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Direktor: Prof.Dr.med Bernd Wolfarth

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Assessment of Functional Status in Patients with Cardiorespiratory Disease using Tele-Accelerometry

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Dr.rer.nat. Melissa Luise Jehn

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Dekan:	Professor Dr. Axel R. Pries
1. Gutachter/in:	Herr Prof. Dr. Klaus-Michael Braumann, Hamburg
2. Gutachter/in:	Herr Prof. Dr. Hubert Wirtz, Leipzig

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ABBREVIATIONS:

COPD = Chronic Obstructive Pulmonary Disease

PROMISE = Predicting Effects and Risk Factors in Exacerbations of Chronic Obstructive Pulmonary Disease (COPD)

GOLD = Global Initiative for Obstructive Lung Disease

BODE Index = Body-Mass Index, Airflow Obstruction, Dyspnoea, and Exercise Capacity Index

MMRC = Modified Medical Research Council Dyspnoea Scale

SGRQ = Saint Georges Respiratory Questionnaire

FEV_1 = Forced Expiratory Volume in one Second

SF - 36 = The Medical Outcomes Short Form 36 Quality of Life Questionnaire

MRproANP = Midregional Proatrial Natriuretic Peptide

MRproADM = Midregional Plasma Pro-Adrenomedullin

WLK = Walking (WLK = 0-5 km/h)

FWLK = Fast Walking (FWLK = > 5 km/h)

TWT = Total Walking Time (TWT = WLK+ FWLK)

CHF = Chronic Heart Failure

TM = Tele-Medicine

6MWT = 6-Minute Walk Test

NYHA = New York Heart Association Functional Class

(TIM-HF) = Telemedical Interventional Monitoring in Heart Failure

MET = Metabolic Equivalent

1. INTRODUCTION

1.1 Definition of Physical Activity

Physical activity can be defined as any bodily movement produced by skeletal muscle that results in energy expenditure (1). It reduces the risk for cardiovascular diseases, diabetes, cancer, and depression (2-8). Moreover adequate levels of physical activity will increase energy expenditure and help control weight, thereby promoting beneficial effects on the metabolic syndrome (i.e. reduction in blood pressure, LDL cholesterol, and blood glucose levels) (1;7). Physical Activity recommendations for the general population include 30 min of moderate intensity activity on ≥ 5 days per week or 20 min of vigorous intensity activity on at least 3 days per week (9). Subcategories of physical activity (PA) include exercise, leisure-time activity, occupational activity, as well as activity of daily living (10). This work will focus on activity of daily living, also known as ambulatory activity and/or functional status.

1.2 Physical Inactivity – General Population

An increasing burden of premature disability and death secondary to lifestyle-related conditions, such as overweight, diabetes, and cardiovascular disease, is related to physical inactivity. It has been identified as the fourth leading risk factor for global mortality causing an estimated 3.2 million deaths worldwide. This follows high blood pressure, (13%), tobacco use (9%) and high blood glucose (6%). Overweight and obesity are responsible for 5% of global mortality (11). Physical inactivity is rising in many countries thereby increasing the prevalence of many chronic diseases (12). It is estimated to be the principal cause for approximately 21–25% of breast and colon cancer, 27% of diabetes and approximately 30% of ischemic heart disease (6;12). Physical inactivity can be the cause of chronic disease as well as the result of chronic disease, especially in the elderly, thereby causing higher overall mortality (13).

1.3 Functional Status / Functional Exercise Capacity

Functional status or functional exercise capacity is an important prognostic parameter in patients with chronic diseases and is defined as the “individual's ability to perform normal daily activities required to meet basic needs, fulfil usual roles, and maintain health and well-being” (14). Both terms, functional status and functional exercise capacity, are often used interchangeably, however the former indicates a person’s self selected daily mobility, whereas the latter reflects the range of mobility that is physically possible to that individual.

In medicine it helps define disease status and is an indicator of the patient's health and well-being. A decrease in functional exercise capacity as a result of age, chronic disease and/or inactivity is tightly linked with an increase in morbidity and mortality (15-17).
In patients with chronic diseases, functional exercise capacity is most often assessed by means of the 6-minute walk test. It is simple to execute and indicates the degree of functional impairment patients suffer from in life. Moreover, it is thought to directly reflect the patient's ability to function in routine daily activities (18-21). Test outcome, in terms of total distance walked in six minutes, is used to assess disease severity and is significantly associated with short-term clinical prognosis (22-24).
The amount of daily physical activity measured by means of accelerometry is also an equivalent measure of functional exercise capacity in patients with chronic diseases (25-27). A number of studies have shown a strong link between accelerometer derived daily activity, disease severity and even mortality in patients with chronic heart and lung disease, cancer, and type II diabetes (17;28-31).

