

Charlson Comorbidity Index does not predict long-term mortality in elderly subjects with chronic heart failure

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Abstract

Background: comorbidity plays a critical role in the high mortality for chronic heart failure (CHF) in the elderly. Charlson Comorbidity Index (CCI) is the most extensively studied comorbidity index. No studies are available on the ability of CCI to predict mortality in CHF elderly subjects. The aim of the present study was to assess if CCI was able to predict long-term mortality in a random sample of elderly CHF subjects.

Methods: long-term mortality after 12-year follow-up in 125 subjects with CHF and 1,143 subjects without CHF was studied. Comorbidity was evaluated using CCI.

Findings: in elderly subjects stratified for CCI (1–3 and ≥ 4), mortality was higher in non-CHF subjects with CCI ≥ 4 (52.4% versus 70%, $P < 0.002$) but not in those with CHF (75.9% versus 77.6%, $P = 0.498$, NS). Cox regression analysis on 12 years mortality indicated that both CCI (HR = 1.15; 95% CI = 1.01–1.31; $P = 0.035$) and CHF (HR = 1.27; 95% CI = 1.04–8.83; $P = 0.003$) were predictive of mortality. When Cox analysis was performed by selecting the presence and the absence of CHF, CCI was predictive of mortality in the absence but not in the presence of CHF.

Conclusion: CCI does not predict long-term mortality in elderly subjects with CHF.

Keywords: Charlson Comorbidity Index, elderly patients, mortality, heart failure, elderly

Introduction

Chronic heart failure (CHF) represents a major public health issue in western countries, being diagnosed in nearly 5 million individuals and accounting for almost 300,000 deaths per year, only in the United States [1–3]. This phenomenon is even more striking in the elderly population, as more than 80% of heart failure patients are aged 65 years or more [4]. In fact, despite the great advances in therapy and management of these patients, CHF still accounts for more than 30% of the causes of hospitalization among older adults [2].

Comorbidity is one of the most important characteristics of elderly patients as the vast majority of people aged ≥ 65 years have one or more chronic medical condition [5–7]. Several authors suggest that the high mortality for CHF among

elderly patients is due, at least in part, to the presence of multiple comorbid conditions [8–10].

To assess the presence and the degree of comorbidity in the elderly, several indexes have been validated and are currently used in geriatric practice. Among these, Charlson Comorbidity Index (CCI) is the most extensively studied comorbidity index [11]. It has been reported to be reliable and to provide a good correlation with mortality and survival outcomes and, mainly, to account for the effect of age [12].

No studies, nevertheless, are available on the ability of CCI to predict mortality in elderly heart failure subjects. For this reason, in this study, we aimed to assess if Charlson Comorbidity Index was able to predict long-term mortality in a random sample of heart failure subjects.

Methods

Study population

The 'Osservatorio Geriatrico Regione Campania' was a cross-sectional study performed in 1992 in Campania, a Region in Southern Italy. The study design is described elsewhere [13]. Briefly, the study sample consisted of 1,780 subjects aged 65 and older randomly selected from the electoral rolls, resident in the five municipalities of Campania, and stratified by a three-step procedure according to age, sex, and size of urban unit.

Of the 1,780 patients, 756 (42.5%) males and 1,024 (57.5%) females, 448 (25.2%) refused to participate in the study resulting in a final study sample of 1,332 subjects, representing an overall participation rate of 74.8%. The mortality of our sample evaluated up to the end of 2003 by means of death certificates was performed in 1,297 of the 1,332 (97.4%) subjects enrolled in 1992; the remaining 35 (2.6%) were unreachable. Of the 1,297 subjects, in 9 subjects (0.06%) data on social support were unavailable. Thus, we studied a final sample of 1,288 subjects (554 male and 734 female), 681 (52.9%) were deceased, 324 men (58.5%) and 357 women (48.6%). However, in the present analysis, 1,268 subjects were considered because in 20 (1.6%) subjects CHF diagnosis was uncertain. All subjects were contacted at home or in their institution and examined by physicians trained to administer a questionnaire including cognitive and depression tests. Data concerning social status and demographic variables were collected.

