ORIGINAL ARTICLE

Three-year survival of patients with chronic systolic heart failure due to hypertension: analysis of prognostic factors

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ABSTRACT

INTRODUCTION   Despite advances in medicine, chronic systolic heart failure (CHF) due to hypertension still constitutes a serious clinical challenge.

OBJECTIVES   The aim of the study was to determine risk mortality factors in a 3-year follow-up of patients with CHF due to hypertension.

PATIENTS AND METHODS   The study involved 140 consecutive stable inpatients with CHF (left ventricular end diastolic diameter >57 mm; left ventricular ejection fraction [LVEF] <40%), without epicardial artery stenosis (>30% vessel lumen), significant heart defect, diabetes, neoplastic, disease, or chronic kidney disease, with a minimum 5-year history of hypertension, and administration of angiotensin-converting enzyme inhibitors (or angiotensin II receptor antagonists), β-adrenolytics, spironolactone and furosemide for 3 or more months. The follow-up began on admission to the hospital after laboratory tests, resting electrocardiogram and echocardiogram, six-minute walk test, coronarography, and endomyocardial biopsy. Late follow-up data was obtained from the follow-up visits or by telephone.

RESULTS   The analysis involved 130 of 140 patients aged 47.8 ±7.9 years. The 3-year mortality rate was 18.5%. Independent risk factors for death were LVEF (hazard ratio [HR], 0.881; 95% confidence interval [CI], 0.797–0.975, P <0.05), serum glucose (HR, 1.266; 95% CI, 1.085–1.627; P <0.05), N-terminal pro-B-type natriuretic peptide (NT-proBNP; HR, 1.369; 95% CI, 1.166–1.671; P <0.001), and bilirubin levels (HR, 1.057; 95% CI, 1.021–1.094; P <0.01).

CONCLUSIONS   Beside LVEF and serum NT-proBNP, other independent risk factors for death in patients with CHF due to hypertension are glucose and bilirubin levels.

INTRODUCTION   Despite advances in the diagnosis and treatment of coronary artery disease and arterial hypertension, the incidence and prevalence of chronic systolic heart failure (CHF) are still on the rise.[1-3] In people aged from 35 to 64 years, arterial hypertension causes a 4-fold increase in the risk of CHF; in elderly patients, the increase is 2-fold.[4,5] Disorders of the circadian rhythm of arterial pressure, such as the absence of night-time dip, are associated with a 2-fold increase in CHF risk.[6]

Hypertension leads to left ventricular (LV) overload and to alterations in cardiac structure and function, referred to as hypertensive heart disease.[7,8] The left ventricle adapts its size and shape to an increased afterload, which requires a greater energy input so as to maintain its cardiac output. Macro- and microangiopathy-related ischemia as well as fibrosis additionally impair the ventricular function. Excessive activation of the neurohormonal system maintains the faulty cycle of remodeling, thereby causing further pro-

gression of changes, with the subsequent release of circulating and tissue neurohormones.[7,8]

CHF risk stratification and evaluation of prognosis enable to identify individuals at highest risk and to implement intensive treatment. The prognosis in CHF is challenging, and the number of independent prognostic parameters is high.[9] This suggests the absence of one straightforward method for the assessment of death risk and exacerbation requiring hospitalization.

The prognostic value of a given parameter depends on the study group, the applied treatment, and follow-up duration.[9,10] The risk evaluated for a small group of selected patients receiving nonoptimal pharmacological treatment cannot be easily extrapolated to the entire population of patients with CHF. The multiple factor analyses available in the literature involve a limited number of parameters, whose prognostic strength may be lost in more comprehensive studies. Furthermore, the significance of various prognostic factors may depend on the etiology of concomitant diseases, and the duration and severity of symptoms.[9,11,12] The changing standards in CHF treatment also complicate the determination of uniform prognostic parameters. The introduction of drugs affecting myocardial remodeling, such as β-adrenolytic drugs and angiotensin-converting enzyme inhibitors (ACEIs), into routine therapy have changed the prognostic value of many known clinical, laboratory, and hemodynamic parameters.[3] There is a paucity of reports concerning the prognostic indices in patients with CHF due to hypertension.[13,14]

The aim of the study was to determine mortality risk factors in a 3-year follow-up period in patients with CHF due to hypertension.

