表 1　患者背景

	DM 群（n=47）	非 DM 群（n=143）	p 値
年齢（歳）	61.0 ± 11.0	58.8 ± 9.6	0.19
身長（cm）	166.5 ± 6.6	167.0 ± 6.0	0.68
体重（kg）	68.8 ± 13.1	66.1 ± 8.5	0.11
BMI（kg /m^2）	24.6 ± 4.0	23.6 ± 2.5	0.06
併存疾患（例）			
高血圧	40	109	0.23
脂質異常症	26	93	0.30
HbA_{1c}（%）	7.6 ± 1.8	5.1 ± 0.3	<0.01
心筋逸脱酵素（IU/l）	227.2 ± 181.9	281.6 ± 305.3	0.28
左室駆出率（%）	49.8 ± 11.9	52.3 ± 10.7	0.20
有意冠動脈狭窄枝数（例）			
0 枝	31	92	0.86
1 枝	12	40	0.45
2 枝	4	11	0.53
投薬内容（例）			
ACE 阻害薬	20	75	0.16
A Ⅱ受容体拮抗薬	22	48	0.08
β 遮断薬	14	56	0.16
硝酸薬	19	41	0.10
Ca 拮抗薬	9	13	0.06
利尿薬	8	16	0.21
経口血糖降下薬	23		
インスリン	18		

平均値 ± 標準偏差
BMI（Body mass index），ACE（アンジオテンシン変換酵素），A Ⅱ（アンジオテンシンⅡ）

表 2　最高酸素摂取量，身体機能指標，自律神経指標

	DM 群（n=47）	非 DM 群（n=143）	p 値
最高酸素摂取量（ml/kg/min）	24.3 ± 4.5	27.1 ± 4.4	<0.01
身体機能指標			
膝伸展筋力（Nm/kg）	1.75 ± 0.37	1.93 ± 0.41	<0.01
握力（kgf）	38.1 ± 7.1	41.3 ± 7.8	0.02
片脚立位時間（秒）	22.2 ± 9.9	28.5 ± 3.6	<0.01
前方リーチ距離（cm）	39.7 ± 4.7	40.6 ± 5.2	0.50
体脂肪率（%）	24.8 ± 4.7	23.9 ± 4.1	0.21
筋肉量（kg）	23.1 ± 3.8	21.9 ± 2.9	0.05
自律神経指標			
% HRR（%）	79.1 ± 16.1	85.6 ± 18.2	0.04
⊿ HR（bpm）	66.0 ± 13.5	75.4 ± 16.3	<0.01

平均値 ± 標準偏差
DM（Diabetes Mellitus），HRR（Heart Rate Reserve），HR（Heart Rate）

表3　DM群の最高酸素摂取量を従属変数とした重回帰分析の結果

独立変数	非標準化係数		t	p値
	β	標準誤差		
定数	8.283	3.787	2.187	0.035
膝伸展筋力	4.505	1.839	2.450	0.019
⊿HR	0.125	0.052	2.407	0.021

重相関係数（R）＝0.58
決定係数（R^2）＝0.30

の低下を指摘しており，本研究では左室拡張能を調査できていないので，この点に関する検討はできていない。

2. DM群の身体機能低下の原因

DMの有無による筋力やバランスなどの身体機能の比較をした報告は多くない。DM患者は筋肉量に対する筋力発揮が弱いことが指摘されている[26]。DM患者は，DEXA法による筋肉量に対する膝伸展筋力（筋力筋量比）が非DM群より低下しており，筋力の質的低下が生じているものと考えられている。本研究結果でも，筋肉量はDM群の方が多いにも関わらず，体重比での膝伸展筋力はDM群の方が低下しており先行研究を支持する結果を得た。また，Andersenら[27]によると，2型DM患者と年齢をマッチングしたコントロール群を比較したところ，DM群では膝関節屈曲筋力で14%，足関節底屈筋力で17%，足関節背屈筋力で14%の有意な低下を認めたとしている。これらの筋力低下は，糖尿病神経障害のスコアと相関を認め，重回帰分析の結果からDM群の筋力低下の原因を糖尿病神経障害の影響と報告している。なお，その研究では上肢の筋力低下はみられていない。以上のことから，糖尿病神経障害患者では，下肢の中でも膝から足部の，より末梢部の筋力低下が生じるものと考えられている。本研究では下肢筋力の指標として膝伸展筋力しか採用していないため，足関節周囲の筋力低下の有無は不明である。また，今回は糖尿病神経障害の検査を行っていないため，DM群における膝伸展筋力低下の原因の検討は不十分である。

その他，Parkら[28]は，高齢2型DM患者では，非DM群と比較して3年の追跡期間において下肢の筋力と筋肉量の低下速度が急速であったと報告している。その報告においてはDM群の筋力低下の具体的な原因は明らかにされていないが，Sarcopenia（加齢性筋肉減少症）や炎症性サイトカインとの関係を指摘している。IL-6やTNFαなど炎症性サイトカインは筋肉組織での異化作用を亢進させるため，筋肉量および筋力低下と関連があると考えられている[29]。DM患者では，これらIL-6などの炎症性サイトカインが増加していると報告されており[30]，推察ではあるが，DM患者の膝伸展筋力の低下には神経障害の有無および身体活動状況以外に，炎症性サイトカインなどの影響も関与している可能性が考えられる。

DM患者のバランス障害は以前から指摘されており，その要因としては糖尿病神経障害による足部からの深部感覚入力の異常が考えられている。また，Ozdirencら[31]の研究では，糖尿病性多発神経障害を認めないDM患者においても，年齢を一致させた健常者と比較して，バランス能力の指標とされる片脚立位時間の短縮が認められている。一方，野村ら[32]は，2型DM患者の片脚立位時間の短縮は糖尿病神経障害による感覚障害の影響以外に，膝伸展筋力低下と関連があることを報告している。本研究では，糖尿病神経障害の有無を判定するアキレス腱反射や振動覚の測定，および足底の感覚障害の評価もできていないが，DM群のバランス能力の低下には，これら糖尿病神経障害の存在や膝伸展筋力の低下が何らかの影響を及ぼしていたものと推察された。

以上のことから，DM患者は運動耐容能以外にも身体機能の低下を認めていることから，筋力やバランス能力を含めた運動機能を評価する必要があると考えられた。

3. DM群の運動耐容能低下の要因

心疾患を併存していないDM患者の運動耐容能が，非DM患者に比し，低下していることは先行研究で指摘されている[31,33]。その運動耐容能の低下の要因としては，糖尿病のコントロール，左心室機能障害，自律神経障害などがあげられている[33]。また，AMI患者においても，DMを合併した患者は合併していない患者と比較し運動耐容能が低下していることが報告されている[6-12]。こうしたDM患者における運動耐容能低下の機序としては，主に自律神経障害の影響が指摘されている[9-12]。これまでDM患者の運動耐容能低下を指摘した研究では，運動機能を含めた検討は少ない。その背景には，臨床において客観的な筋力測定機器の普及が十分ではない可能性があることに加え，DM患者の運動機能の低下に着目した報告[26-28]から年数を経ていないことなどが考えられる。したがって，運動耐容能には複数の要因が関与していることから，多数の臨床指標を用いた

多角的な研究が必要である。

今回，DM群の運動耐容能と年齢，体脂肪率，膝伸展筋力，握力，および⊿HRが単相関することが認められた。これらの指標の中より，DM群の運動耐容能を規定する要因を重回帰分析により解析した結果，⊿HRと膝伸展筋力が抽出された。すなわち，DM群の運動耐容能低下の要因として，従来から指摘されている自律神経障害による心拍応答不全以外とともに膝伸展筋力の低下も関与していることが明らかとなった。山崎ら[15]は，心筋梗塞患者の膝伸展筋力と運動耐容能との間には単相関を認めたと報告している。今回の結果では，DM群は非DM群と比較して膝伸展筋力が有意に低下していることにより，このことが運動耐容能を低下させているひとつの要因になるものと考えられた。

DM患者の血糖コントロール改善を目的とした運動には，有酸素運動とともにレジスタンストレーニングを併用したほうがより効果的である[34)35)]ことから，近年はレジスタンストレーニングが注目されている。また，同様に心臓リハビリテーションの領域においてもレジスタンストレーニングの重要性が指摘されている[36)]。DM群の運動耐容能の低下に膝伸展筋力の低下が関与していることからDMを合併したAMI患者の運動処方にレジスタンストレーニングを選択することは，血糖コントロールの改善のみならず運動耐容能改善にも有用となる可能性がある。

4. 本研究の限界と今後の課題

本研究は後方視研究のため，DM罹病期間や糖尿病神経障害の有無などが不明であるため，それらの影響は検討できていない。今後は，DM群の運動耐容能低下の要因について，DM罹病期間や神経障害などを含めた検討が必要と思われる。さらに，本研究の対象者はトレッドミルによる運動負荷試験が実施できた症例のみであるため，高齢で運動機能の低い症例はほとんど含まれておらず，そうした症例についての検討も今後の課題である。

最後に，本研究は横断研究であり，これらふたつの要因の変化がPeak $\dot{V}O_2$の改善につながるかについては言及できない。したがって，今後は縦断的研究によるさらなる検討を要するものと考えられる。

結　　論

DM群は非DM群と比較しPeak $\dot{V}O_2$，自律神経指標以外にも上下肢筋力，およびバランス機能が低下していた。DM群の運動耐容能低下には，先行研究でその関与が指摘されている自律神経指標（⊿HR）とともに，今回新たに膝伸展筋力の低下が関与することが明らかとなった。

