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Prognostic Factors in Pulmonary Hypertension

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Conflict of interest: We undersign, certificate that we do not have any financial or personal relationships that might bias the content of this work.

ABSTRACT

Background and objectives: *Pulmonary hypertension is a hemodynamic and pathophysiological condition defined as an increase in mean pulmonary pressure more than or equal to 25 mm Hg. Evaluation of pulmonary hypertension severity and prognosis plays a central role in the management of these patients, between diagnosis and therapeutic decision making. The aim of our study was to identify the adverse prognostic factors in patients with pulmonary hypertension and their impact on mortality, quality of life, need for hospitalization and complications during hospitalization.*

Material and methods: *We performed a prospective study that included 553 patients diagnosed with pulmonary hypertension in the Institute of Cardiovascular Diseases of Iasi between 1st November 2008 and 1st July 2011. We analyzed a series of demographic and clinical data, echocardiographic and hemodynamic parameters, which correlated with mortality, WHO functional class, complications and need for hospitalization.*

Outcomes: *We identified as main negative prognostic factors: WHO functional class III and IV, the pulmonary artery systolic pressure value, right chambers dilation, TAPSE, pericardial effusion, cardiac index and right atrial pressure.*

Conclusions: *Pulmonary hypertension, despite the development of treatment methods, remains a serious disease, with progressive and inexorable evolution, but the prognosis of patients with pulmonary hypertension is very variable, depending on the etiology, functional class, clinical, echocardiographic and hemodynamic parameters.*

Keywords: pulmonary hypertension, prognosis, mortality, echocardiography, right heart catheterization

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INTRODUCTION

Pulmonary hypertension (PH) is a hemodynamic and pathophysiological condition defined as an increase of mean pulmonary pressure more than or equal to 25 mmHg at rest (1,2). Evaluation of pulmonary hypertension severity and prognosis plays a central role in the management of these patients, between diagnosis and therapeutic decision making. In patients with untreated idiopathic pulmonary arterial hypertension (IPAH), historical data show a median survival of 6 months in patients with WHO functional class IV, 2.5 years for those in class III and 6 years for functional classes I and II (2). Prognosis is also significantly affected by the etiology of PH (3). Patients with congenital heart diseases have a better prognosis. Survival was significantly higher in patients with Eisenmenger syndrome compared to IPAH patients treated either with conventional therapy or epoprostenol (4,5).

Echocardiography generates several indicators of prognostic value: the existence of pericardial fluid, right atrial area index and left ventricular eccentricity index (6), right ventricular Tei index (7-9) and TAPSE (10). Cardiac catheterization in patients with PH has prognostic value (1,4). Identified parameters include pulmonary artery saturation, right atrium pressure, cardiac output, pulmonary vascular resistance and pronounced vasodilator responsiveness. The pulmonary artery pressure is also prognostic, but towards the final stages of the disease, when the right ventricle becomes insufficient, it may decrease.

The aim of our study was to identify the adverse prognostic factors in patients with pulmonary hypertension and their impact on mortality, quality of life, need for hospitalization and complications during hospitalization. ❑

MATERIALS AND METHODS

We performed a prospective study that included 553 patients diagnosed with pulmonary hypertension in the Institute of Cardiovascular Diseases of Iasi between 2008 and 2011. In order to determine the evolution of the disease we retrospectively analyzed the files of enrolled patients since 1998. Study inclusion criteria were patients with idiopathic arterial pulmonary hypertension and secondary forms of pulmonary hypertension. The classification of patients in clinical classes was performed according to the Dana Point classification of PH (2008). The study had the approval of the ethics committee of our institution. Protocol study included:

