



Decreased physical activity in adults with bronchial asthma



Alex J. van 't Hul^{a,*}, Siete Frouws^b, Edmee van den Akker^c, Rob van Lummel^{b,d},
Anja Starrenburg-Razenberg^c, Alie van Bruggen^c, Gert-Jan Braunstahl^c,
Johannes C.C.M. in 't Veen^c

^a Radboudumc, Department of Pulmonary Diseases, Nijmegen, The Netherlands

^b McRoberts, The Hague, The Netherlands

^c Sint Franciscus Gasthuis, Department of Pulmonary Medicine, Rotterdam, The Netherlands

^d MOVE Research Institute, Faculty of Human Movement Sciences, Amsterdam, The Netherlands

ARTICLE INFO

Article history:

Received 18 November 2015

Received in revised form

12 February 2016

Accepted 21 March 2016

Available online 22 March 2016

Keywords:

Bronchial asthma

Physical activity

Asthma control

Activity monitor

ABSTRACT

Contradictory findings have been reported in the literature on the impact that bronchial asthma may have on habitual physical activity. The present study was designed to compare physical activity, objectively measured with an activity monitor, between adults with bronchial asthma and apparently healthy controls.

Valid registrations of physical activity were obtained in 226 patients with asthma and 201 healthy controls. A multiple general linear model was used to test between group differences and to correct for confounding of the results due to between group differences in BMI and employment status.

In the patients, statistically significantly lower values were found for average steps/day (−1202; CI −1893 to −511; $P = 0.001$), physical activity level based on an estimate of a person's total energy expenditure (−0.035; CI −0.067 to −0.003; $P = 0.034$) and daily time (minutes) spent at vigorous intensive physical activity (−11; CI −17 to −1; $P < 0.001$). In addition, weak albeit significant correlations were found between measures of physical activity and asthma control.

We conclude that bronchial asthma in adults is associated with a significant reduction in physical activity as compared to apparently healthy controls and is accompanied by a lower perceived health status. This is in support of the postulation of PA as potential pathway to better the outcome of care for these patients.

© 2016 Elsevier Ltd. All rights reserved.

1. Introduction

Habitual physical activity (PA) appears to have a protective role on the development of chronic illness in general, as well as in developing bronchial asthma both in children and adults, specifically [1,2]. Moreover, habitual PA seems to be a determinant of the burden of disease in asthmatics. For instance, studies showed a significant association between PA on the one hand, and on the other hand, the likelihood of reporting an asthma exacerbation over 1 year as well as the frequency of seeking medical assistance [3,4]. Conversely, physical training may safely and significantly improve exercise capacity and is found to be associated with improved disease control in adults with asthma [5,6].

Patients diagnosed with bronchial asthma may be susceptible to reduced levels of PA, because exercise and strenuous physical activities are renowned triggers of bronchoconstriction in these patients, resulting in exertional dyspnoea and other respiratory symptoms with exercise avoidance and deconditioning as potential consequence [7]. Indeed, a recent review of the literature on bronchial asthma and aerobic exercise concluded that individuals with asthma are less likely to engage in physical activity than those without asthma [8]. However, two other recent studies showed an absence of reduced PA in asthmatics [9,10]. In addition, an annual survey in the Netherlands concluded that PA of people with bronchial asthma was comparable to the general Dutch population [11].

An important limitation of all published studies on PA in bronchial asthma so far, is the use of subjective, self-report measures of PA, i.e. questionnaires merely. Imperfect measurement properties of PA questionnaires and diaries have been well-documented [12]. Hence, PA is preferably measured with so-called activity monitors.

* Corresponding author. Radboudumc Department of Pulmonology, Internal Postal Code 614, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands.

E-mail address: alex.vanthul@radboudumc.nl (A.J. van 't Hul).

Newly developed technology, using accelerometers, is able to distinguish bodily postures (lying, sitting, standing), has sensitivity to capture also light activities, allows the detection of exercise intensity and to make reliable estimates of energy expenditure [13]. To the best of our knowledge, PA has never been systematically assessed in adults with asthma using accelerometer technology.

The present study aims to compare the level of objectively measured free-living PA between adults with bronchial asthma and an apparently healthy control group.

2. Materials and methods

The present study is a prospective, cross-sectional study with the aim to compare PA between adult patients with bronchial asthma and an apparently, healthy control group, taking into account potential confounding by sex, employment status, age and body mass index.

