



Predictors of activities of daily living at discharge in elderly patients with heart failure with preserved ejection fraction

Kitamura, Masahiro ; Izawa, P. Kazuhiro ; Ishihara, Kodai ; Yaekura, Masakazu ; Nagashima, Hitomi ; Yoshizawa, Takashi ; Okamoto, Nobuhiro

(Citation)

Heart and Vessels, 36(4):509-517

(Issue Date)

2021-04

(Resource Type)

journal article

(Version)

Accepted Manuscript

(Rights)

This version of the article has been accepted for publication, after peer review (when applicable) and is subject to Springer Nature's AM terms of use, but is not the Version of Record and does not reflect post-acceptance improvements, or any corrections. The Version of Record is available online at:...

(URL)

<https://hdl.handle.net/20.500.14094/0100495516>



Predictors of activities of daily living at discharge in elderly patients with heart failure with preserved ejection fraction

Author names and affiliations:

Masahiro Kitamura PhD, MSc ^{a,b,e}, Kazuhiro P. Izawa PhD, MSc ^{b,e}, Kodai Ishihara MSc ^{b,c,e},

Masakazu Yaekura ^d, Hitomi Nagashima ^d Takashi Yoshizawa PhD, MSc ^a, Nobuhiro Okamoto MSc

^a

^a Department of Physical Therapy, Fukuoka Wajiro Professional Training College, 2-1-13 Wajirooka, Higashi-ku, Fukuoka 811-0213, Japan

^b Department of Public Health, Graduate School of Health Sciences, Kobe University, 7-10-2 Tomogaoka, Suma-ku, Kobe 654-0142, Japan

^c Department of Rehabilitation, Sakakibara Heart Institute of Okayama, 5-1-2 Nakaicho, Kita-ku, Okayama 700-0804, Japan

^d Department of Rehabilitation, Shinyukhashi Hospital, Yukuhashi 824-0026, Japan

^e Cardiovascular Stroke Renal Project, Kobe, Japan

Corresponding author: Kazuhiro P. Izawa, PT, PhD, MSc

Graduate School of Health Sciences, Kobe University, 7-10-2 Tomogaoka Suma, Kobe 654-0142,

Japan

Tel: +81-78-792-2555, Fax: +81-78-796-4509

E-mail: izawapk@harbor.kobe-u.ac.jp

Highlights

- We determined predictors of ADL at discharge in elderly patients with HFpEF.
- The cut-off value of LTCI for ADL at discharge was support level 2.
- The cut-off value of walking exercise start day for ADL at discharge was 4.5 days after admission.
- Motor- and cognitive-FIM cut-off values for ADL at discharge were 34.5 and 28.5 points.
- LTCI level, walking exercise start day and motor-/cognitive-FIM at admission may predict ADL at discharge in HFpEF patients.

ABSTRACT

Aims: The purpose of this study was to clarify the predictive factors of activities of daily living (ADL) at discharge in elderly patients with heart failure with preserved ejection fraction (HFpEF).

Methods: Participants were selected from among 598 consecutive hospitalized HF patients based on certain criteria. We investigated patient characteristics, and ADL with the motor and cognitive items of the Functional Independence Measure (FIM). We analyzed the data with the unpaired t-test, Mann-Whitney U test, χ^2 test, logistic regression analysis, and receiver operating characteristic (ROC) curves.

Results: We included 154 patients for further analyses who were divided into the low ADL group (n=75) and high ADL group (n=79). There were significant differences between the two groups in age, long-term care insurance (LTCL) level, New York Heart Association class, creatinine level, albumin level, β -blocker, sitting, standing and walking exercise start days, length of hospital stay, and motor- and cognitive-FIM scores at admission and discharge ($p < 0.05$). The cut-off values of the ROC curves predicting ADL at discharge were LTCL: support level 2 (area under the curve [AUC]: 0.672, $p < 0.001$, sensitivity: 0.573, false-positive rate: 0.278); walking exercise start day: 4.5 days (AUC: 0.694, $p < 0.001$, sensitivity: 0.609, false-positive rate: 0.299); motor FIM score: 34.5 points (AUC: 0.710, $p < 0.001$, sensitivity: 0.633, false-positive rate: 0.280); and cognitive FIM score: 28.5 points (AUC:

0.806, $p < 0.001$, sensitivity: 0.759, false-positive rate: 0.227).

Conclusion: This study revealed several predictors of ADL at discharge and their associated cut-off values in elderly patients with HFpEF.

Keywords: activities of daily living; elderly; heart failure with preserved ejection fraction; hospitalized; walking exercise start day; long-term care insurance

Abbreviations: ACEI, angiotensin converting enzyme inhibitor; ADL, activities of daily living; ARB, angiotensin receptor blocker; AUC, area under the curve; BMI, body mass index; BNP, brain natriuretic peptide; EF, ejection fraction; eGFR, estimated by glomerular filtration rate; FIM, functional independence measure; GNRI, geriatric nutritional risk index; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; LTCI, long-term care insurance; NYHA, New York Heart Association; ROC, receiver operating characteristic.

Funding: The present research received no specific grant from any funding agency in the commercial, public, or not-for-profit sectors.

Introduction

The number of patients worldwide with heart failure (HF) is increasing due to aging, and the associated increase in medical expenses has become a social problem.¹ There are two major categories of HF: HF with preserved ejection fraction (HFpEF) and HF with reduced ejection fraction (HFrEF). The number of HFpEF patients,² which has been increasing in recent years, is equivalent to that of HFrEF patients, and mortality and readmission rates are almost the same.^{3,4} Also, characteristics of patients with HFpEF and HFrEF hospitalized for acute decompensated HF include a high prevalence of frail patients and those with cognitive impairment.⁵ In patients with HFpEF, the proportion of elderly women and the incidences of hypertension, atrial fibrillation, diabetes, kidney disease, obesity, and other conditions are high.^{3,6,7} However, there are few reports on the pathophysiology and treatment of HFpEF compared to HFrEF. In addition, effective treatments that improve the prognosis of HFpEF patients have not been elucidated, and the clinical guidelines for HFpEF patients recommend active diagnosis and management of comorbidities.^{8,9} Therefore, there is a need for evidence of treatment and prognosis associated with HFpEF.

