

The Charlson comorbidity index and short-term readmission in patients with heart failure

A retrospective cohort study

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Abstract

The relationship between the Charlson comorbidity index (CCI) and short-term readmission is as yet unknown. Therefore, we aimed to investigate whether the CCI was independently related to short-term readmission in patients with heart failure (HF) after adjusting for other covariates. From December 2016 to June 2019, 2008 patients who underwent HF were enrolled in the study to determine the relationship between CCI and short-term readmission. Patients with HF were divided into 2 categories based on the predefined CCI (low < 3 and high > =3). The relationships between CCI and short-term readmission were analyzed in multivariable logistic regression models and a 2-piece linear regression model. In the high CCI group, the risk of short-term readmission was higher than that in the low CCI group. A curvilinear association was found between CCI and short-term readmission, with a saturation effect predicted at 2.97. In patients with HF who had CCI scores above 2.97, the risk of short-term readmission increased significantly (OR, 2.66; 95% confidence interval, 1.566–4.537). A high CCI was associated with increased short-term readmission in patients with HF, indicating that the CCI could be useful in estimating the readmission rate and has significant predictive value for clinical outcomes in patients with HF.

Abbreviations: BMI = body mass index, CCI = Charlson comorbidity index, CI = confidence interval, HF = heart failure, NYHA = New York Heart Association, OR = odds ratio.

Keywords: a nonlinear relationship, Charlson comorbidity index, heart failure, short-term readmission

1. Introduction

Heart failure (HF) is the final stage in the development of heart disease and is therefore known as the “last battlefield” in the field of cardiovascular disease.^[1] The overall prevalence of HF in the general population is 1.5% to 2.0%, while in people older than 70 years, it is more than 10%.^[2] Therefore, HF is the main reason for the hospitalization of the elderly.^[3] Despite significant improvements in the outcomes of medical therapy, patients with HF still have a poor prognosis, with 5-year and 10-year survival rates of only 57% and 35%, respectively.^[4,5] Admission rates following hospitalization for HF also remain high, with ≥50% of patients readmitted within 6 months of discharge.^[6] Nearly 80% of costs for HF care are due to hospitalization and short-term readmission.^[7] The identification of high-risk patients for short-term readmission early for timely interventions can improve patient survival and reduce the socioeconomic burden. The high incidence of HF, high

readmission rates, high mortality rates, and high healthcare costs have become common problems in countries worldwide. Accurate assessment of short-term readmission risk and implementation of precise interventions have become an important part of reducing readmission rates and improving health outcomes in patients with HF.

Comorbidities are highly prevalent in patients with HF and affect patient outcomes. Comorbidity is defined as “the presence of more than 1 disorder in a person in a defined period of time.”^[8] HF readmissions were related to no cardiovascular causes and directly associated with an increasing number of comorbidities. Studies have shown that some noncardiac comorbidities, such as chronic kidney disease,^[9] diabetes,^[10] peripheral vascular disease,^[11] and dementia,^[12] increase the risk of HF readmission. The Charlson comorbidity index (CCI) combines both disease numbers and severity into a comorbidity-weighted index.^[13] The CCI has been widely used in clinical research to explore the impact of comorbidities on

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The studies involving human participants were reviewed and approved by the Ethics Committee of Zigong Fourth People's Hospital. The Ethics Committee waived the requirement of written informed consent for participation.

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prognosis.^[14,15] However, few studies have used the CCI to assess the risk of short-term readmission in patients with HF. Therefore, we conducted the present study to further investigate the predictive role of CCI for short-term readmission of patients with HF.

2. Materials and Methods

We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.^[16]

2.1. Database

Data for this retrospective study were obtained from an HF cohort from a hospital in Southwest China. This cohort included all patients with a diagnosis of HF who were admitted to this hospital from December 2016 to June 2019.^[17] The dataset is available at PhysioNet (<https://doi.org/10.13026/8a9e-w734>). The ethics committee of the hospital approved the study with a waiver of informed consent.

2.2. Study population

The definition of HF follows the European Society of Cardiology criteria.^[18] The database contains patients with ICD-9 codes 428, 4280, 4281, 4282, 42820, 42821, 42822, 42823, 4283, 42830, 42831, 42832, 42833, 4284, 42840, 42841, 42842, 42843, and 4289, which include all types of heart failure, including acute heart failure, chronic heart failure, left heart failure, right heart failure, and total heart failure. Patients who had a diagnosis of heart failure on hospital admission were enrolled in our study whether heart failure was the main diagnosis or the secondary diagnosis. We excluded patients under 18 years old and patients with incomplete or inaccessible CCI variables.

