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Original Article

Yearly motor function changes in patients with Duchenne muscular dystrophy, including a COVID-19 behavioral restriction period

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Abstract. [Purpose] This study aimed to assess the motor function status of ambulatory patients with Duchenne muscular dystrophy in 2020, which included a 3-month period of behavioral restriction due to the coronavirus disease of 2019 (COVID-19) pandemic, in comparison to the previous 2 years. [Participants and Methods] A retrospective analysis was conducted on 12 patients (children with mean age: 9.58 ± 3.43 years in 2020). Parameters such as lower leg maximum circumference, 10-m running time, rising-from-the-floor time, ankle joint range-of-motion, 6-min walk distance, and North Star Ambulatory Assessment score were evaluated. [Results] Significant increases in the maximum right thigh circumference and prolonged 10-m running time were observed in 2020. Interestingly, an unexpected improvement in ankle dorsiflexion angle was noted in both ankles. No other statistically significant differences were observed among the assessed time points. [Conclusion] These findings highlight the critical importance of continuous exercise and rehabilitation for ambulatory children with Duchenne muscular dystrophy, emphasizing the potential of rehabilitation to mitigate and restore the transient motor function deterioration observed during periods of behavioral restrictions.

Key words: Duchenne muscular dystrophy, Motor function, Coronavirus disease of 2019 (COVID-19)

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INTRODUCTION

The Japanese government's mandated closure of schools and public institutions in response to the coronavirus disease 2019 (COVID-19) pandemic forced many patients to stay at home during a nearly three-month restriction on activities from April to June 2020. Patients with Duchenne muscular dystrophy (DMD) are at a particularly high risk of immunosuppression due to the long-term use of corticosteroids, which may result in difficulty managing major airway complications and cardiac dysfunction brought on by COVID-19. Moreover, concerns exist on an elevated risk of serious multiorgan complications secondary to COVID-19 infection[1)]. Prevention has therefore become particularly important in this population, incorporating measures to minimize social contact. However, this has resulted in many patients becoming inactive and suffering corresponding drops in motor function[2)]. In our previous study comparing motor function before and after three months of behavioral restrictions, we observed a significant decrease in ankle dorsiflexion range of motion (ROM)[3)].

The present investigation examined the yearly effects of temporary behavioral restrictions in patients with DMD by comparing the changes in motor function during one year in 2020, which included the period of Japanese COVID-19-related behavioral restrictions, with the degrees of change in 2019 and 2018. Such evaluations may help identify what measures should be taken as rehabilitation in the future when patients are forced to restrict their living behaviors.

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PARTICIPANTS AND METHODS

This was a retrospective observational study for the evaluation period from April 2018 to March 2021 that was conducted in the Rehabilitation Department at Shinshu University Hospital.

We enrolled 12 outpatients with ambulatory DMD aged 3–14 years (mean ± standard deviation: 9.58 ± 3.43 years; 2 preschoolers, 8 elementary school students, and 2 middle school students) who were still undergoing rehabilitation at our hospital as of April 2020. We examined the physical characteristics (height, weight, and body mass index [BMI]) and motor function parameters (maximum circumference of both lower legs, 10-meter running time, rising from the floor time, dorsiflexion ROM of both ankles, 6-minute walking distance, and North Star Ambulatory Assessment [NSAA] score) of all participants at each time point.

Motor function data were extracted from medical records from (1) April 2018, (2) March 2019, (3) April 2019, (4) March 2020, (5) April 2020, and (6) March 2021. The changes measured in (1) and (2), (3) and (4), and (5) and (6) were compared over the three periods for each motor function item as the changes in 2018, 2019, and 2020, respectively. The government-mandated period of behavioral restrictions was from April to June 2020. Since no behavioral restrictions were in place in 2018 and 2019, the changes identified in those periods were considered the natural progress of the disease.

This study was approved by the Institutional Ethical Review Board (approval number: 4790) of Shinshu University.

Repeated-measures analysis of variance was used for parametric data, and the Friedman test was used for non-parametric data. As significant differences in height, BMI, maximum circumference of the right lower leg, 10-meter running time, and ROM were present, Bonferroni's multiple comparison test was used as a post-hoc test. The significance level was set at $p<0.05$. All statistical analyses were performed using SPSS version 27 (IBM Corp., Armonk, NY, USA).

