Bratisl Lek Listy 2009; 110 (12)
788 – 794

CLINIAL STUDY

Clinical and hemodynamic picture of Eisenmenger syndrome

Simkova I[1], Tavacova M[1], Kanalikova K[2], Pacak J[1], Kaldararova M[2]

Department of Cardiology, National Institute of Cardiovascular Diseases, Slovak Medical University, Bratislava, Slovakia. **simkova@susch.sk**

Abstract: Eisenmenger syndrome represents a very specific form of pulmonary arterial hypertension (PAH). Unlike patients with idiopathic PAH, in Eisenmenger syndrome the clinical and cardiac status is often relatively stable for a long time. On the other hand, due to cyanosis and due to maladaptive body reactions many non-cardiac complications may occur.
Fourteen patients (pts) with Eisenmenger syndrome were analyzed, with the mean age 41 years. Invasively measured pre-capillary pulmonary hypertension was severe (mean pulmonary arterial pressure 79 mmHg) and a statistically significant difference according to the site of defect was found (pre-tricuspid shunts vs post-tricuspid shunts=57,5 mmHg vs 88 mmHg; p=0.01).
It is neccessary to keep in mind that non-cardiac events and complications may lead to death sooner then the right ventricular dysfunction or PAH *(Tab. 7, Fig. 21, Ref. 16)*. Full Text (Free, PDF) *www.bmj.sk.*
Key words: pulmonary arterial hypertension, Eisenmenger syndrome, cyanosis, a multi-systemic disease, right ventricular function.

Eisenmenger syndrome is a specific form of pulmonary arterial hypertension (PAH) that develops due to a congenital heart defect. Hemodynamically crucial is the presence of a non-restrictive systemic-to-pulmonary connection without pulmonary outflow tract obstruction. For the development and time onset of irreversible pulmonary vascular disease, following factors are important (1, 2) – the site of the defect (pre- or post-tricuspid), the size and the type of the defect, associated extra-cardiac abnormalities and the presence or absence of correction, as well as the time and type of correction.

Unlike patients with other forms of PAH, Eisenmenger syndrome patients act often quite in a unique way. Pulmonary arterial pressure is high, often even suprasystemic. Despite this fact they usually tolerate it well and their clinical status is for long time quite stable and more or less satisfactory, with better survival than patients with other forms of PAH (3, 4). The preserved right ventricular function seems to be crucial – having a "pop-off valve" to the systemic circulation (5, 6). The other important thing is that despite severe PAH the defect with right-to-left shunting enables to maintain sufficient systemic cardiac output, although of course, for the price of systemic O_2 desaturation.

On the other hand, the situation is not too optimistic. Most patients with Eisenmenger syndrome are symptomatic from young age. In later phases of the disease their symptoms may result from heart failure (right ventricular), or from PAH, but more often their symptoms are the result of cyanosis and maladaptive body reactions to systemic desaturation. Eisenmenger syndrome must be considered a multi-systemic disorder (5, 7, 8, 9). The management should be concentrated in specialized centers that can provide both complete diagnosis and therapy of PAH as well as of congenital heart disease (10, 11, 12).

[1]Department of Cardiology, National Institute of Cardiovascular Diseases, Slovak Medical University, Bratislava, and [2]National Institute of Cardiovascular Diseases, Bratislava, Slovakia

Address for correspondence: I. Simkova, MD, PhD, FESC, Dept of Cardiology, National Institute of Cardiovascular Diseases, Slovak Medical University, Pod Krasnou horkou 1, SK-833 48 Bratislava, Slovakia.

Aim of the study

A prospective study, considering Eisenmenger syndrome a multi-systemic disorder, focusing on the clinical and hemodynamic status of the patients.

Patients

We analyzed 14 patients (pts) with Eisenmenger syndrome supervised at our institution during January 2006 – January 2009. They were 10 female (71.4 %) and 4 male (28.6 %), with mean age 41 years (ranged 25–55 years). Majority of them – 8 (57.1 %) were younger than 40 years, 4 pts (28.6 %) were between 40–49 years and 2 pts (14.3 %) were above 50 years of age (Fig. 1).

A pre-tricuspid type of shunt had 4 pts (28.6 %) (all of them atrial septal defect (ASD), 2 pts with additional partial anomalous drainage (PAPVD) of 1–2 pulmonary veins into the right side of the heart) and 10 pts (71.4 %) had a post-tricuspid type of shunt (6 pts (42.9 %) a ventricular septal defect (VSD), 2 pts (14.4 %) an atrio-ventricular septal defect (AVSD), 1 patient (7.1 %) a persistent arterial duct (PDA) and 1 (7.1 %) a common arterial truncus (TAC) (Tab. 1). Simple shunt was present in 10 pts (71.4 %), multiple shunts in 1 pt (7.1 %) and 3 pts (21.4 %) had