1.4 Assessment of Daily Physical Activity

Because inactivity has been identified as such a leading risk factor for developing chronic disease, measurement tools to assess the amount of daily physical activity levels have become increasingly abundant. The most common methods to measure physical activity include activity questionnaires and motion sensors, i.e. accelerometers or pedometers. Several studies have used these tools to assess physical activity under controlled and free living conditions in healthy persons and various patient populations (32-35).
Activity questionnaires are able to cover a wide range of activities, are simple and inexpensive. However, they are skewed by untruthful answers and depend on memory, which can be difficult in elderly patients. Most questionnaires cover moderate intensity activities associated with exercise and/or transport, but are devoid of low intensity activities such as house hold chores, gardening or simply walking around the house (36-39). Specialized questionnaires for patients with functional limitations do exist, albeit it is difficult to generate general questions about detailed activities that address a large population group at the same time (35;40;41).
Motion sensors such as pedometers and accelerometers enable an objective assessment of daily physical activity, however most are limited to movement of the lower extremities, i.e. walking. Pedometers are accurate during moderate walking speeds, but are faulty during low and high movement intensities (32;42;43). Accelerometers provide more detailed

activity data, including exercise frequency, intensity and duration. A drawback is that they can be expensive (~ 800 €) plus require custom made software for data analysis. Two accelerometer models were used to complete the studies presented in this work: the Aipermotion 300 and the Aipermotion 440 (Aipermon® GmbH, Germany). A detailed description can be read under **1.4.2**.

1.4.1 Accelerometers

Accelerometers are small, electronic instruments that are worn close to the body and detect physical movement in one-, two-, or three axes. The difference between uni-, bi- and tri-axial accelerometers lies in the sensitivity and the degree of motion detection, i.e., a tri-axial accelerometer detects wider range of motion compared to a uniaxial accelerometer (44). Accelerometers capture the accelerations of objects and can reflect intensity and frequency of human movement. Integrated with time, accelerometers measure velocity and displacement of the human body. Some accelerometers can respond to gravity, thereby identifying body postures. Most accelerometers can compute physical activity information in order to display energy expenditure. Activity information is often expressed in activity counts and/or steps per day (45). Numerous studies have investigated the validity of these devices finding them reliable in reflecting physical activity levels in healthy persons as well as patients with chronic diseases (33;35;36;46;47).

Limitations in accelerometer derived physical activity assessment do exist. For example, the vibration of vehicle driving can falsely increase accelerometer output in some devices. This can be reduced by filtering the accelerometer signal and/or decreasing its sensitivity (48). The number of consecutive assessment days can also negatively impact the reliability of accelerometer output, especially in patients with chronic diseases (49). A study by Watz et al. demonstrated that 2-3 days of accelerometer assessment are sufficient in patients with advanced heart disease, whereas up to 5 days are needed in patients with only mild chronic disease (31). Moreover, there are marked differences in physical activity levels on weekdays versus weekends. Particularly Sundays deviated from other weekdays by displaying extremely low activity levels (27). Many accelerometers overestimate energy expenditure, particularly in patients with functional limitations due to their altered movement behaviour (50). These factors must be taken into account when employing activity monitors to evaluate habitual physical activity levels in various patient populations.

1.4.2 Aipermon

The AiperMotion 440 (Aipermon® GmbH, Germany) is a three-dimensional accelerometer that is worn at the hip and assesses movement in three axes (x, y, z). Data is stored every minute for 24 hours per day (24 hours). Each one-minute interval is stamped with the according time and date. The output data can then downloaded onto a PC and be viewed via ActiCoach (MPAT2Viewer, Aipermon®). The accelerometer measures daily physical activity including time spent passively (i.e.: min/day sitting), actively (i.e.: movement, but not walking), walking (0-5km/h or 0 – 80 m/min) and fast walking (> 5km/h or 81 – 115 m/min). The device displays the time it is not worn as "resting mode". Moreover, it displays total steps taken, calories and distance (meters) walked. The display of the accelerometer can be hidden, by setting it to a figure picture. This way, patients cannot see the results of their daily activity data and thus be blinded from analysis. The ability to allocate the exact time points of movement is important, because patients with CHF and COPD are more likely to show short activity intervals during the day as opposed to continuous movement.

The AiperMotion 300 device is also a three dimensional accelerometer. This model was customized especially to store data during the 6-minute walk test. It has a "start 6-minute walk test" button and data recording automatically ends once 6 minutes are past. Like the AiperMotion 440, the accelerometer is matchbox sized and worn on hip level. It comes with a pocket pouch that attaches to a person's belt. The device records the total amount of steps taken in six minutes and was especially designed for a large telemedicine project called "Partnership for the Heart" funded by BMWi from 2008-2010 (51;52).

Both devices have been validated in patients with chronic heart failure under laboratory conditions as well as in a field based setting (46). The results proved a step detection accuracy of 99% at walking speeds as low as 20 m/min.