I. Demographic data: sex, age
II. Personal pathologic history – date of diagnosis of PH; for secondary forms of PH – date of diagnosis of the disease which generated PH.
III. The clinical examination aimed to establish the WHO class at admission and the patient status (stable or deteriorating).
IV. Echocardiography was performed in all patients and included the following measurements: systolic pulmonary artery pressure (sPAP), pulmonary acceleration time, pulmonary ejection time and their ratio, left ventricular ejection fraction, TAPSE, right atrium area (indexed to the body surface), right ventricular diameter, presence/ absence of pericardial fluid; by pulsed- wave tissue Doppler at the tricuspid ring we measured the isovolumic contraction time (IVCT), isovolumic contraction velocity (IVCV), isovolumic acceleration (ICA), tricuspid ring systolic velocity (St), E wave (Et), A wave (At) and isovolumic relaxation time (IVRT).
V. Right heart catheterization was performed in 313 patients during the study. All patients signed informed consents. The remaining of the group had previous hemodynamic exams (we used their results only for diagnostic confirmation and not as part of the statistical analysis). The following parameters were calculated: systolic, diastolic and mean pulmonary artery pressure, pulmonary vascular resistance and pulmonary/ systemic resistance ratio, cardiac output, cardiac index, right atrial pressure.
VI. We monitored the following parameters: WHO functional class deterioration; hospitalizations for heart failure phenomena; number of days of hospitalization; need for inotropic support or mechanical ventilation; need of treatment modification; non- cardiac complications (pleural, pericardial, hepatic, renal). We defined renal complications as a rise in serum creatinine of $\geq$0.3 mg/dl or $\geq$50% in less than 48 hours; hepatic complications as hepatic cytolysis syndrome and/or spontaneous INR >1.5; pleural complications as significant pleurisy, which necessitated thoracentesis; pericar-

dial complications as significant amount of pericardial fluid with signs of compression and/or need for pericardiocentesis. Patient monitoring was carried out over 34 months. Patients were examined every 6 months (clinical examination, WHO class assessment and echocardiographic follow- up) or in case of clinical worsening.

Statistical analysis - We used STATISTICA (a dedicated program for medical research) for statistical processing of data. Continuous variables were described as mean ± SD. The χ^2 test was used to compare categorial variables. ANOVA and Kruskal- Wallis test were used to compare means of continuous variables. Survival was calculated using Kaplan- Meier analysis. We performed multivariable analysis for mortality. ❑

RESULTS

Demographic and clinical features of patients are shown in Table 1. IPAH represented 1.26% of the total group. Our analysis confirms the female predominance of the disease. Congenital heart defects generated PH in 48 patients (6.87%). Patients with atrial septal defect (n=21) were significantly older than patients with other malformations (ventricular septal defect, patent ductus arteriosus, complete atrioventricular septal defect, truncusus arteriosus or total anomalous pulmonary venous return) (52.28 ± 20.10 years vs. 27.41 ± 16.10 years, p<0.001), the explanation being PAH late appearance in this condition. In 12 cases the disease was already in stage of Eisenmenger syndrome at diagnosis time. The post-tricuspid shunts (ventricular septal defect and patent ductus arteriosus) reached the stage of Eisenmenger syndrome the most frequently and, for this reason, they have a more severe prognosis.

Echocardiographic and hemodynamic values at baseline are noted in Table 2. Therapeutic options are presented in Table 3. Surgical treatment concerned patients with congenital

	Class 1			Class 2	Class 3	Class 4	Total
	1.1	1.4.1	1.4.4				
Number	7	4	48	370	37	87	553
Male gender [n (%)]	2 (28%)	3 (75%)	22 (46%)	226 (61%)	29 (79%)	31 (36%)	313 (57%)
Age (yrs)	48.7± 18.8	62.75± 11.4	36.2± 20.8	63.6± 11.6	74.1± 6.9	59.7± 14.8	61± 15.5
WHO III - IV [n (%)]	4 (57%)	2 (50%)	25 (52%)	215 (57%)	25 (54%)	52 (60%)	323 (59%)

TABLE 1. Demographical and clinical characteristics.

Parameter	Value
sPAP (echo), mm Hg	61.5 ± 18.22
dPAP (echo), mm Hg	31.32 ± 15.71
LVEF, %	50.84 ± 13.87
PAT, ms	83.9 ± 33.23
PAT/PET	0.48 ± 0.13
TAPSE, mm	18.2 ± 5.9
RVEDD, mm	38.6 ± 7.92
Indexed RA area, cm^2/m^2	14.51 ± 5.47
Pericardial fluid, n (%)	39 (7%)
IVCV (cm/s)	7 ± 2.4
IVCT, ms	55.05 ± 17.43
IVA (m/s^2)	2.7 ± 1
IVRT (ms)	113.81 ± 42.37
Sa (cm/s)	10.43 ± 2.96
Ea (cm/s)	6.1 ± 2.46
Aa (cm/s)	11.26 ± 4.05
sPAP (cath), mm Hg	65.62 ± 25.24
mPAP, mm Hg	42.75 ± 17.3
dPAP, mm Hg	32.75 ± 16.75
PVR, Wood units	13.53 ± 11.1
PVR/SVR	0.4 ± 0.3
CO, l/min	4.47 ± 2. 27
CI, $l/min/m^2$	2.76 ± 1.1
mRAP, mm Hg	11.54 ± 5.5

