Original article

Impact on mortality of systolic and/or diastolic heart failure in the elderly—10 years of follow-up

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A R T I C L E   I N F O

A B S T R A C T

Background/purpose: There is a lack of long-term follow-up studies for elderly patients with heart failure (HF) in primary health care. There is conflicting information on prognostic differences between systolic or diastolic HF in elderly patients. Our aims were, first, to study the association between overall HF or types of HF and all-cause and cardiovascular mortality, and second, to explore the impact of N-terminal prohormone of brain natriuretic peptide (NTproBNP) and comorbidities.
Methods: A longitudinal, prognostic, observational primary health care study with 10 years of follow-up comparing an elderly patient population with HF (systolic and/or diastolic HF) to patients without HF was conducted. HF was diagnosed with echocardiography according to the European Society of Cardiology guidelines.
Results: Seventy-seven of 144 patients (102 women and 42 men; mean age, 77 years) had systolic and/or diastolic HF and were compared with 67 patients without HF (Reference group). During the 10-year follow-up, 71 (49%) patients died (women, 68%; men, 32%). In univariate Cox regression analysis, significant associations were found for overall HF [hazard ratio (HR), 1.86; 95% confidence interval (CI), 1.15 −3.01], isolated systolic HF (HR, 1.95; 95% CI, 1.06−3.61), and combined (systolic and diastolic) HF (HR, 3.28; 95% CI, 1.74−6.14) with all-cause mortality, but not for isolated diastolic HF. Similar results were found for cardiovascular mortality. In multivariate analysis, age (HR, 1.11; 95% CI, 1.06−1.17), kidney dysfunction (HR, 1.91; 95% CI, 1.11−3.29), smoking (HR, 3.70; 95% CI, 2.02−6.77), and NTproBNP (HR, 1.01; 95% CI, 1.00−1.02) significantly predicted all-cause mortality, but not any type of HF.
Conclusion: Patients diagnosed with systolic HF had a worse prognosis for mortality compared to the reference group, but in patients with diastolic HF the prognosis for mortality was similar with that in the reference group. NTproBNP was a valuable prognostic factor in elderly patients. Emphasis should be placed on kidney dysfunction and smoking/having smoked.

1. Introduction

In the elderly population (>75 years), the prevalence of heart failure (HF) is about 10%.[1] The prognosis for patients with HF is poor, comparable to a diagnosis of cancer.[2] Severe systolic HF has the most serious prognosis,[3] but whether diastolic HF has the same ominous prognosis as systolic HF in both younger and elderly patients is a matter of debate.[3–5] Elderly patients, especially females, are known to more often have diastolic HF than younger patients.[6]

However, most HF studies on prognosis are based on younger patients (<70 years) treated in the hospital,[7] but there is limited and conflicting information on prognostic differences between systolic or diastolic HF in elderly patients. Echocardiography is still the gold standard for diagnosis of HF, but there is limited use of echocardiography in primary health care (PHC) so many of these patients may be misdiagnosed and misclassified for prognostic reasons.[8] In PHC, elderly patients often have serious comorbidities, and the contributions of these comorbidities to the prognosis of patients with HF are often overlooked.[9] N-terminal prohormone of brain natriuretic peptide (NTproBNP) is a biomarker used to exclude HF,[10] but is also frequently used for prognostic purposes.[11] Its value in predicting mortality in elderly patients with systolic and/or diastolic HF requires further evaluation.

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There is a lack of long-term follow-up studies for elderly patients with HF in the PHC setting with regard to all-cause as well as cardiovascular mortality, and the prognostic impact of comorbidities.[12] The comorbidities may influence the prognosis beyond the type of HF in the short term; therefore, different follow-up periods need to be evaluated.

1.1. Aims

The primary objective of this study was to investigate the association between overall HF or specific types of HF and all-cause and cardiovascular mortality. The secondary objective was to explore the impact of NTproBNP and comorbidity on the association between overall HF or different types of HF and the risk for all-cause and cardiovascular mortality.

2. Methods

2.1. Study population

Patients were recruited from one PHC selected from northern Sweden between March 30, 2000 and March 11, 2003. The PHC has a catchment area of approximately 7800 inhabitants, of whom many are of advanced age. For many years, a computer-based registry of all patients with a diagnosis of HF had been used by the PHC. In 2001, this registry included 150 patients with a suspected diagnosis of HF on clinical grounds. The patient population comprised both registry patients and incident cases with suspected HF identified by the general practitioner (GP) at the PHC during the recruitment period. All participants had symptoms (mainly dyspnea) indicating chronic HF and were evaluated clinically by a GP prior to being referred for an echocardiography (MO) and subsequent cardiovascular consultation. The study cardiologist (KB) confirmed or refuted the diagnosis of HF based on the GP's pre-specified HF record, echocardiography results, and hospital records.