文　　献

1) http://www.mhlw.go.jp/houdou/2008/12/h1225-5.html（参照　2011-01-26）.
2) Tominaga M, Igarashi K, *et al.*: Impaired glucose tolerance is a risk factor for cardiovascular disease, but not impaired fasting glucose. Diabetes Care. 1999; 22: 920–924.
3) 日本糖尿病学会（編）：糖尿病治療ガイド2010. 文光堂，東京，2010，p80.
4) 加藤丈二，小川洋司，他：再灌流時代における急性心筋梗塞症例の予後規定因子の検討. 東女医大誌. 2007; 77: 759–763.
5) 西山昌秀，井澤和大，他：急性心筋梗塞患者における年度別の臨床的背景についての検討. 理学療法　技術と研究. 2007; 35: 34–37.
6) Izawa K, Tanabe K, *et al.*: Cardiopulmonary response abnormalities during exercise in patients with acute myocardial infarction complicated by non-insulin-dependent diabetes mellitus. Cardiovascular Reviews & Reports. 2001; 22: 534–742.
7) 井澤和大，田辺一彦，他：心筋梗塞患者における糖尿病合併が運動時心血管反応に及ぼす影響. 理学療法学. 2000; 27: 69–74.
8) 後藤葉一，西　　功，他：心臓リハビリテーションにおける疾患管理　現状と今後の課題. 心臓リハ. 2005; 10: 182–186.
9) 鈴木健吾，大宮一人，他：心筋梗塞患者における運動療法の効果：糖尿病の合併の有無による差異. J Cardiol. 2003; 41: 159–168.
10) Kasahara Y, Izawa K, *et al.*: Influence of autonomic nervous dysfunction characterizing effect of diabetes mellitus on heart rate response and exercise capacity in patients undergoing cardiac rehabilitation for acute myocardial infarction. Circ J. 2006; 70: 1017–1025.
11) 伊藤　慎，川上利香，他：糖尿病がある急性心筋梗塞患者における運動耐容能低下の機序. 心臓. 2006; 38: 42–45.
12) Izawa K, Tanabe K, *et al.*: Impaired Chronotropic Response to Exercise in Acute Myocardial Infarction Patients with Type 2 Diabetes Mellitus. Jpn Heart J. 2003; 44: 187–199.
13) Ades PA, Savage PD, *et al.*: Aerobic capacity in patients entering cardiac rehabilitation. Circulation. 2006; 113: 2706–2712.
14) Gadsbøll N, Høilund-Carlsen PF, *et al.*: Cardiac function and maximal exercise capacity early after acute myocardial infarction. Eur Heart J. 1991; 12: 1189–1194.
15) 山﨑裕司，山田純生，他：心筋梗塞患者の下肢筋力　下肢筋力と運動耐容能の関連. 総合リハ. 1994; 22: 41–44.
16) 海鋒有希子，笠原酉介，他：急性心筋梗塞患者における退院時運動耐容能の関連要因に関する検討. 心臓リハビリテーション. 2010; 15: 115–119.
17) 日本糖尿病学会（編）：科学的根拠に基づく糖尿病診療ガイドライン改訂（第2版）. 南江堂，東京，2007，pp7–16.
18) Tanabe K, Yokoyama Y, *et al.*: Effect of anaerobic threshold level exercise training upon oxygen uptake kinetics and sympathetic nervous activity in patients with chronic phase of myocardial infarction. J Noninvasive Cardiol. 1998; 2: 31–37.
19) American College of Sports Medicine: ACSM's Guidelines for Exercise Testing and Prescription. In: Johnson EP (ed): Clinical exercise testing. 6th ed, Williams & Wilkins, Baltimore, 2000, pp91–114.
20) Izawa K, Hirano Y, *et al.*: Improvement in Physiological

Outcomes and Health-Related Quality of Life Following Cardiac Rehabilitation in Patients With Acute Myocardial Infarction. Circ J. 2004; 68: 315–320.
21) 森尾裕志，大森圭貢，他：指示棒を用いたFunctional Reach Testの開発．総合リハ．2007; 35: 487–493.
22) 平木幸治，井澤和大，他：回復期運動療法における体組成の経時的変化についての検討．心臓リハビリテーション．2005; 10: 37–40.
23) Miyatani M, Kanehisa H, *et al.*: Validity of estimating limb muscle volume by bioelectrical impedance. J Appl Physiol. 2001; 91: 386–394.
24) 矢崎晃広，橋本俊雄，他：心筋梗塞患者での冠動脈再狭窄と運動耐容能との関係．日本臨床生理学会雑誌．1997; 27: 181–185.
25) 関　敦，大宮一人，他：心筋梗塞患者におけるBNPと運動耐容能への糖尿病合併の影響．心臓．2001; 33: 11–13.
26) Park SW, Goodpaster BH, *et al.*: Decreased muscle strength and quality in older adults with type 2 diabetes. Diabetes. 2006; 55: 1813–1818.
27) Andersen H, Nielsen H, *et al.*: Muscle Strength in Type 2 Diabetes. Diabetes. 2004; 53: 1543–1548.
28) Park SW, Goodpaster BH, *et al.*: Accelerated Loss of Skeletal Muscle Strength in Older Adults With Type 2 Diabetes. The Health, Aging, and Body Composition Study. Diabetes Care. 2007; 30: 1507–1512.
29) 沖田　実，坂野裕洋：筋力低下のメカニズム．理学療法．2007; 24: 905–913.
30) 小川　渉：Interleukin-6と糖代謝．医学のあゆみ．2006; 219: 463–466.
31) Ozdirenc M, Biberoğlu S, *et al.*: Evaluation of physical fitness in patients with type 2 diabetes mellitus. Diabetes Res Clin Pract. 2003; 60: 171–176.
32) 野村卓生，池田幸雄，他：2型糖尿病患者における片脚立位バランスと膝伸展筋力の関係．糖尿病．2006; 49: 227–231.
33) Fang ZY, Sharman J, *et al.*: Determinants of Exercise Capacity in Patients With Type 2 Diabetes. Diabetes Care. 2005; 28: 1643–1648.
34) Colberg SR, Sigal RJ, *et al.*: Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement executive summary. Diabetes Care. 2010; 33: 2692–2696.
35) Sigal RJ, Kenny GP, *et al.*: Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. Ann Intern Med. 2007; 147: 357–369.
36) 野原隆司（班長）：心疾患におけるリハビリテーションに関するガイドライン（2007年度改訂版）．http://www.j-circ.or.jp/guideline/pdf/JCS2007_nohara_h.pdf（参照　2011-01-26）．

〈**Abstract**〉

Determinants of Exercise Capacity in Acute Myocardial Infarction Patients with Diabetes Mellitus

Koji HIRAKI, PT, MS, Kazuhiro P IZAWA, PT, MS, PhD, Satoshi WATANABE, PT, BS, Yuji MORIO, PT, MS
Department of Rehabilitation Medicine, St. Marianna University School of Medicine Hospital

Yusuke KASAHARA, PT, MS, PhD
Department of Rehabilitation Medicine, St. Marianna University School of Medicine Yokohama City Seibu Hospital

Naohiko OSADA, MD, Kazuto OMIYA, MD
Department of Internal Medicine, St. Marianna University School of Medicine Hospital

Setsu IIJIMA, MD
Graduate School of Comprehensive Human Sciences, University of Tsukuba

Purpose: Acute myocardial infarction (AMI) patients with type 2 diabetes mellitus (DM) have decreased exercise capacity. The purpose of this study was to determine exercise capacity in such patients.

Methods: One hundred ninety male AMI patients were divided into two groups, the DM group (n=47) and the non-DM group (n=143). Peak $\dot{V}O_2$ as an index of exercise capacity was assessed by cardiopulmonary exercise testing performed in each patient at 1 month after the onset AMI.

Results: Peak $\dot{V}O_2$ (24.3 vs. 27.1 ml/kg/min, $p < 0.01$), knee extensor muscle strength (1.75 vs. 1.93 Nm/kg, $p < 0.01$), handgrip strength (38.1 vs. 41.3 kgf, p=0.02), single-leg stance time (22.2 vs. 28.5 sec, $p < 0.01$), % HRR (79.1 vs. 85.6%, p=0.04), and ⊿HR (66.0 vs. 75.4 bpm, $p < 0.01$) were all significantly reduced in the DM group versus the non-DM group. Stepwise linear regression analysis revealed that knee extensor muscle strength and ⊿HR were significant predictors of peak $\dot{V}O_2$ (r=0.58, R^2=0.301, $p < 0.01$).

Conclusions: Knee extensor muscle strength and ⊿HR may predict a reduction in peak $\dot{V}O_2$ in AMI patients with type 2 DM.

Relation Between Sleep Quality and Physical Activity in Chronic Heart Failure Patients

Kazuhiro P. Izawa[1*], Satoshi Watanabe[1], Koichiro Oka[2], Koji Hiraki[1], Yuji Morio[1], Yusuke Kasahara[1], Naoya Takeichi[1], Takae Tsukamoto[3], Naohiko Osada[4], Kazuto Omiya[4] and Haruo Makuuchi[5]

[1]Department of Rehabilitation Medicine, St. Marianna University School of Medicine Hospital, Kanagawa 216-8511, Japan, [2]Faculty of Sport Sciences, Waseda University, Saitama 359-1192, Japan, [3]Department of Nursing, St. Marianna University School of Medicine Hospital, Kanagawa 216-8511, Japan, [4]Division of Cardiology, Department of Internal Medicine, St. Marianna University School of Medicine, Kanagawa, 216-8511 Japan, [5]Department of Cardiovascular Surgery, St. Marianna University School of Medicine, Kanagawa, 216-8511, Japan

Received: June 16, 2011; Accepted: July 25, 2011; Revised: July 21, 2011

Abstract: To determine self-reported sleep quality-related differences in physical activity (PA) and health-related quality of life (HRQOL) and target values of PA for high-quality sleep in chronic heart failure (CHF) outpatients, 149 CHF outpatients (mean age 58 years) were divided into two groups by sleep-quality level determined via self-reported questionnaire: shallow sleep (SS) group ($n = 77$) and deep sleep (DS) group ($n = 72$). Steps were assessed by electronic pedometer, HRQOL was assessed with the Short Form 36 (SF-36) survey, and data were compared between groups. PA resulting in high-quality sleep was determined by receiver-operating characteristics curves. All SF-36 subscale scores except that of bodily pain were significantly decreased in the SS versus DS group. A cutoff value of 5723.6 steps/day and 156.4 Kcal/day for 1 week were determined as target values for PA. Sleep quality may affect PA and HRQOL, and attaining target values of PA may improve sleep quality and HRQOL of CHF outpatients. Patents relevant to heart failure are also discussed in this article.

Keywords: Chronic heart failure, health-related quality of life, physical activity, self-reported sleep quality.

INTRODUCTION

Sleep disorder in chronic heart failure (CHF) patients has been documented in the literature [1-5]. Previous review suggests increased mortality in patients with CHF suffering from sleep disorder in contrast to those without sleep disorder [3]. Ng *et al.* [4] reported that sleep disorder severity was most closely associated with the degree of abnormal ventilatory response during and after exercise in a group of stable CHF patients. Moreover, patients with CHF often report sleeping difficulties (e.g. initiating and maintaining sleep and daytime sleepiness), and this is associated with decreased quality of life (QOL) compared with patients without sleep difficulties [5]. Particularly, excessive sleepiness may affect education, employment, and interpersonal relations, and directly degrade QOL, particularly in relation to functional capacity, health, and the sensation of well-being [6, 7]. Lopes *et al.* [7] previously showed that excessive sleepiness and lack of physical activity affected the QOL of apneic patients, which was worse among sleepy non-physically active subjects and increasingly worse in the subjects with severe apnea. Thus, sleep disorder may cause sleepiness and presumably due to increased sleepiness, it may be related to a reduction in physical activity and health-related quality of life (HRQOL).

There are several methods for diagnosing sleep disorder in CHF patients [3]: polysomnography, portable polysomnograph monitors, questionnaires, and techniques such as heart rate variability [3]. Questionnaires have recently shown promise in screening for sleep apnea. The use of questionnaires to identify patients with a high likelihood of sleep disorder has been advocated in view of the limited accessibility and cost of formal polysomnography. These questionnaires can provide an assessment of the degree of sleepiness or wakefulness, and tools for the assessment of sleep disorder range from more subjective measures such as the Epworth Sleepiness Scale (ESS) [8] to more objective measures such as polysomnography [3, 9].

In the clinical setting, we often ask our CHF patients about sleepiness in relation to their physical condition. Because we think that the amount of sleep a CHF patient gets might influence their level of physical activity or HRQOL, we pose questions such as "Do you sleep well?" and "How was the quality of your sleep, shallow (poor) or deep (good)?" To date, little is known about the determinants of physical activity and HRQOL in relation to differences in sleep quality in CHF outpatients. Therefore, we investigated whether sleep quality is related to differences in physical activity and HRQOL in CHF outpatients and whether there is a target goal for physical activity that improves sleep quality in these patients. We thus hypothesised that shallow (poor) sleep quality might be related to reduced physical activity and HRQOL and could be evaluated by self-reported questionnaire.

