Pinch strength is associated with the prevalence of mild cognitive impairment in patients with cardiovascular disease

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(Degree)
博士（保健学）
(Date of Degree)
2021-03-25
(Date of Publication)
2022-03-01
(Resource Type)
doctoral thesis
(Report Number)
甲第8061号
(URL)
https://hdl.handle.net/20.500.14094/D1008061

博　士　論　文

Pinch strength is associated with the prevalence of mild cognitive impairment in patients with cardiovascular disease

（ピンチ力は、心血管疾患患者で軽度認知障害の有病率と関係している）

令和 3 年　1 月　13 日

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Abstract

Background: The relationship between mild cognitive impairment (MCI) and pinch strength in patients with cardiovascular disease is unclear. The purpose of the present study was to examine the associations among MCI and pinch strength and to determine a pinch strength cut-off value for use in the assessment of MCI.

Methods: We conducted a cross-sectional study of 135 patients with cardiovascular disease but without probable dementia. MCI was estimated with the Japanese version of the Montreal Cognitive Assessment. We classified patients into the normal cognitive group and MCI group and compared their clinical characteristics, handgrip strength, and pinch strength. The relation between MCI and pinch strength was clarified with logistic regression analysis, and the cut-off value for three-fingered pinch strength was determined by receiver operating characteristic curve analysis.

Results: The incidence of MCI was 37.0%. Significant differences between the two groups were identified for age, body mass index, hemoglobin, estimated glomerular filtration rate, albumin, dyslipidemia, use of nitrates, educational background, handgrip strength, and pinch strength. After multivariate analysis, three-fingered pinch strength was significantly associated with MCI (odds ratio 0.77, $p = 0.02$). The cut-off value of three-fingered pinch strength for predicting MCI was 6.75 kgf (area under the curve = 0.71; $p < 0.001$).

Conclusions: Pinch strength was one independent factor significantly associated with MCI in patients with cardiovascular disease. The determination of a cut-off value for three-fingered pinch strength that can predict MCI may be one important factor in the early screening for MCI in the daily clinical setting.

Introduction

The numbers of elderly patients with heart disease and with dementia in Japan are increasing and are becoming public health problems [1–3]. Moreover, cardiovascular disease (CVD) is strongly associated with cognitive dysfunction [4], and cognitive dysfunction in patients with heart disease is associated with increased short- and mid-term progression to death and hospital readmission [5,6] and with functional disability [7].

Mild cognitive impairment (MCI) is thought to be a transitional state between the normal decline in cognitive function that occurs with aging and dementia [8], and early intervention is necessary to prevent dementia from the time of MCI onset or before because 5-10% of healthy elderly people with MCI will develop dementia [9].

In the daily clinical setting, we have observed that in Japanese heart disease patients with cognitive dysfunction, brush pressure is low when writing Japanese calligraphy with a brush on a piece of paper. Previous studies reported that finger dexterity can reflect a decline in cognitive function [10], and finger-tapping frequency of MCI patients is significantly lower than that in patients with normal cognitive function [11]. Furthermore, the decline in handgrip strength from midlife to late life is associated with dementia in Japanese people [12]. From these findings, we hypothesized that pinch strength might reflect a decline in cognitive function and that identification of a relationship between MCI and pinch strength could be one important issue in the early screening of MCI in the daily clinical setting.

To our knowledge, however, the relationship between MCI and pinch strength in patients with CVD is unclear. Thus, the purpose of the present study was to examine the associations between MCI and pinch strength and to determine a pinch strength cut-off value for use in the assessment of MCI.

Methods

Study population

This cross-sectional study comprised 1134 consecutive patients with coronary artery disease (CAD), including acute myocardial infarction, acute coronary syndrome, and stable and unstable angina, who were admitted to the Sakakibara Heart Institute of Okayama from May 2018 to February 2019.

Inclusion criteria included patients who underwent rehabilitation and were admitted for more than 2 days, except those admitted for only one night and two days, for percutaneous coronary intervention. Exclusion criteria included patients who did not give informed consent, underwent coronary artery bypass surgery, had mental disease, experienced a cerebral vascular accident, could not walk without total assistance, had probable dementia as indicated by a Mini-Mental State Examination (MMSE) score below 24 [13,14], and died in hospital.

This study was approved by the Sakakibara Heart Institute of Okayama Ethics Committee (approval no. A2018-0401), and informed consent was obtained from each patient. The present study complied with the principles of the Declaration of Helsinki regarding investigations in human subjects.