2.1. Participants

In total 226 adult patients with bronchial asthma were available for this study. All these patients were newly referred to the outpatient clinic of the pulmonary department of a Dutch Teaching Hospital (Sint Franciscus Gasthuis, Rotterdam, The Netherlands) between January 2013 and March 2015, by their family physician, because of an unsatisfactory response to treatment in primary care. Inclusion criteria were as follow:

(1) Chest physician confirmed diagnosis of bronchial asthma according to Global Initiative for Asthma (GINA) guidelines [14]; (2) on medication regimen as installed by the referring family physician; (3) relative stable state of disease without exacerbation for at least 6 weeks; (4) absence of co-morbidities interfering with PA; (5) age ≥ 18 years.

In addition, 201 apparently healthy subjects could be recruited among employees and relatives of the Sint Franciscus Gasthuis, between January and May 2014, to serve as control group. In order to obtain a convenient control group, employees of different disciplines were approached, i.e. housekeeping, administrative personnel, nurses and physicians. Inclusion criteria were as follow: (1) absence of a known pathologic condition that could impair PA in daily life; (2) a 'no' to all of the following 3 questions: (a) have you ever been diagnosed with asthma, (b) have you ever used inhalation medication for asthma or bronchitis, (c) have you had episodes of shortness of breath in the past 12 months; (3) not involved in strenuous competitive sports activities; (4) absence of co-morbidities interfering with PA; (5) not using drugs for any medical condition; (6) age ≥ 18 years.

2.2. Study procedures

All patients participated in a standardized, diagnostic care pathway for patients with obstructive lung disease in a hospital outpatients setting [15]. This pathway consisted of 2 consecutive sessions of 2–3 h each, separated by one week, in which all assessments were carried out. In the intermediary week, a validated activity monitor measured PA and medication regimes were unaltered.

Control subjects were recruited among personal and relatives of different departments within the hospital via leaflets and 'word-of-mouth'. The same activity monitor was used as in the patients for a similar period of time. However, the controls did not undergo pulmonary function testing, nor were they submitted to the asthma specific health status questionnaires.

The Medical Ethics Committee of the Sint Franciscus Gasthuis declared that this study was outside the remit of the Medical

Research Involving Human Subjects Act (in Dutch: WMO) and gave a written confirmation that neither medical ethical approval nor written informed consent from participants was needed for this kind of study. In the patients, all measurements were part of the routine care in our clinic and data were anonymously processed. Moreover, the wearing of the DynaPort activity monitor was judged not to be harmful, to have a negligible effect on human behavior and not to affect or restrict daily functioning.

2.3. Clinical characteristics of the patients

All patients performed standardized spirometry according to guidelines of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) in order to evaluate the presence and reversibility of airway obstruction on inhalation of 400 mg salbutamol [16]. Asthma control was measured with the Asthma Control Questionnaire (ACQ) and quality of life with the Asthma Quality of Life Questionnaire (AQLQ). Based on the scores of the ACQ, patients were classified as controlled (score < 0.75), partially controlled (score 0.75–1.5) or having uncontrolled bronchial asthma (score > 1.5) [17,18].

2.4. Assessment of physical activity

2.4.1. Activity monitoring device

The DynaPort® MoveMonitor® (McRoberts, The Hague, The Netherlands) activity monitor was used to measure free-living physical activity. The DynaPort consists of a small ($85 \times 58 \times 12$ mm), light case (78 g) containing three orthogonally mounted acceleration sensors, a rechargeable battery, a USB connection and a MicroSD card for raw data storage (204 h). The monitor is worn over the lower lumbar spine, close to the sacrum. The acceleration sensors uses a seismic sensor that responds to both slow and fast changes in acceleration (sample frequency = 100 Hz). These features enable posture as well as motion detection of the subjects. Reliability and validity of the DynaPort MoveMonitor has been extensively documented, most recently in an evaluation by the ProActive consortium [13]. McRoberts MoveMonitor software version 2.8.1 was used to analyze the data from the DynaPort.

Patients as well as control subjects were instructed to wear the monitor for 7 consecutive days, 24 h per day, except while taking a shower or bath and during swimming. They were asked to perform their regular PA as usual. This resulted in a maximum of 6 full days of wearing. Only days with a wearing time of at least 22.5 h were used in the analyses [19]. Patients and subjects were merely included in the analyses if data were available of at least two days of observation for activities and of at least five days for lying, as it has been shown recently, that these are the minimum requirements to obtain reliable registrations [20].

