



OPEN Exploring the potential of handgrip strength as a prognostic marker in acute decompensated heart failure with reduced ejection fraction: a cross-sectional study

Erfan Kohansal^{1,5}, Sara Adimi^{1,5}, Mohammad-saleh Baghi¹, Amirali Soheili¹, Faraz Changizi², Sepehr Jamalkhani¹, Elnaz Hekmat³, Razieh Omidvar¹, Sepideh Taghavi¹, Marzieh Mirtajaddini¹, Zeinab Sadat Fattah Jahromi¹, Mahsa Behnemoon⁴, Majid Maleki¹, Saeideh Mazloomzadeh¹ & Nasim Naderi¹✉

Frailty is associated with poor outcomes in heart failure (HF). Handgrip strength (HGS) is a simple indicator of Physical frailty. We aimed to assess the prognostic value of HGS in patients under 60 years old with acute decompensated HF with reduced ejection fraction (HFrEF). In this cross-sectional study, we enrolled 125 patients with acute decompensated HFrEF. HGS was measured using a manual dynamometer. The primary outcome was in-hospital mortality. Univariate logistic regression analysis was performed to identify risk factors associated with in-hospital mortality. Receiver operating characteristic (ROC) curve analysis was used to assess the predictive value of HGS for in-hospital mortality. The in-hospital mortality rate was 16%. Survivors had numerically higher, though not statistically significant, median HGS compared to non-survivors (18.8 (IQR: 13.2–25.3) kg vs. 13 (IQR: 11.4–19.5) kg; $p = 0.06$). HGS showed negative correlation with length of stay ($\rho = -0.202$, $p = 0.024$) and NT-proBNP levels ($\rho = -0.256$, $p = 0.004$). The area under the ROC curve for overall HGS predicting in-hospital mortality was 0.630 ($p = 0.043$). Lower left ventricular ejection fraction and higher NT-proBNP levels were significantly associated with increased odds of in-hospital mortality in univariate analysis. Lower handgrip strength was associated with longer hospital stay and higher NT-proBNP levels, and demonstrated a modest ability to predict in-hospital mortality. However, further research is necessary to establish standardized measurement methods and optimal prognostic thresholds before handgrip strength can be widely implemented in the management of this patient population.

Keywords Handgrip strength, Acute decompensated heart failure, Heart failure with reduced ejection fraction, Frailty, Prognostic value

Abbreviations

ADHF	Acute decompensated heart failure
AUC	Area under the curve
BMI	Body mass index
BNP	B-type natriuretic peptide
BUN	Blood urea nitrogen
CI	Confidence interval
CKD	Chronic kidney disease
ED	Emergency department

¹Cardiovascular Research Center, Rajaie Cardiovascular institute, Vali-Asr Ave, Tehran 1995614331, Iran. ²School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. ³School of Medicine, Fasa University of Medical Sciences, Fasa, Iran. ⁴Department of Cardiology, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran. ⁵Erfan Kohansal and Sara Adimi contributed equally to this work and share the first authorship. ✉email: naderi.nasim@gmail.com

eGFR	Estimated glomerular filtration rate
ESC	European Society of Cardiology
HF	Heart failure
HFrEF	Heart failure with reduced ejection fraction
HGS	Handgrip strength
IQR	Interquartile range
LVEF	Left ventricular ejection fraction
NT-proBNP	N-terminal pro-B-type natriuretic peptide
OR	Odds ratio
ROC	Receiver operating characteristic

Heart failure (HF) is a significant global health issue, with an estimated 26 million people affected worldwide in 2017¹. The impact of HF extends beyond physical health, as it places a considerable psychological and economic burden on patients, their families, and healthcare systems. Therefore, there is an ongoing need to enhance risk assessment, prevention, and management strategies to reduce the morbidity, mortality, and healthcare costs associated with this condition².

Frailty, a complex and multi-dimensional syndrome characterized by decreased resistance to stressors and increased vulnerability to adverse outcomes, is strongly associated with HF. It is estimated to affect almost 50% of patients with HF, with this number rising to 77% in hospitalized patients due to HF^{3–5}. It has been widely documented that this condition correlates with poor prognosis, including increased rates of hospitalization, functional decline, and mortality^{4,6,7}. Handgrip strength (HGS) is a simple, inexpensive, and reliable measure of muscle strength that is often used as part of the physical/functional component in frailty assessments⁸. A recent meta-analysis by Wang et al. has shown that lower HGS is associated with an increased risk of mortality in patients with HF across various age groups. Importantly, they found no significant effect of age on the relationship between HGS and mortality in HF patients⁹. In HF patients, reduced HGS may reflect skeletal muscle wasting (sarcopenia) and dysfunction, which are common features of the disease and can be evident even in younger HF patients^{5,9}.

