

# The impact of chronic kidney disease on the annual prognosis in patients 80+ years old suffering from chronic heart failure

Anna Cichocka-Radwan, Tomasz Ciurus, Małgorzata Lelonek

Department of Cardiology, Chair of Cardiology and Cardiac Surgery, Medical University of Lodz, Poland

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## Abstract

**Introduction:** It is well known that the function of kidneys is impaired with age.

**Aim:** The purpose of the study was to evaluate whether chronic kidney disease (CKD) is a predictor for 1-year follow-up mortality among hospitalized chronic heart failure (CHF) patients aged 80+.

**Material and methods:** The study included 141 consecutive patients aged 80-92 (mean: 82.4 years, 44.7% men). The prospective analysis contains 61 variables with glomerular filtration rate (GFR) and the occurrence of death at the 1-year follow-up. Patients were divided and analyzed depending on GFR.

**Results:** Chronic kidney disease defined as estimated GFR < 60 ml/min/1.73 m<sup>2</sup> was recorded in 93 patients (66%). A relationship with GFR < 60 was found for older age ( $p = 0.0001$ ), lower body mass index – BMI ( $p = 0.003$ ), more advanced NYHA class III ( $p = 0.007$ ), higher concentrations of N-terminal pro-brain natriuretic peptide – NT-proBNP ( $p = 0.023$ ), lower hemoglobin ( $p = 0.0004$ ) and LVEF ( $p = 0.005$ ), longer hospitalization ( $p = 0.005$ ), more frequent ventricular blocks in ECG ( $p = 0.017$ ) and rarely performed coronary angiography ( $p = 0.021$ ). In turn, GFR < 30 ml/min/1.73 m<sup>2</sup> was recorded in 14 patients (9.9%). Similar relationships as in GFR < 60 were found for GFR < 30 and additionally higher concentrations of high-sensitivity C-reactive protein (hsCRP) ( $p = 0.003$ ), D-dimer ( $p = 0.002$ ) and more frequent dyslipidemia ( $p = 0.004$ ) and left main coronary artery disease ( $p = 0.007$ ). Annual mortality for the total population was 14.2% ( $n = 20$ ) and was higher (16.1%) if GFR was < 60 and even more (21.4%) in GFR < 30. However, the relationship between deaths and GFR was not statistically significant (for GFR < 60,  $p = 0.505$  and GFR < 30,  $p = 0.547$ ).

**Conclusions:** Annual mortality in the patients 80+ who suffered from CHF was high but not statistically significantly associated with CKD.

**Key words:** elderly, heart failure, chronic kidney disease, prognosis.

## Streszczenie

**Wstęp:** Powszechnie wiadomo, że z wiekiem funkcja nerek ulega upośledzeniu.

**Cel:** Ocena wpływu przewlekłej choroby nerek (PChN) na roczne rokowanie pacjentów  $\geq 80$ . roku życia hospitalizowanych z powodu przewlekłej niewydolności serca (PNS).

**Materiał i metody:** Badaniem objęto 141 kolejnych chorych w wieku 80–92 lata (średni wiek: 82,4 roku, 44,7% mężczyzn). Analiza prospektywna zawierała 61 zmiennych z współczynnikiem przesączania kłębuszkowego (GFR) i występowaniem zgonów w obserwacji rocznej. Pacjentów podzielono i analizowano w zależności od GFR.