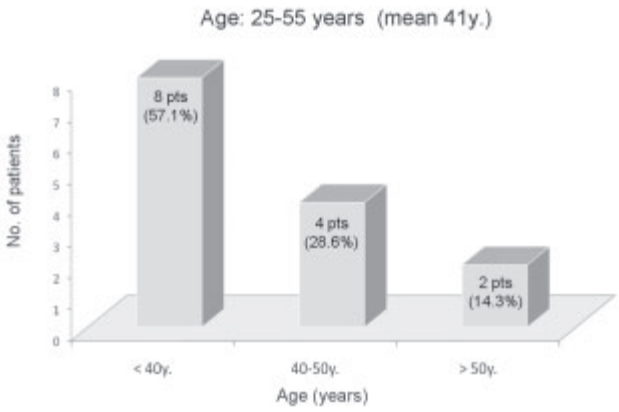

Fig. 1. Age of the patients.

complex cardiac defects with PAH (Tab. 1). Without any intervention were 11 pts (78.6 %), 1 patient had a palliation (pulmonary artery banding, BAP) at 10 months of age and 2 pts (14.3 %) had their defect previously surgically closed (1 patient had a VSD closure at 9 years and 1 pt had an ASD closure at 40 years of age) (Tab. 1). Thus no residual shunts were present, the latter pts developed moderate to severe PAH within 2–5 years after surgery.

Tab. 1. Type and quantification of shunts, surgical correction (ASD – atrial septal defect, PAPVD – partial anomalous pulmonary venous drainage, VSD – ventricular septal defect, AVSD – atrio-ventricular septal defect, TAC – common arterial truncus, PDA – persistent arterial duct, BAP – banding of the pulmonary artery).

Type of shunt	No. of pts	%
▪ pre-tricuspid (ASD / PAPVD)	4	28.6
▪ post-tricuspid	10	71.4
- VSD	6	
- AVSD	2	
- TAC	1	
- PDA	1	
Shunt	**No. of pts**	**%**
▪ simple	10	71.4
▪ multiple	1	7.1
▪ complex	3	21.5
Surgical correction	**No. of pts**	**%**
▪ no	11	78.6
▪ palliation (BAP)	1	7.1
▪ yes	2	14.3

Tab. 2. Medical history.

Anamnestic data	No. of pts	%
Breathlessness	12	85.7
Respiratory disorders (bronchitis, bronchial astma)	4	28.6
Thromboembolic complications	3	21.4
Bleeding / hemoptoe	3	21.4
Syncope / dizziness / headache	3	21.4
Fatigue / muscle pain	4	28.6
Hepatopathy / bile stones	4	28.6
Palpitations	5	35.7
Systemic hypertension	3	21.4
Chest pain	1	7.1
Other	3	21.4

Tab. 3. Clinical findings.

Clinical findings	No. of pts	%
Cyanosis	10	71.4
Clubbing	9	64.3
Heart murmur	13	92.9
Dyspnoea	12	85.7
Hepatomegaly / peripheral edema	6	42.9

Methods

Medical history, patients' present clinical status, laboratory findings and electrocardiogram (ECG), as well as echocardiographic and hemodynamic measurements and current therapy management of the pts were evaluated.

Medical history was obtained from patient's Health card and during a personal interview.

Echocardiography was performed by a single observer with GE Vivid 7 or Philips iE33 ultrasound system, both with digital data archive system. The studies were obtained from standard cardiac projections and all parameters were measured 3 times and the mean value was taken.

A dilated right ventricle (RV) was diagnosed when its diastolic diameter was >30 mm from the parasternal long axis view, or when the RV was larger than the left ventricle (LV) from the apical 4-chamber view, measured at 1/3 of the ventricles below the atrio-ventricular valves. The RV hypertrophy was diagnosed when the RV free wall diastolic diameter from parasternal long axis was >5 mm. RV systolic function was estimated with ejection fraction (EF%), calculated by the Simpson's method (end-diastolic volume (RVEDV) minus end-systolic volume (RVESV)) from the apical 4-chamber view. RV systolic dysfunction was diagnosed when RV EF was <40 %, mildly impaired function when EF was 30–40 %. RV diastolic function was evaluated using trans-tricuspid E/A and TDI E'/A' flow velocity ratios.

Hemodynamic data (pressures and oxygen saturations) were obtained from the right and left heart catheterization, and using standard calculations for pulmonary/systemic flows (Qp/Qs), pressure ratio (PAP/AoP), as well as pulmonary vascular resistance (PVR).

Results

– Medical history (Tab. 2) **and clinical findings** (Tab. 3)

Functional activity of the patients was following – 2 pts (14.3 %) were classified as NYHA II. class, 12 pts (85.7 %) as NYHA III. class.

The most frequent subjective complaint was breathlessness in 12 pts (85.7 %), worsening with exertion. Other respiratory

Tab. 4. Pathological laboratory findings.

