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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Prognosis in children with pulmonary arterial hypertension: 10-year single-centre experience

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Abstract

Background: Pulmonary arterial hypertension (PAH) is a rare progressive disease of the pulmonary arterioles with an unfavourable prognosis.

Aim: To evaluate survival and prognostic factors in patients with PAH diagnosed and treated at a single centre in the years 2004–2013.

Methods: The study included 55 children (33 girls; 66%, 22 boys; 33%), with an average age 6.2 ± 6.0 years, with idiopathic PAH — n = 23 (42%), PAH associated with systemic-to-pulmonary shunts — n = 17 (31%), and PAH after corrective cardiac surgery — n = 15 (27%). Forty-seven of them (87%) were treated with advanced therapy.

Results: During the follow-up with an average time of 5.6 ± 4.7 years 15 (27.3%) children died. The one-, three-, five-, and ten-year survival was, respectively, 83.1%, 77.1%, 70.7%, and 65.2%. The analysis of the survival curves revealed a better prognosis in patients with baseline N-terminal pro-B-type natriuretic peptide (NT-proBNP) level < 605 pg/mL ($p = 0.024$) and a higher probability of survival of three and five years in children at baseline I/II World Health Organisation functional class (WHO-FC). The higher risk of death was associated with a higher pressure in the right atrium (HR 1.23, $p < 0.01$) and higher pulmonary resistance (HR 1.1, $p < 0.01$), whereas no history of syncope had a better prognosis (HR 0.31, $p = 0.03$).

Conclusions: Survival in the study group was comparable to the currently published register data. Mortality risk factors were connected with the severity of the disease at diagnosis.

Key words: pulmonary arterial hypertension, children, survival analysis

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INTRODUCTION

Pulmonary arterial hypertension (PAH) is a rare progressive disease of the pulmonary arterioles with an unfavourable prognosis. Functional and anatomical changes result in an increase of pulmonary artery pressure (PAP) and subsequently lead to right ventricular failure. Detailed guidelines specify diagnostic methods and indications for treatment in adult patients [1, 2]. Based on existing experience, risk factors of poor prognosis, which are indications for treatment intensification, have been specified.

As the pathophysiology of PAH in children and in adults is the same, similar diagnostic methods and treatment strategies are specified for both groups. However, the assessment of prognostic factors is different in the paediatric population. This is due to developmental differences, lack of technical capabilities, and significantly higher risk of some tests in paediatric patients.

The aim of the study was to evaluate survival and prognostic factors in a population of paediatric patients with PAH diagnosed and treated at a single institution according to the same strategy, which change, however, with the development of knowledge and the availability of medication.

METHODS

Between 2004 and 2013, 69 children with PAH were treated in the Department of Paediatric Cardiology. Children with

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a diagnosis of PAH, based on cardiac catheterisation performed at the age of > three months, were included into the study. According to European Society of Cardiology definition, pulmonary hypertension (PH) was diagnosed when mean PAP (mPAP) was ≥ 25 mm Hg, pulmonary capillary wedge pressure (PCWP) < 15 mm Hg, and in patients with shunts, when pulmonary resistance index was of > 3 WU*m^2. Children after cardiac surgery were included into the study on the basis of cardiac catheterisation performed at least one year after surgery.

In the years 2004–2013, data were collected prospectively (incident group). Data of patients remaining under the care of the institution at the beginning of the study in 2004 (prevalent group) were introduced retrospectively on the basis of medical records.

Demographic data including gender, age at diagnosis, and follow-up data from the time of the diagnosis were collected. Additionally, information on the diagnosis of Down syndrome was isolated. In all children echocardiographic study and diagnostic tests, according to the standards [1], were performed to find the causes of PH.

The assessment of severity of the disease at diagnosis was performed on the basis of parameters according to the current guidelines for adults [1]:

- medical history: the presence of syncope;
- physical examination: World Health Organisation functional class (WHO-FC);
- six-minute walk test (6MWT) was not analysed because of the small number of children who were able to perform the test;
- echocardiography — the presence of pericardial effusion, tricuspid annular plane systolic excursion was not included due different normal values depending on age;
- biomarkers — N-terminal pro-B-type natriuretic peptide (NT-proBNP) level — the cut-off was set at 605 pg/mL according to the published results obtained in children [3];
- right heart catheterisation — right atrial pressure, cardiac output (analysed using cardiac index [CI] = cardiac output divided by the body surface area).

