Clinical characteristics of very old patients hospitalized in internal medicine wards for heart failure: a sub-analysis of the FADOI-CONFINE Study Group

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ABSTRACT

The incidence and prevalence of chronic heart failure are increasing worldwide, as is the number of very old patients (>85 years) affected by this disease. The aim of this sub-analysis of the multicenter, observational CONFINE study was to detect clinical and therapeutic peculiarities in patients with chronic heart failure aged >85 years. We recruited patients admitted with a diagnosis of chronic heart failure and present in the hospital in five index days, in 91 Units of Internal Medicine. The patients' clinical characteristics, functional and cognitive status, and the management of the heart failure were analyzed. A total of 1444 subjects were evaluated, of whom 329 (23.1%) were over 85 years old. Signs and symptoms of chronic heart failure were more common in very old patients, as were severe renal insufficiency, anemia, disability and cognitive impairment. The present survey found important age-related differences (concomitant diseases, cognitive status) among patients with chronic heart failure, as well as different therapeutic strategies and clinical outcome for patients over 85 years old. Since these patients are usually excluded from clinical trials and their management remains empirical, specific studies focused on the treatment of very old patients with chronic heart failure are needed.

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Introduction

The incidence and prevalence of chronic heart failure (CHF) are increasing worldwide because of the increased life-span and the improvement of medical treatments.[1] In Italy, the number of patients hospitalized for CHF in 2008 was around 200,000, which represented 2.6% of total admissions, ranking CHF in the second position among all causes of hospitalization.[2] Most of these patients are admitted to Internal Medicine wards because of their advanced age and the presence of comorbidities. Two recent Italian surveys, the TEMISTOCLE[3] and CONFINE[4] studies, found that the mean age of patients admitted to Internal Medicine wards for CHF increased from 77 years in 2002 to 79 years in 2008. Moreover, the number of very old patients (>85 years) was substantial and increasing year-by-year.

Very old patients and patients with comorbidities are usually excluded from randomized clinical trials

and are not, therefore, considered when guidelines are written. The practical consequence of this discrepancy between clinical-trial and real-world populations is that treatments are usually given according to guidelines but only based on extrapolation of data from studies performed in much younger subjects, therefore with lack of evidence that they are of real benefit in elderly/very elderly patients.

This study was aimed at detecting differences between old and very old patients with CHF in an attempt to provide grounds for a more patient-tailored care. For this purpose, data from the more recent survey carried out in Internal Medicine wards thoughout Italy, the CONFINE Study,[4] were re-analyzed to detect peculiarities in clinical presentation, clinical and pathophysiological features, comorbidities and treatments for patients with CHF aged >85 years.

Materials and Methods

The CONFINE Study (Comorbidities and Outcome iN patients with chronic heart Failure: a study in INternal mEdicine units in Italy) was an observational, multicenter study performed in 91 Internal Medicine wards representative of the national setting and associated with the Scientific Society FADOI (Federation of Associations of Hospital Doctors on Internal Medicine).

Patients were recruited according to a spot analysis method in 5 pre-determined days between October 2, 2006 and May 25, 2007. All patients present in the ward on a given index day and admitted with a diagnosis of CHF were enrolled in the study, with no exclusion criteria.

The diagnosis of CHF was made according to the European Society of Cardiology 2005 guidelines.[5] For each patient, the following information relative to the index day, day of hospitalization and day of discharge were collected: age, gender, blood pressure, heart rate, New York Heart Association (NYHA) class, body mass index, electrocardiographic (ECG) records, cause of CHF, comorbidities (see below), laboratory data, and drug treatment with particular reference to cardiovascular therapy. Echocardiograms were performed only in selected centers, depending on instrument availability.

