Correlation of Walking Activity and Cardiac Hospitalizations in Coronary Patients for 1 Year Post Cardiac Rehabilitation: The More Steps, the Better!

Sinann Al Najem^{1,2}, Andreas Groll³, Axel Schmermund^{4,5}, Bernd Nowak^{4,5}, Thomas Voigtländer^{4,5}, Ulrike Kaltenbach⁴, Peter Dohmann⁴, Dietrich Andresen⁶ and Jürgen Scharhag^{2,7}

¹German Heart Foundation, Frankfurt, Germany. ²Institute of Sports and Preventive Medicine, Saarbrücken, Germany. ³Departement of Statistics, TU Dortmund University, Dortmund, Germany. ⁴CCB-Herzwerk, Frankfurt, Germany. ⁵Cardioangiologisches Centrum Bethanien (CCB), Frankfurt, Germany. ⁶Lutheran Hospital Hubertus, Berlin, Germany. ⁷Department of Sports Medicine, Exercise Physiology and Prevention, Institute of Sport Science, University of Vienna, Vienna, Austria.

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ABSTRACT

PROBLEM: Reducing risk by improving fitness is one of the main objectives of cardiac rehabilitation (CR). To estimate how the number of steps/day post-CR affects coronary patients' prognosis, we analyzed its correlation with the occurrence of death, hospitalizations, and heart complaints, and if and how other variables (ejection fraction (EF), gender, age) relate to those.

METHODS: One hundred eleven patients (male = 91, female = 20; average age ± standard deviation (SD): 61 ± 11 years) who had been in CR due to recent coronary revascularization or chronic coronary syndrome could be enrolled. Patients were advised to document their steps (daily), blood pressure (daily), weight (weekly) and occurrences of a cardiac event in a diary for 1 year post-CR. A Cox proportional hazard model was used to examine the influence of steps/day, EF, gender, and age until the occurrence of an event. Kaplan-Meier curves were generated to compare patients' profiles.

RESULTS: Average steps/day of patients post-CR were 7333 (SD 4426). Increased walking activity reduced risk for cardiac hospitalization (constant steps/day: 5000 vs 7500, hazard rate (HR) reduction of 0.43; 10000 vs 12500, HR reduction of 0.20) and risk was higher in patients with an EF<55% versus EF≥55% (HR increase of 2.88). Median follow-up time post-CR was 218 days. No patient died, 25 were hospitalized.

DISCUSSION: Monitoring the number of steps of coronary patients post CR could be valuable for estimating patients' prognosis.

KEYWORDS: Physical activity, coronary heart disease, cardiac rehabilitation, step recommendation, pedometer

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CORRESPONDING AUTHOR: Sinann Al Najem, German Heart Foundation, Bockenheimer Landstr. 94-96, Frankfurt 60323, Germany. Emails: alnajem@herzstiftung. de; sinann.alnajem@googlemail.com

Introduction

The importance of physical activity in avoiding coronary heart disease is well-established, describing an inverse relationship between activity levels and incidence.¹ The same applies to patients who already have coronary artery disease, which is probably best examined in the context of exercise-based cardiac rehabilitation and could be associated with reduced cardiovascular mortality and morbidity.^{2,3} Therefore, cardiac rehabilitation (CR) is classified as a Ia recommendation for coronary patients by the European Society of Cardiology.⁴ Despite its benefits, CR is an underutilized therapy,⁵ and an unmet need exists for CR. According to a recently published study, which aimed to quantify CR density and need in Europe for the first time, on average, only every seventh ischemic heart disease patient undergoes CR.6 We previously reported that physical activity measured in steps/day in cardiac patients remains high for 1 year post-CR, indicating that CR appears to have a sizeable and long-term effect7 showing that the mean steps/day of patients for 1 year after CR was higher than the suggested threshold of >7500 steps/day, which could be associated with a lower risk profile after an acute coronary syndrome.⁸ Compared to activity recommendations of medical associations-which are mostly time-, intensity-, or physical energy expenditurebased9-12-a definition of step goals is complex-especially for ill patients.¹³ Therefore, to estimate if and how the number of steps/day directly affects patients' prognoses, the current study aimed to investigate (a) to what extent the number of daily steps of coronary patients for 1 year post-CR is correlated with the occurrence of death or hospitalization and (b) if and how other variables (ejection fraction (EF), gender, age) relate to those.