Additionally, haemodynamic parameters were analysed: mixed venous saturation, mPAP in relation to the mean systemic pressure, pulmonary resistance index, acute vasoreactivity test performed with nitric oxide in all cases.

Survival analysis was performed for the whole group and the subgroups depending on the time of enrolment (prevalent vs. incident), WHO-FC, diagnosis, the level of NT-proBNP, and administered medication. The time of cardiac catheterisation inclusion into the study was considered as a start point in the incident group, whereas in the prevalent group the point was set at 1st January 2004 (the beginning of the study). The endpoint was death. Lung transplant patients were treated as censored observations. The one-, three-, five-, and ten-year survival period was evaluated. Additionally, we conducted uni- and multivariate analysis of the risk of death, taking the following factors into account: demographic (age at diagnosis, prevalent vs. incident group), clinical (syncope in an anamnesis, Down syndrome, WHO-FC, level of NT-proBNP, treatment), and haemodynamic (mixed venous saturation, right atrial pressure, PAP — absolute value and the value in respect to systemic pressure, cardiac output, pulmonary resistance).

Because of the long follow-up period in patients enrolled in the study, different methods of treatment, based on current knowledge and capabilities, were applied. In the years 2004–2008 and earlier there was only a very limited possibility of treatment with sildenafil administered usually in WHO-FC III (according to contemporary standards) or in selected stable patients in the clinical trial. In the years 2009–2013 the target-oriented therapy in accordance with current standards (2009) was applied, but with no possibility of treatment with prostacyclin or its analogues in outpatient care. Additionally, lung transplant in young children is virtually inaccessible, and the Potts anastomosis was performed for the first time in 2012 [4]. The survival analysis, depending on treatment, was performed for patients taking advanced therapy (limited as above) immediately after the diagnosis or at any time during the course of the disease, as compared with patients who had never been treated with advanced therapy.

Statistical analysis

The data were presented as mean ± standard deviation, and in the case of the qualitative variables as a percentage of the group. The survival analysis was performed using the Kaplan-Meier survival function estimator; the results were shown in survival curves. Confidence intervals for the Kaplan-Meier estimators were not calculated because of the small number of patients. When comparing the significance of the difference between two or more survival functions a log-rank test was used, taking into account the maximum available observation periods, i.e. ten years. Survival analysis in one-, three-, and five-year periods in individual subgroups using the χ^2 test of Pearson with Yates corrections where necessary was performed. For the test adequacy censored observations were eliminated. To assess risk factors, single and multivariable, the Cox proportional hazards model was used. Variables that had in a univariate model a parameter significance of $p < 0.2$ were introduced into the multivariate model, and then stepwise regression in order to select significant variables was used. Missing data were excluded by cases. In all analyses, the level of significance of $p = 0.05$ was adopted. The analyses were done using Statistica 10.0.

RESULTS

Demographic, clinical and haemodynamic characteristics

The study included 55 children (33 girls, 66%; 22 boys, 33%) aged from three months to 17.5 years (mean 6.2 ± 6.0 years, median 3.1). Eighteen children in the group had Down syndrome. In 10 (18.1%) patients, PH was diagnosed before

