

## ORIGINAL ARTICLE

# Physical fitness and activity level in Norwegian adults with achondroplasia

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## Abstract

This cross-sectional Physical Fitness Study compared cardiorespiratory fitness (VO<sub>2</sub> peak), six-minute walk test (6MWT), muscle strength (30sSTS), balance (BESS), and self-reported physical activity level (IPAQ) in Norwegian adults with achondroplasia (ACH) to reference values of average-statured individuals. The feasibility of the physical fitness tests and IPAQ was explored. Forty-three adults (22 women) participated. Mean age was 38 years (range 16–69 years). Mean differences (95% CI) for men and women with ACH compared to reference values were: VO<sub>2</sub> peak, –7.0 ml/min/kg (–13.6 to –0.5,  $p = .037$ ), and –7.9 ml/kg/min (–11.6 to –4.3,  $p < .001$ ); 6MWT –270.8 m (–340.4 to –201.2,  $p < .001$ ), and –196.7 m (–244.3 to –149.0,  $p = .001$ ); 30sSTS –4.6 repetitions (–7.8 to –1.5,  $p = .006$ ), and –1.1 repetitions (–3.4 to 1.1,  $p = .335$ ). There were no differences within ACH participants, except for VO<sub>2</sub> peak, where men performed better. Sufficient physical activity (> 600 metabolic equivalent of task weekly) was achieved by 79% of the participants. The feasibility of the 6MWT and 30sSTS was good. There was a strong correlation between the VO<sub>2</sub> peak and 6MWT (men:  $r = 0.63$ ,  $p = .007$ ; women:  $r = 0.71$ ,  $p < .001$ ). The findings indicate that the 6MWT and 30sSTS test are useful in assessing functional exercise capacity and muscle strength in adults with ACH.

## KEYWORDS

achondroplasia, adult, muscle strength, physical fitness, six-minute walk test

## 1 | INTRODUCTION

Achondroplasia (ACH) is the most common skeletal dysplasia, resulting in disproportionate short stature and rhizomelic shortening of the limbs, in combination with an almost normal trunk length (Horton, Hall, & Hecht, 2007; Pauli, 2019). A high prevalence of medical complications, such as foramen magnum stenosis, limb and spinal deformities in childhood, and spinal stenosis and high prevalence of pain later in life have been reported (Alade et al., 2013; Dhiman et al., 2016; Hunter, Bankier, Rogers, Sillence, & Scott Jr., 1998; Wright & Irving, 2012). Medical complications, disproportionate short

stature, and pain may negatively influence participation in physical activity (Haga, 2004; Takken, van Bergen, Sakkera, Helder, & Engelbert, 2007) and may affect physical activity levels and fitness. Knowledge of physical fitness and activity levels in people with ACH is limited. We only found three studies with focus on physical fitness and strength, comparing healthy peers to people with ACH. One study, in children with ACH, showed reduced physical fitness and low participation in physical activity compared to age-matched peers (Takken et al., 2007). Sims and coworkers (Sims, Onambebe-Pearson, Burden, Payton, & Morse, 2018b) showed that young male adults with ACH had reduced muscle strength compared to healthy young males.

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Stokes et al. (Stokes, Pyeritz, Wise, Fairclough, & Murphy, 1988; Stokes, Wohl, Wise, Pyeritz, & Fairclough, 1990) found a slightly reduced lung capacity in ACH compared to healthy adults, which they did not consider influenced on physical capacity.

The importance of physical fitness, to extend the years of quality living, is extensively justified in the literature for the general population (Blair & Morris, 2009; Bouchard, Blair, & Haskell, 2012). Previous studies have reported that people with ACH have an increased overall mortality compared to the general American population, including 10 times increased heart disease-related mortality (Hecht, Francomano, Horton, & Annegers, 1987; Wynn, King, Gambello, Waller, & Hecht, 2007). Cardio-respiratory fitness (CRF) is well known as a predictor of health and cardiovascular disease in the general population (Kodama et al., 2009; Ladenvall et al., 2016; Myers et al., 2002). A maximum treadmill exercise test is regarded as the reference standard for assessing CRF (Bassett & Howley, 2000) but is a time-consuming and laboratory-dependent test, limiting the applicability in clinical practice. In contrast, the six-minute walk test (6MWT) is a valid clinical functional exercise capacity test (Bohannon & Crouch, 2017). In the general population, studies have shown a high correlation between the 6MWT and CRF (American Thoracic Society, 2002; Burr, Bredin, Faktor, & Warburton, 2011; Enright, 2003).

To assess physical fitness and physical activity level in ACH, we chose well-proven and commonly used clinical assessment tools, due to the lack of instruments validated for ACH. Selection of the physical fitness tests was based on good psychometric properties, the possibility of further use in clinical practice, and low cost without the need for advanced technical equipment. We are not aware of other studies examining physical fitness or levels of physical activity in adults with ACH.