Laboratory findings	No. of pts	%
O_2 saturation < 85%	7	50.0
< 80%	5	35.7
Polyglobulia	9	64.3
Hyperviscose syndrome	9	64.3
Sideropenia	4	28.6
Throbocytopenia	7	50.0
Elevated bilirubin and/or hepatal enzymes	10	71.4
Hyperuricemia	4	28.6
Proteinuria	2	14.3
Hypercholersterolemia	3	21.4
Other	5	35.7

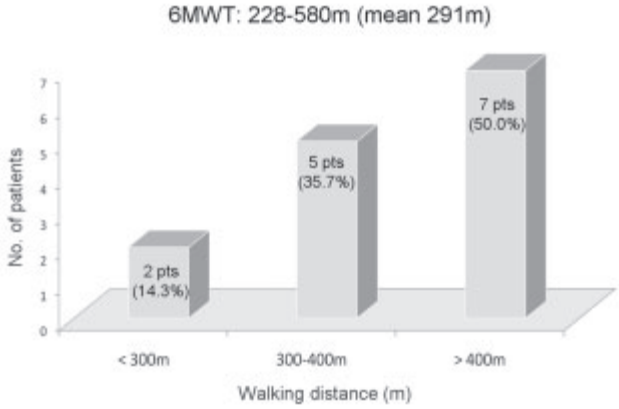

Fig. 2. 6 minute walking test (6MWT).

diseases (recurrent chronic bronchitis and asthma-like symptoms) were found in further 4 pts (28.6 %). Malfunction of the hemocoagulation system was found in 6 pts – thromboembolic complication (deep venous thrombosis and/or pulmonary thromboembolism) in 3 (21.4 %); on the contrary bleeding episodes were present in other 3 pts (21.4 %). Liver disorder or bilirubin metabolism disturbance with bile stones formation was present in 4 pts (28.4 %). Syncope, dizziness and/or headaches experienced 3 pts (21.4 %), complaining of fatigue and/or muscle pain were 4 pts (28.6 %), palpitations were present in 5 pts (35.7 %) and chest pain in 1 patient (7.1 %). Systemic hypertension was an additional diagnosis in 3 pts (21.4 %) Other disorders (kidney stones, thyreoid gland malfunction, oncological disease) were found in 3 pts (21.4 %).

Cyanosis as well as clubbing were present in 10 pts (71.4 %). 2 pts after defect closure and 2 pts with ASD were without cyanosis at rest and they did not develop clubbing either. Heart murmur was audible in 13 pts (92.9 %), mostly systolic 2/6, from tricuspid regurgitation. Dyspnoea at rest or with limited physical activity was present in 12 pts (85.7 %) and signs of right heart failure (hepatomegaly and/or peripheral edema) were present in 6 pts (42.9 %).

Tab. 5. Electrocardiographic (ECG) findings (RV – right ventricle, RBBB – right bundle brunch block, AF – Atrial flutter, SVT – supraventricular tachycardia, SVES – supraventricular extrasystoles, VES – ventricular extrasystoles).

ECG findings	No. of pts	%
RV hypertrophy	14	100.0
RBBB	9	64.3
Arrhythmia	8	57.1
- AF	2	
- SVT	5	
- SVES / VES	5	

– Laboratory findings (Tab. 4)

Oxygen (O_2) saturation was lower than 90% in 10 pts (71.4 %), lower than 85% in 7 pts (50 %) and lower than 80 % in 5 pts (35.7 %). Due to severe cyanosis, secondary polyglobulia and hyperviscose syndrome were present in 9 pts (64.3 %), thrombocytopenia in 7 pts (50 %) and sideropenia in 4 pts (28.6 %). Elevated levels of bilirubin and/or hepatal enzymes were found in 10 pts (71.4 %). Hyperuricemia was in 4 pts (28.6 %), hypercholesterolemia in 3 pts (21.4 %) and proteinuria in 2 pts (14.3 %). Additional other laboratory pathology was found in 5 pts (35.7 %).

– 6 minute walking test (6MWT)

Assessing patients' physical efficiency was done by 6 minute walking test; mean reached distance was 291m (ranged 228–580 m). Distance of more than 400m was achieved by 7 pts (50 %), 300–400 m by 5 pts (35.7 %) and <300 m by 2 pts (14.3 %) (Fig. 2).

– ECG (Tab. 5)

All 14 patients (100 %) showed signs of right ventricular hypertrophy, in 9 pts (64.3 %) a complete or incomplete right

Tab. 6a. Echocardiographic measurements 1 (RV – right ventricle, LAx – long axis projection, 4CH – four-chamber projection, RVAW – right ventricle anterior wall, EF – ejection fraction, E/A TV – transtricuspid diastolic flow, TDI – tissue doppler imaging).