Activities of daily living (ADL) for both HFrEF and HFpEF patients is a useful index related to mortality and readmission rates.¹⁰ Also, ADL is related to walking ability, cognitive function, and living environment, and treatment strategies can be devised based on its analysis.¹¹ In particular, improvement of ADL at discharge by rehabilitation begun at

admission is important because ADL at discharge is associated with readmission.^{12,13} In addition, improvements in safety and activity status have been reported in patients with HFrEF who exercise during hospitalization and after discharge. It is thus becoming clear that ADL-related factors and efficacy of interventions in HFrEF patients are important.¹⁴ However, very few studies have investigated predictors of ADL at discharge in hospitalized HFpEF patients. By assessing predictors of ADL at discharge, evidence of effective intervention during the hospitalization of patients with HFpEF patients may be found.

We hypothesized that among hospitalized elderly patients with HFpEF, those with low ADL would have more comorbidities than those with high ADL, and this factor would affect ADL at discharge. Thus, the purpose of this study was to investigate predictors of ADL at discharge in elderly patients with HFpEF based on indicators assessed at admission and early after admission.

Methods

Study design and subjects

In this retrospective cohort study, we searched the data on 598 consecutive patients with HF who underwent rehabilitation at one acute-care hospital from May 2012 to July 2016. We included patients over the age of 65 who were able to walk at home before admission and had an ejection fraction (EF) of 50% or more and excluded patients who underwent pacemaker

implantation, transfer to other departments and who died during hospitalization. The

Fukuokawajiro Rehabilitation College Ethics Committee approved this study (approval no.

FW-20-03), and informed consent was obtained from each patient.

Measurement

The following patient characteristics and clinical parameters were measured at admission: age, sex, body mass index (BMI), long-term care insurance (LTCI) level, EF, brain natriuretic peptide (BNP), New York Heart Association (NYHA) class, creatinine, estimated glomerular filtration rate (eGFR), hemoglobin, albumin, Geriatric Nutritional Risk Index (GNRI) score, comorbidities, medications, motor Functional Independence Measure (FIM) score and cognitive FIM score. The start days of sitting, standing and walking exercise were determined several days after admission. Motor and cognitive FIM scores and length of hospital stay were assessed at discharge. Characteristics and clinical parameters of the patients were evaluated by retrospectively reviewing their medical records. We divided the patients into two groups, the low ADL group (motor FIM < 75 points) and high ADL group (motor FIM ≥ 75 points) at discharge, on the basis of cut-off values of motor FIM scores determined in a previous study.¹²

HF and HFpEF

The diagnosis of HF was made by a cardiologist based on the Framingham criteria (symptoms related to decreased cardiac output, increased pulmonary wedge pressure and

congestion).¹⁵ Next, based on the guidelines, the patients were classified into three categories "reduced EF ($\leq 40\%$)", "midrange EF (41% to 49%)" and "preserved EF ($\geq 50\%$)" according to the echocardiographic EF obtained at admission. HFpEF patients were defined as those with "preserved EF".^{1,9}

ADL

ADL was assessed by FIM at patient admission and discharge. The FIM, which is composed of two domains, motor and cognitive, was developed to evaluate aspects of rehabilitation in patients with disabilities.^{16,17} The 13 items of the motor domain (motor-FIM) comprise eating, grooming, bathing, dressing upper body, dressing lower body, toileting, bladder and bowel management, transfer to bed, chair, or wheelchair, transfer to toilet, transfer to shower or tub, walking/wheelchair, and stairs. The 5 items of the cognitive domain (cognitive-FIM) comprise comprehension, expression, social interaction, problem solving and memory. Each item can be scored from 1 to 7 points as follows: 1 point for total assistance, 2 points for maximal assistance, 3 points for moderate assistance, 4 points for minimal contact assistance, 5 points for supervision, 6 points for modified independence and 7 points for complete independence. Motor FIM scores range from 13 to 91 points, and cognitive FIM scores range from 5 to 35 points. FIM score measurements were performed by two physiotherapists.

Sitting, standing and walking exercise start day

Hospitalized HF patients perform exercises such as sitting, standing, walking and ADL according to Japanese guidelines.¹⁸ The day after admission that each patient began sitting, standing and walking exercise was determined. Each exercise was guided by a physical therapist or nurse after confirming with the patient's physician that the patient had no symptoms that would prevent mild activity. If the patient could walk, we added exercises to improve the patient's endurance and muscular strength necessary for home life.

Statistical analysis

Patient characteristics and clinical parameters are reported as percentages for categorical variables and mean $\pm$ standard deviation (SD) for continuous variables. The unpaired t-test for normally distributed continuous variables, the Mann-Whitney U test for continuous variables not normally distributed and the chi-square test for categorical variables were used to compare patient characteristics and clinical parameters between the two groups. A logistic regression analysis was used to ascertain whether variables with significant differences between the two groups were independent predictors of motor ADL at discharge. In this analysis, independent predictors were first extracted by univariate analysis, and then multivariate analysis was performed using these predictors as covariates (odds ratio [OR] and 95% confidence interval [CI]). Receiver operating characteristic (ROC) curves were used for the predictors obtained from multivariate analysis, and the area under the curve (AUC) was

calculated to determine the cutoff value of motor ADL and other parameters at discharge. For AUC values, <0.9 indicates high accuracy, $0.7\text{--}0.9$ indicates moderate accuracy, and <0.7 indicates low accuracy.¹⁹ A p-value of <0.05 was considered to indicate statistical significance. Statistical analyses were performed with IBM SPSS 25.0 J statistical software (IBM SPSS Japan, Inc., Tokyo, Japan).

Results

Patient flow

Participant flow in the study is shown in Figure 1. Of the 598 consecutive HF patients who underwent rehabilitation, 186 patients who met the inclusion criteria of 65 years old or older, walking at home before admission and EF of 50% or more were included in this study. However, 32 patients were later excluded because of pacemaker implantation surgery during hospitalization ($n=21$), transfer to other departments ($n=9$) and death during hospitalization ($n=2$). Therefore, 154 patients were included in further analyses (Table 1), and these patients were divided into the low ADL group ($n=75$) and high ADL group ($n=79$).

Patient characteristics

The differences in clinical characteristics of the elderly hospitalized patients with HFpEF in the low ADL group and high ADL group can be compared in Table 2. Compared to the high ADL group, the low ADL group was significantly older and had a higher LTCI level,

higher NYHA class, higher creatinine level, lower serum albumin levels, lower β -blocker use rate, longer number of days to the initiation of sitting, standing and walking exercise, longer length of hospital stay and lower motor FIM and cognitive FIM scores at admission and at discharge ($p < 0.05$).