The main aim of this study was to investigate physical fitness and level of physical activity in a Norwegian cohort of adults with ACH, to compare men versus women with ACH, and ACH versus reference values. We assessed the correlation between age, anthropometrics and physical fitness measures. In addition, we evaluated the feasibility of the 6MWT, the 30-second sit-to-stand test (30sSTS), the Balance Error Scoring System (BESS), and the International Physical Activity Questionnaire (IPAQ) in these individuals.

## 2 | METHODS

### 2.1 | Participants

This cross-sectional study was part of The Norwegian Adult Achondroplasia Study, conducted at Sunnaas Rehabilitation Hospital in collaboration with the National Resource Centre for Rare Disorders. All participants were recruited from this study. Details of design, recruitment, and representativeness of the study sample are presented elsewhere (Fredwall et al., 2020). After inclusion in this study, all participants underwent a medical safety check (medical history, general health evaluation, blood pressure and a cardiopulmonary examination), to clarify for the physical fitness tests.

### 2.2 | Data collection

All physical fitness measures were carried out at Sunnaas Rehabilitation Hospital. Experienced laboratory staff conducted the treadmill and spirometry test, and a physiotherapist (OdV) performed the remaining physical fitness tests. The participants completed the IPAQ, confirmed by a face-to-face interview (OdV). Demographical data, including age, gender, educational level, body measurements (weight, height, sitting height), and smoking status were collected from The Norwegian Adult Achondroplasia Study. Leg length was calculated by subtracting sitting height from standing height.

### 2.3 | Measurements

#### 2.3.1 | Spirometry

As part of the CRF test, all participants completed a spirometry test, measuring Forced Vital Capacity (FVC) and Forced Expiratory Volume, first second (FEV1). We used the instrument VO<sub>2</sub> max 220 (Sensormedics Corporation, Yorba Linda, CA). The spirometry test was conducted in accordance with the recommendations provided by the European Respiratory Society and the American Thoracic Society (Miller et al., 2005). Three technically satisfactory tests were conducted, with the highest FVC and FEV1 used in the analyses. Currently, there are no established spirometry reference values for ACH. However, Stokes et al published spirometry data on adults with ACH (Stokes et al., 1988; Stokes et al., 1990). We used these data to guide an individual clinical assessment of whether the respiratory function could be a potential limiting factor of the physical fitness tests.

#### 2.3.2 | Cardiorespiratory fitness

The CRF was measured by a maximum treadmill exercise test, considered as the gold standard for exercise capacity measurement (Bassett & Howley, 2000). We followed the modified Sunnaas protocol (Lundgaard, Wouda, & Strom, 2017) and the clinician's guide from the American Heart Association (Balady et al., 2010). The CRF outcome was measured as VO<sub>2</sub> peak. After a short warm-up, establishing the self-selected walking speed, the inclination of the treadmill was increased by 2% every minute up to 20% inclination, or until exhaustion. If exhaustion was not reached at the self-selected speed and 20% inclination, the speed was increased every minute by 0.5 km/hr until exhaustion. The test was terminated when the participant achieved exhaustion, despite verbal encouragement. During the test, heart rate (HR) was measured with a HR-monitor (Polar Sports Tester, Polar Electro Inc., Kempele, Finland). Gas exchange variables were measured continuously with a computerized standard open-circuit technique, breath-to-breath spirometer (V<sub>max</sub> Encore 229D, CareFusion Corporation, San Diego, CA). The equipment was calibrated before each test. Blood lactate concentration (mmol/l) was measured two minutes into recovery. The preset criteria for maximal oxygen uptake was set to the achievement of a VO<sub>2</sub> plateau, a respiratory exchange ratio

(RER)  $\geq 1.05$ , lactate  $\geq 5$  mmol/L, and 95% of predicted maximal HR, and a Borg Scale  $\geq 17$ . The Borg scale is a commonly used scale for assessing level of self-perceived exertion, ranging from 6 to 20 points, starting from no exertion to maximum exertion (Borg, 1990). To compare  $\text{VO}_2$  values with the general population, we used the measurement unit ml/kg/min, and the relative  $\text{VO}_2$  was calculated as the absolute value divided by weight (Balady et al., 2010; Bassett & Howley, 2000). Conversion from absolute measurements (liter/min) to ml/kg/min enables comparison, despite differences in body size.

### 2.3.3 | Functional exercise capacity

The 6MWT was conducted according to the American Thoracic Society guidelines (American Thoracic Society, 2002; Enright, 2003). Participants were instructed to walk as fast as possible, without running, back and forth between two cones with a distance of 30 m, on a flat and hard surface for six minutes. We recorded the total walked distance in six minutes (6MWD) up to the nearest meter. After completing the test, participants were asked to rate their perceived exertion on the Borg scale (Borg, 1990).

