Impact of clinical and echocardiographic parameters assessed during acute decompensation of chronic heart failure on 3-year survival

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Abstract

Background: It is unclear whether established risk factors affecting the prognosis of chronic heart failure (CHF) have the same predictive value when assessed during acute haemodynamic decompensation of CHF.

Aim: To investigate the impact of selected clinical and echocardiographic parameters assessed in patients with CHF during emergency admission due to acute CHF decompensation, on 3-year survival.

Methods: This retrospective study involved 100 consecutive patients with CHF (60 women and 40 men at the mean age of 70.4±9.8 years), admitted to hospital due to angina pectoris symptoms or pulmonary oedema. In the echocardiographic study performed within the first 48 hours of in-hospital stay, standard parameters as well as right ventricular systolic pressure (RVSP) were evaluated. In order to identify biological, clinical and echocardiographic factors affecting 3-year survival, both uni- and multivariable Cox proportional hazards regression analyses were carried out.

Results: Forty-four patients died during 3-year follow-up. Univariate regression analysis revealed that age >60 years, sodium serum concentration <140 mmol/L, RVSP >35 mmHg and reduced left ventricular ejection fraction <50% were associated with an increased risk of death. However, multivariate regression analysis showed that only age and sodium concentration were independent risk factors.

Conclusions: Age of over 60 years and sodium concentration below 140 mmol/L seen during acute decompensation were found to be independent predictors of unfavourable outcome in terms of mortality in 3-year follow-up of patients with CHF.

Key words: chronic heart failure, risk factors

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Introduction

Chronic heart failure (CHF) is a heterogeneous syndrome associated with high annular mortality that depends on numerous risk factors [1-3]. Well established risk factors of mortality in this patient population include age, stage of disease, left ventricular ejection fraction (LVEF), ischaemic heart disease, diabetes mellitus, and disorders of peripheral circulation [3]. The aforementioned factors were defined based on population studies performed in stable CHF patients. However, it is not clear what is their predictive value when assessed during acute worsening of CHF.

Patients with CHF die due to sudden cardiac death or progressive haemodynamic pump failure [4]. In the latter case, cardiogenic shock or pulmonary oedema usually lead to death. It was found that if pulmonary oedema was a result of increased arterial blood pressure, one of the commonly accepted risk factors, LVEF, remained unchanged, and the impaired LV relaxation was responsible for the development of haemodynamic decompensation [5]. One can ask if preserved LVEF may have any impact on long-term prognosis in patients with CHF admitted to hospital because of its acute deterioration.

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Reliable measurement of LVEF using echocardiography is rather difficult [6]. Deterioration of LVEF in patients with CHF is considered as an unfavourable predictive factor [6-8]. Degree of pulmonary hypertension (PH) is negatively correlated with LVEF and thus may have an impact on individual long-term risk stratification in patients with CHF [8]. It was shown that PH was an unfavourable prognostic factor in patients with dilated cardiomyopathy accompanied by CHF symptoms [1]. Moreover, PH in patients with systolic CHF indicates a group at markedly increased risk.

Thus, the question arises whether the risk factors with documented influence on prognosis in CHF, have the same predictive value when assessed during acute haemodynamic CHF deterioration and if there are any parameters assessed on hospital admission that might help risk stratification in this patient group.

The purpose of this study was to investigate the impact of selected clinical as well as echocardiographic parameters, assessed at the time of hospital admission due to acute decompensation, on 3-year survival rate of patients with CHF.

Methods

Patients

This was a retrospective study. Our investigation comprised 100 consecutive CHF patients, including 60 women and 40 men at the mean age of 70.4±9.8 years admitted to hospital because of cardiac angina or pulmonary oedema. Patients received standard CHF medical treatment (ACE inhibitors, loop diuretics, spironolactone, and beta-blockers). Patients with acute coronary syndromes were excluded from the study.

Table I. Characteristics of the study group (n=100)

Men	40
Mean age [years]	70.4±9.8
Previous myocardial infarction	26
Arterial hypertension	74
Type 2 diabetes mellitus	31
LVEF ≥50%	59
Other cardiac disease	16
Atrial fibrillation	57
Pneumonia	38
Mean serum Na concentration on admission (mmol/L)	141.4±2.8
Mean serum creatinine concentration on admission (mg/dL)	1.19±0.5

Abbreviations: LVEF – left ventricular ejection fraction

Echocardiographic examination

In all patients echocardiographic examination using a Sonos 100 CF device equipped with a standard probe of 2.5 MHz–5.0 MHz was carried out within the first 48 hours following admission to hospital. Left ventricular end-diastolic dimension (LVDD), right ventricular end-diastolic dimension (RVDD), right ventricular systolic pressure (RVSP) and LVEF were assessed. Evaluation of systolic LV performance was based on modified Simpson's method. To estimate RVSP, simplified Bernoulli model with approximation of the right atrial pressure to 5 mmHg in all patients independently of inferior vena cava dimension and its reaction to breathing was used.