1.5 Assessment of Functional Exercise Capacity in COPD

The prevalence and incidence of Chronic Obstructive Pulmonary Disease (COPD) is rapidly increasing and evidence suggests it to be the third leading cause of death worldwide within the next decade (53-55). COPD is characterized by progressive airflow obstruction and destruction of lung parenchyma caused by chronic exposure to tobacco smoking and/or environmental factors such as indoor/outdoor air pollutants, dust and fumes in genetically susceptible individuals (53). Functional exercise capacity is an independent predictor of mortality in patients with COPD (19;20;53).

Studies have shown, ambulatory physical activity to be significantly associated with disease related symptoms, mortality and long-term prognosis (15;17;29;31;53;56). Evidence suggests that physical activity attenuates and inactivity augments the occurrence of exacerbations in patients with COPD, due to underlying hemodynamic changes and vasoconstriction of the pulmonary vasculature (15). The usefulness of accelerometers to measure daily activity levels in free-living conditions is well documented in patients with COPD. They provide an objective and valid measure of functional exercise capacity that is linearly related to disease severity and mortality (15-17;29;31;47;57-61).

Abundant studies have investigated the positive relationship between daily physical activity levels and clinical symptoms. Although previous investigations have shown only weak correlations between physical activity and lung parameters, particularly the degree of airway obstruction (FEV_1), the level of exertional dyspnea was found to be a significant confounder in regards to walking intensity in patients with COPD (62-64). Seemingly, exertional dyspnea arises from airflow limitation due to bronchoconstriction. This, in turn, limits movement intensity. Watz and colleagues were able to show a linear dependence between MMRC dyspnea scale and physical activity levels in patients with COPD (61). Accelerometer derived physical activity was significantly and inversely related to mMRC scale, meaning that patients with more pronounced dyspnea (mMRC scale III and IV) showed a significantly higher amount of total inactivity and lower amount of measured steps per day, physical activity volume and intensity than patients with lower dyspnea scales (mMRC scale I – II). Albeit, decreased physical activity levels plus increased sedentary time could already be observed in COPD I patients with only mild dyspnea, when compared to age matched healthy controls (31).

Waschki and colleagues demonstrated a significant association between physical activity, exercise intolerance, muscle dysfunction, systemic inflammation, symptoms of dyspnea, impaired health status, degree of emphysema, frequent exacerbations (two or more in the preceding year), and fatigue symptoms in 127 patients with COPD across different study sites (65). MMRC dyspnea scale and level of fatigue were the main independent predictors of total amount of steps per day after adjusting for age, sex, study site and obesity. In addition, they were able to illustrate accelerometer based physical activity to be the strongest predictor of all-cause mortality in patients with COPD (17). Physical inactivity was shown to be an independent predictor of hospital admission due to severe exacerbation and was positively associated with higher numbers of exacerbations per year further increasing mortality risk (15;16).

According to patient reports, the greatest barrier for individuals with COPD to participate in activities of daily living, such as shopping, bathing and cleaning the house, is the patients' subjective perception of breathlessness (66-68). The inability to keep up with their healthy counter parts and perform daily activities like they remember, often leads to severe depression plus decreased quality of life (69). According to epidemiological data, regular physical activity reduces the rapid decline in smoking related lung function thereby alleviating the sensation of breathlessness (70). In addition, the use of walking aids has shown to significantly improve oxygenation and reduce breathlessness in patients with chronic airflow limitation (71;72). Therefore, the promotion of physical activity is an integral part of chronic disease management in patients with COPD with primary goal to reduce progression of disease related signs and symptoms (73). Unfortunately, despite abundant evidence regarding the benefit of physical activity in patients with COPD, recommendations by the treating physician to engage in more physical activity are low and patient adherence to follow activity guidelines is poor (74;75). This should be actively targeted.

1.6 Assessment of Functional Exercise Capacity in Chronic Heart Failure

The prevalence of chronic heart failure (CHF) is high with over 23 million cases worldwide. Over 2.4 million patients are hospitalized each year and nearly 300,000 deaths annually are directly attributable to heart failure (76;77). Patients with CHF suffer from cardiopulmonary and musculoskeletal limitations which greatly impede on their quality of life (78). Consequently, a marked decrease in functional exercise capacity is present. The degree of impairment depends on the severity of heart failure including clinical prognosis (18;79). The New York Heart Association (NYHA) uses the patients' functional capacity to distinguish NYHA functional classes I – IV, by inquiring about the amount of physical activity possible without breathlessness, i.e. flight of stairs climbed or distance walked (80). Sufficient levels of daily physical activity can attenuate disease progression and improve survival rate among CHF patients (81;82). Myers et al. estimated a 12% improvement in survival in patients with cardiovascular disease for every increase in physical activity of 1 MET (83).

