**Prognostic value of geriatric and cardiac parameters for one-year mortality in older heart failure patients. A multicentre, observational, prospective study.**

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# Keywords

Heart failure, prognostic factors, older adults, one-year mortality

# Abstract

PurposeHeart failure is prevalent amongst older people and has a poor prognosis. Aim of this study is to identify potential prognostic, geriatric and cardiac parameters which could help clinicians identify older heart failure patients at high risk for one-year mortality.

MethodsMulticentre, observational cohort study which included 147 heart failure patients aged ≥75 years, hospitalized on the cardiac or geriatric department in two hospitals. One-year survival was the outcome measure. For univariate analysis Chi square test and independent sample T-test were used; for multivariate analysis Logistic regression and Cox regression for time-dependent analysis.

ResultsOne-year mortality was 28% (41/147). One-year survivors and non-survivors did not differ in following characteristics: age, gender, sodium level at hospital discharge, ejection fraction, NYHA Class, basic and instrumental activities of daily living and the presence of a geriatric risk profile. There was a significant lower systolic blood pressure at discharge in non-survivors compared to one-year-survivors *(mean 125,26mmHg vs. 137,59mmHg).* Non-survivors had more severe underlying comorbidities according to the age adjusted Charlson Comorbidity index (CCI) *(mean 8,80 vs. 7,40).*

Both logistic and Cox regression showed a higher risk and rate of mortality with decreasing systolic blood pressure at discharge *(OR 0.963, p=0.001 and HR 0.970, p<0.001)* and with increasing CCI *(OR 1.344, p=0.002 and HR 1.269, p=0.001)*; the other variables were not significantly related.

ConclusionLower blood pressure and more severe comorbidities, but not functionality nor the presence of a geriatric risk profile, are related to one-year mortality in older, in-hospital heart failure patients.

# Introduction

The global population is aging rapidly, leading to a fast growing number of older people living with heart failure [1]. Heart failure is considered the quintessential cardiovascular syndrome of aging and is a chronic, progressive and ultimately lethal condition [1]. Until today, it remains the most common reason for hospitalization in older people [1, 2]. Overall, heart failure remains a condition with a poor prognosis, with increasing mortality rates according to age. One- and five-year mortality was estimated around 7% and 24% for 60-year-olds and increased to 20% and 54% for 80-year-olds in previous literature [2, 3].

Heart failure is defined as a consequence of any structural or functional disorder that impairs the ability of the ventricles to fill with or eject blood, leading to elevated ventricular filling pressures resulting in pulmonary and/or systemic congestion [1, 2, 4]. It is mainly categorized by left ventricular ejection fraction. The European Society of Cardiology guidelines separates patients with heart failure into three categories: patients with reduced EF (< 40%) called HFrEF, mildly reduced EF (40% to 49%) called HFmrEF, and preserved EF ( ≥ 50%), called HFpEF. Often these three categories are reduced to two; HFrEF (EF < 50%) and HFpEF (EF ≥50%) [5, 6, 7]. In older patients, both HFrEF and HFpEF are associated with age related structural changes in other organ systems and comorbid conditions, though their pathophysiology seems to differ significantly [5]. HFrEF is believed to be the result of a substantial loss of cardiomyocytes, acutely or chronically, resulting in systolic dysfunction [6]. The pathophysiology of HFpEF is more associated with left ventricular wall stiffening, resulting in diastolic dysfunction, reduced arterial compliance, left atrial hypertension and pulmonary venous congestion [6]. Previous studies have shown that patients with HFpEF are more often female and have a higher prevalence of comorbidities [5]. They suffer from comorbid conditions such as obesity, diabetes mellitus, chronic kidney disease and physical deconditioning, where patients with HFrEF mostly suffer from arterial disease like carotid and peripheral arterial disease [6]. It is well established that HFpEF nowadays accounts for at least half of the cases of heart failure in patients older than 65 years [5, 6].

Disability is "the difficulty of coping with self-care tasks (Activities of daily living, ADL) and tasks of household management (Instrumental Activities of daily living, IADL)". The likelihood of developing a disability rises steadily with age. Most people with disabilities have more than one type of disability. Disability has been associated with mortality, hospitalization, length of hospital stay and institutionalization. [8, 9, 10, 11, 12].