### 2.3.4 | Functional muscle strength

The 30sSTS test was used to assess functional muscle strength in the lower extremities (Csuka & McCarty, 1985; Jones, Rikli, & Beam, 1999; Tveter, Dagfinrud, Moseng, & Holm, 2014). The test was modified to compensate for low body height. We lowered the chair until the participants achieved 90° of flexion in the hip and knee while seated. Testing started in the sitting position, with arms folded across the chest. Participants were instructed to do as many full “stand-ups” as possible in 30 seconds.

### 2.3.5 | Balance

The BESS was conducted according to the manual (Brown et al., 2014). BESS combines three stances (narrow double leg stance, single leg stance, and tandem stance) on two footing surfaces (firm and foam surface). Participants were asked to hold each stance, with hands on hips and eyes closed, for 20 seconds. According to the scoring manual, any kind of balance reaction (error) created one error-point. A higher score represented a lower performance, with a maximum of 10 points in every stance (total maximum score 60 points). If the participant could not restore balance within 5 seconds, a maximum amount of 10 points was given (Brown et al., 2014).

### 2.3.6 | Physical activity level

The International Physical Activity Questionnaire (IPAQ) is a self-administered questionnaire (Craig et al., 2003; Kurtze, Rangul, &

Hustvedt, 2008). The participants were asked to recall all of their activities during the last seven days, specified in minutes and intensity level. The IPAQ instruction was explained orally to each participant as the intensity concepts needed clarification. For minimizing the errors, all answers were verified by a face-to-face interview with the physiotherapist (OdV) after completing the IPAQ. To calculate the total amount of activity, the reported minutes per activity were multiplied by the number of days per week. Depending on intensity level of the activity, minutes were multiplied by the actual values for the different intensities; for walking, this value is 3.3, for moderate activity 4, and for high intensity 8 (Kurtze et al., 2008). The total amount of activity for a participant in a week is called the metabolic equivalent of task (MET). According to the IPAQ manual, a total MET score of  $>960$  min per day (16 hr) should be excluded. A score exceeding  $>240$  min per day on every intensity value of physical activity was truncated to 240 min per activity value a day. This rule permits a maximum of 28 hours of activity reported for each activity level per week (Schembre & Riebe, 2011; The IPAQ group, 2020).

The activity level per week was graded as insufficiently active ( $< 600$  MET), sufficiently active ( $\geq 600$  MET), or health-enhancing physical activity (HEPA) ( $> 3,000$  MET) (Kurtze et al., 2008).

## 2.4 | Statistics

All data were analyzed using the Statistical Package for Social Sciences (SPSS, IBM, Armonk, NY), version 25. Descriptive statistics for continuous data are presented as mean and SD or as median and range. The categorical data are presented as number (n) and proportions (%). *P* values  $< .05$  were considered statistically significant.

The independent sample *t*-test with 95% confidence intervals (CI) was used to compare mean between groups (ACH men versus women and ACH versus reference values). The assumptions of normal distribution were assessed by histograms, QQ plot, box plot and the Shapiro–Wilk test of normality. For data not normally distributed, the non-parametric Mann–Whitney U Test was used.

Results for CRF, the 6MWT, and the 30sSTS test were compared with reference values developed for the Norwegian general population, matched for gender and age groups by decade (Edvardsen et al., 2013; Tveter, Moseng, Dagfinrud, & Holm, 2013).

As there are no Norwegian reference values for BESS, we used the reference values developed for the Canadian general population, matched for gender, and age groups by decade (Iverson & Koehle, 2013).

The Pearson correlation was used to explore associations between the demographic (age, educational level) and anthropometric (height, weight, leg length) characteristics for both participants (men and women) and physical fitness variables (FVC, FEV1,  $\text{VO}_2$  peak, 6MWT, 30sSTS, and IPAQ). Pearson's correlation was defined as small:  $r = 0.10$ – $0.29$ , medium:  $r = 0.30$ – $0.49$ , and large:  $r = 0.50$ – $1.0$  (Cohen, 1988).

To evaluate the feasibility of the 6MWT, 30sSTS, BESS, and IPAQ, we considered how many participants could perform each item, according to the test manual, and whether any particular problems arose while executing the tests. Using the scoring manual for each

test, we considered the distribution of the results. We also gauged how easy the test was to administer.

## 2.5 | Ethical considerations

The Regional Ethics Committee for Ethics for Medical Health Research in Eastern Norway approved the study (approval number: 2016/2272). A written consent was obtained from all participants prior to taking part in The Physical Fitness Study. The results are reported in accordance with the STROBE guidelines for observational studies (von Elm et al., 2014).

