

Usefulness of physical function sub-item of SF-36 survey to predict exercise intolerance in patients with heart failure

Kensuke Ueno¹, Kentaro Kamiya^{1,2,*}, Nobuaki Hamazaki ¹, Kohei Nozaki³, Takafumi Ichikawa³, Masashi Yamashita ¹, Shota Uchida¹, Masashi Kawabata², Emi Maekawa⁴, Minako Yamaoka-Tojo ^{1,2}, Atsuhiko Matsunaga ^{1,2}, and Junya Ako⁴

¹Department of Rehabilitation Sciences, Graduate School of Medical Sciences, Kitasato University, 1-15-1 Kitasato, Minami-ku, Sagamihara, Kanagawa 252-0373, Japan; ²Department of Rehabilitation, School of Allied Health Sciences, Kitasato University, 1-15-1 Kitasato, Minami-ku, Sagamihara, Kanagawa 252-0373, Japan; ³Department of Rehabilitation, Kitasato University Hospital, 1-15-1 Kitasato, Minami-ku, Sagamihara, Kanagawa 252-0375, Japan; and ⁴Department of Cardiovascular Medicine, School of Medicine, Kitasato University, 1-15-1 Kitasato, Minami-ku, Sagamihara, Kanagawa 252-0374, Japan

Received 23 February 2021; revised 23 April 2021; accepted 25 May 2021

Background	Exercise intolerance is widely known to be a major cardinal symptom in patients with heart failure (HF), but due to the recent coronavirus disease 2019 epidemic, it is still difficult to directly measure exercise tolerance in many hospitals and facilities. The 36-Item Short-Form Health Survey physical functioning (SF-36PF) pertain to lower extremity functioning and walking. The purpose of this study was to investigate whether SF-36PF is a useful predictor of exercise intolerance and to provide its optimal cut-off value for patients with HF.
Methods and results	SF-36PF and 6-min walking distance (6MWD) were evaluated in 372 consecutive patients with HF. Exercise intoler- ance was defined at 6MWD cut-offs of 200, 300, and 400 m. The addition of SF-36PF to the pre-existing determi- nants of exercise tolerance significantly improved the area under the curve scores (0.85 vs. 0.89, $P = 0.011$ for 6MWD <200 m; 0.90 vs. 0.93, $P = 0.001$ for 6MWD <300 m; 0.88 vs. 0.90, $P = 0.021$ for 6MWD <400 m) for the predictive effect on exercise intolerance. The cut-off values of SF-36PF for predicting exercise intolerance defined by 6MWD <200, 300, and 400 m were 45, 50, and 70, respectively.
Conclusions	SF-36PF is a useful tool as an alternative index to predict exercise intolerance in patients with HF.
Keywords	Coronavirus disease 2019 • Heart failure • Exercise intolerance • 6-Min walk distance • 36-Item Short-Form Health Survey physical functioning

Implications for practice

- 36-Item Short Form Health Survey physical functioning (SF-36PF) was useful in predicting exercise intolerance in heart failure patients.
- The cut-off values of SF-36PF scores for exercise intolerance defined at 6-min walking distance <200, 300, and 400 m were 45, 50, and 70, respectively.
- SF-36PF can be worth using in hospitals and in areas where exercise tolerance by other means is difficult to measure.

* Corresponding author. Tel: +81 42 778 9693, Fax: +81 42 778 9686, Email: k-kamiya@kitasato-u.ac.jp

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2021. For permissions, please email: journals.permissions@oup.com.

Introduction

Exercise intolerance is widely known to be a major cardinal symptom, a poor prognostic factor, and an important therapeutic target in patients with heart failure (HF).^{1–5} However, due to the recent coronavirus disease 2019 epidemic, it is anticipated that there are many hospitals and facilities that are restricted from conducting field tests to evaluate exercise tolerance with a high risk of exposure. Moreover, patients are recommended to wear masks during hospitalization, even during exercise tolerance evaluation. However, it has been reported that masks have a marked negative impact on exercise parameters, such as maximum oxygen uptake.⁶ Therefore, another method to evaluate exercise tolerance is required.

The 36-Item Short-Form Health Survey (SF-36) is the most commonly used measure of health status in the world today,⁷ and physical functioning (PF) is one of its sub-items. This subscale consists of 10 items that assess perceived difficulties in physical activities. Most of these items pertain to lower extremity functioning,⁸ and three of them refer specifically to walking.