A higher New York Heart Association (NYHA) class, troponin elevation, elevation of natriuretic peptides (BNP and NT pro-BNP), lower systolic blood pressure, decreased haemoglobin, hyponatremia (sodium levels below 135 mEq/L), extensive comorbidities, elevated heart rate upon admission and a large difference in BUN and creatinine from admission to discharge have all been proven to be linked to a higher mortality rate in patients hospitalized for heart failure [3, 13, 14]. Older adults with a geriatric profile were often excluded in these studies, leading to inconclusive data in this group of patients where disease course is already more heterogeneous and less predictable [15].

Patients with heart failure often experience a variety of debilitating physical and emotional symptoms and are believed to have a similar level of palliative care needs as patients with advanced cancer [3, 16]. Recent systematic reviews and meta-analysis suggest that timely introduction of palliative care in advanced heart failure leads to a positive effect on quality of life, symptom relief, documentation of care preferences, resource use and caregiver outcomes [3, 17]. Therefore, further identifying prognostic factors in older patients with heart failure could lead to an earlier recognition of patients who could benefit from a more palliative oriented approach and/or more individualized care plan [3]. With this study, we want to contribute to this identification and examine which cardiac and geriatric factors could be of predictive value. Furthermore we want to investigate potential differences between patients with HFrEF and HFpEF since HFpEF nowadays accounts for the majority of older patients with heart failure.

# Methodology

In this multicentric cohort study we prospectively included older patients admitted on the acute geriatric and cardiology department in two Belgian hospitals between January 2018 and July 2018. We selected the patients with heart failure, using the following criteria: patients had an ejection fraction of < 50% on transthoracic echocardiograph and/or had a diagnosis of heart failure and/or were being treated with medication, indicating the presence of heart failure. Medication included the use of loop diuretics alone or combined with any of the following drugs: beta blockers, ACE inhibition/ARB inhibitors and/or mineralocorticoid receptor antagonists. For statistical analysis, the simplification was made to categorize patients with an ejection fraction of < 50% as HFrEF and all others as HFpEF. All recruited patients were older than 75 years and were either hospitalized on the cardiology or the geriatric ward. Inclusion criteria did not specify the reason for hospitalization.

In total 655 patients were eligible for inclusion and 248 gave informed consent. Finally, 147 of those had heart failure and were included in this study [Figure 1].

Following characteristics were collected from the medical file: age, gender, weight, systolic blood pressure at discharge, sodium level at discharge, NYHA class, the presence of a geriatric risk profile [18], KATZ scale (basic activities of daily living) [19], Charlson comorbidity index [20], Lawton scale (instrumental activities of daily living) [21] and ejection fraction. Survival status after one year was assessed by telephone call. Firstly the patient or legal representative was contacted, secondly the general practitioner.

SPSS statistical package version 29 was used for statistics. For categorical variables the Chi square test was used and for continuous variables the independent sample T-test. All variables with a p-value < 0.2 in univariate analysis were included in the multivariate analysis and the type of heart failure was forced in the model because this was one of our main research questions. A logistic and cox regression including interaction terms were performed for one-year survival (time).

This study was approved by the ethics committee from UZ Ghent (Belgian Registration number B670201734355A).

# Figure 1. Flow chart patient inclusion

229 patients did not fulfill inclusion criteria:

- 124 patients because of hospitalisation longer than 2 days on another ward

- 13 because of death on admission

- 20 because of already included in the study

- 72 because of length of stay shorter than 2 days

884 patients (75 years and older, from 4 wards) admitted during the study period (January 2018 – July 2018)

study period

655 eligible for inclusion

397 not included in the study:

- 347 because of lack of time of junior doctors to assemble all information and ask for IC

- 50 because of absence of a legal representative

258 were asked for informed consent

10 refused informed consent

248 patients gave informed consent

Selection of patients with heart failure:

- EF < 50%

- History of heart failure on a clinical basis

- Presence of medical heart failure therapy

147 patients aged ≥ 75 with heart failure

# Results

Overall, 65% (89/137) of the study sample suffered from HFpEF and 35% (48/137) of HFrEF. Age, gender, sodium level at discharge, blood pressure at discharge, NYHA class, age adjusted Charlson Comorbidity Index, basic and instrumental activities of daily living and the presence of a geriatric risk profile were all evaluated. None of them differed between patients with HFrEF versus HFpEF [eTable 1, appendix]*.*

One-year mortality was 28% (41/147). We did not find any differences in demographics between survivors and non-survivors. A lower systolic blood pressure at discharge and a higher score on the age adjusted Charlson Comorbidity Index were both linked with a higher risk of mortality in the univariate analysis *(p-value both 0.002)*. The other parameters including premorbid functioning did not show any difference between survivors and non-survivors [Table 1, Figure 2A and Figure 2B].