The following comorbidities were systematically recorded: i) chronic obstructive pulmonary disease (COPD), defined by clinical data or specific therapy; ii) diabetes, defined by prior diagnosis, or specific therapy, or blood glucose >126 mg/dL; iii) systemic hypertension, defined according to the European Society of Hypertension - European Society of Cardiology guidelines;[6] iv) anemia, defined according to the World Health Organization (WHO) definition;[7] v) renal insufficiency, defined by glomerular filtration rate according to the Cockroft-Gault formula; vi) chronic inflammatory diseases (rheumatoid arthritis, systemic lupus erythematosus); vii) brain deficit/dementia, evaluated by the Pfeiffer test;[8] viii) cancer; ix) depression, defined by prior diagnosis, or specific therapy; x) cerebrovascular disease, defined by a history of stroke or transient ischemic attack; and xi) liver cirrhosis.

Disability was evaluated on both the index day and at discharge, by means of the Barthel Index.[9] Quality of life was assessed by administering the Minnesota Living with Heart Failure (MLWHF) questionnaire.[10]

The study was approved by the ethic committees of the participating centers and informed consent for data handling was obtained from the patients, or their relatives in the case of severe cognitive impairment.

Statistics

Patients were divided into two groups according to age, with those age ≤85 years being defined as *old* and those aged >85 years as *very old*. Summary statistics were calculated for all variables. For continuous variables, mean, standard deviation (SD), median, minimum and maximum were assessed. For non-continuous variables, the frequency distribution was considered. The Student t test was used to compare values of blood pressure and heart rate on admission to hospital and at discharge. The association between the occurrence of a negative in-hospital outcome (death or severe clinical worsening) and candidate prognostic factors were evaluated by means of a multi-variable logistic regression. Covariates for these analyses were selected on the basis of their clinical plausibility and the availability of a substantial number of records. The list of covariates included NYHA class (III-IV *vs* I-II), possible presence of concomitant anemia, or dementia, glomerular filtration rate (<60 *vs* ≥60 mL/min), and Barthel Index (≤30 *vs* 31-60 and ≤30 *vs* 61-100). Ejection fraction was not included in the multivariable model because relevant values were available for fewer than two-thirds of the study population. P values ≤0.05 were considered statistically significant. Statistical analyses were carried out using SAS software (version 9.1, SAS Institute).

Results

A total of 1444 subjects were included in the CONFINE study, 692 (48.4%) were male and 737 (51.6%) were female. The mean age of the whole group was 78.7±9.7 years. Approximately one out of four enrolled patients (n=329, 23.1%) were over 85 years (*very old patients*), and 127 of them (8.8%) were over 90. Of the patients over 85 years old, 73.9% were female.

Cardiovascular features and treatments

Among the various causes of CHF defined on the grounds of history and clinical information, hyperten-

sion was the most common in both the very old and old groups of patients, but significantly more frequent in the former, whereas dilated cardiomyopathy was less common in the over 85-year olds (Figure 1).

For about one-third of the patients in both groups, the index hospital admission was their first for CHF (36.3% *vs* 39.4%, P=n.s.).

Most of the patients had NYHA class III or IV CHF, without significant differences between the age groups (Figure 2). Signs and symptoms of congestive heart disease were more common in very old patients than old ones (Table 1) and this was associated with a more pronounced deterioration of renal function (glomerular filtration rate <30 mL/min: 14.2% *vs* 7.2%, P<0.001), and greater prevalence of atrial fibrillation (49.1% *vs* 41.0%, P<0.0001) and atrio-ventricular block (6.6% *vs* 4.8%, P<0.001) in the former.

Mean left ventricular ejection fraction on admission, evaluated in 827 patients, was 42.8±12.8%, with values <30% in 18.1% of patients, between 31-40% in 19.6%, between 41-50% in 34% and >50% in 28% of patients. Older subjects showed a tendency to a higher prevalence of preserved ejection fraction (43.7% *vs* 37.4%, P=n.s.), although the difference was not statistically significant.

The results of the ECG on admission and at discharge, for those patients for whom these data were available (*i.e.* two or more ECG), are presented in Table 2.