Cognitive function, depressive status, disability and social support

The Italian version of the Mini-Mental State Examination (MMSE) validated by Measso [14] was used to measure cognitive mental status. Cognitive impairment was defined as a score of less than 24 on the MMSE. The Geriatric Depression Scale (GDS) [15] was used to evaluate depressive symptoms. Disability was evaluated by means of Basic Activities of Daily Living (BADL) [16] and by means of Instrumental Activity of Daily Living (IADL) [17]. Social support included three categories commonly described as social networks, social relationships and economic support. These items contribute to a total score ranging from 0 to 17, in which the highest score corresponds to the lowest social support level [18].

CHF diagnosis

The diagnosis of CHF was considered possible when (i) participants reported that they had been told by a physician to have CHF, and/or (ii) they had received specific treatment with diuretics and digitalis or vasodilators. The diagnosis was subsequently confirmed by means of a physical examination and a review of medical records. Physical examination was performed to detect the following signs and symptoms: dyspnoea, orthopnoea, tachycardia, atrial fibrillation, jugular venous distension, abdomino-jugular reflux, pulmonary rales, third sound, oedema. Specific aetiology was assessed and all

positive cases were classified by the physician according to New York Heart Association (NYHA) guidelines [19].

Chronic conditions and comorbidity

Chronic conditions were evaluated from past medical history and confirmed by a trained physician through a clinical examination. Comorbidity was evaluated using the Charlson Comorbidity Index (CCI) [20], which considers the following 19 medical conditions: myocardial infarction, angina, cardiovascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease (COPD), connective tissue disease, gastrointestinal disease, slight or serious liver disease, diabetes mellitus complicated or not, stroke, kidney failure, cancer, leukaemia, lymphoma, secondary metastasis, AIDS. The score ranges from 1 to 6 for each item, and total score provides an index of severity. Comorbidity information required to calculate CCI was collected by chart review at the enrolment. We stratified our sample in subjects with a CCI score between 1–3 and ≥ 4 . CCI cut-off 1–3 and ≥ 4 was selected to represent a number of subjects with CHF in order to keep the difference between CCI classes within 10%. Moreover, the presence or the absence of CHF was established before CCI calculation.

Statistical analysis

Data were collected and analysed using the SPSS 13.0 statistics package. Baseline characteristics of the sample are expressed as mean \pm standard deviation. Differences in sex, BADL (1 or more function lost), CHF, COPD, Neurological disease and death were compared with χ^2 analyses. Differences in age, heart rate, systolic, diastolic, pulse and mean blood pressure, social support, drugs number, MMSE, NYHA and CCI were evaluated by one-way ANOVA. Cox regression analysis was performed to evaluate the effect of CCI on long-term mortality independently of the role exerted by age, sex (female), heart rate (bpm), systolic and diastolic blood pressure, social support, drugs number, MMSE, BADL (>1 lost), NYHA, CAD, COPD, Neurological disease, CHF, CCI. In addition, to better assess mortality in relation to severity of comorbidity, Cox regression analysis was performed in subjects with CCI = 1–3 and CCI ≥ 4 with and without CHF, with and without COPD and with and without neurological disease. *P* values less than 0.05 were considered significant.

Results

Our analyses showed that subjects with CHF were older than subjects without CHF and that they had lower social support, but that there was no difference between genders. As expected in CHF elderly subjects, we observed higher heart rate, drugs number and NYHA class than in non-CHF elderly subjects. Accordingly, even GDS score and the prevalence of lost BADL was higher in CHF subjects. Moreover, the presence of other chronic conditions, i.e. chronic obstructive pulmonary disease (COPD), neurological disease, was higher in CHF subjects. Consequently, CCI score, and death

Table 1. Baseline characteristics of 1,268 subjects without and with chronic heart failure stratified by comorbidity