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Methods

Patient selection

Patients were asked to participate in the study on admission to the ambulatory facility, CCB Herzwerk, Frankfurt, Germany (recruiting time between July 2015 and July 2016), where they attended 3 to 4weeks of CR. The study was conducted in accordance with the World Medical Association Declaration of Helsinki, approved by the institutional review board of the ethics committee of the Hessian Medical Association (approval number: FF 47/2015).

Originally, 280 patients provided written informed consent, but 28 of them canceled their study participation already during CR. From this total, patients were only included if they were in CR due to (a) recent coronary revascularization (percutaneous coronary intervention (PCI), coronary stent implantation, or coronary artery bypass grafting (CABG)) or (b) chronic coronary syndrome (CCS).

Furthermore, the following exclusion criteria were determined to ensure the capability of proper walking: peripheral arterial disease; neurological, orthopedic (coxarthrosis or gonarthrosis), and other relevant handicaps that affect walking. Moreover, patients with cardiomyopathies, except those with ischemic cardiomyopathy, and patients with known or suspected heart valve diseases or coronary stenosis for whom further interventions were planned after CR were also excluded. Additionally, to ensure robust and comparable data, we defined a threshold of more than 50% of step data as mandatory during the time of study participation.

Cardiac rehabilitation

In Germany, 3 phases of CR can be distinguished: (I) early mobilization after acute treatment in the hospital, (II) early follow-up treatment, which generally lasts 3 weeks and could be conducted in an inpatient or outpatient setting, and (III) a long-term rehabilitation program, which should guarantee sustainability.14 In our case, we observed patients after Phase II of CR in the ambulatory facility CCB Herzwerk in Frankfurt, where they were supervised by a team of physicians, sport scientists, psychologists, physiotherapists, and social workers. Before starting, the physician and patient determined therapy goals targeting professional reintegration, psychological stability, and improved participation in social and professional life. Afterward, an individualized treatment plan was developed based on personal capacity, including exercise training, outdoor activities (hiking and Nordic walking), and different classes promoting lifestyle changes (healthy eating, smoking cessation, and staying active). Compulsory attendance was 6 hours per day, including 2 hours of recovery. Exercise training comprised daily monitored ergometry training (up to 30 minutes per day), strength training (1 hour per day), gymnastics (3-4 units of 1 hour per week), and coordination training (1 hour twice a week). Among other medical examinations, a blood sample (hemogram, cholesterol, HDL, LDL, creatinine, glomerular filtration rate, sodium, potassium, blood glucose) was taken from every patient during CR. The EF, calculated using the Teichholz formula, was assessed by echocardiography with a General Electric Vivid Pro 7[®] device. For this examination, the EF was used to categorize patients into the following groups:



Heart diaries

Before CR discharge, heart diaries were provided and handed to patients to self-record physical activity, cardiac hospitalizations, and heart complaints post-CR.

Physical activity. Physical activity was assessed via pedometry using Omron Walking Style Pro 2.0® pedometers. Because permanent daily pedometry of up to 1 year post-CR-except during swimming, showering, and sleeping-was desired, we allowed patients to wear them in different positions (attached with a clip on a belt or like a necklace), which does not appear to affect pedometer accuracy.¹⁵ Immediately before discharge, patients were informed about their average steps/day during CR. They were advised to record their daily steps in the heart diary for up to 1 year and instructed regarding its use. As mentioned, permanent continuous pedometry was desired but is unrealistic to achieve over such a long period. Missing days were imputed with patients' mean steps/day. Implausible daily step data (<100 steps/day) were rejected to avoid failure misreading. Step data were only considered up to the date patients stopped recording and thus stopped study participation.

Furthermore, patients could record and specify their training activities—for example, the type of sport—and weekly selfevaluate themselves regarding activity recommendations.

Heart complaints and hospitalizations. Patients were advised to record hospitalizations and complaints post-CR due to cardiac causes in the diary.