*Address correspondence to this author at the Department of Rehabilitation Medicine, St. Marianna University School of Medicine Hospital, 2-16-1 Sugao, Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan;
Tel: +81-44-977-8111 (6157); Fax: +81-44-977-9486;
E-mail: izawapk@ga2.so-net.ne.jp

1574-8901/11 $100.00+.00

The purpose of the present study was to determine 1) differences in physical activity and HRQOL as related to sleep quality and 2) to determine target values of physical activity that would improve sleep quality and HRQOL in outpatients with CHF.

METHODS

Study Design and Subjects

This was a cross-sectional study in which consecutive stable CHF outpatients were selected from 979 cardiac patients with myocardial infarction, coronary artery bypass grafting, valve replacement, or CHF who visited St. Marianna University School of Medicine Hospital from April 2006 to May 2009 for evaluation of self-reported sleep quality as related to physical activity and HRQOL. From these 979 patients, 161 stable CHF outpatients who were beginning a cardiac rehabilitation program at the request of their physician or by their own volition were included in the present study. The inclusion criterion was a left ventricular ejection fraction (LVEF) below 45%. Patients classified as New York Heart Association (NYHA) functional class IV were excluded as were those who had neurological, peripheral vascular, orthopedic, or pulmonary disease Fig. (1).

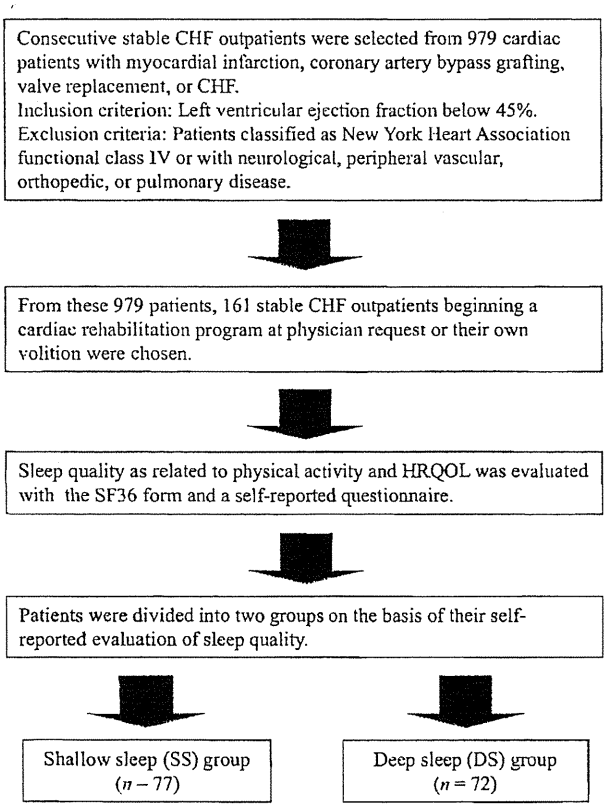

Fig. (1). Diagram of patient selection process.

CHF: chronic heart failure; ESS, Epworth Sleepiness Scale; HRQOL: health-related quality of life.

Clinical Characteristics of the Patients

We evaluated several patient characteristics, including age, sex, body mass index, LVEF, NYHA classification, employment status, etiology of heart failure, and medications. A cardiologist assessed LVEF as the index of cardiac function. An independent investigator determined NYHA classification in all patients.

Self-reported Sleep Quality Questionnaire

First, we asked all patients to determine their quality of sleep, i.e., whether their sleep was shallow (interpreted to mean poor sleep) or deep (interpreted to mean good sleep), in the past 1 week using the self-reported questionnaire. The following question on subjective assessment of sleep quality was embedded in the questionnaire: "How do you assess the quality of your sleep during 1 week: shallow or deep?" All patients choose one of the two choices. We also evaluated sleep quality using the Japanese version of the ESS [10, 11]. The ESS, widely used in many countries to investigate daytime sleepiness, measures the propensity to sleep or doze during active and passive situations commonly encountered during the waking period. The ESS comprises eight questions. By summing the scores (ranging from 0-3) for each question, total scores (0-24) were calculated. The higher the total score, the more severe daytime sleepiness is considered to be, and people with ESS scores of 11 or higher are considered to have excessive daytime sleepiness. In the present study, after evaluation of sleepiness, we calculated the average ESS scores of the patients reporting shallow sleep and those reporting deep sleep.

Physical Activity

We used number of steps and energy expenditure as the indices of physical activity. These indices were estimated by use of an electronic pedometer (Kenz Lifecorder, Suzuken Co., Ltd. Nagoya, Japan). We chose this pedometer because of the reliability and validity of the output data [12, 13]. The Lifecorder records number of steps taken on the basis of physical characteristics (age, sex, height, and weight) entered by the patient. All patients were taught to put on the Lifecorder themselves and were instructed to use the Lifecorder 24 hours a day for 1 week from the time they received it, except while bathing and while sleeping at night. At the end of the 1-week measurement period, the patients were asked to return the Lifecorder to us. For each patient, we calculated the mean number of steps and energy expenditure in Kcal for exercise performed daily over 1 week as follows: mean daily step count = total step count / 7 and mean energy expenditure = Kcal expended over 7 days / 7.

HRQOL

General HRQOL was measured with the Medical Outcome Study 36-item Short Form Health Survey (SF-36) [14]. The SF-36 consists of 36 items representing 8 subscales covering the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The SF-36 is a standardised, generic HRQOL measurement instrument that has been validated in the general normal Japanese population [15, 16]. Multidimensional properties of HRQOL are measured on a scale ranging from 0 to 100; lower scores represent a lower HRQOL and higher scores indicate superior HRQOL.

To compare scores to the normal Japanese population, SF-36 subscale scores were converted into a deviation score adjusted for sex and age based on scores of the Japanese national norm [15, 16]. This is a mean score of 50 with a standard deviation (SD) of ± 10. In the present study, a score < 50 indicates that the score representing the specific health concept was below that of the Japanese national norm after adjusting for age and sex. The questionnaires were computer-scanned and scored by the Public Health Research Foundation (Tokyo, Japan) [16].

Ethics

The present study was approved by the St. Marianna University School of Medicine Institutional Committee on Human Research. Informed consent was obtained from each patient (Approved no. 1480).

Statistical Analysis

Results are expressed as mean (standard error, SE). Parametric and chi-square tests were used to analyze differences between two groups (shallow sleep and deep sleep). Because comparisons were performed between two groups, the unpaired *t*-test was used to test for differences such as clinical characteristics. To compare ESS scores, physical activity, and SF-36 subscale variables between the two groups, one-way ANCOVA with the variables as covariates was performed. Choice of covariates was guided by Chi-square analyses and *t*-tests, which indicated significant differences between the two groups in the clinical characteristic of NYHA class. Receiver-operating characteristic (ROC) curves were constructed by means of plotting true-positive rates (sensitivity) against false-positive rates (1-specificity). ROC curves were constructed after calculation of the sensitivity for physical activity to determine the best cutoff value to obtain deep sleep levels. The area under the curve (AUC) was also calculated and shown with 95% confidence interval (CI). A p value of < 0.05 was considered significant. Statistical analyses were performed with SPSS 12.0 J statistical software (SPSS Japan, Inc, Tokyo, Japan).

RESULTS

Subjects and Response Rate to Questionnaire and Physical Activity and HRQOL Assessment

Of the 161 patients, 12 patients were excluded due to their failure to complete the self-reported sleep questionnaire and/or because of insufficient data to evaluate their physical activity and HRQOL. Therefore, the study sample comprised 149 outpatients who were divided into two groups on the basis of sleep-quality level reported in the self-reported questionnaire: shallow sleep (SS) group, n = 77) and deep sleep (DS) group, n = 72).

Table 1. Clinical Characteristics of the Patients.

Group	Shallow Sleep Group	Deep Sleep Group	t or χ^2 Value	p Value
No. of patients	77	72		
Age (yrs)	56.7 (1.3)	58.7 (1.6)	-0.9*	0.33
Sex male (%)	86.5	81.2	1.2	0.26
BMI (kg/m^2)	23.1 (0.4)	24.0 (0.5)	-1.2*	0.22
LVEF (%)	34.1 (1.4)	36.6 (1.7)	-0.9*	0.33
NYHA class I/II/III (n)	28/32/16	39/26/7	7.8	0.02
Employed (%)	56.1	56.6	0.1	0.99
Etiology (%)				
Cardiomyopathy	49.7	59.4	3.8	0.28
Previous myocardial infarction	23.8	15.1		
Arrhythmia	22.1	20.1		
CABG/VR	6.1	5.4		
Medications (%)				
B blockers	72.0	82.0	0.77	0.59
ARB	52.3	49.2	0.52	0.44
ACEI	53.6	41.1	0.09	0.58
Diuretic	81.7	88.6	0.53	0.56

Values are shown as mean (standard error, SE) unless otherwise noted.
BMI - body mass index; LVEF - left ventricular ejection fraction; NYHA - New York Heart Association; MI - myocardial infarction, CABG - coronary artery bypass grafting; VR - valve replacement; ARB - angiotensin receptor blocker; ACEI - angiotensin converting enzyme inhibitor.
* *t* value.

Clinical Characteristics between Groups

Patient characteristics are summarised in Table 1. Paticnt characteristics, including age, sex, BMI, LVEF, employment, etiology, and medications were almost identical between the two groups. However, NYHA functional class differed significantly between the two groups ($p = 0.02$).

ESS Scores

ESS scores of all 149 outpatients were available for statistical analysis. After adjustment for NYHA class, the mean (SE) ESS score in the SS group was significantly higher than that of the DS group (8.05 [4.14] points, 95% CI: 7.19 -8.91 vs. 5.45 [0.44] points, 95% CI: 4.57 - 6.34, F = 17.30, $p < 0.001$).

Differences in Physical Activity between Groups

After adjustment for NYHA class, step counts in the SS group were found to be significantly lower than those of the DS group (5541.5 [296.5] steps/day for 1 week, 95% CI: 4957.1 - 6129.8 vs. 6811.4 [306.7] steps/day for 1 week, 95% CI: 6208.8 - 7421.3, F = 8.87, $p = 0.003$, Fig. 2). Energy expenditure during exercise in the SS group was also significantly lower than that of the DS group (162.2 [12.6] Kcal, 95% CI: 136.6 - 186.7 vs. 198.6 [13.1] Kcal, 95% CI: 174.1 – 225.6, F = 4.39, $p = 0.038$, Fig. 2).

Differences in HRQOL Subscale Scores between Groups

The data related to SF-36 testing collected from the two groups are presented in Table 2. After adjustment for NYHA class, HRQOL as assessed by the SF-36 scores in the SS group was lower than that of the DS group, and there were significant differences between the groups in all subscale scores except for that of bodily pain.

ROC Curves for Physical Activity

The sensitivities of each cutoff value in the DS group were calculated for both step count and energy expenditure and were used to construct ROC curves Fig. (3). With ROC analysis of deep sleep status, we identified a cutoff value for physical activity of 5723.6 steps/day for 1 week, with a sensitivity of 0.71 and 1-specificity of 0.48. The AUC value was 0.71 (95% CI: 0.623-0.791, $p = 0.0001$). In addition, ROC analysis of deep sleep status identified a cutoff value for energy expenditure for physical activity of 156.4 Kcal/day for 1 week, with a sensitivity of 0.62 and 1-specificity of 0.44. The AUC value was 0.65 (95% CI: 0.558-0.736, $p = 0.0001$) in CHF outpatients.