The following aspects of PA of interest were a priori defined:

1. Compliance with wearing the device, i.e. the number of days when the device was worn for at least 22.5 h/day
2. The daily average time spent in walking, sitting and lying.
3. The number of steps per day. An average of $> 12,500$ steps/day has been proposed to classify subjects as highly active, 10,000–12,500 as active, 7,500–10,000 as somewhat active, 5,000–7,500 as low active and $< 5,000$ as inactive [21].
4. Physical activity level (PAL). PAL is a way to express a person's daily physical activity as a number, and is used to estimate a person's total energy expenditure. A PAL > 1.70 defines an active person, 1.40–1.69 defines a predominantly sedentary person, and < 1.40 defines a very inactive person [19].
5. The time spent at pre-defined levels of energy expenditure:

Light physical activity was defined as an estimated energy expenditure of <3 metabolic equivalents (METs).

The threshold for moderate physical activity was set between 3 and 6 METs.

Vigorous physical activity was defined as physical activity performed at an intensity >6 METs [22].

The data reported represent the mean values calculated over the valid days, i.e. days with a wearing time of at least 22.5 h.

2.4.2. Marshall questionnaire

The Marshall questionnaire is a short, two-item questionnaire allowing subjects to subjectively report compliance with the PA recommendations of the American College of Sports Medicine (ACSM). A score ≥ 4 points indicate good compliance with these recommendations [23].

2.5. Statistical analyses

All analyses were performed on de-identified data in IBM SPSS Statistics (Version 22.0, Armonk, NY: IBM Corp). A valid registration of PA was obtained in 226 out of 236 asthmatics and in 201 out of 216 controls. First, between group differences were checked for sex, employment status, age and BMI using independent T-test and χ^2 test, as these factors are potential confounders for a between group comparison of PA. Statistically significant differences were observed between the 226 patients and the 201 control subjects for sex ($P = 0.003$), employment status ($P < 0.001$), age ($P = 0.001$) and BMI ($P < 0.001$). To check for confounding, linear regression analysis was used. The first step was creation of a linear prediction model for steps/day by group (asthma or control). From these results, the linear regression coefficients (RC) for group (2202 steps/day, $P < 0.001$) present the mean difference between asthmatics and controls in steps/day. In the second step were sex, employment status, age and BMI added to the linear prediction model one by one. A change of more than 10% of the RC was taken as the arbitrary threshold for significant confounding [24]. This was found only for employment status and BMI. In the third and last step a multivariate general linear model was used to test between group differences with the a priori defined measures of PA as dependent variable, group assignment (asthmatics or controls) as fixed factor and employment status and BMI as covariates. A Bonferroni correction was applied to adjust for multiple comparisons. Characteristics of patients and healthy controls are presented as mean and SD (normally distributed variables) or number and percent (dichotomous variables).

3. Results

3.1. Characteristics of the study population

Demographic characteristics of all subjects are provided in Table 1.

Post-bronchodilator pulmonary function as well as health status measurements of the asthmatics are given in Table 2.

Table 1
Demographic characteristics of all subjects.

	Asthmatics (n = 226)	Controls (n = 201)	P-value
Female/male	140/86	152/49	<0.002
Employment (yes/no)	117/109	187/14	<0.001
Age (years)	47.3 $\pm$ 15.3	42.3 $\pm$ 16.3	=0.001
BMI (kg.m ⁻²)	29.8 $\pm$ 6.3	25.1 $\pm$ 4.3	<0.001

Values are expressed as n or mean $\pm$ SD. BMI: body mass index.

Table 2

Pulmonary function measurements and health status measurements of the asthmatics.

	Asthmatics (n = 226)
FEV ₁ (L) (% pred)	2.84 $\pm$ 0.84 (87 $\pm$ 21)
FVC (L) (% pred)	4.09 $\pm$ 1.10 (105 $\pm$ 18)
FEV ₁ /FVC (%)	70 $\pm$ 13
FVCrev (L) (%)	0.13 $\pm$ 0.22 (4 $\pm$ 7)
FEV ₁ rev (L) (%)	0.22 $\pm$ 0.18 (9 $\pm$ 8)
ACQ	1.75 $\pm$ 0.96
ACQ [#]	
Controlled	38 (17%)
Partially controlled	41 (18%)
Uncontrolled	147 (65%)
AQLQtotal	5.15 $\pm$ 1.14
AQLQsymp	5.12 $\pm$ 1.06
AQLQactlim	5.04 $\pm$ 1.50
AQLQemot	5.19 $\pm$ 1.61
AQLQenviron	5.23 $\pm$ 1.39