2.3. Exposure variable

The CCI was used to quantitatively evaluate the comorbidity status of the patients. The CCI scoring criteria were as follows: Point each for myocardial infarction, heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, connective tissue disease, peptic ulcer disease, mild liver disease, and diabetes without complications; Points each for diabetes with complications, hemiplegia, chronic kidney disease, leukemia, malignant lymphoma, and nonmetastatic malignancy; and Points for severe liver disease, while malignancy with metastasis and acquired immunodeficiency syndrome were allotted 6 points. The patient's CCI is the sum of all scores. In the present study, CCI was not included in the age score. A CCI score of < 3 was defined as a low comorbidity group, and a CCI score of ≥ 3 was defined as a high comorbidity group according to a predefined definition. We chose this value because CCI scores of 3 or higher were found to be predictive of higher 1-year mortality rates among patients on their first HF hospitalization^[19] and elder patients experiencing a first acute heart failure hospitalization.^[20]

2.4. Covariates

We collected the following data for this study: the demographic profile, comorbidity, clinician's baseline characteristics, the results of laboratory tests, and drug usage. Demographic profiles, including age and sex, were obtained at the time of admission. Information on comorbidities included in the CCI was extracted from the history of the medical record system. Baseline clinical characteristics, including pulse, systolic blood pressure, diastolic blood pressure, body mass index (BMI), classification by left ventricular ejection fraction value, type of heart

failure, New York Heart Association (NYHA) cardiac function, Killip classification, and Glasgow coma score, were measured at the time of admission. Laboratory tests were performed on the first day of the patient's admission, including serum creatinine, white blood cell count, hemoglobin, platelets, serum calcium, potassium, chloride, sodium, and high-sensitivity troponin. The medications used were those administered on the first day of admission, including furosemide injection, milrinone injection, isoprenaline hydrochloride injection, dobutamine hydrochloride injection, and shenfu injection.

2.5. Follow-up

Patients will be followed up for 28 days, 3 months, and 6 months after discharge.

2.6. Outcomes

The primary outcome was readmission within 6 months, and readmission within 3 months and 28 days were compared as secondary outcomes. Readmission was defined as the first readmission after discharge from the current hospitalization.

2.7. Statistical analysis

All population profiles were described. Normally distributed continuous variables are expressed as the mean (standard deviation) and compared with Student *t* test. Continuous variables with skewed distributions are expressed as medians (quartiles) and compared with the Mann-Whitney test. Categorical variables are expressed as percentages and were analyzed using the chi-square test or Fisher exact test. Logistic regression analysis was used to determine the relationship between CCI and short-term readmission in patients with HF. To determine the independent role of the CCI, we adjusted for multiple variables. Following the use of a generalized additive model to understand the nonlinear relationship between the 2 parameters,^[21,22] the threshold was determined using a 2-stage linear regression model. As part of the sensitivity analysis, CCI was converted into a categorical variable, and median values in each CCI group were used as continuous variables to calculate linear trends.^[23] In addition, stratification and interaction analyses were conducted according to age (<80 and ≥ 80 years), sex, BMI (<25 and ≥ 25), Killip grade (<2 and ≥ 2), NYHA cardiac function classification (IV and No IV), and type of heart failure (total heart failure and not total heart failure). All analyses were conducted in R, version 3.6.3 (R Foundation, Vienna, Austria) and Free Statistics software version (<http://www.clinicalscintists.cn/freestatistics/>) 1.6, and 2-sided *P* < .05 was considered to be statistically significant.

3. Results

3.1. Participant selection

There were 2008 patients with HF in the original database. After excluding patients under 18 years old and without complete CCI information, 2003 patients were included in this study for analysis. The flowchart in Figure 1 shows the process of case screening.

3.2. Baseline demographics and clinical characteristics

The majority (96.4%) of patients had a CCI score ranging from 1 to 4 points; only 2.8% had a CCI score of 0, and 0.8% of patients had a score ≥ 5 (Table S1, Supplemental Digital Content, <http://links.lww.com/MD/I473>). The baseline characteristics of the participants according to CCI are summarized in Table 1 and Table S2, Supplemental Digital Content, <http://links.lww.com/MD/I473>.

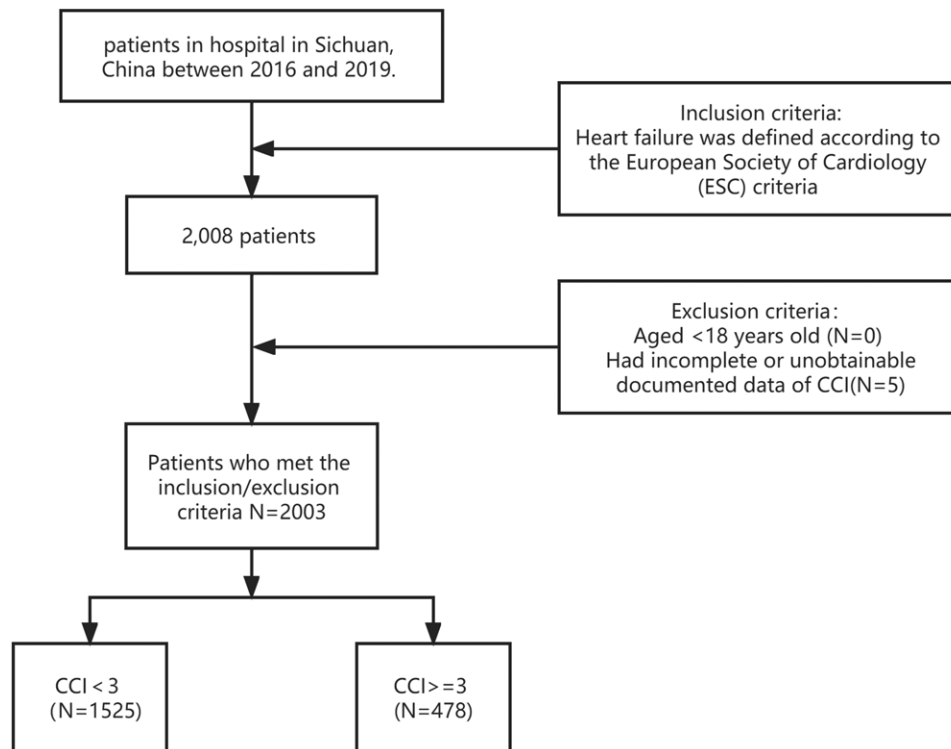


Figure 1. Flowchart of patient selection.