Variables	All (1,268)	no CHF (<i>n</i> = 789)			CHF (<i>n</i> = 125)		
		CCI			CCI		
		1–3 (<i>n</i> = 699)	≥4 (<i>n</i> = 90)	<i>P</i>	1–3 (<i>n</i> = 58)	≥4 (<i>n</i> = 67)	<i>P</i>
Sex female	57.0	55.1	62.2	0.216	53.7	65.7	0.125
Age	74.2 ± 6.3	74.1 ± 6.3	75.4 ± 5.9	0.057	75.7 ± 7.2	76.1 ± 6.3	0.705
Heart rate (bpm)	75.3 ± 10.2	75.5 ± 10.0	75.8 ± 9.6	0.763	78.5 ± 13.5	79.8 ± 12.2	0.577
Systolic BP (mmHg)	145.6 ± 19.3	145.7 ± 19.0	149.0 ± 19.2	0.130	148.5 ± 20.7	147.7 ± 21.4	0.821
Diastolic BP (mmHg)	82.3 ± 9.4	82.4 ± 9.1	84.3 ± 11.0	0.069	83.1 ± 10.2	82.6 ± 11.2	0.781
Pulse BP (mmHg)	63.3 ± 16.1	63.3 ± 16.1	64.3 ± 16.9	0.593	64.5 ± 18.1	65.9 ± 17.4	0.661
Mean BP (mmHg)	118.2 ± 17.7	118.3 ± 17.6	120.5 ± 17.7	0.255	119.9 ± 19.8	120.1 ± 18.9	0.756
Social support	13.0 ± 2.7	13.1 ± 2.6	14.4 ± 2.4	0.000	13.8 ± 2.3	15.0 ± 2.4	0.006
Drugs number	2.2 ± 2.0	2.1 ± 1.8	3.7 ± 2.6	0.000	4.3 ± 1.9	5.1 ± 2.2	0.036
MMSE	25.3 ± 4.8	25.3 ± 4.8	23.7 ± 5.9	0.005	25.4 ± 4.6	21.7 ± 5.8	0.000
GDS	11.3 ± 6.6	11.5 ± 6.2	15.1 ± 6.7	0.000	14.3 ± 5.8	18.0 ± 5.9	0.001
BADL (>1 lost,%)	6.4	5.8	10.3	0.005	11.8	25.0	0.086
NYHA	1.2 ± 0.5	1.15 ± 0.4	1.4 ± 0.7	0.000	2.1 ± 1.0	2.3 ± 0.9	0.179
CHF (%)	9.7	–	–	–	–	–	–
COPD (%)	38.2	48.5	65.6	0.002	60.3	80.6	0.017
Neurological disease	13.0	12.5	53.3	0.000	1.7	43.3	0.000
CCI	1.6 ± 1.6	–	–	–	–	–	–
Death (%)	52.9	52.4	70.0	0.002	75.9	77.6	0.498

CHF, chronic heart failure; CCI, Charlson Comorbidity Index; BP, blood pressure; MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; BADL, basic activity daily living; CAD, coronary artery disease.

rate were significantly higher than in subjects without CHF. MMSE, in contrast, was significantly lower in subjects with CHF than in those without CHF (Table 1).

As we stratified non-CHF elderly subjects for CCI 1–3 and ≥4 (88.6% versus 11.4%, $P < 0.001$) we observed a significant increase of low social support, NYHA class, drugs number, digoxin use, GDS score and the prevalence of BADL lost, as CCI score increased. Moreover, there was an increase of COPD, neurological disease, and a significant decrease in MMSE score, with increasing CCI score (Table 1). Most importantly, death percentage was higher in subjects with CCI ≥ 4 than in those with CCI 1–3 (52.4% versus 70%, $P < 0.002$) (Table 1).

In subject with CHF, stratified for CCI 1–3 and ≥4 (44.6% versus 55.4%, $P = 0.345$, NS) (Table 1), we observed a significant increase of low social support, GDS score and of the prevalence of COPD and neurological disease with a significant decrease in MMSE, in subjects with higher CCI score (Table 1). Interestingly, death rate was similar in subjects with CCI score 1–3 and ≥4 (75.9% versus 77.6%, $P = 0.498$, NS) (Table 1).

Survival probability shows that in subjects without and with CHF survival was 46% and 21%, respectively (Figure 1A in the supplementary data available at *Age and Ageing* online). More interestingly, in subjects without CHF survival was well stratified by CCI score (44% versus 27%) (Figure 1B in the supplementary data) while in subjects with CHF survival was not stratified by CCI score (23% versus 20%) (Figure 1C in the supplementary data).

