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Clinical variables affecting survival in patients with decompensated diastolic versus systolic heart failure

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Abstract *Background* The impact of various clinical variables on long-term survival of patients with acutely decompensated diastolic heart failure (DHF) compared to systolic heart failure (SHF) has not been sufficiently investigated. *Methods* Clinical, laboratory, electrocardiographic and echocardiographic data were collected and analyzed for all-cause mortality in 473 furosemide-treated patients aged ≥60 years, hospitalized for acutely decompensated HF. *Results* Diastolic heart failure patients ($n = 183$) were more likely to be older, female, hypertensive, obese, with shorter preexisting HF duration, atrial fibrillation, lower New York Heart Association (NYHA) class, lower maintenance furosemide dosages, and to receive calcium antagonists. The SHF group (290 patients) demonstrated prevailing coronary artery disease, nitrate or digoxin treatment, and electrocardiographic conduction disturbances ($P \leq 0.01$ in all comparisons). On median 35-month follow-up, the respective one-, three- and five-year survival rates were 82%, 48% and 33% in DHF versus 74%, 46% and 30% in SHF ($P = 0.3$). Higher furosemide daily dosage at discharge (OR = 1.24, 95% CI = 1.11–1.37, $P < 0.001$), increasing age (OR = 1.29, 95% CI = 1.09–1.54, $P = 0.003$), peripheral arterial disease (OR = 1.47, 95% CI = 1.02–2.13, $P = 0.043$), and a history of stroke (OR = 1.44, 95% CI = 0.98–2.1, $P = 0.066$) were most significantly associated with shorter survival in SHF. DHF, in turn, demonstrated higher NYHA class (OR = 2.52, 95% CI = 1.48–4.29, $P < 0.001$), history of non-advanced malignancy (OR = 2.51, 95% CI = 1.3–4.85, $P = 0.012$), and atrial fibrillation (OR = 1.6, 95% CI = 0.97–2.64, $P = 0.066$). Antilipid treatment (OR = 0.56, 95% CI = 0.3–1.02, $P = 0.049$) predicted better survival. *Conclusion* In-patients with acutely decompensated DHF differ from similar SHF subjects with respect to prognostic significance of a number of clinical variables. This observation might carry practical implications.

Key words heart failure – diastolic – systolic – prognosis – mortality

Introduction

Diastolic heart failure (DHF) is a clinical syndrome manifested by symptoms and signs of heart failure (HF), accompanied by normal left ventricular ejection fraction (LVEF) and diastolic dysfunction [3, 7, 26, 32, 34]. LVEF remains preserved in as many as 24% to 55% of HF cases [4, 5, 10, 15, 17, 19, 22, 23, 25, 27–29, 31, 33], and with time the percentage progressively

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increases [25]. Clinical profile of DHF patients substantially differs from those with systolic HF (SHF). Thus, DHF patients are more likely to be older, of female sex, hypertensive, obese, suffering from chronic obstructive pulmonary disease (COPD), atrial fibrillation or receiving calcium antagonists, compared to subjects with SHF [4, 5, 10, 15, 17, 19, 22, 23, 25, 27–29, 31, 33]. Nevertheless, clinical manifestations of HF are ameliorated in DHF patients compared to those with SHF [5, 17, 31]. DHF patients are less likely to demonstrate coronary artery disease (CAD), left bundle branch block on electrocardiogram (ECG), as well as to receive angiotensin-converting enzyme inhibitors or digoxin [4, 5, 10, 15, 17, 19, 22, 23, 25, 27–29, 31, 33].