.com/MD/I474. A total of 37.2% of the patients were older than 80 years, and 42% were male. Two groups were formed based on the CCI: CCI < 3 for the low CCI group and CCI \geq 3 for the high CCI group. The mean CCI score for all patients was 1.9 ± 1.0 , with 3.3 ± 0.5 in the high CCI group and 1.4 ± 0.6 in the low CCI group. Compared to the low CCI group, participants in the high CCI group were more likely to be male and older, and had worse heart function and a higher level of creatinine, white blood cells, and potassium. Additionally, they were more likely to have the following diseases: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, peptic ulcer, solid tumor, and liver disease. Furthermore, they had used higher rates of these drugs: furosemide injection, milrinone injection, and higher readmission rates within 28 days, 3 months, and 6 months.

3.3. Outcomes

A total of 771 patients (38.5%) were readmitted within 6 months, and patients whose CCI scores were high were more likely to have high readmission rates (45.2% vs 36.4%; $P < .001$). Readmission rates within 3 months and 28 days were similar.

3.4. CCI and short-term readmission

The results of the univariate analysis are presented in Table S4, Supplemental Digital Content, <http://links.lww.com/MD/I476>. As a continuous variable, in the unadjusted logistic regression model, the CCI was positively correlated with readmission within 6 months [odds ratio (OR) 1.19, 95% confidence interval (CI) 1.08–1.3]. After further adjustment for all potential covariates, the associations were slightly enhanced but remained significant, with an OR of 1.43 (95% CI 1.22–1.68) (Table S3, Supplemental Digital Content, <http://links.lww.com/MD/I475>). As a categorized variable in the fully adjusted model,

participants in the high CCI group had a 61% increased risk of readmission within 6 months compared with the low CCI group (36.4% vs 45.2%, OR 1.89, 95% CI 1.15–3.11). Similar data were observed for readmission within 3 months and readmission within 28 days (31.8% vs 22.6%, OR 1.55, 95% CI 1.14–2.1, 9.8% vs 6%, OR 1.49, 95% CI 1.12–1.97, respectively) (Table 2). Multivariate logistic regression analysis demonstrated that short-time readmissions were not independently associated with gender (Table S5, Supplemental Digital Content, <http://links.lww.com/MD/I477>).

3.5. Nonlinear relationship between CCI and readmission rates

After adjustment for a series of covariates, the CCI and readmission rates within 6 months exhibited a nonlinear dose-response relationship (Fig. 2). Based on a 2-piecewise linear regression model, we calculated the CCI threshold to be 2.966 (Table 3). If the threshold was reached, the readmission rates within 6 months continued to rise (OR = 2.66; 95% CI: 1.566–4.537; $P < .001$), while if it was below the threshold, there was no significant dose-response curve estimated (OR = 1.267; 95% CI: 0.959–1.674; $P = .0963$).

3.6. Subgroup analyses

In the subgroup analysis conducted for age, sex, BMI, Killip grade, NYHA cardiac function classification, and type of heart failure, the results remained generally similar for the association between CCI and short-term readmission. No significant interactions were observed (Fig. 3).

4. Discussion

In this retrospective study, we demonstrated that CCI scores are associated with short-term readmission in patients with HF.

Table 1

Baseline characteristics of the study participants.