On admission blood pressure and heart rate values were similar in the two groups (systolic blood pressure 140.8±26.7 *vs* 140.8±27.7 mmHg; diastolic blood pressure 81.5±13.5 *vs* 80.5±13.1 mmHg; heart rate 91.6±21.4 *vs* 90.7±2.1 beats/min; P=n.s. for all). Mean hemoglobin levels were slightly lower in very old patients and close to the WHO cut-off value for defining anemia (11.7±2.1 *vs* 12.2±2.2 g/dL; P=n.s.). In the subgroup of patients in whom brain natriuretic peptide

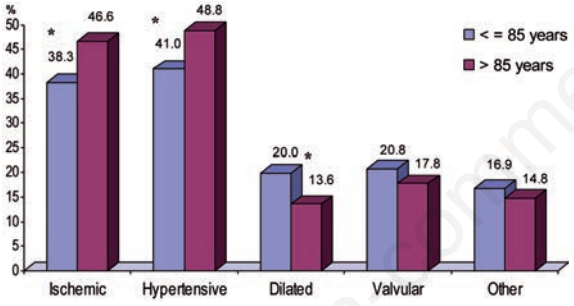

Figure 1. Etiology of chronic heart failure in the two groups. The sum of percentages is more than 100, since more than one cause was present in many patients. *P<0.05.

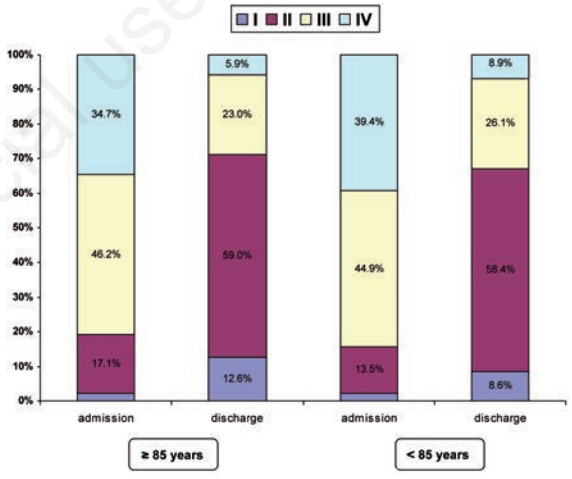

Figure 2. Distribution of New York Heart Association class on admission and at discharge in the two groups of patients (< or ≥ 85 years).

Table 1. Symptomatology and clinical characteristics of patients on admission. Values are expressed as percentages.

	≤85 years (1115 patients)	>85 years (329 patients)	P
Dyspnea	66.5	72.6	<0.05
Wheeze	78.0	84.5	<0.05
Pulmonary edema	21.6	31.9	<0.001
Peripheral edema	70.4	62.9	<0.05
Exertional dyspnea	85.8	83.0	0.21
Hepatomegaly	46.0	31.9	<0.001
Pleural effusion	39.5	49.8	0.001

(BNP) or its N-terminal prohormone (NT-proBNP) was measured, there were no differences in levels between the old and the very old patients.

At discharge there were reductions in the values of systolic blood pressure, diastolic blood pressure, heart rate, and glycemia in both groups, but no differences in BUN, creatinine, uric acid and hemoglobin concentrations (Table 3).

On admission digoxin was used to a larger extent in older patients, while angiotensin-receptor blockers, β-blockers, anti-aldosterone diuretics, calcium channel blockers and oral anticoagulants were used less frequently in the very old patients than in the younger patients (Table 4). Values at discharge are presented in Table 5, showing that there was less use of renin-angiotensin-aldosterone system antagonists (ACE-inhibitors, angiotensin-receptor blockers or both) in both groups, but they were still less used in very old patients. At discharge, β-blockers were being taken by more patients in both groups (Tables 4 and 5) but the

Table 2. Electrocardiogram (ECG) records in the two groups on admission and modification of ECG records in those patients in whom ECG was done at least both on admission and at discharge (503 patients ≤85 years and 137 >85 years).