Clinical characteristics of the patients

Clinical characteristics of the patients were retrospectively evaluated from the medical records. Baseline characteristics assessed included age, sex, body mass index (BMI), educational background (categorized as >13 years of schooling), diagnosis, number of significant coronary artery stenoses (≥75%; especially left main trunk, ≥50%), treatments, New York Heart Association functional class, left ventricular ejection fraction (LVEF) as calculated with the Simpson method for cardiac echocardiography, maximum creatine kinase-myocardial band (CK-MB), serum hemoglobin levels, estimated glomerular filtration rate (eGFR), serum albumin levels, comorbidities, and medications. Laboratory and cardiac echocardiography data were evaluated just prior to patient discharge.

Measurement of cognitive function

The Japanese version of the Montreal Cognitive Assessment (MoCA-J) [15] and the MMSE were used to measure cognitive function in the patients [13,14]. The MoCA-J is used to screen persons with MCI and was reported to have a sensitivity of 93% and specificity of 87% in identifying MCI [15]. The multiple cognitive domains measured by the MoCA-J are visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation. A MoCA-J cutoff point value of 26 was previously used to define MCI [15], and thus we defined patients with MCI as having a MoCA-J score <26 and those with normal cognitive function as having a MoCA-J score ≥26.

Although the MMSE is used globally as a screening tool for dementia [14], it is not sensitive enough to discover early cognitive decline associated with MCI [16]. Thus, we used the MMSE as a means to select the patients with probable dementia for exclusion. A MMSE cutoff score of <24 was used to define probable dementia [14]. Cognitive function assessments were measured by a physical therapist at the time of discharge.

Measurement of handgrip strength and pinch strength

We measured handgrip strength using a grip strength dynamometer (T.K.K.5401; Takei Scientific Instruments Co., Ltd., Niigata, Japan) and pinch strength using a pinch strength dynamometer (Baseline® Hydraulic Pinch Gauge; Fabrication Enterprises Co., Ltd., White Plains, NY, USA) at the time of discharge. Patients were evaluated in the standardized testing position recommended by the American Society of Hand Therapists [17] and the study by Mathiowetz et al. [18] to avoid the Valsalva effect. Patients were seated in a chair with their shoulders neutral and elbows at 90° flexion, forearms neutral in supination/pronation, and the wrist between 0° and 15° ulnar deviation. We measured pinch strength by assessing lateral pinch strength and three-fingered pinch strength. For lateral pinch strength, the pinch strength dynamometer was positioned between the pad of the thumb and the radial side of the middle phalanx of the index finger. For three-fingered pinch strength, the dynamometer was positioned between the pads of the thumb, index, and middle fingers. The higher of the two measured values, which were each measured twice, was recorded, and the right- and left-hand values were averaged to obtain handgrip strength (kg) and pinch strength (kgf) in this study.

Statistical analysis

Patient characteristics and measured outcomes are shown as percentages for the categorical variables and as the mean ± standard deviation for the continuous variables. The unpaired t-test, Welch test, Mann-Whitney U test, and χ^2 test were used as appropriate to evaluate differences in patients' characteristics and in measured outcomes between the MCI and normal cognitive function groups. The relation between MCI and pinch strength was clarified with logistic regression analysis, with the dependent variable being MCI and the independent variables being patient characteristics, handgrip strength, and pinch strength. The covariates entered were those factors that were characteristic of the patients, as guided by significant findings on univariate analyses. Receiver operating characteristic (ROC) curves were constructed by plotting the true-positive rate (sensitivity) against the false-positive rate (1-specificity) to determine the best cut-off value for each value. The area under the curve (AUC) was calculated from the ROC curve for each variable, and the cut-off value was calculated based on the Youden index [19]. AUC values of >0.9 indicate high accuracy, 0.7-0.9 indicate moderate accuracy, and <0.7 indicate low accuracy [20]. The overall level of statistical significance was set at 0.05. Statistical analyses were performed with R ver. 2.8.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Clinical characteristics

A flowchart of patients included in this study is shown in Figure 1. Of the 1134 consecutive patients with CAD, 394 met the inclusion criteria, but 259 patients were subsequently excluded due to the reasons shown in Figure 1. Therefore, 135 patients were ultimately included in our final analysis and were divided into the normal cognitive function group (n = 85, 63.0%) and MCI group (n = 50, 37.0%).

