METHODS

Transposition of Great Vessels with Interventricular Septal Defect and High Pulmonary Hypertension. Hemodynamics and Results of Correction

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Transposition of great vessels (TGV) is a complex congenital heart defect occurring in 7-8% of cases [7]. Fifty-five percent of patients reach the age of one month, 15% of these survive to six months, and only 10% reach the age of one year when the disease progresses naturally. Pulmonary hypertension is one of the complications which greatly affects patient survival. Children more than one year old with even simple TGV have been reported to have pulmonary hypertension in 47% of cases [5,13]. Twenty-five percent of patients with concomitant interventricular septal defect (ISD) develop changes in the lungs and blood vessels by six months which exceed stage III according to the Heath-Edwards (H-E) classification, and these changes are found in 80% of patients more than one year of age. In this case pulmonary hypertension may still progress despite the correction of the defect. The progression rate and severity of pulmonary hypertension are more pronounced with TGV+ISD than in isolated ISD. Besides blood shunt and increased pulmonary blood flow, which are typical for isolated ISD, the following factors play an essential role in TGV: 1) increased bronchial blood flow and low blood oxygenation; 2) disturbances in the blood coagulation system; 3) repeated microembolization of arterioles of the pulmonary circulation with thrombi forming against the background of a high hematocrit [2]; 4) a damaging effect of increased blood viscosity on the vascular wall. These events lead to accelerated intimal proliferation of pulmonary vessels at the level of preacinar arteries, and by 5-6 months cause an occlusion of the lumen with a subsequent increase in pulmonary resistance (PR) [8]. Normal evolution of the vascular wall with the reduction of fetal hypertrophy of the media may occur distal to the occlusion as a result of a sharp drop in the blood flow. This is regarded as a distinctive feature of pulmonary and vascular changes during TGV, which necessitates harvesting of the largest possible piece of lung with preacinar vessels to avoid erroneous results [8]. Biopsy has to be taken from the right lung, since the blood flow tends to pass through the right pulmonary artery in this defect.

It is extremely difficult to evaluate the degree of pulmonary and vascular hemodynamics during heart catheterization. High blood oxygenation in the pulmonary artery does not allow for full use of the method of Fick to estimate pulmonary blood flow due to a low arteriovenous difference. The increased bronchial blood flow and high hematocrit [12] also lead to errors in the estimation of pulmonary blood flow. Along with this, some workers have concluded from their personal experience that the PR param-

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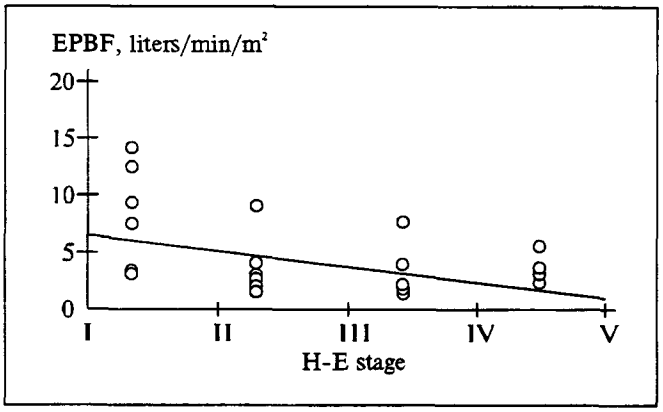

Fig. 1. Correlative dependence between the H–E stage and EPBF in the whole group.

eter provides the most complete information for assesssing the degree of pulmonary hypertension. According to Bush *et al.* [3], correction of the defect is not indicated if PR exceeds 6.5 units/m². Such resistance may produce either H-E stage III or higher or, stage I-II with pronounced medial hypertrophy and a marked constriction of the arterial lumen. In both cases the result will be unsatisfactory. Stark and Clarkson also consider the PR parameter when deciding on possible correction of the defect. The first believes in a successful outcome of the operation if PR does not exceed 10 units/m²; the second considers a PR of 10 units/m² to be the limit and draws a line at the age of six months for the operation. Mahony *et al.* [11] guide themselves exclusively by the age of the patient, believing that a successful outcome is possible only during the first 100 days of life. If the operation is performed at a later age, even though high pulmonary hypertension may not be initially observed, it may develop in 10% of cases at later periods [13]. It has been noted that the absence or insignificant effect of balloon atrioseptotomy indicates the presence of high pulmonary hypertension with vascular changes typical for H-E stage II or III [10].

