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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Cardiogenic pulmonary oedema: alarmingly poor long term prognosis. Analysis of risk factors

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Abstract

Background: Acute heart failure (AHF) is a life-threatening condition associated with poor prognosis.

Aim: To investigate the long term prognosis and identify prognostic factors among patients who were discharged after an episode of cardiogenic pulmonary oedema.

Methods: We enrolled 84 patients (M: 56%, n = 47) who were discharged with cardiogenic pulmonary oedema as a diagnosis. Clinical, biochemical and echocardiographic variables were collected and analysed. The completeness of two- and five-year follow-up was 100% and 96%, respectively.

Results: The median (IQR) age was 74 years (64–81), left ventricular ejection fraction was 35% (27–45), blood pressure on admission was 140/90 mm Hg (115–180/70–100), estimated glomerular filtration rate was 60 mL/min/1.73 m^2 (45–73). Forty per cent (n = 34) of the patients had a history of atrial fibrillation (AF), however, AF was directly involved with pulmonary oedema only in 4% (n = 3) of the cases. Acute myocardial infarction (AMI) accounted for 34% (n = 29) of all the causes of pulmonary oedema and was associated with a better two-year prognosis compared to other causes of pulmonary oedema (p = 0.018). Two- and five-year mortality was 45% (n = 38) and 72% (n = 58), respectively. Co-morbidities were common. Ischaemic heart disease and arterial hypertension were present in 83% and 70% of the patients, respectively. Multivariable analysis identified increased left ventricular mass (RR 3.609, 95% CI 1.235–10.547, p = 0.017) and treatment with long-acting vasodilator drugs (LAVDs) (RR 4.881, 95% CI 1.618–14.727, p = 0.004) as independent negative prognostic factors, whereas in-hospital therapy with beta-blockers created a distinctly protective effect (RR 0.123, 95% CI 0.033–0.457, p = 0.002) in the two-year follow-up. Five-year mortality was independently associated with older age (RR 1.08, 95% CI 1.02–1.14, p = 0.005) and treatment with LAVDs (RR 6.4, 95% CI 1.47–28.14, p = 0.012), while percutaneous coronary intervention (RR 0.17, 95% CI 0.05–0.58, p = 0.004) significantly decreased the risk.

Conclusions: AHF is a heterogeneous syndrome with a very high remote mortality. LAVDs administered during the hospital stay as well as older age on admission correlate with higher long-term overall mortality. In the age of percutaneous coronary intervention, AMI aetiology of pulmonary oedema is no longer a negative prognostic factor for the long-term prognosis.

Key words: acute heart failure, cardiogenic pulmonary oedema, risk factors

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INTRODUCTION

Acute heart failure (AHF) is defined as a rapid onset or change in the signs and symptoms of heart failure (HF) and requires an urgent therapy.

It is often a life-threatening condition associated with a poor prognosis [1]. Pulmonary congestion, being one of the six clinical categories of AHF, is frequent among patients suffering from AHF. According to the latest guidelines, AHF is treated as a heterogeneous syndrome which can be related to systolic or diastolic cardiac dysfunction, abnormalities in cardiac rhythm, pre-load or after-load mismatch. In addition, AHF can be either new onset of HF or decompensation of pre-existing chronic heart failure (CHF) [1]. Due to the fact that about half of HF patients are > 75 years old, while the

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population's average age has been constantly increasing, HF is becoming the most frequent and complex syndrome which concerns the cardiovascular system. As a result, HF has definitely become a major health problem and a considerable drain on the budget [2].

Owing to the poor prognosis of AHF patients, there is a need for appropriate treatment not just after recognising the first symptoms of decompensation but also in further observation. In order to optimise outpatient care and treatment after cardiogenic pulmonary oedema (PE), we must determine the prognostic factors which would be routinely available to physicians. But this can only be done when risk factors affecting post-discharge, and not in-hospital, mortality are elucidated.

METHODS

Patients group

Eighty four consecutive, unselected patients (M: 56%, n = 47) admitted and discharged home from the Cardiology Department of the University Hospital due to cardiogenic PE between 2003 and 2007 were retrospectively identified and followed-up for a period of five years. The completeness of two- and five-year follow-up was 100% and 96%, respectively. The main outcome measure was all-cause mortality, as the most un-biased end point possible. Information about deaths was gathered from the patients' families or the local population registry run by a Government Office.

Definition of prognostic factors

The following factors were analysed: age, gender, heart rate, systolic and diastolic blood pressure measured on admission, body mass index (BMI), coexisting pneumonia, acute myocardial infarction (AMI), estimated glomerular filtration rate (eGFR), serum sodium level (Na^+), haemoglobin, red blood cell count, leukocyte count, selected echocardiographic parameters such us: left atrial diameter, end-diastolic diameter of the right/left ventricle (RVEDd, LVEDd), thickness of the interventricular septum (IVSd), posterior wall thickness (PWT), left ventricular ejection fraction (LVEF) and left ventricular mass (LVM). In-hospital treatment and co-morbidities were included in evaluation of the long-term prognosis. Survival probability was assessed for the two- and five-year observation periods. Two groups of patients were made for each of the follow-up periods (survival and non-survival) and then all of the mentioned variables were analysed.