In patients with CHF, functional exercise capacity is evaluated by means of the 6-minute walk test and/or cardiopulmonary exercise testing. Maximum oxygen consumption (VO_{2peak}) is considered the strongest predictor of survival in patients with CHF and is seen as the gold standard in the assessment of functional capacity and clinical prognosis (18;84).

Likewise, the 6-minute walk test is also widely recognized for its prediction strength regarding short-term mortality in patients with CHF (21;85;86).

A number of studies have shown a significant correlation between accelerometer derived daily activity levels, VO_{2peak} and 6-minute walk distance in patients with CHF (20;23;25;46;87). Accelerometer derived activity levels reflect the patient's coping ability with routine daily activities. A study by Walsh et al., demonstrated daily activity levels, or more specifically inactivity in daily life, to be a better indicator of disease prognosis than cardiopulmonary exercise testing (87).

The bench mark of 3500-5000 steps per day has been set for persons with chronic diseases and less than 25000 steps per week has been associated with an increased mortality risk in patients with chronic heart failure (87;88). On this basis, accelerometry may become a suitable substitute for standardized exercise testing in patients with CHF in order to facilitate continuous patient monitoring.

2 OWN RESEARCH AND PUBLICATIONS

2.1 Tele-Accelerometry in Chronic Heart Failure

The 6-minute walk test is an established measure of functional exercise capacity in Chronic Heart Failure (CHF). In patients with moderate to severe heart failure and marked dyspnoea upon exertion, a 6-minute walk test distance ≤ 350 m has been significantly associated with length of survival and short-term prognosis (23;24). Based in an in-hospital or outpatient setting, the 6-minute walk test is conducted following standard testing requirements with re-tests every six -12 months (89).

This prospective study analysis evaluates the validity of accelerometers to remotely measure 6-minute walk test performance in patients with CHF recruited for the "Telemedical Interventional Monitoring in Heart Failure" (TIM-HF) (clinicaltrials.gov identifier: NCT00543881) trial. TIM-HF is a large multi-centre telemedicine trial that included 710 patients with chronic heart failure (52). Home based telemedicine included daily body weight, blood pressure, ECG and subjective well-being. A subgroup of patients (N = 155) also conducted a regular 6-minute walk test recorded by means of accelerometry. Tele-accelerometry was measured at baseline and on a monthly basis over 12-24 months follow-up using the Aipermotion 300. Exercise data was remotely transmitted via mobile network from the patients' home to the Telemedicine Centre (TMC) in the Charité University Hospital. The parameter of interest was the total amount of steps taken in six minutes.

Our results showed, that 6-minute step frequency has a linear relationship with 6-minute walk distance, meaning the farther the distance walked the higher the total amount of steps taken and vice versa. This is because patients with heart failure regulate their walking speed by adjusting their step frequency not their stride length. Stride length remains roughly the same throughout different walking speeds.

Accelerometer derived 6-minute step frequency proved to be just as robust a parameter of functional exercise capacity as 6-minute walk distance in patients with heart failure. Tele-accelerometry is an instrumental tool for the routine assessment of functional status in a home-based setting in order to document individual change over time. The advantage of this method is its practicality in daily life without the need for in hospital patient consultation.

2.1.1 Tele-Accelerometry as a novel Technique for assessing Functional Status in Patients with Heart Failure: Feasibility, Reliability and Patient Safety

Jehn M, Prescher S, Koehler K, von Haehling S, Winkler S, Deckwart O, Honold M, Sechtem U, Baumann G, Halle M, Anker SD, Koehler F. Int J Cardiol. 2013 Oct 12;168(5):4723-8.

http://dx.doi.org/10.1016/j.ijcard.2013.07.171

2.2 The Value of Physical Activity in COPD

Employing accelerometers to measure habitual levels of physical activity has become common praxis in medical science in order to investigate possible relationships with disease status in Chronic Obstructive Pulmonary Disease (COPD) (27;29;35;47;56;58;90). Patients with COPD show a significant reduction in daily physical activity levels and move at markedly slower intensities compared to age matched healthy controls (63). Previous studies have demonstrated a positive association between disease severity in patients with COPD and reduction in physical activity levels (16;56;59;91). In the following study presented herein, different parameters of accelerometer derived activity data were evaluated in regards to disease severity in 107 patients with COPD.

Data was collected at the Clinic of Pulmonary Medicine of the University Hospital Basel, Switzerland, between November 2008 and March 2010. Included patients received a baseline examination and follow-up assessments every six months. Patient data collected at these visits entailed detailed medical history, in particular smoking status, current medication, co-morbidities, physical examination, quality of life, level of exertional dyspnea (MMRC), spirometry, chest x-ray, 6-minutes walk test and accelerometry. The accelerometers (Aipermotion 440) were given to the patients at one of their scheduled visits and worn continuously for eight days.