Values are expressed as mean $\pm$ SD. FEV₁: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; FVCrev: FVC reversibility on 400 μ g Salbutamol; FEV₁rev: FEV₁ reversibility on 400 μ g Salbutamol; ACQ: Asthma Control Questionnaire; [#]: ACQ categorized as: controlled asthma, ACQ < 0.75; partially controlled asthma, ACQ 0.75–1.5; uncontrolled asthma, ACQ > 1.5; AQLQtotal: Asthma Quality of life Questionnaire total score; AQLQsymp: Asthma Quality of life Questionnaire symptoms score; AQLQactlim: Asthma Quality of life Questionnaire activity limitation score; AQLQemot: Asthma Quality of life Questionnaire emotional function score; AQLQenviron: Asthma Quality of life Questionnaire environmental stimuli score.

3.2. Wearing compliance

Wearing compliance of the DynaPort was very high in the asthma patients. Valid data were available in 226 out of the 236 patients (96%). Six patients were excluded because of a bad-wearing compliance and another four could not be used because of an unexplainable device malfunction. In the control group, wearing compliance was slightly lower but still very acceptable with valid data of 201 out of the 216 subjects (93%). Thirteen control subjects were excluded because of a bad-wearing compliance and another two could not be used because due to an unexplainable device malfunction. The number of days with a valid registration of PA did not differ significantly between asthmatics and controls ($P = 0.90$).

3.3. Comparison of PA between asthmatic patients and healthy controls

Table 3 provides the outcome of the multivariate general linear model. In five out of the eight a priori determined objective PA parameters of interest, significant between group differences were found.

Figs. 1 and 2, represents the distribution of steps/day categories and PAL categories, respectively, in the asthmatic patients and healthy control subjects. A 5 times higher number of patients had less than 5000 steps/day. Eighteen percent of the patients had a PAL of less than 1.4, whereas only four percent of the controls had such a low score.

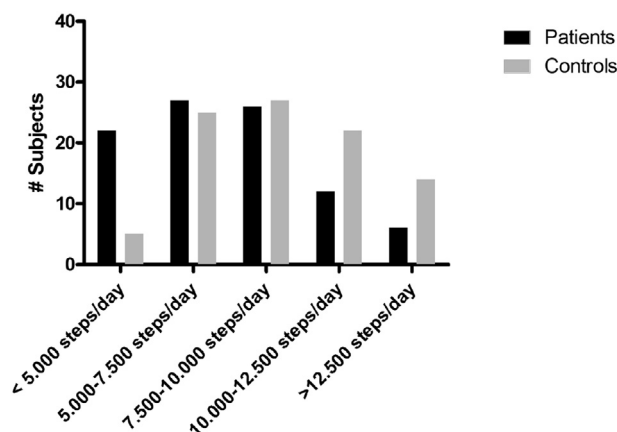
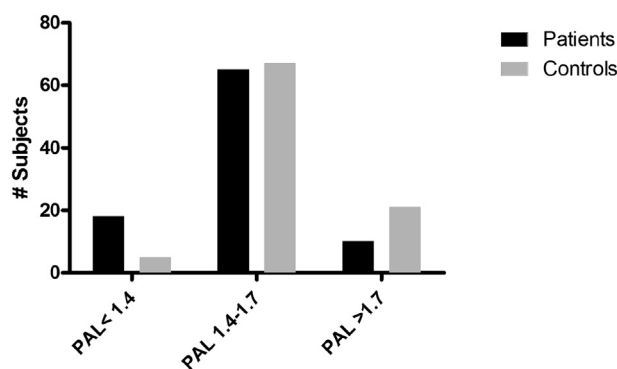
3.4. PA and health status in asthmatics

Significant correlation coefficients were found between ACQ and PAL ($r = -0.23$; $P = 0.001$), ACQ and steps/day ($r = -0.20$; $P = 0.004$) and ACQ and time spent at vigorous exercise (>6 METs) ($r = -0.30$; $P < 0.001$). Between asthmatic patients subdivided according to their ACQ category, significant differences were observed for PAL: 1.58 $\pm$ 0.18 (well controlled) versus 1.54 $\pm$ 0.13 (partially controlled) versus 1.49 $\pm$ 0.13 (uncontrolled); $P = 0.002$,

Table 3

Physical activity comparison between asthmatics and controls.

