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Research paper

Association of objectively measured daily physical activity and health utility to disease severity in chronic heart failure patients: A cross-sectional study ☆

Kazuhiro P. Izawa [a,*], Yusuke Kasahara [b], Satoshi Watanabe [c], Koichiro Oka [d], Peter H. Brubaker [e], Keisuke Kida [f], Yoshihiro J. Akashi [g]

[a] Department of Public Health, Graduate School of Health Sciences, Kobe University, Kobe, Japan
[b] Department of Rehabilitation Medicine, St. Marianna University Yokohama-city Seibu Hospital, Yokohama, Japan
[c] Department of Rehabilitation Center, St. Marianna University School of Medicine Hospital, Kawasaki, Japan
[d] Faculty of Sport Sciences, Waseda University, Tokorozawa, Japan
[e] Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC, USA
[f] Department of Pharmacology, St. Marianna University School of Medicine, Kawasaki, Japan
[g] Division of Cardiology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

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ABSTRACT

Background and aims: Physical activity (PA) levels are related to mortality and morbidity in patients with chronic heart failure (CHF). Health utility (HU), a very important cost-effectiveness analysis for health care and health status, is measured by several preference-based utility measures. This study aimed to evaluate the relation between PA and HU and the effect of disease severity on PA and HU in patients with CHF.
Methods: We enrolled 226 consecutive outpatients with CHF (mean age, 57.5 years; males, 79.6%) in this retrospective cross-sectional study. Patients were divided into three groups by NYHA class for classification of disease severity. Patient characteristics, average step count in steps/day, PA energy expenditure (PAEE) in kcal/day for 7 days as assessed by accelerometer, and HU assessed by Short Form-6D were compared between the groups.
Results: Average step count ($r = 0.37$, $P < 0.01$) and average PAEE ($r = 0.36$, $P < 0.01$) correlated positively with HU in all patients. Patients were classified into three groups by NYHA class: class I ($n = 92$), class II ($n = 97$), and class III ($n = 37$). Average step counts (7618.58, 6452.51, and 4225.63 steps/day, $P < 0.001$), average PAEE (244.65, 176.88, and 103.72 kcal/day, $P < 0.001$), and HU (0.68, 0.63, and 0.57, $P < 0.001$) respectively decreased with the increase in NYHA class ($P < 0.001$).
Conclusion: This study showed a significant relationship of daily PA and HU to disease severity in patients with CHF. Although causation cannot be determined from this study, these results suggest that PA and HU may provide important information related to the severity of disease in patients with CHF.

1. Introduction

Several previous studies reported that not only peak oxygen uptake (VO_2) but also objectively measured physical activity (PA) are related to mortality in cardiac patients, including those with coronary artery disease, cardiac surgery, and chronic heart failure (CHF) [1–7]. Our previous study determined that daily step count objectively measured by accelerometry may be a prognostic indicator of mortality in CHF patients [5]. PA is also associated with health-related quality of life (HRQOL), major adverse cardiac events (MACE), and length of hospital stay in cardiac patients [2,3,5]. One of these studies [2] reported on the effects of leisure-time PA on the prognosis of coronary artery bypass graft surgery and found PA to be an important predictor of MACE and length of hospital stay.

☆ Work was performed in the Department of Rehabilitation Medicine, St. Marianna University School of Medicine Hospital, Kanagawa, Japan.

* Corresponding author at: Department of Public Health, Graduate School of Health Sciences, Kobe University, 10-2 Tomogaoka 7-chome Suma, Kobe 654-0142, Japan.
E-mail address: izawapk@harbor.kobe-u.ac.jp (K.P. Izawa).

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The reported goals of cardiac rehabilitation (CR) for these patients are to improve exercise capacity and HRQOL and to reduce coronary risk factors, subsequent cardiac events, sudden death, all-cause mortality, and hospitalization costs [1,8–12]. Moreover, exercise maintenance in CR patients may be one factor contributing to the improvement of HRQOL and leisure-time objective PA level [3].