CCI	All patients	Low CCI (<3)	High CCI (≥3)	P value
Number, n	2003	1525	478	
Demographics				
Sex, n (%)				< .001
Male	841 (42.0)	609 (39.9)	232 (48.5)	
Female	1162 (58.0)	916 (60.1)	246 (51.5)	
Age, n (%)				.002
<80	1258 (62.8)	986 (64.7)	272 (56.9)	
≥80	745 (37.2)	539 (35.3)	206 (43.1)	
History of disease				
Myocardial infarction, n (%)	141 (7.0)	43 (2.8)	98 (20.5)	< .001
Congestive heart failure, n (%)	1867 (93.2)	1392 (91.3)	475 (99.4)	< .001
Peripheral vascular disease, n (%)	101 (5.0)	31 (2)	70 (14.6)	< .001
Cerebrovascular disease, n (%)	150 (7.5)	67 (4.4)	83 (17.4)	< .001
Dementia, n (%)	115 (5.7)	72 (4.7)	43 (9)	< .001
Chronic obstructive pulmonary disease, n (%)	233 (11.6)	119 (7.8)	114 (23.8)	< .001
Peptic ulcer disease, n (%)	45 (2.2)	20 (1.3)	25 (5.2)	< .001
Solid tumor, n (%)	39 (1.9)	17 (1.1)	22 (4.6)	< .001
Liver disease, n (%)	84 (4.2)	38 (2.5)	46 (9.6)	< .001
Cardiac function				
LVEF, %, (n = 633)	50.6 ± 13.2	50.4 ± 13.3	51.4 ± 12.9	.435
Classification by LVEF value, n (%)				.318
HF _r EF	132 (6.6)	106 (7)	26 (5.4)	
HF _m rEF	152 (7.6)	111 (7.3)	41 (8.6)	
HF _p EF	349 (17.4)	257 (16.9)	92 (19.2)	
Missing data	1370 (68.4)	1051 (68.9)	319 (66.7)	
Type of heart failure, n (%)				.11
Left	477 (23.8)	358 (23.5)	119 (24.9)	
Right	51 (2.5)	45 (3)	6 (1.3)	
Total	1475 (73.6)	1122 (73.6)	353 (73.8)	
NYHA cardiac function, n (%)				< .001
II	352 (17.6)	285 (18.7)	67 (14)	
III	1037 (51.8)	813 (53.3)	224 (46.9)	
IV	614 (30.7)	427 (28)	187 (39.1)	
Killip, n (%)				.016
I	527 (26.3)	426 (27.9)	101 (21.1)	
II	1026 (51.2)	771 (50.6)	255 (53.3)	
III	390 (19.5)	287 (18.8)	103 (21.5)	
IV	60 (3.0)	41 (2.7)	19 (4)	
Scoring system				
GCS	14.8 ± 1.2	14.8 ± 1.1	14.8 ± 1.3	.475
CCI	1.9 ± 1.0	1.4 ± 0.6	3.3 ± 0.5	< .001
Outcome				
Readmission within 28 d, n (%)	139 (6.9)	92 (6)	47 (9.8)	.004
Readmission within 3 mo, n (%)	496 (24.8)	344 (22.6)	152 (31.8)	< .001
Readmission within 6 mo, n (%)	771 (38.5)	555 (36.4)	216 (45.2)	< .001

Data are shown as mean ± standard deviation, median [IQR], and frequency (%).

BMI = body mass index, CCI = Charlson comorbidity index, GCS = Glasgow coma score, HF_pEF = preserved ejection fraction, LVEF = left ventricular ejection fraction, NYHA = New York heart association.

With higher CCI scores, the short-term readmission rate was also significantly higher in patients with HF, and this relationship persisted after adjusting for potential confounders. There was a nonlinear relationship and threshold effect between CCI and readmission within 6 months in patients with HF. When the CCI was >3, the 2 were positively correlated, and when the CCI score was <3, the relationship was not statistically significant. Collectively, our results showed that the CCI score and a CCI ≥ 3 were independent risk factors for short-term readmission in patients with HF.

Our study shows that HF has a high readmission rate that increases with time. Readmission is the admission of a patient to a hospital or other healthcare facility within a short period after discharge. There is no uniform standard for the definition of readmission time. Some scholars recommend 30 days as the readmission time window for HF patients^[4,24]; some scholars use 90 days as the time window, considering that 90 days is the vulnerable period for HF^[25,26]; a few scholars have also set 180 days as the time window for readmission.^[27,28] In contrast, this study

included 28-day, 90-day, and 180-day readmission time windows to explore the relationship between CCI and readmission in patients with HF, and the results were more comprehensive. In our study, the 28-day readmission rate was 6.9%, the 3-month readmission rate was 24.8%, and the 6-month readmission rate was as high as 37.8% in patients with HF. Data from a study conducted by Dustin Harmon showed that 21.2% of patients with heart failure with preserved ejection fraction were readmitted within 90 days of initial discharge.^[11] A study of 1303 samples indicated that the 6-month readmission rate for patients hospitalized for acute decompensated HF was 36.1%.^[28] The results of those previous studies were similar to ours. However, there are several studies whose results differ slightly from ours. In a Korean cohort study of HF, 27.6% of HF patients were readmitted within 30 days of discharge,^[29] a percentage significantly higher than our 6.9%, which may be related to the high CCI score and increased comorbidities. In any case, readmission rates for HF are high, so it is essential to identify risk factors for readmission.

Table 2

Association between CCI and short-term readmission in multiple regression model.

		Model I		Model II		Model III		Model IV	
		OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Readmission within 28-d	CCI < 3	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
	CCI ≥ 3	1.7 (1.18–2.45)	.005	1.62 (1.11–2.34)	.012	2.09 (1.33–3.3)	.001	1.89 (1.15–3.11)	.012
Readmission within 3 mo	CCI < 3	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
	CCI ≥ 3	1.6 (1.28–2.01)	< .001	1.57 (1.24–1.97)	< .001	1.69 (1.27–2.24)	< .001	1.55 (1.14–2.1)	.005
Readmission within 6 mo	CCI < 3	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
	CCI ≥ 3	1.44 (1.17–1.77)	.001	1.41 (1.14–1.74)	.001	1.63 (1.25–2.11)	< .001	1.49 (1.12–1.97)	.006

Model I: didn't adjusted for confounders.

Model II: adjusted for Age, Gender, BMI.

Model III: Model II + NYHA cardiac function classification, Killip grade, type of heart failure, Classification by LVEF value.