	Asthmatics (n = 226)	Controls (n = 201)	Mean difference (CI)	P-value
Marshall Score (pts.)	3.97 (3.61–4.32)	4.28 (3.88–4.67)	–0.31 (–0.90–0.27)	0.29
Time spent walking (hrs.)	1.49 (1.41–1.57)	1.161 (1.53–1.70)	–0.13 (–0.25–0.01)	0.043
Time spent sitting (hrs.)	8.21 (7.95–8.48)	8.58 (8.29–8.86)	–0.36 (–0.78–0.06)	0.091
Daily lying time (hrs.)	10.73 (10.46–11.01)	10.14 (9.85–10.44)	0.59 (0.15–1.03)	0.008
Steps	7593 (7155–8030)	8795 (8326–9263)	–1202 (–1893–511)	=0.001
PAL	1.53 (1.51–1.55)	1.57 (1.55–1.59)	–0.035 (–0.067–0.003)	=0.034
Time spent at light intensive PA (hrs.)	1.76 (1.65–1.88)	1.91 (1.80–2.02)	0.15 (–0.02–0.31)	0.093
Time spent at moderate intensive PA (hrs.)	1.66 (1.58–1.74)	1.64 (1.55–1.72)	0.03 (–0.10–0.15)	0.679
Time spent at vigorous intensive PA (hrs.)	0.34 (0.30–0.38)	0.45 (0.41–0.49)	–0.11 (–0.17–0.005)	<0.001

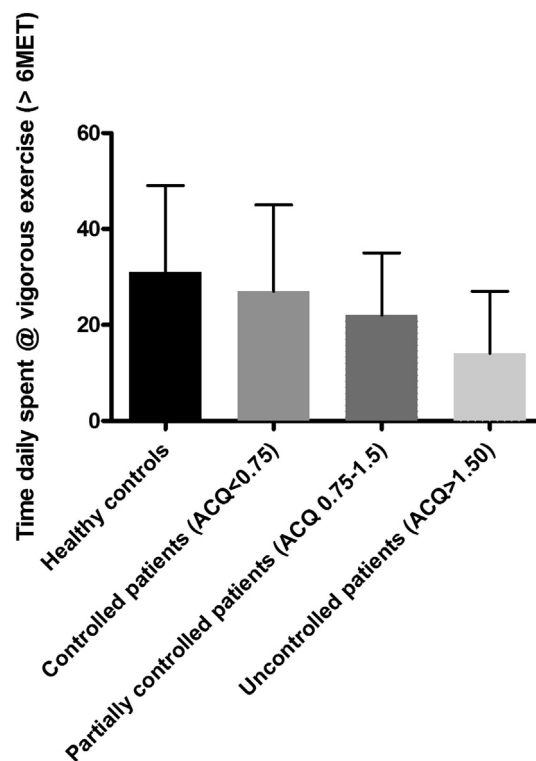
**Fig. 1.** Distribution of the steps/day categories in asthmatics and healthy controls.**Fig. 2.** Distribution of the PAL categories in asthmatics and healthy controls.

for steps/day 8169 ± 3225 (well controlled) versus 8244 ± 2621 (partially controlled) versus 6712 ± 3153 (uncontrolled); $P = 0.005$, and time spent at vigorous exercise (>6 MET): 27 ± 22 versus 22 ± 13 versus 14 ± 13 min/day; $P < 0.001$, for controlled, partially controlled and uncontrolled asthma, respectively. Fig. 3 provides a graphic presentation of the daily time spent at vigorous exercise in healthy controls and asthmatic patients subdivided according to their ACQ category.

4. Discussion

4.1. Main findings

To the best of the authors knowledge this is the first study ever performed in adults with bronchial asthma, using an objective activity monitor to evaluate levels of PA. Our main finding is, that PA is

**Fig. 3.** Daily time spent at vigorous exercise in health controls and asthmatics subdivided according to the ACQ category.

statistically significant lower in adult asthmatics referred to a pulmonologist as compared to an apparently healthy control group. Patients with bronchial asthma had on average, significantly less steps per day (1200), had a 0.035 lower PAL and spent on average 11 min. less at a vigorous exercise intensity per day. In addition, a low habitual PA was found to be associated with poorer asthma control.

4.2. Strengths and limitations of this study

The validity of the findings in our study is strengthened because it comprised: (1) the inclusion of patients only with a pulmonary physician confirmed diagnosis of bronchial asthma, (2) the objective measurement of PA using a validated activity monitor, and, (3) data were checked and corrected for confounders in between group PA comparisons.