LVM was assessed using the mathematical model according to the American Society of Echocardiography: $0.8 \times (1.04 \times [(LVEDd + IVSd + PWT)^3 - (LVEDd)^3]) + 0.6$ [g] normalised to gender [3]. Patients were divided into two groups according to the median value of the LVM assessed separately for males and females. eGFR was calculated using the modification of diet in renal disease (MDRD) formula GFR calculator. The BMI was calculated in the usual way: weight [kg]/height $[m]^2$. Other variables were gathered from medical documentation. The endpoint was defined as all-cause mortality. The start of the follow-up was the day of the discharge. Therefore in-hospital mortality was not an issue, and exclusively out-of-hospital deaths were included.

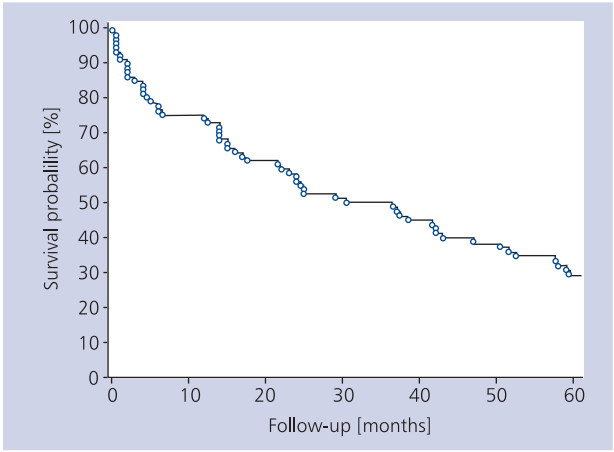

Figure 1. Kaplan-Meier five-year survival curve of the study population — patients with cardiogenic pulmonary oedema who survived in-hospital period

Statistical analysis

Data was tested for normal distribution using the Shapiro-Wilk test. Continuous variables are presented as means ± standard deviation or median and interquartile range (IQR), depending on the type of distribution. The Student's t test, χ^2 test or Mann-Whitney U test were used, as appropriate. Analysis of the long-term data was carried out using the Kaplan-Meier method and by the F Cox test. The logistic regression was used regarding variables affecting the two- and five-year survival rate. Results were presented as relative risks (RR) and 95% confidence intervals (CI). A p value < 0.05 was considered statistically significant. Calculations and statistical analyses were carried out with STATISTICA PL, version 9.0 (StatSoft.Inc. 2009).

RESULTS

Two- and five-year mortality was 45% (n = 38) and 72% (n = 58), respectively. The Kaplan-Meier five-year survival curve is shown in Figure 1. The basic clinical characteristics of the 84 AHF patients who survived the intra-hospital period are summarised in Table 1. The median (IQR) age was 74 years. Males constituted 56% of the patients. The median (IQR) LVEF of all the patients was 35%. Preserved systolic function (LVEF ≥ 45%) was found in 26.2% of patients, whereas 14.3% of them had LVEF ≤ 20% (mostly in males 23.4% vs. females 2.6%, p = 0.0062). Serum sodium level was in the normal range (median: 139 mmol/L) and only 4% (n = 3) of the patients had severe hyponatremia (Na^+ ≤ 130 mmol/L). The commonest drugs administered during the hospital stay were: loop diuretics (92%), angio-

Table 1. Basic clinical characteristics of patients presenting cardiogenic pulmonary oedema who survived intra-hospital period