DISCUSSION

The present cross-sectional study shows a difference in physical activity and HRQOL that appears to be related to the degree of sleep quality attained by CHF outpatients, suggesting that differences in the level of sleep quality might reduce both physical activity, as assessed by the number of steps taken and energy expended on physical activity, and HRQOL. We used a self-reported questionnaire to evaluate sleep quality in which patients were able to choose between shallow (poor) sleep and deep (good) sleep. The question was very simple, and it would be easy to ask patients in the clinical setting. We also evaluated sleep quality status with the ESS instrument because it is well validated, and scores

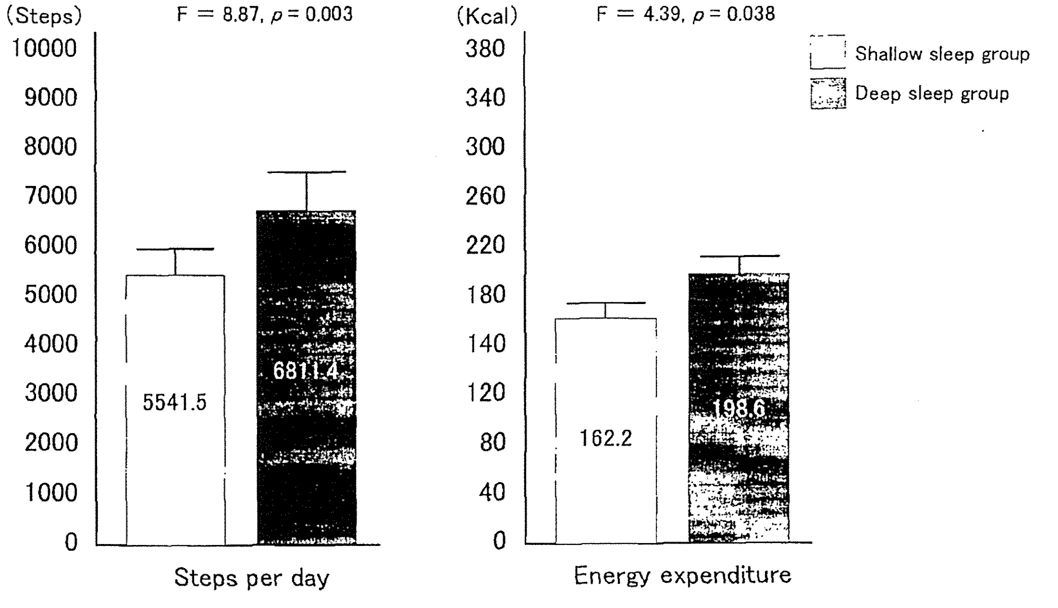

Fig. (2). Comparison of physical activity between the shallow and deep sleep groups in outpatients with CHF.

After adjustment for NYHA class, step counts in the shallow sleep group were significantly lower than those of the deep sleep group (5541.5 [296.5] steps/day for 1 week, 95% CI: 4957.1 - 6129.8 vs. 6811.4 [306.7] steps/day for 1 week, 95% CI: 6208.8 - 7421.3, F = 8.87, $p = 0.003$). Energy expenditure during exercise in the shallow sleep group was also significantly lower than that of the deep sleep group (162.2 [12.6] Kcal, 95% CI: 136.6 - 186.7 vs. 198.6 [13.1] Kcal, 95% CI: 174.1 - 225.6, F = 4.39, $p = 0.038$).

Table 2. Comparison of SF-36 Subscale Scores as an Indicator of Health-related Quality of Life by Sleep Quality.

Group	Shallow Sleep Group	Deep Sleep Group	F Value	*p* Value
No. of patients	77	72		
SF-36 subscales				
Physical functioning	42.7 (1.2) (40.2-45.2)	48.4 (1.3) (45.8-51.0)	9.53	0.002
Role-physical	40.2 (1.5) (37.2-43.3)	47.1 (1.6) (43.9-50.3)	9.19	0.003
Bodily pain	51.4 (1.1) (49.0-53.7)	51.8 (1.2) (49.4-54.3)	0.06	0.794
General health	40.8 (1.0) (38.7-42.9)	47.5 (1.1) (45.4-49.7)	19.7	< 0.001
Vitality	43.1 (1.1) (40.8-45.4)	51.5(1.2) (49.1-53.9)	24.4	< 0.001
Social functioning	42.4 (1.5) (39.4-45.5)	49.2 (1.6) (46.0-52.3)	9.3	0.003
Role-emotional	42.7 (1.5) (39.8-45.7)	48.3 (1.6) (45.2-51.4)	6.4	0.012
Mental health	45.6 (1.1) (43.3-47.8)	51.8 (1.2) (49.4-54.1)	14.2	< 0.001

Values are shown as mean (standard error, SE), (95% confidence interval). Independent variable of analysis of covariance: New York Heart Association class.

from several subject groups have been published [8-11]. Because ESS scores in our study were significantly different between the two groups, we thought that the ESS, as an indicator of the degree of daytime sleepiness, reflected the sleep quality status of CHF outpatients equally as well as did the self-reported questionnaire. As a more subjective indicator of daytime of sleepiness, the ESS score increases as the shallow (poor) sleep quality in CHF outpatients becomes more severe.

Because clinical characteristics of the patients were almost identical between the two groups, these parameters might not influence physical activity and HRQOL. However, more patients were identified as NYHA functional class II or III in the SS group than in the DS group. Itoh *et al.* previously reported that both peak VO_2 and NYHA functional class are related to symptom scores and prognosis in heart failure patients [17]. They reported that peak VO_2 is expressed as a percentage of predicted values determined, and as a result, % peak VO_2 decreases significantly with increasing severity of disease. In other words, peak VO_2 decreases as NYHA functional class increases. In the present study, after adjusting for NYHA functional class, step counts and energy expenditure for physical activity in the SS group were both significantly lower than those in the DS group Fig. (**2**). Thus, shallow (poor) sleep quality in CHF outpatients might influence a reduction in step counts and energy expenditure for physical activity.

As another important outcome of the present study, after adjusting for NYHA functional class, all subscales of the SF-36 for the assessment of HRQOL except for that of bodily pain were also significantly different between groups in relation to sleep quality status Table **2**. Compared with the normal Japanese population, our CHF outpatients in the SS group showed a global reduction in HRQOL as measured by 7 of the 8 SF-36 subscales. Thus, shallow sleep status may have an influence on poor HRQOL. Although the most pronounced loss of HRQOL was observed in the domain of role limitation because of physical problems, SF-36 subscale scores relating to mental status such as social functioning and role-emotional were also low. Thus, poor HRQOL might be indicated not only by scores relating to the physical but also the mental state. Interestingly, the SF-36 bodily pain subscale score did not differ significantly between the two groups, and the score for this parameter reached levels seen in the normal Japanese population. The possibility exists that sleep quality status in our CHF outpatients had no influence on the SF-36 bodily pain subscale score. This finding is consistent with that of an earlier study [18]. Thus, we surmise that the bodily pain subscale may not be appropriate for the evaluation of CHF patients with sleep quality issues. Lopes *et al.* [7] also showed that excessive sleepiness and lack of physical activity affect the QOL of apneic patients, which was worse among sleepy non-physically active subjects and increasingly worse in the patients with severe apnea. Shallow sleep quality may cause sleepiness, and presumably, increased sleepiness may be related to a reduction in physical activity and HRQOL.

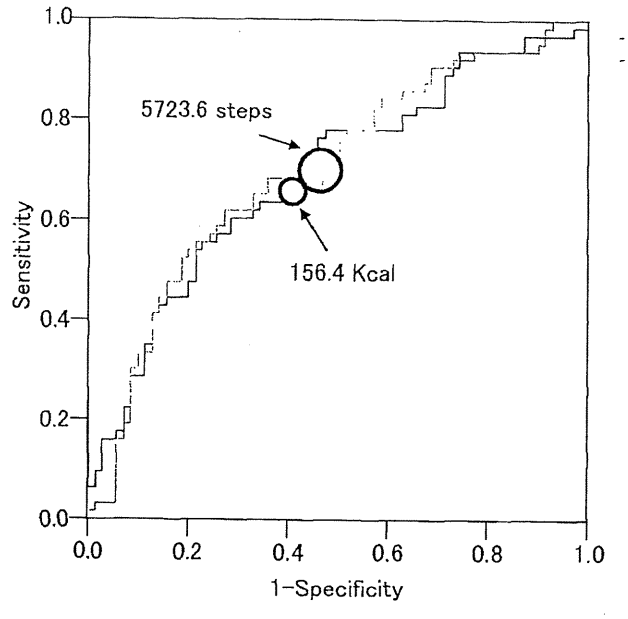

Fig. (3). ROC analysis of physical activity in the deep sleep group.

Sensitivities of each cutoff value in the shallow sleep and deep sleep groups were calculated for both step count and energy expenditure and were used to construct ROC curves. Using ROC analysis of deep sleep status, we identified a cutoff value of 5723.6 steps/day for 1 week for physical activity, with a sensitivity of 0.71 and 1-specificity of 0.48. The AUC value was 0.71 (95% CI: 0.623-0.791, $p = 0.0001$) for physical activity. ROC analysis of deep sleep status identified a cutoff value for energy expenditure of 156.4 Kcal/day for 1 week for physical activity, with a sensitivity of 0.62 and 1-specificity of 0.44. The AUC value was 0.65 (95% CI: 0.558-0.736, $p = 0.0001$) for physical activity in CHF outpatients.

Using ROC analysis of physical activity in the DS group, we identified cutoff values for physical activity of 5723.6 steps/day and 156.4 Kcal/day for 1 week in CHF outpatients Fig. (2). These might be appropriate target values for step count and energy expenditure that may result in improvement of sleep in CHF outpatients. Regarding physical activity and long-term prognosis, Walsh *et al.* [19] previously reported that a reduced level of daily activity is a strong predictor of death in CHF and appears to be a more powerful predictor than the results of laboratory-based exercise tests. They also suggested that from daily activity measured by pedometer, a cutoff value for step count as a predictor of mortality was over 25000 steps/week. This results in a step count of 3571.4 steps/day for 1 week. The step counts in our study were higher compared to their results, and achieving the step count target value shown in the present study might favourably affect mortality in our CHF outpatients.

Savage *et al.* [20] previously reported that the average step count measured by pedometer on days patients attended cardiac rehabilitation was 7387 steps at the beginning of a phase II rehabilitation program. In addition, Ayabe *et al.* [21] suggested that to achieve the total amount of energy expenditure for physical activity generally recommended for the secondary prevention of cardiovascular disease, patients should be encouraged to accumulate 6500-8500 steps/day (200-300 Kcal/day). Thus, physical activity of the subjects in the present study was less than that of these previous studies. Because step counts in CHF patients are reduced according to the severity of the disease, we were not able to compare our results directly with the results of these previous studies; however, the step counts indicated in these previous studies might also be appropriate target values to achieve the energy expenditure recommended for secondary prevention in patients with CHF.