The patients' clinical characteristics can be compared between the two groups in Table 1. Compared with the patients in the normal cognitive function group, those in the MCI group were significantly older and had a lower BMI, lower serum levels of hemoglobin and albumin, lower eGFR, lower levels of dyslipidemia and nitrates use, lower educational background, lower MoCA-J score, lower handgrip strength, and lower lateral and three-fingered pinch strengths ($p < 0.05$).

Table 1

Characteristics of patients in the normal cognitive function group and MCI group.

	Normal cognitive function group (n=85)	MCI group (n=50)	t, χ^2, Z value	p value
Age (years)	65.0 ± 11.7	75.6 ± 10.0	0.45	<0.001
Male, n (%)	73 (86)	38 (76)	2.10†	0.15
BMI (kg/m^2)	24.7 ± 3.9	23.0 ± 3.8	0.20	0.02
Diagnosis, n (%)			0.56†	0.76
Acute myocardial infarction	49 (58)	29 (58)		
Acute coronary syndrome	6 (7)	2 (4)		
Angina	30 (35)	19 (38)		
Significant stenosis of the coronary arteries, n (%)			0.16†	0.93
1-vessel disease	42 (49)	23 (46)		
2-vessel disease	26 (31)	16 (32)		
3-vessel disease	17 (20)	11 (22)		
Treatment, n (%)			0.03†	0.87
Percutaneous coronary intervention	74 (87)	44 (88)		
Medication	11 (13)	6 (12)		
NYHA functional class, n (%)			5.45†	0.07
I	77 (91)	38 (76)		
II	4 (5)	7 (14)		
III	4 (5)	5 (10)		
LVEF (%)	52.9 ± 9.9	53.2 ± 13.2	0.06	0.48
Laboratory data				
Maximum CK-MB (IU/L)	150.0 ± 202.8	123.1 ± 158.1	0.01	0.88
Hemoglobin (g/dL)	13.0 ± 1.6	12.1 ± 2.0	2.77*	0.006
eGFR (mL/min/1.73 m^2)	54.1 ± 21.4	43.2 ± 19.9	0.27	0.002
Albumin (g/dL)	3.6 ± 0.5	3.4 ± 0.4	2.14*	0.03
Comorbidities, n (%)				
Hypertension	45 (53)	30 (60)	0.64†	0.43
Dyslipidemia	48 (57)	19 (38)	4.30†	0.04
Diabetes	35 (41)	24 (48)	0.60†	0.44
Atrial fibrillation	6 (7)	5 (10)	0.36†	0.55
Medication, n (%)				
ACE inhibitor	43 (51)	25 (50)	0.004†	0.95

ARB	26 (31)	14 (28)	0.10†	0.75
β-blocker	71 (84)	39 (78)	0.64†	0.43
Nitrates	15 (18)	2 (4)	5.33†	0.02
Diuretics	21 (25)	18 (36)	1.96†	0.16
Calcium antagonist	22 (26)	14 (28)	0.07†	0.79
Anticholinergics	0 (0)	0 (0)		
Benzodiazepines	6 (7)	7 (14)	1.74†	0.19
Analgesics	5 (6)	3 (6)	<0.001†	0.98
Education background				
>13 years (%)	33 (39)	6 (12)	11.03†	<0.001
MoCA-J (points)	27.8 ± 1.4	21.6 ± 3.0	0.84	<0.001
Handgrip strength (kg)	31.0 ± 8.7	24.0 ± 8.0	4.64*	<0.001
Pinch strength				
Lateral pinch strength (kgf)	8.5 ± 2.0	7.2 ± 2.1	3.60*	<0.001
Three-fingered pinch strength (kgf)	7.8 ± 2.0	6.5 ± 1.7	4.11*	<0.001

Date are presented as mean ± standard deviation or number (%).

Abbreviations: ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; BMI, body mass index; CK-MB, creatine kinase-myocardial band; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; MCI, mild cognitive impairment; MoCA-J, Japanese version of the Montreal Cognitive Assessment; NYHA, New York Heart Association.

* *t* value, † χ^2 value.

Relationship between MCI and pinch strength

The results of the logistic regression analysis are shown in Table 2. After the significant independent variables and covariates were identified in the univariate analysis, the multivariate analysis showed three-fingered pinch strength (odds ratio 0.77, 95% confidence interval 0.61–0.96, p = 0.02) to be associated with MCI after adjustment for covariates. The cut-off value for three-fingered pinch strength determined by the ROC curve analysis was 6.75 kgf (sensitivity, 0.73; specificity, 0.64; AUC = 0.71; 95% confidence interval 0.62–0.80; p < 0.001) (Fig. 2).