	All patients (n = 84)	Two years			Five years		
		Survivors (n = 46)	Non-survivors (n = 38)	P	Survivors (n = 23)	Non-survivors (n = 58)	P
Age [years][1]	74 (64–81)	74.0 (61–82)	73.5 (67–79)	NS	64 (55–79)	76.5 (69–82)	0.025
Male gender	47 (56%)	24 (52%)	23 (61%)	NS	12 (55%)	33 (57%)	NS
LVEF [%][1]	35 (27–45)	35 (28–45)	35 (25–40)	NS	38 (30–48)	30 (25–40)	NS
SBP [mm Hg][1]	140 (115–180)	140 (115–180)	145 (115–180)	NS	140 (110–160)	150 (120–185)	NS
DBP [mm Hg][1]	90 (70–100)	90 (80–105)	90 (70–100)	NS	90 (80–100)	90 (70–105)	NS
HR [bpm][1]	100 (85–120)	100 (90–120)	100 (85–120)	NS	100 (80–100)	100 (90–120)	NS
BMI [kg/m^2][1]	27.3 (24–30)	27.7 (23.8–29.8)	26.2 (24.5–29.5)	NS	26.8 (23.5–28.4)	27.7 (24.2–30.6)	NS
GFR [mL/min/1.73 m^2)][1]	60 (45–73)	60 (45–70)	58 (47–83)	NS	60 (46–70)	58 (45–79)	NS
Na [mmol/L][1]	139 (136–142)	139 (136–141)	140 (136–143)	NS	140 (137–142)	138 (136–142)	NS
RBC [mln/mm^3][2]	4.3 ± 0.6	4.3 ± 0.5	4.2 ± 0.7	NS	4.4 ± 0.6	4.2 ± 0.6	NS
Females[2]	4.1 ± 0.6)	4.0 ± 0.5	4.3 ± 0.7	NS	4.1 ± 0.7	4.2 ± 0.6	NS
Males[2]	4.3 ± 0.6	4.5 ± 0.4	4.1 ± 0.7	0.027	4.6 ± 0.5	4.3 ± 0.6	NS
Hb [g/dL][2]	12.9 ± 1.7	13.0 ± 1.8	12.7 ± 1.7	NS	13.2 ± 2.0	12.7 ± 1.6	NS
Females[2]	12.4 ± 1.6	12.1 ± 1.6	12.8 ± 11.9–14.1	NS	12.2 ± 1.8	12.5 ± 1.6	NS
Males[2]	13.2 ± 1.8	13.9 ± 1.5	12.6 ± 1.8	0.014	14.2 ± 1.9	12.9 ± 1.7	NS
LEU [G/L][1]	9.0 (6.8–11.3)	9.5 (6.6–11.7)	8.65 (6.8–10.8)	NS	9.5 (6.7–13.8)	8.8 (6.8–11.0)	NS
RVEDd [mm][1]	26 (24–29)	26 (24–28)	26 (25–30)	NS	26 (23–28)	26 (24–29)	NS
LA [mm][1]	45 (40–47)	45 (40–46)	45 (40–47)	NS	44 (39–46)	45 (41–47)	NS
PWT [mm][1]	12 (11–13)	11 (10–12)	12 (11–13)	NS	12 (11–13)	12 (11–13)	NS
IVSd [mm][1]	12 (12–14)	12 (11–13)	13 (12–14)	0.030	12 (12–13)	13 (12–14)	NS
LVEDd [mm][1]	56 (50–60)	53 (50–59)	57 (48–64)	NS	54 (50–59)	56 (49–62)	NS
LVM [g][1]	279 (233–318)	262 (223–298)	296 (256–372)	0.008	276 (220–305)	280 (246–338)	NS
Females[1]	250 (218–296)	247 (218–282)	277 (219–311)	NS	271 (218–295)	250 (219–300)	NS
Males[1]	293 (255–347)	282 (235–315)	331 (275–379)	0.034	287 (230–315)	295 (264–350)	NS
Pneumonia	37 (44%)	15 (33%)	22 (58%)	0.020	7 (32%)	29 (50%)	NS

[1]Median (IQR); [2]Mean (SD); IQR — interquartile range; SD — standard deviation; LVEF — left ventricular ejection fraction; SBP/DBP — systolic/diastolic blood pressure on admission; HR — heart rate on admission; BMI — body mass index; eGFR — estimated glomerular filtration rate; RBC — red blood cells; Hb — haemoglobin; LEU — leukocytes; RVEDd — right ventricular end-diastolic diameter; LA — left atrial diameter; PWT — posterior wall thickness; IVSd — interventricular septum diameter; LVEDd — left ventricle end-diastolic diameter; LVM — left ventricular mass