While the prevalence and prognostic impact of physical frailty in patients with acute decompensated heart failure (ADHF) has been reported^{10,11}, the specific role of HGS in patients with HFrEF hospitalized due to ADHF has been less extensively studied⁹. However, notable contributions to this field include the work of Parahiba et al.¹², who investigated HGS in ADHF patients, demonstrating its potential as both a predictor of malnutrition and a prognostic marker for short-term mortality. Despite this valuable research, there remains a need for further investigation to fully elucidate the role of HGS in risk stratification and management of patients with HFrEF hospitalized due to ADHF, particularly in diverse populations and clinical settings.

Based on current literature, we hypothesized that lower handgrip strength would correlate with poorer clinical outcomes in acute decompensated HFrEF patients under 60 years old. This study aims to explore the potential prognostic significance of HGS in patients with HFrEF admitted due to ADHF. By comprehensively assessing HGS and its association with surrogates of clinical outcomes in patients younger than 60 years with acute decompensated HFrEF, we aim to contribute to the growing body of evidence supporting the use of frailty assessment tools in HF management and guide future research and clinical practice.

Materials and methods

Design and population

This cross-sectional study was conducted between April 2023 and October 2023 at Rajaie Cardiovascular Medical and Research Institute, a tertiary care center for heart failure medicine in Tehran, Iran. The study population included adult patients (18–60 years) who were enrolled with a primary diagnosis of ADHF and a diagnosis of chronic heart failure with reduced ejection fraction (HFrEF; left ventricular ejection fraction [LVEF] $\leq 40\%$) for at least three months. The primary decision on ADHF diagnosis, confirmed by a heart failure (HF) specialist according to the 2021 European Society of Cardiology (ESC) guidelines, was made by emergency department physicians¹³. In addition, the management plan was applied and followed by HF specialists considering the ESC guidelines during hospitalization, including the adjustment of diuretics and inotropes (if needed), the initiation or adjustment of medical therapies recommended in the guidelines for HFrEF, including angiotensin receptor/neprilysin inhibitor (or angiotensin-converting enzyme inhibitor if ARNI is not tolerated or contraindicated), a beta blocker, a mineralocorticoid receptor antagonist (MRA), a SGLT2 inhibitor, and a discharge plan.

Exclusion criteria include: (1) patients with acute Denovo heart failure; (2) inability to perform the HGS test with a manual dynamometer due to physical limitations or cognitive impairment; (3) presence of acute conditions, including acute coronary syndrome, acute pulmonary emboli, prosthetic valve malfunction, or cardiogenic shock requiring immediate intervention (mechanical ventilation support, ventricular assist device support, etc.); (4) any uncontrolled chronic condition, excluding heart failure (HF), such as diabetic ketoacidosis, end-stage renal disease (ESRD) requiring hemodialysis, or primary skeletal myopathies, including but not limited to muscular dystrophies, congenital myopathies, metabolic myopathies, and inflammatory myopathies, should be present; (5) The inability to continue the guideline-recommended medical therapies for HFrEF¹⁴; and (6) severe malnutrition or cachexia¹⁵. After screening patients, study physicians enrolled them for further assessment and data collection if they met eligibility criteria.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was reviewed and approved by the Ethics Committee of Rajaie Cardiovascular Medical and Research Institute, Tehran, Iran (IR.RHC.REC.1402.034). Written informed consent was obtained from all study participants prior to their enrollment, and all participants voluntarily provided consent for their medical records to be used in this research. In total, 337 patients were screened, and 125 were identified as eligible for further evaluation.

Patient assessment and data collection

After obtaining informed consent, the patient's assessment was performed within 24 h of hospital admission. Trained physicians (M.B. and A.S.), whose competence in with the instruments was subjectively assessed as satisfactory by an experienced supervisor (S.A.) prior to data collection, performed the HGS assessments. Demographic information (age, sex, and BMI), comorbidities (hypertension, diabetes mellitus, chronic kidney disease, illicit drugs, alcohol, and smoking status), heart failure etiology (ischemic or nonischemic), and other clinical (NYHA class, in-hospital mortality, length of hospital stay) and laboratory data (including NT-Pro-BNP) were obtained from medical records and confirmed during patient assessment. All patients were visited and followed by heart failure experts during their hospital stay. Guideline-directed medical therapies (GDMT) were initiated and adjusted for all patients in the study prior to discharge. The entire study population was monitored for early readmission or all-cause mortality for one month after discharge.

Our primary endpoint was in-hospital mortality, defined as death during the patient's hospitalization for treatment of acute decompensated heart failure (ADHF). Secondary endpoints included length of hospital stay, defined as the number of days a patient remained hospitalized for treatment of ADHF from the day of admission to the day of discharge, and a composite of all-cause mortality and readmission within 1 month of discharge, which included either mortality or readmission to hospital for heart failure within 30 days of discharge from the first hospitalization for ADHF.

