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Hand grip strength is associated with fatigue among men with COPD: epidemiological data from northern Sweden

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ABSTRACT

The aim of this study was to investigate if hand grip strength (HGS) is associated with: 1) fatigue, and specifically clinically relevant fatigue (CRF); 2) low physical activity; and 3) fatigue independent of physical activity level, among individuals with and without COPD. Data were collected from the Obstructive Lung Disease in Northern Sweden (OLIN) COPD-study in 2014. HGS was measured with a hand-grip dynamometer, fatigue and physical activity were assessed by questionnaires; FACIT-Fatigue respectively IPAQ. Among individuals with COPD ($n = 389$), but not without COPD ($n = 442$), HGS was lower among those with CRF than those without CRF, significantly so among men ($p = 0.001$) and close to among women ($p = 0.051$). HGS was not associated with physical activity levels within any of the groups. HGS was associated with fatigue among men, but not women, with COPD independent of physical activity level, age, height, and smoking habits (Beta = 0.190, 95% CI 0.061–0.319, respectively Beta = 0.048, 95% CI –0.056–0.152), while there were no corresponding significant findings among individuals without COPD. In summary, HGS was associated with CRF among individuals with COPD in this population-based study. Among men with COPD, HGS was associated with fatigue independent of physical activity level and common confounders.

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Introduction

Chronic obstructive pulmonary disease (COPD) is estimated to affect over 8%–10% of all adults (Backman et al., 2016; Lamprecht et al., 2015), and the most well-known predictors are increasing age and smoking. The majority of all individuals with COPD have mild to moderate disease (Lindberg et al., 2006). However, merely a third of them are identified by health care (Lamprecht et al., 2015; Lindberg et al., 2006), and this under-diagnosis contributes to a lack of knowledge about COPD in the population. Cardiovascular comorbidities are common (Lindberg, Larsson, Ronmark, and Lundback, 2011), but skeletal muscle abnormalities such as muscle fiber atrophy, muscle fiber shift, weakness, and functional limitations are also frequent (Eisner et al., 2008; Maltais et al., 2014).

Hand grip strength (HGS) correlates strongly to muscle mass and strength in upper and lower extremities in individuals with COPD (Marino et al., 2010),

and is also associated with exercise performance (da Silva et al., 2017; Rausch-Osthoff et al., 2014). There are a few studies of HGS in selected COPD samples, but with contradictory results; some found lower HGS in COPD than controls (Eisner et al., 2008), while others did not find any such differences (Gosselink, Troosters, and Decramer, 2000). Even though we found no difference in HGS when comparing individuals with and without COPD in a recently published population-based study, HGS was clearly associated with COPD severity (Strandkvist et al., 2016).

Physical activity is reduced among patients with moderate to very severe COPD compared to healthy controls (Pitta et al., 2005; Troosters et al., 2010). In a population-based study, the proportion with low physical activity was higher in moderate to severe COPD than in those without COPD (Andersson et al., 2015), and clinically relevant fatigue was associated with low physical activity (Andersson et al., 2015). Fatigue is associated with several chronic diseases (Swain, 2000),

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and is also common in COPD (Stridsman, Mullerova, Skar, and Lindberg, 2013). Among patients with COPD, fatigue seems to be associated with muscle strength (Calik-Kutukcu et al., 2014), and one strategy to gain control over fatigue is to continue with physical activity (Stridsman, Lindberg, and Skar, 2014).

Decreased HGS, increased fatigue and decreased level of physical activity are associated with the burden of COPD, and each of them is a possible target of rehabilitation interventions (Bolton et al., 2013). Still, most studies within this topic include small and selected COPD populations, and furthermore, the relationships between these factors have not been evaluated in the same study. Due to the under-diagnosis, population-based studies are needed to understand the true burden of and relationship between HGS, fatigue, and physical activity in COPD. An increased knowledge is of importance to identify individuals for rehabilitation interventions and also to individualize and monitor effects of rehabilitation efforts. Our hypothesis is that HGS is associated with fatigue and physical activity in individuals with, but not without COPD. The objective of this population-based study was to investigate if: 1) hand grip strength is associated to fatigue, and specifically clinically relevant fatigue, among individuals with and without COPD; 2) hand grip strength is associated to low physical activity among individuals with and without COPD; and 3) hand grip strength is associated to fatigue among individuals with and without COPD, independent of physical activity level.