Table 2. In-hospital treatment of patients with cardiogenic pulmonary oedema

		Two years			Five years		
	All patients (n = 84)	Survivors (n = 46)	Non-survivors (n = 38)	P	Survivors (n = 23)	Non-survivors (n = 58)	P
ACEIs/ARBs	69 (82%)	38 (83%)	31 (82%)	NS	20 (91%)	46 (79%)	NS
BBs	63 (75%)	41 (89%)	22 (58%)	0.001	19 (86%)	40 (69%)	NS
LDs	77 (92%)	42 (50%)	35 (92%)	NS	20 (91%)	54 (93%)	NS
TDs	6 (7%)	4 (5%)	2 (5%)	NS	3 (14%)	3 (5%)	NS
PSDs	68 (81%)	34 (74%)	22 (58%)	NS	17 (77%)	37 (64%)	NS
CCBs	22 (26%)	11 (13%)	11 (29%)	NS	6 (27%)	16 (28%)	NS
Digoxin	29 (35%)	12 (26%)	17 (45%)	NS	4 (18%)	25 (43%)	0.038
NTG	63 (75%)	32 (70%)	31 (82%)	NS	14 (64%)	46 (79%)	NS
LAVDs	31 (37%)	11 (13%)	20 (53%)	0.007	3 (14%)	25 (43%)	0.014
Inotropes:	24 (29%)	16 (35%)	8 (21%)	NS	7 (32%)	15 (26%)	NS
Dopamine	18 (21%)	13 (28%)	5 (13%)	NS	5 (23%)	11 (19%)	NS
Dobutamine	9 (11%)	5 (11%)	4 (11%)	NS	1 (5%)	7 (12%)	NS
Epinephrine	3 (4%)	1 (2%)	2 (5%)	NS	1 (5%)	2 (3%)	NS
Norepinephrine	3 (4%)	1 (2%)	2 (5%)	NS	1 (5%)	2 (3%)	NS
LMWH/UFH	64 (76%)	32 (70%)	32 (84%)	NS	15 (68%)	46 (79%)	NS
ASA	60 (71%)	35 (76%)	25 (66%)	NS	18 (82%)	39 (67%)	NS
APDs	20 (24%)	16 (35%)	4 (11%)	0.009	7 (32%)	10 (17%)	NS
Statins	46 (55%)	31 (67%)	15 (39%)	0.011	18 (82%)	25 (43%)	0.002
$NaHCO_3$	4 (5%)	2 (4%)	2 (5%)	NS	0 (0%)	4 (7%)	NS
GP IIb/IIIa inhibitors	7 (8%)	6 (13%)	1 (3%)	NS	3 (14%)	3 (5%)	NS
ADs	36 (43%)	19 (41%)	17 (45%)	NS	7 (32%)	26 (45%)	NS
Insulin	40 (48%)	24 (52%)	16 (42%)	NS	11 (50%)	26 (45%)	NS
Antibiotics	60 (71%)	29 (63%)	31 (82%)	NS	12 (55%)	46 (79%)	0.027
Iron *i.v.*	4 (5%)	3 (7%)	1 (3%)	NS	2 (9%)	2 (3%)	NS
RBCC	6 (7%)	3 (7%)	3 (8%)	NS	0 (0%)	4 (7%)	NS
PCI	30 (36%)	21 (46%)	9 (24%)	0.037	13 (59%)	14 (24%)	0.003
Coronary stent	21 (25%)	17 (37%)	4 (11%)	0.005	9 (41%)	9 (16%)	0.049
CABG (qualification)	7 (8%)	2 (4%)	5 (13%)	NS	0 (0%)	5 (9%)	NS
NIV	2 (2%)	2 (4%)	0 (0%)	NS	1 (5%)	1 (2%)	NS
IV	9 (11%)	5 (11%)	4 (11%)	NS	2 (9%)	7 (12%)	NS
Cardioversion	2 (2%)	2 (4%)	0 (0%)	NS	0 (0%)	2 (3%)	NS
IABP	7 (8%)	4 (9%)	3 (8%)	NS	2 (9%)	4 (7%)	NS
OADs	6 (7%)	5 (11%)	1 (3%)	NS	1 (5%)	5 (9%)	NS
Opioids	20 (24%)	9 (20%)	11 (29%)	NS	3 (14%)	16 (28%)	NS

ACEIs — angiotensin-conversing enzyme inhibitors; ARBs — angiotensin receptor blockers; BBs — beta blockers; LDs — loop diuretics; TDs — thiazide diuretics; PSDs — potassium-sparing diuretics; CCBs — calcium channel blockers; NTG — nitroglycerin; LAVDs — long-acting vasodilator drugs; LMWH — low-molecular-weight heparin; UFH — unfractionated heparin; ASA — acetylsalicylic acid; APDs — antiplatelet drugs; GP — glycoprotein; ADs — antiarrhythmic drugs; RBCC — red blood cell concentrate; PCI — percutaneous coronary intervention; CABG — coronary artery bypass graft; NIV — noninvasive ventilation; IV — invasive ventilation; IABP — intra-aortic balloon pump; OADs — oral anti-diabetes drugs

tensin-converting enzyme inhibitors/angiotensin receptor blockers (82%), potassium-sparing diuretics (spironolactone 81%), low-molecular-weight heparin/unfractionated heparin (76%), beta-blockers (BBs, 75%), nitroglycerine (75%), acetylsalicylic acid (71%), antibiotics (71%), long-acting vasodilator drugs (LAVDs, 37%) and statins (55%) (Table 2). In relation to the two-year follow-up, higher diameter of IVS (p = 0.030), coexistent pneumonia (p = 0.020) and