Table 2

Univariate and multivariate analysis for the association between MCI and pinch strength in patients with cardiovascular disease.

Variable	Univariate model		Multivariate model	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	1.10 (1.06-1.15)	<0.001	1.09 (1.04-1.14)	<0.001
BMI	0.88 (0.80-0.98)	0.02		
Hemoglobin	0.75 (0.61-0.93)	0.008		
eGFR	0.98 (0.96-0.99)	0.006		
Albumin	0.41 (0.18-0.95)	0.04		
Dyslipidemia	0.47 (0.23-0.97)	0.04		
Nitrates	0.19 (0.04-0.89)	0.04	0.17 (0.04-0.86)	0.03
Handgrip strength	0.91 (0.87-0.95)	<0.001		
Lateral pinch strength	0.73 (0.61-0.88)	<0.001		
Three-fingered pinch strength	0.68 (0.55-0.83)	<0.001	0.77 (0.61-0.96)	0.02

Abbreviations: BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; MCI, mild cognitive impairment; OR, odds ratio.

Logistic regression analyses were conducted with MCI present/MCI absent as the dependent variable. Clinical characteristics, handgrip strength, and pinch strength were included as independent variables. The multivariate model was developed by forward stepwise variable selection.

Discussion

To our knowledge, this is the first study to show an association between MCI and pinch strength in patients with CVD. Three-fingered pinch strength was found to be significantly associated with MCI in patients with CVD after adjustment for covariates.

The prevalence of possible MCI in the present study was 37.0%, which is relatively higher than that of another study that reported the incidence of MCI in Japanese community-dwelling older adults [21]. In this regard, it was reported that the prevalence of dementia was higher in CVD patients [22], and CAD may lead to dementia because it was found to be associated with small vessel disease in the brain [23]. Therefore, it is conceivable that our cohort comprised patients with a relatively high risk of MCI.

We showed that the MCI patients with CVD were significantly older and had a lower BMI, lower serum levels of hemoglobin and albumin, lower eGFR, lower dyslipidemia, lower use of nitrates, lower educational background, and lower MoCA-J than those in the normal cognitive function group. These findings largely agreed with the characteristics of MCI patients reported in previous studies [24–27]. Therefore, it may be possible to partly generalize the characteristics of the MCI patients with CVD.

Three-fingered pinch strength was strongly associated with the incidence of MCI after adjustment for covariates in this study. Moreover, pinch strength would be more useful for detecting MCI than handgrip strength because handgrip strength was included in the covariates. Manual function was reported to be closely associated with cognitive function and requires many processes from perception to cognition [28]. This relationship could be explained by microvascular brain pathology that is associated with motor impairment [29]. Humans adjust finger pressure to precisely grip various visual objects, and this action involves many processes including those related to perception and cognition [28,30]. Furthermore, it was reported that manual dexterity declines in MCI patients [11] and that muscle strength is associated with the incidence of Alzheimer's disease and MCI [31]. Thus, these findings could explain why pinch strength was strongly associated with MCI in the present study, and we interpreted this to indicate that three-fingered pinch strength could be associated with the incidence of MCI in patients with CVD.

The cut-off value for three-fingered pinch strength determined by ROC curve analysis was 6.75 kgf (sensitivity, 0.73; specificity, 0.64; AUC = 0.71; 95% confidence interval 0.62–0.80; $p < 0.001$), and the AUC was 0.71, which indicates moderate accuracy. The determination of a cut-off value for the three-fingered pinch strength that can predict MCI is an important new finding because three-fingered pinch strength can be easily evaluated and associated with activities of daily living (ADL) related to manual function. Three-fingered pinch strength is required in ADL such as grasping a pen and writing, using chopsticks, fastening a button, and tying a string. Another study reported that motor and sensory functions affecting ADL related to manual function are significantly decreased in the elderly [32]. The cut-off value for three-fingered pinch strength in the present study was lower than that of healthy adults of the same age [33]. Thus, as characteristics of MCI patients with CVD, their three-fingered pinch strength is lower and they may have disability of ADL related to manual function as compared to MCI patients without CVD.