Table 1. Comparison of patients characteristics between survivors and non-survivors

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Total** | **Alive after one year** | **Died within one year** | **P-value** |
| **Patients for which one year survival is available** |  n = 147 | n = 106 | n = 41 |  |
| **Demographics** |
| Mean Age |  | 84.3 (5.5) | 84.9 (5.0) | 0.604 |
| Gender | n = 147 |  |  | 0.090 |
|  Male | n = 66 | 43 (40.6%) | 23 (56.1%) |   |
|  Female | n = 81 | 63 (59.4%) | 18 (43.9%) |   |
| **Biochemical factors** |
| Mean Sodium level at discharge  | n = 135 | 140.2 (3.9) | 140.7 (4.0) | 0.512 |
| **Cardiac Clinical factors** |
| Mean Blood pressure at discharge | n = 135 | 137.6 (21.0) | 125.3 (18.7) | 0.002 |
| NYHA class  | n = 135 |  |  | 0.086 |
|  NYHA class I & II |  | 41 (42.3%) | 10 (26.3%) |  |
|  NYHA class III & IV |  | 56 (57.7%) | 28 (73.7%) |  |
| **Comorbidities** |
| Mean score of the ACI (The Charlson Age Comorbidity Index) | n = 147 | 7.4 (2.4) | 8.8 (2.4) | 0.002 |
| **Premorbid Functional Factors** |  |  |  |  |
| KATZ scale  Needs assistance for at least 1 bADLMean score of iADL GRP positive | n = 145 n = 146n = 129 | 23 (21.9%)3.3 (2.2)94 (88.7%) | 6 (15%)3.15 (2.2)35 (85.4%) | 0.3530.7130.583 |
| **Cardiac ultrasound factors** |
| Ejection Fraction  | n = 136 |  |  | 0.814 |
|  Reduced (< 50%) |  | 34 (34.7%) | 14 (36.8%) |  |
|  Preserved ( > 50%) |  | 64 (65.3%) | 24 (63.2%) |  |

Legend: NYHA class: a functional classification that catalogues the extent/severity of heart failure, range I to IV, class I & II = limited restriction secondary to heart failure, class III & IV = moderate to severe limitation secondary to heart failure. CACI: Charlson Age-Comorbidity Index, a combination of age and measure of comorbidity to predict the risk of mortality, high score = higher risk to die. KATZ scale: a scale used to describe basic activities of daily living such as washing, clothing, eating, mobility for short distances and urinary and faecal continence. Documented as ‘dependent’ for basic activities of daily living in case of need for assistance for at least one of these tasks. The Lawton Instrumental Activities of Daily Living Scale (IADL) is an instrument to assess independent living skills. These skills being the ability to use the telephone, to do laundry, food preparation, shopping, housekeeping, handle finance matters, responsibility for own medication and the mode of transportation patients use. A score ranges from 0 (low function, dependent) to 6 (high function, independent), differences between men and women were left out in this dataset. GRP: Geriatric Risk Profile score, range 0-6, high score= high risk. A GRP score ≥ 2 was considered positive.

Percentage documented as percentage of people within the total number survivors/non-survivors. Width of confidence intervals listed for means.

Figure 2A. Boxplot of systolic blood pressure by survival status for HFpEF vs. HFrEF



Figure 2B. Boxplot of Age Adjusted Charlson Comorbidity Index by survival status for HFpEF vs. HFrEF



In the logistic and Cox regression variables with a p-value < 0.2 in the univariate analysis were included. In order to specifically look for a potential difference between patients with HFrEF and HFpEF, the type of heart failure was also included as a covariate and an interaction term was checked for each variable according to type of heart failure. All interaction terms were not statistically significant and thus were left out from the final model as presented in Table 2. The odds of mortality decreased in patients with higher systolic blood pressure at discharge (4% per unit/mmHg blood pressure) (*p = 0.001*) and increased in patients with a higher age adjusted Charlson Comorbidity index (34% per extra ‘point’ on the Charlson comorbidity index) (*p = 0.002*) [Table 2].