Model IV: Model III + systolic blood pressure, diastolic blood pressure, pulse, respiratory support, oxygen inhalation, hemoglobin, platelet, white blood cell, creatinine enzymatic method, potassium, sodium, calcium, chloride, high sensitivity troponin, Furosemide injection, Milrinone injection, Isoprenaline Hydrochloride injection, Dobutamine hydrochloride injection, Shenfu injection, GCS.

CI = confidence interval, CCI = Charlson comorbidity index, OR = odds ratio.

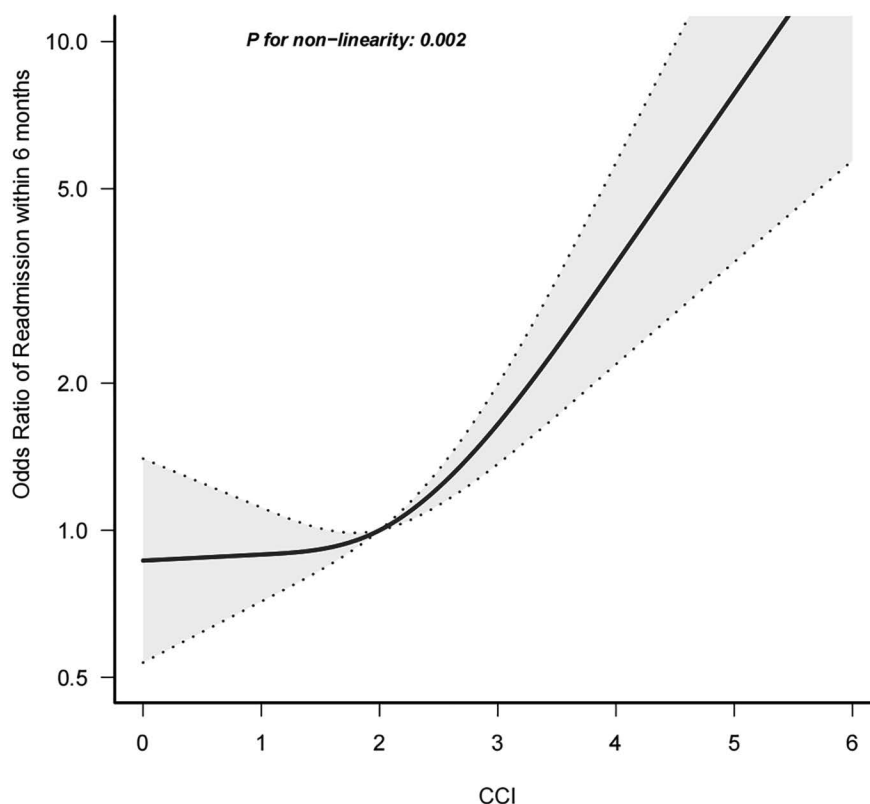


Figure 2. Nonlinear dose-response relationship between CCI and readmission within 6 months. Adjustment factors included age, sex, BMI, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, peptic ulcer disease, solid tumor, liver disease, NYHA cardiac function classification, Killip grade, type of heart failure systolic blood pressure, diastolic blood pressure, pulse, respiratory support, oxygen inhalation, hemoglobin, platelet, white blood cell, creatinine enzymatic method, potassium, sodium, calcium, chloride, high sensitivity troponin, furosemide injection, milrinone injection, isoprenaline hydrochloride injection, dobutamine hydrochloride injection, shenfu injection, GCS. The black line and gray area represent the estimated values and their corresponding 95% confidence intervals, respectively. BMI = body mass index, CCI = Charlson comorbidity index, GCS = Glasgow coma score, NYHA = New York Heart Association.

In our study, the mean CCI was 1.9, which is close to the CCI of 2.0 in a prediction model for HF readmission from a Chinese population.^[25] In other studies, the CCI was higher than ours, such as a mean CCI of 3.5 in an acute HF cohort in Australia^[30] and a mean CCI of 5.2 in a study in Korea.^[29] These findings suggest that patients with HF have a high number of comorbidities and that managing these comorbidities is important for patient prognosis.

We showed in this study that readmission rates increased with increasing CCI, with each point increases in CCI associated with a 43% increase in the risk of readmission within 6 months for

patients with HF. This is consistent with the findings of many studies. An HF cohort study in Japan showed a positive association between CCI and readmission (hazard ratio = 1.087, CI: 1.065–1.108).^[31] An HF cohort study in America showed that each 1-point increase in CCI was associated with a 30% increase in the risk of readmission for congestive HF.^[32] A study conducted by Marco Canepa in Italy showed that in elderly patients with HF, a higher CCI was independently associated with increased readmission.^[33] These results indicated that CCI is a powerful predictor of death and cardiovascular hospitalizations and could help estimate clinical outcomes in patients with HF. Therefore,

Table 3

Threshold effect analysis of CCI on readmission within 6 months.

Threshold of CCI	OR	95% CI	P value
<2.966	1.267	0.959, 1.674	.0963
≥2.966	2.66	1.566, 4.537	< .001
Log-likelihood ratio test			< .001

Adjusted for: Age, Gender, BMI, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, Chronic obstructive pulmonary disease, peptic ulcer disease, solid tumour, liver disease, NYHA cardiac function classification, Killip grade, type of heart failure, systolic blood pressure, diastolic blood pressure, pulse, respiratory support, oxygen inhalation, hemoglobin, platelet, white blood cell, creatinine enzymatic method, potassium, sodium, calcium, chloride, high sensitivity troponin, Furosemide injection, Milrinone injection, Isoprenaline Hydrochloride injection, Dobutamine hydrochloride injection, Shenfu injection, GCS.
CCI = Charlson comorbidity index.