In multivariate analysis, age and use of nitrates were also identified as independent predictors of the incidence of MCI. In past studies, it was reported that aging was associated with MCI [24]. Regarding the use of nitrates, no report, to our knowledge, has indicated a relationship between nitrates and MCI. However, it has been shown that nitric oxide is involved in learning and memory processes [34], and the nitric oxide pathway has been implicated in the pathophysiology of cognitive impairment and dementia [35]. Thus, our results may be associated with these findings.

The present study has several clinical implications. Early diagnosis of MCI in the daily clinical setting is difficult. Thus, we should consider the presence of MCI in patients with CVD who have a three-fingered pinch strength of less than 6.75 kgf. Moreover, ADL requiring pinching ability may be impaired in these patients. Therefore, pinch strength may reflect a decline in cognitive function, and the identification of a cut-off value for three-fingered pinch strength could potentially be one important factor in the early screening of MCI in the daily clinical setting.

There are several limitations in this study. This is a single-center, cross-sectional study with small sample size. Because of the strict inclusion and exclusion criteria, only 12% (135/1134) of the hospitalized patients with CVD could be enrolled as study subjects. Thus, generalizability of the results may be limited. Assessment of cognitive functions was limited to a single screening tool, and imaging data were not analyzed. Assessment only of heart failure and comorbidities was not enough; pinch strength may be influenced not only by MCI but also by sarcopenia, systemic skeletal muscle weakness associated with heart failure, cervical spondylosis, peripheral nerve disease, and patient age and sex. Moreover, the influence of changes in factors such as cognitive function and pinch strength over time is unknown. These issues remain to be resolved in future longitudinal studies.

Conclusions

Pinch strength was one independent factor significantly associated with MCI in patients with CVD. The determination of a cut-off value for three-fingered pinch strength that can predict MCI may potentially be one important factor in the early screening of MCI in the daily clinical setting.

Funding

This work was supported by a JSPS KAKENHI grant (no. JP17K01500).

Conflicts of interest

The authors declare that they have no conflict of interest.

Acknowledgments

We thank the staff members of the Sakakibara Heart Institute of Okayama and Kobe University who collaborated in this study.

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Figure legend

Figure 1 Flow chart of patient selection.
CAD, coronary artery disease; PCI, percutaneous coronary intervention.

Figure 2 Receiver operating characteristic curve for three-fingered pinch strength to predict the incidence of mild cognitive impairment (MCI) in 135 patients with cardiovascular disease. The area under the curve for three-fingered pinch strength is 0.71 with the cut-off value set at 6.75 kgf for prediction of the incidence of MCI (sensitivity, 0.73; specificity, 0.64).

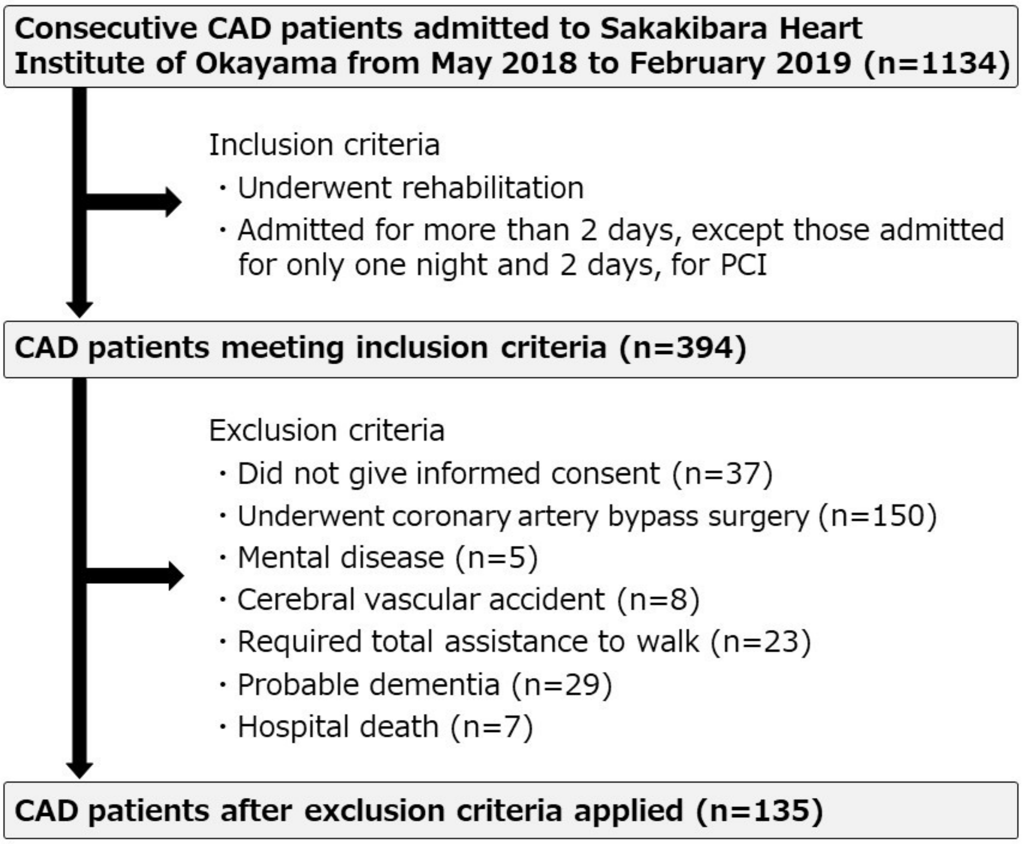
Consecutive CAD patients admitted to Sakakibara Heart Institute of Okayama from May 2018 to February 2019 (n=1134)
Inclusion criteria
・Underwent rehabilitation
・Admitted for more than 2 days, except those admitted for only one night and 2 days, for PCI
CAD patients meeting inclusion criteria (n=394)
Exclusion criteria
・Did not give informed consent (n=37)
・Underwent coronary artery bypass surgery (n=150)
・Mental disease (n=5)
・Cerebral vascular accident (n=8)
・Required total assistance to walk (n=23)
・Probable dementia (n=29)
・Hospital death (n=7)
CAD patients after exclusion criteria applied (n=135)

