Periodic sound-based 6-minute walk test for patients with Duchenne muscular dystrophy: a preliminary study

Hitomi Nishizawa, RPT, MS\textsuperscript{1}, Hirokazu Genno, PhD\textsuperscript{2}, Naoko Shiba, MD\textsuperscript{3}, Akinori Nakamura, MD, PhD\textsuperscript{4}\textsuperscript{*}

\textsuperscript{1} School of Health Sciences, Faculty of Medicine, Shinshu University, Japan
\textsuperscript{2} Corporate Planning, Kissei Comtec Co., Ltd., Japan
\textsuperscript{3} Department of Pediatrics, Shinshu University School of Medicine, Japan
\textsuperscript{4} Intractable Disease Care Center, Shinshu University Hospital: 3-1-1 Asahi, Matsumoto 390-8621, Japan

Abstract. [Purpose] The purpose of this study was to verify if a periodic sound-based 6-minute walk test with the best periodic sound could be used to evaluate physical endurance more precisely than the conventional 6-minute walk test. [Subjects] The subjects were healthy subjects and 6 ambulant patients with Duchenne muscular dystrophy. [Methods] The subjects initially walked for 1 minute to a long-interval metronome sound, and the walking distance was measured. The sound interval was then gradually shortened, and the subjects walked for 1 minute for each of the intervals. The best periodic sound was considered to be the periodic sound used when the subject walked the longest distance in 1 minute, and the process of determining it was referred to as the period shortening walk test. This study administered the 6-minute walk test with the best periodic sound to twenty healthy subjects and 6 ambulant patients with Duchenne muscular dystrophy and compared the walking distance. [Results] The periodic sound-based 6-minute walk test distances in both the healthy subjects and the patients were significantly longer than the conventional 6-minute walk test distances. [Conclusion] The periodic sound-based 6-minute walk test provided a better indication of ambulatory potential in an evaluation of physical endurance than the conventional 6-minute walk test.

Key words: 6-Minute walk test, Best periodic sound, Period shortening walk test

INTRODUCTION

The 6-minute walk test (6MWT) was developed to measure cardiorespiratory function and endurance by assessing the maximum distance that a subject is able to walk in 6 minutes (6-minute walking distance, 6MWD)\textsuperscript{1}. The American Thoracic Society (ATS) has proposed guidelines for safe and accurate performance of the 6MWT, which has demonstrated high accuracy and reproducibility in the evaluation of endurance in patients with cardiorespiratory disorders\textsuperscript{1}. Today, it is used for evaluation of physical endurance in the clinical field of physical therapy\textsuperscript{2–4}. The 6MWT has been reported to be useful for determining the ambulatory capacity of patients with Duchenne muscular dystrophy (DMD)\textsuperscript{5, 6} and for evaluating the natural progression of the disease\textsuperscript{5, 8}. It has also been used in the evaluation of therapeutic efficacy in patients with neuromuscular diseases such as Pompe disease, myotonic dystrophy, and mucopolysaccharidosis\textsuperscript{9–15}. The conventional 6MWT (C6MWT) can be used for patients ≤12 years of age, especially in patients with DMD\textsuperscript{8}, and DMD is often associated with autism or mental retardation\textsuperscript{17, 18}; it is therefore difficult for these patients to follow instructions and accurately perform the 6MWT. The ATS guidelines for the 6MWT simply state the following: “The object of this test is to walk as far as possible for 6 minutes.” However, the ATS guidelines do not provide specific instructions for patients with DMD in regard to stopping or running during the test\textsuperscript{5, 19, 20}. Few studies have addressed the accuracy of 6MWT performance in patients with DMD. Therefore, this study attempted to develop a periodic sound-based 6MWT (PS6MWT) that is appropriate for assessing physical endurance in patients with DMD.