**Wyniki:** Przewlekłą chorobę nerek definiowaną jako GFR < 60 ml/min/1,73 m<sup>2</sup> odnotowano u 93 pacjentów (66%). Udokumentowano zależność pomiędzy GFR < 60 a starszym wiekiem ( $p = 0,0001$ ), niższym wskaźnikiem masy ciała – BMI ( $p = 0,003$ ), bardziej zaawansowaną klasą NYHA III ( $p = 0,007$ ), większym stężeniem N-końcowego propeptydu natriuretycznego typu B – NT-proBNP ( $p = 0,023$ ), mniejszym stężeniem hemoglobiny ( $p = 0,0004$ ), niższą LVEF ( $p = 0,005$ ) oraz dodatkowo dłuższym okresem hospitalizacji ( $p = 0,005$ ), częstszymi wewnątrzkomorowymi blokami przewodzenia ( $p = 0,017$ ) i rzadziej wykonywaną koronarografią ( $p = 0,021$ ). Z kolei GFR < 30 ml/min/1,73 m<sup>2</sup> wykazano u 14 pacjentów (9,9%). Podobnie zależności jak dla GFR < 60 wykazano dla GFR < 30, a ponadto stwierdzono związek z większym stężeniem białka C-reaktywnego oznaczanego metodą wysokiej czułości (hsCRP) ( $p = 0,003$ ) i D-dimerów ( $p = 0,002$ ) oraz częstszym występowaniem dyslipidemii ( $p = 0,004$ ) i choroby pnia tętnicy wieńcowej lewej ( $p = 0,007$ ). Śmiertelność roczna w całej populacji wyniosła 14,2% ( $n = 20$ ) i była wyższa (16,1%), jeśli GRF wynosił < 60 i jeszcze wyższa (21,4%) przy GRF < 30. Związek pomiędzy wystąpieniem zgonu a GFR < 60 i GRF < 30 był jednak nieistotny statystycznie (dla GFR < 60 –  $p = 0,505$ , dla GRF < 30 –  $p = 0,547$ ).

**Wnioski:** Śmiertelność roczna pacjentów  $\geq 80$ . roku życia z przewlekłą niewydolnością serca była wysoka, ale związana nieistotnie statystycznie z przewlekłą chorobą nerek.

**Słowa kluczowe:** starość, niewydolność serca, choroba nerek, rokowanie.

**Address for correspondence:** prof. dr hab. med. Małgorzata Lelonek, Department of Cardiology, Chair of Cardiology and Cardiac Surgery, Medical University, 1/3 Sterling St., 91-425 Lodz, Poland, phone: +48 42 636 44 71, e-mail: mlelonek@poczta.fm

## Introduction

In recent decades, we have observed the systematic extension of the life span in developed countries. Age is the most important and an independent risk factor for chronic heart failure (CHF). The incidence of CHF is estimated as approximately 2-3% in the general population and significantly increases over age 75 up to 10-20% in octogenarians and nonagenarians and is the first reason for hospitalizations [1]. Chronic heart failure is one of the major causes of death for both men and women over 80 years old, and their five-year survival is only 19% [2, 3].

The aging process is also associated with a deterioration in renal function and decrease in GFR of approximately 1 ml/min/1.73 m<sup>2</sup> per year after the fourth decade of life [4]. Prevalence of renal insufficiency with an MDRD-estimated GFR less than 60 ml/min/1.73 m<sup>2</sup> is reported as from nearly 40% in persons aged 60 to one-half of individuals older than 70 years [5, 6]. In most cases in octogenarians and nonagenarians chronic renal insufficiency leads to the terminal state [7].

The prevalence of CHF is already increased in early renal disease and progresses with a decrease in renal function [8]. It was also shown that there is an increased risk of total and cardiovascular mortality in patients with chronic kidney disease (CKD) and CHF compared to individuals with normal renal function in the general population [9]. But what is the prognostic importance of CKD in octogenarians and nonagenarians suffering from CHF?

The aim of the study was to assess the impact of CKD on the one-year outcome of patients aged 80+ hospitalized due to CHF in the cardiac ward.

## Material and methods

### Materials

The study involved 141 consecutive patients during a period of 15 months hospitalized in the Department of Cardiology who were aged 80 years or more (mean age: 82.4 years, 44.7% men) and suffered from CHF. Exclusion criteria were: patients aged < 80, acute heart failure, acute coronary syndrome, severe valvular heart disease, inflammatory process, limited contact with patient due to a significant degree of dementia or acute mental disorder that prevents logical co-operation, and not obtaining written informed consent to the study.