Study Limitations

There are several limitations to the present study. First, diagnosis of sleep quality status cannot be made with the self-reported questionnaire and the ESS. Use of these questionnaires in the present study may weaken the evaluation of sleep quality status in comparison to other methods such as polysomnography. However, the ESS has been shown to be a reliable and valid instrument for screening symptoms of sleep quality in general internal medicine patients and others [3, 10, 11]. The second limitation is the cross-sectional design of the study. It would be highly desirable to document longitudinal change in physical activity for sleep quality and HRQOL in patients with CHF, and evaluation of the effect of improvement in physical activity and HRQOL over the long term after improvement in sleep quality is necessary. Finally, the sensitivity values we chose, 0.71 for deciding physical activity needed for our CHF patients and 0.62 for energy expenditure, may not be considered high. Despite these limitations, we believe the findings of the present study are important because the sample size was adequate to yield significant results from the test instrument scores.

CURRENT & FUTURE DEVELOPMENTS

Sleep quality may affect step count and energy expenditure for physical activity in CHF outpatients. In addition, all SF-36 subscale scores except that for bodily pain were significantly lower in patients reporting shallow sleep than in patients reporting deep, quality sleep. Cutoff values of 5723.6 steps and 156.4 Kcal were determined by ROC analysis to be target values for CHF outpatients to attain improved sleep quality. Future studies will need to be conducted in longitudinal settings and for longer periods to evaluate the effect of improvement of sleep quality on the increase in physical activity of patients with CHF, and long-term follow-up will be required to evaluate whether these benefits continue over time.

The prevalence of poor sleep quality relates to reduced physical activity in CHF patients, and it has negative impact on their reduced HRQOL. Therefore, we believe that assessment of sleep quality and appropriate treatment should be routine practice in the clinical setting of cardiac rehabilitation. Interventions should also be planned to improve the quality of sleep in CHF patients when inadequate sleep affects the physical activity and/or the QOL of these patients.

CONFLICT OF INTEREST

All authors declare no conflicts of interest in relation to the work reported in this manuscript.

ACKNOWLEDGEMENTS

The present study was supported by the Global COE (Centers of Excellence) Program "Sport Sciences for the Promotion of Active Life" from the Japan Ministry of Education, Culture, Sports, Science and Technology.

ABBREVIATIONS LIST

CHF	=	Chronic heart failure
PA	=	Physical activity
HRQOL	=	Health-related quality of life
SS	=	Shallow sleep
DS	=	Deep sleep
SF-36	=	Short Form 36
QOL	=	Quality of life
LVEF	=	Left ventricular ejection fraction
NYHA	=	New York Heart Association
ESS	=	Epworth Sleepiness Scale
AUC	=	Area under the curve
CI	=	Confidence interval
ROC	=	Receiver-operating characteristic

REFERENCES

[1] Kwok, J., Brockway, M., Lee, K., Ni, Q., Pu, Y., Stahmann, J., Zhang, Y., Hartley, J. Method and system for heart failure status evaluation based on a disordered breathing index. US7766840 (**2010**).

[2] Pu, Y., Gropper, C., Lin, D. Detecting sleep disorders using heart activity US20100204586 (**2010**).

[3] Ng AC, Freedman SB. Sleep disordered breathing in chronic heart failure. Heart Fail Rev 2009; 14: 89-99.

[4] Ng AC, Davis GM, Chow CM, Coats AJ, Sindone AP, Freedman B. Impact of sleep disordered breathing severity on hemodynamics, autonomic balance and cardiopulmonary functional status in chronic heart failure. Int J Cardiol 2010; 141: 227-35.

[5] Broström A, Strömberg A, Dahlström U, Fridlund B. Sleep difficulties, daytime sleepiness, and health-related quality of life in patients with chronic heart failure. J Cardiovasc Nurs 2004; 19: 234-42.

[6] Jean-Louis G, Kripke DF, Ancoli-Israel S. Sleep and quality of well-being. Sleep 2000; 23: 1115-21.

[7] Lopes C, Esteves AM, Bittencourt LR, Tufik S, Mello MT. Relationship between the quality of life and the severity of obstructive sleep apnea syndrome. Braz J Med Biol Res 2008; 41: 908-13.

[8] Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991; 14: 540-45.

[9] Sleep-related breathing disorders in adults: Recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999; 22: 667-689.

[10] Takegami M, Sokejima S, Yamazaki S, Nakayama T, Fukuhara S. [An estimation of the prevalence of excessive daytime sleepiness based on age and sex distribution of epworth sleepiness scale scores: a population based survey]. Nippon Koshu Eisei Zasshi 2005; 52: 137-45.

[11] Takegami M, Suzukamo Y, Wakita T, Noguchi H, Chin K, Kadotani H, *et al.* Development of a Japanese version of the Epworth Sleepiness Scale (JESS) based on item response theory. Sleep Med 2009; 10: 556-65.

[12] Schneider PL, Crouter SE, Lukajic O, Bassett DR Jr. Accuracy and reliability of 10 pedometers for measuring steps over a 400-m walk. Med Sci Sports Exerc 2003; 35: 1779-84.

[13] Crouter SE, Schneider PL, Karabulut M, Bassett DR Jr. Validity of 10 electronic pedometers for measuring steps, distance, and energy cost. Med Sci Sports Exerc 2003; 35: 1455-60.

[14] Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992; 30: 473-83.

[15] Fukuhara S, Ware JE Jr, Kosinski M, Wada S, Gandek B. Psychometric and clinical tests of validity of the Japanese SF-36 Health Survey. J Clin Epidemiol 1998; 51: 1045-53.

[16] Fukuhara S, Suzukamo Y, Bito S, Kurokawa K. Manual of SF-36 Japanese version 1.2. Public Health Research Foundation: Tokyo 2001.

[17] Itoh H, Koike A, Taniguchi K, Marumo F. Severity and pathophysiology of heart failure on the basis of anaerobic threshold (AT) and related parameters. Jpn Circ J 1989; 53: 146-54.

[18] Izawa KP, Watanabe S, Omiya K, Yamada S, Oka K, Iijima S, *et al.* Health-related quality of life in relation to different levels of disease severity in patients with chronic heart failure. Journal of the Japanese Physical Therapy Association 2005; 8: 39-45.

[19] Walsh JT, Charlesworth A, Andrews R, Hawkins M, Cowley AJ. Relation of daily activity levels in patients with chronic heart failure to long-term prognosis. Am J Cardiol 1997; 79: 1364-9.

[20] Savage PD, Ades PA. Pedometer step counts predict cardiac risk factors at entry to cardiac rehabilitation. J Cardiopulm Rehabil Prev 2008; 28: 370-7.

[21] Ayabe M, Brubaker PH, Dobrosielski D, Miller HS, Kiyonaga A, Shindo M, *et al.* Target step count for the secondary prevention of cardiovascular disease. Circ J 2008; 72: 299-303.

理学療法学　第 38 巻第 6 号　436 ～ 441 頁（2011 年）

研究論文

慢性腎臓病を合併した慢性心不全患者における運動耐容能とその関連要因の検討*

堀田千晴[1)#]　平木幸治[2)]　渡辺　敏[2)]　井澤和大[2)]
安田　隆[3)]　長田尚彦[4)]　大宮一人[4)]

要旨

【目的】本研究の目的は，慢性心不全（CHF）患者の運動耐容能を腎機能別に調査し，慢性腎臓病（CKD）合併CHF患者の運動耐容能関連要因について明らかにすることである。【方法】男性CHF患者119例を対象に，推算糸球体濾過量（eGFR）を基に，A群（eGFR60以上），B群（eGFR30以上60未満），C群（eGFR30未満）の3群に選別し，運動耐容能および上下肢筋力を比較した。さらにB・C群（CKD群）の運動耐容能関連要因を検討した。【結果】腎機能別の3群間の比較では，運動耐容能，膝伸展筋力，握力は，eGFRが低い群で有意に低値を示した。さらに，CKD群の運動耐容能関連要因を重回帰分析にて検討した結果，膝伸展筋力とeGFR（R = 0.68, R^2 = 0.44, $p < 0.001$）が抽出された。【結語】CHF患者では，腎機能低下にともない運動耐容能は低下した。また，CKD合併CHF患者の運動耐容能関連要因に，膝伸展筋力とともにeGFRが抽出された。

キーワード　運動耐容能，慢性腎臓病，慢性心不全

はじめに

慢性腎臓病（Chronic Kidney Disease；CKD）は，2002年に米国腎臓財団によって定義され，近年急速に普及した疾患概念である。腎機能の悪化は，単に透析導入へとつながるだけでなく，心血管疾患発症のリスクファクターとなることが注目されている。なかでも，腎臓と心臓には病態生理学的に密接な関わりがあり，蛋白尿や腎機能低下が心血管疾患の予後と関連することから，いわゆる「心腎連関」という概念が提唱されている[1)]。

慢性心不全（Chronic Heart Failure；CHF）患者は，本邦において毎年2,000人ずつ増加し続け，2008年には62,688人に達している。今後も高齢化等により，CHF患者は増加すると予想されており[2)]，その予後改善は急務の課題である。CHF患者において，CKDは60.0～77.9%[3)4)]と，高率に合併することが国内外より報告されている。さらにHillegeら[5)]は，CHF患者の予後において，推算糸球体濾過量（estimate glomerular filtration rate；eGFR）はACE阻害薬内服，New York Heart Association（NYHA）心機能分類，左室駆出率（left ventricular ejection fraction：LVEF）よりも強い予後規定因子であると報告しており，腎機能がCHFに相乗的に影響を与える可能性が注目されている。一方，CHF患者の運動耐容能は，予後や患者のQOLと相関があることから，その規定要因や各要因間の関連について先行研究で報告されている[6)]。しかし，CHF患者において腎機能の差異が運動耐容能に与える影響，およびその関連要因について検討したものは少ない。

そこで本研究の目的は，CHF患者の運動耐容能を腎機能別に調査するとともに，CKDを合併したCHF患者における運動耐容能関連要因について明かにすることである。

---

* Determinants of Exercise Capacity in Chronic Heart Failure Patients with Chronic Kidney Disease

1) 川崎市立多摩病院リハビリテーション科
（〒 214-8525　川崎市多摩区宿河原 1-30-37）
Chiharu Hotta, PT, BS: Department of Rehabilitation Medicine, Kawasaki Municipal Tama Hospital
2) 聖マリアンナ医科大学病院リハビリテーション部
Koji Hiraki, PT, MS, Satoshi Watanabe, PT, BS, Kazuhiro P. Izawa, PT, PhD: Department of Rehabilitation Medicine, St. Marianna University School of Medicine Hospital
3) 聖マリアンナ医科大学腎臓・高血圧内科
Takashi Yasuda, MD, PhD: Division of Nephrology and Hypertension, Department of Medicine, St. Marianna University School of Medicine
4) 聖マリアンナ医科大学循環器内科
Naohiko Osada, MD, PhD, Kazuto Omiya, MD, PhD: Division of Cardiology, Department of Medicine, St. Marianna University School of Medicine
E-mail: chiharu-tanaka@marianna-u.ac.jp
（受付日　2011 年 3 月 31 日／受理日　2011 年 7 月 27 日）