Handgrip strength assessment

HGS was measured using a calibrated Jamar[®] handheld dynamometer (Sammons Preston, Bolingbrook, IL, USA). Prior to testing, participants received standard instructions, demonstrations and familiarization with the procedures¹⁶. Manual dynamometry was performed with both hands. Patients performed the test in a seated position with their hips flexed at 90°, arms hanging beside the trunk and elbows flexed at 90°. They were instructed to squeeze the handles with maximum force. The dominant hand was recorded for each patient, and three maximal contractions were required for each hand, with a 1-minute rest between each trial. The average of the three readings was taken as the final score for each hand¹⁷. To compare our results with normal values, we used the handgrip strength data for the Iranian population published by Mohammadian et al.¹⁸.

Statistical analysis

Continuous variables were expressed as medians (interquartile range, IQR). Categorical variables were expressed as numbers (percentages). The Shapiro-Wilk test assessed the normality of the data distribution for all continuous variables.

Due to the non-normal distribution of the data, non-parametric tests were used for the analyses. The Mann-Whitney U test was used to compare continuous variables between two groups, such as HGS (total, dominant hand, and non-dominant hand) between survivors and non-survivors and between readmitted/deceased within one month and not readmitted/deceased within one month.

Spearman's rank correlation coefficient (Spearman's rho) was calculated to assess the relationship between continuous variables, such as total HGS and NT-proBNP levels, and total HGS and the length of hospital stay.

Logistic regression analyses were performed to identify risk factors associated with in-hospital mortality. For the univariate analysis, we selected variables based on their clinical relevance to heart failure outcomes and previous literature. These included demographic factors (age, sex), heart failure characteristics (disease duration, etiology, left ventricular ejection fraction), comorbidities (diabetes mellitus, hypertension, chronic kidney disease), lifestyle factors (smoking), laboratory parameters (hemoglobin, BUN, creatinine, eGFR, NT-proBNP), and our primary variable of interest, handgrip strength (overall, dominant hand, and non-dominant hand). We also constructed three multivariate logistic regression models. For these models, we included variables that showed statistical significance in the univariate analysis or demonstrated a significant correlation/association with in-hospital mortality in other statistical tests. To avoid multicollinearity, we created separate models for overall handgrip strength, dominant hand strength, and non-dominant hand strength (Models 1, 2, and 3, respectively).

Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive value of total HGS, HGS of the dominant hand, and HGS of the non-dominant hand for in-hospital mortality. The area under the curve (AUC) was calculated, and the optimal cutoff value was determined by maximizing the Youden index (sensitivity + specificity minus 1).

A two-sided *p*-value of <0.05 was considered statistically significant. Analyses were performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY). In addition, data visualization was performed using MedCalc[®] Statistical Software Version 22 (MedCalc Software Ltd., Ostend, Belgium).

Results

Baseline characteristics

The study included 125 patients with ADHF with reduced ejection fraction (HFrEF). The median age of the participants was 53 years (IQR: 45–57), with the majority (41.6%) in the 55–60 age group, and 32% (*n* = 40) of the participants being female. The median BMI was 26.6 kg/m² (IQR: 22.6–32.3). Ischemic etiology was present in 52.8% (*n* = 66) of patients, and the median disease duration was 24 months (IQR: 3–90). Comorbidities included hypertension (40.8%, *n* = 51), diabetes mellitus (26.4%, *n* = 33), and chronic kidney disease (23.2%, *n* = 29). The median left ventricular ejection fraction (LVEF) was 15% (IQR: 10–30), and the median level of N-terminal pro-B-type natriuretic peptide (NT-proBNP) was 6500 pg/ml (IQR: 3789–12367). In addition, 54.4% and 40% of the study population fell into NYHA functional classes III and IV, respectively. All patients received tolerable doses of GDMT at the time of discharge. Table 1 summarizes the details of demographic and laboratory data.

	Value* (n = 125)
Age, year	53 (45–57)
Age groups, n (%)	
55–60 years	52 (41.6)
50–54	28 (22.4)
45–49	15 (12)
40–44	19 (15.2)
< 40	11 (8.8)
Female, n (%)	40 (32.0)
BMI, kg/m ²	26.6 (22.6–32.3)
Ischemic etiology, n (%)	66 (52.8)
LVEF, %	15 (10–30)
NYHA Class III, n (%)	68 (54.4)
NYHA Class IV, n (%)	50 (40)
Disease duration, months	24 (3–90)
Disease duration, n (%)	
> 5 years	49 (39.2)
≤ 5 years	76 (60.8)
Hypertension, n (%)	51 (40.8)
Diabetes mellitus, n (%)	33 (26.4)
Smoking, n (%)	26 (20.8)
Chronic kidney disease, n (%)	29 (23.2)
eGFR, mL/min/1.73 m ²	49.9 (35.5–65.2)
NT-proBNP, pg/ml	6500 (3789–12367)
Hemoglobin, g/L	13.0 (11.4–14.3)
White blood cell count; 1000/mm ³	8500 (6500–10500)
Platelet count; 10 ⁶ /mm ³	197 (158–254)
BUN; mg/dL	23 (16–35)
Cr; mg/dL	1.5 (1.1–1.9)
Uric acid; mg/dL	7.9 (5.7–9.9)
Albumin; g/L	38 (34–40)
Aspartate transaminase; IU/L	27 (21–49)
Alanine transaminase; IU/L	25 (16–50)
Alkaline phosphatase; IU/L	192 (149–252)
Cholesterol; mg/dL	133 (103–154)
Thyroid-stimulating hormone; microIU/ml	2.33 (1.25–3.6)
Handgrip assessment, kg	
Total	18.2 (12.2–25.1)
Dominant hand	19.2 (13.7–26.0)
Non-dominant hand	16.2 (11.0–23.0)