Activity data in terms of total walking time (min/day) and walking intensity (m/sec) proved to be a significant and independent predictor of disease severity in patients with COPD. Accordingly, a cut-off value of ≤ 33 min/day for total walking time and ≤ 0.1 min/day for fast walking time predicted the probability of poor prognosis in patients with COPD, i.e. BODE index ≥ 6. Moreover, there was a significant association between total steps per day, 6-minute walk test and COPD severity. Disease severity (GOLD IV) and levels of daily activity showed a strong linear relationship. Albeit, a marked reduction in daily activity volume and intensity was already present in COPD II patients when compared to age matched patients with mild to moderate CHF. This most likely results from the sensation of breathlessness COPD patients feel, even in the early stages of the disease.

The clinical usefulness of our data analyses lies in its potential to use activity monitoring in terms of tele-accelerometry for long-term disease management and patient screening. A reduction in a patient's daily activity level and/or coping abilities might prove to be associated with clinical worsening. This must be investigated in future studies.

2.2.1 Association of Daily Physical Activity Volume and Intensity with COPD Severity

Jehn M, Schmidt- Trucksäss A, Meyer A, Schindler C, Tamm M, Stolz D. Respiratory Medicine 2011 Dec;105(12):1846-52.

http://dx.doi.org/10.1016/j.rmed.2011.07.003

2.3 Physical Activity and Quality of Life in COPD

Functional exercise capacity is strongly affected in patients with Chronic Obstructive Pulmonary Disease (COPD) and is a key performance indicator of mortality in this patient population (15;17;31;56). As previously discussed, the level of accelerometer derived daily physical activity is an equivalent measure of functional exercise capacity in patients with COPD. The latter is typically measured by means of the 6-minute walk test (19).

Nevertheless, there is abundant evidence in literature, demonstrating the applicability of accelerometers to measure functional exercise capacity in terms of daily activity levels in patients with COPD. The data obtained, proved activity measures to relate to respiratory disease severity (15;17;27;29;31;35;47;50;56;59;60;65;91-93). Moreover, reductions in movement capacity due to pulmonary limitations severely impact the patient's quality of life (54;94).

A number of standardized questionnaires have been designed in order to assess quality of life in patients with COPD. These include the Short Form-36 (SF-36) and Saint Georges Respiratory Questionnaire (SGRQ). A significant association between functional exercise capacity assessed by means of the 6-minute walk test and quality of life has previously been validated in patients with COPD (16;27;47). Therefore, we wanted to evaluate, if a positive relationship exists between quality of life and accelerometer derived daily activity as well.

For this investigation, we included 107 patients with COPD (GOLD II-IV). The average age of our recruited patient population was 65.3 ± 10.8 years. During one of their pre-scheduled visits, patients were instructed to fill out both questionnaires. Following this, the accelerometers were handed out to the patients. Accelerometer settings were pre-programmed before giving them to the patients, in order to keep patient handling of the device to a minimum. The output screen was also blinded to the patient by locking it to a running figure (see **1.4.2** for details). This way, they could not see their level of accomplished daily activity. As previously discussed, all patients agreed to wear the accelerometer for 8 consecutive days. We employed the Aipermotion 440 in this study, in order to measure daily habitual activity levels. The device was to be attached upon rising in the morning and only to be taken off for showering, bathing and sleeping.

Accelerometer output data demonstrated, daily walking time and intensity to be significantly and independently predictive of quality of life in patients with COPD. Furthermore, analyses showed an inverse linear relationship between both measures, meaning that patients with the lowest accelerometer activity had the highest disease

severity and the worst outcome regarding health related quality of life. As illustrated by our analysis, daily activity is comparable to the 6-minute walk test in predicting quality of life (19). Quality of life is an important aspect to be integrated into chronic disease management. The advantage of activity monitoring lies in its continuity over a given time period. Walking time and daily walking intensity by means of accelerometry can provide additional information about the patient's functional status and quality of life. This might prove to be useful for therapeutic interventions and clinical prognosis.

2.3.1 Daily Walking Intensity as a Predictor of Quality of Life in Patients with COPD

Jehn M, Schmidt- Trucksäss A, Meyer A, Schindler C, Tamm M, Stolz D. Med Sci Sports Exerc. 2012 Jul;44(7):1212-8.

http://dx.doi.org/10.1249/MSS.0b013e318249d8d8

2.4 Physical Activity and Biomarkers in COPD

Chronic obstructive pulmonary disease is associated with high cardiovascular comorbidity and mortality and the prevalence for cardiovascular related death remains particularly high in patients suffering acute exacerbations of COPD (95-97). The recent TORCH study was able to show that 30% of deaths in COPD patients were related to cardiovascular morbidity and 40% were due to COPD (98). Systemic biomarkers of inflammation and/or cardiac stress have gained in significance regarding their ability to predict clinical prognosis in COPD (65;99;100). Among these are midregional proatrial natriuretic peptide (MRproANP) and plasma pro-adrenomedullin (MRproADM). Both markers of cardiac distress show significant prognostic strength in COPD in terms of hospitalization due to exacerbation and long-term survival (101;102). The purpose of our study was to evaluate the association between prognostic biomarkers (MRproANP and MRproADM) and accelerometer based physical activity in stable COPD patients in order to establish if ambulatory activity monitoring can simplify risk stratification.