In the economic evaluation of hospital costs, several previous studies suggested that health utility (HU), which can be assessed by several preference-based utility measures, is an important measure in the analysis of cost effectiveness in health care [12–17]. One such measure, the recently developed short-form 6D (SF-6D), is an instrument providing a summary score based on the SF-36 measure [18–22]. It was developed to enlarge the bases for economic evaluations while retaining the descriptive richness and sensitivity to change of the SF-36 [18–22]. Economic evaluation of CR has also been reported previously, and the findings have supported the implementation of CR [13–16].

The relation of physiological outcomes such as peak VO_2, hand grip strength, and knee extensor and flexor muscle strength to severity of disease in cardiac patients is well documented [23,24]. In addition, our previous study reported that the eight SF-36 subscale scores of HRQOL and peak VO_2 decreased with increase in the New York Heart Association (NYHA) functional class. In other words, HRQOL decreases as NYHA functional class increases and other physiological measures worsen [23–25].

There is presently very little evidence on the relationship between PA and HU and the effect of differences in disease severity on PA and HU in patients with CHF. In particular, the relation of different levels of disease severity as classified by NYHA functional class to objectively measured daily PA and HU in these patients is unknown. Thus, we hypothesized that a positive correlation would exist between daily PA and HU and that it may be related to differences of disease severity in patients with CHF. Therefore, the purpose of the present study was to evaluate the relation between PA and HU and the effect of disease severity on PA and HU in patients with CHF.

2. Methods

2.1. Participants

This retrospective cross-sectional study included 356 consecutive outpatients with CHF who visited St. Marianna University School of Medicine Hospital from August 2004 to November 2012 for assessment of CHF and who were evaluated by objectively measured PA and HU. Among these 356 patients, those aged 20 to 90 years old were included in the study. Patients classified as functional NYHA class IV and those with neurological, peripheral vascular, orthopedic, or pulmonary disease were excluded.

2.2. Measures

Clinical characteristics of the patients were evaluated by review of medical records and included age, sex, body mass index, left ventricular ejection fraction (LVEF), etiology of cardiac disease, and medications. A cardiologist assessed LVEF as the index of cardiac function by echocardiography and brain natriuretic peptide (BNP) concentration as the objective index of the level of disease severity in all of the patients. NYHA classification was determined in all patients by an independent investigator [24,25].

2.2.1. Objectively measured daily PA

The indices used to assess daily PA included average values of the daily number of steps taken and daily energy expenditure on PA (PAEE) measured over 9 days. They were determined with a Kenz Lifecorder EX 1-axial accelerometer (Suzuken Co., Ltd., Nagoya, Japan), a validated device shown to have good reliability [26,27]. The number of steps taken and PAEE are assessed on the basis of previously entered values of age, sex, height, and weight. The subjects wore the accelerometer at waist level [26,27]. The accelerometer computes daily PAEE every 4 s using body weight (W) and a proprietary manufacturer's factor Ka (exercise index), which is dependent on exercise intensity level: daily energy expenditure (kcal) = Ka (kcal/kg/4 s) × W (kg) [27]. After the subjects wore the device continually for 9 days (from Friday through Monday), data was downloaded into a computer for analysis with Microsoft Excel software. Over the 9-day collection period, PA was assessed during the middle 7 days that included Saturday and Sunday. The averages of daily number of steps taken and daily PAEE were respectively calculated as follows: total step count and kcal expended over 7 days divided by 7. In addition, we did not use the data if we could not obtain 7 consecutive days of data for measurement [4,5].

2.2.2. Health utility

The mean SF-6D utility scores were used to assess HU. The SF-6D was developed as a practical tool for obtaining a preference-based index from SF-36 data [18–21,28]. We initially assessed the patients with the SF-36. However, the SF-6D questionnaire was developed to obtain HU information from the SF-36 questionnaire for use in health economics evaluations and links between psychometric and preference/utility-based measures [18–21,28]. No limitation in any of the SF-36 dimensions indicates that no value is subtracted from the baseline value of 1.0, which indicates perfect health [18–21,28]. The higher the limitation in each domain, the higher is the value subtracted from the baseline score [18–21,28]. After assessing the subjects with the SF-36 (iHope International Co. Ltd., Kyoto, Japan), their scores were converted to mean SF-6D utility scores according to previous studies [18,20,21]. We collected all outcome data from our institution's database from July 2018 to March 2020 and analyzed it. This study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the St. Marianna University School of Medicine Institutional Committee on Human Research (approval no. 4050).