PATIENTS AND METHODS The prospective study involved consecutive patients with stable systolic CHF (New York Heart Association [NYHA] class II and III) without concomitant coronary disease, admitted to the 3rd Department of Cardiology of the Medical University of Silesia, Katowice, Poland, between 2006 and 2007 with the aim to determine disease etiology and treatment intensity, and to consider potential heart transplantation. All patients suffered from long-lasting arterial hypertension. For at least 3 previous months, all patients had been receiving: maximum-tolerated doses of ACEIs (or angiotensin-II-receptor antagonist) and β-receptor antagonists (slow-release metoprolol or carvedilol preparations), spironolactone, and furosemide. The study protocol was approved by the local bioethics committee.

The inclusion criteria were as follows: CHF diagnosed at least 6 months before inclusion to the study, increased LV size (LV end-diastolic diameter >57 mm) associated with impaired systolic function (LV ejection fraction [LVEF] <40%), stable clinical status (NYHA II and III), at least 2 documented incidents of systolic pressure >140 mmHg and/or diastolic pressure >90 mmHg diagnosed less than 5 years before CHF onset.

The exclusion criteria were as follows: epicardial coronary artery stenosis (>30% of vessel lumen) by coronarography, active myocarditis based on myocardial biopsy (Dallas classification), presence of an acquired or congenital heart defect, advanced chronic kidney disease (estimated glomerular filtration rate [eGFR] <30 ml/min/1.73m^2), liver cirrhosis, diabetes, neoplastic diseases, implantable cardioverter-defibrillator (ICD) or a cardiac resynchronization therapy device, and treatment alteration during follow-up.

Hospital admission was the starting point of clinical observation. All patients had medical history taken, followed by physical examination and laboratory tests. Serum concentrations of the following parameters were measured (Cobas Integra analyzer, F. Hoffmann-La Roche Ltd, Switzerland): sodium and potassium, creatinine, total bilirubin, cholesterol, triglycerides, creatine kinase, uric acid, urea, alanine transaminase, aspartate transaminase, alkaline phosphatase, and glucose. In patients with elevated fasting glucose, the oral glucose tolerance test was performed. Blood cells, hemoglobin, and hematocrit were tested with the SF-3000 (SYSMEX Corporation, Japan) or ADVIA 2120 (Siemens, Germany) analyzers. The concentrations of high-sensitivity C-reactive protein were measured by latex-enhanced immunoturbidimetric assay with a 552 nm wavelength, (Cobas Integra 800; Roche). D-dimers were assayed with the immunoturbidimetric method using S.A. LIATEST reagents (STA Compact, Diagnostica Stago, Roche). N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels were measured by immunochemiluminescence (Elecsys 2010, Roche). Next, resting electrocardiography, 6-minute walk test, transthoracic echocardiography (Vivid 5, GE, United States), coronarography, and endomyocardial biopsy were performed. The eGFR was determined using the Modification of Diet in Renal Disease formula.[15] The 3-year follow-up data were obtained during 6 months of follow-up visits or by telephone.

Statistical analysis The normality of distribution was assessed with the Shapiro-Wilk test. Data with normal distribution were expressed as mean ± standard deviations. Nonnormally distributed data and ordinal data were presented as median and interquartile range. Qualitative data were shown as percentages.

For the comparison of data between the 2 groups of patients (death, survival), the following tests were used:

1 for data with normal distribution or after normalization: *t* test for independent data; variance homogeneity was assessed with the Levene's test;

2 for the remaining data: Mann-Whitney *U* test.

