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ORIGINAL ARTICLE

Six-Minute Walk Test in Patients With Down Syndrome: Validity and Reproducibility

Jeroen C. Vis, MD, Hanneke Thoonsen, MD, Marielle G. Duffels, MD, Rianne A. de Bruin-Bon, Sylvia A. Huisman, MD, Arie P. van Dijk, MD, PhD, Elke S. Hoendermis, MD, PhD, Rolf M. Berger, MD, PhD, Berto J. Bouma, MD, PhD, Barbara J. Mulder, MD, PhD

ABSTRACT. Vis JC, Thoonsen H, Duffels MG, de Bruin-Bon RA, Huisman SA, van Dijk AP, Hoendermis ES, Berger RM, Bouma BJ, Mulder BJ. Six-minute walk test in patients with Down syndrome: validity and reproducibility. Arch Phys Med Rehabil 2009;90:1423-7.

Objectives: To examine the validity of the six-minute walk test (6MWT) as a tool to evaluate functional exercise performance in patients with Down syndrome (DS).

Design: Comparison of the six-minute walk distance (6MWD) in 2 distinct groups of DS patients: with and without severe cardiac disease. To test reproducibility, a group of patients with DS performed the 6MWT twice.

Setting: Tertiary referral centers for patients with congenital heart defects and outpatient clinics for people with intellectual disabilities.

Participants: Adult patients with DS with (n=29) and without (n=52) severe cardiac disease categorized by cardiac echocardiography.

Interventions: Not applicable.

Main Outcome Measure: Distance walked on the 6MWT.

Results: The mean 6MWD in the group with severe cardiac disease was 289±104m and in the group without severe cardiac disease 280±104m (P=.70). Older age, female sex, and severe level of intellectual disability were all found to be independently and significantly correlated with a lower 6MWD (r=.67, P<.001). The paired 6MWD was not significantly different (310±88m vs 317±85m; P=.40) in patients who performed the 6MWT twice. The coefficient of variation was 11%.

Conclusions: The 6MWD between the 2 groups was not significantly different. However, the walking distance inversely correlated with the level of intellectual disability. Therefore, the 6MWT is not a valid test to examine cardiac restriction in adult patients with DS.

Key Words: Down syndrome; Exercise test; Rehabilitation.

THE SIX-MINUTE WALK TEST is a practical, simple, and inexpensive exercise test that is easy to perform with minimal equipment. The test measures the distance that a patient can quickly walk on a flat, hard surface in a period of 6 minutes. Because this test is a submaximal exercise test, it reflects the patient's capacity to undertake day to day activities.[1] Furthermore, the 6MWT is currently the test of choice when using a submaximal walk test for clinical or research purposes.[2] Recently, the American Thoracic Society published guidelines for performing 6MWTs in adults in clinical settings.[1] The reliability of the 6MWT has been shown for patients with cardio- and respiratory diagnoses as well as for various other conditions.[3,4] It has been proven to be valid in children.[5-8] The 6MWT has also been used to evaluate treatment response in patients with Eisenmenger syndrome with and without DS.[9-11] To our knowledge, despite its frequent use, the validity of the 6MWT has never been investigated for individuals with DS, and reference values are not available. Because the 6MWT is being used in the clinical setting for patients with DS, research on the 6MWT in DS is particularly relevant. Moreover, several studies[12] have substantiated the physical limitations specific to the condition of DS. Individuals with DS show inferior cardiovascular fitness compared with persons with an intellectual disability but without DS and compared with nondisabled peers. The total heart rate variability is reduced in individuals with DS, manifesting possible autonomic dysfunction in this population.[13] The purpose of this study was to determine whether the 6MWT is a valid tool to evaluate functional exercise performance in individuals with DS.

METHODS

Inclusion

Male and female adults with DS participated in this study. Recruitment took place in different locations: (1) patients that took part in a cardiac screening program for adults with DS. This cardiac screening program took place in The Prinsenstichting and in ASVZ, both institutions for people with intellectual disabilities, and was offered to all adults with DS living in these institutions Patients already treated by a cardiologist, patients with severe Alzheimer's disease, and patients that were not physically able to walk a certain distance were excluded; (2) patients that were followed up at the outpatient departments of adult congenital heart disease of the Academic Medical Centre in Amsterdam and the University Medical

List of Abbreviations

bpm	beats per minute
DS	Down syndrome
6MWD	six-minute walk distance
6MWT	six-minute walk test

From the Department of Cardiology, Academic Medical Centre, Amsterdam (Vis, Thoonsen, Duffels, de Bruin-Bon, Bouma, Mulder); Interuniversity Cardiology Institute of the Netherlands, Utrecht (Vis, Duffels); Prinsenstichting, Institution and Outpatient Clinics for People with Intellectual Disabilities, Purmerend (Huisman); Department of Cardiology, Radboud University Nijmegen Medical Centre, Nijmegen (van Dijk); Department of Cardiology, University Medical Centre Groningen (Hoendermis, Berger); and Department of Cardiology, University Medical Centre Utrecht, Utrecht (Mulder), The Netherlands.