Because all patients referred to our secondary care facility (SFG) during the study period were allocated to our care path, hence included in the present study, patient selection bias was minimized. However, since all patients entering the study were referred

to a pulmonologist our results may not convey to all patients with asthma. Patients referred to secondary care are expected to have a higher impact of the disease on health status. Indeed, in a recent study performed in 12 primary care practices in the UK showed considerable more patients with an ACQ score <2.0 than in our observation (79% versus 43%) [25]. Another study, carried out in primary care in the Netherlands by Metting et al. showed fewer patients with uncontrolled asthma (39% versus 65%) compared to the number in our study [26].

Specific features of the asthma such as presence of exercise induced bronchoconstriction, time of onset of asthma and the medication regime patients were actually on at the time of referral to secondary care were not systematically collected in the present study. The explanation here fore is that we consider our study as a first study into the topic of objectively measured PA in asthmatics. Subsequent studies may address the important questions of the determinants of a low PA such as more detailed pulmonary function impairments.

Our healthy control group consisted of volunteers of hospital staff and their relatives. Controls were included only if they stated to have no (known) pathological conditions and not to experience respiratory symptoms. We did not perform any formal health examination such as pulmonary function testing due to practical reasons. As a consequence, it cannot be ruled out that some controls were not completely healthy. However, if this had been the case, it would have resulted in an underestimation of the contrast we found in PA between patients and controls.

Although accelerometers are considered the criterion method for measuring free living PA, measurements are accepted as being limited in their ability to measure cycling and water based activities [12]. If in asthmatics a larger portion of habitual PA consists of cycling or swimming, this might have biased our results and would have led to an overestimation of the difference in PA as observed in the present study. However, we deliberately decided to measure PA only objectively and declined to add self reported activities in the analysis, because of their well documented methodological shortcomings [12].

Further, our study was not designed to perform an in depth analysis of potential determinants of a low PA in the asthmatics. In patients with COPD multiple, independent factors are found to be associated with PA of which many go beyond markers of pulmonary function impairment. In fact, the severity of the pulmonary dysfunction turned out to be only weakly correlated with PA in COPD patients [27]. In the present study we did not observe any correlation between PA and spirometric measures in asthmatics. The question is whether spirometry adequately mirrors all pulmonary function abnormalities of asthmatics such as bronchial hyper reactivity and/or exercise induced bronchial constriction. In a subset of asthmatics a histamine provocation test was performed but outcomes of this test did not significantly correlated with measures of PA. This suggests that also in asthmatics other factors than pulmonary function impairment are important determinants of PA. Future studies should address this topic as it might include important clues on the pathways to improve free-living PA in asthmatics.

4.3. Implications

Based on PAL, the vast majority of the asthmatics (70%) could be characterised as 'predominantly sedentary' and another 19% as 'very inactive', whereas grounded on steps/day, 53% could be classified as low active and 24% as inactive. These findings are of clinical relevance because inactivity results in deconditioning with a potential detrimental effect on symptoms, disability and health care use in asthmatics [4]. In the present study we observed a

significant association between on the one hand PA, and on the other hand, asthma control in the patients. This finding is in line with a recent study by Haselkorn et al. among 1812 asthmatic patients in the United States. They also observed that patients with uncontrolled asthma were at higher risk for limitations in outdoor activity, physical activity, and daily activity [28]. Obviously, cross-sectional studies are not suited to give insight into the causal relation between PA and asthma control. However, these findings are in concordance with observations that adults who rate themselves as more active, have been found to perceive themselves as healthy, and suggests that preventing or addressing deconditioning might form an important target for therapy in asthma [29]. Indeed, a systematic review demonstrated that physical training could improve cardiopulmonary fitness [30]. Two other studies showed improvements in asthma control and quality of life after an exercise intervention [6,31]. Recent studies aiming to reveal the mechanism behind improved asthma control through exercise training revealed reduction in bronchial hyperresponsiveness and systematic inflammatory response as potential pathways to explain these improvements [32–34]. Whether better exercise capacity, as results of an effective exercise regimen in asthmatics, converts into higher level of habitual PA has to be determined. In COPD there is considerable more research conducted on this theme but is still topic of debate [27].

Self-judgement of PA in the patients based on the Marshall questionnaire showed that 57 patients (61%) comply with the ACSM recommendations on physical activity. However 48 (83%) of this subgroup had a PAL < 1.7 and not less than 15% had a PAL < 1.4, which can be interpreted as very inactive. These findings confirm the inaccuracy and overestimation of individual perceives of PA in asthmatics as found also in general populations [35,36]. Given the association between PA and disease control in asthmatics we believe it is an important outcome that requires objective measurement not only in research but also in the clinical routine of an outpatient clinic.