Predictors of ADL at discharge

The results of the logistic regression analysis are shown in Table 3. In the univariate logistic regression analysis with age, LTCI level, NYHA class, creatinine level, serum albumin levels, β -blocker, sitting, standing and walking exercise start day and motor FIM score and cognitive FIM score at admission as covariates, all of these variables were independent predictors of ADL at discharge with the exception of creatinine level and sitting exercise start day ($p < 0.05$). After univariate analysis identified these significant independent predictors, multivariate logistic regression analysis showed the following covariates to be independent predictors of ADL at discharge: age (OR: 0.86; 95% CI: 0.80–0.92), LTCI level (OR: 0.63; 95% CI: 0.40–0.98), walking exercise start day (OR: 0.83; 95% CI: 0.70–0.99), motor FIM score at admission (OR: 1.04; 95% CI: 1.00–1.08) and cognitive FIM score at admission (OR: 1.10; 95% CI: 1.03–1.19).

Cut-off values of the factors for predicting ADL at discharge

The cut-off values of the four indicators determined from the ROC curve that predict ADL at discharge were as follows. LTCI was support level 2 (AUC: 0.672, $p < 0.001$,

sensitivity: 0.573, false-positive rate: 0.278), walking exercise start day was 4.5 days (AUC: 0.694, $p < 0.001$, sensitivity: 0.609, false-positive rate: 0.299) (Figure 2), motor FIM score was 34.5 points (AUC: 0.710, $p < 0.001$, sensitivity: 0.633, false-positive rate: 0.280) and cognitive FIM score was 28.5 points (AUC: 0.806, $p < 0.001$, sensitivity: 0.759, false-positive rate: 0.227) (Figure 3).

Discussion

To our knowledge, this is the first study to show the relationship between discharge ADL and data at admission in hospitalized elderly patients with HFpEF. After adjusting for confounding factors, age, LTCI level, walking exercise start day and motor-FIM and cognitive-FIM scores at admission were the independent predictors of ADL at discharge.

Characteristics of elderly HFpEF patients with low ADL

The average age of all subjects in the present study was 80 years or older, the proportion of women was high, the rate of hypertension was about 90%, that of atrial fibrillation was about 50%, the average value of eGFR was 42.2 mL/min/1.73 m², indicating low renal function, and the hospital stay was 18 days, which are all similar findings to those of previous studies.^{20,21}

The characteristics of HFpEF patients with low ADL at discharge are older age, higher NYHA class, higher LTCI level, higher creatinine level, lower albumin level, lower β -

blockade use rate, longer number of days to initiation of sitting, standing and walking exercise, longer length of hospital stay and lower motor FIM score and lower cognitive FIM score at admission and discharge. Elderly women with low activity have a high risk of developing HFpEF and a high NYHA class.^{22,23} HFpEF patients have higher creatinine levels with age,²⁴ and HFpEF patients with low nutrition have low ADL at discharge.²⁵ In a previous study of elderly HF patients with a high rate of HFpEF, compared to the high activity group, the low activity group was older and had a higher rate of dementia, lower rate of β blocker usage, poorer motor function,²⁶⁻²⁹ longer time to standing and walking exercise start, longer length of hospital stay and higher LTCI level. Patient characteristics of HFpEF patients with low ADL may be partially similar to those of community-dwelling elderly women and elderly HF patients with low activity reported in previous studies.²⁰⁻²⁸

Predictors and cutoff values for ADL at discharge

The age of HFpEF patients was a predictor of ADL at discharge. The prognosis of HF patients deteriorates with aging and is known to be associated with ADL.^{26,30} Age was a relevant prognostic factor in patients with HFpEF,^{21,24} and its effect on ADL is considered common.

There are few previous studies on the association between pre-hospital LTCI levels and ADL at discharge and readmission in HF patients.^{26,31,32} A previous study of community-dwelling elderly people reported that those with motor-FIM scores of 78 or higher had LTCI

support levels of 1-2, and those with a score less than 78 had care levels of 1-2.³³ In the present study, patients were classified into two groups according to motor-FIM scores at discharge of ≥ 75 points and < 75 points.¹³ The cut-off value of LTCI support level 2 obtained in this study may serve as a predictor of discharge ADL in patients with HFpEF. However, the AUC value indicates low accuracy, and thus, this cutoff value should be treated with some care.¹⁹ Further studies are needed to determine the impact of the LTCI level, such as that on pre-hospital activity, on predicting ADL at discharge.

In regard to the cutoff value of 4.5 days as the start day of the walking exercise, the 4th day as the start day of walking exercise in HF patient has been reported as the cutoff value for gait independence at discharge.²⁸ It has been reported that the cross-sectional area of muscle was reduced by about 10% over the 5 days immediately after admission.³⁴ Early mobilization such as an early start of walking exercise may be important to prevent physical and cognitive deconditioning of HFpEF patients.³⁵ However, the reported AUC for early mobilization was of low accuracy.¹⁹ The cognitive-FIM score was also a predictor in the present study, and previous studies have shown that cognitive function, even when mild, can affect ADL and walking at discharge.^{36,37} In the present study, it was possible that the accuracy of the walking exercise start day was low due to the high proportion of patients with mild cognitive function.

Motor-FIM and cognitive-FIM scores at admission were predictors of motor-FIM score at discharge, and the AUC value of each was of moderate accuracy.¹⁹ FIM on admission for

patients who underwent rehabilitation is known to predict FIM at discharge and outcome.^{38,39}

It may be generally expected that motor-ADL at discharge can be predicted to some extent by motor-ADL at admission. However, it has been shown that cognitive function of elderly dialysis patients at admission affects the achievement of rehabilitation goals,⁴⁰ and a lower cognitive-FIM score at admission affects the motor-FIM score at discharge.⁴¹ In patients with HFpEF, cognitive-ADL at admission may affect motor-ADL at discharge, similar to elderly patients with chronic disease. The average value for motor-FIM score at the time of admission in patients at risk of readmission was reported to be 33–40 points, and that for cognitive-FIM was 25–27 points.^{42,43} Low-difficulty ADL movements such as eating, grooming and bladder and bowel management are reported to be not independent in patients with a motor-FIM score of 30 to 39 points, and these low scores are associated with cognitive decline and old age.^{44,45} The cut-off value obtained for the cognitive-FIM score in the present study is similar to the value for the patient population at risk of readmission and low ADL, and it may be important in understanding the risk of reduced ADL at discharge in patients with HFpEF.

Strengths

This is the first study to determine predictors of ADL at discharge and their associated cutoff values in patients with HFpEF. Age, LTCI level, day of walking exercise start and motor- and cognitive-FIM scores at admission influence ADL at discharge in patients with

HFpEF. These results indicate that interventions to shorten the number of days to the initiation of walking exercise and improve motor and cognitive ADL at admission, and maintaining or improving the LTCI level before admission are the most important factors for improving ADL at discharge in patients with HFpEF.