	≤85 years N=1115	>85 years N=329	P
Sinus rhythm	50.2	42.0	0.001
AF	40.5	48.4	0.001
A-V block	4.3%	6.6%	0,1
RBBB	12.2	13.4	0.6
LBBB	14.7	16.5	0.5
Pace-maker	9.6	12.4	0.001

	≤85 years					>85 years				
	On admission N=503	%	At discharge N=503	%	P	On admission N=137	%	At discharge N=137	%	P
Sinus rhythm	235	46.7	241	47.9	n.s.	53	38.7	60	43.8	n.s.
AF	225	44.7	202	40.2	n.s.	68	38.8	60	43.8	n.s.
A-V block	21	4.2	24	4.8	n.s.	13	9.5	16	11.7	n.s.
RBBB	68	13.5	63	12.5	n.s.	16	11.7	16	11.7	n.s.
LBBB	82	16.3	78	15.5	n.s.	19	13.9	20	14.6	n.s.
Pace-maker	51	10.1	56	11.2	n.s.	17	12.4	17	12.4	n.s.

AF, atrial fibrillation; A-V, atrioventricular; RBBB, right bundle-branch block; LBBB, left bundle-branch block; n.s., not significant.

Table 3. Laboratory tests in both groups on admission and at discharge.

	≤85 years On admission	≤85 years At discharge	P	>85 years On admission	>85 years At discharge	P
SBP mmHg (m±sd)	140.8±26.7	126.1±16.2	0.001	140.8±27.7	125.1±16.9	0.001
DBP mmHg (m±sd)	81.5±13.5	75.2±8.9	0.001	80.5±13.1	74.1±9.3	0.001
Heart rate beats/min (m±sd)	91.6±21.4	79.0±12.0	0.001	90.7±22.1	78.2±12.4	0.001
BUN mg (m±sd)	61.9±46.8	64.5±47.5	0.001	69.2±42.2	73.3±64.2	0.001
Creatinine mg (m±sd)	1.4±0.9	1.5±1.1	n.s.	1.6±0.8	1.6±1.0	n.s.
Uric acid mg (m±sd)	7.4±3.0	8.1±8.7	n.s.	7.6±6.1	6.9±5.3	n.s.
Glycemia mg (m±sd)	137.8±72.9	114.7±45.6	0.001	133.9±60.3	107.4±39.1	0.001
Na mEq/L (m±sd)	138.6±4.9	138.8±5.5	n.s.	139.1±4.9	139.8±5.8	n.s.
K mEq/L mmHg (m±sd)	4.5±3.2	4.4±5.5	n.s.	5.7±5.3	4.7±5.0	n.s.
Hb g/dL (msd)	12.2±2.2	12.2±5.5	n.s.	11.7±2.1	12.1±7.5	n.s.

SBP, systolic blood pressure; DBP, diastolic blood pressure; BUN, blood urea nitrogen; Na, sodium; K, potassium; Hb, hemoglobin; m±sd, mean±standard deviation.

difference was statistically significant only in younger patients.

In both groups, the percentages of patients with atrial fibrillation who were receiving digoxin therapy decreased between admission and discharge (Table 6)

Comorbidities

The distribution of comorbidities is reported in Table 7.

Older patients more frequently had severe limitations of functional status. The mean Barthel Index was 59.3±31.5, and the lowest values were found in very old subjects: the difference between the two age groups was highly significant (64.1±29.9 *vs* 44.0±31.5; P<0.001). Severe cognitive impairment/dementia was more frequent among the very old patients (45.0% *vs* 16.7%, P<0.001).

Cachexia, defined as a body mass index <18.5, was more frequent in very old subjects (15.0 *vs* 4.7%; P<0.001) as was anemia, defined as a hemoglobin <12 g/dL (43.7 *vs* 38.6%; P<0.001). When the most severe forms of anemia were considered (hemoglobin <10 g/dL), these were distributed equally between groups.

Some comorbidities, such as renal insufficiency, hypertension, dementia and anemia could have been changed as a result of treatment or hospitalization, however their frequencies (percent values) were no difference in the two groups on admission and at discharge (Table 8).

Outcomes

The mean duration of the hospital admission in the whole population was 14.1±10.3 days, without differ-

Table 4. Pharmacological treatments used in the two study groups on admission.