A longer walking distance covered in 6 minutes requires a longer stride or a faster cadence. Controlling the stride length is generally difficult, but cadence can be easily adjusted by walking to match a sound. Therefore, a longer 6-minute walking distance might be achieved by adjusting the cadence to as fast as possible. The threshold limit for the cadence may differ among patients, and it is uncertain
whether the walking distance at the fastest cadence would be the maximal distance, without controlling the stride length. Therefore, the best periodic sound (BPS) was determined as the periodic sound when the subjects walked the longest distance in 1 minute.

The purpose of this study was to verify whether the PS6MWT can evaluate physical endurance in patients with DMD more precisely than the C6MWT. This study confirmed the efficacy and safety of the protocol in healthy adult subjects and patients with DMD.

SUBJECTS AND METHODS

Twenty randomly selected healthy males aged 20–26 years were recruited from the School of Health Sciences, Faculty of Medicine, Shinshu University, and 6 ambulant patients with DMD, aged 5–8 years, were recruited from Shinshu University Hospital. None of the selected patients had cardiovascular or respiratory disease. The physical characteristics of the healthy subjects are presented in Table 1, and the clinical profiles of the 6 patients with DMD are presented in Table 2. This study was approved by the institutional ethics committee of the Shinshu University School of Medicine, Japan (approval numbers: healthy subjects, 2,761; patients with DMD, 2,340). The aim and method of this study were explained to all subjects and/or parents, and consent was obtained based on the Declaration of Helsinki.

All tasks were administered by 2 examiners, and one of the examiners followed the patients down the hall. The healthy subjects initially walked for 1 minute to a 110 steps/minute sound rate of a metronome, and the distance was measured. The sound interval was then gradually shortened to yield 120 steps/minute, 130 steps/minute, and up to 180 steps/minute, and each walking distance was measured for 1 minute. Patients with DMD initially walked for 1 minute to the sound rate obtained by rounding off and subtracting 20 steps/minute from the average value of the cadence in the C6MWT. The sound interval was then gradually shortened by 10 steps/minute, and each walking distance was measured for 1 minute. The rest time between the tests was 1 minute, and the measurements were continued until the walking distance was noted to show no increase. The BPS was determined as the periodic sound when the subjects demonstrated the maximum walking distance; this method was named the period shortening walk test (PSWT). A flowchart of the PSWT is presented in Fig. 1A.

In the 6MWT, the subjects walked around 2 cones, which marked the path and were 25 m apart, in the counterclockwise direction. The total walking distance was calculated based on the number of round trips and a ruler set up between

---

Table 1. Physical characteristics of the healthy adult subjects

| n | Group A | Group B | Group A vs Group B |
|---|---------|---------|--------------------|
| 10 | 10 | – |
| Age (years) | 21.9 ± 3.8 | 22.5 ± 2.1 | a |
| Height (cm) | 169.9 ± 4.2 | 172.3 ± 3.2 | b |
| Body weight (kg) | 62.5 ± 4.2 | 69.8 ± 14.5 | a |
| BMI (kg/m²) | 21.6 ± 1.1 | 23.5 ± 4.8 | a |

BMI: body mass index, a Mann-Whitney U test, b Unpaired Student’s t-test.

Table 2. Physical characteristics of the patients with Duchenne muscular dystrophy

| Patient No. | 1 | 2 | 3 | 4 | 5 | 6 |
|-------------|---|---|---|---|---|---|
| Gender      | Male | Male | Male | Male | Male | Male |
| Age (years) | 6 | 5 | 7 | 5 | 4 | 8 |
| Weight (kg) | 17 | 17 | 26 | 16 | 19 | 23 |
| BMD (kg/m²) | 14.0 | 15.1 | 20.4 | 15.2 | 16.6 | 20.1 |
| Gene mutation | DMD del. exons 25-55 | DMD nonsense mutation in exon 21 | DMD nonsense mutation in exon 48 | DMD nonsense mutation in exon 17-19 | DMD del. exons 17-19 | DMD nonsense mutation in exon 44 |
| Serum CK (U/L) | 31,350 | 24,030 | 21,630 | 14,790 | 18,970 | 13,611 |
| Walk alone (months) | 15 | 14 | 18 | 28 | 17 | 21 |
| Developmental disorder | BIQ | BIQ | BIQ, ASD | - | N/A | BIQ, ASD |
| Drug/duration (months) | – | – | Prednisolone / 4 | – | – | – |
| 10 m running (sec) | 3.9 | 4.4 | 2.8 | 4.9 | 5.3 | 4.2 |
| Rising from the floor (sec) | 5.7 | 4.2 | 1.6 | 4.0 | 4.8 | 4.7 |
| NSAA (score) | 27 | 28 | 33 | 25 | 20 | 24 |