DHF is frequently associated with survival rates either better [15, 17, 22, 25, 27–29, 33] or similar [4, 5, 31] to those observed in SHF. Over recent decades, the survival rates were shown to improve in a majority of HF patients, except those with preserved LVEF [25]. However, the regimen of optimal management for DHF patients is still questionable [3, 7]. Information available on the impact of various clinical variables on the long-term survival in the context of DHF versus SHF is scarce [4, 25]. Part of the predictors of death among patients with reduced or preserved LVEF was found to be the same in a number of studies [4, 25]. These predictors included age, renal dysfunction, diabetes mellitus, anemia, peripheral arterial disease, dementia, and hyponatremia [4, 25]. However, while male gender predicted higher mortality rate in patients with preserved LVEF, this was not true for patients with SHF [25]. Furthermore, CAD was found to be associated with high mortality only in patients with reduced LVEF [25]. It is conceivable that the list is still incomplete, and additional clinical variables, not yet evaluated, might also be associated with higher mortality in DHF.

In particular, no sufficient information is available thus far regarding predictors of long-term mortality in furosemide-treated patients, who have been hospitalized for decompensated DHF. The present investigation was undertaken to define a profile of simple bedside variables and to evaluate their impact on long-term survival in such patients as compared to their SHF counterparts.

Methods

Study population

The study population included 473 randomly chosen patients aged ≥60 years, hospitalized for acutely decompensated HF as the primary diagnosis. HF was of various etiologies and was present for at least 3 months prior to admission. The patients had a New York Heart Association (NYHA) grade II-IV, and all of them were routinely maintained with furosemide. Diagnosis of chronic HF was based on data from previous hospitalizations and/or records from outpatient facilities consistent with modified Framingham criteria for HF [4, 24, 25]. Acute decompensation of HF was defined by the presence of an acute increase of shortness of breath (elevation of NYHA grade to III–IV), lung rales, pulmonary vascular enlargement and/or frank edema detected by chest X-ray at the time of admission [2, 15, 33]. Patients with advanced malignant diseases, significant heart-valve or pericardial disease, cor pulmonale, thyrotoxicosis or dialysis-dependent renal failure were excluded from this study. The study was carried out in accordance with the Declaration of Helsinki and was approved by the local Ethics Committee.

Data collection and analysis

On admission, demographic, clinical, ECG, chest X-ray and laboratory characteristics of the patients were recorded. Echocardiographic data were also collected from standard color two-dimensional and Doppler echocardiographic recordings. On discharge, the main underlying cause of HF, duration of hospital stay and recommended medications were registered. Following discharge, patients were contacted annually. At the end of the follow-up period, the collected data were subjected to statistical analysis. Prevalence and eventual association with all-cause mortality were evaluated for the entire patient group and for the SHF and DHF groups separately. Death was confirmed by hospital or outpatient death certificates.

Anemia was defined as hemoglobin <12 g/dl in females and <13 g/dl in males. Renal function was assessed by estimating glomerular filtration rate (GFR) using MDRD equation [21]. The inclusion cut-off for renal dysfunction was estimated GFR <60 ml/min/1.73 m^2 [1, 9]. Cardiac conduction disturbances included atrioventricular or bundle-branch block. SHF was defined as decreased LVEF (<50%). Isolated DHF was diagnosed according to the presence of signs or symptoms of HF simultaneously with preserved LVEF (≥50%) and evidence of diastolic dysfunction (impaired left ventricular relaxation, pseudonormal pattern or restrictive filling, according to the measurement of mitral inflow E to A velocities ratio and deceleration time of E wave) on echocardiogram [3, 7, 16, 26, 32, 34].

Statistical analysis

Statistical analysis was performed using BMDP statistical software [8]. Univariate analysis was applied

using Pearson's χ^2 test for statistical comparison of discrete variables. Analysis of variance (ANOVA) was used for continuous variables. To determine the prognostic significance of variables, survival curves were plotted using Kaplan–Meier method. Mantel–Cox and Breslow's tests were applied to evaluate significance of the differences between the curves. A $P \leq 0.05$ was considered significant. Variables significantly associated with survival ($P \leq 0.1$ by univariate analysis) were further evaluated by Cox proportional-hazards model for identification of parameters most significantly associated with mortality.