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Reprint requests to Jeroen C. Vis, MD, Dept of Cardiology, Academic Medical Centre Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands, e-mail: *j.c.vis@amc.uva.nl.*

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Table 1: Levels of Intellectual Disability

Level	IQ	Adaptive Behavior
Mild	50–69	Capable of personal independence with a little guidance and assistance.
Moderate	35–49	Require assistance with more complex activities; communicate with simple sentences.
Severe	20–34	Require assistance with most ADLs; communicate with words and gestures.
Profound	<19	Require comprehensive care; usually nonverbal; high incidence of secondary disabilities.

Abbreviations: ADLs, activities of daily living; IQ, intelligence quotient.

Centres of Nijmegen and Groningen. All DS patients with Eisenmenger syndrome were included.

After inclusion, subjects were categorized into 2 groups by cardiac echocardiography, a group of patients with DS with severe cardiac disease (Eisenmenger syndrome or severe valve regurgitation) and a group of patients with DS with mild or no cardiac disease. Cardiac echocardiograms were performed by an experienced ultrasound technician and evaluated by a cardiologist. The classification of intellectual disability was obtained from patients' medical files and represents a combination of patient's level of intelligence and adaptive behavior, based on validated psychologic tests.[14] The patient's level of intellectual disability was categorized as mild/moderate or severe/profound (table 1). Informed consent was acquired from all subjects and/or their legal guardians for the complete cardiac screening including the 6MWT. The Institutional Ethics Committee of the Academic Medical Centre in Amsterdam and the University Medical Centres of Nijmegen and Groningen approved the pulmonary hypertension treatment protocol, including the 6MWT, of the Eisenmenger patients.

Six-Minute Walk Test

All 6MWTs were conducted using a lap of 30 or 40m in length on a flat, hard ground in 4 different locations. Testing procedures were performed in a standardized manner in accordance with the guidelines of the American Thoracic Society.[1] Subjects were instructed to walk up and down a corridor, on a course which was marked by 2 orange plastic cones placed 15m or 20m apart. They were instructed to walk as far as possible during 6 minutes, without running or jogging. Resting was allowed if necessary, but walking was to be resumed as soon as subjects were able to do so. The total distance walked in 6 minutes (6MWD) was recorded to the nearest meter. The heart rate and oxygen saturation were measured before the start of the walk, after every lap, and directly after the test by a portable pulse oximeter[a] attached to the subject's wrist and finger. Usage of walking aids was recorded. Data on medical history and the use of medication were obtained from patients' records into an electronic case record file, as were sex and age. Height and weight were measured. The 6MWTs were supervised by the treating physician or a trained medical student, to minimize variability. Because of the setting of a single-visit cardiac screening program in institutionalized patients, we were unable to do a prior familiarization 6MWT trial.

Test-Retest Reliability

A group of patients with Eisenmenger syndrome performed the 6MWT twice. Both tests were performed on the same day, with at least an hour rest in between. Before starting the standardized pulmonary hypertension treatment protocol, patients performed two 6MWTs as a baseline measure.

Statistical Analysis

Descriptive statistics were used to describe patients' characteristics and type of heart conditions. Differences between 2 groups were analyzed by an unpaired Student t test or when appropriate the Mann-Whitney U test for continuous variables and chi-square test for nominal variables. Data are displayed as mean ± SD, and the level of significance was set at P less than .05. A multiple linear regression model of the 6MWD was developed by using those variables found to be significant ($P<.10$) by univariate analysis. Intellectual disability was classified as mild, moderate, severe, or profound. Reliability data were visualized in a Bland-Altman plot[15] in which the difference between the 2 measured 6MWDs is plotted against their mean for each subject. Coefficient of variation was calculated according to the formula: (SD[6MWDdif]/mean[6MWDmean]) * 100%, where 6MWDdif is the first 6MWD minus the second and 6WMDmean is the mean of the two 6MWDs for each subject. Statistical analysis was performed with SPSS 15.0.[b]