Statistical analysis

As the primary statistical approach, a Cox proportional hazard (PH) model was used via the R function coxph from the survival package.^{16,17} We examined the influence of steps/day (daily), EF-group during CR (as a binary variable; EF-group = 1 vs EF-group > 1), gender, and age on time until the occurrence of an event post-CR. The observation time was 1 year. Furthermore, based on the fitted Cox PH model mentioned above, different patient profiles and associated Kaplan-Meier

curves were generated to compare patients with a (constant) walking activity of 5000, 7500, 10000, and 12500 steps/day as well as EF-groups 1 versus 2-4.

Primary outcome

An event was defined as (a) death of cardiac cause or (b) hospitalization due to resuscitation after cardiac arrest, coronary interventions (CABG, PCI, or stent implantation), acute coronary symptoms or worsening angina with objective evidence (chest discomfort, discomfort in other areas of the upper body, shortness of breath, dizziness, nausea), arrhythmia, or cardiac syncopes. Patients' records in the diary (heart complaints and hospitalizations) were checked for such complications.

Results

Dropouts

From 175 eligible patients, 111 sent back their heart diaries (for clinical characteristics of patients refer to Table 1) and were willing to continue study participation. Thus, 64 patients dropped out and were lost to follow-up (Figure 1).

Adverse events

Within the study period post-CR, cardiac hospitalizations were documented for 25 patients within 12 months (Table 2). Finally, no patients died, resulting in an event-free survival of 75%.

We found a significantly increased hazard rate for EF-groups 2-4 ($\hat{\beta} = 1.371$), while the hazard rate significantly decreased with the number of steps/day ($\hat{\beta} = -1.514 \cdot 10^{-4}$). Hence, the risk of an adverse event post-CR, as defined above, was reduced by increased walking activity (Table 3).

The effects of the 2 most relevant predictors of survival are illustrated in Kaplan-Meier curves, comparing the survival curves for a (constant) walking activity of 5000 with 7500 steps/day post-CR (see Figure 2), for a (constant) walking activity of 10000 with 12500 steps/day post-CR (see Figure 3), and EF-group 1 with EF-groups 2-4 (see Figure 4, HR increase of 2.88). However, gender and age showed no statistically significant effects.

Discussion

Our results show that hospitalizations of patients with a higher number of steps/day for 1 year post-CR occur significantly less frequently and later. Furthermore, hospitalizations were more likely and earlier in patients with a lower EF, whereas no significant relationships with hospitalizations were found regarding age and gender.

Activity recommendations

Regarding the risk of coronary artery disease in healthy people (primary prevention), evidence exists for a non-linear doseresponse relationship, showing that individuals performing Table 1. Clinical characteristics of patients in cardiac rehabilitation.

| | N=111 (MALE=91, FEMALE=20) | | | |
|---|-------------------------------|--|--|--|
| Age in years | 61 ± 11 | | | |
| Body Mass Index kg/m ² | 28.17±4.47 | | | |
| EF-group, ^a number of patients (%) | | | | |
| EF-group 1: ≥55% | 91 (82) | | | |
| EF-group 2: <55->45% | 15 (13.5) | | | |
| EF-group 3: ≤45->35% | 3 (2.7) | | | |
| EF-group 4: ≤35% | 2 (1.8) | | | |
| Cardiovascular risk factors, number of patients (%) | | | | |
| Current smoking | 13 (11.7) | | | |
| LDL>100 | 39 (35.1) | | | |
| LDL>70 | 53 (47.7) | | | |
| Hypertension ^b | 20 (18) | | | |
| Diabetes | 26 (23.4) | | | |
| Overweight ^c | 24 (21.6) | | | |
| Nature of coronary artery disease, number of patients (%) | | | | |
| Single vessel | 40 (36) | | | |
| Double vessel | 47 (42.3) | | | |
| Triple vessel | 24 (21.6) | | | |
| Myocardial infarction, number of patients (%) | 52 (46.8) | | | |
| Betablocker medication | 76 (68.5) | | | |

Data presented as mean \pm 1 standard deviation or number of patients (with proportion in brackets).

^aEF: Ejection fraction calculated by Teichholz's formula and assessed via echocardiography.

^bHypertension was defined as systolic blood pressure >140 mmHg. ^cOverweight was defined as BMI (kg/m²) >30.