2.3. Statistical analysis

Results are expressed as mean ± standard deviation (SD). The relation between PA and HU data in all subjects was assessed by Pearson's correlation coefficient. One-way analysis of variance (ANOVA) and χ^2 tests were used to test for differences in clinical characteristics, PA, and HU between the three groups by NYHA class I, II, and III. Because comparisons between the three groups were performed for disease severity and the sample across the PA and HU values, Tukey's post hoc test was used to test for differences between three independent groups. A P value of <0.05 was considered to indicate statistical significance. Statistical analyses were performed with IBM SPSS 26.0 J statistical software (IBM SPSS Japan, Inc., Tokyo, Japan).

3. Results

3.1. Patient characteristics

Of the 356 potential subjects, 258 met the inclusion criteria; however, 32 additional patients were excluded because the data necessary to evaluate their clinical characteristics, exercise capacity, PA, and/or HU were either incomplete or missing. Thus, 226 patients were included for analysis on the basis of the inclusion criteria and available data (Fig. 1). These 226 patients were divided into three groups by NYHA class: class I ($n = 92$), class II ($n = 97$), and class III ($n = 37$). With the exception of BNP concentration, clinical characteristics of the patients were similar between the three groups in the present study (Table 1).

3.2. Relation between daily PA and HU

There was a positive correlation between daily PA and HU as measured by average step count ($r = 0.37$, $P < 0.01$), and average PAEE

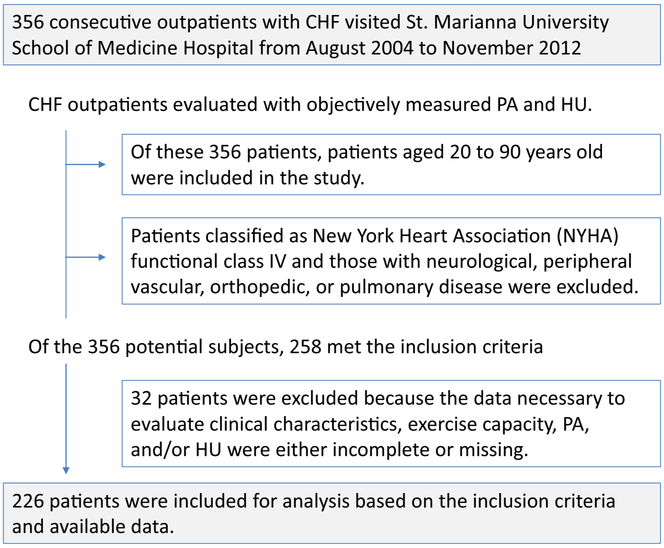

Fig. 1. Patient flow chart.

Table 1
Demographic and clinical characteristics.

Group	NYHA I	NYHA II	NYHA III	F or χ^2# value	*P* value
No. of patients	92	97	37		
Age (yrs)	56.5 ± 10.9	59.1 ± 12.4	61.2 ± 11.3	2.35	0.09
Male (%)	86.9	75.2	72.9	5.20#	0.07
BMI (kg/m^2)	24.1 ± 4.5	23.4 ± 4.4	22.9 ± 3.4	1.27	0.28
LVEF (%)	36.6 ± 12.6	36.7 ± 14.8	30.9 ± 11.7	2.56	0.08
BNP (pg/mL)	108.9 ± 123.3†‡	223.8 ± 247.0*,‡	426.8 ± 399.7*,†	21.15	<0.001
Etiology (%)					
Cardiomyopathy	73.9	55.7	56.8	8.19#	0.09
CABG/ Postoperative valvular disease	8.7	15.5	10.8	–	–
Myocardial infarction	17.4	28.8	32.4	–	–
Medications (%)					
Beta blockers	86.9	88.6	86.5	0.12#	0.94
ARB	44.6	46.4	48.6	0.13#	0.93
ACEI	50.0	49.5	70.2	5.01#	0.08
Diuretic	81.5	79.4	94.5	4.46#	0.10

NYHA = New York Heart Association; BMI = body mass index; LVEF = left ventricular ejection fraction; BNP = brain natriuretic peptide; CABG = coronary artery bypass grafting; ARB = angiotensin receptor blocker; ACEI = angiotensin converting enzyme inhibitor.
# χ^2 value.
* Significantly different compared with the NYHA I group.
† Significantly different compared with the NYHA II group.
‡ Significantly different compared with the NYHA III group.