Table 1. Baseline demographics and clinical characteristics. BUN, blood urea nitrogen; Cr, creatinine; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; BMI, body mass index. *Values are presented as median (interquartile range) for continuous variables and n (%) for categorical variables.

The median total hand grip strength (HGS) was 18.2 kg (IQR: 12.2–25.1), with the HGS of the dominant hand being 19.2 kg (IQR: 13.7–26) and the HGS of the non-dominant hand being 16.2 kg (IQR: 11–23) (Table 1). Looking at the normal values of HGS in different age and sex subgroups of the Iranian population¹⁸, the HGS values were below the lower limit of the norm in 81.2% of men and 50% of women.

Analysis of factors associated with overall HGS revealed several significant relationships (Tables S1 and S2). Age showed a weak negative correlation with HGS ($r = -0.184$, $p = 0.040$), while NT-proBNP levels demonstrated a stronger negative correlation ($r = -0.256$, $p = 0.004$). The scatterplot (Fig. 1) shows the relationship between HGS and NT-proBNP levels in the study population. The 95% confidence interval for the Spearman's rho correlation coefficient ranged from -0.417 to -0.079 , further confirming the significant inverse relationship between these two variables. Gender was significantly associated with HGS, with males having higher median HGS (21.3 kg, IQR: 13.5–27.7) compared to females (13.4 kg, IQR: 8.9–17.6) ($p < 0.001$). Smoking status was also associated with HGS, with non-smokers showing higher median HGS (25 kg, IQR: 17.2–28.5) compared to

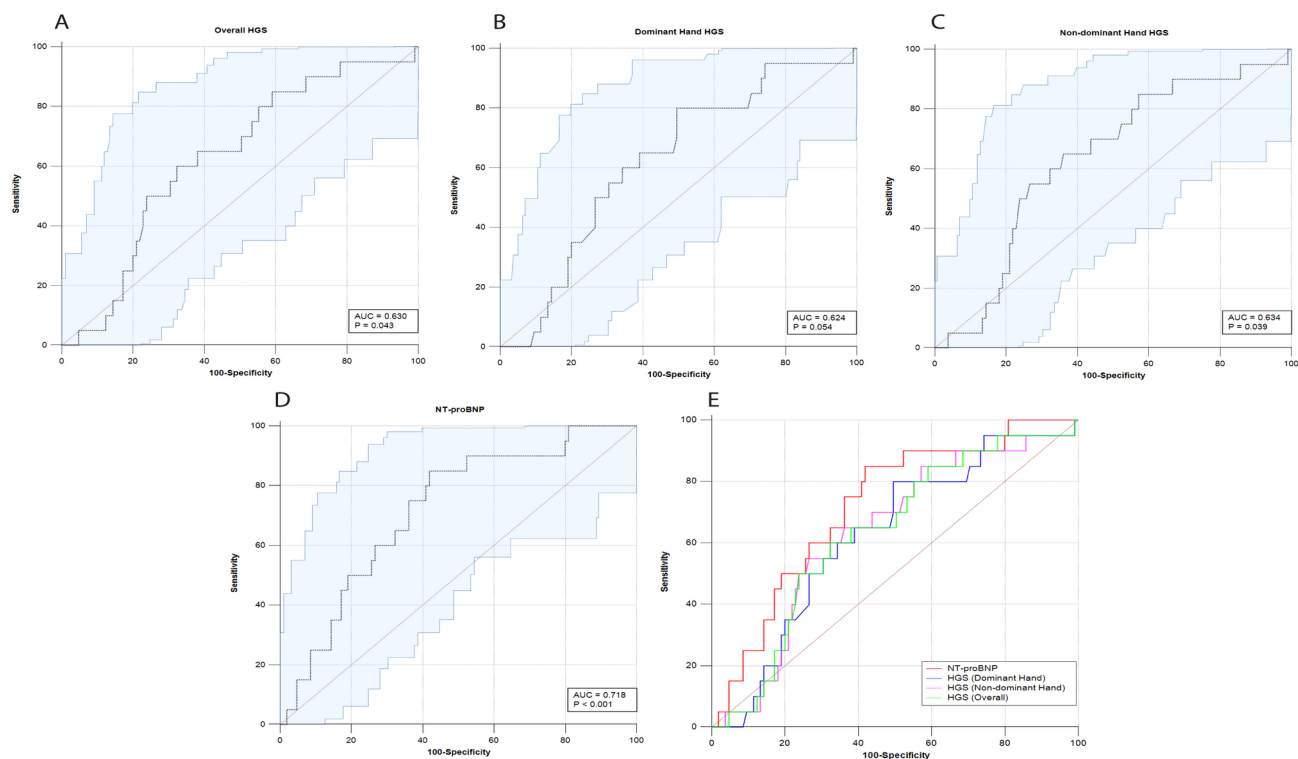


Fig. 1. Scatter plot showing the correlation between handgrip strength and NT-proBNP levels.