Echocardiographic measurements /1.		
▪ RV dilatation (LAx: RV > 30 mm / 4CH: RV > LV)	No. of pts.	%
no	4	28.6
yes	10	71.4
▪ RV hypertrophy (RVAW > 5 mm)	No. of pts.	%
yes	14	100
▪ RV systolic dysfunction (EF < 40%)	No. of pts.	%
no	10	71.4
yes	4	28.6
▪ RV diastolic dysfunction (E/A TV / TDI)	No. of pts.	%
no	2	14.3
yes	12	85.7

Tab. 6b. Echocardiographic measurements 2 (TAPSE – tricuspid annulus excursion).

Echocardiographic measurements / 2.	
▪ RV anterior free wall diastolic diameter (RVAW)	
7-17 mm	(mean 11.5 mm)
▪ Tricuspid regurgitation peak gradient (TR)	
48-129 mmHg	(mean 101mmHg)
▪ RV ejection fraction (EF)	
30-69 %	(mean 49%)
▪ TAPSE	
12-26 mm	(mean 21 mm)

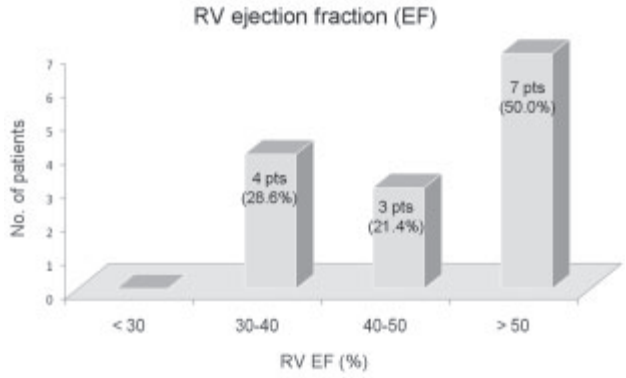

Fig. 3. Echocardiographic measurement of right ventricular ejection fraction (RV EF).

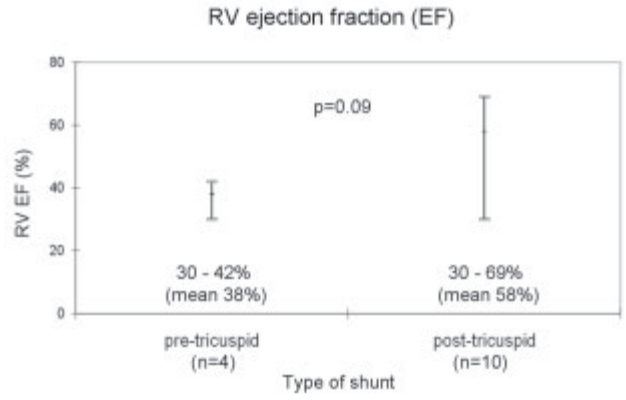

Fig. 4. Echocardiographic right ventricular ejection fraction (RV EF) according to type of shunt.

bundle brunch block were present. Arrhythmias were present in 8 pts (57.1 %) – in 2 pts intermittent or permanent atrial flutter, in 5 pts paroxysms of supraventricular tachycardia and in 5 pts supraventricular or ventricular extrasystoles.

– Echocardiographic measurements (Tab. 6a, 6b)

RV dilatation was present in 10 pts (71.4 %). RV hypertrophy was in all 14 (100 %) patients, with RV free wall (RVAW)

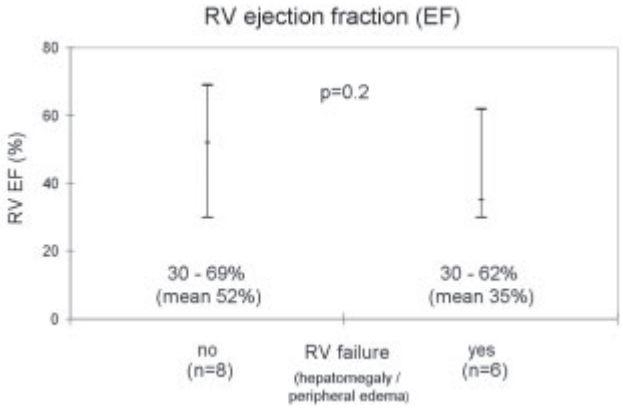

Fig. 5. Echocardiographic right ventricular ejection fraction (RV EF) according to clinical signs of right ventricular (RV) failure (hepatomegaly/peripheral edema).