Results

Baseline characteristics

We investigated 473 HF patients, 290 (61%) with SHF and 183 (39%) with DHF. Their baseline characteristics are presented in Table 1. Hypertension was the most frequently observed primary underlying cause of DHF, while the main etiology of SHF appeared to be CAD. DHF patients demonstrated a shorter duration of preexisting HF (18.7 ± 24 months for DHF vs. 28.9 ± 25 months for SHF, $P < 0.001$), as well as a prolonged hospitalization time (7.3 ± 4 days for DHF vs. 6.3 ± 4 days for SHF, $P = 0.009$).

Older age, female sex, hypertension, obesity and atrial fibrillation were found more common in DHF compared to SHF ($P \leq 0.01$ for each). In contrast, CAD, higher NYHA grade and cardiac conduction disturbances were more prevalent in the SHF group ($P < 0.001$ in all comparisons). With respect to prevalence of diabetes mellitus, renal dysfunction, dyslipidemia, anemia, COPD, peripheral arterial disease, non-advanced malignancy and history of stroke, no statistically significant differences were observed between the DHF and SHF groups.

Compared to SHF patients, those with DHF showed an increased frequency of left ventricular hypertrophy and thicker interventricular septum, but fewer segmental wall motion abnormalities and a smaller left ventricular end-diastolic diameter on echocardiographic examination ($P < 0.001$ in each comparison).

Significant differences were also observed between the treatment regimens of the two groups. Thus, patients with DHF received lower daily furosemide dosages on admission and discharge ($P < 0.001$). These patients were more frequently discharged with prescription of calcium channel blockers ($P < 0.001$) or anticoagulants ($P = 0.01$). Finally, they were less likely to be treated with nitrates ($P < 0.001$), digoxin ($P = 0.004$) or antiplatelet agents ($P = 0.04$). Treatment regimens with other relevant medications were comparable in both groups.

Survival

Mean and median follow-up periods in the whole patient group were 47.5 months and 35 months, respectively. During the study period, 231 out of 473 (49%) patients died. The registered one-, three- and five-year survival rates were 77%, 47% and 32%. Fig. 1 illustrates the survival curves of the DHF vs. SHF groups. The respective mean survival durations as well as the one-, three- and five-years survival rates showed no statistically significant difference between the two groups (49 months, 82%, 48% and 33% for DHF, and 45.9 months, 74%, 46% and 30% for SHF, $P = 0.3$).

Association of various variables with survival: univariate analysis

Variables associated with shorter survival within the entire group were as follows: longer period of preexisting HF ($P = 0.04$), higher NYHA class ($P = 0.002$), anemia ($P = 0.05$), renal dysfunction ($P < 0.001$), atrial fibrillation ($P = 0.008$), COPD ($P = 0.01$), peripheral arterial disease ($P = 0.002$), history of stroke ($P = 0.01$), hypermagnesemia ($P = 0.004$), higher furosemide dosages (>80 mg/day) on discharge ($P = 0.02$), and digoxin treatment ($P = 0.03$). Treatments with β-receptor blockers ($P = 0.01$) or antiplatelet agents ($P = 0.004$) were, by contrast, associated with better survival.

When the two groups were analyzed separately, shorter survival in the SHF group (Table 2) was associated with higher NYHA class ($P = 0.046$), presence of CAD ($P = 0.03$), renal dysfunction ($P = 0.006$), COPD ($P = 0.01$), history of stroke ($P = 0.01$), peripheral arterial disease ($P < 0.001$), higher furosemide dosages ($P < 0.001$), and abnormal levels of serum magnesium (either hypomagnesemia or hypermagnesemia, $P = 0.002$). By contrast, treatment with β-receptor blockers ($P = 0.03$) predicted better survival in SHF.