RESULTS

Of the 12 patients enrolled, one 3-year-old child did not receive steroid therapy. The height and BMI values of the participants in April of each year were all statistically comparable (all $p<0.001$) (Table 1).

Regarding motor function, right leg circumference had significantly increased in 2020 as compared with 2018 ($p=0.03$, Table 2), while 10-meter running time was significantly slower in 2020 than in 2019 ($p=0.03$, Table 2). Unexpectedly, bilateral ankle dorsiflexion ROM had increased significantly in 2020 versus 2018 (right: $p=0.03$, left: $p=0.02$, Table 2). No significant differences were identified for rising from the floor time (Table 2), 6-minute walking distance, or NSAA score (Table 2).

DISCUSSION

This study investigated the yearly changes in motor function of DMD patients including a period containing government-mandated behavioral restrictions due to COVID-19. We observed significantly larger right lower leg circumference and slower 10-meter running time in 2020, whereas bilateral ankle dorsiflexion angle was significantly wider. No significant changes were observed for other motor function endpoints. A negative correlation has been reported between rising from the floor time and 6-minute walking distance, with a rise time between 10 and 30 seconds being associated with a high risk of walking ability loss within the following two years[4]. Such a result can also be used as an indicator of gait maintenance. The absence of any significant difference in rising from the floor time showed that our cohort had maintained its gait ability. This confirms that no significant difference in the 6-minute walking distance was present and simultaneously supports the report that there is a negative correlation between the rise time from the floor and the 6-minute walking distance[5].

The maximum circumference of the right lower leg was significantly increased in 2020 as compared with 2018, suggesting the progression of pseudohypertrophy, although this could not be clearly distinguished from spontaneous progression. Since the participants ranged in age from 6 to 14 years, the increase in maximum lower leg circumference might have been due to growth, which could be considered a confounding factor. We observed the tendency for a larger maximum circumference in the right leg throughout the study. This may be attributed to it being the patient's dominant foot; only one patient was left-handed. Although it is also important to consider the influence of the pivot foot, neither the patients nor their guardians

Table 1. Physical characteristics of study participants (n=12)

	April 2018	April 2019	April 2020	Comparison of 3 groups
Height (cm)	117.8 ± 12.8	118.8 ± 15.2	123.3 ± 14.6	a
BMI (kg/m^2)	19.3 ± 3.3	20.5 ± 4.0	22.0 ± 4.8	b

Values are expressed as the mean ± standard deviation.
a, b: $p<0.001$ (repeated-measures analysis of variance).
BMI: body mass index.

Table 2. Comparison of the amount of change in each motor function assessment parameter

Parameter	April 2018	April 2019	April 2020	Comparison of 3 groups
Maximum circumference of the lower leg: Right side (cm)	0.1 ± 0.37	0.60 ± 0.97	1.20 ± 1.23	c
Maximum circumference of the lower leg: Left side (cm)	1.80 ± 1.41	0.50 ± 1.33	1.70 ± 1.09	
10-meter running time (sec)	0.66 ± 0.65	0.45 ± 1.18	−0.07 ± 4.34	d
Rising from the floor time (sec)	4.05 ± 8.4	1.68 ± 3.2	1.43 ± 8.0	
Ankle joint dorsiflexion angle: Right side (degrees)	−5.83 ± 4.49	−0.83 ± 4.49	0.00 ± 7.91	e
Ankle joint dorsiflexion angle: Left side (degrees)	−6.25 ± 4.62	−0.42 ± 4.32	−0.83 ± 7.86	f
6-minute walking distance (m)	22.6 ± 48.6	−31.6 ± 83.4	−41.5 ± 40.5	
NSAA score	−2.9 ± 6.19	−1.8 ± 2.04	−3.5 ± 3.58	