BMI: body mass index; DMD: Duchenne muscular dystrophy; del.: deletion; N/A: not applicable; CK: creatine kinase; BIQ: borderline IQ; ASD: autistic spectrum disorder; NSAA: North Star ambulatory assessment.
Healthy adults were allocated randomly into two groups (Group A and B), and all patients with DMD were allocated into the Group A. PSWT: period shortening walk test; DMD: Duchenne muscular dystrophy; PS6MWT: periodic sound-based 6-minute walk test; C6MWT: conventional 6-minute walk test; BPS: best periodic sound.

Ten healthy adult subjects were randomly allocated to each of the 2 groups (group A or B). There were no differences in age, height, body weight, and body mass index (BMI) between the 2 groups (Table 1). The task order in group A was (1) C6MWT, (2) PSWT, and (3) PS6MWT; in group B, the order was (1) PSWT, (2) PS6MWT, and (3) C6MWT. The interval between tasks was 20–30 minutes for healthy subjects. In patients with DMD, the task order in group A was (1) C6MWT, (2) PSWT, and (3) PS6MWT. The interval between the tasks was 2–4 weeks. The allocation of subjects is presented in Fig. 1B.

Further, in each task, a monitor (RCX5, Polar Electro, Finland) was used to measure heart rate at 1 Hz, the number of steps (steps/min) was measured, and a 3-axis accelerometer (JD Mate, Kissei Comtec, Matsumoto, Japan) was used to measure energy expenditure (EE) at 1 Hz; these measurements were performed continuously. Before and after tasks, systolic and diastolic blood pressure (SBP and DBP, respectively) were measured with a hemodynamometer (H55, Terumo, Tokyo, Japan), and the oxygen saturation (SpO2) was measured with a pulse oximeter (BO-650, Japan Precision Instruments, Shibukawa, Japan). The degree of fatigue was also assessed with the Borg CR10 scale, but only in healthy subjects21, 22. The sound was generated by a metronome (ME-110, Yamaha Corporation, Hamamatsu, Japan).

The variance of normality of the data was tested by the Shapiro-Wilk test. Comparison between the 2 groups was performed using the unpaired Student t-test or Mann-Whitney U-test for non-repeated measures and using the paired Student t-test or Wilcoxon signed-rank test for repeated measures. In the comparison among 3 or more-sample designs, one-way analysis of variance (ANOVA) or Friedman test was used in the case of 1 factor, and two-way ANOVA was used in 2 factors. In multiple comparisons, as a post hoc test, Bonferroni correction or the Wilcoxon signed-rank test was used, as appropriate. Correlation between the 2 groups was examined using the Pearson product-moment correlation coefficient. Results were expressed as means ± standard deviation (SD). Statistical significance was set at p < 0.05.

All analyses were conducted using the PASW Statistics software (version 18.0, SPSS, Inc., Chicago, IL, USA).