150 minutes of moderate leisure-time physical activity per week had a 14% lower risk of coronary heart disease. Conversely, engaging in 300 minutes per week lowered the risk by only up to 20% compared to individuals who reported no leisure-time physical activity.¹ Compared to the risk of heart failure, the evidence is similar, identifying a dose-dependent risk overall but especially in heart failure patients with a preserved EF.^{18,19} In contrast to the risk of coronary heart disease, where every activity increase is beneficial, a special amount-meeting or exceeding physical activity recommendations-appears relevant.¹⁹ Our results principally match the dose-response relationship for developing coronary heart disease, proclaiming that "some activity is better than none" and "additional benefits occur with more physical activity."1 Likewise, the risk reduction was higher when comparing moderate with low than when comparing moderate with high mean steps/day in patients for 1 year



Figure 1. Patient flow diagram.

Table 2. Steps/day and cardiac events post-cardiac rehabilitation (median follow-up time 218 days).

| | N=111 (MALE=91, FEMALE=20) |
|--|----------------------------|
| Steps/day post cardiac rehabilitation | 7333 ± 4426 |
| Number of patients with a steps/day mean for 1 year post cardiac rehabilitation ≥10000 (%) | 21 (19) |
| Number of patients with a steps/day mean for 1 year post cardiac rehabilitation ≥7500-<10000 (%) | 28 (25) |
| Number of patients with a steps/day mean for 1 year post cardiac rehabilitation ≥5000-<7500 (%) | 38 (34) |
| Number of patients with a steps/day mean for 1 year post cardiac rehabilitation ${<}5000$ (%) | 24 (22) |
| Reasons for cardiac rehabilitation, number of patients (%) | |
| Percutaneous transluminal angioplasty (PTCA) | 2 (1.8) |
| Percutaneous coronary intervention (PCI) | 100 (90.1) |
| Coronary artery bypass graft (CABG) | 6 (5.4) |
| Coronary artery disease | 3 (2.7) |
| Cardiac hospitalizations post cardiac rehabilitation | |
| Number of patients within 6 months | 19 (17) |
| Number of patients within 12 months | 25 (23) |
| Causes for cardiac hospitalizations | |
| Acute coronary symptoms (chest discomfort, pain) | 9 (8.11) |
| Coronary intervention | 4 (3.6) |
| Dyspnea | 2 (1.8) |
| Arrythmia | 4 (3.6) |
| Syncopes | 1 (0.9) |

Data presented as mean \pm 1 standard deviation or number of patients (with proportion in brackets).

| PARAMETRIC COEFFICIENTS | COEF | EXP(COEF) | SE(COEF) | Z | PR(>IZI) |
|---------------------------|------------|-----------|-----------|--------|-----------|
| EF>1 | 1.371e+00 | 3.9380 | 4.172e-01 | 3.285 | 0.00102** |
| Steps per day | -1.514e-04 | 0.9998 | 6.524e-05 | -2.321 | 0.02027* |
| Gender (male=1, female=0) | 7.751e-01 | 2.1709 | 7.405e-01 | 1.047 | 0.29522 |
| Age (in years) | 1.033e-02 | 1.0104 | 1.951e-02 | 0.529 | 0.59664 |

Table 3. Estimated coefficients reflecting the influence of steps/day (on a daily basis) post cardiac rehabilitation (CR), ejection fraction (EF)-group during CR (as a binary variable), gender and age on time until the occurrence of an event post CR based on a Cox proportional hazard (PH) model.

Abbreviation: EF > 1, ejection fraction <55%.

P*-value < .05. *P*-value < .01.



Figure 2. Survival function (including 95% CI as shaded area), here representing the probability over time an individual is free of an adverse event, with respect to a cardiac hospitalization comparing patients with an average of 5000 and 7500 steps per day for 1 year post cardiac rehabilitation.

post-CR. For example, if we compare a mean of 5000 steps/ day, classified as a sedentary threshold in healthy individuals, with a mean of 7500 steps/day (Figure 2), classified as a "somewhat active" threshold,²⁰ our results determine a risk reduction in terms of the hazard by 32%. Due to the underlying proportional hazards assumption of the Cox model, also comparing, for example, a mean of 10000 steps/day, classified as an "active" threshold, with 12500 steps/day (Figure 3), classified as "highly active,"20 the risk is lowered equivalently by 32%. However, absolute risk reduction differs, showing a decreased hazard of 0.43 when comparing means of 5000 and 7500 steps/day. Conversely, the hazard decreased by 0.20 when comparing means of 10000 and 12500 steps/day. Consequently, the difference from patients augmenting a small number of steps/day to patients augmenting a moderate number appears more relevant regarding prognosis than when comparing patients with high and very high numbers of steps.