Limitations

As limitations of this study, it was a single-center study with a small sample size. Also, we were not able to investigate physical or cognitive function, FIM gain and factors such as readmission and death in the study patients. Further, as no comparison was made with patients with HFrEF in this study, the findings are limited only to the characteristics of HFpEF patients.

Conclusions

This study found age, LTCI level, day of walking exercise start and motor-FIM and cognitive-FIM scores at admission to be predictors of ADL at discharge in patients with HFpEF and determined the cutoff values for these predictors.

Conflicts of interest:

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

Acknowledgements

This study was benefitted by the support and encouragement of Masashi Kanai, Masato Ogawa, Asami Ogura, Ikkou Kubo, Yuji Kanejima, Hiroto Ogi and Dr. Shinichi Shimada, Department of Public Health, Graduate School of Health Sciences, Kobe University.

References

1. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P (2016) 2016 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. *Rev Esp Cardiol (Engl Ed)* 69:1167.
2. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM (2006) Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med* 355 (3):251–259.
3. Tsuchihashi-Makaya M, Hamaguchi S, Kinugawa S, Yokota T, Goto D, Yokoshiki H, Kato N, Takeshita A, Tsutsui H (2009) Characteristics and outcomes of hospitalized patients with heart failure and reduced vs preserved ejection fraction. Report from the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD). *Circ J*

73:1893–1900.

4. Tsuji K, Sakata Y, Nochioka K, Miura M, Yamauchi T, Onose T, Abe R, Oikawa T, Kasahara S, Sato M, Shiroto T, Takahashi J, Miyata S, Shimokawa H (2017) Characterization of heart failure patients with mid-range left ventricular ejection fraction-a report from the CHART-2 Study. *Eur J Heart Fail* 19 (10):1258–1269.
5. Warraich HJ, Kitzman DW, Whellan DJ, Duncan PW, Mentz RJ, Pastva AM, Nelson MB, Upadhy B, Reeves GR (2018) Physical function, frailty, cognition, depression, and quality of life in hospitalized adults ≥ 60 years with acute decompensated heart failure with preserved versus reduced ejection fraction. *Circ Heart Fail* 11 (11):e005254.
6. Pandey A, LaMonte M, Klein L, Ayers C, Psaty BM, Eaton CB, Allen NB, de Lemos JA, Carnethon M, Greenland P, Berry JD (2017) Relationship between physical activity, body mass index, and risk of heart failure. *J Am Coll Cardiol* 69 (9):1129–1142.
7. Gu J, Yin ZF, Zhang HL, Fan YQ, Zhang JF, Wang CQ (2020) Characteristics and outcomes of transitions among heart failure categories: a prospective observational cohort study. *ESC Heart Fail* 7 (2):616–625.
8. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM,

- Ruschitzka F, Rutten FH, van der Meer P (2016) 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 37 (27):2129–2200.
9. Tsutsui H, Isobe M, Ito H, Ito H, Okumura K, Ono M, Kitakaze M, Kinugawa K, Kihara Y, Goto Y, Komuro I, Saiki Y, Saito Y, Sakata Y, Sato N, Sawa Y, Shiose A, Shimizu W, Shimokawa H, Seino Y, Node K, Higo T, Hirayama A, Makaya M, Masuyama T, Murohara T, Momomura SI, Yano M, Yamazaki K, Yamamoto K, Yoshikawa T, Yoshimura M, Akiyama M, Anzai T, Ishihara S, Inomata T, Imamura T, Iwasaki YK, Ohtani T, Onishi K, Kasai T, Kato M, Kawai M, Kinugasa Y, Kinugawa S, Kuratani T, Kobayashi S, Sakata Y, Tanaka A, Toda K, Noda T, Nochioka K, Hatano M, Hidaka T, Fujino T, Makita S, Yamaguchi O, Ikeda U, Kimura T, Kohsaka S, Kosuge M, Yamagishi M, Yamashina A (2019) JCS 2017/JHFS 2017 Guideline on Diagnosis and Treatment of Acute and Chronic Heart Failure - Digest Version. *Circ J* 83 (10):2084–2184.
 10. Dunlay SM, Manemann SM, Chamberlain AM, Cheville AL, Jiang R, Weston SA, Roger VL (2015) Activities of daily living and outcomes in heart failure. *Circ Heart Fail* 8 (2):261–267.
 11. Asiri FY, Marchetti GF, Ellis JL, Otis L, Sparto PJ, Watzlaf V, Whitney SL (2017)

- Effect of home-based rehabilitation on activities of daily living and gait in older adults with heart failure at risk for falling: a retrospective cohort study. *Physiother. Theory Pract* 33 (12):943–953.
12. Kitamura M, Izawa KP, Taniue H, Mimura Y, Imamura K, Nagashima H, Brubaker PH (2017) Relationship between activities of daily living and readmission within 90 days in hospitalized elderly patients with heart failure. *Biomed Res Int* 2017;7420738.
 13. Takabayashi K, Kitaguchi S, Iwatsu K, Morikami Y, Ichinohe T, Yamamoto T, Takenaka K, Takenaka H, Muranaka H, Fujita R, Nakajima O, Yokoyama R, Terasaki Y, Nishio H, Masai M, Koito H, Okuda M, Uwatoko H, Kawakami Y, Matsumoto S, Kitamura T, Nohara R (2019) A decline in activities of daily living due to acute heart failure is an independent risk factor of hospitalization for heart failure and mortality. *J Cardiol* 73(6):522–529.
 14. Cattadori G, Segurini C, Picozzi A, Padeletti L, Anzà C (2018) Exercise and heart failure: an update. *ESC Heart Fail* 5(2):222–232.
 15. Patrick A. McKee, William P. Castelli, Patricia M. McNamara, William B. Kannel (1971) The Natural History of Congestive Heart Failure: The Framingham Study. *N Engl J Med* 23;285(26):1441-1446.
 16. Ottenbacher KJ, Hsu Y, Granger CV, Fiedler RC (1996) The reliability of the functional independence measure: a quantitative review. *Arch Phys Med Rehabil* 77(12): 1226–

1232.