The purpose of this study was to investigate whether SF-36PF is a useful predictor of exercise intolerance and to provide its optimal cut-off value for patients with HF.

Methods

Study population

A single-centre retrospective study was conducted. The study population consisted of 1014 consecutive patients who were admitted to Kitasato University Hospital with a diagnosis of HF from January 2015 to September 2018. Exclusion criteria were as follows: discharged or died before the measurement, unstable medical condition, severe disability, refused to measure 6-min walking distance (6MWD), missed measurement, and patients who were missed for any of the variables used in the multivariate analysis. A total of 372 patients who underwent evaluation of both SF-36PF and 6MWD at discharge were finally included in the study (Figure 1). The study was performed following the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Kitasato University Hospital (B18-075). Data on all variables were collected from electronic medical records. B-type natriuretic peptide (BNP) concentration was measured using a commercially available immunoradiometric assay (Shionogi, Osaka, Japan). Simpson's method was used to estimate left ventricular ejection fraction (LVEF) on two-dimensional echocardiograms. 6MWD was measured according to the American Thoracic Society guidelines,⁹ and measurements were supervised by technicians. We measured 6MWD in the flat in-hospital hallway, which was marked at 1 m intervals. Patients were instructed to walk as far as possible along a straight line, and the distance, expressed in metres, was recorded at the end of a 6-min period. SF-36PF consist of 10 activities related to mobility and physical movements,¹⁰ ranging from 0, indicating severely restricted physical activity, to 100, indicating unrestricted physical activity. SF-36PF was evaluated at the same time as 6MWD tests, and the measurement was supervised by technicians.

Statistical analysis

Continuous variables are expressed as the median and interquartile range, and categorical variables are expressed as numbers and percentages. Exercise intolerance was defined at the established 6MWD cut-offs of 200,¹ 300,^{2–4} and 400 m.^{5,11} Statistical analysis of 6MWD cut-off values was performed using the areas under the curve scores (AUCs) and the 95% confidence interval (CI) of receiver operating characteristic (ROC) curves. These measures were used to compare the accuracy of adding SF-36PF to predictive models using pre-existing determinants of exercise tolerance. Pre-existing determinants of exercise tolerance were defined as follows: age, sex, body mass index, LVEF, New York Heart Association functional class (NYHA class), log BNP, haemoglobin, albumin, and length of stay. Generally, an AUC equal to 0.7–0.8 is considered acceptable, an



Table I Patient characteristics

Characteristics	All patients (n = 372)	
Age (years)	74 (67–81)	
Sex, male (%)	222 (59.7)	
Body mass index (kg/m^2)	21.5 (19.4–24.5)	
lschaemic heart disease (%)	129 (34.7)	
Left ventricular ejection fraction (%)	41.4 (30.0–60.0)	
New York Heart Association	80 (21.5)	
functional Class III or IV (%)		
Medications (%)		
ACE inhibitor or ARB	314 (84.4)	
Beta-blockers	290 (78.0)	
Aldosterone blockers	196 (52.7)	
Diuretic agents	326 (87.6)	
Comorbidities (%)		
Hypertension	253 (68.0)	
Diabetes	140 (37.6)	
Current smoker	71 (19.5)	
Chronic obstructive pulmonary disease	38 (10.2)	
Chronic kidney disease	287 (77.2)	
Laboratory data		
Haemoglobin (g/dL)	12.0 (10.5–13.8)	
Albumin (g/dL)	3.5 (3.1–3.8)	
B-type natriuretic peptide (pg/mL)	421 (203–876)	
SF-36 physical functioning, scores	60 (35–85)	
6MWD (m)	338 (227–429)	
6MWD <200 m (%)	66 (17.7)	
6MWD <300 m (%)	147 (39.5)	
6MWD <400 m (%)	250 (67.2)	
Length of stay (days)	18 (13-28)	

Values are median (interquartile range) or n (%).

6MWD, 6-min walking distance; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blockers; SF-36, 36-Item Short-Form Health Survey.