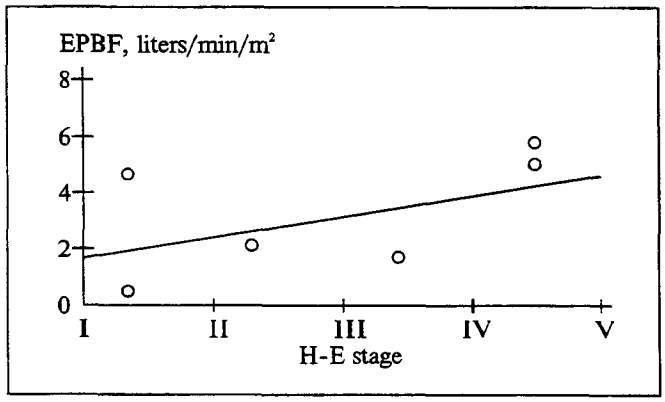

Fig. 2. Correlative dependence between the H–E stage and ESBF in patients with intact interatrial septum.

Hospital lethality during TGV+ISD may reach 23% [1,6,14-16], the major cause being high pulmonary hypertension. Taking into consideration this fact and the difficulty of evaluating accurately the degree of pulmonary and vascular changes, Lindesmith *et al.* were the first to introduce and perform in 1972 a palliative operation using the Mustard procedure. The operation involved hemodynamic correction of both blood flows without blocking ISD. Kirklin *et al.* [9] recommend either palliative operations after Mustard or transfer of the great vessels in all patients with PR of more than 10 units/m². Such an operation may be accompanied by a decrease in pulmonary artery pressure at later periods, which in some cases will allow a radical correction of the defect to be performed at the second step [9]. Hospital lethality during this operation is reported to be low and is not even mentioned in many studies [4], allowing us to introduce the concept of two-stage correction of TGV+ISD with high pulmonary hypertension.

The Research Center for Cardiovascular Surgery (RCCS) has a broad experience in the surgical correction of TGV+ISD. However, there are still no clear-cut criteria for correction of the defect in the case of high pulmonary hypertension. The present study aimed to develop such criteria.

MATERIALS AND METHODS

Forty-six patients diagnosed with TGV+ISD and high pulmonary hypertension were under treatment at RCCS from 1986 to April 1994. Forty of them had atrial septal defect. Their age varied from 2 to 57 months (15 months on average). Clinical examination involved heart catheterization and angiocardiography. The following hemodynamic parameters were estimated during catheterization: degree of pulmonary hypertension, mean pressure in the pulmonary artery, PR, PR ratio to the general peripheral resistance, arteriovenous difference between the pulmonary and systemic circulation, pulmonary blood flow, arteriovenous and venous-arterial blood shunt; blood oxygenation in pulmonary artery aorta and left atrium. The degree of atrial septal defect was documented by echocardiography. An open biopsy of the lung was performed in 36 patients to evaluate the severity of pulmonary hypertension. Morphological changes were assessed by autopsy data in six patients. The stage of morphological changes was evaluated according to the H-E system in the course of bioptate analysis. Radical or hemodynamic correction was performed in 31 patients: in 25 patients using the Mustard procedure, in three patients us-

ing the Sening procedure, and in three patients by transfer of great vessels. A palliative operation after Mustard was performed in six patients.