TABLE 2. Echocardiographic and hemodynamic characteristics.

heart diseases and left heart valvular disease. Seven patients showed inadequate clinically response to the initial specific therapy and needed treatment augmentation to combination therapy (4 cases- phosphodiesterase type-5 inhibitor and prostanoids, 3 cases- endothelin receptor antagonist and phosphodiesterase type-5 inhibitor).

We recorded 25 deaths in the studied group (4.52% mortality). There were no significant differences between genders (13 male patients and 12 female) (p 0.27). Average age at death was 64.72 years (range between 1 and 92 years). Age was not an independent risk factor for death (mean age 64.72 years vs. 61.03 years, p = 0.24).

Mortality depending on the etiology of the general group is presented in Figure 1. The highest mortality was recorded for idiopathic PH and the lowest in patients with congenital heart diseases, but the difference is not statistically significant (χ^2 2.59, p = 0.1).

Among the deceased patients, one was in functional class II WHO, two in class III and 22 in functional class IV. Functional class IV was associated with a relative risk of death of 36.27, p<0.001 and the combined analysis of class III and IV WHO showed a relative risk of 21.27, p<0.001. The difference in survival between III and IV WHO classes is statistically significant (χ^2 4.09576, p<0.001). The difference is even more marked between WHO class II and IV, respectively (χ^2 4.21073, p<0.001). Kaplan-Meier survival curves according to the WHO class are shown in Figure 2.

The average systolic pulmonary artery pressure determined by echocardiography (sPAP) in the deceased patients group was of 75.65 ± 14.67 mmHg. The ANOVA test for comparing mean values of sPAP depending on the patient's vital status shows that there was a statistically significant difference between patients who died and alive patients (in this subgroup, mean sPAP is 60.72 ± 18.12 mmHg, p<0.001). In order to determine the influence of sPAP on survival we can set a "cut off" value function of the quartiles of the variable, then setting the corresponding survival rates. For sPAP the value of 70 mmHg represents a "cut off" value. Figure 3 shows the regression analysis for the correlation between sPAP and the months of survival. sPAP value is strongly correlated with survival duration (r 0.52, p<0.001). Figure 4 shows the Kaplan Meier survival curve according to the cut off value found in our study, and this value is statistically significant (χ^2 = -2.47957, p= 0.01).

Treatment	Number (%)
Oral anticoagulation	195 (35.6%)
Surgery	159 (28.75%)
Calcium channel blockers	44 (7.95%)
PDE-5 I	27 (4.88%)
ERA	20 (3.61%)
Prostanoids	9 (1.62%)
Combination therapy	7 (1.26%)

TABLE 3. Therapeutic options.

ERA = endothelin receptor antagonists; PDE-5 I = phosphodiesterase type-5 inhibitor

Left ventricle ejection fraction was 44.74 ± 21.12% in deceased patients group vs 51.01 ± 13.56% in survivors (p 0.03). We found no correlation between the value of left ventricular ejection fraction and survival (r 0.0203, p = 0.747).

The pulmonary acceleration time (PAT) is strongly correlated with severity of PH. Kruskal-Wallis test shows highly significant statistical variation of PAT according to the severity of PH (p <0.001). The ANOVA test shows, however, that this difference doesn't reach statistical significance in terms of mortality (p = 0.14). PAT correlates inversely with survival time (there is a decrease of the range of survival with decreasing values of PAT), but not statistically significant (r = - 0.29, p = 0.059).