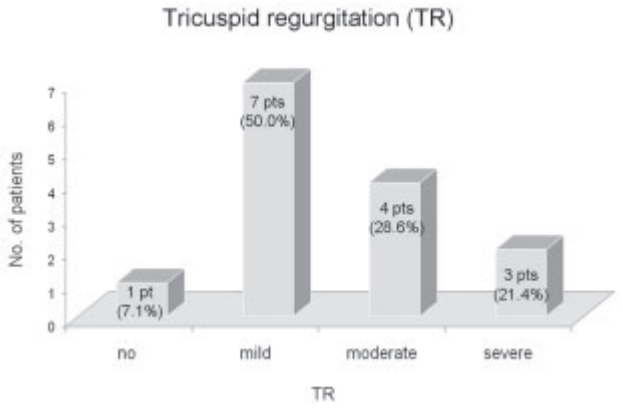

Fig. 6. Echocardiographic tricuspid regurgitation (TR).

diastolic diameter 7–17 mm (mean 11.5 mm). RV EF was 30–69 % (mean 49 %). Figure 3 shows number of pts according to RV EF. Good systolic RV function (EF >40 %) was in 10 pts (71.4 %) and the presence of decreased RV function (EF <40%) was found in 4 pts (28.6 %), though in all of them the RV function was only mildly decreased (EF 30–40 %). When evaluating RV function according to the type of shunt, there was a difference (although statistically not significant, p=0.09) between pts with pre-tricuspid and post-tricuspid type of shunting (Fig. 4). In pts with pre-tricuspid shunts the RV EF was 30–42 % (mean 38 %), when in 2 of 4 pts in this group the RV function was mildly impaired (EF 30–40 %) and in the other 2 pts the EF was just above 40 %. On the contrary, in pts with post-tricuspid shunts the RV EF was 30–69 % (mean 58 %), when only 2 of 10 pts had RV EF <40 %. Evaluating RV ejection fraction according to clinical signs of RV failure (hepatomegaly and /or peripheral edema) showed a difference, although statistically not significant (p=0.2). In pts with no signs of RV failure the RV EF was higher – 30–69 % (mean 52 %), compared to pts with signs of RV failure, where RV RF was 30–62 % (mean 35 %) (Fig. 5). Diastolic dysfunction type I. was present in 12 pts (85.7 %).

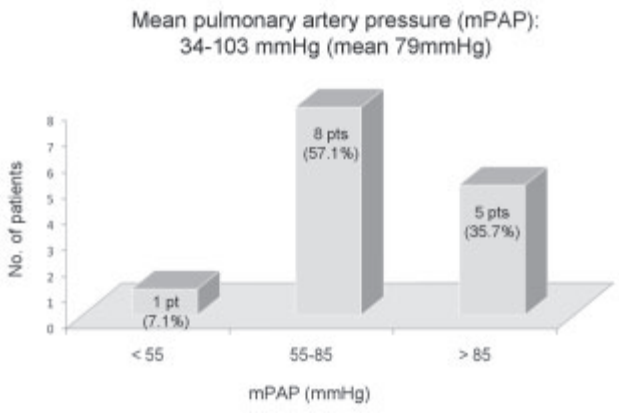

Fig. 7. Invasive measurement of mean pulmonary artery pressure (mPAP).

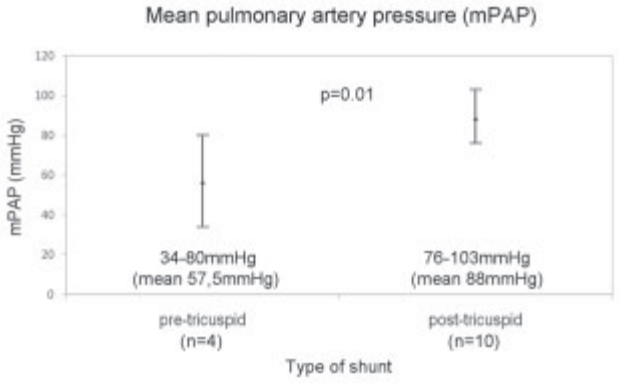

Fig. 8. Invasive measurement of mean pulmonary artery pressure (mPAP) according to the type of shunt (pre-tricuspid vs post-tricuspid).

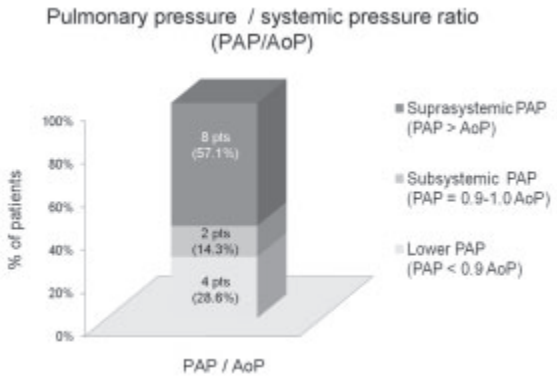

Fig. 9. Pulmonary-to-systemic pressure ratio (PAP — pulmonary artery pressure, AoP - systemic arterial pressure).

Without any tricuspid regurgitation (TR) was only one pt (7.1 %). Most common finding was mild TR – in 7 pts (50 %), in 4 pts (28.6 %) was moderate TR and 2 pts (14.3 %) severe TR (Fig. 6). Mean tricuspid regurgitation gradient was 101 mmHg (ranged 48–129 mmHg).