	Value (n = 125)	P-value
In-hospital mortality, n (%)	20 (16)	
HGS (kg), median (IQR)		
Survived	18.8 (13.2–25.3)	0.066
Not-survived	13.0 (11.4–19.5)	
Readmission/mortality within one month, n (%)	35 (33.3)*	
HGS (kg), median (IQR)		
Admitted/ not-survived	17.6 (12.4–25.1)	0.758
Not-admitted/ survived	19.2 (9.4–25.1)	
Length of stay in hospital (days), median (IQR)	9 (6–16)	
Length of stay in hospital correlation with HGS [‡]	–0.202	0.024

Table 2. Patients' outcome and its association with handgrip strength. [‡]Spearman's rho correlation coefficient.

*This number is calculated out of 105 hospital-survived patients. Significance value bold (P -value < 0.05).

smokers (16.1 kg, IQR: 11.6–23) ($p=0.002$). Patients without chronic kidney disease had higher median HGS (19.1 kg, IQR: 13–25.4) compared to those with the condition (14.1 kg, IQR: 10.7–19.7) ($p=0.028$).

Other factors, including BMI, LVEF, disease duration, eGFR, heart failure etiology, NYHA class, hypertension, and diabetes mellitus, did not show significant associations with overall HGS.

Association between HGS and patient outcomes

The median duration of hospitalization was nine days (IQR: 6–16). A significant, albeit weak, negative correlation was observed between HGS and length of stay (Spearman's rho = -0.202 , $P=0.024$). The in-hospital mortality rate was 16% ($n=20$). Patients who survived had a numerically higher, but not statistically significant, median HGS of 18.8 kg (IQR: 13.2–25.3) than those who did not survive (13 kg, IQR: 11.4–19.5; $P=0.066$). Of the patients who survived hospitalization ($n=105$), 33.3% ($n=35$) were readmitted or died within one month. However, there was no significant difference in HGS between patients who were readmitted or died within one month and those who were not ($P=0.758$) (Table 2).

Risk factors for in-hospital mortality

Univariate logistic regression was performed to identify risk factors associated with in-hospital mortality (Table 3). On analysis, two variables were found to be significantly associated with in-hospital mortality,

Variable	Univariate analysis				Model 1				Model 2				Model 3			
	OR	95% CI		P-value	OR	95% CI		P-value	OR	95% CI		P-value	OR	95% CI		P-value
		Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper	
Male	0.497	0.149	1.540	0.217	2.241	0.587	8.563	0.238	2.271	0.591	8.729	0.233	2.182	0.576	8.265	0.251
Age	1.015	0.951	1.083	0.659	0.994	0.926	1.066	0.856	0.993	0.926	1.056	0.871	0.994	0.927	1.066	0.871
Disease duration > 5 years	1.692	0.647	4.428	0.284	–	–	–	–	–	–	–	–	–	–	–	–
Ischemic etiology	1.111	0.425	2.904	0.830	–	–	–	–	–	–	–	–	–	–	–	–
Diabetes mellitus	0.265	0.058	1.213	0.087	–	–	–	–	–	–	–	–	–	–	–	–
Hypertension	0.571	0.204	1.603	0.288	–	–	–	–	–	–	–	–	–	–	–	–
Chronic kidney disease	2.667	0.967	7.354	0.058	1.697	0.542	5.315	0.364	1.700	0.543	5.328	0.362	1.702	0.544	5.322	0.361
Smoking	1.589	0.428	5.900	0.489	1.594	0.381	6.675	0.523	1.619	0.387	5.767	0.509	1.574	0.376	6.594	0.535
Serum hemoglobin	0.911	0.725	1.146	0.428	–	–	–	–	–	–	–	–	–	–	–	–
Serum BUN	1.010	0.983	1.036	0.478	–	–	–	–	–	–	–	–	–	–	–	–
Serum creatinine	1.348	0.857	2.120	0.197	–	–	–	–	–	–	–	–	–	–	–	–
eGFR	1.004	0.990	1.019	0.541	–	–	–	–	–	–	–	–	–	–	–	–
LVEF	0.935	0.881	0.993	0.029	0.955	0.893	1.020	0.171	0.955	0.894	1.020	0.173	0.954	0.893	1.020	0.171
NT-proBNP	1.467	1.167	1.817	0.014	0.530	0.311	1.091	0.435	0.533	0.314	1.095	0.430	0.535	0.314	1.094	0.429
Overall HGS	0.953	0.897	1.013	0.125	0.952	0.885	1.024	0.185	–	–	–	–	–	–	–	–
Dominant hand HGS	0.957	0.903	1.014	0.135	–	–	–	–	0.954	0.889	1.023	0.186	–	–	–	–
Non-dominant hand HGS	0.951	0.892	1.013	0.121	–	–	–	–	–	–	–	–	0.952	0.883	1.025	0.194