## 3 | RESULTS

### 3.1 | The study participants

Figure 1 shows the physical tests used and the patients included in the study tests. A total of 43 out of 50 participants in the Norwegian Adult Achondroplasia Study were enrolled in The Physical Fitness

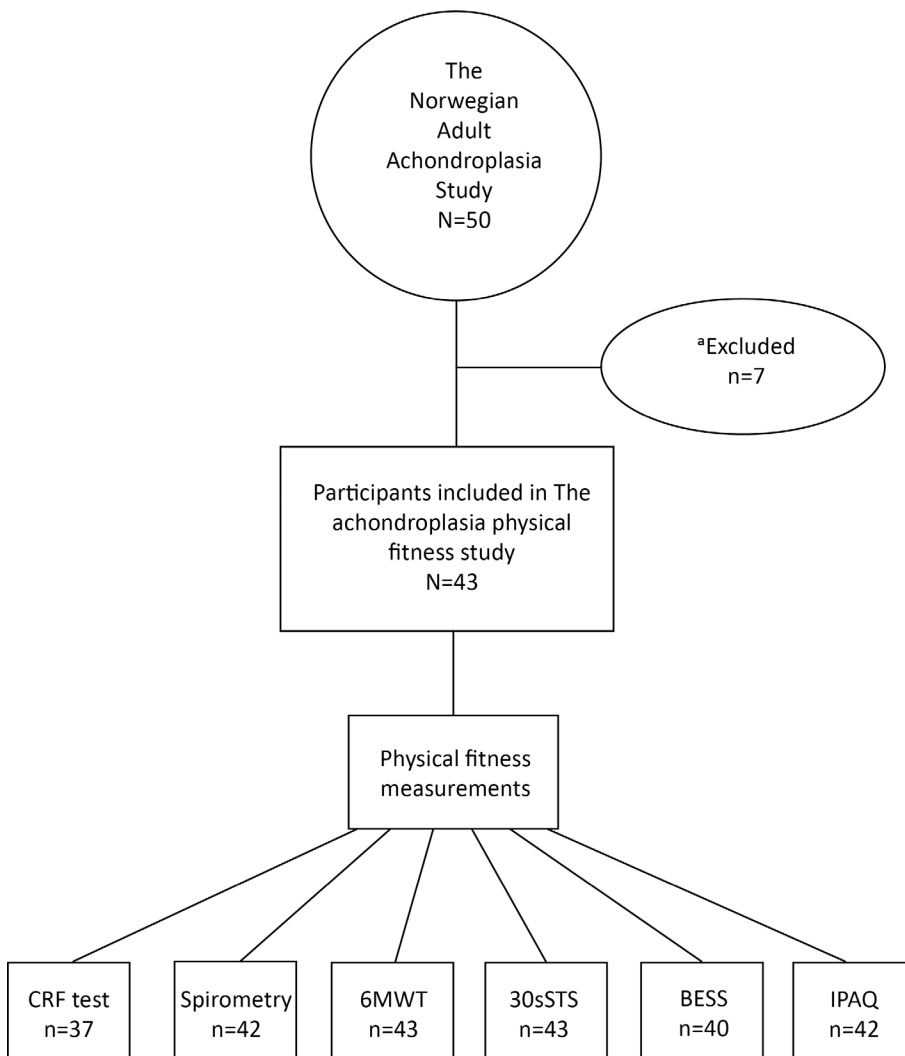
Study, all with genetically confirmed ACH (Fredwall et al., 2020). Due to comorbidity, five out of 43 participants were not medically cleared to perform the CRF test. One refused to participate in both the CRF and spirometry tests. Nine subjects had to terminate before exhaustion set in, because of pain or numbness in their legs. Their test results qualified as peak performance. Three out of 43 could not carry out the balance test (BESS), due to problems with independent standing over time. One IPAQ form was excluded, due to the registration involving more than 960 minutes (16 hr) of activity a day.

Demographic, anthropometric, and spirometry measures for men and women with ACH are presented in Table 1. Height, weight, sitting height, leg length, and spirometry results were all higher in men compared with women.

### 3.2 | Physical fitness in adults with ACH

#### 3.2.1 | Comparisons

Table 2 shows the physical fitness test results for men and women with ACH. There were no differences between men and women,



**FIGURE 1** Flowchart for the achondroplasia physical fitness study (N = 43). Abbreviations: CRF, cardiorespiratory fitness test; 6MWT, six-minute walk test; 30sSTS, 30-second sit-to-stand test; BESS, balance error scoring system; IPAQ, international physical activity questionnaire. <sup>a</sup>Five were not able to attend the hospital, one was permanent wheelchair user and one was undergoing limb lengthening