Methods

Design

The cross-sectional data were collected from the population-based Obstructive Lung Disease in Northern Sweden (OLIN) longitudinal COPD study, and the study design has previously been described in detail (Lindberg and Lundback, 2008). The study was approved by the Regional Ethical Review Board at Umeå University, Sweden. All participants gave written informed consent before data collection.

Participants

All individuals with airway obstruction, $FEV_1/(F)VC < 0.70$ (COPD, $n = 993$), were identified from four adult population-based adult cohorts during 2002–2004, together with a sex- and age-matched reference group without obstructive lung function impairment (non-COPD). The study population ($n = 1\ 986$; 902 women, 1,084 men) has been invited to annual examinations since

2005 with a basic program including spirometry and a structured interview (Lindberg and Lundback, 2008). The current study is based on data collected during 2014 when measurements of HGS as well as questionnaires for assessment of fatigue and physical activity were included in addition to the basic program. In total 831 individuals, whereof 389 with COPD participated (Figure 1).

Outcome measures

HGS was measured by a hand-grip dynamometer, Jamar® (Mathiowetz, Weber, Volland, and Kashman, 1984), in kilogram (kg). The participants were instructed to sit down with their elbows flexed at an angle of 90 degrees, with the dynamometer held by the hand in a neutral position (Bohannon et al., 2006). Three attempts were performed with each hand, and the highest value was used for analysis.

Fatigue was assessed by the validated and symptom-specific questionnaire, the Functional Assessment of Chronic Therapy-Fatigue (FACIT-Fatigue) (Al-Shair et al., 2012; Cella et al., 2002). The scale has 13 items and measures the intensity of fatigue and its impact on daily life during the last week, with a higher score (0–52) indicating less fatigue. Clinically relevant fatigue (CRF) was defined as a FACIT-Fatigue score of ≤ 43 (Cella et al., 2002; Stridsman, Mullerova, Skar, and Lindberg, 2013).

Physical activity was assessed with the Swedish version of the International Physical Activity Questionnaire (IPAQ) short form modified for the elderly (Hurtig-Wennlof, Hagstromer, and Olsson, 2010), previously used in COPD research (Andersson et al., 2015; Todt et al., 2015). The total time is weighted by a metabolic equivalent of task, MET (1 MET = resting metabolic rate, $3.5\text{ ml O}_2\text{ kg}^{-1}\cdot\text{min}^{-1}$), resulting in a body weight-adjusted activity estimate, expressed as MET-minutes/week (min/w). Physical activity was categorized into three levels: 1) low; 2) moderate; and 3) high, based on reported time of walking, moderate and/or vigorous activity, in combination with a weighted factor for the different activities (International Physical Activity Questionnaire, 2005). Low activity was defined as not meeting the recommended minimum physical activity level defined as at least 30 min of moderate physical activity five days of the week (Garber et al., 2011; Nelson et al., 2007).

The spirometry was performed using a dry volume spirometer, Minhjard Vicatest, according to American Thoracic Society standards (American Thoracic Society, 1995) but with a repeatability criterion of 5%. COPD was defined as $FEV_1/\text{best of VC or FVC} < 0.70$, using the highest value pre- or post-bronchodilation, and severity-grading was based on $FEV_1\%$ of predicted value according to the Global Initiative for Chronic Obstructive Lung