Table 1. Demographic, clinical, and haemodynamic characteristics at diagnosis

Characteristic		Overall (n = 55)	Survivors (n = 37)	Others (n = 18)**
Age at diagnosis [years]*		6.2 ± 6.0	6.7 ± 6.0	5.1 ± 6.0
Gender	Male	22 (40%)	15 (41%)	7 (39%)
	Female	33 (60%)	22 (59%)	11 (61%)
Prevalent/incident		10/45	6/31	4/14
		(18%/82%)	(16%/84%)	(22%/78%)
Follow up [years]*		5.6 ± 4.7	6.6 ± 4.6	3.6 ± 4.2
WHO-FC	II	35 (64%)	24 (65%)	11 (61%)
	III	17 (31%)	12 (32%)	5 (28%)
	IV	3 (5%)	1 (3%)	2 (11%)
Syncope		10 (18%)	5 (14%)	5 (28%)
Down syndrome		18 (33%)	14 (38%)	4 (22%)
Diagnosis	IPAH	23 (42%)	15 (41%)	8 (44%)
	APAH-CHD	17 (31%)	13 (35%)	4 (22%)
	APAH-CHDpostop	15 (27%)	9 (24%)	6 (33%)
6MWT desaturation [%]*		12.2 ± 11.5	13.1 ± 12.2	8.0 ± 9.9
		(n = 10)	(n = 8)	(n = 2)
NT-proBNP [pg/mL]*		2198 ± 2091	2078 ± 2184	2460 ± 1955
		(n = 32)	(n = 22)	(n = 10)
NT-proBNP (n = 32)	< 605 pg/mL	11 (34%)	9 (43%)	2 (18%)
	> 605 pg/mL	21 (66%)	13 (62%)	8 (73%)
Pericardial effusion on echo		0	0	0
Haemodynamic*	MVO (%HbO2)	65.4 ± 8.2	65.6 ± 7.2	64.8 ± 10.5
		(n = 42)	(n = 29)	(n = 13)
	Mean RAP [mm Hg]	9.0 ± 4.1	8.5 ± 3.4	10.2 ± 5.3
		(n = 51)	(n = 35)	(n = 16)
	Mean PAP [mm Hg]	56.9 ± 13.7	56.6 ± 13.9	57.5 ± 13.6
	Mean PAP/SAP	0.9 ± 0.2	0.9 ± 0.2	0,9 ± 0,2
	CI [L/min/m^2]	3.4 ± 1.5	3.7 ± 1.7	2.8 ± 1.0
		(n = 41)	(n = 28)	(n = 13)
	PVRI [WU*m^2]	15.3 ± 9.5	12.9 ± 7.3	20.9 ± 11.8
		(n = 43)	(n = 30)	(n = 13)
AVT (n = 42)	Positive	3 (7%)	1 (3%)	2 (15%)
	Negative	39 (93%)	28 (97%)	11 (85%)
Advanced therapy after diagnosis		41 (75%)	29 (78%)	12 (67%)
Advanced therapy during disease course		47 (85%)	33 (89%)	14 (78%)

*Data are presented as mean ± standard deviation; **Deaths and lung transplantations; in brackets percentage of overall, survivors, and others; WHO-FC — World Health Organisation functional class; APAH-CHD — pulmonary hypertension associated with systemic-to-pulmonary shunts; APAH-CHDpostop — pulmonary hypertension after corrective cardiac surgery without significant shunt; IPAH — idiopathic pulmonary hypertension; 6MWT — six-minute walk test; NT-proBNP — N-terminal pro-B-type natriuretic peptide; MVO — mixed venous oxygenation; RAP — right atrial pressure; PAP — pulmonary artery pressure; SAP — systemic arterial pressure; CI — cardiac index; PVRI — pulmonary vascular resistance index; AVT — acute vasoreactivity test

2004 (prevalent group). The observation period was from 0 (death during diagnostic catheterisation of the right heart) to 19 years (mean 5.6 ± 4.7 years, median 3.9), and the period of observation in the study of 0 to 10 years (mean 4.3 ± 3.3 years). During this period, three (5.4%) patients underwent lung transplantation and 15 (27.3%) children died. Causes of death included progressive right ventricular failure (n = 10), sudden death (n = 3), and PH crisis due to anaesthesia for cardiac catheterisation (n = 2). The demographic data are shown in Table 1.

At diagnosis, 35 (64%) children were in class II WHO-FC, 17 (31%) in III, and three (5%) in class IV. Ten patients had a history of fainting. Idiopathic or familial pulmonary hypertension (IPAH/FPAH) was diagnosed in 23 (42%) children (IPAH 22, FPAH 1), pulmonary hypertension associated with systemic-to-pulmonary shunts (APAH-CHD) in 17 (31%), and pulmonary hypertension after corrective cardiac surgery without significant shunt (APAH-CHDpostop) in 15 (27%) patients. FPAH was diagnosed based on history of PH in the patient's sister; genetic tests were not performed. There was no pericardial effusion in any patient. NT-proBNP levels ranged from normal (< 120 pg/mL) in three children to 7716 pg/mL. In haemodynamic study the PAP ranged from 32 to 90 mm Hg and pulmonary resistance from 3.7 to 48 WU*m^2. Suprasystemic pulmonary artery pressure (mPAP/mSAP > 1) was found in 13 (24%) children, and significantly reduced cardiac output (CI < 2.5 L/min/m^2) in the 12 of 41 (29%). A positive vasoreactivity test was achieved only in three children. Detailed clinical and haemodynamic data for the group are shown in Table 1.