RESULTS

In total, 54 patients with DS living in the participating institutions performed the 6MWT. Ten patients were not able to perform the 6MWT because they sat in a wheelchair; 9 refused to perform the test. Twenty-seven DS patients with Eisenmenger syndrome from the outpatient clinics performed the 6MWT. Fourteen of them performed the 6MWT twice. In total, 81 adults with DS (mean age, 39±11y; 65% men) could be included in this study and were divided into 2 groups: 29 patients with severe cardiac disease (mean age, 36±10y; 52% men) and 52 patients with mild or no cardiac disease (mean age, 41±11y; 73% men). The baseline characteristics are summarized in table 2. The type of heart conditions in both groups are shown in table 3.

Six-Minute Walk Distance

The mean walking distance did not differ significantly between the patients with severe cardiac disease and patients with mild or no cardiac disease (289±105m vs 280±104m, $P=.70$) (fig 1). The mean peak heart rate, measured during the 6MWT, was not statistically different ($P=0.7$) in the severe group (109±17bpm) compared with the group with mild or no car-

Table 2: Patient Characteristics

Characteristics	Severe CD n=29	No or Mild CD n=52	P
Male sex (%)	52	73	.050
Age (y)	36±10	41±11	.020
Height (cm)	153±10	156±9	.240
Weight (kg)	59±9	67±9	<.001
BMI (kg/m^2)	25±3	28±4	.003
Intellectual disability			.340
Mild/moderate	18	35	
Severe/profound	5	17	

NOTE. Values are expressed as mean value ± SD or as otherwise indicated.
Abbreviations: BMI, body mass index; CD, cardiac disease.

Table 3: Type of Heart Conditions

Type of Condition	Severe CD n (%)	No or Mild CD n (%)
Eisenmenger syndrome	27	0
ASD	1 (3)	0
VSD	13 (41)	0
AVSD	15 (47)	0
PAD	3 (9)	2
Valve regurgitation		
Trace	9 (17)	23 (26)
Mild	20 (37)	51 (58)
Moderate	14 (26)	14 (16)
Severe	11 (20)	0

NOTE. Values are numbers of congenital heart defects or valve regurgitations (% of total number of congenital heart defects or valve regurgitation). One patient can have several defects. Total sample size was n=29 and n=52 for severe CD and no or mild CD, respectively.
Abbreviations: ASD, atrial septal defect; AVSD, atrioventricular septal defect; CD, cardiac disease; PAD, patent arterial duct; VSD, ventricular septal defect.

diac disease (107±18bpm), nor was the increase in heart rate (28±11bpm vs 25±18bpm, $P=0.5$) between both groups during the 6MWT. The lowest level of oxygen saturation reached during the 6MWT was lower for the severe group (70±12%) than for the group with mild or no cardiac disease (94±5%) ($P<.001$). Twenty-two patients needed a walking aid during the test (accompanied by a guardian or a rolling walker).

Factors Influencing the Six-Minute Walk Distance

Multivariate analysis indicated that 45% of the variation in distance walked by the subjects could be accounted for by the combined factors of sex, age, and level of intellectual disability

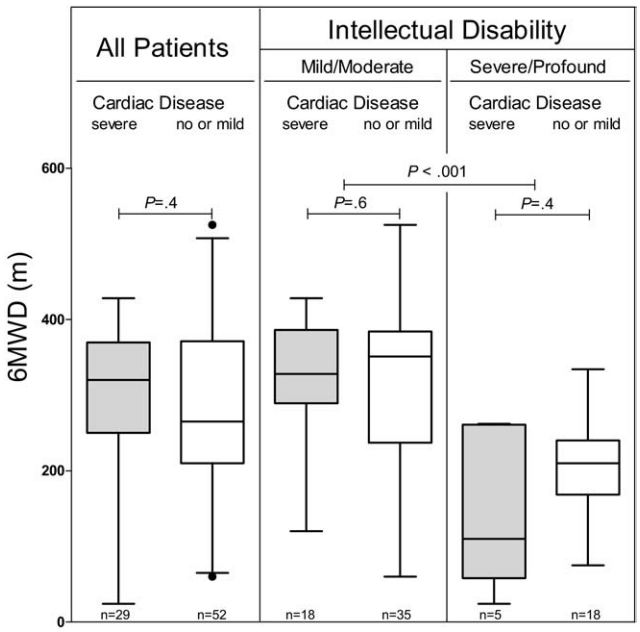

Fig 1. Distance walked by the group with severe cardiac disease and the group with no or mild cardiac disease for all patients and for 2 subgroups divided by level of intellectual disability. Representations are median and centiles.