Values are expressed as the mean ± standard deviation.
c: p=0.03 (repeated-measures analysis of variance from 2018 to 2020).
d: p=0.03 (repeated-measures analysis of variance from 2019 to 2020).
e: p=0.03 (repeated-measures analysis of variance from 2018 to 2020).
f: p=0.02 (repeated-measures analysis of variance from 2018 to 2020).
NSAA: North Star Ambulatory Assessment.

were able to express which foot was the pivot foot. The 10-meter running time was significantly slower in 2020 than in 2019. This parameter did not differ significantly between 2018 and 2019, suggesting a stronger progression of symptoms in 2020. Indeed, it appears the continuation of normal exercise at the level of daily living is essential. A 30-foot running time is reportedly useful for predicting DMD prognosis until the patient becomes unable to walk[6], and may be suitable as a guide for maintaining motor function even during behavioral limitations. To ensure opportunities for continued exercise and evaluation of 10-meter running time in all situations, telerehabilitation systems will be required. Specifically, for family members who have devices such as smartphones and tablets, it is possible to use them to conduct online conferences. For family members without access to an online conferencing system, physiotherapists can also provide care via the telephone.

Unexpectedly, bilateral ankle dorsiflexion ROM was significantly improved in 2020 over 2018. In our previous study of the same participants in 2020, which compared changes in motor function immediately before and after behavioral restrictions from April to June, ankle dorsiflexion angle was 3.8- to 4.5-fold worse after restrictions compared with natural history[4]. Ankle joints naturally stiffen by 0.4° per month in DMD without treatment[7]. Considering these factors, the three-month restriction in the early 2020 period could have been an exceptional situation with extremely low physical activity. In the same previous study, despite 90% of parents reporting stretching at home during the relevant period, the patients' ankle contractures worsened. Even after the movement restrictions were lifted, the patients voluntarily refrained from going out, although rehabilitation was resumed at the same frequency as before the COVID-19 outbreak. Thus, resuming rehabilitation might be one of the factors that contributed to improvements in joint ROM in this study. We routinely teach all patients stretching and have a night splint made at the age 4 or 5 years as several reports have shown that such devices maintain ankle joint angles[8–10]. We presumed these measures also exerted a positive influence. Although a previous study[4] suggested that a limitation of physical activity due to behavioral restrictions might adversely affect joint ROM more quickly than gross motor function, joint ROM in our investigation could have deteriorated temporarily, but then returned to a previous state once the patient was freed from extreme behavioral limitations and became able to resume rehabilitation.

However, this result does not imply that all patients showed improvement. ROM gradually improved from 2018 to 2020, which might have been partly because younger patients were more active than older ones during the study period as they started steroid regimens[11, 12] and wearing night splints[8], and partly because patients who were unable to walk were excluded from this study. In addition, the frequency of rehabilitation visits varied from patient to patient. We additionally compared the amount of change in all items in a high-frequency group of 6 patients who received rehabilitation at least once every 2 months with a low-frequency group of 6 patients who received rehabilitation less than once every 3 months. Although there was a significant difference in the change of NSAA score within 2020 (p=0.01; unpaired t-test), no significant differences in the other items were seen for any time (data not shown). Hence, differences in the frequency of rehabilitation appeared not to influence the results.

Although the strengths of our study included the fact that the same assessments were conducted by the same rater over an extended period of time prior to behavioral restrictions, this report had several limitations. Strictly speaking, the reasons for the year-to-year improvement in ankle dorsiflexion angle and the causes for recovery from temporary deterioration should be considered different; however, our data do not allow a clear distinction. Another limitation was a small sample size. Our preliminary findings require confirmation in larger, independent cohorts.

Based on a 3 year history including the period of Japanese government-imposed behavioral restrictions due to the COVID-19 pandemic, 3 months of behavioral restrictions appeared to have significant detrimental effects on maximum lower leg circumference and 10-meter running time. In the meantime, ankle ROM exhibited recovery to a previous state after temporary deterioration. This study suggests that transient ROM declines may be slightly ameliorated by a subsequent

return to physical activity, especially the reinitiation of rehabilitation. Our results highlight that ongoing rehabilitation and opportunities for exercise are important to slow the progression of symptoms in ambulatory DMD patients.

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Conflict of interest

None of the authors have any conflict of interest to disclose.

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