RESULTS

In healthy adult subjects, the SBP, maximum heart rate (HRmax), and CR10 score showed significant interaction effects between the evaluated points (pre vs. post) and tests (C6MWT vs. PS6MWT) (Table 3). The EE and number of steps were significantly different between the C6MWT and PS6MWT. A significant difference in the 6MWD was obtained between the C6MWT (665.1 ± 73.8 m) and PS6MWT (791.3 ± 61.3 m) (p < 0.001) (Table 3). The HRmax for the PS6MWT was significantly higher than that for the C6MWT (p < 0.001), and the HRmax for the PSWT was significantly higher than that for the C6MWT (p < 0.01) and lower than that for the PS6MWT (p < 0.001). The SBP, DBP, HRmax, and CR10 score after the PSWT were significantly higher than those before the PSWT (p < 0.001) (Table 4). The 1-minute walking distance in the PS6MWT was significantly longer than that in the C6MWT (p < 0.001). The distance covered in the first minute was significantly longer than that in the second (p < 0.001) and third minutes (p < 0.01) (Fig. 2). Among the walking distances for each sound interval in the PSWT, the 1-minute distance at ‘free’ speed (no sound) was significantly shorter than that with the BPS (Fig. 3A). The distance with the BPS was significantly longer than those of the sound rates with −20, −10, and +10 steps/min compared with the BPS. The number of steps at each sound interval in the PSWT was increased until it reached +10 steps/minute compared with the BPS (Fig. 3B). The results also indicated that the 1-min walking distance with the BPS in the PSWT was significantly correlated with the 6MWD in the PS6MWT (r = 0.738, p < 0.001) but not with that in the C6MWT (Fig. 4).

In the results of the patients with DMD, the 6MWD in
Table 3. Changes in clinical parameters between before (pre) and after (post) the C6MWT and PS6MWT in the healthy adult subjects

|                  | C6MWT       | PS6MWT      |
|------------------|-------------|-------------|
|                  | Pre         | Post        | Pre         | Post        | Pre vs. Post | C6MWT vs. PS6MWT | Interaction |
| SBP (mmHg)       | 122.7 ± 9.8 | 135.0 ± 13.5| 122.9 ± 13.0| 146.8 ± 13.4| ***a         | ***a            | ***a        |
| DBP (mmHg)       | 74.6 ± 9.1  | 79.1 ± 9.3  | 76.2 ± 11.1 | 83.2 ± 8.7  | b            | ***b           | b           |
| SpO2 (%)         | 98.0 ± 0.6  | 97.9 ± 0.3  | 98.3 ± 0.5  | 98.0 ± 0.6  | b            | b             | b           |
| HRmax (bpm)      | 79.7 ± 10.9c| 133.5 ± 25.1d| 78.4 ± 14.6d| 161.9 ± 24.3d| ***a         | ***a           | ***a        |
| CR10             | 0.2 ± 0.4   | 3.1 ± 1.4   | 0.2 ± 0.3   | 5.8 ± 1.4   | ***b         | ***b           | ***b        |
| EE (kcal/kg/min) | 120.1 ± 17.4d| 147.7 ± 10.8d| 0.105 ± 0.017d| 0.130 ± 0.020d| ***c         | ***c           | ***c        |
| Distance (m)     | 665.1 ± 73.8d| 791.3 ± 61.3d| 0.105 ± 0.017d| 0.130 ± 0.020d| ***c         | ***c           | ***c        |
| Number of steps (steps/min) | 120.1 ± 17.4d| 147.7 ± 10.8d| 0.105 ± 0.017d| 0.130 ± 0.020d| ***c         | ***c           | ***c        |

***p<0.001. a ANOVA. b ANOVA (no normality). c Measured before the C6MWT or PS6MWT while sitting on a chair. d Measured during the C6MWT or PS6MWT. e Wilcoxon signed-rank test. C6MWT: conventional 6-minute walk test; PS6MWT: periodic sound-based 6-minute walk test; SBP: systolic blood pressure; DBP: diastolic blood pressure; SpO2: oxygen saturation; HRmax: maximum heart rate; CR10: Borg CR10 Scale; EE: energy expenditure