In the DHF group (Table 3), shorter survival was associated with longer period of preexisting HF, higher NYHA class, renal dysfunction, history of non-advanced malignancy, atrial fibrillation and treatment with digoxin ($P = 0.048$, 0.008, 0.04, 0.02, 0.001 and 0.02, respectively). By contrast, antiplatelet and antilipid agents administration predicted longer survival ($P = 0.04$ and 0.01, respectively).

Table 1 Baseline characteristics of the entire group and of SHF versus DHF groups

Variable	Entire group (n = 473)	SHF group (n = 290)	DHF group (n = 183)	P^a
Age (years), mean ± SD	73.4 ± 10	72.2 ± 10	75.3 ± 10	<0.001
Female sex	43.3%	30.7%	63.4%	<0.001
Primary underlying cause of chronic HF				
Ischemic	61.7%	92.8%	12.6%	<0.001
Hypertensive	28.8%	2.4%	70.5%	
Others	9.5%	4.8%	16.9%	
Preexisting HF duration (months), mean ± SD	24.9 ± 25	28.9 ± 25	18.7 ± 24	<0.001
Duration of hospitalization (days), mean ± SD	6.7 ± 4	6.3 ± 4	7.3 ± 4	0.009
NYHA functional class (prior to HF decompensation)				
II	53.9%	46.9%	65%	<0.001
III–IV	46.1%	53.1%	35%	
Comorbid conditions				
Hypertension	78.6%	71.7%	89.6%	<0.001
Coronary artery disease	75.5%	92.4%	48.6%	<0.001
Dyslipidemia	56%	56.6%	55.2%	0.8
Diabetes mellitus	46.9%	48.3%	44.8%	0.5
Anemia	56.7%	57.6%	55.2%	0.6
Renal dysfunction	69.6%	70.3%	68.3%	0.6
Chronic atrial fibrillation	21.8%	17.9%	27.9%	0.01
Chronic obstructive pulmonary disease	26.4%	28.3%	23.5%	0.3
Obesity (body mass-index ≥30 kg/m^2)	26.7%	19.6%	38.1%	<0.001
History of stroke	22.6%	22.4%	23%	0.9
Peripheral arterial disease	24.1%	26.2%	20.8%	0.2
History of non-advanced malignancy	11.6%	11.7%	11.5%	0.9
Clinical data				
Jugular venous distension	42.1%	41.7%	42.6%	0.8
Bilateral ankle edema	42.3%	41.4%	43.7%	0.6
Electrocardiographic findings				
Sinus rhythm	69.8%	74.8%	61.7%	0.003
Atrial fibrillation	27.1%	22.1%	35%	0.003
Other rhythm patterns	3.1%	3.1%	3.3%	0.6
Cardiac conduction disturbances	54.3%	60.7%	44.3%	<0.001
Echocardiographic findings				
Left ventricular ejection fraction (%), mean ± SD	41.2 ± 14.4	31.3 ± 8	57 ± 5	<0.001
Left ventricular hyperthrophy	53.7%	35.5%	82.5%	<0.001
Segmental wall motion abnormalities	69.1%	93.8%	30.1%	<0.001
Interventricular septal thickness (mm), mean ± SD	12.3 ± 2.5	11.4 ± 2.2	13.5 ± 2.2	<0.001
Left ventricular end-diastolic diameter (mm), mean ± SD	51 ± 8	55 ± 9	46 ± 5	<0.001
Laboratory data				
Estimated GFR (ml/min/1.73 m^2), mean ± SD	51.8 ± 23	51.1 ± 24	52.9 ± 21	0.4
Serum creatinine (normal <107 μmol/l), mean ± SD	124 ± 62	133 ± 62	115 ± 53	<0.001
Serum C-reactive protein (normal 0–5 mg/dl), mean ± SD	40.4 ± 56	41.4 ± 59	39.2 ± 54	0.8
Blood hemoglobin (g/dl), mean ± SD	12.2 ± 2	12.3 ± 2	12 ± 2	0.07
Hyponatremia (<135 mmol/l)	17.5%	17.2%	18%	0.9
Hypokalemia (<3.3 mmol/l)	4%	3.4%	6.6%	0.2
Hypomagnesemia (<0.7 mmol/l)	4.9%	3.8%	6.6%	0.2
Hypermagnesemia (>1.1 mmol/l)	4.7%	5.9%	2.7%	0.1
Medications prescribed on discharge				
Furosemide daily dosage (mg), mean ± SD				
On admission	67 ± 41	73 ± 44	58 ± 34	<0.001
On discharge	87 ± 49	94 ± 53	74 ± 40	<0.001
β-receptor blockers	57.9%	59.7%	55.2%	0.4
Angiotensin-converting enzyme inhibitors	50.1%	48.3%	53%	0.4
Angiotensin receptor blockers	13.7%	15.9%	10.4%	0.1
Calcium channel blockers	31.3%	23.4%	43.7%	<0.001
Nitrates	40%	46.2%	30.1%	<0.001
Digoxin	18.8%	23.1%	12%	0.004
Thiazide diuretics	11.4%	10%	13.7%	0.2
Aldosterone antagonists	11%	13.1%	7.7%	0.07
Antiarrhythmics	19%	20.3%	16.9%	0.4
Antiplatelet agents	72.3%	75.9%	66.7%	0.04
Anticoagulants	24.7%	20.7%	31.1%	0.01
Antilipid agents	43.6%	46.2%	39.3%	0.2