対象および方法

1. 対象

対象は，2003年1月から2009年9月の間に，聖マリアンナ医科大学病院に心不全治療目的に入院し，退院後の外来にて心肺運動負荷試験（Cardio pulmonary exercise test；CPX）を施行した男性119例である。除外基準は，CPX中に心電図上の虚血や致死性不整脈を認めた症例，負荷終了時ガス交換比1.0未満の症例，血液疾患等を合併した症例，維持透析療法を施行している症例とした。

対象者を，eGFR（単位：ml/min/1.73m^2）を基に，A群（非CKD群；eGFR60以上），B群（GFR中等度低下群；eGFR30以上60未満），C群（GFR高度低下群；eGFR30未満）と定義し，3群に選別した。また，CKD合併CHF患者における運動耐容能の関連要因を検討する際には，B群とC群を併せ，「CKD群」と定義した。なお，CKD群ではeGFRが3ヵ月間以上にわたり60 ml/min/1.73m^{2}未満が持続していることを確認した。

2. 倫理的配慮

本研究は，聖マリアンナ医科大学生命倫理委員会の承認を得て実施した（承認番号第340号）。本研究の参加に際し，対象者に研究の趣旨，内容，および調査結果の取り扱い等に関して説明し同意を得た。

3. 調査・測定項目

1）患者背景

調査項目は，年齢，身長，体重，Body Mass Index（BMI），血液生化学検査値（血清クレアチニン［Cr］，eGFR，ヘモグロビン［Hb］，脳性ナトリウム利尿ペプチド［BNP］），LVEF，NYHA心機能分類，基礎疾患，服薬状況とした。これらについては，CPXと同一日もしくはその直近のものを診療記録より後方視的に調査した。

2）最高酸素摂取量（peak $\dot{V}O_2$）

退院後の心不全安定期の外来にて，自転車エルゴメータ（LODE社製，CORIVAL400）を用いた症候限界性CPXを施行した。CPXは，3分間の安静後に，3分間の0または20 wattsのウォーミングアップ，その後6秒間に1 wattずつ増加するramp負荷を用いたプロトコルにて実施した。CPX中は，運動負荷試験装置（フクダ電子社製，ML-5000）にて，心拍数，ST-T変化および不整脈の有無を連続的に監視し，12誘導心電図を1分毎に記録した。血圧の測定は，自動血圧計（日本コーリン社製，STBP-780）にて1分間毎に血圧値を記録した。運動負荷試験終了基準は米国スポーツ医学会の中止基準[7]を満たす徴候の出現，あるいは負荷の増加にも関わらず酸素摂取量の増加を認めない，leveling offの状態とした。負荷終了後は，クーリングダウンを施行後，座位にて運動負荷終了5分後まで呼気ガス分析を施行した。呼気ガス分析は呼気ガス分析装置（ミナト社製，AE-300S aero monitor）を用い，breath by breath法で連続的に分析を施行後，検査中の$\dot{V}O_2$の最高値をpeak $\dot{V}O_2$として算出した（ml/kg/min）。

3）上下肢筋力

下肢は膝伸展筋力，上肢は握力を採用した。両指標はともに，CPXと同一日に測定を実施した。具体的方法については以下に示す。

(1) 膝伸展筋力

等速性下肢筋力測定装置（Biodex社製，SYSTEMS2®）を用い，膝伸展筋力を測定した。先行研究に準じ[8]，対象者は，坐位80°の姿勢で坐り，体幹，腰部，大腿部をストラップで固定した。抵抗パッドは内果の中枢側10 cmに固定した。検査中は0～90°の間で膝屈曲に対する可動域を設定し，3回のwarming-upを行った後に，角速度60°/secの等速運動を計5回繰り返した。測定結果は付属のソフトウェアを使い算出し，得られた最大膝伸展筋力を体重で除した値（Nm/kg）を採用した。

(2) 握力

握力は油圧式握力計（Sammons Prestons社製，Jamar® Hand Dynamometer-5030J1）を用い，測定した。先行研究に準じ[8]，測定肢位は，座位，肘関節屈曲90°，前腕中間位にて握力を左右2回測定し，左右の最大値の平均値（kgf）を採用した。

4. 統計処理

eGFRを基に選別した3群間の比較は，NYHA心機能分類，基礎疾患，服薬状況にχ^2検定を，正規性の得られなかったCr, BNPにKruskal-Wallisの検定を使用した。正規性の得られたその他の指標には一元配置分散分析を用い，多重比較にはBonferoniの検定を用いた。また，CKD群を対象とした，運動耐容能とその関連要因の検討には，Spearmanの相関係数とステップワイズ重回帰分析を用いた。解析には，SPSS 12.0J（SPSS Japan, Inc, Tokyo, Japan）を使用し，統計学的有意判定の基準は，5%未満とした。

結　　果

1. 患者背景

eGFRにより重症度別に選別した3群間の患者背景の比較を表1に示す。年齢，Cr，eGFR，Hb，BNPは3群間に主効果を認め，eGFRが低値な群ほど，年齢，Cr，BNPは有意に高く，Hbは有意に低かった（$p < 0.001$）。またNYHA心機能分類の比較より，eGFRが低い群ほど心不全重症度の高い者の割合が多かった（$p =$

表1 腎機能別の患者背景の比較

	A群 非CKD群 (n=54)	B群 GFR中等度低下群 (n=52)	C群 GFR高度低下群 (n=13)	p 値
年齢（歳）	48.4 ± 12.8	62.9 ± 12.0	69.7 ± 7.3	< 0.001
BMI（kg/m^2）	25.3 ± 5.7	24.7 ± 3.6	21.9 ± 2.2	0.06
Cr（mg/dl）*	0.85 (0.55－1.04)	1.16 (0.95－1.78)	2.44 (1.81－4.61)	< 0.001
eGFR（$ml/min/1.73\ m^2$）	79.6 ± 13.5	49.5 ± 8.1	22.0 ± 5.4	< 0.001
Hb（g/dl）	14.7 ± 1.6	13.5 ± 1.5	11.3 ± 1.7	< 0.001
BNP（pg/ml）*	67.9 (4.0－518.0)	133.5 (4.0－1577.5)	213.0 (77.4－1190.0)	< 0.001
LVEF（%）	38.0 ± 13.7	38.5 ± 16.1	30.4 ± 13.0	0.28
NYHA心機能分類（度） (I / II / III)	33/20/1	21/21/10	1/8/4	0.001
基礎疾患（症例数）				
虚血性心疾患	6	10	4	0.070
心臓外科術後	4	11	2	
高血圧	1	5	0	
不整脈	3	2	0	
拡張型心筋症	40	24	7	
服薬（症例数）				
β 遮断薬	44	33	8	0.086
利尿薬	42	48	12	0.079
ACE阻害薬	34	24	2	0.006
ARB	19	25	9	0.068

* Cr，BNPは中央値（最小値―最大値），ほか指標は平均値±標準偏差を示す．
CKD：chronic kidney disease, GFR：glomerular filtration rate, BMI：Body mass index, Cr：血清クレアチニン，eGFR：estimate glomerular filtration rate, Hb：ヘモグロビン，BNP：脳性ナトリウム利尿ペプチド，LVEF：left ventricular ejection fraction, NYHA：New York Heart Association, ACE：angiotensin converting enzyme, ARB：angiotensin II receptor blocker

表2 腎機能別のpeak $\dot{V}O_2$ および上下肢筋力の比較

	A群 非CKD群 (n=54)	B群 GFR中等度低下群 (n=52)	C群 GFR高度低下群 (n=13)	p 値
peak $\dot{V}O_2$（ml/kg/min）	22.7 ± 4.1	19.8 ± 5.8	15.3 ± 3.8	< 0.001* ¶ §
膝伸展筋力（Nm/kg）	1.99 ± 0.40	1.74 ± 0.38	1.41 ± 0.30	< 0.001* ¶ §
握力（kgf）	43.8 ± 8.8	37.4 ± 7.8	33.8 ± 5.7	< 0.001* §

平均値±標準偏差を示す．
CKD：chronic kidney disease, GFR：glomerular filtration rate
*：A群 vs B群（$p < 0.05$），¶：B群 vs C群（$p < 0.05$），§：A群 vs C群（$p < 0.05$）

0.001)。服薬状況では，ACE阻害薬のみで有意差を認め，eGFRが低いほどACE阻害薬を内服している割合が低かった（$p = 0.006$）。

2. 運動耐容能および筋力の比較

3群間の運動耐容能，および上下肢筋力（膝伸展筋力，握力）を比較した結果を表2に示す。運動耐容能，膝伸展筋力，握力はいずれも，3群間に主効果を認め（$p <$ 0.001），多重比較において一部を除き各群間にも有意差を認め，eGFRが低い群で有意に低値を示した。

3. CKD合併CHF患者の運動耐容能と関連要因の検討

peak $\dot{V}O_2$ と各因子の関係を，単相関で検討した結果を表3に示す。CKD合併CHF患者において，peak $\dot{V}O_2$ は年齢，Hb，eGFR，BNP，膝伸展筋力，握力と有意な相関を認めた（$p < 0.05$）。以上より，peak $\dot{V}O_2$ を従属

表 3 CKD 群における peak $\dot{V}O_2$ と各因子間の関係

	相関係数 (r)
年齢	− 0.47 *
BMI	0.22
eGFR	0.52 *
Hb	0.44 *
BNP	− 0.50 *
LVEF	0.17
膝伸展筋力	0.58 *
握力	0.49 *

* $p < 0.05$
CKD：chronic kidney disease, BMI：Body mass index, eGFR：estimate glomerular filtration rate, Hb：ヘモグロビン, BNP：脳性ナトリウム利尿ペプチド, LVEF：left ventricular ejection fraction

表 4 CKD 群における peak $\dot{V}O_2$ と各因子の重回帰分析

	β	p
年齢	− 0.17	0.14
eGFR	0.27	0.02
Hb	0.04	0.75
BNP	− 0.15	0.17
膝伸展筋力	0.51	< 0.001
握力	0.27	0.05
重相関係数（R）	0.68	
決定係数（R^2）	0.44	

CKD：chronic kidney disease, eGFR：estimate glomerular filtration rate, Hb：ヘモグロビン, BNP：脳性ナトリウム利尿ペプチド

変数，独立変数を前述した単相関を認めた項目とし，重回帰分析を施行した。その結果，peak $\dot{V}O_2$ の関連要因として，膝伸展筋力と eGFR（$R = 0.68$, $R^2 = 0.44$, $p < 0.001$）が抽出された（表 4）。

考　　察

本研究の目的は，CHF 患者の運動耐容能を腎機能別に調査し，CKD を合併した CHF 患者における運動耐容能の関連要因を明らかにすることである。患者背景，上下肢筋力の腎機能別の比較，および CKD 合併 CHF 患者における運動耐容能とその関連要因について以下に考察する。

1. 腎機能別に選別した 3 群間の比較

<患者背景>

患者背景を腎機能別に比較した結果，腎機能が低下するほど，Hb は有意に低く，年齢，BNP は有意に高い結果であった。

CKD 患者では，腎でのエリスロポエチン産生低下により，「腎性貧血」をきたすことが知られており[1]，腎機能の指標である GFR は，加齢とともに低下することが報告されている[9]。また，BNP は CHF の重症度指標として広く用いられているが，腎機能低下により循環血液量増加，血圧上昇等の影響で高値となることが報告されている[10]。以上より，本研究の患者背景における Hb，年齢，BNP の差異は，腎機能低下自体の影響と考えられた。また NYHA 心機能分類の比較より，eGFR が低い群ほど心不全重症度の高い者の割合が多かった。これは先行研究[11]とも一致した見解であることから，腎機能低下にともなう CHF の重症化は，患者背景の特徴の一つであると思われた。