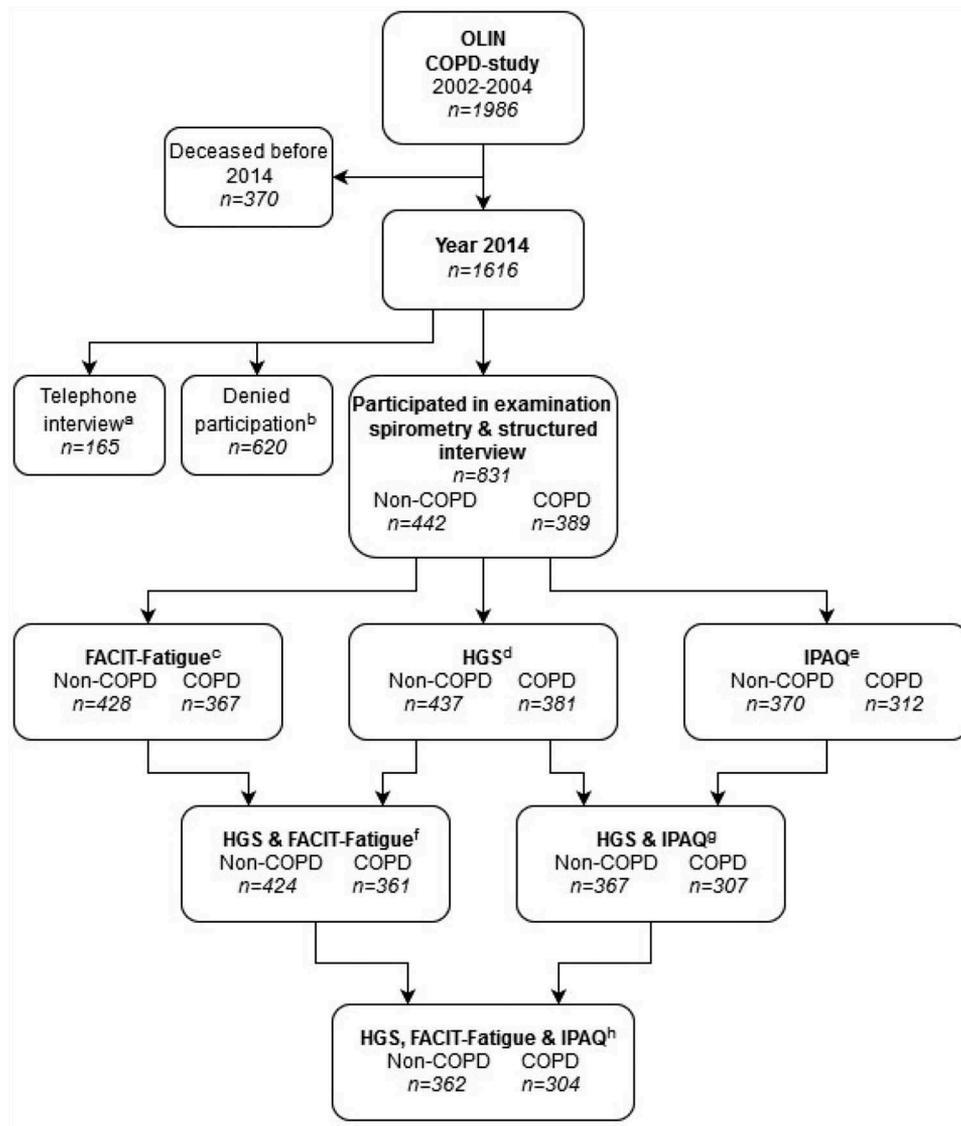


Figure 1. Flow chart, recruitment of study population.

Notes: ^aIndividuals who were unable to attend examination; ^bIndividuals who denied participation or could not be located; ^cIndividuals with complete data on FACIT-Fatigue; ^dIndividuals with complete data on HGS; ^eIndividuals with complete data on IPAQ; ^fIndividuals with complete data on HGS & FACIT-Fatigue; ^gIndividuals with complete data on HGS & IPAQ; ^hIndividuals with complete data on HGS, FACIT-Fatigue & IPAQ.

Disease (GOLD) document, GOLD 1–4 (Vogelmeier et al., 2017). In 21 cases spirometry was missing, and in those cases the latest previous spirometry was used (2010–2013). The OLIN reference values based on healthy non-smokers were applied for FEV₁ (Backman et al., 2015).

Data analysis

All analyses were stratified by sex. All individuals with complete data on spirometry and HGS, FACIT-Fatigue or IPAQ, respectively or combinations thereof, were included in the analysis (Figure 1). Differences in proportions were analyzed with the Chi-2 test, and

differences in mean values between groups were analyzed with the student's *t*-test. The non-parametric Mann-Whitney *u*-test was used for non-normally distributed data. *P*-values < 0.05 were considered statistically significant. The relationships between HGS, fatigue, and physical activity among individuals with respectively without COPD were analyzed by multiple linear regression in three different models, I-III, including fatigue (I), low (II), or both (III). All models were adjusted for age, height, and smoking habits. Statistical analyses were performed with Statistical Package for the Social Sciences, Version 23 (IBM Corporation, Armonk, NY, USA).

Results

Basic characteristics of the study population are shown in Table 1. The COPD group included (n = women/men): GOLD 1; n = 87/96, GOLD 2; n = 72/107, and GOLD 3–4; n = 5/14. Respiratory symptoms and current smoking were more common among those with than without COPD. Mean HGS was significantly lower in COPD than non-COPD among both women and men (Table 1).

