Sleep apnoea and hypoventilation in patients with five major types of muscular dystrophy

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ABSTRACT

Background The characteristics of and relationship between sleep apnoea and hypoventilation in patients with muscular dystrophy (MD) remain to be fully understood.

Methods We analysed 104 in-laboratory sleep studies of 73 patients with MD with five common types (DM)—Duchenne, Becker MD, CMD—congenital, LGMD—limb-girdle and DM—myotonic dystrophy). We used generalised estimating equations to examine differences among these types for outcomes.

Results Patients in all five types had high risk of sleep apnoea with 53 of the 73 patients (73%) meeting the diagnostic criteria in at least one study. Patients with DM had higher risk of sleep apnoea compared with patients with LGMD (OR=5.15, 95% CI 1.47 to 18.0; p=0.003). Forty-three percent of patients had hypoventilation with observed prevalence higher in CMD (67%), DMD (48%) and DM (44%). Hypoventilation and sleep apnoea were associated in those patients (unadjusted OR=2.75, 95% CI 1.15 to 6.60; p=0.03), but the association weakened after adjustment (OR=2.32, 95% CI 0.92 to 5.81; p=0.08).

In-sleep average heart rate was about 10 beats/min higher in patients with CMD and DMD compared with patients with DM (p=0.0006 and p=0.02, respectively, adjusted for multiple testing).

Conclusion Sleep-disordered breathing is common in patients with MD but each type has its unique features. Hypoventilation was only weakly associated with sleep apnoea; thus, high clinical suspicion is needed for diagnosing hypoventilation. Identifying the window when respiratory muscle weakness begins to cause hypoventilation is important for patients with MD; it enables early intervention with non-invasive ventilation—a therapy that should both lengthen the expected life of these patients and improve its quality.

INTRODUCTION

Muscular dystrophy disorders are a heterogeneous group of inherited genetic diseases characterised by progressive skeletal muscle weakness including diaphragm weakness and cardiomyopathy and wasting. Respiratory insufficiency and cardiomyopathy are two major causes for mortality and morbidity in those patients. Chronic respiratory insufficiency results in alveolar hypoventilation and hypercapnia, both are common in patients with muscular dystrophy. Early treatment of cardiomyopathy improves outcomes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Sleep apnoea and hypoventilation are common in patients with muscular dystrophy (MD); however, the characteristics of sleep-disordered breathing among patients with the five types are less known. This study looks into five major types of MD (Duchenne MD, Becker MD, congenital MD, LGMD—limb-girdle and DM—myotonic dystrophy).

WHAT THIS STUDY ADDS

⇒ Not all types of MD have the same degree and characteristics of sleep-disordered breathing. Importantly, hypoventilation was only weakly associated with sleep apnoea in patients with MD. Moreover, we found that patients with DM had significantly higher risk of sleep apnoea compared with patients with LGMD.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Specific attention should be paid to each type of MD. Because of the weak association between sleep apnoea and hypoventilation, high clinical suspicion is needed so that hypoventilation can be diagnosed early to allow for timely intervention with non-invasive ventilation and thus better outcome.
of diseases caused often by mutations (repeat expansions) in genes coding for proteins involving muscle structure formation, functions, and/or repair. DM is characterised by progressive muscle weakness, wasting and complex extramuscular manifestations including those in the cardiac and central nervous systems; its two principal subtypes are caused by mutations in two different genes: the DMPK gene for DM1 and the CNBP gene for DM2. CMD refers to a heterogeneous group of often severe muscular dystrophies that become apparent at or near birth.

Sleep-disordered breathing (sleep apnoea and hypoventilation) is common in patients with muscular dystrophy. Sleep apnoea occurs when normal breathing during sleep is interrupted. Sleep-related hypoventilation refers to breathing that is too slow or shallow during sleep resulting in impaired gas exchange as evidenced by an increase in partial arterial carbon dioxide (pCO₂) pressure. Possible differences in characteristics of sleep-disordered breathing among patients with the five major types are less well understood. Moreover, little is known about the relationship between sleep apnoea and hypoventilation in those patients. In this report, we analysed baseline and sleep variables obtained from 104 in-laboratory polysomnography (PSG) studies on 73 patients diagnosed with one of the five major types of muscular dystrophy. Our goals were: (1) to compare average values of selected clinical variables among muscular dystrophy types; (2) to examine the association of hypoventilation and sleep apnoea with clinical variables and types; and (3) to characterise the association between hypoventilation and sleep apnoea in these patients.