RESULTS

Six patients died of high pulmonary hypertension during hemodynamic and radical correction (19%). Three out of six patients died of pulmonary hypertension (50%) after the palliative Mustard procedure. Hemodynamic parameters in the whole group were as follows: pulmonary hypertension was 85±19%; mean pressure in the pulmonary artery was 50±14 mm Hg; PR was 8±5 units/m^2; pulmonary blood flow was 7.6±4.2 liters/min/m^2; efficient systemic blood flow (ESBF) was 4.3±2.9 liters/min/m^2; efficient pulmonary blood flow (EPBF) was 4.7±3.2 liters/min/m^2; blood oxygenation was: in the aorta 61±13%, in the pulmonary artery 87±6%, in the left atrium 88±9%. Analysis of pulmonary biopsy revealed stage I-II in 13 patients, stage II-III in 14 patients, stage III-IV in eight patients, and stage IV-V in five patients. Correlation analysis of hemodynamic parameters and lung morphology data demonstrated a high relationship between the severity of cardiovascular changes according to the H-E system and the patients' age (r=0.694), as well as the degree of EPBF and ESBF (r=-0.654 and r=0.568, respectively, Fig. 1). Furthermore, the EPBF value correlated with the value of pulmonary blood flow (r=0.617) and PR (r=-0.595). The degree of blood oxygenation in the aorta was found to be dependent on the degree of atrial septal defect (r=0.870). These results suggest that PR and EPBF decrease (shunt from the right to the left ventricle) and ESBF increases (shunt from the left to the right ventricle) as the pulmonary and vascular changes progress.

Hemodynamics and pulmonary and vascular changes according to the H-E system were assessed by comparative analysis. Table 1 shows that EPBF of less than 4 liters/min/m^2 most probably corresponds to pulmonary and vascular changes of stage III-IV or IV-V. If PR is more than 10 units/m^2,

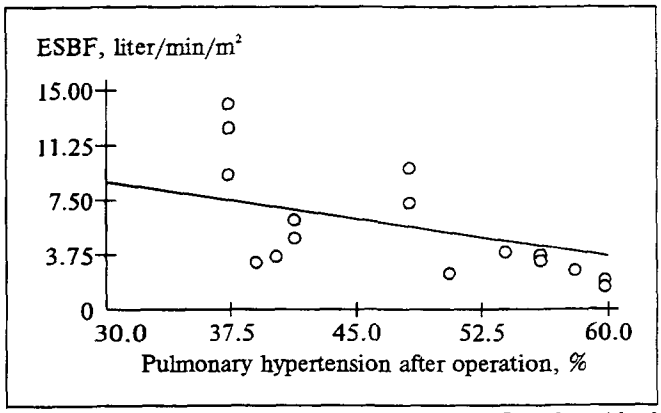

Fig. 3. Correlative dependence between EPBF and residual pulmonary hypertension after correction of congenital heart defect.

it is safe to speak about stage IV-V. Significant differences in patients' ages at different stages provide an important additional factor for the evaluation of pulmonary hypertension. Patients more than one year old were more likely to develop severe and irreversible pulmonary and vascular changes. There were no significant differences in ESBF during the various morphological stages. Along with this, ESBF appeared to increase as the severity of vascular changes increased. EPBF exceeded ESBF at stages I-II and II-III, whereas the latter prevailed at stages III-IV and IV-V.

Six patients with intact interatrial septum were used for subsequent analysis. In this group the anatomy of the defect itself excludes high blood oxygenation in the systemic ventricle due to blood bypass at the atrial level. The distinctive feature of the group was a 100% pulmonary hypertension in all patients, including three patients under nine months and one patient under four months. The ESBF parameter was dependent on the mean pressure in the pulmonary artery (r=0.877) and on the H-E stage (r=0.570) (Fig. 2). The findings demonstrated that ESBF increased with the severity of pulmonary and vascular changes and with an increase in PR.