Follow-up

Three-year follow-up was based on information regarding deaths obtained from the official governmental database. Patient characteristics are presented in Table I.

The study was approved by the Bioethical Committee of Warmińsko-Mazurska Izba Lekarska in Olsztyn.

Statistical analysis

Uni- and multivariate analyses were performed to evaluate the predictive value of individual factors on mortality. Cox proportional hazards model was used. The following variables were analysed: presence of arterial hypertension based on previously established diagnosis or previously initiated anti-hypertensive therapy, diabetes mellitus based on previously established diagnosis or initiated medical therapy, history of myocardial infarction, valvular heart disease, persistent atrial fibrillation, sinus rhythm, pulmonary hypertension (RVSP >35 mmHg) and concomitant infection, including pneumonia, and selected laboratory as well as echocardiographic parameters. Variables found to be of statistical significance ($p < 0.05$) in the univariate analysis were entered into the multivariate one. Finally, for the parameters that reached significance in the multivariate analysis, survival curves were computed using the Kaplan-Meier method. Statistical analysis was carried out employing the SAS statistical software package.

Results

Forty-four patients out of 100 died during 3-year follow-up. Because of the small number of subjects in the study, no further statistical analysis of causes of death was performed. Only all-cause mortality was analysed.

Clinical and echocardiographic variables that were analysed to evaluate their impact on survival rate are outlined in Table I. Significant predictors of mortality in the univariate analysis were age >60 years, sodium concentration <140 mmol/L, RVSP >35 mmHg and LVEF

Table II. Value of selected clinical, laboratory and echocardiographic variables in predicting 3-year survival – univariate Cox proportional regression analysis

Variable	HR	95% CI	P
Gender	0.96	0.52–1.77	0.9
Age >60 years	1.05	1.01–1.09	0.003
Myocardial infarction	1.55	0.82–2.93	0.17
Arterial hypertension	1.24	0.61–2.51	0.54
Diabetes mellitus	1.77	0.97–3.24	0.06
Atrial fibrillation	0.85	0.46–1.53	0.59
Pneumonia	1.12	0.61–2.04	0.71
LVDD	0.92	0.66–1.29	0.65
RVDD	1.22	0.74–2.01	0.42
LVEF <50%	0.97	0.94–0.99	0.039
RVSP >35 mmHg	2.05	1.13–3.74	0.018
Na >140 mmol/L	0.86	0.77–0.97	0.013
Creatinine ≥1.2 [mg/dl]	1.06	0.47–2.42	0.870

Abbreviations: RVDD – right ventricular end-diastolic dimension, LVDD – left ventricular end-diastolic dimension, RVSP – right ventricular systolic pressure, Na – serum sodium concentration, creatinine – serum creatinine concentration, HR – hazard ratio, CI – confidence interval

<50% (Table II). RVSP >35 mmHg was found in 43 patients, sodium level <140 mmol/L in 27 patients and LVEF <50% in 41 patients.

After including these four parameters into the multivariate analysis only age >60 years and sodium concentration <140 mmol/L remained significant (p=0.0006 and p=0.03, respectively) (Table III).

Table III. Value of selected clinical, laboratory and echocardiographic variables in predicting 3-year survival – multivariate Cox proportional regression model

Variable	HR	95% CI	P
Age >60 years	1.05	1.02-1.09	0.0006
Na 140 mml/L	0.87	0.87-0.77	0.033
LVEF <50%	0.97	0.94-1.00	0.073
RVSP >35 mmHg	1.55	0.82-2.92	0.17

For these parameters, the Kaplan-Meier survival curves were computed and are presented in Figures 1 and 2.

Discussion

Acute decompensation of heart failure is one of the predominant reasons of hospital admissions. Still, data regarding patients suffering from this disease characteristic are limited. In the Euro-Heart Failure Survey [9], women accounted for approximately half of patients, and 51% of them were older than 75 years of age. Among men only 30% were older than 75. Impaired systolic function was observed more frequently in men than in women (51% and 28%, respectively), in contrast to diastolic heart failure which was demonstrated more often in female than in male patients (45% and 22%, respectively); diabetes mellitus was concomitant pathology in 20% of the whole population. In the ADHERE Registy (Acute Decompensated Heart Failure National Registry) the mean age of patients was 75.3 years, women accounted for 52%, and in 46% of patients impaired LV systolic function was noted, while diabetes