Values are percentages of presenting cases unless stated otherwise
[a]Statistical comparison between groups of patients with SHF versus DHF. *SHF* systolic heart failure, *DHF* diastolic heart failure, *HF* heart failure, *SD* standard deviation, *NYHA* New York Heart Association, *GFR* glomerular filtration rate

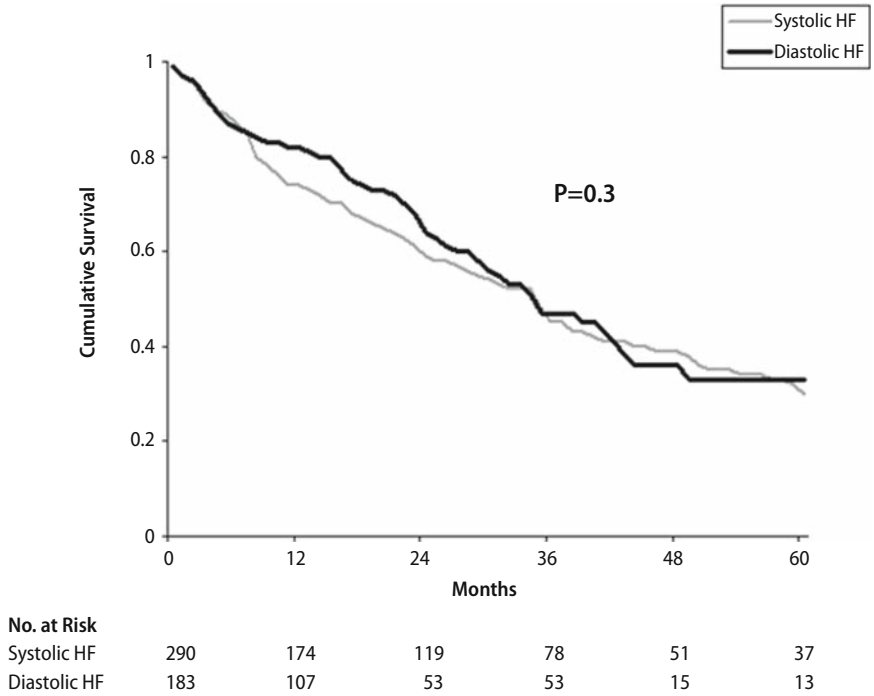

Fig. 1 The Kaplan–Meier estimates of survival in the diastolic versus systolic heart failure (HF) groups