Correlation analysis of the group of patients who had undergone correction of the defect combined with ISD plastic surgery demonstrated a de-

Table 1. Age and Hemodynamics at Various H–E Stages (n=46, $M\pm m$)

Index	H-E stage:			
	I-II	II-III	III-IV	IV-V
Age, months	6±3*	11±7*	22±15*	33±17
ESBF, liters/min/m^2	2.4±1.6	3.8±2.2	4.8±3.6	7.0±2.9
EPBF, liters/min/m^2	8.1±2.1*	4.5±2.0*	3.0±1.7*	2.4±1.7
PR, units/m^2	8±5	7±3	9±3*	14±4

Note. * p<0.05. Here and in Table 2: n = number of patients.

Table 2. Hemodynamics in Groups of Surviving and Deceased Patients ($n=32$, $M\pm m$)

Hemodynamics	Surviving patients (n=26)	Deceased patients (n=6)
EPBF, liters/min/m^2	7.0±3.4	2.6±0.9
ESBF, liters/min/m^2	3.0±2.0	6.5±3.0
Blood oxygenation in left atrium, %	91±4	85±5
Pulmonary hypertension postoperation, %	49±11	67±10

Note. All indexes are significant.

pendence between the value of residual pulmonary hypertension postoperation and baseline parameters of EPBF and ESBF (r=-0.546 and r=0.591, respectively). Postoperative pressure remained high with little EPBF and increased ESBF (Fig. 3). Among the patients who survived the operation twelve were at stage I-II, nine at stage II-III, and two at stage III-IV. Among the deceased patients stage II-III was observed in three and stage III-IV in three. Comparative hemodynamics of the two groups revealed significant differences in some parameters (Table 2).

The findings suggest that patients at stages II-III and III-IV are likely to have a high residual pulmonary hypertension if EPBF decreases to less than 3 liters/min/m^2 and ESBF increases to more than 3 liters/min/m^2. Residual pulmonary hypertension is more than 60% in all cases and may cause death in the early postoperative period. The decreased blood oxygenation in the left atrium of the deceased patients was probably associated with the abundant bronchial blood flow, which compensated for the increase in ESBF during serious sclerotic changes in pulmonary vessels. This allowed the speculation that the operability of such patients is doubtful if blood oxygenation in the left atrium decreases by more than 85%.

The six patients who had undergone the palliative operation after Mustard showed the following hemodynamics: pulmonary hypertension was 98±4%; PR was 12±4 units/m^2, and EPBF was 3.4±1.7 liters/min/m^2, and ESBF was 5.2±1.6 liter/min/m^2; blood oxygenation was: in the aorta 58±14%, and in the pulmonary artery 87±4%. Open biopsy of the lung revealed stage II-III in two patients and stage IV-V in three patients. The three patients with stage IV-V died soon after the operation. Pressure of the venous ventricle decreased to 60-70% of the systemic value in the two patients with stage II-III. We are planning to close ISD in these patients at the second step of the operation.

The findings suggest the following conclusions:

1. EPBF is found to prevail with low pulmonary hypertension. Development of a 100% pulmonary hypertension with pronounced vascular sclerosis of the lungs changes the direction of blood shunt via ISD, while ESBF is increased.

2. The severity of pulmonary and vascular changes depends on blood flow parameters and patient age. If ESBF dominates over EPBF in a child older than one year, pulmonary and vascular changes are likely to exceed stage III.

3. The degree of hypoxemia mainly depends on the degree of atrial septal defect.

4. The decrease in blood oxygenation in the left atrium is probably linked with the elevated bronchial blood flow with growing severity of pulmonary and vascular changes and prevalence of ESBF.

5. An EPBF of more than 7 liters/min/m^2, an ESBF of not more than 3 liters/min/m^2, and a patient age of less than twelve months can be regarded as criteria for successful surgical intervention.

6. Patients whose hemodynamics do not fall within these criteria should undergo an open biopsy of the lung. A palliative operation after Mustard is indicated if there are changes typical for stage III-IV.

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