higher LVM (p = 0.008) were more common among the non-survivor group. Lower red blood cell count and haemoglobin level were characteristic only for males who did not survive to two-year follow-up (p = 0.027; p = 0.014, respectively). Furthermore, non-survivors less frequently received BBs (p = 0.001), antiplatelet drugs (p = 0.009), statins (p = 0.011), percutaneous coronary intervention (PCI, p = 0.037) and implantation of the coronary stent (p = 0.005), whereas they more frequently received LAVDs (p = 0.007) (Table 2). At the five-year follow-up, there were no statistically significant differences between the survivor group and the non-survivor group apart from age (p = 0.025). Those who did not survive to five-year follow-up were treated more often with digoxin, LAVDs and antibiotics. Simultaneously, statins, PCI and implantation of a coronary stent were less frequently needed during the hospital stay. Univariate analysis revealed the following variables were associated with a poor two-year prognosis: therapy without PCI treatment, antiplatelet drugs (clopidogrel/ticlopidine), statins, BBs; higher RVEDd; increased LVM; coexistent pneumonia, aetiology of cardiogenic PE other than AMI, treatment without coronary stent implantation and LAVDs. Multivariable analysis identified increased LVM (RR 3.609, 95% CI 1.235–10.547, p = 0.017) and treatment with LAVDs (RR 4.881, 95% CI 1.618–14.727, p = 0.004) as independent negative prognostic factors in the two-year follow-up, whereas in-hospital therapy with BBs was independently associated with better prognosis (RR 0.123, 95% CI 0.033–0.457, p = 0.002) (Table 3).

Five-year survival tended to be better among younger patients who were not treated with antibiotics, LAVDs, digoxin and those who underwent PCI or had a coronary stent implanted during the hospitalisation. LAVDs (RR 6.4, 95% CI 1.47–28.14, p = 0.012) and older age (RR 1.08, 95% CI 1.02–1.14, p = 0.005) were independently associated with higher five-year mortality, while treatment with PCI improved prognosis (RR 0.17, 95% CI 0.05–0.58, p = 0.004) (Table 4, Figs. 2–4). LVEF measured on admission did not impact on long-term mortality (Fig. 5). Co-morbidities were common. Most of the patients (n = 70; 83%) had ischaemic heart disease (IHD), and 17 (20%) had mitral insufficiency. Arterial hypertension, diabetes, chronic lung disease (chronic obstructive pulmonary disease) and previous history of neoplasm were present in 70% (n = 59), 43% (n = 36), 15% (n = 13) and 8% (n = 7) of the patients, respectively. Forty per cent (n = 34) of the patients had a history of atrial fibrillation (AF), however, AF was considered to be directly involved with the development of PE only in 4% (n = 3) of the cases. In 34% (n = 29) of the patients, AMI was assumed to be the trigger of AHF and this was associated with a better two-year prognosis compared to other causes of PE (Table 5). Nevertheless, in the four-month period after being discharged, AMI seemed to have a negative impact on mortality. Of those patients, 69% had ST-elevation myocardial infarction (STEMI, n = 20), whereas the other 31% had an myocardial infarction without ST-elevation (NSTEMI, n = 9). PCI was performed after initial stabilisation in 66% (n = 19) of the AMI cases. Another 24% (n = 7) of the patients with AMI were scheduled for elective coronary artery bypass graft.

Table 3. Variables independently associated with two-year mortality among patients presenting acute cardiogenic pulmonary oedema who survived intra-hospital period

	RR	95% CI	P
Univariate analysis			
AMI	0.317	0.118–0.852	0.020
Pneumonia	2.842	1.150–7.023	0.022
Left ventricular mass	2.836	1.131–7.110	0.024
RVEDd	1.148	1.011–1.304	0.030
Beta-blockers	0.168	0.053–0.528	0.002
LAVDs	3.535	1.376–9.084	0.008
APDs	0.221	0.065–0.746	0.014
Statins	0.316	0.127–0.784	0.012
PCI	0.370	0.141–0.966	0.039
Coronary stent	0.200	0.060–0.676	0.009
Multivariate analysis			
Left ventricular mass	3.609	1.235–10.547	0.017
LAVDs	4.881	1.618–14.727	0.004
Beta-blockers	0.123	0.033–0.457	0.002

RR — relative risk; CI — confidence interval; AMI — acute myocardial infarction RVEDd — right ventricular end-diastolic diameter; LAVDs — long-acting vasodilator drugs (molsidomin, isosorbide mononitrate); APDs — antiplatelet drugs (clopidpogrel/ticlopidine); PCI — percutaneous coronary intervention

Table 4. Variables independently associated with five-year mortality among patients with cardiogenic pulmonary oedema who survived in-hospital period

	RR	95% CI	P
Univariate analysis			
Antibiotic	2.95	1.03–8.49	0.042
LAVDs	3.60	1.07–12.13	0.036
Digoxin	3.60	1.07–12.13	0.036
Coronary stent	0.24	0.08–0.72	0.010
Age	1.06	1.02–1.11	0.008
PCI	0.21	0.07–0.58	0.003
Multivariate analysis			
LAVDs	6.43	1.47–28.14	0.012
Age	1.08	1.02–1.14	0.005
PCI	0.17	0.05–0.58	0.004

RR — relative risk; CI — confidence interval; LAVDs — long-acting vasodilator drugs (molsidomin, isosorbide mononitrate); PCI — percutaneous coronary intervention