**TABLE 1** Characteristics and anthropometric measures in men and women with achondroplasia, N = 43

	Achondroplasia men n = 21		Achondroplasia women n = 22		Differences		
	Mean (SD)	Range	Mean (SD)	Range	Mean difference	95% confidence interval	p-value
Age (years)	39.3 (17.8)	16–69	35.7 (15.9)	16–69	3.6	–6.8 to 13.9	.493
Height (cm)	136.2 (8.6)	117–155	129.1 (7.8)	115–145	7.1	2.0 to 12.1	.007
Weight (kg)	64.9 (16.3)	44–96	54.4 (9.8)	32–69	10.5	2.1 to 18.9	.016
Sitting height (cm)	87.9 (3.6)	80–94	84.7 (4.0)	77–92	3.2	0.9 to 5.6	.009
leg length (cm) <sup>a</sup>	48.2 (5.9)	37–61	44.4 (5.8)	36–56	3.9	0.3 to 7.4	.036
FVC (liter)	3.3 (0.7)	2.0–5.0	2.8 (0.6)	1.5–4.2	0.6	0.2 to 1.0	.008
FEV1 (liter)	2.7 (0.7)	1.6–4.3	2.3 (0.6)	0.9–3.6	0.4	0.0 to 0.8	.045
Education level	N	%	N	%			
High school	12	57	12	55			n.s
College/university	9	43	10	46			n.s
Smokers	0	0	1	5			n.s

Abbreviations: FEV1, forced expiratory volume, first second; FVC, forced vital capacity; n.s, not significant.

<sup>a</sup>Leg length = calculated by standing height – sitting height. Level of significance  $\leq 0.05$ .

**TABLE 2** Physical fitness in men and women with achondroplasia, N = 43

	Achondroplasia men, n = 21		Achondroplasia women, n = 22		Differences		
	n	Mean (SD)	n	Mean (SD)	Mean difference	95% confidence interval	p value
CRF (VO <sub>2</sub> peak)	17	37.1 (11.8)	20	28.4 (6.6)	8.8	2.1 to 15.4	.012
6MWT (m)	21	421.9 (150.1)	22	446.8 (105.4)	–24.9	–104.4 to 54.7	.531
30sSTS (repetitions)	21	22.3 (6.6)	22	23.7 (5.0)	–1.4	–5.0 to 2.2	.423
		Median (range)		Median (range)	Median difference		
BESS (reactions)	19	33.0 (11.0–55.0)	21	22.0 (7.0–42.0)	11.0		.363
IPAQ (MET)	21	2,577 (0–8,799)	21	1,560 (0–6,506)	1,017		.204

Abbreviations: BESS, balance error scoring system, scoring balance reactions; CRF, cardiorespiratory fitness, presented as peak oxygen uptake (VO<sub>2</sub> peak) (milliliter/kilogram/minute); IPAQ, international physical activity questionnaire, in metabolic equivalent of task (MET); 30sSTS, 30 seconds sit-to-stand test, scoring full “stand-ups”; 6MWT, six-minute walk test, walked distance in six minutes, up to the nearest meter.

Level of significance  $\leq 0.05$ .

except for VO<sub>2</sub> peak (95% CI 2.1 to 15.4,  $p = .012$ ). The IPAQ scores for men showed that 81% (17/21) accomplished the recommended physical activity level of a minimum of 600 MET weekly, and women 76% (16/21) > 600 MET weekly.

Tables 3 and 4 show physical fitness differences between study participants and age-matched reference values for the general population, separated for men and women. The participants with ACH had lower physical fitness scores for all measurements, except for the 30sSTS-test in women (95% CI –3.4 to 1.1,  $p = .335$ ).

In the total study sample, all physical fitness results showed considerable variation (Tables 3 and 4). Of all participants completing the CRF test, 19% (7/37) performed at the mean or higher than the mean reference values, while 81% (30/37) performed below. The 6MWD varied from 133 to 624 m, with a mean (SD) perceived exertion while walking of 13.6 (1.9), graded by the Borg scale. All participants walked shorter compared to age matched reference values. The 30sSTS test varied from eight to 34 repetitions, and 74% (32/43) performed similar or below mean reference values.

Regarding the BESS test, 79% (34/43) were either unable to perform the test ( $n = 3$ ) or performed very poorly ( $n = 31$ ).

The IPAQ scores for the total study sample showed that 79% (33/42) accomplished the recommended physical activity level of a minimum of 600 MET, including 37% (16/42) who reported health-enhancing physical activity levels (> 3,000 MET), while 21% (9/42) had an insufficient activity level (< 600 MET).