In the years 2009–2013, in 25 children oral therapy — sildenafil (n = 12), bosentan (n = 12), and bosentan + sildenafil (n = 1) — was administered after diagnosis. One child who died immediately after cardiac catheterisation received epoprostenol and nitric oxide. Prior to 2009, treatment with sildenafil was administered immediately after diagnosis in 15 of 29 children, wherein qualification for the treatment was not affect by the patient's condition, but by the drug's availability. Another seven children with hypertension diagnosed before 2009 began advanced pharmacotherapy at a later date.

Survival analysis

Survival of one, three, five, and ten years for the entire studied population was, respectively, 83.1%, 77.1%, 70.7%, and 65.2%. These data are illustrated by a Kaplan-Meier curve (Fig. 1). The fact that the slope of the survival curve in the first years after diagnosis is greater than in the next years draws attention and suggests a difference in the probability of survival in the group of prevalent and incident patients (Fig. 1).

Figure 1 shows the survival curves in both groups. In the studied population no significant statistical difference in the probability of survival between the two groups was shown. This result may be associated with the small number of children diagnosed before the study (prevalent). The suggestion of better prognosis for prevalent patients seems to be confirmed by the fact that in this group no mortality was observed > two years after diagnosis, in a follow-up period of max. 9.3 years, mean 5.0 ± 2.4 years.

Diagnosis. Influence of diagnosis (IPAH, APAH-CHD, APAH-CHDpostop) on prognosis was analysed by assessing one-, three-, five-, and ten-year survival, which was, respectively, IPAH 86.7%, 81.7%, 72.6%, and 72.6%; APAH-CHD 93.8%, 87.1%, 79%, and 68.4%; and APAH-CHDpostop 66.7%, 60.0%, 60.0%, and 60.0% (Fig. 2).

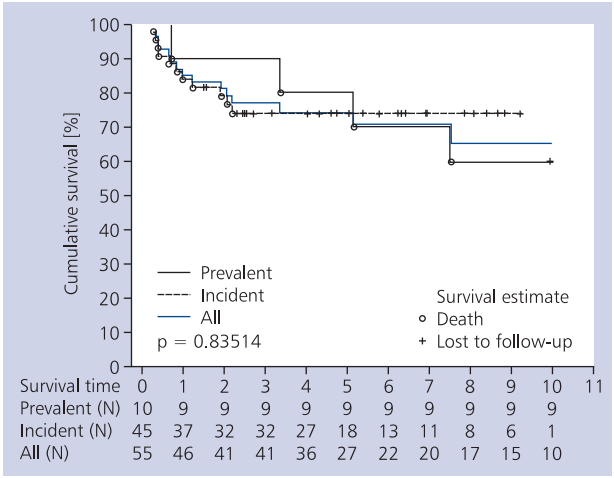

Figure 1. Kaplan-Meier curves for survival for the entire cohort, and prevalent and incident subgroups

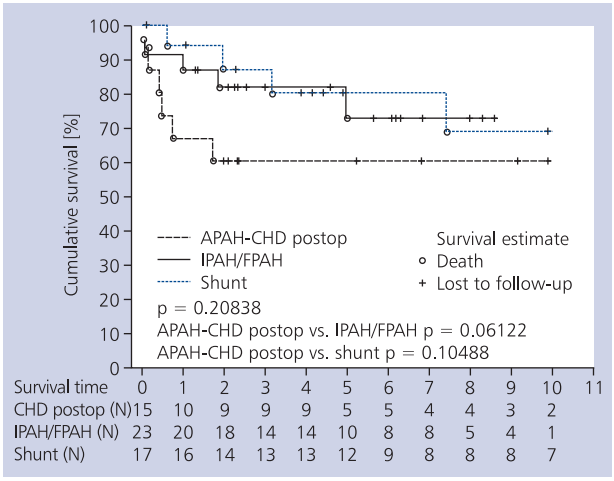

Figure 2. Kaplan-Meier curves for survival for the patients with IPAH (IPAH/FPAH), APAH-CHD (shunt), and APAH-CHDpostop; abbreviations — see the text

Although the survival analysis of Kaplan-Meier showed no statistically significant difference in the likelihood of survival between the groups, the curve suggests a worse prognosis in children with congenital heart defects after cardiac surgery in a shorter period of follow-up (< five years). The lack of statistical significance may be due to the low number of patients.