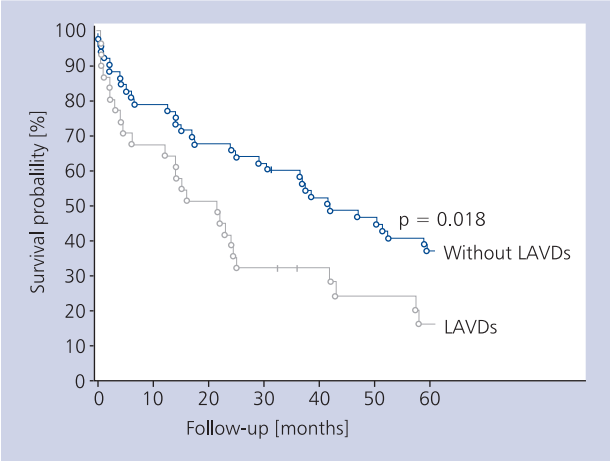

Figure 2. Kaplan-Meier five-year survival curve of the study population divided into two groups regarding in-hospital treatment with long-acting vasodilator drugs (LAVDs). LAVDs as independent negative prognostic factor (RR 6.4, 95% CI 1.47–28.14, p = 0.012)

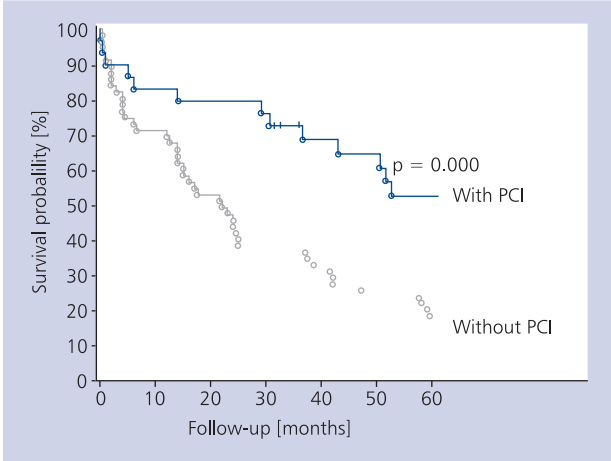

Figure 4. Kaplan-Meier five-year survival curve of the study population divided into two groups regarding in-hospital treatment with percutaneous coronary intervention (PCI). PCI as independent positive prognostic factor (RR 0.17, 95% CI 0.05–0.58, p = 0.004)

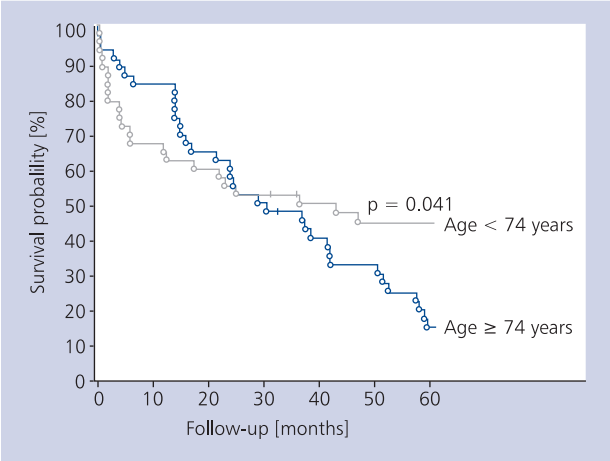

Figure 3. Kaplan-Meier five-year survival curve of the study population divided into two groups regarding median age. Older age as independent negative prognostic factor (RR 1.08, 95% CI 1.02–1.14, p = 0.005)

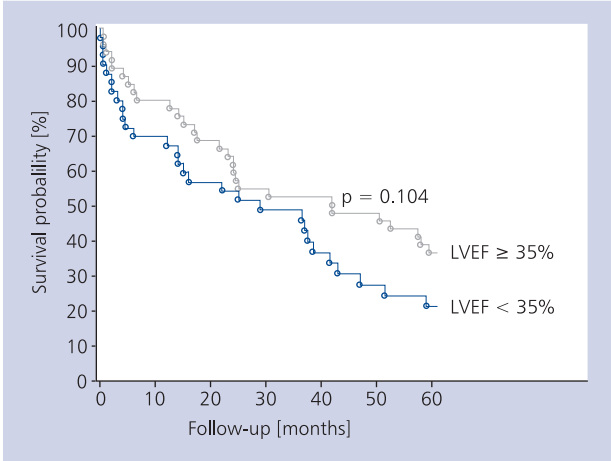

Figure 5. Kaplan-Meier five-year survival curve of the study population divided into two groups regarding left ventricular ejection fraction (LVEF) measured on admission to the hospital

Table 5. Aetiology of pulmonary oedema. Patients presenting acute cardiogenic pulmonary oedema

		Two years			Five years		
	All patients (n = 84)	Survivors (n = 46)	Non-survivors (n = 38)	P	Survivors (n = 23)	Non-survivors (n = 58)	P
AMI	29 (34%)	21 (46%)	8 (21%)	0.018	10 (41%)	17 (29%)	NS
Other*	55 (66%)	25 (54%)	30 (79%)	0.018	13 (59%)	41 (71%)	NS

AMI — acute myocardial infarction; *arterial hypertension, valvular heart disease (mitral insufficiency, complex mitral valve disease, aortic insufficiency), dilated cardiomyopathy, atrial fibrillation

DISCUSSION

The prevalence of HF is increasing due to the ageing population and improved survival after acute coronary syndromes (ACS) [4]. As a result, the incidence of exacerbation escalates too. Although the vast majority of patients with AHF symptomatically improve during their hospitalisation, their post-discharge mortality still remains very high [5]. Moreover, the long-term prognosis seems to be worse among European patients than non-European patients [6]. However, such data is still missing for Poland. In our report, the overall post-discharge mortality seems to be similar to other accessible data [6–8].