METHODS
Subjects and study protocol
A retrospective in-laboratory PSG data review was conducted for studies carried out between January 2004 and December 2021 in an American Academy of Sleep Medicine (AASM)-accredited sleep laboratory at the University of North Carolina at Chapel Hill (UNC-CH) on patients with a diagnosis of muscular dystrophy.

In-laboratory PSG study
Routine level 1 in-laboratory PSG studies were carried out at UNC-CH hospitals. Each in-laboratory PSG included at least six channel electroencephalograms, two electro-oculograms, submental and bilateral tibialis surface electromyograms and an ECG. Additional recordings included airflow from nasal pressure and nasal/oral thermocouple, chest and abdominal movement via respiratory impedance plethysmography belts, end-tidal CO₂ via a BCI capnograph sampled through a nasal cannula and arterial blood oxygen via a finger probe. Transcutaneous CO₂ was used when end-tidal CO₂ measurement was not feasible in selected patient groups such as the very young. Time-locked digital video was recorded with the PSG. The multichannel polysomnogram was recorded digitally and stored using a Stellate Systems polygraph, Grass Systems polygraph, and Natus polygraph between 2004 and 2012, between 2013 and 2018, and 2019 and 2021, respectively.

Studies before 2007 were scored using the guidelines from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. Studies from September 2007 until June 2016 were scored with the 2007 guidelines from the AASM scoring manuals. Subsequent studies were scored with the 2016 guidelines.

For all three periods, respiratory events were required to be a minimum of two breaths in duration. Hypopnoeas were required to be associated with at least 3% desaturation or arousal or 4% desaturation if the patient was on certain insurance such as Medicare. Diagnoses of obstructive sleep apnoea (OSA) and hypoventilation were based on the criteria by International Classification of Sleep Disorders-3.

Briefly, mild, moderate and severe sleep apnoea were defined based on the apnoea–hypopnoea index (AHI) but, by convention, with different ranges depending on the patient’s age at PSG. For those younger than 13 years old, mild, moderate and severe were defined, respectively, by the following ranges: 1.5≤AHI<5, 5≤AHI<10 and AHI≥10; for those at or above 18 years old, the corresponding ranges were: 5≤AHI<15, 15≤AHI<30 and AHI≥30. For teenagers between the ages of 13 and 18 years, criteria were chosen at the discretion of the reading physician. Hypoventilation was also defined differently depending on the patient’s age. For those under the age of 18 years, hypoventilation was defined as having greater than 25% of time in sleep spent with partial pressure of CO₂ (pCO₂) or surrogate measurements >50 mm Hg and a more than 10 mm Hg increase in pCO₂ in sleep in comparison with awake. For those 18 years and older, hypoventilation required having greater than 10 min with pCO₂ or surrogate measurements >55 mm Hg. Each sleep study was initially scored by an AASM board-certified sleep technologist and finalised by an AASM-certified physician. Paediatric studies were all scored by AASM board-certified sleep physicians specialised in children. Additional information can be found in the online supplemental materials.

Data
We included 96 diagnostic PSG studies and 8 split-night sleep studies. For a split-night study, we used data only from the diagnostic portion of the study.

We extracted patient details from electronic medical records including data on arterial blood gases (ABGs), maximal inspiratory/expiratory pressure (MIP/MEP) as measures of respiratory muscle strength, echocardiogram, Epworth Sleepiness Scale score, beta-blocker prescription, whether the patients were on ventilator at the time of study, status of tracheostomy and other relevant information (online supplemental table 1). For inclusion, these variables had to be measured within ±6 months of the sleep study. Specifically, we looked at the
date of the sleep study and then at the closest clinical record before or after that date within 6 months.

From the sleep study records, we extracted the basic variables: sex, age (years), weight (kg), height (cm), body mass index (BMI) and muscular dystrophy type, as well as PSG-specific variables. These included baseline variables: oxygen saturation (%), end-tidal CO₂ (mm Hg), heart rate (beats/min) and respiratory rate (breaths/min), as well as variables measured during sleep: average and peak heart rate, average and peak end-tidal CO₂ and overall AHI. Some PSG studies did not record all these variables, so our data have sporadic missing values.

Statistical analysis
We computed the age-adjusted and gender-adjusted BMI z-scores using weight (kg) and height (cm) according to the method proposed by Centers for Disease Control and Prevention.⁹ We then categorised these z-scores into three groups: z-score <-2, -2 ≤ z-score ≤2 and z-score >2. For some statistical analyses, we transformed continuous variables like age (by the base-2 logarithm) to improve model fit. Using the criteria delineated earlier, we also created binary (present or absent) variables for hyperventilation and sleep apnoea.