WHO-FC. For the purpose of statistical analysis patients were divided into two groups: WHO-FC I–II (n = 35) and WHO-FC III–IV (n = 20). One-, three-, five-, and ten-year survival rates were, respectively, as follows: WHO-FC I–II 85.4%, 85.4%, 77.0%, and 70.5%; WHO-FC III–IV 79.2%, 62.2%, 62.2%, and 62.2% (Fig. 3).

There was no statistically significant difference between the curves, but separate analysis of one-, three-, and five-year survival rates (after the elimination of censored observations)

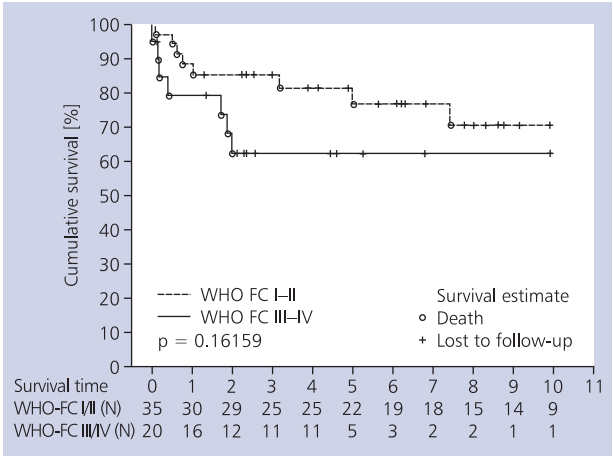

Figure 3. Kaplan-Meier curves for survival for the patients in the World Health Organisation functional class (WHO-FC) I–II group and the WHO-FC III–IV group

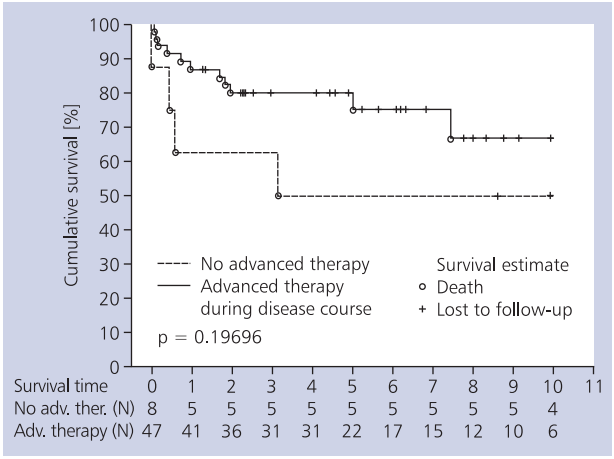

Figure 5. Kaplan-Meier curves for survival for the patients on advanced therapy and without advanced therapy during disease course

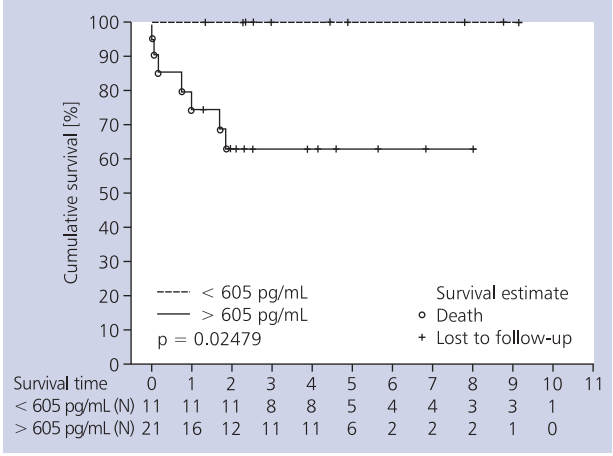

Figure 4. Kaplan-Meier curves for survival for the patients with N-terminal pro-B-type natriuretic peptide (NT-proBNP) > 605 pg/mL and < 605 pg/mL

revealed significantly higher risk of death within three and five years after diagnosis for the patients in III–IV WHO-FC ($p = 0.01$, $p = 0.05$).

NT-proBNP. The only factor that influenced the prognosis in children with PH (evaluated using survival analysis of Kaplan-Meier) was the level of NT-proBNP. A statistically significant difference in survival curves (NT-proBNP > 605 pg/mL and < 605 pg/mL) was shown ($p = 0.024$) (Fig. 4).