For the comparison of dichotomous variables, the χ^2 test or its modifications were applied. For the evaluation of the effect of continuous and dichotomous data on the incidence of death during late follow-up, the Cox proportional hazard was used. Variables of the single factor

analysis which proved to be statistically significant ($P < 0.05$), taking into consideration the collinearity of variables, were included in the multiple factor analysis using Cox proportional hazard, the backward elimination method.

The results are presented as hazard ratio (HR) with a 95% confidence interval (CI), Wald statistics, and the respective level of significance. To obtain the cut-off points for the parameters that reached statistical significance in the multiple factor analysis, appropriate receiver operator characteristics (ROC) curves were plotted. The results are presented as the area under the curve and sensitivity and specificity with 95% CI and the respective levels of significance. The comparison of death incidence in the groups of patients depending on the cut-off point was performed with the Kaplan-Meier curves and the log-rank test. A P level of less than 0.05 was considered statistically significant. All data were analyzed using the Statistica 8.0 PL version.

RESULTS Based on the inclusion and exclusion criteria, 140 of 238 patients were included in the analysis. In 82 of 98 patients who were not included in the study, significant coronary stenosis was observed on coronarography. In 16 patients, active myocarditis was diagnosed. In 10 of 140 patients, significant treatment alterations were observed in late follow-up: 2 patients did not follow the recommended pharmacotherapy, while 8 had an ICD implanted.

The final analysis included 130 inhospital patients receiving optimal pharmacotherapy. ACEIs were used by 121 patients (93%); the remaining patients received angiotensin-II-receptor antagonists. β-adrenolytics were administered to 118 patients (91%), loop diuretics (furosemide or torasemid) to 104 (80%), and spironolactone to 120 (92%). Digitalis glycosides were used in 78 patients (60%), acenocoumarol in 18 (14%), and statins in 29 (22%). Treatment was continued throughout the entire follow-up period.

Twenty-four patients (18.5%) died during follow-up. The cause of death was not determined in 14 patients. Based on the clinical data and postmortem examination, the causes of death in the remaining 10 patients were: sudden cardiac death in the asystolic mechanism (2 patients), pulmonary embolism (2 patients), failure of the heart as a pump (5 patients), and stroke (1 patient). Patients who died had a 3-fold longer history of the disease, higher NT-proBNP levels, and lower LVEF. They more frequently suffered from disturbed carbohydrate metabolism (higher fasting glycemia and hemoglobin A_{1c} [HbA_{1c}] levels) and had higher bilirubin levels (**TABLE 1**).

The multiple factor analysis of Cox proportional hazard, adjusted for patient's age, revealed that significant risk factors for death included LVEF, and serum NT-proBNP, glucose, and bilirubin levels (**TABLE 2**).

The **FIGURE** presents the Kaplan-Meier curves for the incidence of death, depending on the cut-off

points obtained from the ROC curves. Bilirubin levels over 17.4 µmol/l had the highest predictive sensitivity (**TABLE 3**). During follow-up, death was statistically significantly more frequent and occurred earlier in patients with higher levels of NT-proBNP, glucose, and bilirubin as well as lower LVEF.

DISCUSSION Patients with CHF analyzed in our study were free from coronary disease (excluded by coronarography) and myocarditis (Dallas criteria). They had long-term arterial hypertension, which was the only tangible factor likely to have caused LV dysfunction, followed by symptomatic CHF. The incidence of death in the analyzed group was low and reached 18.5%. The optimal pharmacotherapy throughout the entire study likely contributed to the positive outcome. Furthermore, the study included stable patients with CHF of nonischemic etiology, which has a much better prognosis than coronary CHF. The independent risk factors for death during follow-up were LVEF and serum NT-proBNP, glucose, and bilirubin levels.