	≤85 years (1115 patients)	>85 years (329 patients)	P
Digoxin, No. (%)	303 (27.2)	117 (35.6)	<0.01
ARB, No. (%)	168 (15.1)	36 (10.9)	<0.05
ACE-inhibitor, No. (%)	551 (49.4)	168 (51.1)	0.8
Furosemide, No. (%)	494 (44.3)	149 (45.3)	0.95
Spironolactone, No. (%)	237 (21.2)	49 (14.9)	<0.01
β-blockers, No. (%)	290 (26.0)	42 (12.8)	<0.001
Calcium channel blockers, No. (%)	157 (14.1)	36 (10.9)	0.1
Acetylsalicylic acid, No. (%)	353 (31.6)	122 (37.1)	0.1
Oral anticoagulants, No. (%)	281 (25.2)	38 (11.6)	<0.001
Allopurinol, No. (%)	167 (15.0)	56 (17.0)	0.43

ARB, angiotensin-receptor blocker; ACE, angiotensin-converting enzyme.

Table 5. Pharmacological treatments used in the two study groups at discharge.

	≤85 years (1096 patients)	>85 years (329 patients)	P
Digoxin, No. (%)	274 (25.0)	111 (33.7)	<0.01
ARB, No. (%)	312 (28.5)	81 (24.6)	<0.05
ACE-inhibitors, No. (%)	200 (18.2)	61 (18.5)	0.8
Furosemide, No. (%)	756 (69.0)	231 (70.2	0.95
Spironolactone, No. (%)	308 (28.1)	81 (24.6)	<0.01
β-blockers, No. (%)	327 (29.8)	53 (16.1)	<0.001
Calcium channel blockers, No. (%)	149 (13.6)	28 (8.5)	0.1
Acetylsalicylic acid, No. (%)	345 (31.5)	117 (35.6)	0.1
Oral anticoagulants, No. (%)	268 (24.5)	40 (12.2)	<0.001
Allopurinol, No. (%)	218 (19.9)	58 (17.6)	0.43

ARB, angiotensin-receptor blocker; ACE, angiotensin-converting enzyme.

ences between groups (14.2±10.5 in old *vs* 14.0±9.4 in very old patients). During the stay in hospital, disability worsened more in very old subjects than in old ones (Barthel Index score: –7.6±15.5 *vs* –5.0±12.8; P<0.01). NYHA class improved in both groups (Figure 1). Only 5.9% of old and 8.9% of very old patients were discharged in NYHA class IV (P<0.0001).

Sixty patients (4.4%) died during hospitalization, the majority (75%) of them because of cardiovascular events. The mortality rate was lower in the old patients (3.3%) than in the very old ones (7.0%) (P<0.0001). Twenty-six of the very old patients (7.9%) had a poor outcome (in-hospital death or worsening of clinical condition that required transfer to the Intensive Care Unit).

By means of multivariable analysis, patients with less disability (Barthel Index) had a significantly lower risk of adverse outcome. A trend toward worse outcome was present in patients with higher NYHA class at hospital admission, and those with severe cognitive impairment/dementia (Figure 3).

Table 6. Difference in prevalence of treatment with digoxin in patients with atrial fibrillation between admission and discharge.

	≤85 years with AF on admission (454 patients)		P	>85 years with AF on admission (159 patients)		P
	On admission, No. (%)	At discharge, No. (%)		On admission, No. (%)	At discharge, No. (%)	
Digoxin	218 (50.5)	183 (44.7)	n.s.	85 (53.0)	66 (41.5)	n.s.

AF, atrial fibrillation; n.s., not significant.

Table 7. Distribution of comorbidities in the two groups of patients.