Sixty-one variables were investigated: age, gender, New York Heart Association (NYHA) functional class, selected risk factors including body mass index (BMI), arterial blood pressure, impaired glucose and lipid metabolism, results of basic laboratory tests (creatinine, glomerular filtration rate [GFR] estimated by Cockcroft-Gault's model, white blood cells, hemoglobin, glucose and lipid levels) and selected biomarkers, including high-sensitivity troponin T (hsTnT) and N-terminal pro-brain natriuretic peptide (NT-proBNP). Next, the analysis involved: 12-lead resting electrocardiography (ECG), heart rhythm (sinus rhythm or atrial arrhythmias) and ventricular conduction abnormalities. In addition, we

analyzed the burden of comorbidities and results of echocardiography and coronary angiography.

Echocardiography and coronary arteriography were performed according to the ESC and ASE/EAE recommendations. Using M-mode, 2-dimensional and Doppler echocardiographic examinations, left ventricular systolic (LVSD) and diastolic dimensions (LVDD), left ventricular end-systolic (LVESV) and end-diastolic volume (LVEDV) and left ventricular ejection fraction (LVEF), diastolic relaxation disturbances and septal diameter were assessed. Coronary arteriography was performed as needed using a femoral or radial approach. The degree of luminal obstruction in conventional visual quantification of coronary arteriography was evaluated to calculate the sclerotic alteration in coronary arteries (stenosis  $\geq$  50% of the left main coronary artery and  $\geq$  75% of other coronary arteries).

Participants were prospectively followed with observation for one year and the information on survival was collected by a cardiologist contacting them or their families by telephone. The cause of death was established during an interview based on the medical record or post mortem chart if available or based on an interview with a family member if the patient died outside the hospital. Patients were divided and analyzed depending on GFR: GFR < 30, GFR 30-60 and GFR > 60 ml/min/1.73 m<sup>2</sup>.

The study was approved by the Bioethical Committee of the Medical University of Lodz.

### Statistical analysis

Calculations were performed using the statistical package STATISTICA PL 10. Quantitative variables were characterized giving the basic descriptive statistics: number of observations (*N*), mean, median, minimum (Min) and maximum value (Max), the first (Q25) and third (Q75) quartiles, and standard deviation (SD). The hypothesis of normal distribution was verified using the Shapiro-Wilk test of normality. In the case of qualitative variables for each category there was given a variable number of observations with a given variant (*N*) and the corresponding percentage.

Differences between two independent variables for continuous data were analyzed using Student's *t* test (if the variable distribution was normal in both groups), and Mann-Whitney's test (in the absence of normal distribution). The independence  $\chi^2$  test with Yates' correction was used to investigate whether there is a relationship between GFR and the various qualitative variables. To compare three independent samples – GFR < 30, GFR 30-60, and GFR > 60 – the parametric ANOVA (with post-hoc tests) was used.

*P* values < 0.05 were considered statistically significant.

## Results

The causes of hospitalization of studied patients were: NYHA II – 35.5%, NYHA III – 38.3%, NYHA ambulatory IV – 14.9% or reduced exercise tolerance in 42.3% and in 30.2% peripheral edema. Most patients had arterial hypertension (85.8%), overweight or obesity (70.2%) and stable coro-

nary heart disease (70.2%). Slightly fewer were burdened by dyslipidemia (43.3%), impaired glucose metabolism (36.9%) and thromboembolism (14.9%). A common phenomenon was also the coexistence of other noncardiac diseases (82.3%) and polypharmacy. The participants used on average 7.3 drugs daily (ranges 6-10) and were hospitalized at the ward for on average 5.33 days. Most often the studied patients suffered from CKD with GFR < 60 ml/min/1.73 m<sup>2</sup> – 66% (*n* = 93). GFR < 30 was present in 9.9% of patients (*n* = 14), lung disease in 27.6% (chronic obstructive pulmonary disease 12.8%; bronchitis, emphysema and tuberculosis 12.8% and asthma 2.2%), anemia in 28.3% and cancer in 12.8%.