Table 3. Logistic univariate and multivariate analysis to identify risk factors of in-hospital mortality. Significance value bold (P -value < 0.05).

including LVEF (OR=0.935, 95% CI: 0.881–0.993, P =0.029) and NT-proBNP levels (OR=1.467, 95% CI: 1.167–1.817, P =0.014). Although not statistically significant, diabetes mellitus (P =0.087) and chronic kidney disease (P =0.058), as well as hand grip strength (P =0.06) (total, dominant, and non-dominant hand), showed a trend towards association with in-hospital mortality in this univariate analysis. Multivariate logistic regression models were also constructed (Models 1, 2, and 3 in Table 3), which included variables such as gender, age, chronic kidney disease, smoking status, LVEF, NT-proBNP, and various measures of HGS. However, in these adjusted models, none of the variables retained statistical significance.

Predictive value of handgrip strength for in-hospital mortality: a ROC curve analysis

Figure 2 presents the ROC curves for predicting in-hospital mortality using HGS measurements and NT-proBNP levels. As shown in panel A, the AUC for overall HGS was 0.630 (95% CI: 0.539–0.714, p =0.043), indicating a statistically significant, albeit modest, discriminatory ability to predict in-hospital mortality. However, it also indicates a potential for false positives if HGS were to be used as a prognostic tool. Similarly, the AUC for HGS of the non-dominant hand was 0.634 (95% CI 0.543–0.718, p =0.039), and the AUC for HGS of the dominant hand was 0.624 (95% CI 0.533–0.709, p =0.054) (Panels B and C). These results suggest that HGS, particularly when measured in total or in the non-dominant hand, has a comparable predictive value for in-hospital mortality in this patient population.

Overall HGS and HGS for the dominant and non-dominant hands had optimal cutoff values of 14.4 kg (sensitivity: 60%, specificity: 67.62%), 20.33 kg (sensitivity: 80%, specificity: 50.46%), and 14.7 kg (sensitivity: 66%, specificity: 63.81%), respectively. The Youden index was highest for HGS of the dominant hand (0.3048), followed by HGS of the non-dominant hand (0.2881) and HGS total (0.2762). However, the optimal cutoff value for HGS of the dominant hand (≤ 20.33) had a lower specificity (50.46%) than the other two variables.

NT-proBNP demonstrated the highest predictive ability with an AUC of 0.718 (p <0.001), as shown in panel D. Panel E provides a visual comparison of the ROC curves for NT-proBNP and all HGS measurements. While NT-proBNP appears to have slightly better predictive performance, the curves for the HGS measurements closely follow each other, indicating similar predictive abilities among the different HGS measures. Additionally, pairwise comparisons of the ROC curves revealed no statistically significant differences between the AUCs of NT-proBNP and any of the HGS measurements, or among the different HGS measurements themselves (Table S3); suggesting that the predictive performance of HGS measurements for in-hospital mortality is not significantly different from that of NT-proBNP, a well-established biomarker in heart failure.

Discussion

The importance of frailty and sarcopenia in adult patients with HF younger than 60 years has been emphasized in recent studies from our institute^{5,19}. In our current study, we investigated the prognostic value of HGS, a key component of physical frailty assessment, in patients with acutely decompensated HFrEF with a mean age of 53 years. In our study, a trend was observed for the association between HGS and in-hospital mortality (P =0.06). Additionally, the length of hospital stay was significantly longer in patients with lower HGS scores. Chung et al., Parahiba et al., Tanaka et al., Wang et al., and Singh et al. demonstrated that lower HGS was associated with an increased risk of death in patients with heart failure^{9,12,20–22}. Furthermore, we found no significant difference