Based on the analysis of 300 patients with stable CHF and LVEF below 45%, Richards et al.[16] claimed that NT-proBNP concentration above the median of 99 pmol/l (equivalent to 850 ng/l) led to an almost 5-fold increase in the risk of all-cause death.[16] In the Val-HeFT study, involving 5000 patients with mild and moderate CHF, NT-proBNP levels 500 ng/l higher than the baseline values were associated with an increased risk of death and rehospitalization.[17] In the study by Masson et al.,[18] the NT-proBNP concentration above 1000 ng/l in patients with CHF was associated with higher mortality. According to Bettencourt et al.,[19] changes in NT-proBNP levels during hospitalization due to CHF exacerbation were independent risk factors for death and hospitalization during a 6-month follow-up.[19] The BATTLESCARED study showed that after a 3-year follow-up, NT-proBNP-dependent therapy caused a significant reduction in mortality among elderly patients (>75-years old), but had no prognostic effect in younger age groups.[20] Another study, involving 181 patients with noncoronary CHF, aged 59 ±13 years, mainly with the NYHA class III (88.4%) showed that NT-proBNP concentration above 975 pg/ml was associated with a significantly higher mortality risk in a 1-year follow-up (relative risk, 4.72; $P < 0.001$).[21] Wedel et al.[22] evaluated the incidence of adverse events and deaths in 3342 patients with the NYHA classes II–IV, aged above 60 years. The authors showed that the log-transformed concentration (NT-proBNP) was a statistically significant risk factor for all-cause death (HR, 1.59; $P < 0.001$). According to the current standards of management, natriuretic peptides are recognized diagnostic and prognostic markers in CHF; nevertheless, the results available in the literature show substantial differences in the prognostic value of NT-proBNP, depending on the studied group.[9,10] Therefore, it

TABLE 1 Patient characteristics by survival/death

Parameter	Total	Survival	Death	P
	n = 130 (100%)	n = 106 (81.5%)	n = 24 (18.5%)	
age, y	48.8 ±7.9	49.3 ±7.3	46.5 ±10.0	NS
men, n (%)	107 (82.3)	88 (83.0)	19 (79.2)	NS
CHF duration, mo	13.0 (7.0–38.0)	12.0 (7.0–36.0)	36.0 (9.0–66.0)	<0.05
NYHA II, n (%)	96 (76.8)	80 (78.4)	16 (69.6)	NS
NYHA III, n (%)	29 (23.2)	22 (21.6)	7 (30.4)	NS
BMI, kg/m²	28.7 ±4.51	28.8 ±4.3	28.4 ±5.6	NS
hsCRP, mg/l	4.0 ±5.5	3.6 ±5.5	5.7 ±5.5	<0.01
D-dimer, μg/ml	0.37 ±0.31	0.35 ±0.31	0.43 ±0.29	NS
hemoglobin, mmol/l	9.1 ±0.9	9.1 ±0.8	8.9 ±1.1	NS
sodium, mmol/l	138.2 ±3.8	138.4 ±3.7	137.3 ±3.9	NS
potassium, mmol/l	4.49 ±0.46	4.48 ±0.44	4.55 ±0.54	NS
glucose, mmol/l	5.9 ±1.4	5.7 ±1.2	6.5 ±2.2	<0.05
hemoglobin A_{1c}	5.7 ±0.2	5.2 ±0.2	5.8 ±0.3	<0.01
IFG, n (%)	39 (30.0)	18 (17.0)	21 (87.5)	<0.001
creatinine, μmol/l	86.9 ±17.3	87.7 ±18.5	83.7 ±10.6	NS
eGFR, ml/min/1.73 m²	85.6 ±19.0	84.9 ±19.3	88.3 ±18.1	NS
NT-proBNP, pg/ml	1383.9 ±1589.6	970.9 ±1272.3	3017.1 ±1692.7	<0.001
bilirubin, μmol/l	20.4 ±11.7	18.7 ±9.8	28.2 ±15.9	<0.01
cholesterol, mmol/l	5.34 ±1.22	5.29 ±1.20	5.56 ±1.30	NS
triglycerides, mmol/l	1.96 ±1.00	2.02 ±1.04	1.69 ±0.77	NS
LVEF, %	30.8 ±7.3	31.7 ±7.3	26.7 ±5.9	<0.01
LVEDV, mm	211.8 ±73.2	202.5 ±69.1	254.5 ±77.7	<0.01
LVESV, mm	146.9 ±61.7	138.2 ±69.1	187.3 ±68.6	<0.01
LVM, g	357.7 ±85.2	353.6 ±86.2	377.1 ±79.8	NS
LA, mm	43.0 ±5.7	42.4 ±5.6	45.5 ±5.5	<0.05
RV, mm	26.8 ±7.3	25.5 ±6.6	32.7 ±7.5	<0.001
atrial fibrillation, n (%)	18 (14.1)	13 (12.4)	5 (21.7)	NS
LBBB, n (%)	28 (26.4)	23 (26.1)	5 (21.7)	NS