AUC equal to 0.8-0.9 is considered excellent, and an AUC >0.9 is considered outstanding.¹² In addition, based on the ROC curves, the maximum values of the Youden index were calculated to determine the

Results

This study included 372 HF patients. The median age of the patients was 74 years. Of these, 59.7% of patients were male, 21.5% of the patients belonged to NYHA Class III or IV, and the median 6MWD was 338 m (*Table 1*).

optimal cut-off value of SF-36PF scores for exercise intolerance defined

by 6MWD <200, 300, and 400 m, respectively.

The addition of SF-36PF to the pre-existing determinants of exercise tolerance significantly improved the AUCs [0.85 (95% CI 0.79–0.89) vs. 0.89 (95% CI 0.84–0.92), P = 0.011 for 6MWD <200 m; 0.90 (95% CI 0.87–0.93) vs. 0.93 (95% CI 0.91–0.95), P = 0.001 for 6MWD <300 m; 0.88 (95% CI 0.84–0.91) vs. 0.90 (95% CI 0.87–0.93), P = 0.021 for 6MWD <400 m, *Figure 2*] for the predictive effect on exercise intolerance.

The cut-off values of SF-36PF for predicting exercise intolerance based on the Youden index for 6MWD < 200, 300, and 400 m were 45, 50, and 70, respectively.

Conclusion

This study shows that SF-36PF is useful in predicting exercise intolerance and provides an optimal cut-off value according to the degree of exercise intolerance.

The usefulness of using subjective measures to predict exercise tolerance in patients with HF has been widely reported. The NYHA class assesses the difficulty of physical activity and is commonly used in clinical practice to assess exercise tolerance.² The specific activity scale links basic activities of daily living to oxygen uptake and is useful for assessing exercise tolerance.¹³ In contrast, SF-36PF includes questions on physical functions, such as stair climbing and long-distance



Figure 2 The complementary role of 36-Item Short-Form Health Survey physical functioning to pre-existing determinants of exercise tolerance in predicting exercise intolerance in 372 heart failure patients. AUCs, area under the curve scores; SF-36PF, 36-Item Short-Form Health Survey physical functioning.

walking, and reportedly has a moderate correlation with exercise tolerance.¹⁴ Moreover, it was reported that SF-36PF was determined to a considerable degree (51%) by NYHA class and the 6MWD.¹⁴ Therefore, SF-36PF may be useful in predicting exercise tolerance but has not been widely reported. To the best of our knowledge, this is the first study to provide an optimal cut-off value according to the exercise intolerance degree.

SF-36PF has been translated into more than 170 countries languages and can be used anywhere through both postal surveys and telephone interviews. Therefore, the increased risk of relevant infective transmission in exercise tolerance assessments¹⁵ can be reduced and will also help mitigate the shortage of medical resources associated with the recommendation to wear personal protective equipment. Moreover, although the demand for inpatient to outpatient follow-up in HF cases is increasing, the ongoing pandemic requires strict rules of social distancing. As a result, field tests are currently expected to be limited. Therefore, we consider that the cut-off values of SF-36PF for predicting exercise intolerance obtained in the present study can be worth using in many types of hospitals and health care facilities and in areas where 6MWD and cardiopulmonary exercise testing are difficult to measure.

Some limitations will need to be considered in this study, such as a single-centre retrospective study and conducted only on Asian patients hospitalized for HF. Also, impaired autonomic regulation and peripheral vascular maladaptation, which have been reported as determinants of exercise tolerance, were not investigated.¹⁶ However, we believe that the SF-36PF is a useful measure for predicting exercise intolerance in patients with HF in any clinical setting, as its usefulness is consistent even after adjustment for existing HF severity. Additionally, self-reported questionnaires may have a limitation in patients with cognitive dysfunction or very old patients.

In conclusion, SF-36PF is a useful tool as an alternative index to predict exercise intolerance in patients with HF and can be a valid alternative in facilities and areas where evaluation of exercise tolerance for nursing care and risk stratification is difficult.

Conflict of interest: The authors declare that there is no conflict of interest.

Data availability

The data underlying this article cannot be shared publicly due to the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

References

1. Alahdab MT, Mansour IN, Napan S, Stamos TD. Six minute walk test predicts long-term all-cause mortality and heart failure rehospitalization in African-

American patients hospitalized with acute decompensated heart failure. J Card Fail 2009; 15:130-135.