Table 4. Changes in clinical parameters between before (pre) and after (post) the PSWT in the healthy adult subjects

|                  | Pre         | Post        |
|------------------|-------------|-------------|
|                  | SBP (mmHg)  | Post        |
|                  | 120.3 ± 12.0| 141.4 ± 13.2|
|                  | DBP (mmHg)  | Post        |
|                  | 72.9 ± 9.5  | 83.3 ± 10.6 |
|                  | SpO2 (%)    | Post        |
|                  | 97.9 ± 0.5  | 98.2 ± 0.6  |
|                  | HRmax (bpm) | Post        |
|                  | 75.9 ± 14.1c| 148.2 ± 24.4d|
|                  | CR10        | 0.1 ± 0.2   |

***p<0.001. a Paired Student’s t-test. b Wilcoxon signed-rank test. c Measured before the PSWT while sitting on a chair. d Measured during the PSWT. PSWT: period shortening walk test; SBP: systolic blood pressure; DBP: diastolic blood pressure; SpO2: oxygen saturation; HRmax: maximum heart rate; CR10: Borg CR10 Scale

Table 5. Changes in clinical parameters between before (pre) and after (post) the C6MWT and PS6MWT in the patients with Duchenne muscular dystrophy

|                  | C6MWT       | PS6MWT      |
|------------------|-------------|-------------|
|                  | Pre         | Post        | Pre         | Post        | Pre vs. Post | C6MWT vs. PS6MWT | Interaction |
| SBP (mmHg)       | 101.7 ± 14.4| 98.6 ± 15.7 | 84.4 ± 15.4 | 97.1 ± 14.3 | d            | d              | d           |
| DBP (mmHg)       | 61.3 ± 8.0  | 64.3 ± 14.2 | 55.7 ± 10.2 | 56.5 ± 5.8  | d            | d              | d           |
| SpO2 (%)         | 98.5 ± 0.5  | 98.8 ± 0.4  | 98.7 ± 0.5  | 98.3 ± 0.5  | a            | a              | a           |
| HRmax (bpm)      | 98.6 ± 11.5b| 144.5 ± 11.0c| 96.7 ± 12.3b| 149.7 ± 10.3b| ***d         | d              | d           |
| EE (kcal/kg/min) | 0.100 ± 0.013c| 0.116 ± 0.020c| 0.116 ± 0.020c| 0.116 ± 0.020c| e            | e              | e           |
| Distance (m)     | 386.2 ± 33.4c| 427.4 ± 32.5c| 427.4 ± 32.5c| 427.4 ± 32.5c| ***c         | ***c           | ***c        |
| Number of steps (steps/min) | 143.2 ± 10.6d| 151.0 ± 10.6d| 151.0 ± 10.6d| 151.0 ± 10.6d| e            | e              | e           |

***p<0.001; **p<0.01; *p<0.05. a ANOVA. b ANOVA (no normality). c Measured before the C6MWT or PS6MWT while sitting on a chair. d Measured during the C6MWT or PS6MWT. e ANOVA. f Paired Student’s t-test. C6MWT: conventional 6-minute walk test; PS6MWT: periodic sound-based 6-minute walk test; SBP: systolic blood pressure; DBP: diastolic blood pressure; SpO2: oxygen saturation; HRmax: maximum heart rate; EE: energy expenditure
the PS6MWT (427.4 ± 32.5 m) was significantly longer than that in the C6MWT (386.2 ± 33.4 m) (p < 0.01). The HRmax after the PSWT was significantly increased compared with that before the PSWT (p < 0.01) (Table 6). The 1-min walking distance in the PS6MWT was significantly longer than that in the C6MWT (p < 0.001). The correlation analysis was performed using the Pearson product-moment correlation coefficient. C6MWT: 6-minute walk test; PS6MWT: periodic sound-based 6-minute walk test; BPS: best periodic sound.