Fatigue in non-COPD and COPD by sex, and association with HGS

Among men, but not women, the median FACIT-Fatigue score was lower, and the proportion with clinically relevant fatigue (CRF) was higher in COPD than non-COPD (Table 2). Among individuals with COPD, those with CRF had lower mean HGS than those without CRF, significantly so among men ($p = 0.001$) and close to among women ($p = 0.051$), while in non-COPD corresponding comparisons were non-significant. Among men with CRF, those with COPD had lower HGS than those without (Table 3).

Physical activity in non-COPD and COPD by sex, and association with HGS

Among women, the distribution of the proportions with low, moderate and high physical activity level differed between COPD and non-COPD, and MET min/w was 33.5% lower among women with than without COPD ($p = 0.002$) (Table 2). Corresponding analyses among men revealed no significant differences. In both sexes, the proportion with low physical activity level was similar among those with and without COPD; among women 13.6% and 10.4% ($p = 0.386$), and among men 18.9% and 13.3% ($p = 0.140$). HGS was also similar among individuals with low physical activity and moderate-to-high activity in all groups (Table 4). Among men with low physical activity, HGS was lower among those with than without COPD, while corresponding findings were found among women with moderate-high physical activity (Table 4).

Associations between HGS, fatigue, and physical activity

Among men with COPD, HGS was associated with FACIT-fatigue score also when adjusted for age, smoking

Table 1. Basic characteristics of individuals participating in clinical examination and measure of hand grip strength (HGS), comparing individuals with and without COPD, among women and men, respectively.

Variables	Women			Men		
	Non-COPD n = 198 ^a	COPD n = 164 ^a	<i>p</i> -value ^b	Non-COPD n = 239 ^a	COPD n = 217 ^a	<i>p</i> -value ^b
Age, mean (SD)	70.3 (9.8)	72.8 (8.7)	0.011	70.1 (9.0)	71.6 (9.0)	0.083
Smoker, n (%)	17 (8.6)	29 (17.7)		10 (4.2)	45 (20.5)	
Ex smoker, n (%)	71 (35.9)	75 (45.7)		122 (51.0)	116 (53.5)	
Non smoker, n (%)	110 (55.6)	60 (36.6)	<0.001	107 (44.8)	56 (25.8)	<0.001
Height, mean (SD)	160.3 (6.7)	159.8 (6.6)	0.460	173.8 (7.1)	174.3 (6.7)	0.425
BMI, kg/m ² , mean (SD)	27.8 (4.7)	26.6 (4.6)	0.015	27.4 (3.73)	26.9 (4.0)	0.111
FEV ₁ ,% pred, mean (SD)	99.4 (14.0)	81.2 (15.9)	<0.001	95.1 (13.4)	76.5 (17.5)	<0.001
Any respiratory symptoms, n(%)	77 (38.9)	97 (59.1)	<0.001	105 (44.9)	147 (67.7)	<0.001
Heart disease, n (%)	18 (9.1)	21 (12.8)	0.225	46 (19.2)	51 (23.5)	0.296
HGS, mean (SD)	24.6 (6.8)	22.8 (5.5)	0.008	43.3 (9.6)	41.1 (9.5)	0.013

Notes: ^aIndividuals with complete data on HGS; ^bComparing non-COPD and COPD, *p*-values < 0.05 in bold

Abbreviations: BMI, Body mass index; HGS, Hand grip strength; FEV₁,% pred, Forced expiratory volume in one second percent of predicted; SD, Standard deviation

Table 2. Comparing A) fatigue assessed by the FACIT-fatigue questionnaire, and B) physical activity assessed by the IPAQ questionnaire, between individuals with and without COPD, among women and men, respectively.