- Bittner V, Weiner DH, Yusuf S, Rogers WJ, McIntyre KM, Bangdiwala SI, Kronenberg MW, Kostis JB, Kohn RM, Guillotte M. Prediction of mortality and morbidity with a 6-minute walk test in patients with left ventricular dysfunction. SOLVD Investigators. JAMA 1993;270:1702–1707.
- 3. Metra M, Ponikowski P, Dickstein K, McMurray JJV, Gavazzi A, Bergh C-H, Fraser AG, Jaarsma T, Pitsis A, Mohacsi P, Böhm M, Anker S, Dargie H, Brutsaert D, Komajda M; on behalf of the Heart Failure Association of the European Society of Cardiology. Advanced chronic heart failure: a position statement from the Study Group on Advanced Heart Failure of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2007;**9**:684–694.
- 4. Fang JC, Ewald GA, Allen LA, Butler J, Westlake Canary CA, Colvin-Adams M, Dickinson MG, Levy P, Stough WG, Sweitzer NK, Teerlink JR, Whellan DJ, Albert NM, Krishnamani R, Rich MW, Walsh MN, Bonnell MR, Carson PE, Chan MC, Dries DL, Hernandez AF, Hershberger RE, Katz SD, Moore S, Rodgers JE, Rogers JG, Vest AR, Givertz MM. Advanced (stage D) heart failure: a statement from the Heart Failure Society of America Guidelines Committee. J Card Fail 2015;21:519–534.
- Newman AB, Simonsick EM, Naydeck BL, Boudreau RM, Kritchevsky SB, Nevitt MC, Pahor M, Satterfield S, Brach JS, Studenski SA, Harris TB. Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. JAMA 2006;295:2018–2026.
- Fikenzer S, Uhe T, Lavall D, Rudolph U, Falz R, Busse M, Hepp P, Laufs U. Effects of surgical and FFP2/N95 face masks on cardiopulmonary exercise capacity. *Clin Res Cardiol* 2020;109:1522–1530.
- Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30: 473–483.
- Rogers WH, Wittink H, Wagner A, Cynn D, Carr DB. Assessing individual outcomes during outpatient, multidisciplinary chronic pain treatment by means of an augmented SF-36. *Pain Med* 2000;**1**:44–54.
- ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111–117.
- Ware JE, Snow KK, Kosinski M, Gandek B. SF-36 Health Survey Manual and Interpretation Guide. Boston, MA: New England Medical Center, The Health Institute; 1993.
- 11. Morley JE, Abbatecola AM, Argiles JM, Baracos V, Bauer J, Bhasin S, Cederholm T, Stewart Coats AJ, Cummings SR, Evans WJ, Fearon K, Ferrucci L, Fielding RA, Guralnik JM, Harris TB, Inui A, Kalantar-Zadeh K, Kirwan B-A, Mantovani G, Muscaritoli M, Newman AB, Rossi-Fanelli F, Rosano GMC, Roubenoff R, Schambelan M, Sokol GH, Storer TW, Vellas B, von Haehling S, Yeh S-S, Anker SD. Sarcopenia with limited mobility: an international consensus. J Am Med Dir Assoc 2011;**12**:403–409.
- Mandrekar JN. Receiver operating characteristic curve in diagnostic test assessment. J Thorac Oncol 2010;5:1315–1316.
- Goldman L, Hashimoto B, Cook EF, Loscalzo A. Comparative reproducibility and validity of systems for assessing cardiovascular functional class: advantages of a new specific activity scale. *Circulation* 1981;64:1227–1234.
- Juenger J, Schellberg D, Kraemer S, Haunstetter A, Zugck C, Herzog W, Haass M. Health related quality of life in patients with congestive heart failure: comparison with other chronic diseases and relation to functional variables. *Heart* 2002; 87:235–241.
- Faghy MA, Sylvester KP, Cooper BG, Hull JH. Cardiopulmonary exercise testing in the COVID-19 endemic phase. Br J Anaesth 2020;125:447–449.
- Del Buono MG, Arena R, Borlaug BA, Carbone S, Canada JM, Kirkman DL, Garten R, Rodriguez-Miguelez P, Guazzi M, Lavie CJ, Abbate A. Exercise intolerance in patients with heart failure. J Am College Cardiol 2019;73: 2209–2225.