The baseline characteristics of patients depending on GFR < 30, GFR 30-60 and GFR > 60 ml/min/1.73 m<sup>2</sup> are presented in Tables I-IV. The total CKD group with GFR < 60 was slightly older (83.3 vs. 81.5 years, *p* = 0.0001), with lower BMI (26.07 vs. 28.05, *p* = 0.003) and was admitted to the ward for longer hospitalization (6.58 vs. 4.71, *p* = 0.005). A relationship with GFR < 60 was found for more advanced NYHA class III (*p* = 0.007), higher concentration of NT-proBNP (*p* = 0.023), lower hemoglobin (*p* = 0.0004), lower LVEF (*p* = 0.005), more frequent ventricular blocks in ECG (*p* = 0.017), and rarely performed coronary angiography (*p* = 0.021). Compared to patients with GFR > 60, patients with CKD did not differ in either cardiovascular (20.8% vs. 19.4%, *p* > 0.05) or non-cardiac comorbidities (77.1% vs. 84.9%, *p* > 0.05) or in other analyzed variables.

Similarly, a relationship with GFR < 30 ml/min/1.73 m<sup>2</sup> was found for advanced NYHA class: III (*p* = 0.017) and IV (*p* = 0.003), higher concentrations of NT-proBNP (*p* = 0.003), lower hemoglobin (*p* = 0.0001), more frequent ejection fraction (EF) < 45% (*p* = 0.004) and ventricular blocks in the electrocardiogram (*p* = 0.023), rarely performed coronary angiography (*p* = 0.032), and additionally with less frequent hypertension (*p* = 0.049), higher concentrations of hsCRP (*p* = 0.003) and D-dimer (*p* = 0.002), more frequent dyslipidemia (*p* = 0.004) and left main coronary artery disease (*p* = 0.007) (Tables I-IV).

In our study cardiac catheterization was done in 51.1% (*n* = 72) and was least frequent when GFR was < 30 (Table IV). Percutaneous coronary intervention was performed in 44.4% (*n* = 32) of patients diagnosed by catheterization. Coronary artery bypass graft (CABG) was performed only in 34.5% (*n* = 10) of patients with angiographic indications for this treatment, in 50% of patients with GFR < 30 (*n* = 1 in a group of 2 patients), in 35.3% with GFR = 30-60 (6/17 patients), and in 30% of patients with GFR > 60 (3/10 patients). The others were not operated on because of a high EuroSCORE, coexistence of noncardiac diseases with poor prognosis (life expectancy < 1 year) and disseminated atherosclerosis in coronary arteries.

Annual mortality for the total population was 14.2% (*n* = 20) and was higher (16.1%, *n* = 15) if GFR was < 60 and even more (21.4%, *n* = 3) when GFR was < 30. There was a relationship between deaths and GFR < 60 and GFR

**Tab. I.** Clinical characteristics of the studied population

Factor	GFR < 30 patients <i>n</i> = 14	GFR = 30-60 patients <i>n</i> = 79	GFR > 60 patients <i>n</i> = 48	<i>p</i> ANOVA
Age [years]	83 82-85*	83 81-85*	81 80-82*	<b>0.0003</b>
Male sex	5 (35.7)	34 (43.0)	24 (50.0)	0.579
Overweight + obesity	7 (53.9)	56 (70.9)	36 (76.6)	0.276
BMI [kg/m <sup>2</sup> ]	25.2 ± 3.8 20.7-29.0	26.2 ± 3.2 18.3-34.6	28.1 ± 3.8 20.7-37.9	<b>0.004</b>
Hypertension	9 (64.3)	69 (87.3)	39 (81.3)	<b>0.049</b>
Systolic blood pressure [mmHg]	122.5 ± 12.9 100-145	141.1 ± 22.7 90-200	138.5 120-150*	<b>0.005</b>
Diastolic blood pressure [mmHg]	72.3 ± 9.0 55-90	80 70-90*	80 70-85*	<b>0.031</b>
Lipid disorders	10 (71.4)	25 (31.7)	26 (54.2)	<b>0.004</b>
Impaired glucose metabolism	9 (34.3)	29 (36.7)	14 (29.1)	0.057
Hospitalization [days]	7 4-11*	5 3-8*	4 3-6*	<b>0.006</b>
Number of drugs/person/day	7.9 ± 1.2 6-10	7 6-9*	7 6-9*	0.360