Treatment. A group of patients who received advanced pharmacological treatment ($n = 47$) comprised the group of children who had never received specific treatment for PAH ($n = 8$) (Fig. 5).

The probability of one-, three-, five-, and ten-year survival in the group of treated children was, respectively, 86.6%, 79.5%, 74.8%, and 66.5% and in untreated — 62.5%, 62.5%, 50.0%, and 50.0%. The survival in the treated patients seems to be higher, although no statistically significant difference between these groups was found, which may be due to the small number of patients untreated with advanced therapy.

Analysis of risk factors

Taking the collected data presented in Table 1 into account, uni- and multivariate survival analysis for the entire examined population was performed (Table 2). Higher risk of death is associated with higher pressure in the right atrium (HR 1.23, $p < 0.01$) and with higher pulmonary resistance (HR 1.1, $p < 0.01$). However, no syncope revealed in anamnesis influenced better prognosis (HR 0.31, $p = 0.03$). In a multivariate analysis, the only statistically significant factor of the increased risk of death was higher right of atrial pressure (HR 1.44, $p = 0.02$) (Table 2).

DISCUSSION

Pulmonary arterial hypertension is a rare disease. In adults, morbidity is recognised at 15–52 per million [5, 6], and in children even less (PAH prevalence excluding APAH-CHD ≥ 3.7 per million) [7]. Therefore, epidemiological data and data on diagnosis and prognosis usually come from registers, especially in the paediatric population. According to the data collected from all nine paediatric reference centres in Poland, dealing with PH, the annual incidence in children in our country is 3.3 per million, while the prevalence is 13.8–15.8 per million (unpublished data of the national consultant in paediatric cardiology). A unique feature of this study is the analysis of a series of patients in one centre, which ensures uniform standards of diagnosis and treatment, and coverage of the whole population of children fulfilling the inclusion criteria. The limitation, however, is the fact that until 2008 only monotherapy was applied, and not in all patients requiring

Table 2. Cox proportional hazards model of survival

Characteristic	N	Death — HR	95% CI	P
Univariate analysis				
Age at diagnosis	55	0.91	0.81–1.02	0.11
Incident vs. prevalent	55	0.89	0.28–2.89	0.85
Syncope (– vs. +)	55	0.31	0.10–0.90	0.03
Down syndrome (– vs. +)	55	1.60	0.51–5.06	0.42
WHO (I–II vs. III–IV)	55	0.46	0.16–1.3	0.14
NT-proBNP (< 1400 vs. > 1400 pg/mL)	32	0.13	0.02–1.09	0.06
Advanced therapy after diagnosis (– vs. +)	55	0.87	0.29–2.59	0.80
Advanced therapy during disease course (– vs. +)	55	2.10	0.66–6.67	0.21
MVO	42	0.93	0.86–1.02	0.13
Mean RAP	51	1.23	1.06–1.43	< 0.01
Mean PAP	55	1.01	0.97–1.04	0.79
Mean PAP/SAP	55	4.18	0.45–38.96	0.21
Cardiac index	41	0.72	0.39–1.32	0.28
PVRI	43	1.10	1.03–1.18	< 0.01
Multivariate analysis				
mRAP	27	1.44	1.07–1.92	0.02

Blue font — statistically significant p-values; HR — hazard ratio; CI — confidence interval; other abbreviations as in Table 1

treatment, and since 2009 the advanced treatment was not fully available for the most seriously ill children (no possibility to use prostacyclin and its analogues in out-patient care, no possibility of lung transplant in young children). In addition, during the 10 years of recruitment, in 2009, the treatment guidelines changed [1]. The same problems, which can cause difficulties in comparing the results of studies depending on the population, are also highlighted by other authors [8, 9].

Survival analysis

One-, three-, five-, and ten-year survival rates in the study group were 83.1%, 77.1%, 70.7%, and 65.2%, respectively. This is clearly better than historical data prior to the specific pharmacotherapy era: one-, three-, and five-year survival rates for non-responders in acute vasodilator test: 66%, 52%, and 35%, respectively [10]. The results were compared with available data from current records of children with PH. Survival in our study was lower than in cases when the modern therapy was applied: the United Kingdom registry in [11] 90.5%, 82.8, 64.2%, REVEAL (United States) 96%, 84%, 74%, respectively [9]. Our results are similar to the results of the Dutch registry [12] from the years 1993 to 2008, which also deal with a historical group of children not treated with advanced drugs (87%, 78%, 73%, respectively). The question of whether the ability to use all the treatment options in a small number of the most severely ill patients could improve the survival in the studied group, remains open. However during long-term follow-up (10 years) the survival rate in the study population decreased with the time, also in the group treated with advanced therapy. This information has some clinical significance, pointing to the progression of the disease despite treatment (in children the probability of dying of natural causes within 10 years is close to 0).