Figure 1

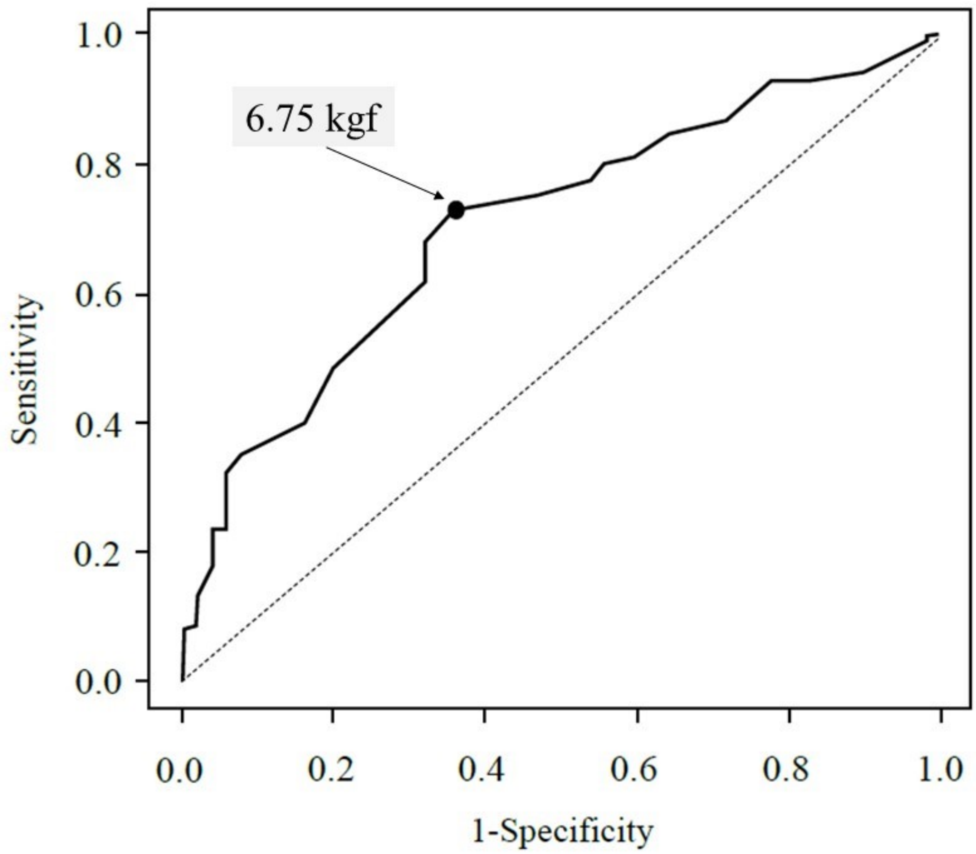
6.75 kgf
1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
0.0
0.2
0.4
0.6
0.8
1.0
1-Specificity

Figure 2