Data are expressed as *N* (%), mean ± SD and ranges in normal distribution, median and interquartile ranges (IQR) in non-normal distribution (\*)

GFR – glomerular filtration rate (ml/min/1.73 m<sup>2</sup>) estimated by Cockcroft-Gault's model, BMI – body mass index

Age: #*p* = 0.005, GFR < 30 vs. GFR > 60, ##*p* = 0.002, GFR = 30-60 vs. GFR > 60

BMI: *p* = 0.023, GFR = 30-60 vs. GFR > 60

Hypertension: *p* = 0.049, GFR < 30 vs. GFR > 60

Systolic blood pressure: #*p* = 0.004, GFR < 30 vs. GFR > 60, ##*p* = 0.0049 GFR < 30 vs. GFR = 30-60

Diastolic blood pressure: *p* = 0.032, GFR < 30 vs. GFR = 30-60

Lipid disorders: *p* = 0.004 GFR < 30 vs. GFR > 60

Hospitalization: *p* = 0.012 GFR < 30 vs. GFR > 60

**Tab. II.** Electrocardiographic and echocardiographic characteristics of the studied population

Factor	GFR < 30 patients <i>n</i> = 14	GFR = 30-60 patients <i>n</i> = 79	GFR > 60 patients <i>n</i> = 48	<i>p</i> ANOVA
Electrocardiography (ECG)				
Heart rate/min	63 60-75*	70 60-80*	70 60-75*	0.440
Ventricular blocks	5 (35.7)	20 (35.6)	4 (8.3)	<b>0.023</b>
Atrial arrhythmia	4 (28.6)	17 (21.8)	15 (31.2)	0.589
Echocardiography				
EF [%]	43 22-61*	55 43-64*	63 54-67*	<b>0.007</b>
EF < 45%	6 (50.0)	18 (26.1)	4 (8.7)	<b>0.004</b>
LVDD [mm]	5.8 ± 1.4 4-8.2	5.1 4.2-5.9*	5.1 ± 0.7 3.7-6.4	0.412
LVSD [mm]	4.3 ± 1.7 2.1-6.9	3.2 2.7-4.2*	3.5 ± 0.8 2.2-5.2	0.345
LVEDV [ml]	97.5 93-102*	90.2 86-129*	86.8.3 ± 30.6 44-153.7	0.230
LVESV [ml]	40.5 37-44*	39.5 24.6-91*	27 22-47*	0.257
Septal hypertrophy	2 (15.4)	28 (40.0)	17 (36.2)	0.237
Diastolic relaxation disturbances	5 (41.7)	24 (34.8)	23 (48.9)	0.312

Data are expressed as *N* (%), mean ± SD and ranges in normal distribution, median and interquartile ranges (IQR) in non-normal distribution (\*)

GFR – glomerular filtration rate (ml/min/1.73 m<sup>2</sup>) estimated by Cockcroft-Gault's model, EF – ejection fraction, LVSD – end-diastolic dimension of the left ventricle, LVSD – end-systolic dimension of the left ventricle, LVESV – left ventricular end-systolic volume, LVEDV – left ventricular end-diastolic volume

Ventricular blocks: *p* = 0.023, GFR < 30 vs. GFR > 60

EF: *p* = 0.014, GFR < 30 vs. GFR > 60

EF < 45%: *p* = 0.004, GFR < 30 vs. GFR > 60

< 30 but it was not statistically significant (respectively *p* = 0.505 and *p* = 0.547). The proportion of hospital mortality and deaths during a year of observation was 0.7% (*n* = 1) and 19.71% (*n* = 27). One person (with GFR = 30-60) died in hospital due to decompensated HF. The cause of death during a year of follow-up was difficult to state by the patients' family in 51.9%, while in 25.9% it was due to cardiovascular reasons (decompensated heart failure – 19.9%, myocardial infarction – 6%) and in 22.2% noncardiac (stroke – 14.8%, pneumonia – 7.4%). Annual mortality in the group of non-operated patients with angiographic indications for CABG was 22.7% compared to 14.3% in the operated group (*p* > 0.05).