	≤85 years (1090 patients)	>85 years (328 patients)	P
Renal insufficiency, No. (%)			
Not present	635 (58.3)	157 (47.9)	<0.001
GFR 60-89 mL/min	164 (15.0)	49 (14.9)	0.96
GFR 30-59 mL/min	195 (17.9)	70 (21.3)	0.16
GFR 15-29 mL/min	92 (8.4)	51 (15.5)	<0.001
Hemodialysis	4 (0.4)	1 (0.3)	0.4
Diabetes, No. (%)	386 (35.4)	74 (22.6)	<0.001
Hypertension, No. (%)			
Not present	404 (37.1)	122 (37.2)	0.81
Mild (≥140/85-159/99 mmHg)	379 (34.8)	111 (33.8)	0.71
Moderate (≥160/100-179/109 mmHg)	250 (22.9)	74 (22.6)	0.64
Severe (≥180/110 mmHg)	57 (5.2)	21 (6.4)	0.2
Chronic obstructive pulmonary disease,* No. (%)	277 (25.5)	79 (23.8)	0.7
Dementia,° No. (%)			
Not present	437 (40.1)	68 (20.7)	<0.001
Mild (3-4)	108 (9.9)	41 (12.5)	0.28
Moderate (5-6)	123 (11.3)	47 (14.3)	<0.001
Severe (≥7)	55 (5.0)	25 (7.6)	<0.001
Chronic inflammatory diseases, No. (%)	81 (7.4)	25 (7.6)	0.47
Cachexia, No. (%)	51 (4.7)	44 (13.4)	<0.001
Anemia (WHO criteria), No. (%)	420 (38.5)	152 (46.3)	<0.05
Cerebrovascular disease, No. (%)	199 (18.2)	27 (8.2)	<0.05
Cancer, No. (%)	112 (10.3)	33 (10.1)	0.92
Disability: Barthel index,# No. (%)			
0-30	132 (12.1)	98 (29.9)	<0.001
31-60	213 (19.5)	72 (21.9)	0.48
61-100	436 (40.0)	73 (22.2)	<0.001

GFR, glomerular filtration rate. *Diagnosed on the basis of history, clinical examination and/or instrumental investigations; °evaluated on the basis of 950 Pfeiffer tests; #the lower the index, the greater the disability.

Discussion

The main findings of this study are that CHF in very old patients was, in comparison to that in relatively younger patients: i) more frequently due to systemic hypertension and less frequently to dilated cardiomyopathy; ii) characterized by a higher prevalence of comorbidities, namely, impaired renal function, cachexia and disability; and iii) associated with greater in-hospital deterioration of disability and mortality.

Very old patients were treated less frequently with β-blockers, angiotensin- receptor blockers, aldosterone antagonists and oral anticoagulants, but more frequently with digoxin.

Age is unquestionably a very important variable to be taken into account in the population admitted to hospital, especially in Internal Medicine wards. The data of the CONFINE study are very similar to those of the Italian National Health System database, indicating that majority of patients admitted for CHF are over 70 years old. However, roughly one fourth of these patients are over 85 years and six out of ten are re-admitted to hospital once or more within 1 year. The clinical characteristics of these patients have rarely been described in detail, mainly because they are generally excluded from large clinical trials.[11] This real-life study describes the clinical characteristics of very old patients admitted to Internal Medicine wards because of CHF.

Not surprisingly, compared to CHF subjects ≤85 years old, those older than 85 years were found to be more critically ill, with a higher prevalence of congestion and renal function impairment, and tended to improve more slowly during hospitalization, thus being discharged with a slightly higher NYHA. Atrial fibrillation was frequently observed in very old patients and its overall prevalence was higher than that reported in CHF clinical trials, once again underlying the difference between the world of trials and that of real life. Conversely, the prevalence of CHF with preserved ejection fraction was about 30% in the older group, which is consistent with other studies.[12]

The present study also highlights important differences in treatment between old and very old patients. The latter were undertreated with β-blockers, despite these being generally recommended in elderly patients because they are relatively well tolerated.[13] It must be noted, however, that some data show greater benefits with β-blockers in patients with systolic heart failure, whereas left ventricular ejection fraction is frequently preserved in older patients.[14] Angiotensin-converting enzyme inhibitors were equally used in old and very old patients, despite doubts recently raised regarding their benefits in old patients.[15] By contrast, angiotensin-receptor blockers were underused in older patients, which can be ascribed to the fear of renal function deterioration in old patients already being treated with angiotensin-converting enzyme inhibitors for comorbidities. The ob-

Table 8. Changes in the prevalences of some comorbidities in the two groups between admission and discharge.