Figure 3. Survival function (including 95% CI as shaded area), here representing the probability over time an individual is free of an adverse event, with respect to a cardiac hospitalization comparing patients with an average of 10000 and 12500 steps per day for 1 year post cardiac rehabilitation.

However, our results must be treated with caution, and comparison is difficult. A recently published meta-analysis states that activity monitors have the potential to enhance physical activity, but the effect might be overestimated due to publication bias.²¹ Overall, activity measurements differ with all their advantages and disadvantages.²² In our study, physical activity was directly measured via pedometry, an objective assessment tool that precisely measures steps but not the frequency, intensity or duration of an activity. Conversely, questionnaires generally have good usability but are vulnerable to recall bias, especially in older populations,²³ and can be inaccurate in recording distance or calculating energy expenditure.²⁴ Despite their limitations, pedometers can approximately indicate a person's general activity. Furthermore, the importance of intensity, duration, and frequency, and whether the physical activity volume alone is decisive, remains unclear because most studies do not consider the total energy expenditure.²⁵



Figure 4. Survival function (including 95% CI as shaded area), here representing the probability over time an individual is free of an adverse event, with respect to a cardiac hospitalization for 1 year post cardiac rehabilitation, comparing patients with an ejection fraction (EF) \geq 55% (EF 1) and <55% (EF > 1).

Moreover, it is questionable whether increased benefits are related to higher intensity levels or whether only the total volume of energy expenditure is higher and, therefore, the leading cause.¹⁰ Regarding the guidelines of medical associations, moderate or vigorous activities-or a combination-are recommended,⁹ resulting in an energy expenditure of at least 500 to 1000 metabolic equivalents of task-minutes per week.¹⁰ Secondary prevention recommendations are similar; however, training must be individualized considering risk determinants, especially in patients with a moderate or high risk,^{11,12} because-paradoxically-training may trigger sudden cardiac arrest in patients with cardiovascular diseases.²⁶ Therefore, activity recommendations in coronary patients must be individually tailored, which could lead to restrictions in, for example, competitive sports requiring vigorous effort.¹¹ Nevertheless, all chronic coronary disease patients should be encouraged to train.27 This could even be shown to be superior to stent implantation regarding event-free survival and exercise capacity over 1 year in selected patients with stable coronary disease.²⁸ Furthermore, vast evidence exists for the effectiveness (reduced cardiac mortality, reduced hospital readmissions) of exercise-based CR, especially in coronary patients,^{2,3} which due to its prevalence, represents the majority of patients in CR (approximately 80%—unstable angina pectoris: 3%, NSTEMI: 22.1%, STEMI: 39.2%, elective PCI: 1%, CABG: 20.1%).29

The more steps, the better prognosis?

Although we did not aim to determine whether the general recommendation of $10\,000$ steps/day for healthy people^{30,31}