Data are presented as mean ± standard deviation, median (interquartile range), or number (percentage) of patients.

Abbreviations: BMI – body mass index, CHF – chronic heart failure, eGFR – estimated glomerular filtration rate, IFG – impaired fasting glucose, hsCRP – high-sensitivity C-reactive protein, LA – left atrium, LBBB – left bundle branch block, LVEDV – left ventricular end-diastolic volume, LVEF – left ventricular ejection fraction, LVESV – left ventricular end-systolic volume, LVM – left ventricular mass, NS – nonsignificant, NT-proBNP – N-terminal pro-B-type natriuretic peptide, NYHA – New York Heart Association, RV – right ventricle

TABLE 2 Results of a multifactor analysis by Cox proportional hazard stepwise regression analysis

Parameter	HR	95% CI	X²	P
NT-proBNP, ng/ml	1.369	1.166–1.671	13.25	<0.001
bilirubin, μmol/l	1.057	1.021–1.094	9.74	<0.01
LVEF, %	0.881	0.797–0.975	5.98	<0.05
glucose, mmol/l	1.266	1.085–1.627	3.49	<0.05

Abbreviations: CI – confidence interval, HR – hazard ratio, others – see **TABLE 1**

is questionable whether the determination of one value as the cut-off point is possible and whether the NT-proBNP concentration should be treated as a continuous variable associated, from a given value on, with an increase in the risk of death and cardiovascular complications.