Most patients in the present study were elderly men with multiple coexistent diseases, among which IHD and arterial hypertension were the most frequently found. Those findings are comparable with other AHF reports [8, 9]. In the present study, five-year overall mortality was increased by older age on admission, and by therapy with LAVDs and without PCI during the hospital stay. Similarly to the findings of Sosin et al. [6], older age was predictive of five-year death whereas, unlike other reports [10, 11], it was not associated with two-year mortality. AMI was the aetiology of cardiogenic PE in one third of the enrolled patients and was associated with better two-year prognosis. It is likely that those with a more severe condition caused by left ventricle systolic dysfunction, revealed by the AMI, died before admission to the hospital, in hospital, or in the four-month period after discharge. Contradicting previous reports [8, 12, 13], recent data has revealed that ACS does not seem to play a substantial role in the short-term prognosis [11, 14]. The main therapeutic option for AMI lies presently in the restoration of perfusion as soon as possible to salvage as much of the jeopardised myocardium as possible.

Prompt diagnosis, combined with invasive intervention and pharmacological treatment after discharge, may preserve myocardial function and reduce mortality and chronic disability. Thus, AMI in some of the cases might be only a temporary reason for failing heart function, unlike arterial hypertension or valvular heart disease. Having a better remote prognosis might be associated with more favourable left ventricle remodelling among these patients. Especially in the age of PCI, AMI aetiology of PE does not seem to be a negative prognostic factor for the long-term prognosis. Our data supports the notion that early intervention, even in elderly patients with ACS, may improve prognosis [9]. In-hospital treatment with LAVDs was found to be another very important factor affecting two- and five-year prognosis. Almost all patients to whom LAVDs were administered had had previously diagnosed IHD. Therefore, the influence of in-hospital use of LAVDs might be the equivalent of symptomatic suboptimally treated IHD. In the last 20 years, the long-term nitrate use in IHD has been found to be a factor that increases remote mortality [15–17]. In our report, BBs predicted only two-year prognosis, while not having a significant impact on further outcome. Unlike other previously published data [10, 18], reduced left ventricular systolic function was not an independent negative prognostic factor, either in the two- or the five-year follow-up. The downward trend in LVEF value was seen solely among those who did not survive five years after being discharged compared to the survivors group. The explanation for not finding a statistically significant difference in two-year observation might be higher LVEF among patients with aetiology of PE other than AMI who had worse two-year prognosis compared to AMI patients (median 36.5%, IQR 25–45 vs. 30%, IQR 28–48, respectively). This may point to problems of out-patient care. Patients without the in-hospital diagnosis of myocardial infarction usually are less intensively treated, with less common visits. Moreover, an adverse two-year prognosis of those patients might be connected with more commonly increased LVM. Prompt and appropriate treatment for AMI makes it only a transient cause of HF in contrast to other aetiologies of PE, such as arterial hypertension which gradually leads to left ventricular hypertrophy. Increased LVM results in deterioration of left ventricular diastolic filling as well as its systolic function. Impaired diastolic function has been shown to be associated with adverse prognosis in patients with HF [19]. Echocardiographic parameters being easy and commonly available make the two-dimensional echocardiography, undertaken in the acute phase of HF, very helpful in detecting patients who need closer outpatient monitoring [19].

The mortality of the patients in our study population is alarmingly high. Nearly 25% of patients died within six months of discharge, and only 50% survived more than 30 months. We must stress that patients who present cardiogenic PE have a very poor long term prognosis and require particular out-patient care, even if LVEF is not severely impaired (Fig. 5). Extremely high, exceeding 70%, five-year mortality in patients with PE should be compared with the five-year prognosis of patients with STEMI treated with PCI, in whom more than 75% of patients survive five years after the event [20]. This finding should influence the thinking of cardiologists and primary care physicians who treat patients discharged with the diagnosis of PE.

Limitations of the study

Several limitations should be mentioned. First, our study might be potentially limited by the retrospective nature of the analysis, which meant we were not able to assess the re-admission rate or changes of the patients' clinical and biochemical parameters during the follow-up period. Nevertheless, our purpose was to evaluate the long-term prognosis in patients with PE on the basis on information routinely available to physicians. Second, due to arrhythmias, echocardiographic parameters of diastolic function had not been assessed in the entire group, and therefore, could not be used to characterise patients with diastolic HF. The single centre character and relatively small number of patients enrolled make this study

more liable to the bias associated with organisational characteristics of healthcare.