No. at Risk						
Systolic HF	290	174	119	78	51	37
Diastolic HF	183	107	53	53	15	13

Variables most significantly associated with survival

When Cox proportional-hazards model was applied to scrutinize the entire patient group (Table 4), the following variables emerged as the most significantly associated with lower survival: atrial fibrillation ($P = 0.006$), higher NYHA class ($P = 0.007$), higher furosemide dosages on discharge ($P = 0.01$), peripheral arterial disease ($P = 0.015$), renal dysfunction ($P = 0.023$), non-advanced malignancy ($P = 0.026$), and increasing age ($P = 0.044$).

Variables most significantly associated with mortality in SHF differed from those in DHF group (Table 4). In SHF, higher furosemide daily dosages ($P < 0.001$), older age ($P = 0.003$), peripheral arterial disease ($P = 0.043$), and history of stroke ($P = 0.066$) were most significantly associated with shorter survival. In the DHF group, higher NYHA class ($P < 0.001$), history of non-advanced malignancy ($P = 0.012$), and atrial fibrillation ($P = 0.066$) were most significantly associated with poor survival, while treatment with antilipid agents predicted better survival ($P = 0.049$).

Discussion

The main objective of the present investigation was to compare the profiles of the patients with DHF and SHF with respect to their bedside clinical variables, and to evaluate their impact on long-term survival. We have found that the two groups substantially differed in their demographic, clinical, ECG and echocardiographic characteristics. Although the two groups did demonstrate similar results with respect to the long-term survival, different clinical variables were associated with prolongation of their vitality.

In relevant publications, the reported diversity in prevalence and prognosis of DHF vary, depending on the methods used for diagnostic purposes, the study design, the cut-off value of LVEF, and the disease process underlying DHF [4, 25, 34]. HF with preserved LVEF has been studied in various distinct populations. These included outpatients [5, 10, 19], inpatients hospitalized for disorders other than HF [15, 22], inpatients with new onset HF [4], patients hospitalized for newly diagnosed or worsened HF [23, 25, 28, 29, 33], a whole population of patients admitted to cardiology service [31], males [30], African–American patients [18], and patients older than 70 years [27]. In our present investigation, we concentrated on a different study population, consisting of older furosemide-treated patients diagnosed for chronic HF prior to hospitalization for acute HF decompensation and subsequently subjected to extensive follow-up period. Their relatively long pre-existing HF course was intended to minimize diagnostic bias, common in a setup of a newly diagnosed DHF. Moreover, all of our patients had a rather severe clinical profile of HF, thus requiring a maintenance furosemide treatment.

Table 2 Variables associated with survival in the systolic heart failure group (univariate analysis)

Variable	Mean survival duration (months)	*P*
Age group (years)		0.4
<70	51.1	
70–80	46.9	
≥80	32	
Gender		0.5
Male	44.5	
Female	47.9	
New York Heart Association functional class		0.046
II	53.3	
III–IV	39.7	
Coronary artery disease		0.03
Yes	43.7	
No	73.1	
Renal dysfunction		0.006
Yes	40	
No	58	
Chronic obstructive pulmonary disease		0.01
Yes	39	
No	48.8	
History of stroke		0.01
Yes	34.6	
No	49	
Peripheral arterial disease		<0.001
Yes	31.3	
No	50.5	
Serum magnesium		0.002
Hypomagnesemia	35.4	
Normal	47.3	
Hypermagnesemia	28.3	
Furosemide daily dosage on discharge (mg)		<0.001
≤80	53	
>80	32	
Treatment with β-receptor blockers		0.03
Yes	53.1	
No	40.3	

Table 3 Variables associated with survival in the diastolic heart failure group (univariate analysis)