($r = 0.36$, $P < 0.01$) correlated positively with the SF-6D score for HU in all patients (Fig. 2).

3.3. Difference in daily PA and HU measures between the three NYHA functional classes

There were significant differences between the three groups of patients in average step count, average PAEE of PA, and SF-6D score for HU (Table 2). The greatest decreases observed in average step count, average PAEE, and SF-6D score were those in the NYHA class III patients, and higher functional class was associated with poorer average step count, average PAEE, and SF-6D score.

4. Discussion

The present study is the first, to our knowledge, to examine the relationship between objectively measured physical activity levels (steps and PAEE) and HU and to evaluate their relation to disease severity in patients with CHF. As a result, average step count and average PAEE correlated positively with HU in all patients. In addition, the indices of average step count, PAEE, and HU decreased in accordance with the increase in NYHA class.

With the exception of BNP concentration, the clinical characteristics of the present study patients were similar and not significantly different between the three groups (Table 1). Many previous studies have reported that BNP increases as CHF severity increases, and thus, BNP is a well-known, independent factor for mortality from CHF [29,30]. In the present study, BNP concentration increased as NYHA functional class increased, as was shown in several earlier studies [24,30]. Therefore, we believe that BNP reflects the severity of CHF similar to the NYHA classification.

There was a positive correlation between PA and HU as measured by average step count, and average PAEE correlated positively with SF-6D in all of the study patients (Fig. 2). Previously, we also reported that at >18 months after myocardial infarction, cardiac patients who continued to exercise maintained both objectively measured daily PA and HRQOL as assessed by the SF-36 compared to the patients who did not maintain exercise [3]. Thus, exercise may be one of the factors contributing to the maintenance of these two indices [3], suggesting a potential link between PA and HRQOL during this time.

There were significant differences between the three patient groups in average step count, average PAEE, and SF-6D scores. The greatest decreases observed in these three measures were those in the NYHA class III patients, in whom higher functional class was associated with poorer values of average step count, average PAEE, and SF-6D score (Table 2).

A recent study reported in Japanese populations that the highest age-adjusted mean number of steps for men was 8235 steps/day in 2000, whereas it was 7667 steps/day in 2015, and those for women were 7474 steps/day in 1998 and 6691 steps/day in 2015 [31]. Compared to the values in this previous study, the average step count in our NYHA I patients of 7618.58 was slightly reduced, but step counts in both our NYHA II and III patients of 6452.51 and 4225.63, respectively, were reduced even more.

Previously, we found that an exercise capacity of ≥4 METs in males with CHF was equivalent to a mean daily step count of approximately 4397 steps of PA [4]. We also found that middle- and older-aged CHF patients with a measured exercise capacity of ≥5 METs could complete approximately 6000 steps/day [6]. Although there are differences in METS and numbers of steps taken between these previous studies and the present study, the results of the present study indicate that the exercise intensity and amount of exercise that can be achieved by CHF patients may differ according to their NYHA class.

The average values of PA obtained in the present study patients can be easily measured and potentially useful for predicting cardiac-related mortality in CHF outpatients [5,32]. Values reported in previous studies ranged from 3571 to 4889 steps/day [5,32]. The step count value for PA of 4226 steps/day in our NYHA class III patients with CHF was similar to those of these previous studies [5,32]. Thus, the step count value of NHYA III patients would appear to indicate lower PA than that of the NYHA I and II patients and that NYHA III patients might not have the reserve capacity for PA that the NYHA I and II patients do. NYHA class III CHF patients might have a poorer prognosis from the viewpoint of the PA compared with that for the NHYA class I and II patients.