## Discussion

The main finding of our study was that the mortality rate throughout the year of observation in patients over 80 years old suffering from CHF was higher if renal insufficiency occurs. However, we did not reveal a statistically significant relationship between deaths and GFR (*p* > 0.05).

In the general population hospitalized due to CHF, renal dysfunction, which occurs frequently, has been recognized as an adverse prognostic factor among cardiologists [10]. Most studies that observed high mortality in heart failure and renal insufficiency included patients aged ≥ 65 years old but a subgroup of octogenarians and nonagenarians was not distinguished, making direct comparisons unfeasible.

In Fried's study elevated creatinine was a significant predictor of all-cause (*p* < 0.001) and cardiovascular mortality (*p* < 0.001) as well as CHF (*p* < 0.001) in 5808 patients older than 65 years who were followed for a median of 7.3 years. A linear increase in cardiovascular risk was observed with increasing creatinine [11]. The observation of the oldest patients was made by Mogensen *et al.* [12]. They reported that mortality risk in a similar follow-up time as in the report of Fried – between 6 and 8 years in patients aged > 85 years – was associated with renal insufficiency (HR = 1.36, *p* < 0.0001) but had less prognostic importance than in younger patients (*p* for interactions < 0.003) [12]. Unfortunately, there is no analysis in terms of annual follow-up in this survey.

In turn, in the subgroup of patients > 80 years old with CHF in Forman's study, worsened renal function defined as a rise in serum creatinine of > 0.3 mg/dl (26.5 μmol/l) occurred in 26.9% and was associated with death during hospitalization, complications and, similarly to our study, longer length of stay [13].

The standard clinical measures of renal function – serum creatinine, which partly reflects muscle mass, and creatinine-based estimates of glomerular filtration rate (GFR) – may be less correlated with actual GFR in the elderly and insensitive for detecting renal insufficiency [14]. Some studies suggest that cystatin C, a novel serum meas-

**Tab. III.** Biochemical characteristics of the studied population

Biochemical characteristics	GFR < 30 patients <i>n</i> = 14	GFR = 30-60 patients <i>n</i> = 79	GFR > 60 patients <i>n</i> = 48	<i>p</i> ANOVA
Creatinine [mg/dl]	1.9 1.8-3*	1.1 0.9-1.3*	0.8 ± 0.16 0.5-1.2	<b>0.000</b>
Glucose [mmol/l]	6.3 5.1-9.6*	6.0 5.3-6.9*	5.8 5.4-6.4*	0.663
NT-proBNP [pg/ml]	9314.4 ± 8722.2 884-23491	1206 411.2-3212*	527.5 257.1-1098*	<b>0.003</b>
hsTnT [ng/l]	31 15-51*	18.5 11-36*	12 10-26*	0.083
hsCRP [mg/l]	14.4 ± 10.6 1.2-30.2	2 1.1-6.5*	1.95 1.1-4*	<b>0.003</b>
D-dimer [pg/ml]	3.06 1.9-5.1*	0.6 0.5-1.4*	0.8 ± 0.6 0.01-1.9	<b>0.002</b>
White blood cells [10 <sup>3</sup> /μL]	7.5 5.8-9*	6.8 5.6-8.9*	6.8 ± 1.8 2.1-11.2	0.465
Hemoglobin [g/dl]	11.5 ± 1.2 9.1-13.7	12.5 11.8-13.8*	13.6 12.5-14.6*	<b>0.0001</b>
Anemia	11 (84.6)	36 (45.6)	7 (14.6)	<b>0.000</b>
Total cholesterol [mg/dl]	3.9 ± 1.1 2.1-5.6	4.3 ± 1.1 2.5-7.7	4.4 ± 0.9 2.9-6.3	0.663
Low-density lipoprotein [mg/dl]	2.2 ± 0.7 1.0-3.2	2.1 1.7-2.8*	2.4 ± 0.7 1.3-3.7	0.897
High-density lipoprotein [mg/dl]	1.1 ± 0.5 0.6-1.8	1.4 ± 0.4 0.7-2.7	1.4 ± 0.4 0.7-2.2	0.189
Triglyceride [mg/dl]	2.5 2.2-4.4*	2.5 2.0-3.8*	2.9 ± 1.9 0.4-7.8	0.871

Data are expressed as *N* (%), mean ± SD and ranges in normal distribution, median and interquartile ranges (IQR) in non-normal distribution (\*).

