)** Sensitivity/specificity analysis of AASM criteria. + = meets criteria, − = does not meet critera, AASM = American Academy of Sleep Medicine, DMD = Duchenne muscular dystrophy. NIV = noninvasive ventilation, NPV = negative predictive value, PPV = positive predictive value.

compared with AASM criteria. As a result, compared with AASM criteria, the use of DMD disease-specific criteria to identify SDB may result in a greater proportion of children initiating NIV therapy. Earlier detection of SDB and initiation of NIV may have improved outcomes for survival and quality of life.[25] Earlier initiation of NIV is likely to impact several factors including health care utilization, lung function, and NIV adherence.[26,27] Prospective, randomized trials are needed to determine if the earlier prescription of NIV for mild to moderate SDB is associated with improved clinical outcomes.

Interestingly, 24.1% of children who met hypoventilation criteria based on DMD-specific criteria but who did not meet AASM criteria were not prescribed NIV. Furthermore, 41% of the DMD criteria patients and 35% of the AASM criteria patients were not initiated on NIV despite meeting 1 or more criteria for SDB. On the other hand, of the 34 patients meeting neither AASM nor DMD criteria, 9 (26%) were still initiated on NIV after diagnostic PSG. This suggests that there are additional factors influencing the initiation or deferral of NIV therapy in children with DMD diagnosed with SDB, regardless of the diagnostic criteria based on PSG alone. Multiple factors have been identified that can influence medical decision-making and these include resource availability, physician experience, medical communication, and provider autonomy.[28,29] In the past decade, there has also been an increasing emphasis on the use of family- and patient-centered shared medical decision-making.[30–32] The latter has contributed to additional factors influencing clinician decision-making, including parental education, patient and family care goals, as well as health literacy. Future studies are required to investigate specific factors influencing the initiation or deferral of NIV therapy for children with DMD meeting criteria for SDB.

Although we conducted a multicenter study, which improved the generalizability of our results, there are some notable limitations to our study that require consideration. First, this is a retrospective review of a study period during which the majority of the PSGs were conducted prior to the publication of the DMD-specific guidelines. Therefore, we are extrapolating on the reason for the prescription of NIV based on the AASM criteria and the DMD-specific criteria alone. Second, we do not have qualitative or survey data to assess the reasons for the subset of children with DMD not started on NIV despite meeting AASM criteria. To date, there are no substantiated criteria to start NIV in children. Clinical judgment, physician experience, and center-specific protocols also appear to be affecting the prescription of NIV in this population. Therefore, it is very important to develop a strong collaborative relationship between sleep medicine and other specific clinical specialties in order to enhance the diagnostic evaluation and treatment outcome of patients with DMD. Finally, our study, due to its retrospective nature, could not assess the utility of either the AASM criteria or the DMD-specific criteria to improve hard clinical outcomes such as improvements in sleep quality, reduced pneumonias, reduced hospitalizations, or slower decline of pulmonary function tests. Therefore, future prospective, multicenter studies are needed to examine factors affecting NIV prescription based on both AASM and DMD disease-specific criteria as well as the long-term clinical outcomes in children prescribed NIV based on the different criteria.

CONCLUSIONS

Overall, a greater proportion of children met DMD criteria compared with AASM criteria. Factors influencing the initiation of NIV in children with DMD criteria–diagnosed SDB are multifactorial, including older age, lower baseline SpO_2, lower SpO_2 nadir, and higher peak of $etCO_2$. Future studies should address whether the prescription of NIV for children with DMD based on AASM or DMD-specific criteria is associated with different clinical outcomes.

ABBREVIATIONS

AASM, American Academy of Sleep Medicine
AHI, apnea-hypopnea index
BMI, body mass index
CAHI, central apnea-hypopnea index
CSA, central sleep apnea
DMD, Duchenne muscular dystrophy
$etCO_2$, end-tidal carbon dioxide
FVC, forced vital capacity
NIV, noninvasive ventilation
NMD, neuromuscular disease

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OAHI, obstructive apnea-hypopnea index
OSA, obstructive sleep apnea
PSG, polysomnogram/polysomnography
SD, standard deviation
SDB, sleep-disordered breathing
SpO_2, oxygen saturation
$tcCO_2$, transcutaneous carbon dioxide
TST, total sleep time

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DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. Work for this study was performed at Rady Children's Hospital, San Diego, California, and The Hospital for Sick Children, Toronto, Ontario, Canada. The authors report no conflicts of interest.

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