Variable	Mean survival duration (months)	*P*
Age group (years)		0.1
<70	57.7	
70–80	44.5	
≥80	35.5	
Gender		0.8
Male	46.2	
Female	48.3	
Preexisting heart failure duration (years)		0.048
≤2	49.5	
>2	42.7	
New York Heart Association functional class		0.008
II	56.9	
III–IV	24.9	
Renal dysfunction		0.04
Yes	41	
No	60	
History of non-advanced malignancy		0.02
Yes	25	
No	52.5	
Atrial fibrillation		0.001
Yes	59.3	
No	35.7	
Treatment with digoxin		0.02
Yes	34.6	
No	51.7	
Treatment with antiplatelet agents		0.04
Yes	58.8	
No	34.6	
Treatment with antilipid agents		0.01
Yes	63.5	
No	41.6	

Similar to data from previous relevant studies, our DHF patients were more likely to be older, females, hypertensive, obese, with atrial fibrillation, lower NYHA class, and receiving calcium channel blockers [4, 5, 10, 15, 17, 19, 22, 23, 25, 27–29, 31, 33]. On the other hand, SHF patients were more likely to suffer from CAD, cardiac conduction disturbances as well as to receive nitrates, digoxin or antiplatelet agents [4, 5, 10, 15, 17, 19, 22, 23, 25, 27–29, 31, 33]. Furthermore, the respective mean daily furosemide dosages on admission (58 vs. 73 mg) and discharge (74 vs. 94 mg) were lower in the DHF group compared to the SHF patients. In addition, our DHF patients were more frequently treated with anticoagulants, probably due to the higher prevalence of atrial fibrillation, compared to previous reports [22, 29, 31].

The preexisting HF period was shorter in our DHF patients compared to the SHF group. Similarly, abridged or comparable preexisting diagnosis periods were previously reported for patients hospitalized

Table 4 Variables most significantly associated with low survival (Cox proportional-hazards model)

Variable	*P*	Odds ratio	95% confidence interval
Entire group			
Atrial fibrillation	0.006	1.51	1.13–2.01
New York Heart Association grade	0.007	1.46	1.11–1.93
Furosemide daily dosage on discharge[a]	0.01	1.14	1.04–1.26
Peripheral arterial disease	0.015	1.47	1.09–1.99
Renal dysfunction	0.023	1.42	1.04–1.95
History of non-advanced malignancy	0.026	1.56	1.07–2.27
Age[b]	0.044	1.17	1.0–1.37
Systolic heart failure group			
Furosemide daily dosage on discharge[a]	<0.001	1.24	1.11–1.37
Age[b]	0.003	1.29	1.09–1.54
Peripheral arterial disease	0.043	1.47	1.02–2.13
History of stroke	0.066	1.44	0.98–2.1
Diastolic heart failure group			
New York Heart Association grade	<0.001	2.52	1.48–4.29
History of non-advanced malignancy	0.012	2.51	1.3–4.85
Treatment with antilipid agents	0.049	0.56	0.3–1.02
Atrial fibrillation	0.066	1.6	0.97–2.64

[a]For each 40 mg increment
[b]For each 10 years increment

with compensated or exacerbated HF [15, 28, 29]. The reason for the shorter duration of preexisting diagnosis in DHF might be a progressive decline of LVEF over time in part of the patients, eventually resulting in SHF [6]. Duration of hospital stay was longer in our DHF group (7.3 vs. 6.3 days). In one of a few relevant studies, the mean hospital stay tended to rise in patients with decreased versus preserved LVEF (15 vs. 13.6 days, respectively [31]), while in others it was similar in both groups (5 vs. 4.9 days [33], and 7.9 versus 7.5 days [28], respectively). Local differences in the routine of medical services may be, in part, responsible for the latter. On echocardiography, DHF in our patients was characterized by more frequent left ventricular hypertrophy, together with less common segmental wall motion abnormalities and lower values of left ventricular end-diastolic diameter, compared to the SHF group. Similar data have been previously reported [3, 5, 15, 17, 19, 34]. Most of these dissimilarities reflect the differences in pathophysiology between the two HF groups [3, 7, 34].