GFR – glomerular filtration rate (ml/min/1.73 m<sup>2</sup>) estimated by Cockcroft-Gault's model, NT-proBNP – N-terminal pro-brain natriuretic peptide, hsTnT – high-sensitivity troponin T, hsCRP – high-sensitivity C-reactive protein

Creatinine: \**p* = 0.0001, GFR < 30 vs. GFR = 30-60, \*\**p* = 0.000 GFR < 30 vs. GFR > 60, \*\*\**p* = 0.000 GFR = 30-60 vs. GFR > 60

NT-proBNP: #*p* = 0.031 GFR < 30 vs. GFR = 30-60, ##*p* = 0.002 GFR < 30 vs. GFR > 60

hsCRP: \**p* = 0.005 GFR < 30 vs. GFR = 30-60, \*\**p* = 0.002 GFR < 30 vs. GFR > 60

D-dimer: \**p* = 0.002 GFR < 30 vs. GFR = 30-60, \*\**p* = 0.011 GFR < 30 vs. GFR > 60

Hemoglobin: #*p* = 0.024 GFR < 30 vs. GFR = 30-60, ##*p* = 0.000 GFR < 30 vs. GFR > 60, \*\*\**p* = 0.014 GFR = 30-60 vs. GFR > 60

Anemia: *p* = 0.000 GFR < 30 vs. GFR > 60

**Tab. IV.** Angiographic characteristics of the studied population

Factor	GFR < 30 patients <i>n</i> = 14	GFR = 30-60 patients <i>n</i> = 79	GFR > 60 patients <i>n</i> = 48	<i>p</i> ANOVA
Cardiac catheterization	4 (28.6)	37 (46.8)	31 (64.6)	<b>0.032</b>
Left main coronary artery disease	2 (40.0)	4 (9.1)	1 (2.4)	<b>0.007</b>
1 – vessel coronary artery disease	1 (20.0)	3 (5.5)	4 (9.8)	0.439
2 – vessel coronary artery disease	2 (40.0)	13 (23.2)	11 (26.8)	0.689
3 – vessel coronary artery disease	1 (20.0)	16 (28.6)	10 (24.4)	0.850

Data are expressed as *N* (%).

GFR – glomerular filtration rate (ml/min/1.73 m<sup>2</sup>) estimated by Cockcroft-Gault's model

Cardiac catheterization: *p* = 0.032 GFR < 30 vs. GFR > 60

Left main coronary artery disease: *p* = 0.007 GFR < 30 vs. GFR > 60

ure of renal function, may better approximate GFR than creatinine [15, 16]. Its associations with CHF outcomes in elderly was compared in Shlipak's study [17]. Each standard deviation increase in cystatin C (0.35 mg/l) was associated with a 31% greater adjusted mortality risk (95% confidence interval [CI]: 20-43%, *p* < 0.001), whereas each standard de-

viation increase in creatinine (0.39 mg/dl) was associated with a 17% greater adjusted mortality risk (95% CI: 1-36%, *p* = 0.04).

Chronic heart and renal failure are called the two new epidemics [7]. These diseases mainly affect the elderly; the prevalence of each increases with every successive decade

of age. Hence, the burden associated with these disorders is expected to grow because of the aging of the population. Many of the randomized clinical trials have excluded elderly patients or patients with significant co-morbidities. In particular, participants aged  $\geq 75$  years have been barely represented in large trials and most of the data come from registries [18]. The number of studies on mortality and factors affecting the prognosis in heart failure in the elderly is small [19, 20].