We used generalised estimating equations (GEE) with an exchangeable correlation structure when examining associations. Model specification differed somewhat for different response variables. For binary responses, such as apnoea or hyperventilation, our GEE models used a binomial distribution with the logistic link function; for continuous responses, such as heart rate, our GEE models used a normal distribution with the identity link function.

Although we have a reasonably large collection of patients with muscular dystrophy with PSG data, our sample, containing approximately 100 PSG studies, supports only small numbers of predictors in individual statistical models and limits statistical power. Consequently, we examined associations between response variable and individual predictor variables including adjustment for a few selected covariates. In general, we report p values without accounting for multiple testing although we employ the Tukey-Kramer procedure for pairwise comparisons among types. For model fitting, we used PROC GENMOD in SAS (V.9.4) (details in online supplemental materials).

Patient and public involvement
Neither patients nor the public had any involvement with planning, conducting or reporting this research.

RESULTS
We identified 104 PSG studies from 73 unique patients with confirmed diagnosis of one of the five major types of muscular dystrophy (table 1). The most frequently represented among the major types were DMD (37% of patients) and DM (33% of patients); BMD, CMD and LGMD made up approximately 7%, 10% and 14% of patients, respectively. Of the 73 patients, 57 (78%) contributed one study, 7 (10%) had two studies, 7 (10%) had three studies and 1 (1%) had four studies. One patient (1%) with congenital DM had eight studies (online supplemental table 2). At least one patient of each type had more than one study. The patient who had eight studies was diagnosed with congenital DM type 1. Of the 31 consecutive pairs of studies from patients with multiple studies, their separation in time ranged from 0 to 10 years, with 17 (55%) within 2 years of the previous study. The patients’ pulmonologists or neurologists ordered all PSGs. All patients with DMD and BMD were male, consistent with these types being X linked recessive diseases. All patients with CMD except one were also male. Approximately half of the patients with LGMD and the DM were male.

Brief summary of the clinical variables
We sought certain both PSG and non-PSG-related clinical variables from patient medical records within ±6 months of each PSG study. These included ABGs, beta-blocker prescription, echocardiogram, MIP/MEP, vital status, tracheostomy status, Epworth Sleepiness Scale, ventilator status at PSG study, among others (table 1 and online supplemental table 1). For many subjects, some variables were not recorded during the 6-month window around the PSG. For example, MIP/MEP was recorded for 29, marked as ‘unable’ for 8 and unrecorded for 67 of 104 PSG studies; these factors were not routinely assessed by their pulmonologists for patients with DM and for the young because of small nostrils and other constraints. Among the 49 studies with ABG (pCO₂) measurements, 35 (71%) had borderline to elevated levels (pCO₂ ≥45 mm Hg or bicarb >30 mEq/L). Among the 27 studies with MIP measurements, 22 (81%) had reduced pressures. Similarly, among the 27 with MEP measurements, 20 (74%) had reduced pressures. Eight of the 67 studies (12%) with echocardiograms showed reduced left ventricular ejection fraction. Five patients (three DM, one CMD and one DMD) had tracheostomy. Among the 73 patients, 14 (1 BMD, 2 CMD, 3 DM, 6 DMD and 2 LGMD) are known to have died, 1 has unknown vital status; the remainder are alive. Among the 14 deaths, the median and average age at death were 21 and 25 years old.

Age and BMI in the patients under study
Based on all 104 studies, patients with DMD and CMD had the youngest median ages (13 and 14 years, respectively); whereas patients with DM, LGMD and BMD had older median ages (22, 23 and 18 years, respectively) (table 2 and online supplemental table 3).

Based on 103 studies (information on BMI was missing for one study), the median BMI z-score for patients with BMD or DMD either approached or exceeded the 90th
percentile (z=1.28) in the general population (table 2). BMI z-score for patients with CMD was below the average z-score (z=0) in the general population in over 75% of the studies. Some patients showed signs of malnourishment at the time of study with BMI z-scores less than −2. Eleven of the 72 patients had at least one study with a BMI z-score greater than 2, indicative of overweight; eight of these were patients with DMD.
Sleep apnoeas and AHI in patients with muscular dystrophy
Fifty-three of the 73 patients (73%) were diagnosed with sleep apnoea (table 3). Four of the five patients with BMD exhibited severe primary OSA.