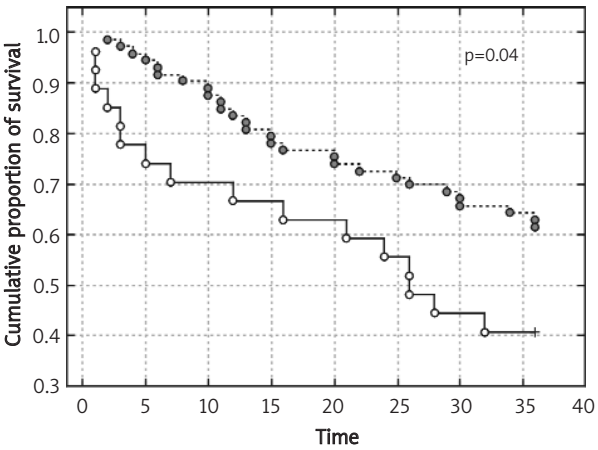

Figure 1. Kaplan-Meier survival curves for patients, with Na ≥140 mmol/L (dotted line) and <140 mml/L (solid line) during 36-month follow-up.

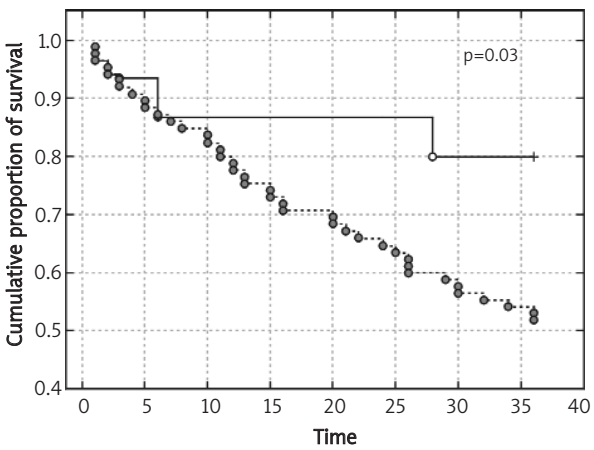

Figure 2. Kaplan-Meier survival curves for two patient >60 years (dotted line) and <60 years (solid line) during 36-month follow-up

mellitus was diagnosed more frequently among patients enrolled into the registry (44%) [10]. In the EPICAL trial, mean age of patients admitted to hospital due to severe heart failure was 65 year old, ischaemic aetiology accounted for 45%, 75% of them were male patients, concomitant arterial hypertension was found in 43% and atrial fibrillation in 24% of patients [11].

In our series patients were of similar age (median 70.4 years), and the women-to-men ratio was similar (3:2) to that in the first of the two mentioned trials. Incidence of systolic heart failure in our study was 41% which is similar to the rate found in the ADHERE trial [10]. Moreover, patients had lower rate of ischaemic aetiology of heart failure (26%), higher prevalence of arterial hypertension (74%) as well as atrial fibrillation (57%), and all presented rates were similar to those reported in the literature.

In our patients, the most powerful predictors of death were decreased serum sodium concentration and age >60 years in the multivariate Cox proportional analysis, and additionally two echocardiographic parameters, RVSP and LVEF, in the univariate regression analysis.

Hyponatremia is a recognised independent predictor of unfavourable outcome in patients with stable CHF. In the EPICAL study which evaluated patients in acute heart failure decompensation accompanied by impaired LV function, one of the predictors of increased mortality was serum sodium concentration <138 mmol/L [11]. In our study, threshold of sodium concentration was higher: 140 mmol/L. Although both values of sodium concentration are within the normal range, such concentrations are associated with increased risk of death. It is assumed that in patients with CHF baroceptor dysfunction leads to decreased sodium concentration, which is an important linkage between vasomotor and neuroendocrine disturbances. Water and sodium balance depend on activity of mechanisms promoting renal sodium and water retention, i.e. increased sympathetic tone, renin-angiotensin--aldosterone (RAA) system and vasopressin secretion. This equilibrium may be influenced by the activity of mechanisms promoting natriuresis and diuresis such as renal dopamine, PGE2 and PGI2 production and release of ANP by atrial cardiomyocytes. Moreover, impaired renal perfusion caused by decreased cardiac output leads to upregulation of the RAA system and increased release of vasopressin. Additionally, in patients with CHF, increased endothelin-1 (ET-1) production, suppressed nitric oxide (NO) synthesis and development of renal resistance to natriuretic action of ANP, BNP and other natriuretic peptides were shown [12-15].