could be an appropriate goal for coronary patients, we observed that most of our patients (81%) did not achieve this number. Moreover, according to smartphone data, the general population also does not meet this recommendation.³² Conversely, the mean steps/day of our patients for 1 year after CR was 7345 (SD 4448), much higher than for the general population, and met on average the suggested range of 6500 to 8000 steps for secondary cardiovascular prevention,³³ which is a somewhat theoretical recommendation associating this range with an energy expenditure of 1500 to 2200 calories per week. Another study suggests a threshold of >7500 steps/day, showing that this number is associated with a lower risk profile (blood pressure, lipid profile) in patients for 1 year after an acute coronary syndrome.8 In contrast to the above recommendations, which describe the relationship between steps and risk factors, we aimed to correlate the patient prognosis for a cardiac event directly with their number of daily steps after CR, and we demonstrated that coronary patients with a higher number of steps are hospitalized less often due to cardiac symptoms. Nevertheless, it remains unclear whether the prognosis of these patients was worse anyway, which could have led to reduced activity. The observation that hospitalizations were also more frequent in patients with a low EF supports this probable cause (prognosis was worse anyway), especially because the EF is a valuable marker for the patient prognosis.34 Furthermore, a reduced EF (<50%) is a feature of a high probability of exercise-induced adverse cardiac events³⁵ and is, therefore, consistent with activity restrictions (competitive sports).^{11,35} In a former study,7 we identified reduced walking activity for 1 year post-CR in patients with a lower EF. Furthermore, factors such as higher age, a higher New York Heart Association class, overweightness, or obesity, smoking behavior (smokers and exsmokers), and being female were associated with reduced walking activity, whereas the reduced walking activity in females compared to males could also be caused by the way and time of wearing (for example, leaving the pedometer in a handbag). Regarding this study, gender and age were unrelated to cardiac events; however, due to their relationship with the number of steps post-CR-assumable-they could indirectly influence the patient prognosis. Due to study design no causalities can be derived from our results; therefore, we could not support thresholds for step goals such as 10000^{30,31} or 7500⁸ steps/day, nor warn against augmenting less than 5000 steps/ day, often classified as a sedentary threshold.³⁶ In ill patients, walking behavior must also be viewed as a result of ability. Therefore, we would recommend an individual approach to understanding steps/day as a baseline orientation, which should be increased in patients and adapted based on capacities and preferences. Especially in patients with low step numbers, reasons should be sought since the number of steps/day appears a valuable marker regarding prognosis (cardiac hospitalizations) for 1 year post-CR in coronary patients.

Limitations

Our study findings are limited and must be treated with caution. First, they describe the prognosis of patients after CR-participation in an ambulatory facility (CCB Herzwerk) in Frankfurt. Second, measuring activity via pedometry is generally limited due to its inability to measure the frequency, intensity, duration, and type of activity. Therefore, it is impossible to determine whether activity guidelines were met. We instructed patients to self-evaluate weekly whether they met activity recommendations and record further training information-for example, non-walking activities (type of sport). Regrettably, most of them failed to provide this information in the diary. Therefore, we could not examine this data. Third, steps/day after CR was correlated with the EF of patients determined during CR, which possibly could have changed afterward. Fourth, we asked patients to wear the pedometers permanently for better wearing compliance-except during sleeping, swimming, and showering-because the pedometer is not waterproofed. Therefore, pedometers were also worn during non-walking activities, which probably led to miscounts.²² We attempted to collect and analyze further activity information (eg, type of sport); however, the data quality was poor, with numerous missing values, and no conclusions could be derived from it. Fifth, no information was provided about the activity behavior of patients before CR or illness. Although comparison was impossible, an activity increase can be expected due to CR as well as the proportionally high average number of steps/day compared to the general population.³² Sixth, due to the high demands on the patient (daily pedometry and recording), dropouts occurred and lowered the number of participants during the year post-CR. Possibly, motivated patients would rather participate in such a study and stick to it. However, in our case, we believe that an absolute representative study population is not particularly relevant because we focused on the relationship between step counts and the occurrence of an adverse event.

Author Contributions

Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data Curation, Writing- Original draft, Visualization, Project Administration: SA; Conceptualization, Methodology, Software, Formal analysis, Data Curation, Writing – Review & Editing, Visualization: AG; Conceptualization, Methodology, Resources, Writing – Review & Editing: AS; Methodology, Resources, Writing – Review & Editing: BN; Conceptualization, Methodology, Resources, Data Curation, Writing – Review & Editing: UK; Conceptualization, Methodology, Resources, Writing – Review & Editing: TV; Conceptualization, Resources, Data Curation, Writing – Review & Editing: PD, Conceptualization, Methodology, Writing – Review & Editing: DA; Conceptualization, Methodology, Formal analysis, Writing – Review & Editing, Supervision; JS.

ORCID iDs

Sinann Al Najem D https://orcid.org/0000-0003-4458-950X Andreas Groll D https://orcid.org/0000-0001-6787-9118

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