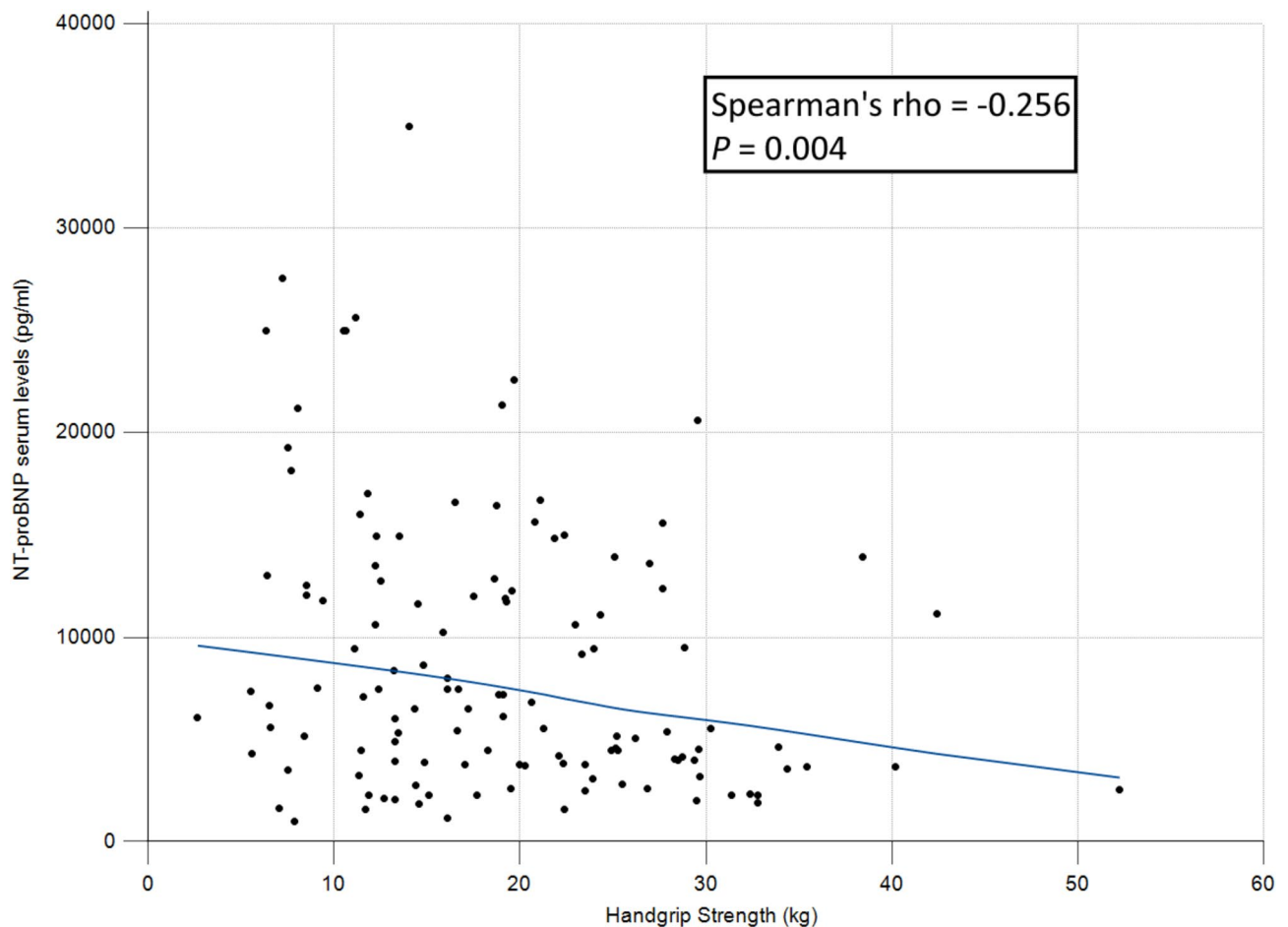


Fig. 2. ROC curves for predicting in-hospital mortality. (A) Overall HGS; (B) dominant Hand HGS; (C) non-dominant Hand HGS; (D) NT-proBNP; (E) visual comparison of ROC curves for NT-proBNP and all HGS measurements.

in HGS between patients who were readmitted or died within one month and those who were not ($p=0.896$). This is in contrast to Joyce et al., who found that poor HGS was associated with a higher risk of readmission or emergency department visit within 6 months in hospitalized patients with heart failure²³.

Singh et al. also found in a prospective study of 210 chronic HF patients that HGS alone had good predictive accuracy for mortality (area under the curve: 0.75, $p < 0.001$), with a cutoff value of 16.95 kg having a sensitivity of 72% and specificity of 63%²¹. Our study determined that the most effective threshold for overall HGS to predict in-hospital mortality was 14.4 kg. This threshold had a sensitivity of 0.6 and a specificity of 0.67. Although this threshold value can help identify patients at high risk, its moderate specificity indicates that it may also result in a significant number of false positives, potentially exaggerating the risk of death in certain patients.

The suggested prognostic value of HGS in young HF patients is thought to be due to its ability to detect the systemic effects of HF on skeletal muscle function and the general state of frailty, independent of the aging process^{9,24}. Reduced muscle strength, as measured by HGS, may result from the complex interplay of factors in HF, including decreased cardiac output, chronic inflammation, metabolic dysfunction, and neurohormonal activation²⁴. In addition, poor HGS could be a sign of an advanced stage of heart failure and be helpful in distinguishing those patients who require more comprehensive heart failure care and treatment²⁵.

