Chronic heart failure in the very elderly: Clinical status, survival, and prognostic factors in 188 patients more than 70 years old

Mariantonietta Cicoira, MD, Constantinos H. Davos, MD, PhD, Viorel Florea, PhD, DSc, Waqar Shamim, MD, Wolfram Doehner, MD, Andrew J. S. Coats, DM, and Stefan D. Anker, MD, PhD
London, United Kingdom, Verona, Italy, and Berlin, Germany

Background Chronic heart failure (CHF) is a frequent disease with a dismal prognosis, but little is known about survival in the very elderly. There are no data on the prognostic value of cardiopulmonary exercise testing in this population. We aimed to assess exercise capacity, survival, and prognostic parameters in elderly patients with CHF.

Methods We evaluated 188 patients with CHF >70 years old (mean 77 ± 4 years, range 70-94 years) seen at our heart failure clinic between March 1992 and June 1998. A cardiopulmonary exercise test was performed in 102 patients (peak VO₂ 15.3 ± 4.7, VE/VCO₂ slope 39.6 ± 15.01). All patients were followed up for at least 12 months. The prognostic end point of the study was all-cause mortality.

Results At the end of follow-up (16 ± 10 mo, range 12-41 mo), 67 patients (35.6%) had died (1-year mortality rate 26% [95% confidence interval 20.32]). In univariate analysis New York Heart Association class (NYHA) (relative risk [RR] = 2.56, P < .0001), VE/VCO₂ (RR = 1.041, P < .0001), peak VO₂ (RR = 0.87, P = .0007), and fractional shortening (RR = 0.95, P < .0001) predicted mortality. Peak VO₂ predicted mortality independently of age, NYHA class, and left ventricular ejection fraction. A subgroup of 12 patients with dynamic left ventricular outflow tract obstruction during stress had an excellent outcome, with a 100% survival at the end of follow-up (mean 16 ± 7 mo, range 12-39 mo).

Conclusions The prognosis in elderly patients with CHF is poor. Valid exercise testing results can be obtained in more than 50% of elderly patients with CHF. NYHA class and peak VO₂ are the strongest prognostic factors in this population.

(Am Heart J 2001;142:174-80.)
elderly patients with CHF with and without systolic dysfunction.

Thus we aimed to analyze survival in a large population of very elderly patients with CHF to more accurately describe the effects of systolic function on prognosis and, finally, to determine the prognostic relevance of markers of clinical status and exercise test characteristics in this population.

Methods

We evaluated 188 consecutive patients with CHF who were >70 years old seen at the Heart Failure Clinic of the Royal Brompton Hospital between March 1992 and June 1998 (134 men, 54 women, mean age ± SD 76.7 ± 4.5 years). In this time period a total of 580 patients was seen in our clinic (ie, the elderly representing 32% of our CHF population). The diagnosis of heart failure was based on a history of dyspnea and symptomatic exercise intolerance with signs of pulmonary congestion or peripheral edema or documentation of left ventricular enlargement or dysfunction by chest x-ray film, echocardiography, or radionuclide ventriculography. The medical regimen of all the enrolled patients was optimized and stable for at least 4 weeks. Standardized medications included digoxin, angiotensin-converting enzyme (ACE) inhibitors, diuretics, calcium antagonists, nitrates, β-blockers, and aspirin or warfarin in varying combinations (Table I). Resting LVEF and right ventricular ejection fractions (RVEF) were determined in 105 (56%) and 64 (34%) patients, respectively, by radionuclide ventriculography.

Echocardiography

Echocardiography at rest was performed in 166 patients (88%) with a Hewlett-Packard Sonos echocardiograph with a 2.5-MHz transducer with the patients in the semilateral position. Left ventricular end-diastolic (LVEDD) and end-systolic diameters (LVESD) were measured from the M-mode recording with a paper speed of 100 mm per second of the left ventricular minor axis on the parasternal view with the cursor on the tips of the mitral leaflets with the leading-edge method. LVEF was calculated according to the standard dimensions cubed formula: (LVEDD³ – LVESD³)/LVEDD³. Preserved systolic function was defined as LVEF >45% on radionuclide ventriculography or echocardiography, if radionuclide ventriculography was not available.