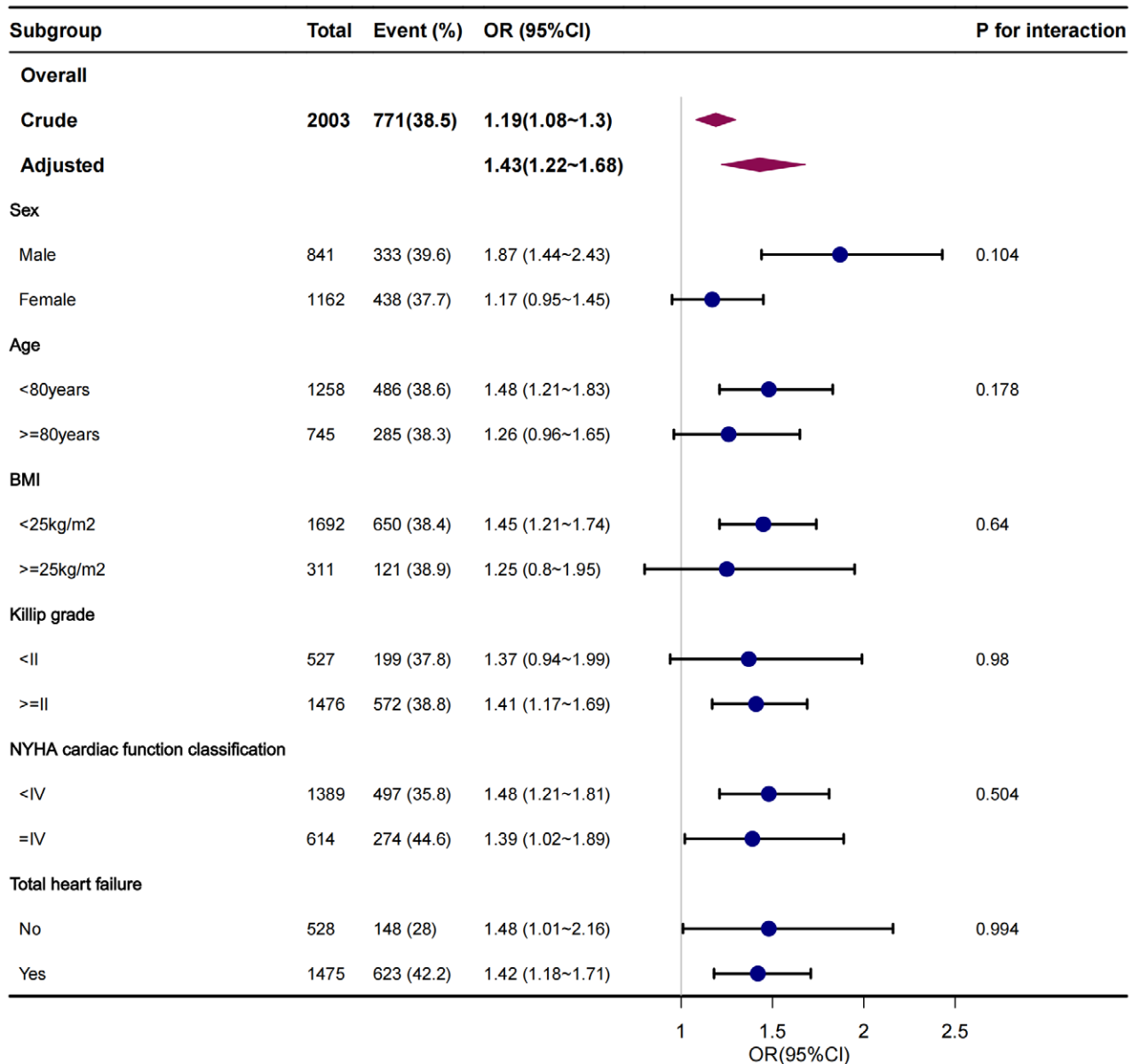


Figure 3. Risk of the primary outcome for CCI in different subgroups of patients. Odds ratio (OR) was adjusted for age, sex, BMI, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, peptic ulcer. disease, solid tumor, liver disease, NYHA cardiac function classification, Killip grade, type of heart failure systolic blood pressure, diastolic blood pressure, pulse, respiratory support, oxygen inhalation, hemoglobin, platelet, white blood cell, creatinine enzymatic method, potassium, sodium, calcium, chloride, high sensitivity troponin, furosemide injection, milrinone injection, isoprenaline hydrochloride injection, dobutamine hydrochloride injection, shenfu injection, GCS. CI = confidence interval, BMI = body mass index, CCI = Charlson comorbidity index, GCS = Glasgow coma score, NYHA = New York Heart Association, OR = odds ratio.