Table 4: Predictors for 6MWD

Variables	6MWD Univariate β	P	Multivariate β	P
Severe ID	–0.54	<.001	–0.41	<.001
Age	–0.37	.001	–0.29	.030
Male sex	0.25	.020	0.31	.001
Walking aid	–0.39	.001		
Height	0.20	.070		
BMI	0.07	.560		
Severe CD	0.04	.720		

Abbreviations: BMI, body mass index; CD, cardiac disease; ID, intellectual disability.

($r=.67$, $P<.001$). There was a significant difference in mean walking distance between the group with a mild/moderate level of intellectual disability (318±92m) and the group with a severe/profound level of intellectual disability (195±84m, $P<.001$). The level of intellectual disability was an independent factor for 6MWD. Figure 1 shows that within the 2 groups of intellectual disability, the severity of cardiac disease had no influence on 6MWD. In addition, the 6MWD did not correlate with height, body mass index, or use of a walking aid (table 4).

Test-Retest Reliability

Test-retest reliability was evaluated in 14 patients (mean age, 32y; range, 19–44y; 50% men). There was no significant difference between the 2 walking distances reached (310±88m vs 317±85m; $P=0.4$). The results of the reliability test are shown in the Bland Altman plot[15] (fig 2). The coefficient of

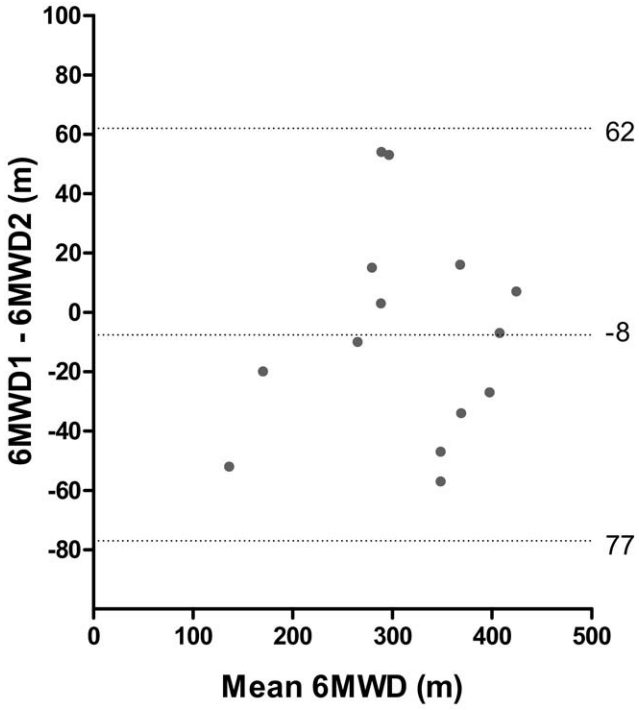

Fig 2. Bland and Altman plot for data from the two 6MWTs. The difference between the first and second 6MWD plotted against the subject's mean of the two 6MWTs. The center dashed line equals the mean difference between the 2 tests and outer dashed lines equal ±2 SD of the mean.

variation was 11%. In 8 of 14 patients, the individual best test was the second test.

DISCUSSION

In this study, we found that the 6MWD was not dependent on severity of cardiac disease in patients with DS. Therefore, the 6MWT is not a valid test to examine cardiac restriction in patients with DS. The level of intellectual disability was negatively correlated with the 6MWD and it was found to be an independent predictor of the 6MWD. The test-retest reliability of the 6MWT in patients with DS was adequate.

Six-Minute Walk Distance in the Down Syndrome Population

For the first time, 6MWD has been show to correlate with intellectual disability rather than with the severity of cardiac disease in patients with DS. The mean 6MWD in the group of 52 adults with DS without significant cardiac disease was 280±104m. Published data on mean 6MWD in healthy populations showed much longer walking distances. Troosters et al[16] found an average 6MWD of 631±93m in 51 healthy subjects aged 50 to 85 years. Gibbons et al[17] observed a somewhat longer mean walking distance of 698±96m in a younger population of 79 healthy subjects with a mean age of 41 years. The shorter walking distances in our DS population without a significant heart defect are consistent with the literature on lower cardiovascular fitness levels in this population. Fernhall et al[18] reported that individuals with intellectual disability have low levels of cardiovascular fitness and that these values may be negatively affected by DS. It has been suggested that persons with intellectual disability have a very inactive lifestyle, resulting in low fitness levels and a high incidence of obesity.[19,20] Lavay et al[21] stated that persons with intellectual disability lack a required certain degree of motivation to successfully fulfill a cardiovascular fitness test. In our opinion, understanding of the test procedure also has a major effect on test results of the 6MWT because the study showed that 29% of the variation in distances walked by the subjects could be accounted for by level of intellectual disability alone.