	≤85 years					>85 years				
	On admission N=1090		At discharge N=977			On admission N=328		At discharge N=296		
	No.	%	No.	%	P	No.	%	No.	%	P
Renal insufficiency, No. (%)										
Not present	635	58.3	588	60.2	n.s.	157	47.9	150	50.7	n.s.
GFR 60-89 mL/min	164	15.0	158	16.2	n.s.	49	14.9	47	15.9	n.s.
GFR 30-59 mL/min	195	17.9	156	16.0	n.s.	70	21.3	56	18.9	n.s.
GFR 15-29 mL/min	92	8.4	70	7.2	n.s.	51	15.5	42	14.2	n.s.
Hemodialysis, No. (%)	4	0.4	5	0.5	n.s.	1	0.3	1	0.3	
Hypertension, No. (%)										
Not present	404	39.2	513	56.4	0.001	122	39.9	154	54.1	0.05
Mild: ≥140/85-159/99 mmHg	379	34.3	369	34.8	n.s.	111	33.1	116	38.3	n.s.
Moderate: ≥160/100-179/109 mmHg	250	21.9	91	8.5	0.001	74	20.7	26	26.0	0.01
Severe: ≥180/110 mmHg	57	4.6	4	0.3	0.001	21	6.3			
Dementia, No. (%)										
Not present	922	83.3	832	83.8	n.s.	192	55.1	171	54.0	n.s.
Mild (3-4)	102	9.6	88	9.4	n.s.	64	20.2	70	24.7	n.s.
Moderate (5-6)	42	4.5	36	4.4	n.s.	47	16.1	38	14.4	n.s.
Severe (≥7)	24	2.6	21	2.5	n.s.	25	8.7	17	7.0	n.s.
Anemia (WHO criteria), No. (%)	420	38.6	348	36.0	n.s.	152	43.7	122	40.7	n.s.

GFR, glomerular filtration rate; n.s., not significant.

served underuse of anti-aldosterone drugs can be explained by the concomitant use of angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, β-blockers, and the presence of impaired renal function, which could lead to life-threatening hyperkaliemia, as previously reported.[16] Digoxin was used in a large proportion of patients (around 30%) and more frequently in the very old group. This is in line with the current still large use of this drug, despite the alert of a narrower therapeutic window in old patients.[17] The higher prevalence of atrial fibrillation in the older group probably does not account for this tendency and this is underlined in both groups by the reduction of digoxin therapy at discharge of the patients who were on digoxin treatment at admission.

Patients over 85 years had a greater burden of comorbidities in comparison with relatively younger subjects. Nearly 30% of patients over 85 years old had had a previous transient ischemic attack or stroke, which contrasts with an approximate 11% prevalence of cerebrovascular events in the general population of the same age of either sex.[18] A greater prevalence of stroke in the heart failure population has already been reported[19] and it has been shown that the risk of stroke increases with depression of ventricular function.[20] This adds to the doubled increase of risk per decade above the age of 55.[21]

Renal function was preserved in about 60% of old patients and nearly 50% of very old patients, yet glomerular filtration rate below 30 mL/min occurred more frequently in very old patients, which is in line with data available in the literature.[22]

Recent studies have shown that a body mass index between 30 and 34.9 kg/m^2 is associated with better outcome in patients with CHF,[23] whereas cachexia and malnutrition make prognosis worse.[24] In the present study, cachexia was observed in 4.7% of old and 15% of very old subjects. Moreover, older patients had more frequent and more severe anemia, a condition that is known to be commonly associated with CHF[25] and negatively affects prognosis.[26] This latter was not confirmed in our study in the subgroup of very old patients, probably due to limited statistical power of the multivariable analysis that we conducted.