An earlier report [33] suggested that patients should be encouraged to expend 200–300 kcal/day to achieve the overall amount of PAEE

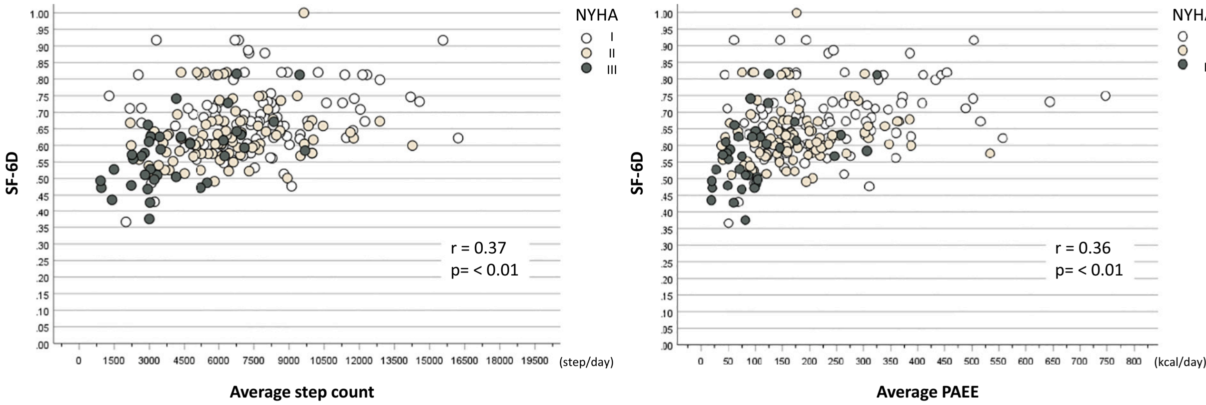

Fig. 2. Relation between daily PA and HU. There was a positive correlation between PA and HU as measured by average step count, and average PAEE correlated positively with the SF-6D score in all study patients. PA = physical activity; HU = health utility; PAEE = energy expenditure on PA; SF-6D = short form-6D.

Table 2
PA and HU in relation to disease severity in the study patients.

Group	NYHA I	NYHA II	NYHA III	F value	*P* value
No. of patients	92	97	37		
PA					
Average step count (steps/day)	7618.58 ± 3010.17[†‡]	6452.51 ± 2333.18[*,‡]	4225.63 ± 2279.77[*,†]	21.15	<0.001
Average PAEE (kcal/day)	244.65 ± 136.77[†,‡]	176.88 ± 87.58[*,‡]	103.72 ± 74.95[*,†]	22.22	<0.001
HU					
SF-6D	0.68 ± 0.11[†,‡]	0.63 ± 0.86[*,‡]	0.57 ± 0.10[*,†]	16.95	<0.001

NYHA = New York Heart Association; PA = physical activity; PAEE = energy expenditure on PA; HU = Health Utility; SF-6D = Short Form-6D.
[*] Significantly different compared with the NYHA I group.
[†] Significantly different compared with the NYHA II group.
[‡] Significantly different compared with the NYHA III group.

considered necessary for the secondary prevention of cardiovascular disease. In the present study, PAEE in the NYHA I patients was similar to that of this earlier study at 245 kcal, but the respective values of 177 kcal and 104 in our NYHA II and III CHF patients were much lower than those recommended in that study [33]. Because there are differences in step counts and PAEE between the present study and those of these previous studies that might relate to several factors such as age difference, etiology and severity of disease, and socio-environmental factors, the present results could not be compared directly with those of the previous studies.

A recent systematic and meta-analysis review reported that among 541 cardiac patients (age, 60.8 years; men, 79.6%.) from 6 studies in whom step counts were used to evaluate PA in the intervention and control groups, self-monitoring significantly increased PA (95% confidence interval, 1916–3090 steps/day, $P < 0.05$) [34]. As the age and sex characteristics of the present study patients were similar to those of the patients in these 6 previous studies, self-monitoring for PA might be a useful interventional strategy to improve PA in patients with CHF. We suggest that patients measure their current PA with smartphone applications or PA meters after baseline goals are set for each patient's PA level. Based on this, patients can record their daily PA. Encouraging patients to reach their PA goals can increase their self-efficacy, and repetition of physical exercise will eventually lead to increased levels of PA.