Cox regression analysis on 12 years mortality indicated that both CCI score (Hazard ratio = 1.15; 95% confidence interval = 1.01–1.31; $P = 0.035$) and CHF

Table 2. Cox regression analysis on 12 years' mortality

Variables	B	Exp B	95% CI	<i>P</i>
Age	0.139	1.149	1.11 – 1.17	0.000
Sex (female)	–0.921	0.398	0.29 – 0.53	0.000
Heart rate (bpm)	0.002	1.002	0.98 – 1.01	0.820
Systolic blood pressure	0.005	1.005	0.99 – 1.01	0.290
Diastolic blood pressure	–0.001	0.999	0.98 – 1.01	0.951
Social support	0.400	1.491	1.18 – 1.87	0.001
Drugs number	0.087	1.091	1.01 – 1.17	0.027
MMSE	–0.024	0.977	0.94 – 1.00	0.150
GDS	0.002	1.002	0.97 – 1.02	0.874
BADL (≥1 lost)	1.231	3.424	1.40 – 8.34	0.007
NYHA	0.209	1.232	0.93 – 1.61	0.132
CAD	0.265	1.303	0.68 – 2.47	0.417
COPD	–0.081	0.922	0.66 – 1.27	0.626
Neurological disease	–0.399	0.671	0.41 – 1.09	0.113
CHF	0.328	1.276	1.04 – 8.83	0.003
CCI	0.143	1.153	1.01 – 1.31	0.035

MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Scale; BADL, basic activity of daily living; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CHF, chronic heart failure; CCI, Charlson Comorbidity Index.

(Hazard ratio = 1.28; 95% confidence interval = 1.04–8.83; $P = 0.003$) were predictive of mortality in a multivariate model adjusted for sex, age and several other variables (Table 2). Moreover, when Cox analysis was performed by selecting the presence and the absence of a specific disease, CCI score was predictive of mortality in the absence but not in the presence of CHF (Figure 1A). In contrast, CCI score was still predictive both in the absence and in the presence of COPD and neurological disease (Figure 1B and C).

Charlson Comorbidity Index does not predict long-term mortality in elderly subjects with CHF