One hundred and five COPD patients (GOLD II, N = 29; GOLD III, N = 51, GOLD IV = N = 25) were consecutively included in this sub-study at the Clinic of Pulmonary Medicine of the University Hospital Basel, Switzerland. Mean age of patient population was 66.1 ± 8.7 years and 71% were men. Assessment of daily activity levels was done with the Aipermotion 440 (8-day accelerometry). Blood samples were taken during one of the scheduled visits every six months in order to evaluate levels of MRproANP and MRproADM.

Our results indicate that daily walking activity is an independent predictor of circulating MRproANP and MRproADM levels in stable COPD patients, two prognostic biomarkers markedly elevated upon exacerbation of COPD. The daily amount of physical activity was inversely proportional to levels of circulating MRproADM across increasing GOLD stages. Thus GOLD IV patients presented with lowest levels of daily walking activity and highest levels of circulating MRproADM. MRproADM is a surrogate marker known to indicate overall cardiopulmonary distress including the development of transient myocardial dysfunction due to its counter regulatory properties in response to bronchoconstriction, pulmonary arterial hypertension, airway inflammation and/or infection during exacerbation of COPD (102).

Employing activity monitors in stable COPD patients might simplify risk stratification by identifying patients at risk for exacerbation early on. Subsequent future studies should evaluate if continuous activity monitoring can ascertain patients at risk for exacerbation and

if changes in daily physical activity are directly associated to changes in circulating biomarkers of cardiac distress.

2.4.1 Associations of Daily Walking Activity with Biomarkers Related to Cardiac Distress in Patients with Chronic Obstructive Pulmonary Disease

Jehn M, Schindler C, Meyer A, Tamm M, Koehler F, Witt C, Schmidt-Trucksäss A, Stolz D. Respiration. 2013;85(3):195-202.

https://doi.org/10.1159/000345218

2.5 Tele-monitoring during Heat Stress in COPD

A report from the Centre for Health and Global Environment at Harvard Medical School, proclaims there to be a dramatic increase in the number, duration and intensity of extreme weather events, including heat waves (103). The ramifications this will have for human health, in particular patients with respiratory diseases, remains a question yet to be answered. An abundance of epidemiological data reflect a rise in morbidity and mortality during heat waves in patients with respiratory diseases, including Chronic Obstructive Pulmonary Disease (COPD) (104-107).

A primary reason for hospital admissions in elderly patients is acute exacerbation of COPD. Research suggests, that these extreme temperatures fluxes further aggravate this condition (104;108). Elderly patients (> 65 years of age) with COPD are negatively affected by heat stress and experience a heightened medical vulnerability. This is due to a reduction in lung perfusion and bronchial mucosa, triggered by hot air loaded with air pollutants (104;107;109).

Continuous ambulatory activity by tele-accelerometry is a surrogate marker of functional exercise capacity in COPD. Our main objective was to investigate the association between summer heat stress exposure and a possible reduction in clinical status in patients with COPD. In order to do so, we installed a tele-monitoring system in the patients' home that would allow us to observe, if continuous patient monitoring reduces the risk of exacerbation during and outside periods of heat stress.

The length of patient observation lasted nine months. Patients were randomized in either the telemedicine group (TG, N = 32) or the control group (CG N = 30). Mean age of our patient cohort was 65.7 ± 10.3 years with moderate to severe disease status (GOLD II-IV). Patient care was based on current guidelines for COPD and entailed an initial baseline visit as well as regular follow-ups at 3, 6, and 9 months. We recorded detailed medical history, current medication, duration of disease, co-morbidities, physical examination, quality of life (SGRQ (110)), modified Medical Research Council Dyspnoea Scale (mMRC), spirometry, COPD Assessment Test (CAT), and an accelerometer based 6-minute walk test. Patients in the telemedicine group had to complete the CAT and spirometry test on a daily basis. Accelerometer based six-minute walk test with the Aipermotion 300 was performed on a weekly basis. All three testing modalities were conducted in the patient's home without professional assistance. Patient data was transmitted via mobile network directly to the study centre at the Charité University Hospital, in Berlin. Weather data was obtained

from the local weather station (Tempelhof, Berlin, Germany; maintained by the Deutscher Wetterdienst).

Our data analyses demonstrated a significant worsening in clinical status, lung function and exercise capacity on heat stress days (29.0 ± 2.5 °C) compared to thermal comfort days (21.0 ± 2.9 °C) in the telemedicine group. This indicates that heat stress aggravates COPD symptoms by putting patients at greater risk for exacerbation. When comparing the entire patient cohort at the 9-month follow-up visit, we found that patients who had received continuous tele-monitoring however, had significantly improved in clinical and functional status whereas control patients had not. Overall, the telemedicine group also showed a significantly lower number of exacerbation related hospital admissions over the study duration when compared to the control group.