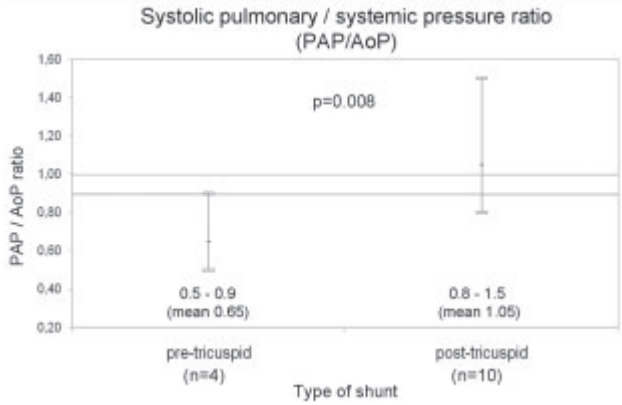

Fig. 10. Pulmonary-to-systemic pressure ratio according to the type of shunt (PAP – pulmonary artery pressure, AoP – systemic arterial pressure).

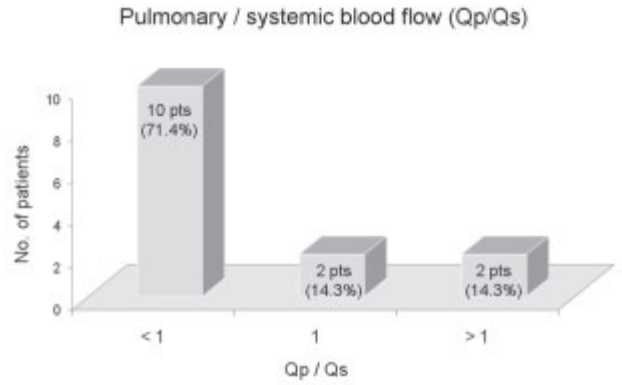

Fig. 11. Invasively measured pulmonary-to-systemic blood flow (Qp – pulmonary blood flow, Qs – systemic blood flow).

– Hemodynamic data

All pts had pre-capillary type of pulmonary hypertension with normal pulmonary wedge pressures. Mean pulmonary artery pressure (mPAP) was 34–103 mmHg (mean 79 mmHg), 5 pts (35.7 %) had mPAP >85 mmHg, 8 pts (57.1%) 55-85mmHg and only one pt had mPAP <55 mmHg (Fig. 7). A statistically significant difference (p=0.01) in mPAP was found between pre-tricuspid (34–80 mmHg, mean 57.5 mmHg) and post-tricuspid shunts (76–103 mmHg, mean 88 mmHg) (Fig. 8). Suprasystemic systolic pulmonary artery pressure (pulmonary/systemic pressure ratio (PAP/AoP) >1) was present in 8 pts (57.1 %), subsystemic pulmonary artery pressure (PAP/AoP between 0.9–1) was in 2 pts (14.3 %) and pulmonary artery pressure lower than systemic pressure in 4 pts (28.6 %) (Fig. 9). Comparing pre- and post-tricuspid shunts a significant difference (p=0.008) was found – the PAP/AoP ratio in pre-tricuspid shunts was 0.5–0.9 (mean 0.65), on the other hand in post-tricuspid shunts it was 0.8–1.5 (mean 1.05) (Fig. 10). Pulmonary/systemic flow ratio (Qp/Qs) <1 was calculated in 10 pts (71.4 %), Qp/Qs=1 was in 2 pts (14.3 %) and Qp/Qs >1 was in 2 pts (14.3 %) (Fig. 11). PVR >8 Wood

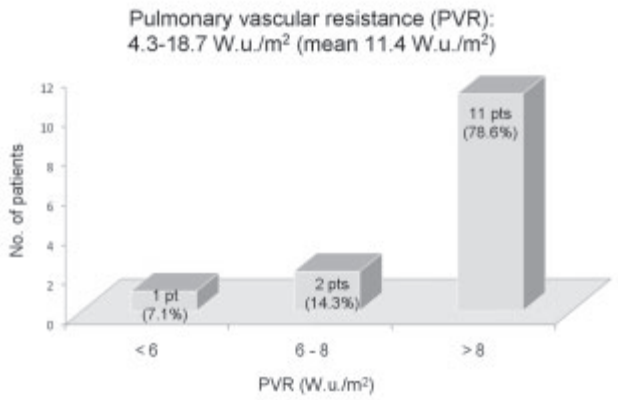

Fig. 12. Invasively measured pulmonary vascular resistance (PVR) (W.u./m² – Wood units per patient's body surface area).

units per m2 of patients' body surface area (W.u./m²) was calculated in 11 pts (78.6 %), 6–8 W.u./m² in 2 pts (14.3 %), and PVR <6 W.u./m² only in one pt (7.1 %) (Fig. 12).