<上下肢筋力>

CHF 患者において，上下肢筋力の指標である膝伸展筋力と握力は，腎機能が低いほど有意に低下した。

前述の通り，本研究の対象者は腎機能が低下するほど高齢になる傾向を示しているため，腎機能低下に伴う上下肢筋力の低下が年齢の影響を受けた可能性は否定できない。しかし，太田ら[12]は健常高齢男性（平均 70 歳）の膝伸展筋力を 2.3 Nm/kg と報告しており，本研究の CKD 群だけでなく，非 CKD 群（平均 48 歳）であっても健常値と比較して筋力低下を認めた。

一方，Izawa ら[13]は，CHF 患者における重症度別の運動耐容能および上下肢筋力は，重症度に伴い低下することを報告している。患者背景より，腎機能低下群において重症 CHF 患者の割合が多いことが示されていることから，上下肢筋力の低下は CHF の重症度による影響を受けた可能性が考えられる。また先行研究において透析前 CKD 患者の下肢筋力は，同年代の健常者と比較し低下していることが報告されている[14)15]。CKD 患者における筋力低下の原因としては，栄養不良，蛋白の喪失，異化状態，炎症マーカーの亢進，身体活動低下など複数要因の関与が報告されている[16]。しかし，本研究ではこれら原因を追及する指標については評価していないことから，腎機能と上下肢筋力の関係について明確に言及することはできない。

以上より，本研究対象者の上下肢筋力低下は加齢の影響より，CHF の重症度や腎機能低下の影響が関与しているものと考えられた。

2. CKD 合併 CHF 患者における運動耐容能とその関連要因の検討

CHF 患者の運動耐容能は，腎機能が低下するほど有意に低値を示した。また CKD 合併 CHF 患者を対象に，運動耐容能の関連要因を検討した結果，膝伸展筋力と eGFR が抽出された。

Clyne ら[17]は，GFR と運動耐容能に正の相関がある

ことを報告している。CKD合併CHF患者の運動耐容能関連要因を単相関で検討した結果，運動耐容能は腎機能とも関連のある指標（Hb，年齢，BNP）と関係を認めた。このことが，運動耐容能低下を相乗的に低下させたことにより，その関連要因にもeGFRが抽出された可能性がある。しかし今回調査した指標以外にも，心臓の拡張能や神経体液性因子，骨格筋の代謝といった腎機能により変動し，かつ運動耐容能に影響をおよぼし得る要因が多数存在する。今後はさらに指標を増やし，より多角的に検討する必要がある。

また先行研究よりCHF患者，CKD患者各々の運動耐容能において，筋力は重要な規定要因のひとつと考えられている[18)19)]。さらにCKD患者において貧血と運動耐容能の関連は多く報告されているが，一定の見解は得られていない。CKD診療ガイド[1)]より，腎性貧血の治療目標は，Hb値で10～12 g/dlが勧められるとされている。患者背景より，C群（GFR高度低下群）におけるHb平均値は11.3 g/dlであり，本研究のCKD患者において，貧血は軽度であったと予測される。Leikisら[20)]は，貧血のないCKD患者を対象に運動耐容能低下の関連要因を検討し，下肢筋力に注目することが重要であると報告しており，本研究と同様の結果を示している。非透析CKD患者における運動療法の効果を示した研究はわずかであるが，先行研究ではCKD患者を対象に運動療法介入を行い，筋力向上により運動耐容能が改善することが報告されている[21)]。このことから，CKD合併CHF患者においてリハビリテーション介入による筋力強化の重要性が示唆された。

3. 本研究の理学療法意義

前述のとおり，CHF患者において腎機能が低下している者は，運動耐容能だけでなく上下肢筋力の低下を認めていることから，理学療法介入時には運動機能を評価する必要があると考えられた。さらに，CKDを合併したCHF患者の運動耐容能は，膝伸展筋力とeGFRが独立した関連要因として抽出されたことから，それら症例の運動耐容能改善には筋力トレーニングを処方することが有用となる可能性がある。また，理学療法介入前には腎機能にも着目する必要性が示唆された。今後は，今回抽出された膝伸展筋力とeGFRのふたつの要因がどの程度低下すると運動耐容能に影響を与えるのか，具体的な基準値を検討していく必要があると考えられた。

4. 研究の限界

腎機能により対象者を選別した結果，年齢やCHF重症度などの患者背景要因に差異を生じ，腎機能自体の影響を検討することが難しかった。今後はさらに対象者を増やし，これらの影響を除外しての検討が必要である。

結　論

CHF患者では，腎機能低下にともない運動耐容能および上下肢筋力が低下した。また，CKD合併CHF患者の運動耐容能の関連要因として，膝伸展筋力とともにeGFRが抽出された。

文　献

1) 松尾清一，飯野靖彦，他：CKD診療ガイドライン．日本腎臓学会（編），東京医学社，東京，2007，pp19-26.
2) 厚生統計協会：国民衛生の動向・厚生の指標（2008年）．廣済堂，東京，2008.
3) 平光伸也，宮城島賢二，他：心腎連関における貧血の関与を探る．Vascular Medicine. 2008; 4: 322-326.
4) Heywood JT, Fonarow GC, *et al.*: High prevalence of dysfunction and its impact on outcome in 118, 465 patients hospitalized with acute decompensated heart failure. —Areport from the ADHERE database. J Cardiac Fail. 2007; 13: 422-430.
5) Hillege HL, Girbes AR, *et al.*: Renal function, Neurohormonal Activation, and Survival in Patients with chronic heart failure. Circulation. 2000; 102: 203-210.
6) 伊藤春樹：心不全の運動療法の実際．臨床成人病．1999; 29: 1033-1040.
7) American College of Sports Medicine: ACSM's Guidelines for Exercise Testing and Prescription. In: Johnson EP (ed): Clinical exercise testing. 6th ed, Williams & Wilkins, Baltimore, 2000, pp91-114.
8) Izawa KP, Oka K, *et al.*: Gender-related differences in characteristics and physiological and psychosocial outcomes of Japanese patients at entry into phase II cardiac rehabilitation. J Rehabil Med. 2008; 40 (3): 225-230.
9) Davies DF, Shock NW: Age changes in glomerular filtration rate, effective renal plasma flow, and tubular excretory capacity in adult males. J Clin Inv. 1950; 29: 496-507.
10) Carr SJ, Bavanandan S, *et al.*: Prognostic potential of brain natriuretic peptide (BNP) in predialysis chronic kidney disease patients. Clin Sci (Lond). 2005; 109 (1): 75-82.
11) Wiley L, Switzer P, *et al.*: Association of B-type natriuretic peptide levels with estimated glomerular filtration rate and congestive heart failure. CM & R. 2010; 1: 7-12.
12) 太田壽城，小林　規，他：高齢者の歩行に関する研究—第1報　動的筋力および全身持久力からみた高齢者の歩行運動—．スポーツ医・科学．1991; 5 (1): 31-36.
13) Izawa KP, Watanabe S, *et al.*: Muscle strength in relation to disease severity in patients with congestive heart failure. Am J Phys Med Rehabil. 2007; 86 (11): 893-900.
14) Padilla J, Krasnoff J, *et al.*: Physical functioning in patients with chronic kidney disease. J Nephrol. 2008; 21 (4): 550-559.
15) Heiwe S, Tollback A, *et al.*: Twelve weeks of exercise training increases muscle function and walking capacity in elderly predialysis patients and healthy subjects. Nephron. 2001; 88 (1): 48-56.
16) Patel DR, Raj VM, *et al.*: Chronic kidney disease, exercise, and sports in children, adolescents, and adults. Phys Sportsmed. 2009; 37: 11-19.
17) Clyne N, Jogestrand T, *et al.*: Progressive decline in renal function induces a gradual decrease in total hemoglobin and exercise capacity. Nephron. 1994; 67 (3): 322-326.

18) 野原隆司：Annual Review 循環器 2001. 山口 徹他（編），中外医学社，東京，2001，pp101-105.
19) 橋本俊雄，笹島 忠，他：慢性腎不全患者における運動耐容能．臨床スポーツ医学．1992; 9 (1): 39-44.
20) Leikis MJ, Mckenna MJ, *et al.*: Exercise performance falls over time in patients with chronic kidney disease despite maintenance of hemoglobin concentration. Clin J Am Soc Nephrol. 2006; 1: 488-495.
21) Clyne N, Ekholm J, *et al.*: Effects of Exercise Training in Predialytic Uremic Patients. Nephron. 1991; 59: 84-89.

〈Abstract〉

Determinants of Exercise Capacity in Chronic Heart Failure Patients with Chronic Kidney Disease

Chiharu HOTTA, PT, BS
Department of Rehabilitation Medicine, Kawasaki Municipal Tama Hospital

Koji HIRAKI, PT, MS, Satoshi WATANABE, PT, BS, Kazuhiro P. IZAWA, PT, PhD
Department of Rehabilitation Medicine, St. Marianna University School of Medicine Hospital

Takashi YASUDA, MD, PhD
Division of Nephrology and Hypertension, Department of Medicine, St. Marianna University School of Medicine

Naohiko OSADA, MD, PhD, Kazuto OMIYA, MD, PhD
Division of Cardiology, Department of Medicine, St. Marianna University School of Medicine

Purpose: The purpose of this study was to investigate both the exercise capacity of chronic heart failure (CHF) patients exercise capacity according to renal function and the determinants of exercise capacity in CHF patients with chronic kidney disease (CKD).
Methods: The study population was comprised of 119 male CHF patients. Patients were divided into three groups according to their estimated glomerular filtration rate (eGFR): group A (eGFR $\geqq$ 60), group B (30 $\leqq$ eGFR $<$ 60), and group C (eGFR $<$ 30). After dividing the patients into groups, exercise capacity and knee extensor and hand grip muscle strength were compared among the three groups. Furthermore, groups B and C were defined as the CKD group, and relevant factors related to exercise capacity were examined.
Results: Exercise capacity and all muscle strength indices decreased as eGFR decreased. Stepwise linear regression analysis revealed that knee extensor muscle strength and eGFR were significant important factors in predicting exercise capacity in CHF patients with CKD (R= 0.68, R^2=0.44, $p < 0.001$).
Conclusions: In CHF patients, exercise capacity decreased with declining renal function. Moreover, knee extensor muscle strength and eGFR were determined to be important factors in predicting exercise capacity in CHF patients with CKD.