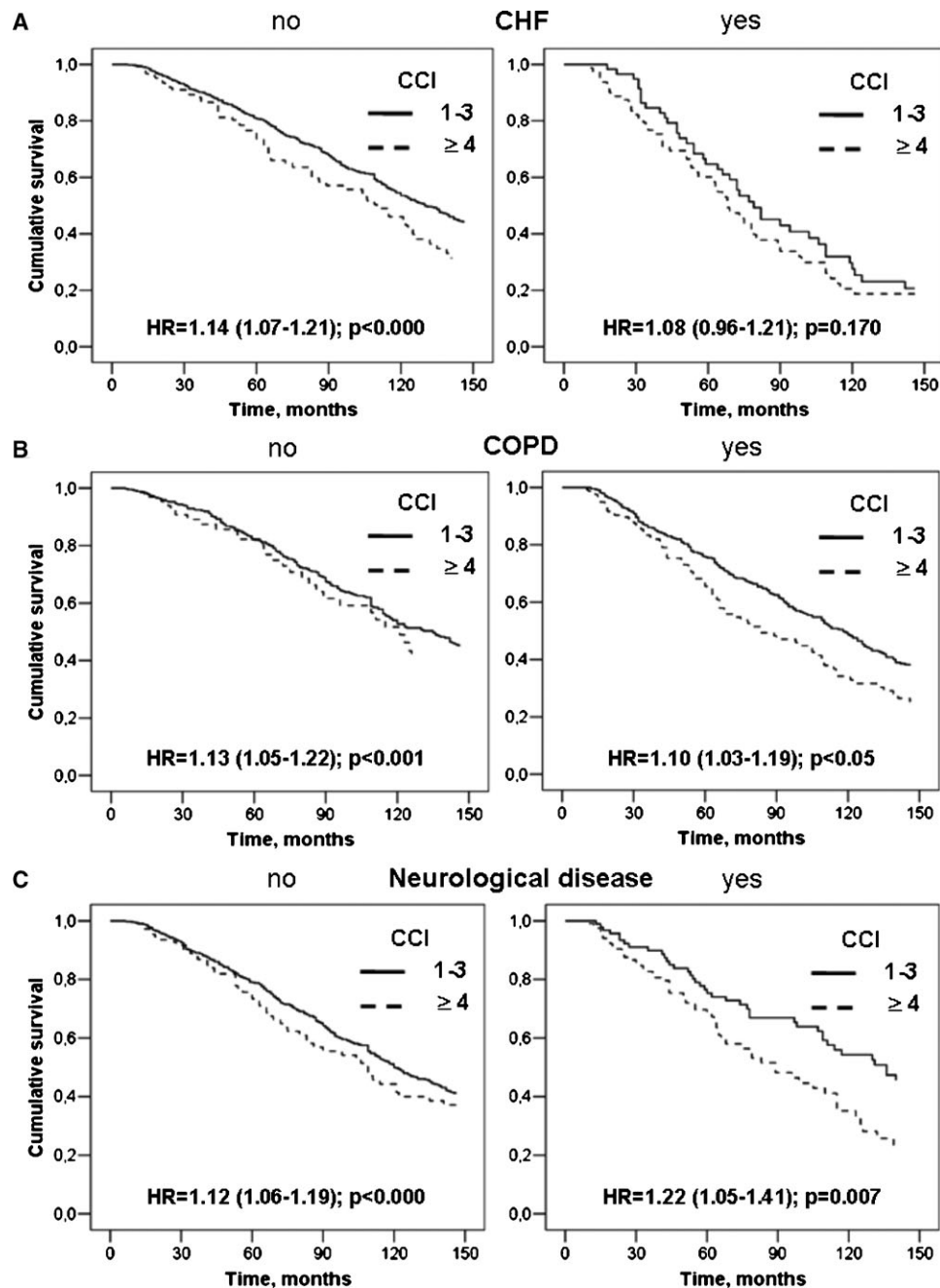


Figure 1. Survival probability according to Cox analysis in elderly subjects with and without chronic heart failure (CHF), (A), in those with and without Chronic Obstructive Pulmonary Disease (COPD), (B), and in those with and without Neurological disease (C) stratified for Charlson Comorbidity Index (CCI) score.

Discussion

Our results show that in subjects without CHF, at a 12-year follow-up, survival progressively decreased as age and CCI score increased. In contrast, subjects with CHF showed decreasing survival rates with advancing age but not with increasing CCI score. In addition, both CCI and CHF were predictive of 12 years mortality in a multivariate model. Moreover and more importantly, Cox regression analysis by the presence and the absence of a specific disease confirmed

that CCI is predictive of mortality in the absence but not in the presence of CHF. Thus, CCI did not predict long-term mortality in elderly subjects with CHF.

CHF in the elderly

Several epidemiological studies reported how CHF has become, in the last decades, a social burden [1, 21]. Recent studies, performed in different European countries, reported an increasing prevalence of heart failure subjects up to 10

times more in persons aged 65–74 and 20 times more in those aged 85 or more, with respect to the general population [21, 22]. Accordingly, in our sample the prevalence of heart failure subjects was $\approx 10\%$, the mean age being 74.2 ± 6.3 years, and 12 years mortality was $\approx 80\%$. These data confirm the fact that CHF is mainly a geriatric disease [4, 23–27].

Comorbidity in the elderly

Comorbidity represents one of the major characteristics of the elderly population, and in the last decade its impact has been studied in different settings. Several reports showed the increasing rates of comorbidity in western countries [5, 6, 28]. Wolff *et al.* [5] reported that in 1999, 82% of Medicare beneficiaries aged ≥ 65 had 1 or more chronic conditions and that 65% had multiple chronic conditions. In this report the authors found that more than half of all study participants had a chronic condition related to a disease of the circulatory system, followed by endocrine, nutritional and metabolic diseases. Van den Akker *et al.* [6] reported that among patients referring to a network of general practitioners in the south of Netherlands, male subjects aged 60–79 and ≥ 80 had a mean number of diseases of 2.42 and 3.24, respectively. In the female population, these values were 2.61 and 3.57 in subjects aged 60–79 and ≥ 80 . Accordingly, in our sample, a significant increase in the prevalence of BADL lost, chronic obstructive pulmonary disease, neurological disease, and NYHA class and a significant decrease in MMSE score characterized subjects with the highest CCI. More importantly, death percentage was higher as CCI score increased.