appropriate interventions should be implemented to reduce hospitalization rates in patients with HF. For the first time, we found

a nonlinear relationship and threshold effect between CCI scores and readmission rates in HF patients. At a CCI >3, the risk of

readmission within 6 months was consistently higher, whereas, at a CCI <3, the relationship with readmission rates was not significantly different. The risk of readmission within 6 months was 1.61-fold higher in patients with high CCI scores (≥ 3) than in those with CCI scores < 3. This study highlights the importance of comorbidity as a core factor in HF readmission rates. The possible reasons for this are as follows: some comorbidities included in the CCI, such as myocardial infarction and diabetes mellitus, are underlying conditions for the development of HF, predispose to HF and are important in the instability and progression of HF.^[34] Additionally, comorbidities and HF have bidirectional effects that influence each other and are interconnected through multiple common mechanisms, including inflammation,^[35] endothelial dysfunction,^[36] excessive renin-angiotensin-aldosterone system activation, and sympathetic nervous system activation.^[37]

The relationship between gender and readmission in patients with HF is indeed a question worth studying. However, there are some conflicting results.^[38,39] Our study showed no significant correlation between the 2. The inconsistency of these findings may be related to the sample size and follow-up time, and further expansion of the sample size and longer follow-up time is needed in the future to clarify the relationship.

The CCI can be used as a predictor of the risk of readmission for HF. Several studies have shown that the CCI predicts readmission within 30 days^[40] and within 90 days^[11] in cases of preserved ejection fraction. The LACE index is a commonly used and effective predictive model for predicting HF readmission, and the CCI is an important part of it. One study conducted by Tan incorporated 3 indicators, NT-proBNP, erythrocyte distribution width, and CCI, to build a prediction model to predict readmission of patients with HF within 90 days of discharge and performed an internal validation which showed that the model had a C-index of 0.73, with good discrimination.^[25] In conclusion, the CCI has an important predictive value for readmission in HF.

Some limitations still need to be considered. First, this is a single-center study using a public database, with possible misclassification problems and some limitations on the extrapolation of results. Second, although we adjusted for more variables, there may be variables that may affect the results that were not adjusted for. This is a common problem in all observational studies. Finally, because the rehospitalization for the same cause is particularly frequent in patients with cardiovascular pathologies^[41], but this study did not record in detail whether the specific reason for readmission was due to recurrent HF or other comorbidities, we could only calculate the all-cause readmission rate of patients and not their readmission rate for recurrent HF. Hence, we should more deeply investigate the role of CCI in HF readmission by breaking down the reasons for patient readmission in further studies. There is a nonlinear relationship between CCI and readmission. For this reason, in future work it could be hypothesized to consider readmissions as successive “states” and to study the effect of the CCI on the transitions of the state through a Markov model.^[15]

5. Conclusion

In conclusion, a high CCI was associated with increased short-term readmission in patients with HF, indicating that the CCI could be useful in estimating the readmission rate and has significant predictive value for clinical outcomes in patients with HF.

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References

- Braunwald E. Heart failure. *JACC Heart Fail.* 2013;1:1–20.
- Mosterd A, Hoes AW. Clinical epidemiology of heart failure. *Heart.* 2007;93:1137–46.
- Groenewegen A, Rutten FH, Mosterd A, et al. Epidemiology of heart failure. *Eur J Heart Fail.* 2020;22:1342–56.
- Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. *Circulation.* 2018;137:e67–e492.
- Jones NR, Roalfe AK, Adoki I, et al. Survival of patients with chronic heart failure in the community: a systematic review and meta-analysis. *Eur J Heart Fail.* 2019;21:1306–25.
- Butt JH, Fosbøl EL, Gerds TA, et al. Readmission and death in patients admitted with new-onset versus worsening of chronic heart failure: insights from a nationwide cohort. *Eur J Heart Fail.* 2020;22:1777–85.
- Shafie AA, Tan YP, Ng CH. Systematic review of economic burden of heart failure. *Heart Fail Rev.* 2018;23:131–45.
- Spoorthy MS, Chakrabarti S, Grover S. Comorbidity of bipolar and anxiety disorders: an overview of trends in research. *World J Psychiatry.* 2019;9:7–29.
- Groenewegen A, Rutten FH, Mosterd A, et al. Prognostic impact of chronic kidney disease in patients with heart failure. *Perm J.* 2019;23:18–273.
- Kruik-Kollöffel WJ, Vallejo-Yagüe E, Movig KLL, et al. Non-cardiovascular medication and readmission for heart failure: an observational cohort study. *Int J Clin Pharm.* 2022;44:762–8.
- Harmon D, Rathousky J, Choudhry F, et al. Readmission risk factors and heart failure with preserved ejection fraction. *J Am Osteopath Assoc.* 2020;120:831–8.
- Yap NLX, Kor Q, Teo YN, et al. Prevalence and incidence of cognitive impairment and dementia in heart failure – a systematic review, meta-analysis and meta-regression. *Hellenic J Cardiol.* 2022;67:48–58.
- Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373–83.
- Kachlíková M, Sabaka P, Koščálová A, et al. Comorbid status and the faecal microbial transplantation failure in treatment of recurrent *Clostridioides difficile* infection - pilot prospective observational cohort study. *BMC Infect Dis.* 2020;20:52.
- Bartolomeo N, Trerotoli P, Moretti A, et al. A Markov model to evaluate hospital readmission. *BMC Med Res Methodol.* 2008;8:23.
- Elm E von, Altman DG, Egger M, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ.* 2007;335:806–8.
- Zhang Z, Cao L, Chen R, et al. Electronic healthcare records and external outcome data for hospitalized patients with heart failure. *Sci Data.* 2021;8:46.
- Ponikowski P, Voors AA, Anker SD, et al. 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.* 2016;37:2129–200.
- Jong P, Vowinkel E, Liu PP, et al. Prognosis and determinants of survival in patients newly hospitalized for heart failure: a population-based study. *Arch Intern Med.* 2002;162:1689–94.
- Formiga F, Moreno-Gonzalez R, Chivite D, et al. High comorbidity, measured by the Charlson comorbidity index, associates with higher 1-year mortality risks in elderly patients experiencing a first acute heart failure hospitalization. *Aging Clin Exp Res.* 2018;30:927–33.
- Kong X, Huang X, Zhao M, et al. Platelet count affects efficacy of folic acid in preventing first stroke. *J Am Coll Cardiol.* 2018;71:2136–46.
- Yu X, Chen J, Li Y, et al. Threshold effects of moderately excessive fluoride exposure on children’s health: a potential association between dental fluorosis and loss of excellent intelligence. *Environ Int.* 2018;118:116–24.
- Park S-Y, Freedman ND, Haiman CA, et al. Association of coffee consumption with total and cause-specific mortality among nonwhite populations. *Ann Intern Med.* 2017;167:228–35.
- Shin S, Austin PC, Ross HJ, et al. Machine learning vs. conventional statistical models for predicting heart failure readmission and mortality. *ESC Heart Fail.* 2021;8:106–15.