Dilatation of right cavities was a major prognostic factor, negatively correlated with mortality. Right ventricular end diastolic diameter in deceased patients was in average of 45.47 ± 8.77 mm and of 38.22 ± 7.78 mm for the rest of the group (p<0.001). Right atrium area (indexed to the body surface area) was closely correlated with the risk of death (p<0.001); the mean area of deceased patients was 19.06 ± 7 mm/m², compared to 15.18 ± 5.31 mm/

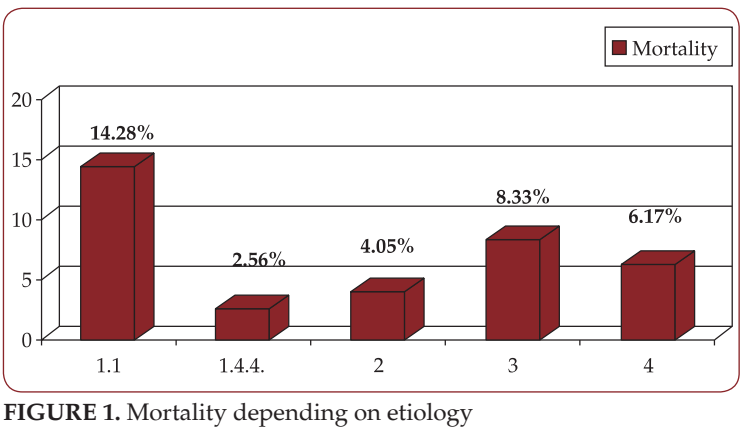

FIGURE 1. Mortality depending on etiology

	DEATH Param.	DEATH Std.Err	t	p	DEATH exp (ß)	-95.00% Cnf.Lmt	+95.00% Cnf.Lmt
Intercept	0.181640	0.29835	0.6088	0.54659		-0.42406	0.787342
sPAP	-0.00220	0.00201	1.3881	0.02813	**1.743998**	1.00628	3.001884
LVEF	-0.00291	0.00362	-0.8043	0.42661	-0.15584	-0.01027	0.004442
TAPSE	0.003991	0.00575	0.6938	0.49233	0.141463	-0.00768	0.015667
RVEDD	-0.00403	0.00476	-0.8470	0.40273	-0.17161	-0.01370	0.005636
Indexed RA area	0.002841	0.00598	0.4747	0.63791	0.093861	-0.00930	0.014992
RAP	0.025920	0.01043	2.4829	0.01797	**2.686186**	1.04727	4.047113
CI	-0.02119	0.03544	-0.5979	0.55369	-0.12429	-0.09315	0.050760
WHO class 1	0.032404	0.11552	0.2805	0.78074	0.078467	-0.20211	0.266925
WHO class 2	0.026661	0.08196	0.3252	0.74689	0.094303	-0.13972	0.193048
WHO class 3-4	-0.10117	0.07288	-1.0940	0.17386	-0.36750	-0.24914	0.046790

TABLE 4. Multivariable analysis of mortality.

m^2 in living patients. Right ventricular dysfunction was also associated with higher risk of death - average TAPSE in deceased patients was 12.23 ± 4.83 mm and 18.49 ± 5.8 mm in the remaining patients ($p<0.001$). Pericardial fluid was associated with a relative risk of death of 3.5 (confidence interval 1.49 to 8.21), $p = 0.04$.