Comorbidity and CHF in the elderly

In the vast majority of elderly patients CHF almost never occurs as an isolated condition [7]. Brown and Cleland reported that $\approx 12\%$ of CHF admission was associated to COPD, $\approx 9\%$ to chronic renal failure, and $\approx 6\%$ to cerebrovascular accident [9]. The National Heart Failure Project found that COPD, stroke and dementia are very prevalent among elderly CHF patients [29]. These chronic comorbid conditions have implications for the care of elderly CHF patients and negatively affect clinical outcomes, especially increasing the rates of re-hospitalizations [4, 10]. Recently, Braunstein *et al.* brilliantly studied the impact of non-cardiac comorbidity on one-year preventable hospitalizations and mortality in elderly CHF patients. They observed that, of nearly 122,000 patients, only 4% had heart failure alone and that $\approx 40\%$ had 5 or more non-cardiac comorbid conditions. In their sample, Braunstein *et al.* describe the relationship between the number of non-cardiac comorbidities and the probability of hospitalization. Interestingly, they found that the occurrence of multiple comorbid conditions dramatically raised the probability of rehospitalization in patients with CHF [10].

CCI and mortality in CHF elderly subjects

CCI was able to predict three years mortality in patients with COPD [30], five years mortality in non-surgical patients attending the emergency department [31], and 18 months mortality in elderly patients with community-acquired pneumonia seen at an acute care hospital [32]. Even in surgical setting, it was recently shown that CCI could be a good predictor of five-year survival in patients undergoing non-small cell lung cancer resection [33]. Accordingly, in our sample CCI is able to predict mortality both in the presence or the absence of highly elderly prevalent diseases such as COPD and neurological disease. However, no specific data are available on the ability of CCI to predict long-term mortality in elderly patients with CHF. Recently, Jong *et al.*, by using the Canadian Institute for Health Information database, retrospectively analysed nearly 40,000 consecutive patients with first-time admissions for heart failure and could observe that the presence of comorbidities, as identified by CCI, was independently associated with poorer 1 year survival [34]. However, this study was not designed on the elderly population. In contrast, in our sample death rates did not show any significant increase in CHF-elderly subjects with higher CCI score, while it was observed in non-CHF elderly subjects. In other words, the presence of CHF abolishes the CCI predictive power on long-term mortality. This phenomenon is not present when considered other highly prevalent elderly diseases such as COPD or neurological diseases. In fact, CCI predicts long-term mortality when the analysis was performed both in the absence and in the presence of COPD and neurological disease.

CCI was developed and validated by Charlson in 1987 based on 1-year mortality in a cohort of breast cancer patients [20]. It is derived by summing the weights assigned to all health problems affecting a patient from a list of 19 medical conditions and, as above reported, it has been tested in a variety of settings and patient populations. However, to our knowledge, the predictive accuracy of the CCI has never been investigated in community-dwelling elderly CHF subjects and on such a long-term follow-up. In our setting, in fact, it showed some important limitations. Our opinion is that certain pathological conditions, such as acquired immunodeficiency syndrome, are heavily weighted in the index yet rarely encountered in the elderly community-dwelling setting, while other highly elderly prevalent conditions, such as CHF, are probably underestimated. Several authors have recommended the original list of comorbidities to be expanded and the weights re-estimated to improve its ability to control confounding in a given study [35–38].

Conclusion

Our results confirm the ability of CCI to predict mortality in elderly subjects, but show that this ability is lost in elderly subjects with CHF. These findings suggest that CHF within the CCI is probably underestimated and should be more heavily weighted.

Key points

- Comorbidity plays a critical role in the high mortality for chronic heart failure in the elderly.
- Charlson Comorbidity Index is the most extensively studied comorbidity index.
- Charlson Comorbidity Index does not predict long-term mortality in elderly subjects with chronic heart failure.

Supplementary Data

Supplementary data are available at *Age and Ageing* online.

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