2.2. Diagnosis and types of HF

Global left ventricular systolic function was assessed as normal or depressed including mildly, moderately, or severely depressed. Normal systolic function corresponded to an ejection fraction (EF) of $\geq$55%, and severely depressed systolic function was considered to be an EF of <30%.

To evaluate the diastolic function (1) we used the mitral valve inflow pattern as the ratio of early and atrial filling velocities of the left ventricle; (2) the pulmonary vein flow was examined in the apical four-chamber view in the right upper pulmonary vein; and (3) we used the isovolumic relaxation time measured in the four-chamber view with the cursor placed between the aortic valve and the mitral valve.

In summary, if any of the above-described diastolic variables were abnormal, then diastolic dysfunction was established[13–15] (see Table 1).

Diagnosis of HF was established according to the European guidelines.[15] Patients diagnosed with left ventricular dysfunction alone had abnormal systolic and/or diastolic LV function, but had symptoms considered to be caused primarily by factors other than cardiac diseases.

We classified 170 patients (121 women and 49 men) as having HF (systolic and/or diastolic HF) or not having HF (Fig. 1). This patient population has been described in detail previously.[16]

In the present longitudinal, prognostic, observational study, 144 patients from the study population were included. Patients diagnosed with left ventricular dysfunction were excluded (Fig. 1). Of the 144 included patients, 77 had overall HF (systolic and/or

Table 1
Distribution of echocardiographic variables for systolic and diastolic HF.[a]

Diagnostic variables	Systolic HF ($n = 28$)	Diastolic HF ($n = 28$)
EF $\geq$ 55%	3	28
EF 30−<55%	23	0
Abnormal E/A		15
Abnormal IVRT		13
Abnormal S/D		5
Normal E/A	13	9
Normal IVRT	8	9
Normal S/D	9	15

E/A = ratio of early (E) and atrial (A) filling; EF = ejection fraction; HF = heart failure; IVRT = isovolumic relaxation time; S/D = ratio of systolic (S) and diastolic (D) components in the pulmonary vein inflow.

[a] Classification for diastolic HF is as follows. The E/A ratio was classified as age-dependent and considered abnormal when $E/A < 1$ (40−49 years), $E/A < 0.9$ (50−59 years), $E/A < 0.8$ (60−69 years), $E/A < 0.7$ (70−80 years), and $E/A < 0.7$ (>80 years).[1] The relation between the S and D components of the pulmonary vein inflow was assessed and $S/D < 1$ was considered abnormal in age > 60 years and $S/D < 0.9$ was considered abnormal in age < 60 years. The IVRT value was also classified by age as follows: IVRT >85 milliseconds (40−49 years), IVRT > 90 milliseconds (50−59 years), IVRT > 95 milliseconds (60−69 years), and IVRT > 100 milliseconds (>70 years) is abnormal value and <70 ms is abnormal in all ages.[13,14]

diastolic HF) and were compared with 67 patients with no HF (reference group). The types of HF were defined as follows: overall HF included the three types of HF—isolated systolic HF, isolated diastolic HF, or combined systolic/diastolic HF (combined HF).

In short, details of the patients' medical history—such as hypertension, myocardial infarction (MI), atrial fibrillation (missing, $n = 30$), valvular heart disease, stroke, pulmonary disease, kidney dysfunction (creatinine > 100 μmol/L; missing, $n = 5$), diabetes (both types 1 and 2), smoking habits (both smoker and ex-smoker, missing, $n = 10$), use of alcohol (yes/no; missing, $n = 16$), weight (missing, $n = 8$), symptoms, and evidence-based medical treatment associated with prognosis—were collected from the GP's case record when the patients were examined at baseline.

2.3. NTproBNP

For analysis of NTproBNP, blood samples (plastic EDTA tubes) were taken from fasting patients who had rested for 20 minutes. After 5 minutes, the samples were centrifuged (1500−2000 × g) for 10 minutes at 4°C then stored frozen at −70°C. NTproBNP was analyzed with Roche Elecsys proBNP immunoassay (Roche Diagnostic Corporations, Indianapolis, Indiana, USA; NtproBNP with missing information, $n = 11$).

2.4. Outcome classification

Death certificates were used to identify all-cause mortality, and cardiovascular mortality was defined as International Classification of Diseases-10 codes 100−199. The same classification was used for both 3-year mortality and the 10-year follow-up (median, 4.17 years) for the 144 patients in this study.

2.5. Statistical analysis

Baseline characteristics were described as frequencies or means and standard deviations. Differences between groups were tested with the Student t test for normally distributed data, Mann−Whitney U test was used for nonnormally distributed continuous variables, and the Chi-square test was used for categorical variables. The association between baseline characteristics and mortality for 3-year was analyzed with logistic regression analysis and at 10 years of follow-up with Cox regression analysis. In multivariate logistic or Cox regression analyses, Model 1 included