Factors influencing Six-Minute Walk Distance

Other researchers[4-7] investigating the 6MWT in various populations have observed significant relationships between the distance walked and height, weight, and body mass index. However, in our DS population, only age, sex, and level of intellectual disability were independent predictors of walking distance in multivariate analysis ($r=.67$, $P<.001$). Although the guidelines for the 6MWT[1] label "impaired cognition" as a source of 6MWD variability, the relation of intellectual disability and 6MWD has never been studied before. Other factors that were not studied, such as motivation, mood,[2] and motor development, may play a role as well.

Learning Effect

A notable finding in this study is that in repeated testing, 6MWD was either increased (57%) or decreased during the second 6MWT. This finding contrasts several studies showing that walking distance tends to increase with repeated test administration.[16,17,22,23] This learning effect may be caused by improved coordination, finding optimal stride length, and overcoming anxiety.[1] The magnitude of the reported learning effect is quite variable between studies and ranges from around 4.5% to 33% of the initial distance walked.[22] Because the distance walked tends to plateau after 3 walks, 1 to 2 practice walks have been suggested. The absence of a learning effect in this study may possibly be the result of the restricted learning capacities of our DS population.

Feasibility of the Six-Minute Walk Test

Because communicating with persons with an intellectual disability can be difficult, an objective test to determine cardiorespiratory fitness can offer a solution. In theory, the 6MWT could have been fit for use in a DS population. The act of walking is familiar to all, as opposed to cycling, running, stepping, or treadmill walking, which are used in other tests of cardiorespiratory fitness. Therefore, reconsidering the design of the 6MWT to improve the test's validity in patients with DS might prove to be worthwhile. Some other studies concerning field testing in intellectually disabled persons have paired subjects with a partner while testing.[24-27] This is a modification that should be given serious consideration because these subjects lack motivation, necessary knowledge, and ability regarding proper pacing techniques. In their review on measuring the cardiovascular endurance of persons with an intellectual disability, Lavay et al[21] stressed the importance of proper test familiarization in this type of population. Every effort should be made to familiarize and accommodate the person during the procedure. Because the 6MWT does not reflect cardiorespiratory fitness in patients with DS, it is not fit to monitor changes in cardiorespiratory fitness in time within each individual patient either.

Study Limitations

Our study has a few limitations. These include possible recruitment bias because of the selected patient population. Patients were recruited from tertiary referral centers for patients with congenital heart defects and from outpatient clinics for people with intellectual disabilities. Moreover, the absence of the description of a patient's usual physical activity may lead to a comparability bias. We were unable to use a totally standardized test protocol. We followed the guidelines for 6MWT in a clinical setting[1] in all but 2 aspects: (1) the Eisenmenger patients performed the test on a 10-m longer corridor and had to walk less turnarounds than the other individuals. However, in a previous study, the course length had no significant effect on walking distance.[28] (2) A standardized explanation of the test and timing and wording of encouragement during testing was impossible because of the large variety of the subjects in motivation and level of intellectual disability. Another limiting factor is the size of the study sample, especially of the reliability study. However, with respect to this population, sample size was quite reasonable compared with other studies concerning cardiorespiratory fitness tests in patients with an intellectual disability.[24-27,29] No familiarization techniques were used in our study. Lavay et al[21] states that in every cardiovascular fitness test familiarization with the mode of exercise is an important concept. Persons with an intellectual disability may be apprehensive to attempt new test procedures and/or to use a certain piece of exercise equipment, which may influence test results.

CONCLUSIONS

The findings of this study suggest that the 6MWT does not appear to be a valid indicator of cardiorespiratory fitness in adult patients with DS. The 6MWT appeared to be inversely related to intellectual disability in these patients. Future studies are needed to investigate other parameters that can be used to assess functional capacity in individuals with DS or modifications that can improve the validity of the 6MWT for this population.

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