Variables	Women			Men		
	Non-COPD	COPD	<i>p</i> -value ^a	Non-COPD	COPD	<i>p</i> -value ^a
Fatigue						
A	n = 195 ^b	n = 155 ^b		n = 233 ^b	n = 212 ^b	
FACIT-Fatigue, median (IQR)	48 (43–51)	47 (39–50)	0.098	48 (43–51)	46 (39–50)	0.002
CRF, n (%)	54 (27.7)	55 (35.5)	0.118	64 (27.5)	81 (38.2)	0.016
IPAQ						
B	n = 164 ^c	n = 134 ^c		n = 206 ^c	n = 178 ^c	
IPAQ category Low, n (%)	17 (10.4)	19 (14.2)		28 (13.6)	33 (18.5)	
IPAQ Moderate	52 (31.7)	64 (47.8)		55 (26.7)	48 (26.8)	
IPAQ High	95 (57.9)	51 (38.1)	0.003^b	122 (59.2)	97 (54.5)	0.382 ^b
METmin/w, median (IQR)	3 649 (1 926–5 358)	2 428 (1 358–4 638)	0.002	3746 (1 773–6 635)	3 356 (1 145–5 999)	0.315

Notes: ^aComparing non-COPD and COPD, *p*-values < 0.05 in bold; ^bIndividuals with complete data on FACIT-Fatigue; ^cIndividuals with complete data on IPAQ; ^dComparing the proportions of all three IPAQ categories between non-COPD and COPD.

Abbreviations: CRF, Clinically relevant fatigue; IPAQ, International Physical Activity Questionnaire; MET, Metabolic equivalent of task; IQR, Interquartile range

Table 3. Comparing mean HGS (SD) among those with and without clinically relevant fatigue (CRF) in COPD and non-COPD, among women and men, respectively.

Categories	Women		p-value ^b
	Non-COPD n = 194 ^a	COPD n = 152 ^a	
	Mean HGS (SD)	Mean HGS (SD)	
Non-CRF	25.1 (6.5)	23.7 (5.0)	0.054
CRF	23.2 (7.2)	21.9 (5.9)	0.323
p-value	0.069 ^c	0.051 ^d	

Categories	Men		p-value ^b
	n = 230 ^a	n = 209 ^a	
	Mean HGS (SD)	Mean HGS (SD)	
Non-CRF	44.2 (9.5)	43.1 (8.7)	0.313
CRF	42.0 (9.2)	38.6 (9.7)	0.035
p-value	0.114 ^c	0.001^d	

Notes: ^aIndividuals with complete data on HGS and FACIT-Fatigue; ^bComparing mean HGS between non-COPD and COPD; ^cComparing mean HGS between non-CRF and CRF in non-COPD; ^dComparing mean HGS between non-CRF and CRF in COPD. CRF is defined as a FACIT-Fatigue score of ≤ 43 . Abbreviations: HGS, Hand grip strength; CRF, Clinically relevant fatigue; SD, standard deviation

Table 4. Comparing mean HGS (SD) between those with a category of low and moderate/high physical activity level according to IPAQ, among women and men, respectively.

Categories	Women a		p-value ^b
	Non-COPD n = 164 ^a	COPD n = 132 ^a	
	Mean HGS (SD)	Mean HGS (SD)	
IPAQ Low	25.5 (9.0)	23.8 (4.5)	0.506
IPAQ Moderate-High	25.2 (6.7)	22.8 (5.4)	0.002
p-value	0.875 ^c	0.459 ^d	

Categories	Men		p-value ^b
	n = 203	n = 175	
	Mean HGS (SD)	Mean HGS (SD)	
IPAQ Low	45.7 (10.3)	39.6 (9.7)	0.022
IPAQ Moderate-High	43.6 (9.1)	42.6 (9.1)	0.318
p-value	0.103 ^c	0.121 ^d	

Notes: ^aIndividuals with complete data on HGS and IPAQ; ^bComparing mean HGS between non-COPD and COPD; ^cComparing mean HGS between IPAQ low and IPAQ moderate-high in non-COPD; ^dComparing of mean HGS between IPAQ low and IPAQ moderate-high in COPD. Abbreviations: HGS, Hand grip strength; IPAQ, International Physical Activity Questionnaire; SD, standard deviation

habits, and height (model I), and it was independent of physical activity level (model III) (Table 5). These associations remained significant also when COPD disease severity, assessed as FEV₁% of predicted, was included in the models. Among women with COPD, as well as among men or women without COPD, the corresponding analyses yielded no significant results (Table 5). When substituting FACIT-Fatigue score with CRF in the models, the association with HGS among men with COPD in model I, but not in model III, remained significant (Beta = - 2.66, 95% CI -4.61 to -0.70).