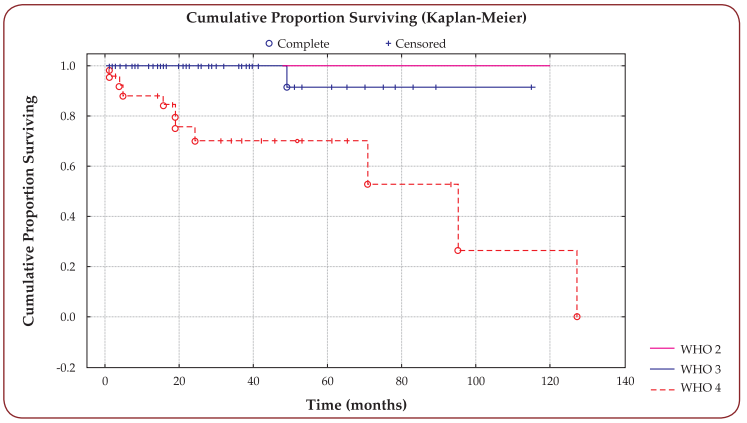

FIGURE 2. Kaplan-Meier survival curves according to the WHO class

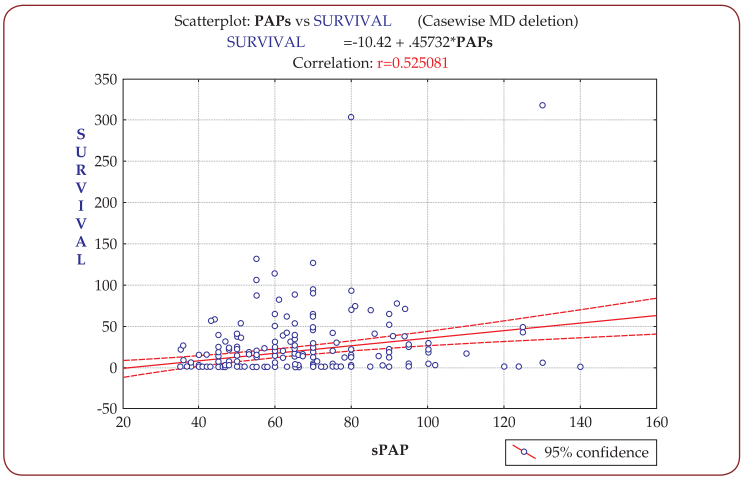

FIGURE 3. Regression analysis for the correlation between sPAP and survival

Among the studied hemodynamic parameters, the right atrium pressure (RAP) and the decreased cardiac index had the greatest impact on mortality. The RAP of deceased patients was 29.66 ± 3.05 mmHg compared to 11.3 ± 5.39 mmHg in survivors ($p < 0.001$). The cardiac index in patients who died was on average 1.63 ± 0.6 l/min/m^2, compared to 2.56 ± 1.17 l/min/m^2 in survivors ($p = 0.009$).

The results of multivariable analysis for mortality are shown in Table 4. Only right atrial pressure ($p = 0.017$) and sPAP ($p = 0.028$) reached statistical significance.

Among the deceased patients, four died after cardiac surgery (valvular replacement); the dead IPAH patient was receiving phosphodiesterase type-5 inhibitor and oral anticoagulation; four patients with thromboembolic PH were on oral anticoagulation; the rest had no specific PH medication.

In order to see if sPAP value has other prognostic implications, we divided patients into two groups (sPAP lower, respectively higher than 70 mmHg) and we analyzed the need for hospitalization due to heart failure phenomena and the average period of hospitalization for each group. For patients with sPAP lower than 70 mm Hg, the average number of hospitalizations for clinical worsening and heart failure phenomena during the monitoring period was 1.1 ± 0.35 vs 1.39 ± 0.9 hospitalizations for patients with severe PH ($p<0.001$). The average duration of hospitalization was 7.82 ± 4.08 days in the first group, respectively 12.96 ± 7.84 days in the second group ($p <0.001$). The impact of PH severity on the need for mechanical ventilation, inotropic support and

non-cardiac complications is presented in Table 5.

Using the risk stratification recommended by the ESC Guidelines (good prognosis – patients with functional classes I and II, negative prognosis - patients with functional classes III and IV), we divided patients into a first group of classes I and II and a second group that included patients with functional classes III and IV and we studied a series of clinical, echocardiographic and hemodynamic parameters. The results are presented in Table 6. ❑

DISCUSSIONS

There is a lack of consensus on factors that predict mortality and prognosis in patients with pulmonary arterial hypertension. A recent meta-analysis (11) addressing IPAH identified no less than 107 factors that have been associated with mortality in different studies. There are conflicting reports on the prognostic value of many of them. The first ten identified as prognostic factors were functional class, heart rate, six minutes walking distance, pericardial effusion, mPAP, right atrial pressure, cardiac index, stroke volume index, PVR, mixed venous