17. Aziz EF, Javed F, Pratap B, Musat D, Nader A, Pulimi S, Alivar CL, Herzog E, Kukin ML (2011) Malnutrition as assessed by nutritional risk index is associated with worse outcome in patients admitted with acute decompensated heart failure: an ACAP-HF data analysis. *Heart Int* 6 (1):e2.
18. JCS Joint Working Group (2014) Guidelines for Rehabilitation in Patients with Cardiovascular Disease (JCS 2012). *Circ J* 78:2022–2093.
19. Akobeng AK (2007) Understanding diagnostic tests 3: receiver operating characteristic curves, *Acta Paediatr* 96:644–647.
20. Nagai T, Yoshikawa T, Saito Y, Takeishi Y, Yamamoto K, Ogawa H, Anzai T (2018) Clinical characteristics, management, and outcomes of Japanese patients hospitalized for heart failure with preserved ejection fraction - A report from the Japanese Heart Failure Syndrome With Preserved Ejection Fraction (JASPER) Registry. *Circ J* 82(6):1534–1545.
21. Goyal P, Almarzooq ZI, Horn EM, Karas MG, Sobol I, Swaminathan RV, Feldman DN, Minutello RM, Singh HS, Bergman GW, Wong SC, Kim LK (2016) Characteristics of hospitalizations for heart failure with preserved ejection fraction. *Am J Med* 129(6):635.e15–e26.

22. LaMonte MJ, Manson JE, Chomistek AK, Larson JC, Lewis CE, Bea JW, Johnson KC, Li W, Klein L, LaCroix AZ, Stefanick ML, Wactawski-Wende J, Eaton CB (2018) Physical activity and incidence of heart failure in postmenopausal women. *JACC Heart Fail* 6(12):983–995.
23. Snipelisky D, Kelly J, Levine JA, Koepp GA, Anstrom KJ, McNulty SE, Zakeri R, Felker GM, Hernandez AF, Braunwald E, Redfield MM (2017) Accelerometer-measured daily activity in heart failure with preserved ejection fraction: Clinical correlates and association with standard heart failure severity indices. *Circ. Heart Fail* 10(6):e003878.
24. Tromp J, Shen L, Jhund PS, Anand IS, Carson PE, Desai AS, Granger CB, Komajda M, McKelvie RS, Pfeffer MA, Solomon SD, Køber L, Swedberg K, Zile MR, Pitt B, Lam CSP, McMurray JJV (2019) Age-related characteristics and outcomes of patients with heart failure with preserved ejection fraction. *J Am Coll Cardiol* 74(5):601–612.
25. Kinugasa Y, Kato M, Sugihara S, Hirai M, Yamada K, Yanagihara K, Yamamoto K (2013) Geriatric nutritional risk index predicts functional dependency and mortality in patients with heart failure with preserved ejection fraction. *Circ J* 77(3):705–711.
26. Chivite D, Formiga F, Corbella X, Conde-Martel A, Aramburu Ó, Carrera M, Dávila MF, Pérez-Silvestre J, Manzano L, Montero-Pérez-Barquero M (2018) Basal functional

- status predicts one-year mortality after a heart failure hospitalization in elderly patients
– The RICA prospective study. *Int J Cardiol* 254:182–188.
27. Conde-Martel A, Formiga F, Pérez-Bocanegra C, Armengou-Arxé A, Muela-Molinero A, Sánchez-Sánchez C, Diez-Manglano J, Montero-Pérez-Barquero M (2013) Clinical characteristics and one-year survival in heart failure patients more than 85 years of age compared with younger. *Eur J Intern Med* 24(4):339–345.
 28. Ozawa T, Saitoh M, Hori K, Sakamoto J, Akiho M, Nakazawa M, Hara M, Okamura, D (2015) Initiation of early mobilization to maintain walking ability at discharge in heart failure patients with clinical scenarios 1 and 2. *Journal of the Japanese Physical Therapy Association* 42:26–34. (In Japanese).
 29. Kitamura M, Saitoh K, Mizutani M, Yokoi T, Yekura M, Mimura Y, Nagashima H (2016) Recovery process of mobility and prognosis of walking independence in elderly patients with heart failure. *Journal of the Japanese Physical Therapy Association* 43:47–55. (In Japanese).
 30. Yamashita M, Kamiya K, Hamazaki N, Matsuzawa R, Nozaki K, Ichikawa T, Nakamura T, Maekawa E, Yamaoka-Tojo M, Matsunaga A, Ako J (2020). Prognostic value of instrumental activity of daily living in initial heart failure hospitalization patients aged 65 years or older. *Heart Vessels* 35(3):360–366.

31. Kitamura M, Mimura Y, Taniue H, Yoshitake K, Nagashima H, Izawa KP (2016)
Predictors of independent walking at hospital discharge in elderly heart failure patients.
Int J Cardiol 203:609–611.
32. Greysen SR, Stijacic Cenzer I, Auerbach AD, Covinsky KE (2015) Functional
impairment and hospital readmission in Medicare seniors. JAMA Intern Med
175(4):559–565.
33. Takahashi K, Saito M, Inaba S, Morofuji T, Aisu H, Sumimoto T, Ogimoto A, Ikeda S,
Higaki J (2016) Contribution of the long-term care insurance certificate for predicting
1-year all-cause readmission compared with validated risk scores in elderly patients
with heart failure. Open Heart 3(2):e000501.
34. Llano-Diez M, Renaud G, Andersson M, Marrero HG, Cacciani N, Engquist H,
Corpeño R, Artemenko K, Bergquist J, Larsson L (2012) Mechanisms underlying ICU
muscle wasting and effects of passive mechanical loading. Crit Care 16(5):R209.
35. Kono Y, Izawa H, Aoyagi Y, Ishikawa A, Sugiura T, Mori E, Yanohara R, Ishiguro T,
Yamada R, Okumura S, Fujiwara W, Hayashi M, Saitoh E (2020). Predictive impact of
early mobilization on rehospitalization for elderly Japanese heart failure patients. Heart
Vessels 35(4):531–536.