We examined differences in the prevalence of sleep apnoea among the types by fitting a logistic regression model adjusted for age, sex and three categories of BMI z-score using GEE. Although sleep apnoea prevalence tended to increase with age, the evidence was inconclusive (OR 1.03 per year, 95% CI 0.99 to 1.06; p=0.08). Neither were extremely high BMI z-scores (>2) associated with apnoea compared with scores between −2 and 2 (OR Table 2

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BMI (kg/cm²)
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BMI z-score
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<td>1.53</td>
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*Number of PSG studies.
BMD, Becker muscular dystrophy; BMI, body mass index; CMD, congenital muscular dystrophy; DM, myotonic dystrophy; DMD, Duchenne muscular dystrophy; LGMD, limb-girdle muscular dystrophy; PSG, polysomnography.

Table 3

<table>
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<th>Type</th>
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<tr>
<td>LGMD†</td>
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<td>40</td>
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<tr>
<td>Overall</td>
<td>73</td>
<td>20</td>
<td>27</td>
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</table>

*Percentages use the type-specific total number of patients (column 2) as the denominator. Apnoea percentages may not sum to 100 due to rounding.
†One of 10 patients with LGMD was missing hypoventilation status; thus, the denominator for hypoventilation was 9 for LGMD and 72 overall.
BMD, Becker muscular dystrophy; CMD, congenital muscular dystrophy; DM, myotonic dystrophy; DMD, Duchenne muscular dystrophy; LGMD, limb-girdle muscular dystrophy.

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0.71, 95% CI 0.19 to 2.67; p=0.61); however, extremely low BMI z-scores were associated with lower prevalence of apnoea (OR 0.19, 95% CI 0.04 to 0.91; p=0.04). Female patients had lower prevalence of sleep apnoea (OR 0.41, 95% CI 0.15 to 1.08; p=0.07) compared with male patients, though not significantly. Adjusted estimates of the odds of sleep apnoea differed across muscular dystrophy types with DM exhibiting the highest odds and LGMD the lowest, but estimates were imprecise (online supplemental table 4A). In comparisons among all possible pairs of types, only the OR comparing DM with LGMD was statistically significant after adjustment for multiple testing (OR=5.15, 95% CI 1.47 to 18.0; p=0.003) (online supplemental table 4B).

We also examined differences in mean AHI among muscular dystrophy types by fitting a regression model using GEE, adjusting for age, sex and category of BMI z-score. Based on this model, each 10-year age increase was associated with a slight increase in AHI (1.5 events/hour, 95% CI 0.5 to 2.4; p=0.002). Female patients had about the same AHI on average as male patients (mean difference=−1.3 events/hour, 95% CI −4.5 to 2.3; p=0.52). Although patients with extremely low BMI z-scores (<−2) tended to have lower AHI than the reference group (−2≤ z-score ≤2), the difference was not statistically significant (mean difference=−3.3 events/hour, 95% CI −7.5 to 0.5; p=0.08). For those with extremely high BMI z-scores (>2), mean AHI was similar to the reference group (mean difference=1.1 events/hour, 95% CI −5.5 to 7.7; p=0.74). Mean AHI appeared to differ among muscular dystrophy types. Patients with BMD had the highest observed mean AHI, over 10 events/hour higher than any other type, and patients with CMD and LGMD had the lowest (online supplemental table 3). The same relationship held after adjustment for these covariates, but confidence limits were broad (online supplemental table 5A). In comparisons of all possible pairs of types, only the BMD versus LGMD difference was statistically significant after correction for multiple testing (online supplemental table 5B).

**Hypoventilation in patients with muscular dystrophy**

Among the 104 PSG studies, 54 and 89 had recordings for average end-tidal CO$_2$ (mean 44.3 mm Hg, range 26.4–62.0 mm Hg) and peak end-tidal CO$_2$ (mean 51.7, range 35.2–90 mm Hg) during sleep, respectively (online supplemental table 3). Correlation between age and average CO$_2$ or peak CO$_2$ was small (Spearman correlation coefficient 0.13 and 0.03, respectively). Among the 72 patients with hypoventilation status, 30 (42%) were diagnosed with hypoventilation at least once. Patients with CMD were most likely to be diagnosed with hypoventilation (table 3), consistent with the finding that patients with CMD showed the highest mean end-tidal CO$_2$ levels at baseline and during sleep (online supplemental table 3). Hypoventilation was common in the following types: 57% of CMD, 52% of DMD and 42% of DM. Patients with BMD and LGMD were the least likely to exhibit hypoventilation (table 3); in fact, none of the seven PSG studies on five patients with BMD yielded a diagnosis of hypoventilation.