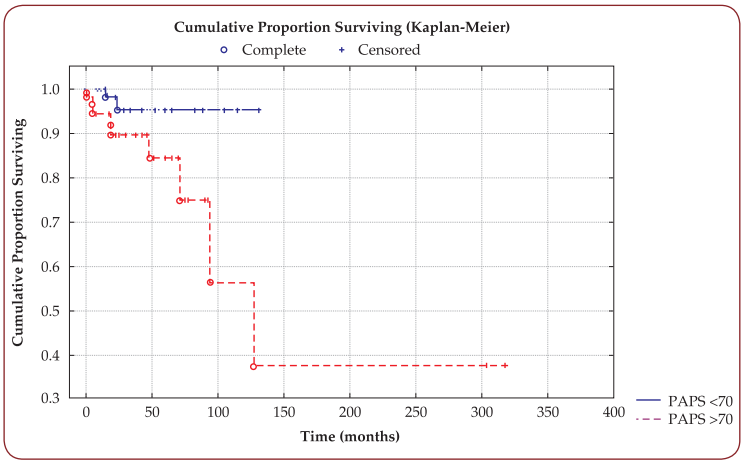

FIGURE 4. Kaplan Meier survival curve according to the cut off value of sPAP

Complication	sPAP<70 mm Hg N = 376	sPAP>70 mm Hg N = 177	χ^2	p
Mechanical ventilation, n (%)	2 (0.53%)	6 (3.39%)	7	0.008
Inotropic support, n (%)	15 (3.99%)	10 (5.65%)	0.76	0.38
Renal, n (%)	7 (1.86%)	10 (5.65%)	5.79	0.01
Hepatic, n (%)	24 (6.38%)	23 (12.99%)	6.76	0.009
Pleural, n (%)	15 (3.99%)	7 (3.95%)	0.0004	0.98
Pericardial, n (%)	4 (1.06%)	10 (5.65%)	10.25	0.001

TABLE 5. Rate of complications according to PH severity.

Parameter	WHO I- II (n = 232)	WHO III- IV (n = 321)	F	p
sPAP, mm Hg	49.89 ± 10.97	69.56 ± 17.79	3.85	<0.001
PAT, ms	96.81± 42.82	76.17 ± 22.22	7.74	0.006
PAT/PET	0.4 ± 0.08	0.31± 0.08	23.89	<0.001
TAPSE, mm	21.1± 4.65	16.3 ± 5.31	51.52	<0.001
EDRVD, mm	35.59 ± 6.63	40.49 ± 8.13	50.97	<0.001
Indexed RA area, cm^2/m^2	12.57 ± 3.9	16.10 ± 5.8	75.75	<0.001
IVCV, cm/s	7.28 ± 2.82	6.94 ± 2.34	0.2	0.6
IVCT, ms	48.83 ± 13.89	58.45 ± 18.40	3.74	0.05
IVA, m/s^2	3 ± 1.2	2.1 ± 0.7	8.76	0.005
Et, cm/s	7.22 ± 2.73	5.1 ± 2.2	9.19	0.004
At	12.33 ± 3.67	10.65 ± 4.57	1.77	0.18
St	11.16 ± 2.5	9.87 ± 2.41	4.02	0.05
IVRT, ms	109.72 ± 37.1	121.73 ± 47.28	0.86	0.35
mPAP, mm Hg	32.05 ± 8.96	51.97 ± 17.55	34.42	<0.001
RAP, mm Hg	6.22 ± 2.25	16.04 ± 3.95	103.2	<0.001
CI, $l/min/ m^2$	3.1± 1.07	2.1± 0.75	40.9	<0.001
PVR, Wood units	5.25 ± 4.65	23.81 ± 11.25	46.68	<0.001
PVR/SVR	0.19 ± 0.16	0.61 ± 0.27	46.53	<0.001
Pericardial fluid, n (%)	2 (0.86%)	37 (11.52%)	χ^2 = 23.36	<0.001

TABLE 6. Echocardiographic and hemodynamic parameters according to WHO class.

pressure of oxygen or saturations. Our study identifies echocardiographic and hemodynamic parameters associated with unfavourable outcomes in patients with both idiopathic and secondary forms of PH. We found significant correlation between these parameters and mortality, need for hospitalization, number of days of hospitalization, need for inotropic support and mechanical ventilation and occurrence of non- cardiac complications. The sPAP, determined by echocardiography, has not classically been seen as a prognostic factor (6). Yet, LeTourneau and his colleagues found that sPAP above 50 mm Hg in patients with chronic organic mitral regurgitation was an independent predictor of mortality after cardiac surgery (12). In another study, sPAP >60 mmHg correlated with a composite end point of cardiac death, readmission for heart failure or fatal arrhythmia in a group of patients undergoing restrictive mitral annuloplasty for severe functional mitral regurgitation secondary to advanced cardiomyopathy (13). In our study, we found that severe PH (defined as sPAP >70 mmHg) is closely related to increased mortality, survival duration, number of hospitalizations for clinical worsening and heart failure phenomena and longer hospitalization duration. We also found a statistically higher risk of patients with sPAP >70 mmHg for mechanical ventilation and renal, hepatic and pericardial complications. We found no association between sPAP value and need for inotropic support or pleural complications. Prognostic value of sPAP remained significant in multivariable analysis.