Another independent risk factor in the analyzed group of patients was elevated fasting plasma glucose. The ROC curve analysis showed that the cut-off point beyond which there was a significant increase in mortality risk in the study group was 5.7 mmol/l, while the upper limit of the normal range for blood glucose concentration in the general population is 5.6 mmol/l. Although the 2 groups of patients (death, survival) differed significantly with regard to the concentrations of both glucose and HbA_{1c}, the glucose concentration was considered in a multifactor
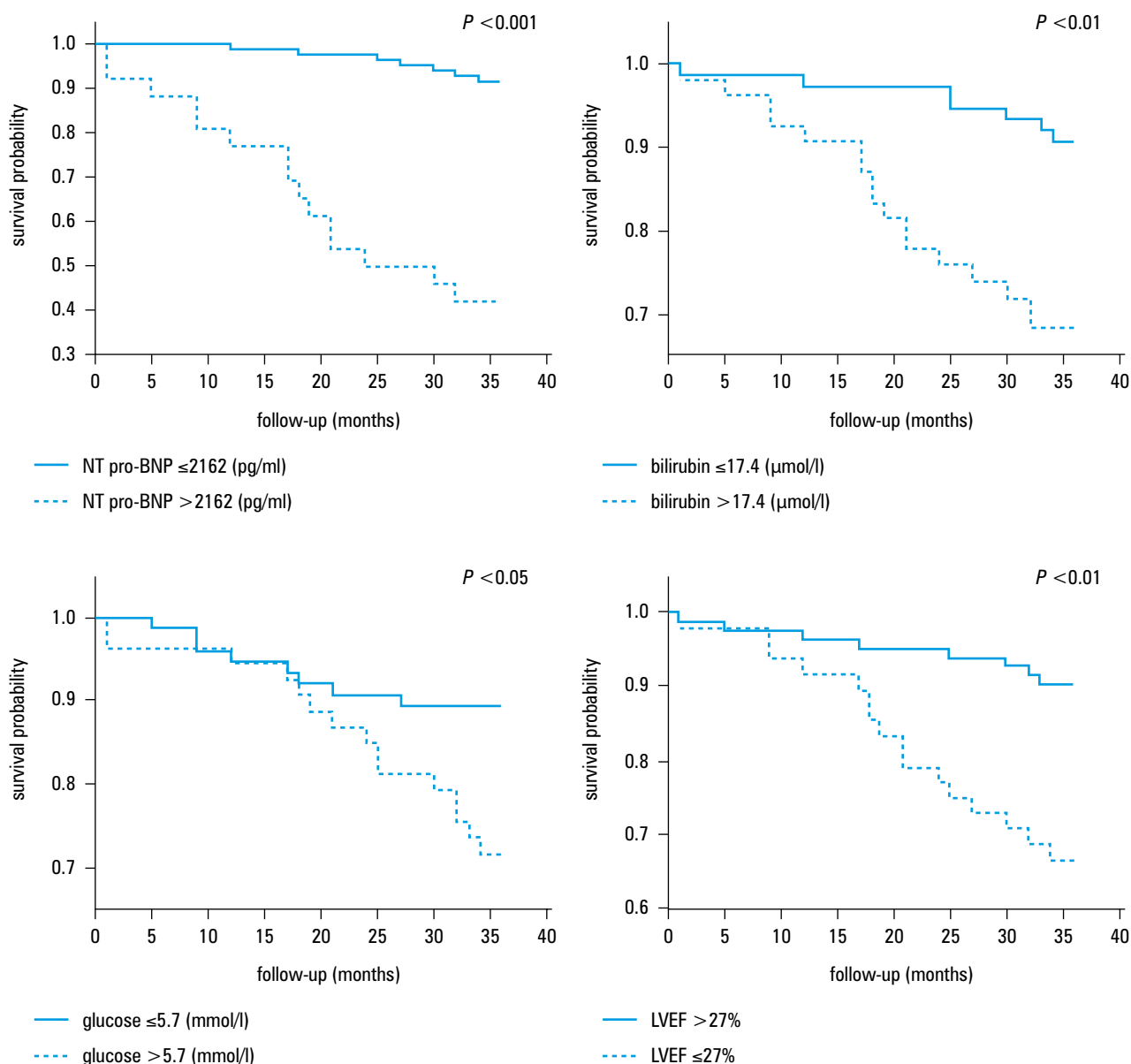
FIGURE Kaplan-Meier curves illustrating survival probability depending on the cut-off point
Abbreviations: see TABLE 1

analysis. In our opinion, fasting glucose levels have the highest practical value because its measurement is considerably cheaper than that of HbA$_{1c}$ and, importantly, its measurement is performed routinely in all patients with CHF. HbA$_{1c}$ determination is generally recommended in patients with diagnosed diabetes to monitor treatment efficacy. This has been confirmed by Thrainsdottir et al.[23] who showed that both diabetes and impaired glucose tolerance were independent risk factors for all-cause death.

Matsue et al.[24] analyzed 136 patients with CHF to determine the prognostic value of prediabetes on prognosis in a 150-day follow-up. Compared with our population, the analyzed patients were older and the inclusion criteria included both systolic and diastolic CHF. Unlike in our study, an elevated fasting glucose concentration was not an adverse prognostic factor.[24] The meta-analysis conducted by Countinho et al.[25] showed that only postprandial hyperglycemia, and not elevated fasting glucose concentration, was a factor that increased the risk of adverse cardiac events.

The results of the above studies confirm the adverse effect of insulin resistance on long-term prognosis in CHF patients. Still, obesity does not account for insulin resistance in the poor-prognosis group as the body mass index of the patients who survived tended to be slightly higher.