36. Ishihara K, Izawa KP, Kitamura M, Shimogai T, Kanejima Y, Morisawa T, Shimizu I (2019) Influence of mild cognitive impairment on activities of daily living in patients with cardiovascular disease. *Heart Vessels* 34(12):1944–1951.
37. Ohta Y, Nomura E, Hatanaka N, Osakada Y, Matsumoto N, Sasaki R, Tsunoda K, Takemoto M, Tadokoro K, Hishikawa N, Wakutani Y, Yamashita T, Sato K, Omote Y, Abe K (2019) Female dominant association of sarcopenia and physical frailty in mild cognitive impairment and Alzheimer's disease. *J Clin Neurosci* 70:96–101.
38. Ng YS, Jung H, Tay SS, Bok CW, Chiong Y, Lim PA (2007) Results from a prospective acute inpatient rehabilitation database: clinical characteristics and functional outcomes using the Functional Independence Measure. *Ann Acad Med Singapore* 36(1):3–10.
39. Sansone GR, Alba A, Frengley JD (2002) Analysis of FIM instrument scores for patients admitted to an inpatient cardiac rehabilitation program. *Arch Phys Med Rehabil* 83(4):506–512.
40. Farragher J, Einbinder Y, Oliver MJ, Nachman J, Chow E, Jassal SV (2020) Importance of early inpatient geriatric rehabilitation on outcomes in individuals on dialysis. *Arch Phys Med Rehabil* 101(2):227–233.
41. Goda A, Ohsugi H, Sasaki Y, Ohgi S (2017) The relationship between cognitive function at admission and FIM effectiveness in orthopedic inpatients. *The Journal of Japan Society for Early Stage of Dementia* 10:43–51. (In Japanese).

42. Galloway RV, Karmarkar AM, Graham JE, Tan A, Raji M, Granger CV, Ottenbacher KJ (2016) Hospital readmission following discharge from inpatient rehabilitation for older adults with debility. *Phys Ther* 96(2):241–251.
43. Hoyer EH, Needham DM, Miller J, Deutschendorf A, Friedman M, Brotman DJ (2013) Functional status impairment is associated with unplanned readmissions. *Arch Phys Med Rehabil* 94(10):1951–1958.
44. Tsufi T, Sonoda S, Chino N (1996) The ADL structure for stroke patients at admission and discharge based on the Functional Independence Measure. *The Japanese Journal of Rehabilitation Medicine* 33(5):301–309. (In Japanese).
45. Nagai S, Okuyama Y, Sonoda S, Nitta O, Nobotachi N, Sakamoto R, Teranishi T, Kaneda Y (2010). Time course analysis of FIM motor items by severity on admission of post-stroke hemiplegia patients. *Rigakuryoho Kagaku* 25(1):1–6. (In Japanese).

Credit author statement:

Masahiro Kitamura conceptualized and designed the study, collected data, conducted initial analyses, and drafted the initial manuscript; Kazuhiro P. Izawa, Kodai Ishihara, Masakazu Yaekura, Hitomi Nagashima, Takashi Yoshizawa and Nobuhiro Okamoto reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of this work.

Table 1 Characteristics of the patients with HFpEF

	All HFpEF patients n=154
Age, years	83.4±5.9
Sex, male, %	40.2
BMI, kg/m ²	22.2±4.4
LTCI level, none/support1,2/care1,2,3; %	42/20/24/11/3/0
Clinical parameters	
NYHA class I/II/III/IV, %	1/14/49/36
EF, %	61.5±7.6
BNP, pg/mL	642.3±463.7
Creatinine level, mg/dL	1.6±1.4
Hemoglobin level, g/dL	10.7±2.5
eGFR, mL/min/1.73 m ²	42.4±22.2
Albumin level at discharge, g/dL	3.6±0.4
GNRI	95.6±11.4
Comorbidity, %	
Hypertension	88.2
Diabetes	33.7
Ischemic heart disease	45.3
Atrial fibrillation	47.9
Orthopedic disease	38.4
Neurological disease	25.4
Respiratory disease	20.8
Medications, %	
Catecholamine	10.4
Diuretic	92.8
ACEI/ARB	42.2
β-blockers	47.8

Rehabilitation progress

Sitting exercise start, day	2.6±4.4
Standing exercise start, day	3.8±3.9
Walking exercise start, day	5.9±5.1
Length of hospital stay, days	18.2±9.2
Motor-FIM score at admission, points	34.9±14.6
Motor-FIM score at discharge, points	69.9±10.0
Cognitive-FIM score at admission, points	26.8±7.0
Cognitive-FIM score at discharge, points	30.2±4.8

Values are presented as mean ± standard deviation or %.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; BNP, brain natriuretic peptide; EF, ejection fraction, eGFR, estimated glomerular filtration rate; FIM, Functional Independence Measure; GNRI, Geriatric Nutritional Risk Index; HFpEF, heart failure with preserved ejection fraction; LTCI, long-term care insurance; NYHA, New York Heart Association.

Table 2 Characteristics of patients with HFpEF and low vs. high ADL

	Low ADL n=75	High ADL n=79	<i>t</i> , χ^2 , or <i>Z</i> value	<i>p</i> value
Age, years	85.9±5.4	80.8±6.3	5.4*	<0.001
Sex, male, %	38.7	41.8	0.15	0.69
BMI, kg/m ²	21.7±5.2	22.6±3.7	12.2*	0.22
LTCI level, none/support1,2/care1,2,3; %	42/20/24/11/3/0	72/18/8/1/0/1	21.4	<0.001
Clinical parameters at admission				
NYHA class I/II/III/IV, %	1/5/48/45	1/11/51/38	11.2	0.01
EF, %	49.1±14.0	46.1±16.3	0.8 [†]	0.41
BNP, pg/mL	619.6±494.8	665.0±432.6	0.4 [†]	0.23
Creatinine level, mg/dL	1.7±1.5	1.5±1.3	2.1 [†]	0.04
Hemoglobin level, g/dL	10.4±2.4	11.0±2.5	1.6*	0.11
eGFR, mL/min/1.73 m ²	39.0±21.5	45.9±23.0	1.9*	0.06
Albumin level, g/dL	3.5±0.4	3.7±0.4	2.3*	0.02
GNRI	94.6±11.1	96.5±11.8	1.0*	0.30
Comorbidity, %				
Hypertension	85.3	91.1	1.26	0.26
Diabetes	32.0	35.4	0.20	0.65
Ischemic heart disease	38.7	51.9	2.7	0.10
Atrial fibrillation	44.0	51.9	1.0	0.33
Orthopedic disease	41.3	35.4	0.6	0.45
Neurological disease	26.7	24.1	0.1	0.71
Respiratory disease	20.0	21.5	0.1	0.82
Medications, %				
Catecholamine	9.3	11.4	0.1	0.68
Diuretic	90.7	94.9	0.3	0.30
ACEI/ARB	42.7	41.8	0.1	0.91
β-blockers	38.7	57.0	0.1	0.02

Rehabilitation progress				
Sitting exercise start, day	3.1±3.3	2.1±2.8	2.9 [†]	0.004
Standing exercise start, day	4.6±4.7	3.0±3.1	2.7 [†]	0.008
Walking exercise start, day	7.6±6.2	4.2±4.0	4.1 [†]	<0.001
Length of hospital stay, days	20.1±11.8	17.9±9.0	2.4 [†]	0.013
Motor FIM score at admission, points	28.8±12.0	40.9±17.3	4.5 [†]	<0.001
Motor FIM score at discharge, points	57.0±16.1	82.8±3.9	10.7 [†]	<0.001
Cognitive FIM score at admission,	23.4±6.9	30.3±7.0	7.5 [†]	<0.001
Cognitive FIM score at discharge, points	26.7±6.7	33.6±2.8	7.5 [†]	<0.001

Values are presented as mean ± standard deviation or %.