Interactions between the heart and the kidneys and their impact on mortality have been known and discussed for decades. Patients with CKD have a substantially increased risk of cardiovascular disease compared with the general population. In end-stage renal disease they have a more than 10-fold increased risk of cardiovascular death than do age- and gender-matched controls in the general population [21]. The high prevalence of established traditional risk factors for atherosclerosis and hemodynamic overload, characteristic of chronic uremia, undoubtedly contributes to the accelerated rate of CHF. In our study of participants hospitalized for CHF, we revealed a relationship between  $\text{GFR} < 60$  or even  $\text{GFR} < 30$  and more advanced NYHA class, higher concentration of NT-proBNP and lower LVEF in the  $\text{GFR} < 60$  group or more frequent  $\text{LVEF} < 45\%$  in the  $\text{GFR} < 30$  group. Nevertheless, people  $> 75$  years old without heart failure have 2-3-fold higher serum concentration of NT-proBNP, which is related mostly to the reduction of GFR. Moreover, in Pfisterer's study heart failure therapy guided by N-terminal BNP in patients aged 75 years or older did not improve overall clinical outcomes or quality of life compared with symptom-guided treatment, in contrast to those aged 60 to 75 years [22]. Similarly, CKD patients even without CHF typically develop edema and complain of shortness of breath. Surely more advanced NYHA class, higher concentration of NT-proBNP and lower LVEF are factors of poor prognosis in CHF patients, but these issues in CKD and elderly age are very complex and require further studies.

Other variables which were associated with CKD in our study were: lower BMI and hemoglobin, higher concentrations of hsCRP and D-dimer, more frequent dyslipidemia, and ventricular blocks in ECG. Some of them, such as anemia or higher concentrations of D-dimer and hsCRP, are CKD- and CHF-dependent or may also exacerbate CHF and CKD symptoms.

Nevertheless, cardiorenal patients have been excluded from studies based on modern cardiology treatment, even though it appears that most treatments, if tolerated, are equally effective in cardiorenal patients [23]. Patients with renal insufficiency in the oldest age groups were generally less likely to receive beneficial treatment recommended by the guidelines during hospitalization and at discharge, especially invasive treatment. Routinely, in our study patients were evaluated using a scale of perioperative risk – the European System for Cardiac Operative Risk Evaluation (EuroSCORE) – and assessed by the Heart Team, and thus disqualified from operations. However, it was reported that in the group of octogenarians in 62.7% with impaired

renal function preoperative mortality risk assessment determined on the basis of EuroSCORE I and EuroSCORE II may be overestimated [24]. Very common undertreatment can contribute to high and excess mortality of the oldest cardiorenal patients.

### Limitations

The main limitation of this study is the relatively small number of participants, which was connected with the period of enrollment. The size of the subpopulation probably influenced the results.

Furthermore, we used each patient's baseline weight in calculating their creatinine clearance by Cockcroft-Gault's model. 27.7% of the patients in the present study were believed to be fluid overloaded on examination by experienced heart failure clinicians. It is possible that the baseline weight of some patients was higher than their true "dry" weights. This would tend to overestimate the patient's creatinine clearance. Also, calculated creatinine clearance tends to overestimate GFR [25]. However, both of these biases would work to weaken the observed association between GFR and cardiovascular outcomes, which suggests that the present data may underestimate the association between renal function and outcomes. Moreover, we did not have particular data on urinalyses or structural abnormalities of the kidneys in these patients. Thus, we cannot definitively classify patients with creatinine clearances between 60 and 90 ml/min as having kidney disease or not.

Finally, it was a hospital-based, short-term study. Therefore, patients with CHF treated exclusively on an outpatient basis were not included. The study needs to be validated in a general very elderly CHF population. Further multicenter investigations should explore the association between renal function and prognosis in patients 80+ years old with CHF to compare the results and provide generalized conclusions.

### Conclusions

Even though chronic renal insufficiency is an important adverse prognostic factor in the general population with CHF and is more common in older patients, the relationship between annual mortality and CKD in octogenarians and nonagenarians hospitalized due to CHF in our study did not reach statistical significance. Undoubtedly, more randomized trials in geriatric patients should investigate the role of renal insufficiency as a prognostic factor in CHF.

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### Disclosure

The authors report no conflict of interest.

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