We found no significant influence of age or gender on mortality in patients with PH. Age impact on PAH prognosis is controversial in literature. One recent study identified male gender and age over 60 years as an independent predictor of increased mortality (14). Extremes of age (<14 years or >65 years are considered to carry a poor prognosis in IPAH (1). However, it seems that children have an increased vasodilator response, more reversible lesions and a better prognosis (15-18). The highest mortality in our group was recorded for IPAH and the lowest in patients with congenital heart diseases. Even the difference is not statistically significant, this finding is consistent with literature data showing that IPAH patients have a poor prognosis and patients with congenital heart disease, even with Eisenmenger syndrome, have a longer natural history (4,5).

We found a significant number of clinical, echocardiographic and hemodynamic parameters associated with mortality. WHO classes III and IV, as reported in many previous studies (1, 11, 14, 19), despite large interobserver variation, remain a strong predictor of mortality. Right atrium enlargement, right ventricle dilation and dysfunction, pericardial fluid, decreased cardiac index and elevated right atrial pressure correlate in our study both with mortality and functional class. These findings are consistent with other literature data (6,11,14,20). Right ventricle dilation has recently been associated with poor outcome in patients with IPAH (21). In our study, left ventricle systolic function was associated with mortality, but not with survival time. This finding is a consequence of the group structure, with more than half of patients having class II PH.

In multivariable analysis, right atrial pressure had the strongest impact on mortality. Our study comes to confirm the strong predictive value of mRAP (1,3,14). RAP was overall the most powerful predictor of survival both by univariate and multivariate analysis in patients receiving either conventional therapy or epoprostenol (3). The NIH registry identified mRAP, cardiac index and mean pulmonary artery pressure as important predictors of survival (1). Our analysis confirms the importance of hemodynamic parameters obtained by right cardiac catheterization.

Most hospitalizations and deaths in our group were due to right heart failure. Elevated right atrial pressure is due to severe functional tricuspid regurgitation and/ or elevated right diastolic pressure, both a consequence of right ventricular failure. Early diagnosis of right ventricle dysfunction may identify a high risk category of patients, which need aggressive therapy. Identifying accurate and reliable non invasive parameters for the functional assessment of the right ventricle still remains a challenge (22). In univariable analysis, TAPSE was associated with mortality and worse functional class. Using pulsed-wave tissue Doppler at the tricuspid ring, we found significant differences between WHO classes for tricuspid ring systolic velocity (St), isovolumic contraction time and isovolumic acceleration time. Studies have shown that tricuspid ring systolic velocity and IVA strongly correlate with right ventricle ejection fraction determined by MRI or radionuclide ventriculogram (22). Abnormal right ven-

tricle filling, expressed by decreased Et value (which we found statistically significant in patients with WHO class III and IV) and inverted Et/At, indicates an impaired right ventricle relaxation. This abnormality occurs early in patients with PAH (23). Thus, tissue Doppler parameters may be an useful tool for early detection of right ventricle diastolic and/ or systolic dysfunction and risk stratification.

Limits of the study: The heterogeneity of our group represented one limitation of the study. Detailed analysis for each clinical class is further needed. Another limitation is the reduced number of patients with IPAH, which made a separate statistic analysis irrelevant. Due to group heterogeneity, treatment analysis was also difficult. The significant number of patients surgically treated imposes a separate analysis of this group. Last but not least, the great number of patients with clinical class 2 (left heart diseases) had a considerable impact on some particular findings, such as significance of decreased LVEF. ❑

CONCLUSIONS

Pulmonary hypertension, despite the development of treatment methods, remains a serious disease, with progressive and inexorable evolution. PH severity and the onset of right ventricular dysfunction are associated with increased mortality, functional class deterioration, increased complications and need for hospitalization. The prognosis of patients with PH is very variable, depending on etiology, functional class and clinical, echocardiographic and hemodynamic parameters. Knowledge of these parameters allows early identification of high risk patients, which require close monitoring and aggressive therapeutic approach.