Interestingly, an elevated bilirubin concentration was an independent prognostic factor in our study. CHF is known to be associated with clinical, biochemical, and histological features of liver damage since hepatic flow decreases with the decrease of stroke volume. This leads to venous hypertension with impaired blood flow in portal circulation and the ensuing impaired oxygen supply to hepatic cells. Liver damage in CHF often has a subclinical course, with only a slight increase in bilirubin concentrations. The cut-off point for this parameter obtained from our analysis corresponds to the upper limit of the normal range for the general population. In our study, bilirubin was determined at baseline in patients receiving optimal treatment for at least 3 months. In further follow-up, bilirubin concentration, being

TABLE 3 Results of the receiver operating characteristic curve analysis

Parameter	P	AUC ±95% CI	Cut-off point	Sensitivity ±95% CI	Specificity ±95% CI
NT-proBNP, ng/ml	<0.001	0.861	>2162	68.2	87.3
		0.781–0.919		45.1–86.1	78.5–93.5
bilirubin, μmol/l	<0.01	0.704	>17.4	70.8	64.8
		0.618–0.781		48.9–87.3	54.8–73.8
LVEF, %	<0.001	0.712	≤27	66.7	69.8
		0.626–0.788		44.7–84.3	60.1–78.3
glucose, mmol/l	<0.05	0.643	>5.7	65.2	63.8
		0.553–0.726		42.7–83.6	53.9–73.0

Abbreviations: AUC – area under the curve, others – see **TABLES 1** and **2**

CHF-control-dependent, may provide an indication for treatment intensification. The results of our analysis are in line with the results obtained by Shinagawa et al.[26] who, based on the analysis of more than 180 patients with systolic CHF and admitted to the hospital due to circulatory decompensation, concluded that elevated total bilirubin concentration (HR, 1.896) on admission was an independent risk factor for death or hospitalization due to CHF exacerbation. Bilirubin correlated with central venous pressure, pulmonary capillary wedge pressure, and the cardiac index. Several other studies also demonstrated that serum bilirubin concentrations correlated with hemodynamic parameters.[27,28]

The retrospective analysis of over 100 patients conducted by Lau et al.[27] showed a strong correlation between cholestasis indices and severity of tricuspid insufficiency. Poelzl et al.[28] followed over 1000 patients for 36 months. The median age of the patients was 61 years, and the median LVEF was 28%. The majority of patients in that study suffered from nonischemic CHF (almost 70%), and bilirubin concentrations as a prognostic factor reached statistical significance only in a single-factor analysis. The independent prognostic factors for death were (depending on the model) 2 cholestasis indices: alkaline phosphatase and γ-glutamyltranspeptidase.

Another independent prognostic factor in the analyzed group of patients was LVEF measured by two-dimensional echocardiography. The available data on the significance of baseline LVEF for prognosis in CHF patients are ambiguous. To a large extent, this seems to be linked with constantly changing treatment standards and methods of treatment, etiology, and concomitant diseases. Not without significance is the fact that LVEF measured by two-dimensional echocardiography is assessed by simplified calculations in which the LV shape is brought down to an ellipsoid. Moreover, the result of the examination depends on the operator's expertise. Analyzing 314 patients with CHF of various etiology, de Groote et al.[29] proved the independent prognostic significance of LVEF measured by echocardiography in a group of patients with nonischemic CHF. Also Martinez-Selles et al.[30] confirmed the prognostic

value of LVEF in 701 consecutive hospitalized patients with CHF in long-term follow-up as part of the HOLA registry. LVEF measured by two-dimensional echocardiography and selected scintigraphic parameters were independent risk factors for all-cause death in a mean follow-up period of 9.1 ±4 years in the study by Momose et al.[31]