5. Conclusions

In summary, results from this cross-sectional comparison between people referred to secondary care and a pulmonary physician confirmed diagnosis of bronchial asthma, and an apparently healthy control group, showed a statistically lower level of habitual PA in asthmatics. The frequent incidence of a low PA and significant association with poor asthma control suggest the clinical significance of a low habitual PA in asthma and is in support of the postulation of PA as potential pathway to better the outcome of care for these patients.

References

- [1] D.E. Warburton, C.W. Nicol, S.S. Bredin, Health benefits of physical activity: the evidence, *Cmaj*. 174 (6) (2006) 801–809.
- [2] M. Eijkemans, M. Mommers, J.M. Draaisma, C. Thijs, M.H. Prins, Physical activity and asthma: a systematic review and meta-analysis, *PLoS One*. 7 (12) (2012) e50775.
- [3] J. Garcia-Aymerich, R. Varraso, J.M. Anto, C.A. Camargo Jr., Prospective study of physical activity and risk of asthma exacerbations in older women, *Am. J. Respir. Crit. Care Med.* 179 (11) (2009) 999–1003.
- [4] S. Dogra, J. Baker, C.I. Arden, The role of physical activity and body mass index in the health care use of adults with asthma, *Ann. Allergy Asthma Immunol.* 102 (6) (2009) 462–468.
- [5] K.V. Carson, M.G. Chandratilleke, J. Picot, M.P. Brinn, A.J. Esterman, B.J. Smith, Physical training for asthma, *Cochrane Database Syst. Rev.* 9 (2013) CD001116.
- [6] S. Dogra, J.L. Kuk, J. Baker, V. Jamnik, Exercise is associated with improved asthma control in adults, *Eur. Respir. J.* 37 (2) (2011) 318–323.
- [7] C.J. Clark, Asthma and exercise: a suitable case for rehabilitation? *Thorax*. 47 (10) (1992) 765–767.
- [8] K.M. Avallone, A.C. McLeish, Asthma and aerobic exercise: a review of the