There are several possible reasons for our relatively different study results. First, it is important to note that our study was conducted at a tertiary referral center for heart failure. Therefore, our study population may represent a more advanced and severe stage of heart failure compared to the general heart failure population. The HGS levels, which were below the lower limit of normal in approximately 70% of our study population, a relatively high in-hospital mortality rate (16%), a significant early readmission rate despite attempts to achieve GDMT, and a negative correlation between NT-ProBNP levels and HGS emphasize the severity of the disease in our patient population.

Although several studies have provided convincing evidence for the prognostic value of HGS in HF patients, several limitations should be considered. First, the cutoff values for the definition of low HGS varied across studies, ranging from 16.95 kg to 25.5 kg^{12,21}. This heterogeneity may reflect differences in patient population, measurement methods, and study design, but it also underscores the need for standardized definitions of frailty and low HGS in HF patients. Second, most studies were conducted in single centers or specific populations

(e.g., elderly, acutely decompensated HF), which may limit the generalizability of results to the broader HF population. Third, the retrospective nature of some studies may introduce potential biases, such as selection and information bias, which could compromise the validity of the results.

Therefore, the generalizability of our results to other heart failure populations treated under different conditions may be limited. The high mortality and readmission rates observed in our studies underscore the complexity and severity of heart failure cases treated at our tertiary referral center. Future studies conducted in various clinical settings and patient populations are needed to validate our results and gain a deeper understanding of the prognostic value of handgrip strength and other factors across the spectrum of heart failure severity and treatment strategies.

This study has several strengths, including the focus on a specific patient population (acutely decompensated HFrEF in patients younger than 60 years old) and the comprehensive assessment of HGS and its relationship to various clinical outcomes. However, despite the valuable insight provided by the present study, it has some limitations. First, it is crucial to acknowledge that our study primarily assesses muscle strength via HGS measurement and does not constitute a comprehensive frailty evaluation. While HGS is a valuable component of physical function assessment, it does not capture the full spectrum of muscle function or the multidimensional nature of frailty. Therefore, our findings should be interpreted in the context of muscle strength rather than overall frailty. Second, the relatively small sample size may have limited the power to detect significant associations between HGS and mortality in the univariate analysis. As a single-center study conducted at a tertiary referral center for heart failure, our results may not be generalizable to all ADHF patients or to those treated in different clinical settings. Third, the severity of heart failure in our cohort, as evidenced by the high in-hospital mortality rate (16%) and significant early readmission rate, may differ from that seen in other centers or in the general heart failure population. Fourth, our study did not collect detailed data on specific treatments beyond GDMT or non-pharmacological interventions. Finally, the cross-sectional nature of our study limits our ability to assess changes in HGS over time and their relationship to long-term outcomes.

Despite these limitations, the consistent results of several studies with different designs, populations and statistical methods provide strong evidence for the association between reduced HGS and increased mortality risk in HF patients. The simplicity, low cost and ease of use of HGS measurement make it an attractive tool for risk stratification in clinical practice, especially in resource-limited settings. In addition, incorporating HGS into existing risk prediction models can improve their accuracy and help identify high-risk patients who may benefit from targeted interventions such as exercise training, nutritional support and medication optimization.

Conclusion

The assessment of HGS in patients with HF, especially those with ADHF and reduced EF aged less than 60 years, offers some potential prognostic insights that could aid clinical decision-making. The simplicity and relatively low cost of the test may suggest wider applicability. However, it is important to point out that further research is needed to clarify the measurement methods and determine optimal prognostic thresholds.

Data availability

All data gathered and analyzed during this study are included in this published article. In addition, the dataset used is available from the corresponding author upon reasonable request.

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Author contributions

E.K.: Conceptualization; Methodology; Data curation; Formal analysis; Writing—original draft. S.A.: Conceptualization; Methodology; Data curation; Writing—review & editing. M.B.: Investigation; Methodology. A.S.: Investigation; Methodology. F.C.: Investigation; Methodology; Visualization. S.J.: Writing—review & editing; Formal analysis. E.H.: Writing—review & editing. R.O.: Supervision; Investigation; Methodology. S.T.: Supervision; Investigation; Methodology. M.M.: Supervision; Investigation; Methodology. Z.A.F.J.: Investigation; Methodology. M.B.: Investigation; Methodology. M.M.: Investigation; Methodology. S.M.: Data curation; Formal analysis. N.N.: Conceptualization; Supervision; Methodology; Writing—review & editing.

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Declarations

Competing interests

The authors declare no competing interests.

Ethical approval and consent to participate

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was reviewed and approved by the Ethics Committee of Rajaie Cardiovascular Medical and Research Center, Tehran, Iran (IR.RHC.REC.1402.034). In addition, written, signed, and dated informed consent was obtained from all study participants before enrollment. All participants voluntarily consented to have their medical records used in this research.

Additional information

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Correspondence and requests for materials should be addressed to N.N.

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