Deterioration of cognitive function in CHF has already been reported,[27] and age is likely the strongest link between these conditions.[28] Because cognitive deterioration correlates with disability,[29] it is not surprising that the latter is more evident and more frequent in older subjects. Moreover, hospitalization tself brings about a further worsening of disability and this effect was more pronounced in the older group of the present study. Cognitive impairment/dementia and disability were the strongest independent predictors of

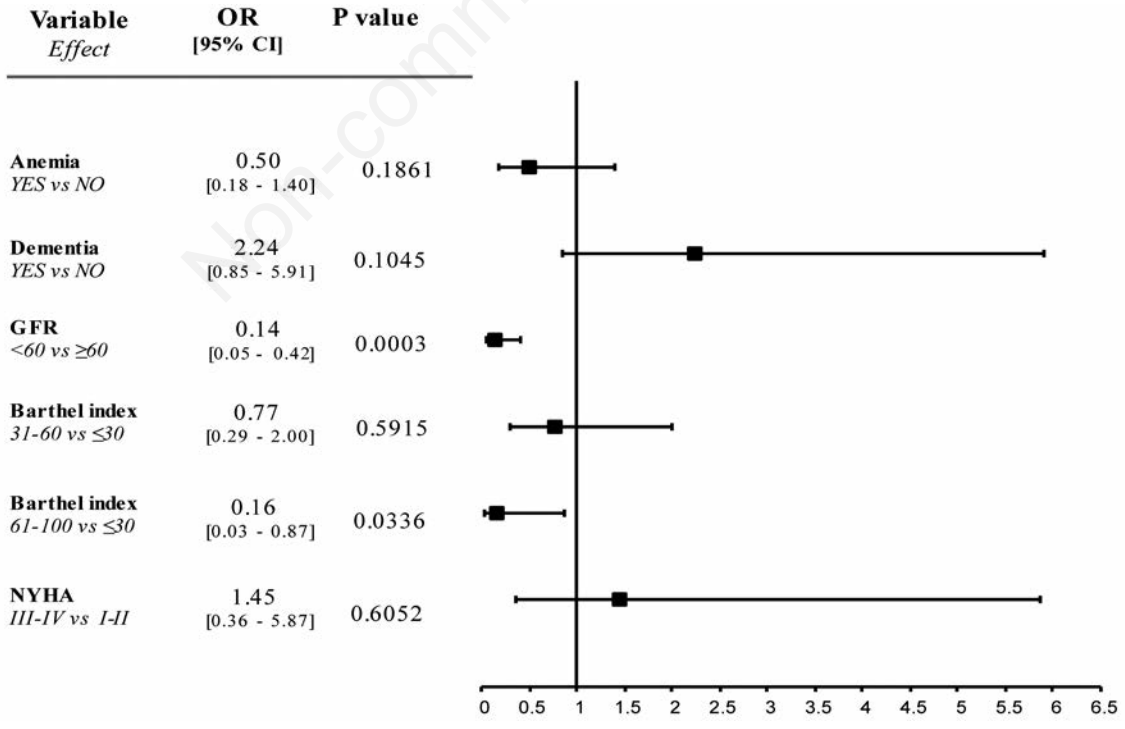

Figure 3. Multivariable analysis investigating correlations between negative hospital outcome (all-cause death or clinical worsening) and a number of variables in the group of very old patients. OR, odds ratio; CI, confidence interval; GFR, glomerular filtration rate; NYHA, New York Heart Association.

in-hospital adverse outcome in very old patients enrolled in our study.

Conclusions

The present survey shows that there are important age-related differences between patients with CHF, which may have an impact on therapeutic strategies. These differences are mainly related to the presence of multiple morbid conditions, complications and altered cognitive status. Since these are usually criteria for exclusion from clinical trials, treatment of old and very old patients with CHF will remain empirical until prospective trials are available in which real-world elderly patients are included. The results of studies focused on these aspects might influence physicians' attitudes and lead to clinical, social and economic changes in the treatment of very old patients with CHF.

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