### 3.2.2 | Correlations

Table 5 shows the correlations between age, anthropometrics, and physical fitness measures in men and women with ACH. In men with ACH, increased age and weight were strongly associated with decreased physical fitness performance (VO<sub>2</sub> peak, 6MWT, 30sSTS test), and the VO<sub>2</sub> peak, 6MWT, and 30sSTS test were moderately to strongly associated to each other. In women with ACH, we found a moderate association between age and VO<sub>2</sub> peak, and a strong

**TABLE 3** Physical fitness in men with achondroplasia ( $n = 21$ ) compared to reference values

	n	Achondroplasia men	Reference values <sup>a</sup>	Differences		
		Mean (SD)	Mean (SD)	Mean difference	95% confidence interval	p value
CRF (VO <sub>2</sub> peak)	17	37.1 (11.8)	44.1 (5.6)	-7.0	-13.6 to -0.5	.037
6MWT (m)	21	421.9 (150.1)	692.7 (33.6)	-270.8	-340.4 to -201.2	<.001
30sSTS (repetitions)	21	22.3 (6.6)	26.9 (2.2)	-4.6	-7.8 to -1.5	.006
		Median (range)	Median (range)	Median difference		
BESS (reactions)	19	33.0 (11.0–55.0)	11.5 (10.0–20.0)	21.5		<.001

Abbreviations: BESS, balance error scoring system, scoring amount of balance reactions; CRF, cardiorespiratory fitness, presented as peak oxygen uptake (VO<sub>2</sub> peak) (milliliter/k gram/ minute); 30sSTS, 30 seconds sit-to-stand test, scoring amount of full “stand-ups”; 6MWT, six-minute walk test, walked distance in six minutes, up to the nearest meter.

<sup>a</sup>Reference values developed for the Norwegian general population. For the BESS we used the reference values developed for the Canadian general population. Level of significance  $\leq .05$ .

**TABLE 4** Physical fitness in women with achondroplasia ( $n = 22$ ) compared to reference values

	n	Achondroplasia women	Reference values <sup>a</sup>	Differences		
		Mean (SD)	Mean (SD)	Mean difference	95% confidence interval	p value
CRF (VO <sub>2</sub> peak)	20	28.4 (6.6)	36.3 (4.5)	-7.9	-11.6 to -4.3	<.001
6MWT(m)	22	446.8 (105.4)	643.5 (24.1)	-196.7	-244.3 to -149.0	<.001
30sSTS (repetitions)	22	23.7 (5.0)	24.8 (1.5)	-1.1	-3.4 to 1.1	.335
		Median (range)	Median (range)	Median difference		
BESS (reactions)	21	22.0 (7.0–42.0)	11.9 (11.0–20.0)	10.1		<.001

Abbreviations: BESS, balance error scoring system, scoring amount of balance reactions; CRF, cardiorespiratory fitness, presented as peak oxygen uptake (VO<sub>2</sub> peak) (milliliter/k gram/ minute); 30sSTS, 30 seconds sit-to-stand test, scoring amount of full “stand-ups”; 6MWT, six-minute walk test, walked distance in six minutes, up to the nearest meter.

<sup>a</sup>Reference values developed for the Norwegian general population. For the BESS, we used the reference values developed for the Canadian general population. Level of significance  $\leq .05$ .

**TABLE 5** Correlations between age, anthropometrics and physical fitness measures in men and women with achondroplasia,  $N = 43$ 

	Achondroplasia men						Achondroplasia women					
	CRF (VO <sub>2</sub> peak) $n = 17$		6MWT (m) $n = 21$		30sSTS (repetitions) $n = 21$		CRF (VO <sub>2</sub> peak) $n = 20$		6MWT (m) $n = 22$		30sSTS (repetitions) $n = 22$	
	Pearson r	p value	Pearson r	p value	Pearson r	p value	Pearson r	p value	Pearson r	p value	Pearson r	p value
Age (years)	-0.74	.001	-0.55	.010	-0.68	.001	-0.45	.045	-0.25	.270	-0.46	.032
Height (cm)	-0.16	.549	0.05	.819	-0.35	.119	0.35	.132	0.12	.605	-0.55	.008
Weight (kg)	-0.70	.002	-0.56	.008	-0.67	.001	-0.27	.258	-0.38	.084	-0.32	.145
Leg length (cm) <sup>a</sup>	0.23	.380	0.05	.825	-0.35	.125	0.14	.559	0.19	.393	-0.62	.002
6MWT (m)	0.63	.007					0.71	<.001				
30sSTS (repetitions)	0.71	.001	0.79	<.001			0.21	.385	0.32	.152		
IPAQ (MET)	0.02	.951	0.51	.017	0.40	.070	0.34	.153	0.43	.051	0.32	.162

Abbreviations: CRF, cardiorespiratory fitness, presented as peak oxygen uptake (VO<sub>2</sub> peak) (milliliter/k gram/ minute); IPAQ, international physical activity questionnaire, counting metabolic equivalent of task minutes (MET); 30sSTS, 30 seconds sit-to-stand test, scoring amount of full “stand-ups”; 6MWT, six-minute walk test, walked distance in six minutes, up to the nearest meter.

<sup>a</sup>Leg length = standing height - sitting height. Level of significance  $\leq .05$ .

association between the 6MWT and VO<sub>2</sub> peak. Higher VO<sub>2</sub> peak was associated with increased 6MWD in both men and women with ACH.

For men, higher muscle strength in the lower extremities (30sSTS) was associated with higher VO<sub>2</sub> peak.