The Kaplan-Meier analysis showed that scintigraphy data were more useful in determining prognosis in the first 3 years of follow-up, while LVEF proved more useful in a 10-year prognosis. Solomon et al.[32] analyzed the prognostic value of LVEF in over 7000 patients with CHF in the NYHA classes II–IV. Arterial hypertension was present in approximately 50% of the patients. Patients were followed up for a median period of 38 months; mean LVEF was 38% (median, 36%). In patients with LVEF below 45%, LVEF was a potent prognostic factor for death.[32]

The strength of our study is the homogeneity of the analyzed group: all patients underwent coronarography and endomyocardial biopsy, the inclusion and exclusion criteria were precisely stipulated, and the pharmacotherapy was optimal. Patients with ICDs implanted during long-term follow-up were excluded from the study; all-cause death was the endpoint of the study and the implantation of an ICD would potentially have affected the result of the analysis and distort the homogeneity of the group. Still, the percentage of patients undergoing this form of treatment was very small. It is understandable considering the fact that the follow-up began in 2006–2007 when CHF management was regulated by the 2005 standards recommending the use of ICDs in secondary prevention and in selected patients with postinfarction CHF.

In conclusion, beside LVEF and serum NT-proBNP levels, also glucose and bilirubin levels are independent risk factors for death in patients with CHF due to hypertension.

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Trzyletnie przeżycie chorych z przewlekłą skurczową niewydolnością serca w przebiegu nadciśnienia tętniczego – analiza czynników prognostycznych

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STRESZCZENIE

WPROWADZENIE   Pomimo postępu w medycynie przewlekła skurczowa niewydolność serca (PNS) w przebiegu choroby nadciśnieniowej stanowi nadal istotny problem kliniczny.

CELE   Celem badania było określenie czynników ryzyka zgonu w 3-letniej obserwacji chorych z PNS w przebiegu nadciśnienia tętniczego.

PACJENCI I METODY   Badano 140 kolejnych hospitalizowanych, stabilnych chorych z PNS (wymiar końcowo-rozkurczowy lewej komory >57 mm, frakcja wyrzutowa lewej komory [*left ventricular ejection fraction* – LVEF] <40%), bez przewężeń tętnic nasierdziowych (>30% światła naczynia), istotnej wady serca, cukrzycy, choroby nowotworowej i przewlekłej choroby nerek, z co najmniej 5-letnim wywiadem nadciśnienia tętniczego, którzy przez 3 miesiące lub dłużej otrzymywali inhibitory konwertazy angiotensyny (lub antagonistów receptora angiotensyny II), β-adrenolityk, spironolakton i furosemid. Trzyletnią obserwację rozpoczęto przy przyjęciu do szpitala po wykonaniu badań laboratoryjnych, spoczynkowego badania elektrokardiograficznego i echokardiograficznego, testu 6-minutowego marszu, koronarografii i biopsji endomiokardialnej. Dane dotyczące obserwacji odległej uzyskiwano na podstawie dokumentacji ambulatoryjnej wizyt kontrolnych lub przez kontakt telefoniczny.

WYNIKI   Do analizy zakwalifikowano 130 ze 140 chorych w wieku 47,8 ±7,9 roku. Trzyletnia śmiertelność wyniosła 18,5%. Niezależnymi czynnikami ryzyka zgonu były: LVEF (hazard względny [*hazard ratio* – HR] = 0,881; 95% przedział ufności [*confidence interval* – CI]: 0,797–0,975; p <0,05), stężenie glukozy w surowicy (HR = 1,266; 95% CI: 1,085–1,627; p <0,05), stężenie N-końcowego fragmentu propeptydu natriuretycznego typu B (NT-proBNP; HR = 1,369; 95% CI: 1,166–1,671; p <0,001) oraz stężenie bilirubiny (HR = 1,057; 95% CI: 1,021–1,094; p <0,05).

WNIOSKI   Poza LVEF i stężeniem NT-proBNP w surowicy, niezależnymi czynnikami ryzyka zgonu chorych z PNS w przebiegu nadciśnienia tętniczego są stężenia glukozy i bilirubiny.

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