The HU indices also decreased with increases in NYHA class. Shiroiwa et al. [22] reported on 1143 adult respondents (aged 20 to 70 years or older) who were randomly sampled from across Japan using data from the Basic Resident Register. The mean scores of the SF-6D in this general Japanese population classified according to sex and age categories were as follows: 20–29 years, 0.731 in males, 0.727 in females; 30–39 years, 0.729 in males, 0.695 in females; 40–49 years, 0.704 in males, 0.688 in females; 50–59 years, 0.741 in males, 0.704 in females; 60–69 years, 0.691 in males, 0.658 in females; and ≥ 70 years, 0.674 in males, 0.635 in females [22]. The average age and percentage of males in the present study were 56.5 years and 86.9% in NYHA I, 59.1 years and 75.2% in NHYA II, and 61.2 years and 72.9% in NHYA III. The SF-6D values of the present study were 0.68 in NYHA I, 0.63 in NYHA II, and 0.57 in NHYA III and tended to be lower than those of the general Japanese population. In particular, the SF-6D value in NHYA III was the lowest. Therefore, the HU value was also considered to be lower in the CHF patients than that in the general Japanese population, and it decreased further depending on disease severity.

In a cost-utility analysis carried out in tandem with a randomized controlled trial using the SF-6D in learning and coping strategies in CR that comprised 825 patients over 18 years of age admitted with ischemic heart disease or heart failure, Dehbarez et al. reported mean SF-6D scores of 0.739 at baseline, 0.798 at 2 months after intervention, and 0.794 after 5 months of follow-up [35]. Although there were differences in etiologies between the Dehbarez et al. study and the present study, the respective mean SF-6D utility scores in the present study of 0.68 in NYHA I, 0.63 in NYHA II, and 0.57 in NHYA III 0.72, were lower than those of the patients studied by Dehbarez et al. Therefore, we need to evaluate whether HU continues to change over the long term following a phase II CR program. In addition, this information may be useful for calculating quality-adjusted life year (QALY) in economic evaluations [22] and examining the QOL score of CHF patients in future trials.

4.1. Study limitations

This study has several limitations. This is a retrospective cross-sectional study with a small sample size that used mean scores for PA and PAEE assessment that were obtained only over one 7-day period. Data on the timing of PA and HU in relation to cardiac-related mortality or re-hospitalization including information on length of diagnosis, recent hospitalization, or CHF exacerbation for the patients in the 3 NYHA classes were not assessed due to the limited amount of related data available. Further, correlational analyses do not determine causality. The present study comprised subjects who were predominantly male. In future work, a higher percentage of females should be evaluated to determine the possible effects of gender difference. Also, the reasons for impaired PA outcomes were not ascertained. For example, other conditions, such as depression or intensity of PA, may also result in lower HU values. We did not determine BMI, body composition, lean body mass, or PA in relation to local community environments [36]. We also did not investigate heart failure types such as heart failure with reduced, mid-range, or preserved ejection fraction [37]. Therefore, further study is needed to investigate the relation between PA outcomes and other many factors. The primary aim of the present study was to assess the differences in the severity of illness and the relationship to PA and HU. Nevertheless, it would be of interest to document the longitudinal changes in PA and HU in patients with CHF. Future work should also be directed toward interventions to determine whether increased PA correlates with increased HU by NHYA class in patients with CHF.

5. Conclusions

The results of this study indicate a significant relationship of daily PA and HU to disease severity in patients with CHF and that the average step counts in our CHF patients were reduced compared to those previously reported in Japanese populations. Although causation cannot be determined from this study, these results suggest that PA and HU may provide important information related to the severity of disease in patients with CHF. The PA levels determined in this study could be used by clinicians or patients as minimum target values based on disease severity in patients with CHF of different NYHA functional class. Future longitudinal studies will be required to evaluate the effect of improvement of these values in patients with CHF. In addition, long-term follow-up will be needed to evaluate possible time-related benefits of this improvement.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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