Cardiopulmonary exercise testing

Symptom-limited cardiopulmonary exercise testing with respiratory gas exchange was performed in 123 patients (65%) by the modified Bruce protocol. Of the remaining 65 patients, 23 (12%) were not able to exercise because of neurologic disorders, 22 (12%) were judged too compromised or physically too frail because of severe heart failure, 15 (8%) had moderate to severe claudication, and 5 (3%) refused to perform the test. Oxygen consumption was measured online every 10 seconds by a standard inert gas dilution technique (Amis 2000, Odense, Denmark). Patients were encouraged to exercise to exhaustion. The peak oxygen consumption (VO2) was defined as the highest VO2 observed during exercise. The anaerobic threshold was defined as the VO2 at which expired carbon dioxide increased nonlinearly relative to oxygen consumption. Age-, weight-, and sex-adjusted predicted VO2 was determined according to the treadmill equations of Wasserman et al. In 102 (83%) of the 123 exercise tests, patients achieved a respiratory exchange ratio >1.00, indicating the achievement of anaerobic exercise conditions. The remaining 21 tests were considered submaximal and were therefore excluded from further analyses.

Follow-up

All patients were followed up by the Royal Brompton Hospital Heart Failure Clinic. The primary end point of the study was all-cause mortality because in many cases death occurred outside the hospital and it was not possible to establish whether it was of cardiac origin. We aimed at a follow-up time of at least 12 months for survivors; this was achieved in all cases.

Statistical analysis

Results are presented as the mean ± SD. Intergroup differences among clinical, hemodynamic, and exercise capacity variables were compared with the unpaired Student t test. A P value <.05 was considered statistically significant. The Cox proportional hazards model was used to assess the impact of clinical history and test results on time to death. Death was censored as a binary event, with time to follow-up coded in months. Multivariate regression analysis was performed on significant univariate predictors with P < .01. Kaplan-Meier cumulative survival plots were constructed to estimate survival data after 6, 12, 24, and 48 months. Statistical analysis was performed with a standard statistical program package (StatView, version 4.5, Abacus Concepts Inc).

Results

The clinical characteristics of the study population are summarized in Table I. Twenty-three (12%) patients had CHF of New York Heart Association (NYHA) functional class I, 81 (43%) class II, 62 (33%) class III, and 22 (12%) class IV. A total of 85% were taking an ACE inhibitor, 72% a diuretic, and only 15% a β-blocker. The etiology of CHF was ischemic heart disease in 123 patients (66%), idiopathic dilated cardiomyopathy in 27 (14%), valvular heart disease in 13 (7%), restrictive in 10 (5%), hypertrophic cardiomyopathy in 3 (2%), and dynamic left ventricular outflow tract obstruction (DVLVOTO) in 12 (6%). This represents a condition of phasic obstruction of the left ventricular outflow tract during systole, particularly during stress. In our patients diagnosis was made on the basis of a transthoracic echocardiography performed during infusion of low-dose dobutamine, as previously described. According to our definition, 90 patients (48%) had preserved systolic function.

The mean peak VO2 was 15.37 ± 4.7 mL/min/kg (for the other results, see Table I). There was no statistically significant difference in the mean peak VO2 and the re-
piratory ratio between patients with reduced and preserved LVEF. Age did not significantly correlate with the VE/VCO2 slope ($r = 0.005$), and there was only a weak correlation between age and peak VO2 ($r = 0.17, P = .08$).

Of the 188 patients with CHF, 61 (32.4%) died after a mean of 9 ± 6 months (range 1-41 months). Survivors were followed-up for a mean of 18 ± 7 months (range 12-56 months). The cumulative survival of all patients was 87% at 6 months (95% confidence interval [CI] 82%-92%), 74% at 12 months (95% CI 67%-80%), 61% at 24 months (95% CI 53%-69%), and 47% at 48 months (95% CI 28%-65%). No patient received heart transplantation during follow-up.

In univariate analysis, peak VO2 ($P = .0007$), VE/VCO2 ($P < .0001$), NYHA functional class ($P < .0001$), and LVEF ($P = .0002$) were the strongest predictors of mortality. The prognostic value of these factors was also independent of age (Table II). Furthermore, in a bivariate model peak VO2 predicted survival independently of sex ($P < .05$). In 2 models of multivariate analysis, considering age, NYHA class, LVEF, and peak VO2, peak VO2 was an independent predictor of impaired survival (Table III). The presence of one or two risk factors, defined as peak VO2 <14 mL/min/kg and relation of minute ventilation to carbon dioxide consumption (VE/VCO2) slope >34.5 was related to a poor outcome ($P = .0053$) (Figure 1).