Physical activity in relation to exercise capacity in chronic heart failure patients

Kazuhiro P. Izawa [a,*], Satoshi Watanabe [a], Koichiro Oka [b], Koji Hiraki [a], Yuji Morio [a], Yusuke Kasahara [a], Naoya Takeichi [a], Takae Tsukamoto [c], Naohiko Osada [d], Kazuto Omiya [a,d]

[a] Department of Rehabilitation Medicine, St. Marianna University School of Medicine Hospital, Kanagawa 216-8511, Japan
[b] Faculty of Sport Sciences, Waseda University, Saitama 359-1192, Japan
[c] Department of Nursing, St. Marianna University School of Medicine Hospital, Kanagawa 216-8511, Japan
[d] Division of Cardiology, Department of Internal Medicine, St. Marianna University School of Medicine, Kanagawa 216-8511, Japan

ARTICLE INFO

Article history:
Received 15 July 2011
Accepted 25 July 2011

Keywords:
Physical activity
Exercise capacity
Steps
Chronic heart failure

Historically, peak oxygen uptake (peak VO_2) as an index of exercise capacity is one important criterion used to evaluate chronic heart failure (CHF) patients for heart transplantation worldwide [1,2]. Mancini et al. [2] reported that cardiac transplantation can be safely deferred in ambulatory heart failure patients with severe left ventricular dysfunction and a peak VO_2 of >14 ml/min/kg (4 metabolic equivalents: METs). Several previous reports have suggested that not only peak VO_2 but also physical activity is an equally strong predictor of survival in patients with stroke, myocardial infarction, pulmonary disease, arrhythmia, and CHF [3,4].

Although individual perceptions may differ regarding the value of exercise considered important in the design of strategies to improve physical activity in CHF patients, only a few studies have addressed this issue.

The purpose of the present study was to determine (1) differences between physical activity in the performance of exercise capacity of ≥4 METs, and (2) levels of physical activity required to attain an exercise capacity of ≥4 METs in outpatients with CHF.

This was a cross-sectional study in which consecutive 145 stable male CHF outpatients who were beginning a cardiac rehabilitation (CR) program were included.

We evaluated several patient characteristics, including left ventricular ejection fraction (LVEF), brain natriuretic peptide (BNP) concentration, and New York Heart Association (NYHA) functional class.

All 145 patients underwent symptom-limited cardiopulmonary exercise testing (CPX) via a ramp cycle ergometer (CORIVAL 400 ergometer) protocol during stable male CHF.

Peak VO_2 was measured throughout the exercise period with an AE-300S aero monitor and calculated on a personal computer [4,5]. METs for each patient were calculated as follows: METs = peak VO_2 ml/kg/min/3.5 ml/kg/min. After CPX, we further divided the patients into two groups according to exercise capacity: ≥4 METs (group A, $n=113$) and <4 METs (group B, $n=32$).

We used number of steps as the indices of physical activity. These indices were estimated by use of an accelerometer-equipped electronic pedometer (Kenz Lifecorder). All patients were taught to put on the Lifecorder themselves and were instructed to use the Lifecorder 24 h a day for 1 week, except while bathing. For each patient, we calculated the mean number of steps for 1 week as follows: mean daily step count = total step count/7 (steps/day for 1 week).

The present study was approved by the St. Marianna University School of Medicine Institutional Committee on Human Research. Informed consent was obtained from each patient.

Results are expressed as mean ± standard error (SE). The unpaired t-test and chi-square test were used to analyze differences such as clinical characteristics between groups A and B. In addition, analysis of covariance was performed to adjust for the effect of age, BNP, and NYHA functional class on mean daily step count between the two groups. Receiver-operating characteristic (ROC) curves were constructed by means of plotting true-positive rates (sensitivity) against false-positive rates (1-specificity) following calculation of the sensitivity for mean daily step count of an exercise capacity of ≥4 METs to determine the best cutoff value. A p value of <0.05 was considered significant. Statistical analyses were performed with SPSS 12.0 J statistical software.

Patient characteristics were almost identical between groups A and B. However, age ($p<0.001$), BNP concentration ($p<0.001$), and NYHA functional class ($p<0.001$) differed significantly between groups A and B (Table 1).

After adjustment for age, BNP concentration, and NYHA functional class, mean daily step counts of physical activity ($p<0.001$) in the CHF patients were significantly higher in group A than in group B (Table 2).

The sensitivities of each cutoff value for group A (≥4 METs) were calculated and used to construct ROC curves for the CHF patients (Fig. 1). Using ROC analysis of exercise capacity of ≥4 METs, we identified a cutoff value for daily step count of physical activity of 4397.1 steps/day for 1 week, with a sensitivity of 0.80, 1-specificity of 0.21, and area under the curve value of 0.83 (95% confidence interval: 0.76–0.89, $p<0.001$).

The present study shows that for CHF outpatients, there are differences in mean daily step counts of physical activity in relation to an exercise capacity threshold of ≥4 METs. Although the data was adjusted for age, BNP concentration, and NYHA functional class, group B

Table 1
Clinical characteristics of the patients.

Group	A (≥4 METs)	B (<4 METs)	t and χ^2 value	P value
No. of patients	113	32		
Age (yrs)	58.4 ± 1.1	67.8 ± 1.9	3.87[a]	<0.001
BMI (kg/m^2)	23.8 ± 0.3	22.6 ± 0.8	1.64[a]	0.10
LVEF (%)	30.4 ± 1.2	28.1 ± 1.9	1.03[a]	0.31
BNP (pg/ml)	174.4 ± 20.6	460.4 ± 59.1	5.68[a]	<0.001
NYHA (I/II/III)	56/53/4	0/12/20	68.7	<0.001
Etiology (%)				
Cardiomyopathy	48.1	42.8	4.33	0.22
Previous myocardial infarction	31.2	39.2		
Arrhythmia	15.1	10.7		
CABG/VR	5.6	7.3		
Medications(%)				
B blockers	78.9	82.1	1.39	0.46
ARB	44.3	56.6	3.49	0.09
ACEI	47.1	46.4	0.04	1.00
Diuretic	86.5	92.8	0.83	0.36

METs, metabolic equivalents; BMI, body mass index; LVEF, left ventricular ejection fraction; BNP, brain natriuretic peptide; NYHA, New York Heart Association; MI, myocardial infarction; CABG, coronary artery bypass grafting; VR, valve replacement; ARB, angiotensin receptor blocker; ACEI, angiotensin converting enzyme inhibitor.
[a] t value.

* Corresponding author at: Department of Rehabilitation Medicine, St. Marianna University School of Medicine Hospital, 2-16-1 Sugao, Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan. Tel.: +81 44 977 8111x6155; fax: +81 44 977 9486.
E-mail address: izawapk@ga2.so-net.ne.jp (K.P. Izawa).

Table 2
Differences in physical activity adjusted for age, BNP concentration, and NYHA functional class.

Group	A (≥4 METs)	B (<4 METs)	F value	P value
No. of patients	113	32		
Mean daily step counts of physical activity (steps/day for 1 week)	6947.5±268.1 (6417.4–7477.5)	4399.1±588.6 (3235.3–5562.9)	14.4	<0.001

Strength values are shown as mean±standard error (95% confidence interval). Independent variables of analysis of covariance: age, BNP, and NYHA functional class. BNP, brain natriuretic peptide; METs, metabolic equivalents; peak VO_2, peak oxygen uptake; NYHA, New York Heart Association.

patients attained significantly lower mean step counts of physical activity than did group A patients (Table 2). Thus, we suggest that an exercise capacity threshold of ≥4 METs has some influence on the mean step count that can be generated.

ROC analysis in the present study showed that an exercise capacity of ≥4 METs in male CHF patients was equivalent to a mean daily step count of approximately 4397.1 steps (Fig. 1). A previous review of pedometer use to measure physical activity reported that the expected number of steps per day for individuals living with disabilities and chronic illnesses was in the range of 3500 to 5500 steps [6]. This value was similar to our present result in male CHF patients. Another study also suggested that a cutoff value of 3571.4 steps (calculated value based on a reported pedometer score of 250×10^2 steps per week = 25,000 - steps/7 days) as an index of the daily activity level of CHF patients was related to mortality and that this parameter appears to be a more powerful index than laboratory-based exercise testing variables such as peak VO_2 and exercise time [5]. Mean step counts attained by patients in our study are superior to those of this previous study.

We found that an exercise capacity of ≥4 METs in male CHF outpatients was equivalent to a mean daily step count of approximately 4397.1 steps of physical activity for 1 week. These values may be useful target goals for improvement of exercise capacity in male CHF outpatients at entry into a phase II CR program.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology (Shewan and Coats 2010; 144:1–2).

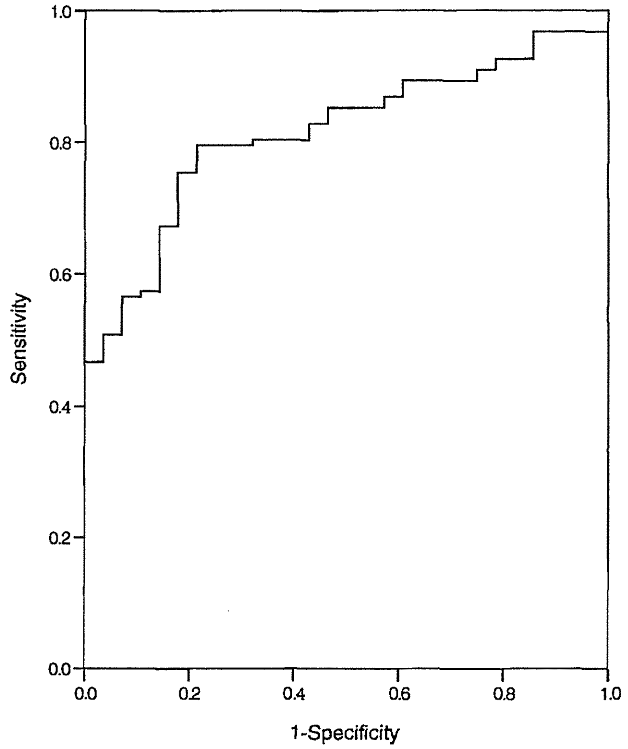

Fig. 1. Cutoff value for daily step counts of physical activity identified by ROC analysis of exercise capacity of ≥4 METs in group A. Cutoff value of daily step counts of physical activity = 4397.1 steps/day for 1 week, with a sensitivity of 0.80, 1-specificity of 0.21; and AUC value of 0.83 (95% CI: 0.76–0.89, $p<0.001$).

References

[1] Osada N, Chaitman BR, Miller LW, et al. Cardiopulmonary exercise testing identifies low risk patients with heart failure and severely impaired exercise capacity considered for heart transplantation. J Am Coll Cardiol 1998;31:577–82.
[2] Mancini DM, Eisen H, Kussmaul W, Mull R, Edmunds Jr LH, Wilson JR. Value of peak exercise oxygen consumption for optimal timing of cardiac transplantation in ambulatory patients with heart failure. Circulation 1991;83:778–86.
[3] Walsh JT, Charlesworth A, Andrews R, Hawkins M, Cowley AJ. Relation of daily activity levels in patients with chronic heart failure to long-term prognosis. Am J Cardiol 1997;79:1364–9.
[4] Myers J, Kaykha A, George S, et al. Fitness versus physical activity patterns in predicting mortality in men. Am J Med 2004;117:912–8.
[5] Seo Y, Roberts BL, Piña I, Dolansky M. Predictors of motor tasks essential for daily activities among persons with heart failure. J Card Fail 2008;14:296–302.
[6] Tudor-Locke CE, Myers AM. Methodological considerations for researchers and practitioners using pedometers to measure physical (ambulatory) activity. Res Q Exerc Sport 2001;72:1–12.

doi:10.1016/j.ijcard.2011.07.069