We examined differences in the prevalence of hypoventilation among muscular dystrophy types by fitting a logistic regression model adjusted for age, sex and three categories of BMI z-score using GEE. The prevalence of hypoventilation was constant with age (OR 1.00 per year, 95% CI 0.98 to 1.03; p=0.86). Those with extreme BMI z-scores (<−2 or >2) had similar prevalence of hypoventilation compared with those with intermediate scores (z-score <−2: OR 0.40, 95% CI 0.06 to 2.79; p=0.35 and z-score >2: OR 1.31, 95% CI 0.54 to 4.97; p=0.69). Adjusted estimates of the odds of hypoventilation differed across muscular dystrophy types with CMD exhibiting the highest odds and LGMD the lowest, but estimates were imprecise (online supplemental table 6A). In comparisons among all possible pairs of types, none of the pairwise differences were statistically significant after adjustment for multiple comparisons (online supplemental table 6B).

**Association of hypoventilation and sleep apnoea or AHI in patients with muscular dystrophy**

We examined the relationship between sleep apnoea and hypoventilation among the 102 studies encompassing 71 patients where both were recorded with BMI available. We considered the association first without adjusting for any covariates and again after simultaneously adjusting for age, sex, three categories of BMI z-score and muscular dystrophy type by fitting logistic models using GEE. Among 68 PSG studies where the patient exhibited sleep apnoea, the patient also exhibited hypoventilation in 28 of them; whereas in the 34 PSG studies where the patient did not have sleep apnoea, only 7 had hypoventilation (GEE unadjusted OR 2.75, 95% CI 1.15 to 6.60; p=0.03). After adjustment for covariates, the association weakened slightly (adjusted OR 2.31, 95% CI 0.92 to 5.81; p=0.08).

We also examined the relationship between AHI and hypoventilation by replacing sleep apnoea with AHI in the GEE logistic model. The odds of hypoventilation were estimated to increase slightly with increasing AHI, but the association was not statistically significant (adjusted OR for a 5 events/hour increase in AHI: 1.02, 95% CI 0.79 to 1.31; p=0.89). A plot of AHI against age with points coded by hyperpnea status and type failed to show a clear relationship of hypoventilation status or type to AHI (figure 1).

**Heart rates in patients with muscular dystrophy**

Mean baseline heart rates were 79, 96, 85, 98 and 84 beats/min (overall mean 90 beats/min) for patients with BMD, CMD, DM, DMD and LGMD, respectively (online supplemental table 3). Likewise, during sleep, the mean heart rates were 67, 90, 77, 93 and 79 beats/min (overall mean 83 beats/min), and mean peak heart rates were 113, 126, 115, 126 and 112 beats/min (overall mean 119 beats/min).
beats/min), respectively. Patients with DMD had significantly higher baseline heart rate and average and peak heart rates during sleep by about 10 beats/min (online supplemental table 7A), than those of patients with DM (p=0.003, p<0.0001 and p=0.02, respectively) (online supplemental table 7B and figure 2). Similarly, patients with CMD had significantly higher baseline heart rate and average and peak heart rates during sleep than those of patients with DM, again with mean differences near 10 beats/min (p=0.03, p<0.0001 and p=0.0006, respectively).

**DISCUSSION**

Our finding is consistent with sleep-disordered breathing being common in patients with muscular dystrophy. Among the five common muscular dystrophy types, sleep apnoea tended to be mild for patients with LGMD and severe for patients with BMD, an observation based on very few subjects of each type. Hypoventilation is also a major concern for patients with muscular dystrophy. Patients with CMD had the highest prevalence of hypoventilation, but it was also common in patients with DMD and DM; patients with LGMD had the lowest prevalence though differences in hypoventilation prevalence among types were not statistically significant. In a recent study of patients with DMD in their early teens, 34 ~34% had hypoventilation; this proportion is somewhat lower than in our patients with DMD. Hypoventilation in patients with muscular dystrophy is usually most severe in rapid eye movement sleep.

Unlike conditions related to skeletal muscle weakness, hypoventilation due to respiratory muscle weakness can be treated with non-invasive ventilation such as bilevel positive airway pressure. Our results support the importance of nocturnal hypoventilation monitoring for patients with muscular dystrophy as part of disease management, because of the high prevalence of hypoventilation and progressive nature of the diseases in patients with muscular dystrophy. Non-invasive mechanical ventilation can be a valuable modality for patients with muscular dystrophy for more favourable outcomes and better survival.