Patients with preserved systolic function (LVEF >45%) had a better prognosis compared with the group of patients with reduced systolic function, with a 12-month survival rate of 86% (95% CI 79%-93%) versus 62% (95% CI 52%-71%), respectively ($P = .0019$) (Figure 2). Among those with a normal LVEF, the subgroup of patients with DLVOTO had a particularly favorable prognosis, with 100% survival at the end of follow-up (mean follow-up 16 ± 8 months, range 12-39 months).

**Discussion**

In the current study we describe survival in 188 patients with CHF >70 years old and the feasibility of exercise testing and the impact of its results on prognosis assessment in this population. Overall prognosis in this patient group was poor, with a mortality rate of 26% at 12 months. Cardiopulmonary exercise testing was performed in >50% of patients, and peak VO2 was the strongest predictor of impaired survival in the study population.

Although the prevalence of CHF in the very elderly is increasing, few data are available regarding survival in this population. The impact of age on survival in patients with CHF is far from being clearly established. Some authors describe a negative effect of age on survival in patients with CHF, whereas others do not confirm this finding. In the Veterans Administration Heart Failure Trial (V-HeFT) design an age limit of 75 years was imposed, and the study included only men.

| Age (y) [n = 188] | 76.6 ± 4.5 | 75.7 | 70-94 |
| NYHA class | 2.3 ± 0.8 | 2 | 1-4 |
| Men [%] | 134 [71] | — | — |
| Atrial fibrillation [%] | 56 [29] | — | — |
| LVEF [%] [n = 105] | 38 ± 17 | 39 | 8-91 |
| RVEF [%] [n = 68] | 39 ± 13 | 37 | 5-72 |
| LVEDD [mm] [n = 166] | 59 ± 13 | 60 | 30-92 |
| LVESD [mm] [n = 166] | 46 ± 16 | 45 | 14-86 |
| LAD (mm) [n = 166] | 48 ± 10 | 46 | 20-82 |
| Peak VO2 (mL/min/kg) [n = 102] | 15.3 ± 4.7 | 15.1 | 6.5-28.9 |
| VE/Vco2 slope [n = 102] | 39.6 ± 15 | 36.42 | 7.9-74 |
| Exercise duration [min] [n = 102] | 5.8 ± 2.2 | 5.3 | 1.2-13 |
| Systolic BP (mm Hg) [n = 188] | 133 ± 22 | 130 | 80-190 |
| Diastolic BP (mm Hg) [n = 188] | 76 ± 10 | 75 | 45-100 |
| Resting heart rate [beats/min] [n = 188] | 77 ± 11 | 78 | 50-110 |
| Plasma sodium [mmol/L] [n = 188] | 138 ± 3 | 139 | 124-145 |
| Total protein [g/L] [n = 188] | 69 ± 7 | 69 | 44-103 |
| Albumin [g/L] [n = 188] | 38 ± 5 | 39 | 21-47 |
| Urea [mmol/L] [n = 188] | 9 ± 5 | 9 | 3.2-47 |
| Creatinine [µmol/L] [n = 188] | 123 ± 49 | 113 | 5-631 |
| Hemoglobin [g/dL] [n = 188] | 12.6 ± 1.7 | 12.5 | 7-21.4 |
| Cholesterol [mmol/L] [n = 188] | 5.8 ± 1.5 | 5.7 | 2.9-12.9 |

NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LAD, left atrial diameter; VO2, oxygen consumption; VE/VCO2, slope of the relationship of minute ventilation to carbon dioxide production; BP, blood pressure.
Other studies included only patients with left ventricular dysfunction,\(^\text{18}\) which cannot be representative of the whole population of this age. Senni et al\(^\text{9}\) studied a larger population of elderly patients with CHF in the community, with a 12-month survival rate of 76%, which is similar to the outcome in our population.

### Cardiopulmonary exercise testing in the very elderly

In our study elderly patients with left ventricular systolic dysfunction had a worse prognosis than did patients with preserved left ventricular systolic function. However, LVEF cannot be used as a marker of the disease because signs and symptoms of CHF can be determined even in presence of normal systolic left ventricular function. This is even more important in the elderly, considering the high prevalence of isolated diastolic dysfunction in this subgroup and the atypical presentation of symptoms. An objective parameter is needed to characterize the severity of the disease in this population. Peak VO\(_2\) is an useful predictor of morbidity and mortality in patients with CHF,\(^\text{20,21}\) but in prognostic studies of elderly patients with CHF cardiopulmonary exercise testing has not been performed\(^\text{9,22,23}\) or was performed only in patients with systolic dysfunction\(^\text{24}\) and, conversely, studies on the prognostic value of peak VO\(_2\) included only younger patients.\(^\text{19,20,25}\) Therefore the clinical relevance of cardiopulmonary exercise testing in a population of very elderly patients with CHF with and without systolic dysfunction has not been established clearly.