ACEI, angiotensin-converting enzyme inhibitor; ADL, activities of daily living; ARB, angiotensin receptor blocker; BMI, body mass index; BNP, brain natriuretic peptide; EF, ejection fraction, eGFR, estimated glomerular filtration rate; FIM, Functional Independence Measure; GNRI, Geriatric Nutritional Risk Index; HFpEF, heart failure with preserved ejection fraction; LTCI, long-term care insurance; NYHA, New York Heart Association.

Table 3 Univariate and multivariate analysis for ADL at discharge

	Univariate analysis			Multivariate analysis		
	OR	95% CI	<i>p</i> Value	OR	95% CI	<i>p</i> Value
Age	0.86	0.80-0.92	<0.001	0.83	0.75-0.92	<0.001
LTCI level	0.49	0.34-0.70	<0.001	0.63	0.40-0.98	0.044
NYHA	0.48	0.30-0.78	0.003	1.00	0.45-2.23	0.993
Creatinine level	0.87	0.69-1.10	0.241			
Albumin level	2.56	1.12-5.85	0.026	2.14	0.70-6.60	0.184
β-blocker	2.10	1.10-4.00	0.024	1.29	0.51-3.29	0.588
Sitting exercise start	0.89	0.79-1.01	0.067			
Standing exercise start	0.89	0.81-0.98	0.020	1.13	0.94-1.37	0.190
Walking exercise start	0.87	0.80-0.94	0.001	0.83	0.70-0.99	0.045
Motor-FIM score at admission	1.06	1.03-1.08	<0.001	1.04	1.00-1.08	0.045
Cognitive-FIM score at admission	1.16	1.10-1.23	<0.001	1.10	1.03-1.19	0.008

CI, confidence interval; FIM, Functional Independence Measure; LTCI, long-term care insurance; NYHA, New York Heart Association; OR, odds ratio.

Figure Legends

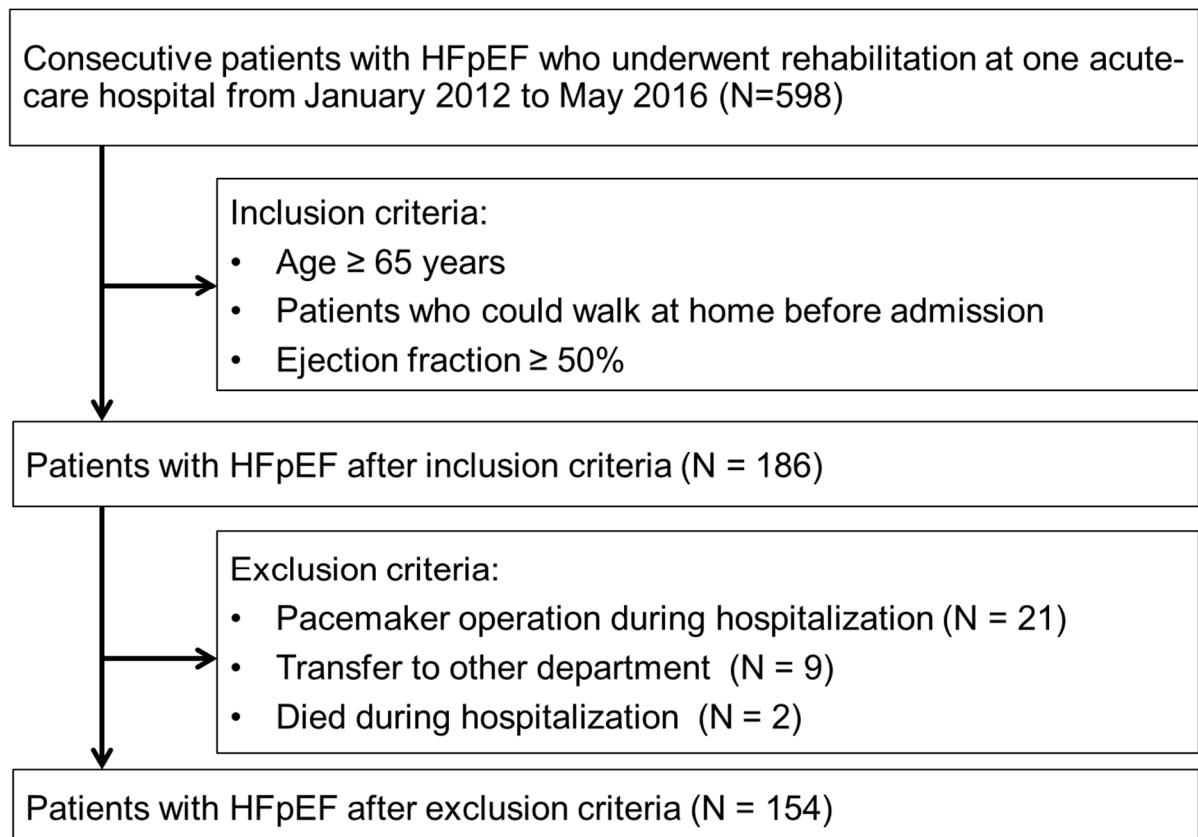


Fig. 1. Patient flow. HFpEF, heart failure with preserved ejection fraction.