### 3.3 | Feasibility

All participants were able to perform the 6MWT without pausing, including those three participants who used walking aids (two men and one woman). During the project, we became aware that several participants stumbled or tripped, although none fell. Their total perceived exertion on the Borg scale ranged from eight to 18. We observed that those with good walking speed had high step frequency (steps/min).

After individual chair adjustment, all participants could perform the 30sSTS test. Even those with some balance issues were able to complete the test with a satisfying degree of quality, and in accordance with the manual.

We experienced several challenges in performing the balance test (BESS). The BESS results were low; 78% (31/40) performed poorly or very poorly, and three participants were not able to perform the test at all. Only 13% (5/40) achieved performances within the predicted range or above. The participants had particular difficulties in performing the more advanced one-foot positions and tandem stance on the foam pad. On the one-foot stand, 85% (33/40) had a maximum amount of error, while 58% (23/40) experienced largely the same with the tandem stance; this stance's starting position was demonstrated to be difficult, due to short legs and broad thighs.

We found the 6MWT and 30sSTS test easy to assess and score in adults with ACH, while BESS was technically difficult to both perform and score.

All participants needed assistance in filling out the IPAQ. Particularly difficult was grading the intensity of the reported activity, or the amount of time spent on physical activity for the last seven days. We experienced that the participants had difficulty in recalling their daily life activities, although regular exercise seemed to be easier. Moreover, the IPAQ items 3a and 3b, inquiring about walking habits, were not applicable to wheelchair users.

## 4 | DISCUSSION

This study investigated physical fitness and level of physical activity in a Norwegian cohort of adults with ACH, including feasibility of use of the physical fitness tests. We found low levels of physical fitness in adults with ACH compared to reference values, and with considerable variance, despite a relatively high reported level of physical activity. The 6MWT and 30sSTS tests were feasible, and appeared to be useful in assessing exercise capacity and muscle strength in this population. To our knowledge, this is the first study to investigate physical fitness, activity level, and feasibility of commonly used physical fitness tests in adults with ACH.

### 4.1 | Physical fitness

The respiratory function was assessed by spirometry, and compared with values reported by Stokes et al. (Stokes et al., 1988; Stokes

et al., 1990). Based on this comparison, and the clinical interpretation of the absolute spirometry results (in liter), we considered that lung capacity did not limit the performance of the physical fitness tests in this study.

The mean  $VO_2$  peak was significantly lower for both men and women, compared with reference values matched for age groups and gender (Edvardsen et al., 2013), and with a pronounced variation. Our results are consistent with Takken et al. (2007), who found a low mean  $VO_2$  peak in children with ACH. As for the general population, the  $VO_2$  peak values in ACH were influenced by age and gender (Bouchard et al., 2012). When body weight increases, the amount of oxygen per kilo ( $VO_2$  peak measured in ml/kg/min.) decreases. Sims, Onambélé-Pearson, Burden, Payton, and Morse (2019) found a higher body fat percentage in people with ACH. This might explain the relative low  $VO_2$  peak, potentially reflecting high body fat instead of low  $VO_2$  peak. Comparing  $VO_2$  peak results based on fat free mass would therefore have been relevant.

An interesting finding was that men had a higher  $VO_2$  peak compared to women with ACH, but there was no gender difference in the 6MWD. This might be explained by the higher body weight of men, which is associated with shorter walking distance and lower oxygen uptake per kilo. The women in this study sample were also slightly younger. As symptomatic spinal stenosis influences on walking distance, and spinal stenosis becomes significantly more prevalent with increasing age (Fredwall et al., 2020), this may be the cause of relative short 6MWD for men in this study.

The strong correlation (men:  $r = 0.63$ ; women:  $r = 0.71$ ) between the  $VO_2$  peak and the 6MWD in our study population is consistent with the general population (Burr et al., 2011), indicating that the 6MWT is applicable for assessing exercise capacity in adults with ACH.

As expected, the mean 6MWD was significantly lower in the both men and women with ACH, compared with matched reference values (Enright et al., 2003; Tveter et al., 2013). Surprisingly, we found no association between body height, sitting height, or leg length and walking distance in our study sample. One possible explanation might be the observed increased step frequency, compensating for the short stride length. Walking speed is determined by step length and step frequency (speed m/s) (Whittle, 2007, p.57). Hence, increased step frequency might compensate for short legs (Sims, Onambélé-Pearson, Burden, Payton, & Morse, 2018a). To achieve high step frequency, muscle strength plays a central role. In men with ACH, the 6MWD increased with good muscle strength. This is consistent with Gurses, Zeren, Denizoglu Kulli, and Durgut (2018), who found a moderate correlation between 6MWD and muscle strength (30sSTS) in healthy young adults.