Discussion

To the best of our knowledge, this is the first study, which is also a population-based study, to investigate the relationship between hand grip strength, fatigue, and physical activity among men and women, with and without COPD. Among individuals with COPD, those with clinically relevant fatigue had lower mean HGS compared to those without, significantly so among men, and close to among women. There were no differences in HGS when comparing individuals with low physical activity and those with moderate-to-high physical activity in any of the groups. Among men, but not women with COPD, HGS was associated with fatigue also after adjustment for age, smoking habits, and height, and this association was independent of physical activity level as well as disease severity assessed as FEV₁% of predicted. Corresponding analyses among individuals without COPD yielded no significant results.

In this report, based on data collected in 2014, mean HGS was lower among individuals with than without COPD, although no such difference was observed in the same cohort 5 years earlier (Strandkvist et al., 2016). Without a direct comparison between the groups over time, the differences are hard to evaluate. There may be differences in the process of aging among individuals with and without COPD (MacNee, 2016), but also differences regarding muscle strength associated with changes in physical activity over time. However, the observed increased fatigue and decreased physical activity level among individuals with COPD when compared to those without COPD is similar as previously found (Andersson et al., 2015; Stridsman, Mullerova, Skar, and Lindberg, 2013).

The current study indicates that there is an association between fatigue and HGS among individuals with COPD; those with CRF had lower HGS than those without. Our results correspond well with the findings in a previous study where quadriceps muscle strength predicted both physical and general fatigue among patients with COPD when assessed by the Multidimensional Fatigue Inventory questionnaire (Lewko, Bidgood, and Garrod, 2009). In our study, fatigue was associated with HGS independent of height, age, smoking habits, and low physical activity among men with COPD, while corresponding analyses among women yielded no significant results. However, we did no direct comparison between men and women. It has been reported that women with severe COPD suffer more from fatigue than men (Gift and Shepard, 1999), while another study concluded that there were no

program for individuals with COPD may improve muscle strength, fatigue as well as physical activity (Bolton et al., 2013). Individuals with COPD suffering from fatigue described that physical activity, such as walks or exercise, contributed to control their fatigue (Stridsman, Lindberg, and Skar, 2014). Exercise capacity and the experience of fatigue are associated among both men and women, and it has been suggested that endurance exercise training might have beneficial effects on fatigue (Todt et al., 2014). However, fatigue may also be an obstacle to COPD rehabilitation: among patients who chose not to participate or withdrew from the participation in a pulmonary rehabilitation program, lack of perceived benefit and being unwell were central themes contributing to non-participation. A minor theme was the subjective feeling of fatigue; some participants did not attend rehabilitation due to lack of required energy levels, and some felt too tired to complete the program (Keating, Lee, and Holland, 2011).

The strength of this epidemiological study is the large study population in which classification of COPD was based on post-bronchodilator spirometry. A majority of those with COPD had mild to moderate disease, GOLD 1 and 2, corresponding to what have been shown by other population-based studies (Lindberg et al., 2006). The population-based study design further means that the results will not be affected by the well-known under-diagnosis of COPD, and the results are considered generalizable to COPD in the general population. Another strength is that well-validated methods, measurement of HGS, and questionnaires for assessment of fatigue and physical activity, were used. Further, these three methods are simple, cheap, and easy to implement in clinical practice.

Despite the fact that this study presents new and original data regarding the relationships between HGS, fatigue and physical activity in a population-based setting, it is not possible to evaluate cause and effect due to the cross-sectional study design. Further, when assessing physical activity by a questionnaire, it is common that the study participants overestimate their physical activity, compared to when assessed by objective methods, such as accelerometers (Dyrstad, Hansen, Holme, and Anderssen, 2014). However, this bias is probably fairly evenly distributed, and may thus not affect the comparison between groups or the observed significant associations in the current study.

Conclusion

In this population-based study, individuals with COPD and clinically relevant fatigue had lower hand grip strength than those without clinically relevant fatigue, significantly so among men and close to among women. There was no clear association between hand

grip strength and level of physical activity within any of the groups. Fatigue was associated with hand grip strength among men with COPD also when adjusted for age, smoking habits, and height, independent of physical activity level and disease severity assessed as FEV₁% of predicted. No such associations were found in corresponding analyses among women with COPD or individuals without COPD. The relationships between hand grip strength, fatigue, and physical activity are complex, however, each of them is a possible target of interventions. We suggest further evaluation of these simple and cheap methods, easy to implement in clinical practice, as screening tools to identify individuals with COPD for rehabilitation and for follow-up during rehabilitation programs.

Declaration of interest

The authors declare no conflict of interest toward this study.

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