Nevertheless, real life medicine is strongly affected by healthcare organisation, not only by the pathophysiology of the disease. Despite these limitations, our study reflects real life medical practice and suggests that variables such as LVM, age, in-hospital treatment with LAVDs, BBs and PCI are important long-term independent prognostic factors among patients with cardiogenic PE.

CONCLUSIONS

Despite increasing knowledge on AHF, the post-discharge mortality among cardiogenic PE patients remains very high. Several clinical and echocardiographic factors were identified as associated with a poor long-term prognosis of the PE patients who survived the in-hospital period. LAVDs administered during the hospital stay, as well as older age on admission, correlate with higher long-term overall mortality. In the age of PCI, AMI aetiology of PE is no longer a negative prognostic factor for the long-term prognosis.

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Kardiogenny obrzęk płuc jest związany z alarmująco wysoką śmiertelnością. Analiza czynników ryzyka niekorzystnego rokowania

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Streszczenie

Wstęp: Ostra niewydolność serca (AHF) jest stanem zagrażającym życiu obarczonym poważnym rokowaniem. Aby w pełni zoptymalizować opiekę nad chorym z AHF, ważne jest określenie głównych czynników rokowniczych.

Cel: Celem pracy była identyfikacja czynników ryzyka oraz ocena 2- i 5-letniego rokowania pacjentów z kardiogennym obrzękiem płuc, jako specyficzną postacią kliniczną ostrej lewokomorowej niewydolności serca.

Metody: Retrospektywną analizą objęto 84 pacjentów (M: 56%, n = 47) hospitalizowanych i wypisanych ze szpitala w latach 2003–2007 z powodu kardiogennego obrzęku płuc. Chorych obserwowano przez 5 lat; 100% pacjentów ukończyło 2-letni, a 96% 5-letni okres obserwacji.

Wyniki: Mediana (rozstęp międzykwartylowy, IQR) wieku grupy badanej wynosiła 74 lata (64–81), frakcji wyrzutowej lewej komory 35% (27–45), ciśnienia tętniczego przy przyjęciu 140/90 mm Hg (115–180/70–100), oszacowanej filtracji kłębuszkowej 60 ml/min/1,73 m^2 (45–73). Migotanie przedsionków (AF) w wywiadzie zanotowano u 40% (n = 34) pacjentów, choć jedynie w 4% przypadków uznano to za główną przyczynę wystąpienia obrzęku płuc. Ostry zawał serca (AMI) w 34% (n = 29) przypadków był bezpośrednią przyczyną obrzęku płuc (69%, n = 20 z uniesieniem odcinka ST; 31%, n = 9 bez uniesienia odcinka ST) i wiązał się z lepszym odległym rokowaniem w porównaniu z innymi przyczynami AHF (p = 0,018). Za pomocą przezskórnej interwencji wieńcowej (PCI) leczono 66% (n = 19) pacjentów z AMI. Dwuletnia i pięcioletnia śmiertelność wynosiła odpowiednio 45% (n = 38) i 72% (n = 58). Choroba niedokrwienna serca (83%) i nadciśnienie tętnicze (70%) były najczęściej stwierdzanymi współwystępującymi chorobami wśród badanej populacji. W analizie wieloczynnikowej zmiennymi związanymi z gorszym 2-letnim rokowaniem były: zwiększona masa lewej komory (RR 3,609; 95% CI 1,235–10,547; p = 0,017), terapia długodziałającymi wazodylatatorami — LAVDs (RR 4,881; 95% CI 1,618–14,727, p = 0,004), natomiast stosowanie leków beta-adrenolitycznych (RR 0,123; 95% CI 0,033–0,457; p = 0,002) wiązało się z lepszym rokowaniem. Czynnikami zwiększającymi śmiertelność 5-letnią były: LAVDs (RR 6,4; 95% CI 1,47–28,14; p = 0,012) i starszy wiek (RR 1,08; 95% CI 1,02–1,14; p = 0,005), podczas gdy leczenie za pomocą PCI zdecydowanie poprawiało rokowanie odległe (RR 0,17; 95% CI 0,05–0,58; p = 0,004).

Wnioski: Ostra niewydolność serca jest heterogennym zespołem z bardzo wysoką śmiertelnością odległą. Choroba niedokrwienna serca i nadciśnienie tętnicze są najczęściej stwierdzanymi schorzeniami współtowarzyszącymi. LAVDs i starszy wiek przy przyjęciu zwiększają śmiertelność 5-letnią. W dobie PCI zawałowa etiologia obrzęku płuc nie jest już czynnikiem pogarszającym odległe rokowanie.

Słowa kluczowe: ostra niewydolność serca, kardiogenny obrzęk płuc, czynniki ryzyka

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