While the mean muscle strength for men with ACH was reduced compared to the reference values, women with ACH had results similar to the reference values, both for absolute values and range (Tveter et al., 2013). Takken et al. (2007) explained reduced muscle strength in children with ACH by differences in biomechanical conditions, reduced muscle volume, and inactivity. Sims et al. (2018b) found reduced muscle volume and high muscle fat infiltration. These findings require further studies.

## 4.2 | Physical activity level

Self-reported physical activity levels were relatively high in our study population, as 79% reported  $\geq 600$  MET, and with a particularly high amount of high-intensity activities. Despite the relatively high intensity activity reported in our material, we found low values of  $VO_2$  peak, which is surprising, given that high-intensity activities should result in high  $VO_2$  peak values. A possible explanation might be that individuals with ACH tend to report their strenuous everyday activities as high-intensity activities, as described by Johansen, Andresen, Naess, and Hagen (2007). Recall bias and coincidental high reporting of activity could also affect our results. Also notable is the fact that we did not present our oxygen uptake results based on fat free mass. Eliminating high body fat percentage could decrease the difference between the ACH group and the general population, as suggested by Sims et al. (2019).

## 4.3 | Feasibility of the physical fitness tests for ACH

The 6MWT was technically easy to perform and well tolerated for adults with ACH. The possibility of using walking aids made it possible for all participants to walk for six minutes. We found a somewhat low Borg scale score, which could indicate low level of intensity. The strong correlation between the 6MWT and  $VO_2$  peak in adults with ACH, including feasibility, suggests that the 6MWT could be a useful instrument in assessing functional exercise capacity in adults with ACH.

The 30sSTS test was also well tolerated and easy to perform in adults with ACH. No advanced or specialized equipment was necessary, and the 30sSTS results showed a normal distribution. In contrast, the BESS test was technically difficult to administer and resulted in only 13% of participants scoring within the normal range. According to the test manual, there is no distinction between small and big balance reaction “errors”. Some starting positions were impossible for participants due to short legs and broad thighs, creating difficulties in keeping the balance and increasing the total score. Hence, BESS appeared not to be feasible for use in the ACH population. The test is designed for athletes, and does not seem to be valid for testing balance in adults with ACH.

To our knowledge, balance has not previously been reported as a problem in ACH. In several of the participants, we noticed a waddling and wide-based gait, and some stumbling while performing the 6MWT. This might be a sign of decreased balance or altered gait, as described by Sims et al. (2018a). We are not aware of other studies investigating balance in adults with ACH.

## 4.4 | Strengths and limitations

Strengths of this study are the broad recruitment of participants, including 50% of the total estimated Norwegian adult ACH

population, and all participants being genetically confirmed (Fredwall et al., 2020). The sample's anthropometric measurements (height, weight, and sitting height) are representative of adults with ACH in Europe (Merker et al., 2018a; Merker et al., 2018b).

There are also limitations to this study. Assessing physical fitness and activity level in ACH is challenging, due to the complexity of the concept of physical fitness. The impact of several of the physiological factors in ACH, and the lack of knowledge about psychometric properties for physical fitness measures, are unknown and could affect the results. To overcome these challenges, we applied clinically well-established and commonly used measurements, along with the gold standard laboratory CRF test.

Self-reported physical activity level (IPAQ) is well known to pose a risk of recall bias, leading to under- or overestimation of physical activity (Kowalski, Rhodes, Naylor, Tuokko, & Macdonald, 2012; Kurtze, Gundersen, & Holmen, 2003; Prince et al., 2008). The high amount of reported activity minutes in our study suggest low validity of the IPAQ for adults with ACH. Further studies are needed to explore the validity of IPAQ for adults with ACH, before this test is applied in other clinical studies of this condition.

There is also a risk of selection bias, which includes having recruited the healthiest participants, since those with a comorbidity were excluded from the CRF test. However, by including them, the physical fitness level would likely have been even lower. Five young participants (aged 16–18 years) were included in the study. Excluding these participants in the analysis did not have considerable effect on the outcome, but would have reduced the statistical power.

Despite having recruited a large proportion of the total estimated Norwegian population of ACH adults, the sample size limits the possibilities of statistical analyses, and the associations should therefore be interpreted with caution.

## 5 | CONCLUSIONS

This cohort of Norwegian adults with ACH had overall low physical fitness levels, with achievements within a wide range, compared to Norwegian population reference values. There were no gender differences within the ACH study sample, except for  $VO_2$  peak, where men performed better. There was a high correlation between  $VO_2$  peak and the 6MWT. The 6MWT and 30sSTS test were feasible to administer in this population, and appeared to be useful in assessing exercise capacity and muscle strength in adults with ACH.

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**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

**DATA AVAILABILITY STATEMENT**

The Norwegian South Eastern Regional Committee for Medical and Health Research Ethics restrict the data for this study. Due to these restrictions, potentially identifying patient's information, data are not available.

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