– Therapy (Tab. 7)

All 14 patients (100 %) received anticoagulants, 4 pts (28.4 %) required cardiotonic and 7 pts (50 %) also diuretic therapy. Calcium channel blockers were used in 7 pts (50 %), intermittent iron substitution in 4 (28.4 %) sideropenic pts and long-term oxygen therapy in 2 pts (14.3 %). Medical antiarrhythmic therapy was required in 4 pts (28.6 %). Additional medicamentous therapy was needed in 11 pts (78.6 %).

Since 2006 at our institution specific treatment of PAH was included into therapy in 10 pts (71.4 %), all of them were at time of study evaluation on endothelin-receptor antagonists, in 2 pts (14.3 %) combined with phosphodiesterase-5 inhibitors (9, 10).

Discussion

Patients with Eisenmenger syndrome were mostly in the NYHA class III (85.7 %), less frequently in NYHA II (14.3 %).

Tab. 7. Therapy (PAH – pulmonary arterial hypertension).

Therapy	No. of pts	%
Cardiotonics	4	28.6
Diuretics	7	50
Calcium channel blockers	7	50
Iron substitution	4	28.6
Oxygen therapy	2	14.3
Antiarrhythmics	4	28.6
Other	11	78.6
Specific threatment of PAH	10	71.3
- Endothelin-receptor antagonists	10	
- Phosphodiesterase inhibitors (combination th.)	2	

None of them were in NYHA IV; but none of them were in NYHA class I either, although the majority (57.1 %) were younger than 40 years of age. Evaluating 6MWT showed relatively good exercise tolerance compared to other forms of PAH (1, 4, 5) – as 50 % of patients were able to achieve a distance >400 m, 35.7 % walked between 300–400 m and only 14.3 % achieved <300 m. On the other hand, none of the patients were asymptomatic, with the most frequent subjective complaint – breathlessness – present in 85.7 %. Also signs of at least mild to moderate RV failure (hepatomegaly and/or peripheral edema) were present in 42.9 % of patients.

Cyanosis with systemic O_2 desaturation (<90 %) was present in 71.4 % of patients; above all in 50 % of patients the O_2 saturation was less then 85 % and in 35.7 % even less then 80 %. Severe systemic desaturation leads to many clinical complications and laboratory changes. In alignment with other studies (5, 7, 8, 13) secondary erythrocytosis and hyperviscose syndrome was found in 2/3 of our patients (64.3 %) and sideropenic were about 1/3 (28.6 %) of them. Low iron levels were found as a compensatory mechanism in patients with cyanosis and erythrocytosis (7, 8), its frequency is increasing with age, and usually can be drawn back to repeated phlebotomies. Nevertheless, serious non-cardiac complications resulting from cyanosis suffered as many as 42.8 % of our Eisenmenger patients – 21.4 % had thromboembolic complications and 21.4 % serious bleeding events. In studies (3, 8, 14, 15), these types of complications are reported in 11–100 % of patients. Arrhytmias, particularly supraventricular, are very common like in our study group (in almost 60 %), are usually poorly tolerated and cause important morbidity and mortality (1, 7, 16).

Despite high (even suprasystemic) pulmonary arterial pressure in patients with Eisenmenger syndrome, their RV function is usually better compared to patients with other forms of PAH.

The anatomy and the function of the RV are crucial for the survival and relative well-being of Eisenmenger patients (5, 6, 8). All of our patients presented with RV hypertrophy (with mean wall thickness 11.5 mm). Good RV ejection function (EF >40 %) was found in 71.4 % of patients, and only mildly decreased RV function (EF 30–40 %) in the rest of them. As previously reported there is a difference in RV picture between pre- and post-tricuspid type of defects (5, 6). Although not statistically significant, RV EF in patients with pre-tricuspid shunts was worse (mean EF 38 %) compared to patients with post-tricuspid shunts (mean EF 58 %), as well the RV EF showed worse in patients with clinical sings of RV failure (mean EF 35 %) then in those without hepatomegaly and/or peripheral edema (mean EF 52 %). Mild tricuspid regurgitation was present in 50 % of patients, but on the other hand only 14.3 % had severe tricuspid regurgitation. Diastolic dysfunction type I as a result of RV hypertrophy was present in 85.7 % of patients.

Invasive hemodynamic data showed pre-capillary pulmonary hypertension with the mean value of mPAP 79 mmHg. There was a statistically significant difference of pulmonary artery pressures according to the site of defect (mean mPAP 57.5 mmHg in pre-tricuspid defects and 88mmHg in post-tricuspid defects) and

from another point of view – in pre-tricuspid defects the pulmonary artery pressure was about 2/3 of systemic pressure (mean PAP/AoP ratio = 0.65), whereas in post-tricuspid defects it was slightly suprasystemic (mean PAP/AoP ratio = 1.05). This may show the ability of RV to tolerate much higher pressures in a post-tricuspid type of defect, either due to the "fetal picture" of the ventricle with more prominent RV hypertrophy or perhaps due to a more effective ventricular interdependence.