Risk factors

Data from recent publications on risk factors of death in children with PAH are presented in Table 3.

The prognostic usefulness of the WHO-FC and the level of NT-proBNP were proven in each of the cited studies in which they were dealt with. This result is consistent with observations in adults [14–16]. None of the studies confirmed the impact of the duration of follow-up (prevalent vs. incident) on the results of the survival analysis postulated by French authors [17]. There was also no difference in prognosis depending on the diagnosis confirmed if it concerned a distinction between IPAH and APAH-CHD. Some authors have noted that APAH-CHDpostop has a poorer prognosis than other forms of paediatric PH. This is probably due to closure of a shunt in patients developing PH despite surgery (pathophysiology like IPAH). Periodic right-to-left flow through the defect could prevent acute right heart failure, while surgery excludes this mechanism. Such patients have the poorest prognosis [11]. This fact in the observation period < five years is also suggested by the results of the presented analysis.

Evaluation of mPAP is crucial in the diagnosis of PH. The value of this parameter as a prognostic factor was not confirmed in any of these publications; this may be due to the pathophysiology of the disease. In the initial period the

Table 3. Predictors of poor outcome in children with pulmonary arterial hypertension — review of current publications compared to presented data [10, 12, 13]

	van Loon [12], Netherlands	Moledina [13], United Kingdom	Barst [10], United States	Żuk, Poland
Date of publication	2010	2010	2012	2014
N	52	64	216	55
Diagnosis	PAH	IPAH	PAH	PAH
Study period	1993–2008	2001–2007	2006–2009	2004–2013
PREDICTORS				
Age at diagnosis	No	No	Yes	No
Gender	No	Yes	No	No
Failure to thrive		Yes		
Prevalent/incident		No	No	No
Down syndrome				No
IPAH vs. APAH	No		No	No
WHO-FC	Yes	Yes		Yes*
Syncope in history		No	No	Yes
NT-proBNP	Yes		Yes[a]	Yes[b]
Uric acid	Yes			
MVO	Yes**			No
Mean RAP		No		Yes
PVRI		No	Yes	Yes
Mean PAP		No		No
Systolic BP	Yes		No	
Diastolic BP	Yes**			
Mean SAP		No		
Mean PAP/SAP	Yes		No	No
CI	Yes**	No	Yes	No
AVT	No	No	Yes	No

Blank cells — characteristic not considered; Yes (blue font) — statistically significant predictor of death; No — characteristic considered, but without predictive value; *Statistically significant only in three- and five-year follow-up period; **After correction for cohort (according to specific PAH therapy) loss of predictive values; [a]Cut-off 300 pg/mL — data obtained at enrolment, no at diagnosis; [b]Cut-off 605 pg/mL; BP — blood pressure; other abbreviations as in Table 1

pressure in the pulmonary artery rises, while later, with the development of severe heart failure, it decreases [18]. A single measurement without analysis of other parameters does not explain the severity of the disease. Additionally, the absolute value of mPAP is not as important as its relation to the mean systemic pressure (mPAP/mSAP). However, the prognostic usefulness of this parameter has been shown only in one of three studies. Other risk factors of death are different in different publications. In this material these factors are associated with both severity of changes in the pulmonary circulation (pulmonary resistance) and with the function of the right ventricle (right atrial pressure, syncope) [19]. In multifactorial analysis the only significant factor was right atrial pressure, which reveals the important role played by the right ventricle in predicting prognosis [20]. This was confirmed in numerous publications [16, 21, 22], and right atrial pressure was incorporated to guidelines as a one of the haemodynamic determinants of prognosis [1]. Noteworthy is the assessment of cardiac output, which, from the pathophysiological point of view, should be a significant independent risk factor for mortality, but this has been demonstrated only in one out of four analyses. In these studies the cardiac output during the first diagnostic cardiac catheterisation was measured. Because it is known that as the disease progresses it leads to the failure of both ventricles and a decrease of the cardiac output [18]. The specific pharmacotherapy of PH inhibits the progress of the disease. In case of failure of pharmacotherapy the modification of cardiac output by Potts anastomosis or atrioseptostomy is possible. Therefore, in assessing of the prognosis the often-repeated non-invasive measurement of cardiac output would be of greater importance than the initial catheterisation diagnostic test.