Left ventricular EF is a simple and very important parameter widely employed for the assessment of cardiac performance. Preload, afterload and myocardial contractility determine LVEF value. Large clinical trials involving patients with systolic heart failure documented unfavourable predictive value of decreased LVEF. An inverse correlation between LVEF and cardiovascular mortality in the course of heart failure was shown in the CONSENSUS, SOLVD, SAVE, DIG, V-HeFT I and II trials. Although CHF patients with LVEF ≥50% have similar risk of repeated hospital admissions caused by either CHF deterioration or acute circulatory destabilization to patients with decreased LVEF, mortality in patients with preserved LVEF is lower than in patients with impaired LVEF [16-18]. According to Gandhi et al., if increased arterial blood pressure leads to pulmonary oedema, and LVEF as an established risk factor is unchanged, impairment of LV relaxation is responsible for the development of haemodynamic deterioration [5]. Patients in our series had well preserved LVEF (mean value 55.5%), and patients with LVEF >50% accounted for 59% of the investigated population. However, all examined patients were acutely decompensated, similarly to the patients in Gandhi's et al. report.

It is thought that PH in the course of CHF is a result of impaired NO endothelial synthesis and increased release rate of endothelin by the endothelial cells of the pulmonary circulation [19]. Moreover, it may also be facilitated by both embolic and thrombotic components that are difficult to assess, resulting from either vasoconstriction, pulmonary vasculature remodelling or enhanced platelet activity [20, 21]. Numerous reports have shown that RV function significantly affects survival of patients with CHF [6-8, 22]. In a report by Ghio et al. [8] RVEF and PH, which is negatively correlated with RVEF, were found to be independent predicting factors. Thus, the presence of PH in patients with systolic heart failure identifies a group at markedly higher risk. Abramson et al. [23], investigating 108 consecutive patients with symptomatic HF accompanied by impaired LV systolic function, showed that peak velocity of tricuspid regurgitation exceeding 2.5 m/s (25 mmHg) was the most powerful variable predicting death and repeat hospitalisation during 28-month follow-up (mortality of 57% in comparison to 17%, mortality and rehospitalisation rate of 89% vs 32%).

In our study, LVEF <50% and RVSP >35 mmHg reached statistical significance only in univariate logistic regression analysis (p=0.039 and p=0.018), and thus were not found to be independent mortality predictors.

Conclusions

Age of over 60 years and sodium concentration below 140 mmol/L seen during acute decompensation were found to be independent predictors of unfavourable outcome in terms of mortality during 3-year follow-up of patients with CHF.

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Wartość rokownicza klinicznych i echokardiograficznych parametrów ocenianych w okresie ostrej dekompensacji przewlekłej niewydolności serca. Wynik 3-letniej obserwacji

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Streszczenie

Wstęp: Nie jest jasne, czy powszechnie akceptowane czynniki ryzyka wpływające na rokowanie w przewlekłej niewydolności serca (PNS) mają takie samo znaczenie prognostyczne, jeśli oceniane są w okresie nagłego hemodynamicznego pogorszenia PNS.

Cel: Analiza wpływu wybranych klinicznych i echokardiograficznych zmiennych, stwierdzanych podczas przyjęcia do szpitala chorych z PNS z powodu jej ostrej dekompensacji, na 3-letnie przeżycie.

Metody: Badanie retrospektywne, którym objęto 100 kolejnych wypisanych pacjentów z PNS (60 kobiet i 40 mężczyzn w średnim wieku 70,4±9,8 lat), przyjętych z objawami astmy sercowej lub obrzęku płuc. W badaniu echokardiograficznym wykonanym w ciągu pierwszych 48 godz. poza standardowymi parametrami określono ciśnienie skurczowe w prawej komorze (RVSP). Zastosowano jedno- i wieloczynnikową analizę regresji logistycznej Cox, aby określić biologiczne, kliniczne i echokardiograficzne zmienne wpływające na 3-letnie przeżycie.

Wyniki: W trakcie 3-letniej obserwacji zmarło 44 chorych. Niezależnymi czynnikami ryzyka zgonu były stężenie sodu w surowicy krwi poniżej 140 mmol/L, (p=0,0003) i wiek powyżej 60. roku życia (p=0,03). Natomiast wśród zmiennych echokardiograficznych istotność statystyczną obserwowano jedynie w analizie jednoczynnikowej dla RVSP powyżej 35 mmHg (p=0,018) i frakcji wyrzutowej lewej komory poniżej 50% (p=0,039).

Wnioski: Wiek powyżej 60. roku życia i stężenie sodu poniżej 140 mmol/L stwierdzane w okresie ostrej dekompensacji okazały się niezależnymi czynnikami wpływającymi niekorzystnie na 3-letnie przeżycie chorych z PNS.

Słowa kluczowe: przewlekła niewydolność serca, czynniki ryzyka

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