Study limitation

Despite the success of the last years in pediatric cardiology diagnosis and surgical strategies with a decreasing number of new Eisenmenger patients, there is still a group of them from past decades. Due to the irreversibility of their PAH changes and due to no real possibility to provide them with any sufficient treatment options, for a long time patients with Eisenmenger syndrome were considered as "not interesting". As in our country no registry of Eisenmenger patients is available, so it is difficult to evaluate those who are asymptomatic or with low level of symptoms and are tolerating their symptoms well. This showed also to be the crucial study limitation, as to our institution were referred only patients with complications and/or with progressive subjective deterioration. On the other hand, interestingly no patients in the NYHA IV class were present in our cohort. It may show that once patients develop severe symptoms, PAH has a fast and progressive course, or that they die suddenly of non-cardiac complications in lower NYHA classes.

Conclusion

Patients with Eisenmenger syndrome represent a complicated group of PAH patients with the ultimate necessity to understant their anatomy and physiology. Despite severe PAH (with even suprasystemic pulmonary pressures), these patients often show a relatively good clinical status and exercise tolerance for a long time. A preserved good RV function (having a "pop-off valve" to the systemic circulation and ventricular interdependence) and its chronic adaptation for functioning in high pressure system (RV hypertrophy) is crucial.

On the other hand, due to cyanosis and body maladaptations resulting from cyanosis, Eisenmenger syndrome has to be considered a multi-systemic disease and all possible complications need to be expected. When these complications are misunderstood or not properly managed, any stress situation (even a simple disease or a surgery) may be fatal. It is neccessary to keep in mind that in patients with Eisenmenger syndrom these non-cardiac events and complications may lead to death sooner then heart (right ventricular) dysfunction or pulmonary hypertension.

References

1. Oechslin E. Eisenmengers syndrome. 363—377. In: Gatzoulis MA, Webb GD, Daubeney PEF. Diagnosis and management of adult congenital heart disease. London; Churchill Livingstone 2003.

2. Galic N. Classification of patients with congenital systemic-to-pulmonary shunt associated with pulmonary arterial hypertension: Current status and future directions. 11—17. In: Beghetti M, Barst RJ, Naeije R, Rubin LJ. Pulmonary arterial hypertension related to congenital heart disease. Munich; Elsevier GmbH, Urban & Fischer Verlag 2006.

3. Diller G-P, Gatzoulis MA. Pulmonary vascular disease in adults with congenital heart disease. Circulation 2007; 115: 1039—1050.

4. Galic N, Torbicki A, Barst R et al. ESC Guidelines — Guidelines on diagnosis and treatment of pulmonary arterial hypertension. Eur Heart J 2004; 25: 2243—2278.

5. Diller G-P, Dimopoulos K, Kafka H et al. Model of chronic adaptation: right ventricular function in Eisenmenger syndrome. Eur Heart J Supplements 2007; 9 (Suppl H): H54—60.

6. Hopkins WE. The remarkable right ventricle in patients with Eisenmenger syndrome. Coronary Artery Dis 2005; 16: 16—25.

7. Somerville J. How to manage the Eisenmenger syndrome. Int J Cardiol 1998; 63: 1—8.

8. Krishna R, Kumar RK, Sandoval J. Advanced pulmonary vascular disease: the Eisenmenger syndrome. Cardiol Young 2009; 19 (E-Suppl 1): 39—44.

9. Kaldararova M. Why is pulmonary hypertension still so frustrating? Bratisl Lek Listy 2009; 110 (9): 536—543.

10. Simkova I, Pacak J, Vulev I et al. Initial experiences with novel therapy for pulmonary hypertension in Slovakia. Bratisl Lek Listy 2006; 107: 239—247.

11. Jansa P, Aschermann M, Riedel et al. Recommendations for diagnosis and treatment of pulmonary arterial hypertension in Czech Republic. Cor et Vasa 2004; 46: K35—K44.

12. Jansa P, Ambroz D, Maresova J et al. Pulmonary arterial hypertension – Contemporary management strategy. Bratisl Lek Listy 2009; 110 (10): 603—608.

13. Diller G-P, Dimopoulos K, Broberg CS et al. Presentation, survival prospects, and predictors of death in Eisenmenger syndrome: a combined retrospective and case-control study. Eur Heart J 2006; 27: 1737—1742.

14. Daliento L, Somerville J, Presbitero P et al. Eisenmenger syndrome. Factors relating to deterioration and death. Eur Heart J 1998; 19: 1845—1855.

15. Beghetti M, Galic N. Eisenmenger syndrome. A clinical perspective in a new therapeutic era of pulmonary arterial hypertension. J Amer Coll Cardiol 2009; 53: 733—740.

16. Kaldararova M, Balazova E, Bordacova L et al. Arrhythmias in congenital heart defects. Bratisl Lek Listy 2007; 108: 14—19.

Received June 28, 2009.
Accepted September 20, 2009.