In this study, we were able to demonstrate a beneficial effect of tele-monitoring in our patient population. Implementing this system during prolonged heat exposure can help to improve risk stratification in patients and possibly reduce the number of total exacerbations by allowing for early-on identification of high-risk patients by the treating doctor. Adaptation strategies must be in place to protect vulnerable patients at risk for heat stress in order to reduce poor outcome. These include, but are not limited to, tele-accelerometry, patient schooling about proper adaptive behaviour during heat stress, as well as necessary adjustments in pharmacological therapy.

2.5.1 Tele-monitoring reduces Exacerbation of COPD in the Context of Climate Change - a Randomized Controlled Trial

Jehn M, Donaldson G, Kiran B, Liebers U, Mueller K, Scherer D, Endlicher W, Witt C. Environ Health. 2013 Nov 21;12:99.

http://dx.doi.org/10.1186/1476-069X-12-99

3 DISCUSSION

3.1 The Value of Telemedicine

Specialized outpatient management programs for patients with chronic diseases have become increasingly abundant in medicine. These include tele-medicine and/or structured support programs for afflicted patients. A variety of tele-medical concepts have been developed and implemented in order to deliver structured patient care over a large geographical area thereby reducing health care costs (52). These concepts range from basic telephone support to complex technologies in order to assess a patient's clinical status (111). Their efficacy, however, on improving patient outcome is still an on going debate among medical professionals and thus remains unclear.

3.2 Clinical Application of Tele-Accelerometry

The use of accelerometers to measure functional exercise capacity in patients with chronic diseases, in particular CHF and COPD, has found widespread acceptance in theory, but is rarely applied in clinical praxis to actively guide patient evaluation and therapy (25;31;35;46;56;87;112). For example, all modern implantable cardiac devices are equipped with accelerometers, however these captured activity logs are difficult to interpret and seem of limited use in routine clinical patient evaluation (113). The first large tele-medical study to successfully include accelerometers in their remote technological data transfer system was the Tele-medical study “Interventional Monitoring in Heart Failure” (TIM-HF) (26;52). This innovative study concept incorporated exercise testing as an integral part of the telemedicine setting to objectively evaluate a patient's clinical and functional status. Direct data transfer including weight, blood pressure, ECG, and accelerometer based 6-minute walk testing allowed for tight patient monitoring, even during exercise. Nevertheless, here too, real time physical activity data was not used to actively guide patient evaluation, but rather gathered over the course of the study duration and analysed retrospectively. The results showed that, in theory, tele-accelerometry was feasible and safe in patients with chronic heart failure.

3.3 Disadvantages of Tele-Accelerometry

Although the prognostic utility of accelerometry has been widely established in patients with chronic diseases, the method in itself bears certain restrictions. Accelerometry lacks a defined gold standard in terms of measurement methodology. There is a paucity of standardized reference parameters that enable the uniform interpretation of accelerometer

based physical performance. This unconformity in data output between different accelerometer devices limits the comparability of studies regarding their data output. Moreover, many external factors can influence accelerometer based daily activity measures, which are difficult to control for. For example, the majority of health professionals agree, that patients with high levels of daily physical activity have a better prognosis than inactive patients. But it is difficult to distinguish between a patient's true physical capacity (i.e. functional capacity) and his or hers actual state of being (i.e. functional status). The former indicates the physically ability of a person when maximally challenged, whereas the latter illustrates the actual doing of a person, i.e. due to a lack of motivation or bad weather.

3.4 Number of Required Monitoring Days

A further uncertainty in accelerometer derived daily activity is the number of required monitoring days in order to obtain a reliable measurement. Howell et al. monitored daily physical activity in 60 heart failure patients over 9 months and reported that six minutes of maximum daily activity was sufficient to determine functional exercise capacity and to predict HF hospitalization and/or mortality (112). However the number of consecutive monitoring days needed for this to bear significance, was not determined in this study. According to literature, the number of required monitoring days always depends on the patient population being studied. Pitta et al, measured daily physical activity levels in a group of COPD patients and concluded that two days (N=2) of activity monitoring are enough to achieve an intraclass reliability coefficient of >0.7, the minimal value required for the reliability of a variable to be considered acceptable (27). Our own investigation showed, that a minimum of four days (N=4) of activity monitoring is needed in order to predict NYHA functional class in patients with CHF (25). A study by Trost et al. demonstrated that up to seven monitoring days (N=7) are required to provide reliable estimates of daily activity levels in healthy adolescents (49). The latter however used a uniaxial accelerometer instead of a triaxial accelerometer, which is less sensitive in motion detection. Moreover, elderly individuals with chronic diseases tend to strictly adhere to their same daily routine, which adolescents do not. It is possible, that this factor also plays an eminent role, when accounting for the discrepancy in monitoring days.