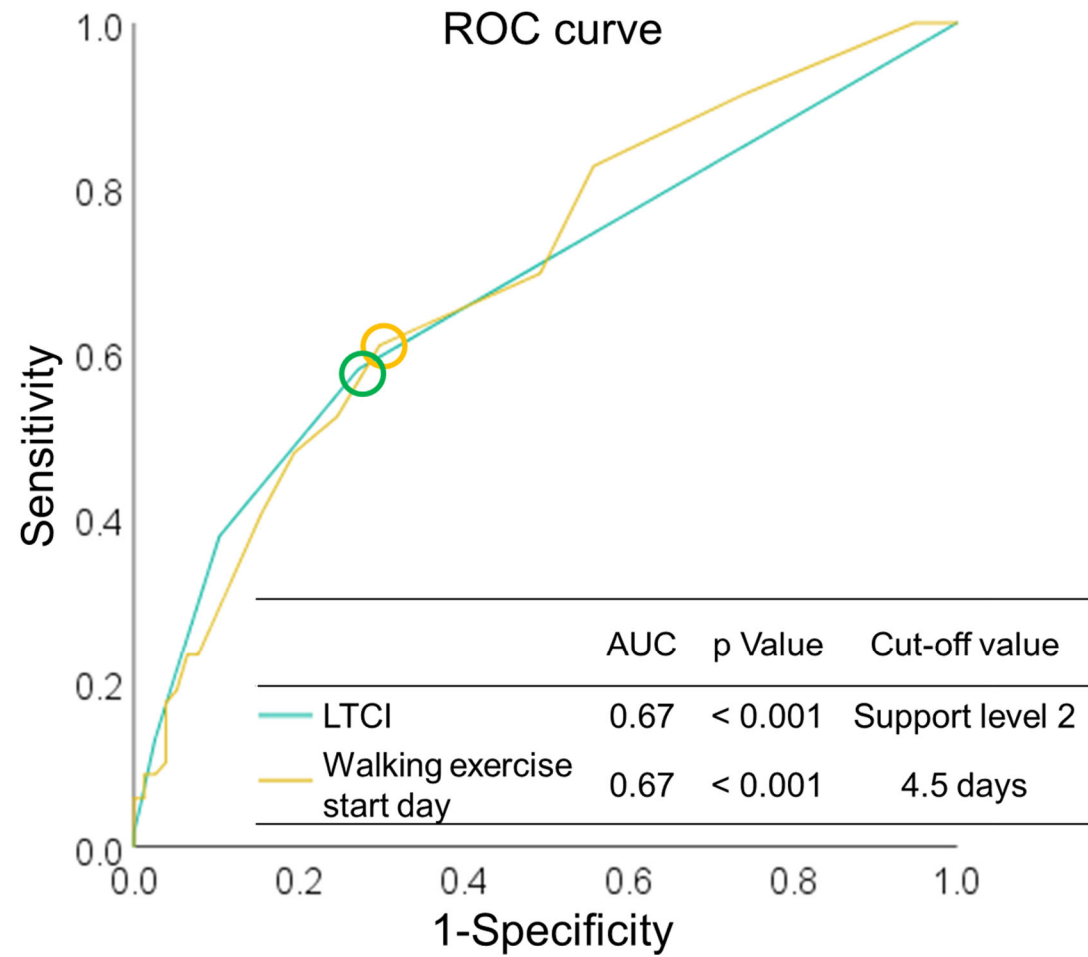


Fig. 2. Cut-off value of LTCL levels and walking exercise start day.

AUC, area under the curve; LTCI, long-term care insurance; ROC, receiver operating characteristic.

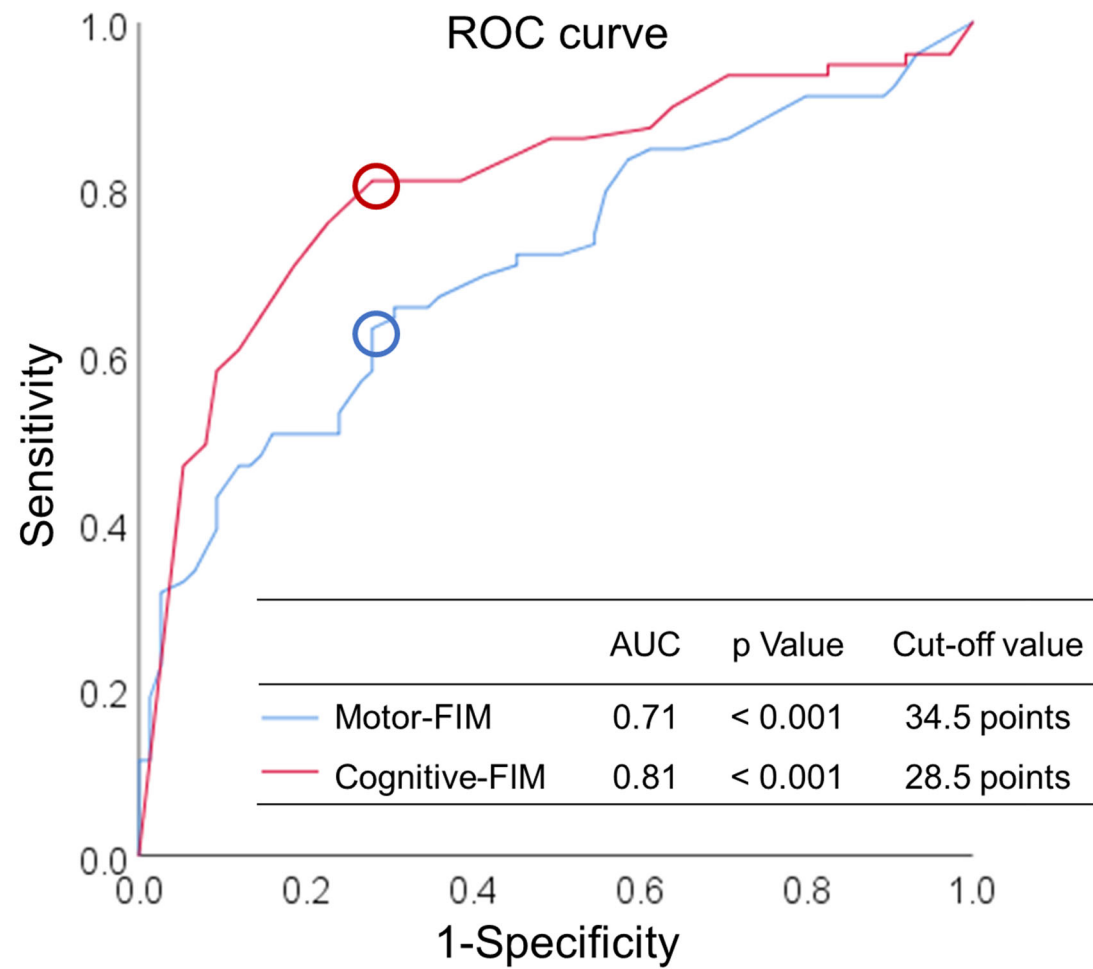


Fig. 3. Cut-off value of motor- and cognitive-FIM points.

AUC, area under the curve; FIM, Functional Independence Measure; ROC, receiver operating characteristic.