Table 2. Logistic regression to evaluate odds of one-year mortality

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Odds** **ratio** | **95%****Confidence** **Interval****Lower** | **95%****Confidence** **Interval****Upper** | **Significance****P value**  |
| **Gender** | 0.520 | 0.225 | 1.202 | 0.126 |
| **Age adjusted Charlson Comorbidity Index** | 1.344 | 1.114 | 1.623 | 0.002 |
| **Type of Heart failure (HFrEF vs HFpEF)**  | 0.642 | 0.262 | 1.574 | 0.333 |
| **NYHA class (I/II vs. III/IV)** | 2.024 | 0.806 | 5.086 | 0.133 |
| **Systolic Blood pressure at discharge** | 0.963 | 0.941 | 0.985 | 0.001 |

The Cox regression showed that rate of mortality increased with 27% per higher score/unit on the age adjusted Charlson Comorbidity Index (*p = 0.001*) and decreased with 3% per higher unit/systolic blood pressure at discharge (*p < 0.001*) [Table 3].

Gender, type of heart failure and NYHA class were not statistically associated with status and/or rate of mortality.

Table 3. Cox regression analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Hazard ratio** | **95% Confidence Interval****Lower** | **95% Confidence Interval****Upper** | **Significance****P value**  |
| **Gender** | 0.694 | 0.353 | 1.361 | 0.287 |
| **Age adjusted Charlson Comorbidity Index** | 1.269 | 1.101 | 1.464 | 0.001 |
| **Type of Heart failure (HFrEF vs HFpEF)**  | 0.835 | 0.425 | 1.641 | 0.601 |
| **NYHA class (I/II vs. III/IV)** | 1.218 | 0.572 | 2.591 | 0.609 |
| **Systolic Blood pressure at discharge** | 0.970 | 0.952 | 0.987 | <0.001 |

# Discussion

This study is one of the first combining cardiac and geriatric parameters as potential prognostic factors in an older heart failure population, with a focus on the difference between HFrEF and HFpEF. Systolic blood pressure at discharge and the extent of underlying comorbidities were predictive of status and rate of one-year mortality in both types of heart failure. None of the other parameters we studied, including basic and instrumental activities of daily living and the presence of a geriatric risk profile, were predictive for one-year mortality in patients with HFrEF or HFpEF.

Previous studies in heart failure patients did show that patients with HFpEF are more often female and have more severe comorbidities, which was not the case in our study. The fact that the patients in our cohort were older, with a mean age of 84 years in both patient groups, could potentially explain why comorbidities were quite numerous in both patient groups. Several other studies focused on geriatric parameters as potential predictive parameters in older patients with heart failure [8, 9, 22, 23]. These studies showed that mobility disability, low physical activity, weight loss, slow walking speed, weak grip strength and exhaustion were linked with a higher readmission risk and a higher long-term mortality risk [8, 9]. In line with these findings, we hypothesized that geriatric parameters would have shown prognostic value, but this was not the case. There is extensive research available on the prognostic value of certain cardiac parameters where lower systolic blood pressure (systolic and/or diastolic) has already been linked to a higher mortality in heart failure patients [16, 24, 25, 26]. Our study supports this previous finding and confirms that this routine clinical, cardiac parameter can contribute to predicting the risk of mortality. The same cannot be said about the included geriatric parameters [24]. This observation could be attributed to the predominance of cardiovascular-related causes of death in older heart failure patients, which appear to be independent of their functional abilities [27]. It could also be that the presence of a low systolic blood pressure and extensive comorbidity limits (optimization of) heart failure therapy. The fact that ADL was scored as a dichotomic variable in this study (defining a patient as dependent or independent) could be an explanation for the lack of predictive value of the geriatric parameters. Dividing these functional parameters into subcategories would be a more refined approach for future studies. Furthermore, there was no information available on which heart failure medication a patient received, which could also be of added value.

We consider our study to have several strengths. First of all, the patient cohort consists of patients older than 75 years and was assembled from both the cardiac and the geriatric ward. This leads to a very realistic and heterogeneous patient cohort, where ‘the most frail’ patients were not excluded. Secondly, we used multiple parameters (basic activities of daily living, instrumental activities of daily living and the presence of a geriatric risk profile) to describe a patient’s functional status, leading to a broad perspective on the patient’s capabilities.