**DISCUSSION**

Among the healthy controls, it was found that the 6MWD in the PS6MWT was significantly longer than that in the C6MWT. The 6MWD in the C6MWT was influenced by age, height, weight, and gender. Therefore, subjects with similar physical characteristics were selected. Previous studies reported 6MWD values for the 6MWT in healthy adults of 670.1 m and 654.7 m; the walking distances were comparable to the data for the C6MWT in the present study (Table 3). The PS6MWT was also safe to administer, with no subjects falling or stopping exercise.

The SBP, HRmax, and CR10 score showed significant interactions between the evaluated points and tests, suggesting that the physical load in the PS6MWT was greater than that in the C6MWT. The results showed a highly positive correlation between the 1-min walking distance with the BPS in the PSWT and the 6MWD in the PS6MWT. Because HRmax was significantly lower during the PSWT than during the PS6MWT, the PSWT could be conducted at a lower physical load and may be available for clinical use.

**Table 6.** Changes in clinical parameters between before (pre) and after (post) the PSWT in the patients with Duchenne muscular dystrophy

| Pre       | Post     | Pre vs. Post |
|-----------|----------|--------------|
| SBP (mmHg)| 101.0 ± 14.5 | 99.3 ± 11.3  |
| DBP (mmHg)| 62.9 ± 16.6  | 62.1 ± 13.7  |
| SpO2 (%)  | 98.2 ± 0.7   | 98.5 ± 0.8   |
| HRmax (bpm)| 111.0 ± 8.0 | 149.8 ± 10.9 |

*Measured before the PSWT sitting on a chair. **Measured during the PSWT. SBP: systolic blood pressure; DBP: diastolic blood pressure; SpO2: oxygen saturation; HRmax: maximum heart rate.

Subjects have been reported to be influenced by age, height, weight, and gender. Therefore, subjects with similar physical characteristics were selected. Previous studies reported 6MWD values for the 6MWT in healthy adults of 670.1 m and 654.7 m; the walking distances were comparable to the data for the C6MWT in the present study (Table 3). The PS6MWT was also safe to administer, with no subjects falling or stopping exercise.

The SBP, HRmax, and CR10 score showed a significant interaction between the evaluated points and tests, suggesting that the physical load in the PS6MWT was greater than that in the C6MWT. The results also indicated a highly positive correlation between the 1-min walking distance with the BPS in the PSWT and the 6MWD in the PS6MWT. Because HRmax was significantly lower during the PSWT than during the PS6MWT, the PSWT could be conducted at a lower physical load and may be available for clinical use.
evaluation of physical endurance.

Next, the same experiment was performed in 6 patients with DMD. The results showed that the 6MWD in the PS6MWT was significantly longer than that in the C6MWT (Table 5). It has been reported that a decrease of motivation or concentration can affect the 6MWT performance in children with DMD(20). Several studies have reported that some patients were unable or unwilling to complete the 6MWT, even with permitted rest periods(20, 26, 27). The 2-minute walk test (2MWT) has been recommended for healthy adults, healthy children, and cardiac surgery patients(26-28). A previous study suggested that the 6MWD and 2-minute walking distance were highly correlated in the 6MWT(29). However, if the subjects were instructed to complete the test in just 2 minutes, the walking distance on the 2MWT might be further prolonged. A better method may be to stop at 2 minutes during the 6MWT, but this cannot be done repeatedly because of the difference in motivation of the subjects regarding the tests. The 6MWT was originally developed to evaluate cardiorespiratory endurance. In this respect, it is necessary to confirm if the 2MWT is indicative of physical endurance in patients with DMD. Moreover, the results also indicated a significant correlation between the 1-minute walking distance with the BPS and the 6MWD in the PS6MWT. The PSWT is expected to be a better indicator of ambulatory potential in an evaluation of physical endurance compared with the C6MWT in patients with DMD.

Cardiorespiratory dysfunctions progress along with the disease course in DMD(30). The results revealed that the patients did not show any adverse changes including the SpO2, and none of the patients dropped out or wanted to stop the task halfway; therefore, it was considered that this experiment was conducted in a safe manner.