Survival analyses based on data from large registries for adults with PAH allowed the creation of risk calculators [21, 22]. They include various parameters — the United Kingdom [21]: age, gender, aetiology, 6MWT, and haemodynamic studies (right atrial pressure and the cardiac output); United States [22]: aetiology, age, sex and co-morbidities, the WHO-FC, blood pressure and heart function, 6MWT, BNP or NT-proBNP, pericardial effusion in echo, pulmonary function tests (DLCO), and haemodynamic studies (right atrial pressure and pulmonary resistance). These calculators are used to assess the prognosis, but can also be useful in planning treatment strategies (aggressive or less aggressive). Due to developmental differences, they cannot be used in the paediatric population. The creation of such risk calculators for children with PH is very difficult due to the relatively small number of patients.

CONCLUSIONS

In the study group of children with PAH, prognosis was associated with the severity of disease at diagnosis with risk factors such as syncope, WHO-FC III/IV, elevated NT-proBNP level, high pulmonary vascular resistance, and high right atrial pressure. The survival rate in the study group was comparable to the currently published data from registries.

Conflict of interest: *none declared*

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Rokowanie u dzieci z tętniczym nadciśnieniem płucnym: 10-letnie doświadczenia jednego ośrodka

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Streszczenie

Wstęp: Tętnicze nadciśnienie płucne (PAH) jest rzadką postępującą chorobą tętniczek płucnych o niekorzystnym rokowaniu.

Cel: Celem pracy była ocena przeżycia i czynników rokowniczych w populacji pacjentów z PAH diagnozowanych i leczonych w jednym ośrodku w latach 2004–2013.

Metody: Badaniem objęto 55 dzieci (33 dziewczynki, 66%; 22 chłopców, 33%) w wieku średnio 6,2 ± 6,0 lat z idiopatycznym PAH (n = 23, 42%), w przebiegu wady (APAH-CHD) (n =17, 31%) oraz po leczeniu operacyjnym wady serca (n = 15, 27%). Analizowano dane demograficzne, kliniczne i hemodynamiczne uzyskane w momencie rozpoznania. Ze względu na małą liczbę pacjentów, którzy nigdy nie zostali poddani zaawansowanej terapii (8 vs. 47), nie analizowano wpływu leczenia na przeżycie.

Wyniki: W okresie obserwacji trwającym średnio 5,6 ± 4,7 roku 15 (27,3%) dzieci zmarło. Przeżycie 1-, 3-, 5-, 10-letnie wyniosło odpowiednio 83,1%; 77,1%; 70,7% i 65,2%. Analiza krzywych przeżycia wykazała lepsze rokowanie u pacjentów z wyjściowym stężeniem N-końcowego fragmentu propeptydu natriuretycznego typu B (NT-proBNP) < 605 pg/ml (p = 0,024) oraz wyższe prawdopodobieństwo przeżycia 3- i 5-letniego u dzieci wyjściowo w I/II klasie czynnościowej wg Światowej Organizacji Zdrowia (WHO-FC). Na postawie analizy czynników ryzyka ustalono, że wyższe ryzyko zgonu wiąże się z wyższym ciśnieniem w prawym przedsionku (HR 1,23; p < 0,01) oraz wyższym oporem płucnym (HR 1,1; p < 0,01), natomiast brak omdleń w wywiadzie wpływa na lepsze rokowanie (HR 0,31; p = 0,03).

Wnioski: W badanej grupie dzieci z nadciśnieniem płucnym rokowanie wiązało się z zaawansowaniem choroby w chwili rozpoznania, a czynnikami ryzyka niekorzystnego przebiegu były omdlenia, WHO-FC III/IV, podwyższone stężenie NT-proBNP, wysoki opór płucny i wysokie ciśnienie w prawym przedsionku. Przeżycie w badanej grupie jest porównywalne z aktualnie publikowanymi danymi z rejestrów.

Słowa kluczowe: tętnicze nadciśnienie płucne, dzieci, analiza przeżycia

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