Peak VO\(_2\) is a key parameter for the correct timing of heart transplantation. In our population this therapeutic option is ruled out by definition because an age limit of 70 years was imposed to enter the trial; nevertheless, we would like to underline the feasibility of exercise testing even in very elderly patients with CHF. Peak VO\(_2\) remains a milestone for a complete evaluation of individual patients with heart failure because it allows a better understanding of the severity of the disease in this population. In the future nonsurgical therapeutic approaches may also use peak VO\(_2\) for stratification of therapy. Many authors reported the beneficial effects of cardiac rehabilitation and exercise training on exercise capacity and reduction of myocardial infarction and all-cause mortality.\(^\text{26,27}\) and these benefits seem to be particularly striking in elderly patients compared with younger patients.\(^\text{28}\) Unfortunately, despite the positive effects of cardiac rehabilitation in elderly patients,
Figure 1

Kaplan-Meier survival curves of 102 patients with CHF >70 years old divided according to the presence or absence of 1 or 2 risk factors, defined as peak VO₂ <14 mL/min/kg and VE/VCO₂ slope >34.5.

Figure 2

Kaplan-Meier survival curves of 188 patients with CHF >70 years old divided according to the presence or absence of left ventricular systolic dysfunction (LVEF <45%).
elderly patients are often not referred to attend these programs.39

**Left ventricular function**

The prognostic value of left ventricular dysfunction has been consistently reported, but some authors have shown that ejection fraction might not be the strongest prognostic factor in CHF.30,31 In our study, patients with diastolic dysfunction had a better prognosis compared with the group with reduced LVEF, confirming previously reported data.21,23 It has been recently identified that a particular subgroup of elderly patients with normal or even increased rest ejection fraction and impaired exercise tolerance will have a DLVOTO during low-dose dobutamine infusion.14 The prevalence of DLVOTO has been recently reported to be 17.5%,32 but its prognostic relevance has never been described. In our population 12 patients (6% of total) had a known DLVOTO, and interestingly they had a 100% survival at the end of follow-up. Therefore they might represent a subgroup of those with preserved LVEF with a particularly favorable outcome, with pathophysiologic mechanisms and natural history different from patients with “pure” diastolic dysfunction.

**Limitations**

In the current study we found a 32% prevalence of patients >70 years old, in contrast to the report of Senni et al9 of 88% of patients >65 years old. This apparent discrepancy might depend on a different selection of patients. In fact, our patients were referred to a tertiary care institution, whereas in the study of Senni it was population based. Therefore in our study we are not able to describe a real prevalence of the disease, but the real advantage of a study conducted in a tertiary center is the possibility of collecting large numbers of data that, to the opposite, would be extremely difficult in a population-based study. Another limitation of the current study is the lack of Doppler parameters, which were not measured on a routine basis. Nevertheless, the diagnostic and prognostic role of Doppler parameters in patients with isolated diastolic dysfunction is far from being established clearly.33 Finally, we would like to underline the importance of a complete clinical evaluation in elderly patients with CHF, including cardiopulmonary exercise testing, which can be performed in more than 50% of patients with CHF who are >70 years old. This could add important information regarding the severity of the disease and may be useful to guide individualized treatment.

**Conclusions**

This study shows that prognosis in very elderly patients with CHF is poor, and the strongest prognostic factors are NYHA class and peak VO2. Hemodynamic parameters such as LVEF play an important role; in fact, patients with impaired systolic function are at higher risk of death than are patients with preserved systolic function. We identified a small subgroup of patients with dynamic left ventricular outflow obstruction with a particularly favorable outcome. We would like to underline the importance of a complete clinical evaluation in elderly patients with CHF, including cardiopulmonary exercise testing, which can be performed in more than 50% of patients with CHF who are >70 years old. This could add important information regarding the severity of the disease and may be useful to guide individualized treatment.

**References**

17. Judge K, Pawitan Y, Caldwell J. Congestive heart failure in patients...