In this study, a 6MWT based on a regular metronome sound was developed, and the BPS, that is, the sound used when the subject walked the longest distance in 1 minute, was determined. The PS6MWT was administered to healthy young adults and ambulant patients with DMD, and the 6MWD was compared between the PS6MWT and C6MWT. All subjects showed a significantly longer 6MWD in the PS6MWT than in the C6MWT, and the 1-minute walking distance with the BPS was significantly correlated with the PS6MWT distance. Both the PS6MWT and PSWT may be useful in the evaluation of physical endurance.

ACKNOWLEDGEMENTS

This study was supported by an Intramural Research Grant (26–6) for Neurological and Psychiatric Disorders of the National Center of Neurology and Psychiatry (NCNP).

REFERENCES

1) ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories: ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med, 2002, 166: 111–117. [Medline] [CrossRef]
2) Tao W, Van D, Li JH, et al.: Gait improvement by low-dose botulinum toxin A injection treatment of the lower limbs in subacute stroke patients. J Phys Ther Sci, 2015, 27: 759–762. [Medline] [CrossRef]
3) An HJ, Kim JI, Kim YR, et al.: The effect of various dual task training methods with gait on the balance and gait of patients with chronic stroke. J Phys Ther Sci, 2014, 26: 1287–1291. [Medline] [CrossRef]
4) Park IM, Lee YS, Moon BM, et al.: A comparison of the effects of over-ground gait training and treadmill gait training according to stroke patients’ gait velocity. J Phys Ther Sci, 2015, 25: 379–382. [CrossRef]
5) McDonald CM, Henricson EK, Han JI, et al.: The 6-minute walk test as a new outcome measure in Duchenne muscular dystrophy. Muscle Nerve, 2010, 41: 500–510. [Medline] [CrossRef]
6) McDonald CM, Henricson EK, Han JI, et al.: The 6-minute walk test in Duchenne/Becker muscular dystrophy: longitudinal observations. Muscle Nerve, 2010, 42: 966–974. [Medline] [CrossRef]
7) Goemans N, van den Hauwe M, Wilson R, et al.: Ambulatory capacity and disease progression as measured by the 6-minute-walk distance in Duchenne muscular dystrophy subjects on daily corticosteroids. Neuromuscular Disorders, 2013, 23: 618–623. [Medline] [CrossRef]
8) McDonald CM, Henricson EK, Abresch RT, et al.: FTC124-GD-007-DMD Study Group: The 6-minute walk test and other endpoints in Duchenne muscular dystrophy: longitudinal natural history observations over 48 weeks from a multicenter study. Muscle Nerve, 2013, 48: 343–356. [Medline] [CrossRef]
9) Wraith JE, Clarke LA, Beck M, et al.: Enzyme replacement therapy for mucopolysaccharidosis I: a randomized, double-blinded, placebo-controlled, multinational study of recombinant human alpha-L-iduronidase (laronidase). J Pediatr, 2004, 144: 581–588. [Medline] [CrossRef]
10) Muenzer J, Wraith JE, Beck M, et al.: A phase II/III clinical study of enzy -

This content is from a copyrighted source and is for personal use only. No further reproduction or distribution is permitted without permission from the copyright holder.
walk test for older adults living in long-term care. Physiother Can, 2009, 61: 78–87. [Medline] [CrossRef]

28) Brooks D, Parsons J, Tran D, et al.: The two-minute walk test as a measure of functional capacity in cardiac surgery patients. Arch Phys Med Rehabil, 2004, 85: 1525–1530. [Medline] [CrossRef]

29) Bohannon RW, Bubela D, Magasi S, et al.: Comparison of walking performance over the first 2 minutes and the full 6 minutes of the Six-Minute Walk Test. BMC Res Notes, 2014, 7: 1–6. [CrossRef]

30) Weir NA, Brown AW, Shlobin OA, et al.: The influence of alternative instruction on 6-min walk test distance. Chest, 2013, 144: 1900–1905. [Medline] [CrossRef]