We have also found similar long-term survival in patients with DHF and their SHF counterparts, despite their milder clinical profile (lower NYHA class and lower maintenance furosemide dosages). In a number of previous studies, patients with preserved LVEF were reported to have either better [15, 17, 22, 25, 27–29, 33] or similar [4, 5, 31] prognosis, compared to those with reduced LVEF, the outcome greatly depending on the choice of inclusion criteria and diagnostic methods [4, 25, 34].

In the present investigation, one-year survival rates were found comparable in both groups and similar to those reported recently for hospitalized patients with new-onset HF [4]. On the other hand, information concerning the impact of various clinical variables on the long-term survival in the context of DHF vs. SHF was rather limited [4, 25]. Several predictors of death among patients with reduced and preserved LVEF were found to be similar in a handful of studies [4, 25]. These predictors included age, renal dysfunction, diabetes mellitus, anemia, peripheral arterial disease, dementia, and hyponatremia [4, 25]. However, while male sex was associated with a higher mortality rate only in patients with preserved LVEF, such association was evident only in patients with CAD and reduced LVEF [25].

In the present study, application of univariate statistical analysis combined with further evaluation by Cox proportional-hazards model enabled us to uncover profound differences in the statistical significance of the death predictors between SHF and DHF among our patients. In accordance with previously reported data [4, 25, 27, 33], only higher NYHA class and renal dysfunction were associated with shorter survival in both HF groups. One can conclude that renal insufficiency not only contributed to the severity of HF, but was also responsible for increased mortality of HF patients, by aggravating the impairment of their hemodynamics, electrolyte, acid base, immunological and other mechanisms [9].

In the SHF group, CAD, COPD, peripheral arterial disease, history of stroke, higher furosemide dosages (>80 mg/day) on discharge and abnormal levels of serum magnesium were also found to be significant predictors of poor survival, while treatment with β-receptor blockers was associated with better survival. On evaluation by Cox proportional-hazards model, higher furosemide daily dosages, older age, peripheral arterial disease and history of stroke emerged as the variables most significantly associated with shorter survival in SHF, this being consistent with the reported data [4, 11, 12, 14, 20, 25, 33].

Univariate analysis of the DHF group revealed longer preexisting HF duration, history of non-advanced malignancy, atrial fibrillation and treatment with digoxin to be significantly associated with poor survival. Of interest, treatment with antiplatelet or antilipid agents was also associated with better survival. In accordance with these results, two recent publications reported history of cancer [4] and atrial fibrillation [22] to be the predictors of death in HF patients with preserved LVEF. Moreover, in DHF patients, treatment with digoxin was associated with shorter survival [22], while use of aspirin [22] or statins [13, 22] with longer survival. This detrimental effect of atrial fibrillation on survival in DHF may encourage the attempts to convert atrial fibrillation to sinus rhythm in order to, hopefully, improve the prognosis. The observed negative association of digoxin treatment with survival by us and by others [22] was not evident in ambulatory patients with mild to moderate chronic DHF [1].

In conclusion, we have found that bedside clinical variables, as well as their ability to predict survival, differ between patients with decompensated DHF and SHF. The study might be defined as epidemiologic, since the subject cohort and the duration of surveillance were sufficient. It should be noted, however, that the main limitation of this study was that diastolic dysfunction was not assessed according to the currently used guidelines, since the study started before the latter were introduced. It is possible that improvement in management of relevant comorbidities (including renal dysfunction, peripheral arterial disease, atrial fibrillation, malignancy) as well as pharmacologic measures, such as diminishing maintenance dosages of furosemide in SHF, may substantially decrease these patients' mortality. Bearing in mind that optimal treatment of DHF patients has not been established thus far, these two main outcomes of the present study, namely limiting the digoxin treatment and maximizing the antiplatelet and antilipid agents, should be a subject of further research.

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