References

1. **Galié N, Hoeper M, Humbert M, et al. –** Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J* 2009;30:2493-2537
2. **Ginghina C, Enache R –** Hipertensiunea pulmonara. În Mic tratat de cardiologie. Ed. Ginghina C, Bucuresti, Editura Academiei Române 2010:621-54
3. **McLaughlin VV, Presberg KW, Doyle RL, et al. –** Prognosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest.* 2004 Jul; 126 (1 Suppl):78S-92S
4. **Hopkins WE, Ochoa LL, Richardson GW, et al. –** Comparison of the hemodynamics and survival of adults with severe primary pulmonary hypertension or Eisemenger syndrome. *J Heart Lung Transplant* 1996;15:100-105
5. **Kuhn KP, Byrne DW, Arbogast PG, et al. –** Outcome in 91 consecutive patients with pulmonary arterial hypertension receiving epoprostenol. *Am J Respir Crit Care Med* 2003;167: 580-6
6. **Raymond RJ, Hinderliter AL, Willis PW, et al. –** Echocardiographic predictors of adverse outcomes in primary pulmonary hypertension. *J Am Coll Cardiol* 2002;39:1214-9
7. **Zacharska-Kokot E –** The myocardial performance index in children after surgical correction of congenital malformations with intracardiac shunt. *Kardiol Pol.* 2007;65:143-50
8. **Blanchard DG, Malouf PJ, Gurudevan SV, et al. –** Utility of right ventricular Tei index in the noninvasive evaluation of chronic thromboembolic pulmonary hypertension before and after pulmonary thromboendarterectomy. *JACC Cardiovasc Imaging*. 2009;2:143-9
9. **Ciurzynski M, Bienias P, Lichodziejewska B, et al. –** Assessment of left and right ventricular diastolic function in patients with systemic sclerosis. *Kardiol Pol.* 2008;66:269-76
10. **Forfia PR, Fisher MR, Mathai SC, et al. –** Tricuspid annular displacement predicts survival in pulmonary hypertension. *Am J Respir Crit Care Med.* 2006;174:1034-41
11. **Swiston JR, Johnson SR, Granton JT –** Factors that prognosticate mortality in idiopathic pulmonary arterial hypertension: a systematic review of the literature. *Respir Med* 2010; 104:1588-607
12. **Le Tourneau T, Richardson M, Juthier F, et al. –** Echocardiography predictors and prognostic value of pulmonary artery systolic pressure in chronic organic mitral regurgitation. *Heart* 2010;96:1311-7
13. **Kainuma S, Taniguchi K, Toda K, et al. –** Pulmonary hypertension predicts adverse cardiac events after restrictive mitral annuloplasty for severe functional mitral regurgitation. *J Thorac Cardiovasc Surg* 2011:142:783-92
14. **Benza RL, Miller DP, Gomberg-Maitland M, et al. –** Predicting survival in pulmonary arterial hypertension: Insights from the Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL). *Circulation* 2010:122:164-72
15. **Haworth SG, Hislop AA –** Treatment and survival in children with pulmonary arterial hypertension: the UK Pulmonary Hypertension Service for Children 2001–2006. *Heart* 2009;95:312-7
16. **Fraisse A, Jais X, Schleich JM, et al. –** Characteristics and prospective 2-year follow-up of children with pulmonary arterial hypertension in France. *Arch Cardiovasc Dis.* 2010;103:66-74
17. **Ivy DD, Rosenzweig EB, Lemarie JC, et al. –** Long-term outcomes in children with pulmonary arterial hypertension treated with bosentan in real-world clinical settings. *Am J Cardiol* 2010;106:1332-1338
18. **Barst RJ, Ertel SI, Beghetti M, et al. –** Pulmonary arterial hypertension: a comparison between children and adults. *Eur Respir J* 2011;37:665-677
19. **Kurzyna M, Zylkowska J, Fijalkowska A, et al. –** Characteristics and prognosis of patients with decompensated right ventricular failure during the course of pulmonary hypertension. *Kardiol Pol.* 2008;66:1033-9
20. **Miura Y, Fukumoto Y, Sugimura K, et al. –** Identification of new prognostic factors of pulmonary hypertension. *Circ J* 2010;74:1965-71
21. **Zeng WJ, Sun YJ, Xiong CM, et al. –** Prognostic value of echocardiographic right/left ventricular end-diastolic diameter ratio in idiopathic pulmonary arterial hypertension. *Chin Med J* (Engl). 2011;124 :1672-7
22. **Jurcut R, Giusca S, La Gerche A, et al. –** The echocardiographic assessment of the right ventricle: what to do in 2010? *Eur J Echocardiogr* 2010;11:81-96
23. **Huez S, Vachiéry JL, Unger P, et al. –** Tissue Doppler imaging evaluation of cardiac adaptation to severe pulmonary hypertension. *Am J Cardiol* 2007;100:1473-8