3.5 Standard Exercise Testing by means of Tele-Accelerometry

Recently, our research group introduced an approach to combine tele-accelerometry with the 6-minute walk test, in order to obtain a more compact measure of physical performance that can be interpreted by many. Detailed information about this approach can be read

under point **2.1**. We considered activity data obtained during a standardised exercise test to have higher precision than measures of arbitrary daily activity levels. Our data not only showed that it is feasible to remotely conduct the 6-minute walk test using tele-accelerometry, but that 6-minute walk step frequency is a valid indicator of functional capacity in patients with heart failure. If needed, step frequency can then be mathematically converted into 6-minute walk distance, in order to compare performance with other published reference values. The advantage of using a standardized exercise test to measure functional performance as opposed to measures of daily activity levels is, that individual performance is not significantly influenced by external factors, such as differences in daily routine or weather. Moreover, the information is consolidated. This theory was successfully replicated in patients with COPD in order to remotely monitor functional status (92).

3.6 Limitations to Standard Exercise Testing

The use of tele-accelerometry to assess 6-minute walk test performance possesses the same limitations the exercise test has on its own. For once, a certain disease severity must be present to offer prognostic insight, as not all patients are cardio-respiratory challenged by the 6-minute walk test (24;114). A supervised first test is recommended as a reference for all consecutive testing, in order to familiarize the patient with testing procedures. This requires time and staff resources, especially in large studies including ≥ 100 patients. Previous studies have reported that the 6-minute walk test lacks discrimination strength between survivors and non-survivors in chronically ill patients, thereby providing little prognostic insights (18;79;115). Small differences are often difficult to interpret, because these differences might be statistically significant but not clinically relevant. On the other hand, Pinto-Plata and colleagues were able to show that every reduction of 50 meters increases the probability of death by 18% (19). Moreover, investigators from the Study of Left Ventricular Dysfunction (SOLVD) reported, that 6-minute walk distance was a significant independent predictor of long term mortality (12).

3.7 Comparing Methodologies – Daily Activity vs. 6-Minute Walk Test

The use of tele-accelerometry to assess functional exercise capacity in patients with COPD and CHF, as well as other chronic illnesses, has clinical potential. Which of the two approaches presented herein, i.e. 24 hour monitoring of daily activity, or 6-minute walk test step frequency, is the better indicator of clinical prognosis has yet to be determined. Accelerometer derived daily activity levels have already been ascertained in literature in terms of predicting outcome in COPD and CHF (17;87). The next step would be to

associate 6-minute step frequency with clinical prognosis in this patient population and/or patients with other chronic diseases. Both approaches enable continuous patient monitoring. This would open the possibility to recognise decreases in functional capacity as soon as they occur without progressing silently until the next hospital examination is scheduled. Further studies are needed however, in which tele-accelerometry is incorporated as a surrogate marker in deciding treatment evaluation and to actively guide prognosis.

4 SUMMARY

This work illustrates two different approaches of using tele-accelerometry to measure functional exercise capacity in patients with chronic diseases. In the first approach we demonstrated that it is possible to remotely conduct a standardized exercise test in patients with chronic heart failure using tele-accelerometry. The association of 6-minute walk test step frequency is interchangeable with 6-minute walk distance. The second approach shows daily physical activity to be a solid indicator of functional exercise capacity in patients with CHF and COPD. Daily walking time and intensity can be used to predict the probability of poor prognosis (NYHA IV, BODE index > 6). In particular walking intensity proved to be a key indicator of disease status in this patient population. Continuous monitoring of daily activity enables patient screening and improves long-term chronic disease management.

Moreover, our findings emphasize an independent and significant association between accelerometer based functional exercise capacity and health related quality of life in patients with COPD. The amount of daily walking activity is indicative of patients' functional status and directly linked to disease severity. Using tele-accelerometry to monitor quality of life can be useful to guide therapeutic interventions.

Our data also illustrates that daily walking activity is significantly and independently associated with prognostic biomarkers of cardiac distress in patients with COPD, in particular MRproADM. Employing activity monitors in stable COPD patients not only enables continuous patient monitoring in a real life setting, but can also reduce the risk for exacerbation in COPD.

Last but not least, we demonstrated a relationship between functional capacity and heat stress in our patient population. Tele-accelerometry is applicable to monitor functional capacity in patients with COPD during periods of extreme outside temperatures. Heat stress negatively impacts clinical and functional status in patients with COPD and makes patients more vulnerable for disease related morbidity. Continuous tele-monitoring reduces

exacerbation frequency and should be implemented on top of regular patient care during prolonged heat exposure.

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7 DISCLOSURE

Erklärung

§ 4 Abs. 3 (k) der HabOMed der Charité

Hiermit erkläre ich, dass

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