- [25] Tan B-Y, Gu J-Y, Wei H-Y, et al. Electronic medical record-based model to predict the risk of 90-day readmission for patients with heart failure. *BMC Med Inform Decis Mak.* 2019;19:193.
- [26] Formiga F, Masip J, Chivite D, et al. Applicability of the heart failure readmission risk score: a first European study. *Int J Cardiol.* 2017;236:304–9.
- [27] Disdier Moulder MP, Larock JM, Garofoli A, et al. Family help with medication management: a predictive marker for early readmission. *Mayo Clin Proc Innov Qual Outcomes.* 2017;1:211–8.
- [28] Salah K, Kok WE, Eurlings LW, et al. A novel discharge risk model for patients hospitalised for acute decompensated heart failure incorporating N-terminal pro-B-type natriuretic peptide levels: a European collaboration on acute decompensated heart failure: ELAN-HF Score. *Heart.* 2014;100:115–25.
- [29] Chung JE, Noh E, Gwak HS. Evaluation of the predictors of readmission in Korean patients with heart failure. *J Clin Pharm Ther.* 2017;42:51–7.
- [30] Newton PJ, Si S, Reid CM, et al. Survival after an acute heart failure admission. Twelve-month outcomes from the NSW HF Snapshot study. *Heart Lung Circ.* 2020;29:1032–8.
- [31] Aizawa H, Imai S, Fushimi K. Factors associated with 30-day readmission of patients with heart failure from a Japanese administrative database. *BMC Cardiovasc Disord.* 2015;15:134.
- [32] Chin MH, Goldman L. Correlates of early hospital readmission or death in patients with congestive heart failure. *Am J Cardiol.* 1997;79:1640–4.
- [33] Canepa M, Leporatti L, Persico L, et al. Frequency, characteristics and prognostic impact of hospital readmissions in elderly patients with heart failure: a population study from 2013 to 2017 in Liguria, Northern Italy. *Int J Cardiol.* 2022;363:111–8.
- [34] McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European society of cardiology (ESC) with the special contribution of the heart failure association (HFA) of the ESC. *Rev Esp Cardiol (Engl Ed).* 2022;75:523.
- [35] Kumar P, Lim A, Poh SL, et al. Pro-Inflammatory derangement of the immuno-interactome in heart failure. *Front Immunol.* 2022;13:817514.
- [36] D'Amario D, Migliaro S, Borovac JA, et al. Microvascular dysfunction in heart failure with preserved ejection fraction. *Front Physiol.* 2019;10:1347.
- [37] Garcia-Garduño TC, Padilla-Gutierrez JR, Cambrón-Mora D, et al. RAAS: a convergent player in ischemic heart failure and cancer. *Int J Mol Sci.* 2021;22:7176.
- [38] Hoang-Kim A, Parpia C, Freitas C, et al. Readmission rates following heart failure: a scoping review of sex and gender based considerations. *BMC Cardiovasc Disord.* 2020;20:223.
- [39] Giorgi A de, Boari B, Tiseo R, et al. Hospital readmissions to internal medicine departments: a higher risk for females? *Eur Rev Med Pharmacol Sci.* 2016;20:4557–64.
- [40] Regmi MR, Bhattarai M, Parajuli P, et al. Heart failure with preserved ejection fraction and 30-day readmission. *Clin Med Res.* 2020;18:126–32.
- [41] Fabbian F, Boccafogli A, Giorgi A de, et al. The crucial factor of hospital readmissions: a retrospective cohort study of patients evaluated in the emergency department and admitted to the department of medicine of a general hospital in Italy. *Eur J Med Res.* 2015;20:6.