- empirical literature, *J. Asthma*. 50 (2) (2013) 109–116.
- [9] T. Ritz, D. Rosenfield, A. Steptoe, Physical activity, lung function, and shortness of breath in the daily life of individuals with asthma, *Chest* 138 (4) (2010) 913–918.
 - [10] C. Jerling, E. Martinander, A. Bjerg, et al., Asthma and physical activity - A population based study results from the Swedish GA(2)LEN survey, *Respir. Med.* 107 (11) (2013) 1651–1658.
 - [11] D. Baan, M. Heijmans, Mensen met astma in beweging, Factsheet, NIVEL (2012).
 - [12] F. Pitta, T. Troosters, V.S. Probst, M.A. Spruit, M. Decramer, R. Gosselink, Quantifying physical activity in daily life with questionnaires and motion sensors in COPD, *Eur. Respir. J.* 27 (5) (2006) 1040–1055.
 - [13] H. Van Remoortel, Y. Raste, Z. Louvaris, et al., Validity of six activity monitors in chronic obstructive pulmonary disease: a comparison with indirect calorimetry, *PLoS One* 7 (6) (2012) e39198.
 - [14] From the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA), 2014. Available from: <http://www.ginaasthma.org/>.
 - [15] E.F. van den Akker, A.J. van 't Hul, N.H. Chavannes, et al., Development of an integral assessment approach of health status in patients with obstructive airway diseases: the CORONA study, *Int. J. Chron. Obstruct Pulmon Dis.* 10 (2015) 2413–2422.
 - [16] M.R. Miller, J. Hankinson, V. Brusasco, et al., Standardisation of spirometry, *Eur. Respir. J.* 26 (2) (2005) 319–338.
 - [17] E.F. Juniper, P.M. O'Byrne, G.H. Guyatt, P.J. Ferrie, D.R. King, Development and validation of a questionnaire to measure asthma control, *Eur. Respir. J.* 14 (4) (1999) 902–907.
 - [18] E.F. Juniper, G.H. Guyatt, P.J. Ferrie, L.E. Griffith, Measuring quality of life in asthma, *Am. Rev. Respir. Dis.* 147 (4) (1993) 832–838.
 - [19] H. Watz, B. Waschki, T. Meyer, H. Magnussen, Physical activity in patients with COPD, *Eur. Respir. J.* 33 (2) (2009) 262–272.
 - [20] K.S. van Schooten, S.M. Rispens, P.J. Elders, P. Lips, J.H. van Dieen, M. Pijnappels, Assessing physical activity in older adults: required days of trunk accelerometer measurements for reliable estimation, *J. Aging Phys. Activit.* 23 (1) (2015) 9–17.
 - [21] C. Tudor-Locke, C.L. Craig, Y. Aoyagi, et al., How many steps/day are enough? For older adults and special populations, *Int. J. Behav. Nutr. Phys. Act.* 8 (2011) 80.
 - [22] C.E. Garber, B. Blissmer, M.R. Deschenes, et al., American college of sports medicine position stand. quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise, *Med. Sci. Sports Exerc.* 43 (7) (2011) 1334–1359.
 - [23] A.L. Marshall, B.J. Smith, A.E. Bauman, S. Kaur, Reliability and validity of a brief physical activity assessment for use by family doctors, *Br. J. Sports Med.* 39 (5) (2005) 294–297 discussion 294–297.
 - [24] H. Groepenhoff, N. Westerhof, W. Jacobs, A. Boonstra, P.E. Postmus, A. Vonk-Noordegraaf, Exercise stroke volume and heart rate response differ in right and left heart failure, *Eur. J. Heart Fail.* 12 (7) (2010) 716–720.
 - [25] H. Pinnock, C. Burton, S. Campbell, et al., Clinical implications of the Royal College of Physicians three questions in routine asthma care: a real-life validation study, *Prim. Care Respir. J.* 21 (3) (2012) 288–294.
 - [26] E.I. Metting, R.A. Riemersma, J.H. Kocks, M.G. Piersma-Wichers, R. Sanderma, T. van der Molen, Feasibility and effectiveness of an Asthma/COPD service for primary care: a cross-sectional baseline description and longitudinal results, *NPJ Prim. care Respir. Med.* 25 (2015) 14101.
 - [27] H. Watz, F. Pitta, C.L. Rochester, et al., An official European Respiratory Society statement on physical activity in COPD, *Eur. Respir. J.* 44 (6) (2014) 1521–1537.
 - [28] T. Haselkorn, H. Chen, D.P. Miller, et al., Asthma control and activity limitations: insights from the Real-world Evaluation of Asthma Control and Treatment (REACT) study, *Ann. Allergy Asthma Immunol.* 104 (6) (2010) 471–477.
 - [29] E.M. van Sluijs, S.J. Griffin, M.N. van Poppel, A cross-sectional study of awareness of physical activity: associations with personal, behavioral and psychosocial factors, *Int. J. Behav. Nutr. Phys. Act.* 4 (2007) 53.
 - [30] M.G. Chandratilleke, K.V. Carson, J. Picot, M.P. Brinn, A.J. Esterman, B.J. Smith, Physical training for asthma, *Cochrane database Syst. Rev.* 5 (2012) CD001116.
 - [31] C.A. Mancuso, T.N. Choi, H. Westermann, S. Wenderoth, M.T. Wells, M.E. Charlson, Improvement in asthma quality of life in patients enrolled in a prospective study to increase lifestyle physical activity, *J. Asthma*. 50 (1) (2013) 103–107.
 - [32] A. Franca-Pinto, F.A. Mendes, R.M. de Carvalho-Pinto, et al., Aerobic training decreases bronchial hyperresponsiveness and systemic inflammation in patients with moderate or severe asthma: a randomised controlled trial, *Thorax* 70 (8) (2015) 732–739.
 - [33] R.A. Silva, F.M. Almeida, C.R. Olivo, B.M. Saraiva-Romanholo, M.A. Martins, C.R. Carvalho, Exercise reverses OVA-induced inhibition of glucocorticoid receptor and increases anti-inflammatory cytokines in asthma, *Scand. J. Med. Sci. Sports* 26 (1) (2016) 82–92.
 - [34] H.A. Scott, J.R. Latham, R. Callister, et al., Acute exercise is associated with reduced exhaled nitric oxide in physically inactive adults with asthma, *Ann. Allergy Asthma Immunol.* 114 (6) (2015) 470–479.
 - [35] S.A. Adams, C.E. Matthews, C.B. Ebbeling, et al., The effect of social desirability and social approval on self-reports of physical activity, *Am. J. Epidemiol.* 161 (4) (2005) 389–398.
 - [36] J.M. Tucker, G.J. Welk, N.K. Beyler, Physical activity in U.S.: adults compliance with the Physical Activity Guidelines for Americans, *Am. J. Prev. Med.* 40 (4) (2011) 454–461.