A first limitation to our study is the dependency on the completeness of medical records, making it impossible to refine some parameters. As a frailty tool is not part of routine assessment in the two hospitals, we had to rely on bADL and iADL and GRP scores as geriatric parameters. A second limitation is that we potentially missed a number of patients with heart failure in our selection process. We used 3 criteria to select the patients with heart failure in our cohort: previous diagnosis, echocardiographic data and/or the use of specific heart failure medication. This implies we potentially missed a group of patients with heart failure who do not take any of these medications and/or with an incomplete medical file.

Based on our findings, we propose to use systolic blood pressure and the severity of a patient’s comorbidities for evaluating the risk of mortality. These parameters are both easy to obtain in daily clinical practice.

Patients with a lower systolic blood pressure and/or with extensive comorbidities could in our opinion benefit from timely introduction of an advanced care planning and a more palliative oriented approach. For now, we could not demonstrate any prognostic value of functional/geriatric parameters in older patients with heart failure. Blood pressure and comorbidity seem of greater value for predicting one year mortality, even in patients hospitalized on the geriatric ward. Further research in larger patient groups is required to determine if functional parameters and/or frailty tools (such as the widespread Rockwood Clinical Frailty Scale) could be of added value in predicting the risk of mortality in older, geriatric heart failure patients. When setting up further research projects we recommend including the subcategories/questions of the different functional/geriatric parameters, providing information on heart failure medication, adding parameters that probe for frailty/physical functioning, adding the risk of readmission and cause of death as outcome parameters.

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# Conflicts of interest

The authors declare that there are no conflicts of interest.

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# Appendix

eTable 1. Characteristics of patients with heart failure with reduced ejection fraction versus heart failure with preserved ejection fraction.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | Total | HFrEF | HFpEF | P-value |
| Total patients for which EF is available  | n = 137 | n =48  | n = 89 |  |
| Demographics  |
| Mean age  | n = 137 | 84.50 (5.6) | 84.40 (5.2) | 0.921 |
| Gender  | n = 137 |  |  | 0.413 |
|  Male  | n = 62 | 24 (50%) | 38 (42.7%) |   |
|  Female  | n = 75 | 24 (50%) | 51 (57.3%) |   |
| Biochemical factors |
| Sodium level at discharge (mean)  | n = 136 | 139.8 (4.3) | 140.7 (3.6) | 0.205 |
| Cardiac Clinical factors |
| Blood pressure at discharge mean  | n = 136 | 129.9 (20.8) | 136.3(20.877) | 0.093 |
| NYHA class  | n = 136 |  |  | 0.085 |
|  NYHA class I & II  |  | 13 (27.7%) | 38 (42.7%) |  |
|  NYHA class III & IV  |  | 34 (72.3%) | 51 (57.3%) |  |
| Comorbidities |
| Mean score of ACI (The Charlson Age Comorbidity Index)  | n = 137 | 8.1 (2.2) | 7.4 (2.4) | 0.113 |
| Premorbid Functional Factors |
| KATZ scale  | n = 135 |  |  | 0.201 |
|  Needs assistance for at least 1 ADL |  | 34 (72.3%) | 72 (81.8%) |  |
| Mean score of iADL  | n = 136 | 3.4 (2.2) | 3.26 (2.2) | 0.674 |
| GRP positive  | n = 120 | 41 (85.4%) | 79 (88.8%) | 0.571 |

Legend: NYHA class: a functional classification that catalogues the extent/severity of heart failure, range I to IV, class I & II = limited restriction secondary to heart failure, class III & IV = moderate to severe limitation secondary to heart failure. CACI: Charlson Age-Comorbidity Index, a combination of age and measure of comorbidity to predict the risk of mortality, high score= higher risk to die. KATZ scale: a scale used to describe basic activities of daily living such as washing, clothing, eating, mobility for short distances and urinary and faecal continence. Documented as ‘dependent’ for basic activities of daily living in case of need for assistance for at least one of these tasks. The Lawton Instrumental Activities of Daily Living Scale (IADL) is an instrument to assess independent living skills. These skills being the ability to use the telephone, to do laundry, food preparation, shopping, housekeeping, handle finance matters, responsibility for own medication and the mode of transportation patients use. A score ranges from 0 (low function, dependent) to 6 (high function, independent), differences between men and women were left out in this dataset. GRP: Geriatric Risk Profile score, range 0-6, high score= high risk. A GRP score ≥ 2 was considered positive.

Percentage documented as percentage of people within the total number of people diagnosed with HFrEF/HFpEF. Width of confidence intervals listed for means.