Our analysis also revealed that sleep apnoeic events and hypoventilation events in patients with muscular dystrophy were mildly associated, though of borderline statistical significance. This finding has important clinical implications. Unlike obese hypoventilation, which is strongly associated with OSA, hypoventilation in patients with muscular dystrophy is only marginally associated with OSA. Thus, for patients with muscular dystrophy, treating OSA may not provide equal relief for hypoventilation and vice versa; both conditions may need to be managed concomitantly. Hypoventilation commonly occurs alongside sleep apnoea especially for those with obesity. Chronic hypoventilation in patients with muscular dystrophy is likely related to the underlying aetiology of the disease rather than to other conditions such as obesity, though we did see a tendency toward higher prevalence of hypoventilation among the most obese patients. Chronic weakening of respiratory muscles including diaphragm in patients with muscular dystrophy is likely the major contributor of hypoventilation in those patients. Monitoring and diagnosing early muscle weakness in those patients are important for appropriate early intervention. Once sleep-disordered breathing has developed, both sleep apnoeas and hypoventilation may need to be monitored and managed alongside.

Consistent with our findings, patients with CMD and DMD had high heart rate during sleep. For patients...
with muscular dystrophy, routine cardiology follow-up for the risk of cardiomyopathy and early pharmacological intervention may be needed especially for those with DMD and CMD.

Lastly, not all types of muscular dystrophy have the same degree and characteristics of sleep-disordered breathing or the same clinical manifestations. Specific attention should be paid to each type. For instance, patients with CMD tend to have severe muscle weakness. As a result, those patients had the lowest average BMI z-scores and the highest risk of hypoventilation compared with patients with other types. Mean AHI appeared to differ among muscular dystrophy types. DM had statistically significant higher odds of sleep apnoea compared with LGMD. Patients with BMD exhibited the severest primary OSA compared with all other types. Hypoventilation was common in the following types: 57% of CMD, 52% of DMD and 42% of DM. Patients with DMD had significantly, or nearly significantly, higher baseline heart rate and average and peak heart rates during sleep than those of patients with DM. Similarly, patients with CMD had significantly higher average and peak heart rates during sleep than those of patients with DM.

This study has several limitations. Despite having one of the largest collections of diagnostic PSG studies of patients with muscular dystrophy ever reported, our small sample size limited our ability to probe associations; consequently, CIs were wide and statistical power was restricted. BMD, CMD and LGMD had especially small samples. Our sample size was too small to probe some questions of interest such as whether the association of hypoventilation and sleep apnoea differed among the types. Further, our tertiary data collection may skew our sample of patients toward the more severe spectrum; how well the patients in our study represent the disease population is difficult to assess. Our analysis included PSG studies spanning 17 years during which different PSG technologies and scoring criteria were used. The changes in scoring criteria during the study period may have influenced scoring of hypopnoea events. We did not attempt to rescore all original studies using a single scoring criterion. Our analysis also did not consider medication use and other potential clinical confounders.

CONCLUSIONS
Sleep-disordered breathing is common among the patients with muscular dystrophy. Not all types of muscular dystrophy have the same degree and characteristics of sleep-disordered breathing or the same clinical manifestations. Specific attention should be paid to each type. Patients with DM had the highest odds of sleep apnoea, significantly higher than patients with LGMD who had the lowest odds. Patients with DMD had the highest proportion with moderate to severe OSA. Patients with CMD had the highest odds of hypoventilation followed by DMD. Hypoventilation was mildly associated with sleep apnoea after adjusting for age, sex, BMI and type, although the statistical significance of the association was borderline. Thus, CO₂ retention may be an independent process from upper airway obstructive breathing. Early diagnosis of muscle weakness is critical for early intervention with non-invasive ventilation and will have a positive effect on the quality of care of a patient with muscular dystrophy and, thus, life expectancy.46

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Contributors ZJF identified the research question. ZJF, LL and DMU were responsible for the study design and research protocol, and for drafting the manuscript. DMU, MS, LL and MA were responsible for the statistical analysis. LL, DSCY, YL and ZJF were responsible for data collection. PH, BV and ZJF were the clinicians on this project. All other authors contributed to writing, reviewing and editing the manuscript. ZJF is the guarantor for this paper, accepts full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish.

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Data availability statement Data are available upon reasonable request. The data used in this study are stored on a secure drive at the National Institute of Environmental Health Sciences (NIH). All requests for data sharing will be considered on an individual basis and data will be made available to facilitate replication of the results.

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