Detection of Transposition of the Great Arteries in Fetuses Reduces Neonatal Morbidity and Mortality

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Background—Transposition of the great arteries (TGA) is a life-threatening malformation in neonates, but it is amenable to complete repair. Prenatal detection, diagnosis, and early management may modify neonatal mortality and mortality.

Methods and Results—Preoperative and postoperative morbidity and mortality were compared in 68 neonates with prenatal diagnosis and in 250 neonates with a postnatal diagnosis of TGA over a period of 10 years. The delay between birth and admission was 2±2.8 hours in the prenatal group and 73±210 hours in the neonatal group (P<0.01). Clinical condition at arrival, including metabolic acidosis and multiorgan failure, was worse in the neonatal group (P<0.01). Once in the pediatric cardiology unit, the management was identical in the 2 groups (atrioseptostomy, PGE, infusion, operation date). Preoperative mortality was 15 of 250 (6%; 95% CI, 3% to 9%) in the neonatal group and 0 of 68 in the prenatal group (P<0.05). Postoperative mortality was not different (25 of 235 versus 6 of 68), but hospital stay was longer in the neonatal group (30±17 versus 24±11 days, P<0.01). In addition, postoperative mortality was significantly higher in the neonatal group (20 of 235 versus 0 of 68, P<0.01); however, the known risk factors for operative mortality were identical in the 2 groups.

Conclusions—Prenatal diagnosis reduces mortality and morbidity in TGA. Prenatal detection of this cardiac defect must be increased to improve early neonatal management. In utero transfer of fetuses with prenatal diagnosis of TGA in an appropriate unit is mandatory. (Circulation. 1999;99:916-918.)

Key Words: heart defects, congenital ■ transposition of great vessels ■ pediatrics ■ echocardiography

Progress has been made in fetal cardiac screening both by first-line sonographers and by the development of targeted education programs in various countries. However, whether and to what extent fetal cardiac screening modifies neonatal prognosis remains unknown. It is of note that the impact of routine screening for congenital heart diseases in reported series appeared to be small. In addition, in well-defined birth populations, survival of infants who were diagnosed as having congenital heart disease in utero was not improved. Transposition of the great arteries (TGA), however, is a very peculiar congenital heart defect in which the dramatic changes that occur after birth may lead to rapid hemodynamic compromise and death. Immediate balloon atrial septostomy and prostaglandin infusion are frequently life-saving. Therefore, we sought to determine whether prenatal detection of TGA reduced neonatal morbidity and mortality.

Methods

Population
Two hundred fifty consecutive newborn infants with postnatal diagnosis of TGA (neonatal group) were compared with 68 consecutive newborn infants in whom the diagnosis of TGA was made during the fetal life (prenatal group). These simultaneous series were collected over a period of 10 years (1988 to 1997).

Two hundred sixty-one patients had an isolated TGA, 204 of 250 (81.6%) in the neonatal group and 57 of 68 (83.8%) in the prenatal group (P<0.05). In addition, patients with TGA and ventricular septal defect and/or coarctation of the aorta were also included, because early management of these patients is identical to the management of isolated TGA. The distributions of associated anomalies were not different in the 2 groups (see the Table).

Patients who had an anatomic contraindication for an arterial switch repair were excluded, namely TGA with subpulmonic stenosis, univentricular heart or multiple ventricular septal defect with TGA, and straddling of the mitral valve. Infants with extracardiac malformations were also excluded. Patients with a postnatal diagnosis of TGA referred from abroad or from a pediatric unit outside our sanitary area were excluded as well. Patients with a prenatal diagnosis of TGA were always born in an obstetric unit <10 minutes distant from our institution.

Prenatal diagnosis was performed between 18 and 34 weeks of gestation (mean, 26.5±7 weeks). The cardiac malformation was suspected by the first-line ultrasonographers at routine obstetric scanning. These ultrasonographers were trained to routinely screen fetuses for great-vessel anomalies. Detailed fetal echocardiography was performed by 2 of us (L.F., J.L.) with an Acuson XP128.

Postnatal Evaluation
Preoperative evaluation included age at arrival in our pediatric intensive care unit, hemodynamic condition (mechanical ventilation, metabolic

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Comparison of Characteristics of Patients in the Prenatal and Postnatal Groups

|                                | Postnatal Group | Prenatal Group | P  
|--------------------------------|-----------------|----------------|-----
| Isolated TGA                   | 204             | 57             | NS  
| Associated defects             | 46              | 11             | NS  
| VSD                            | 31              | 8              | NS  
| VSD+CoA                        | 14              | 3              | NS  
| CoA                            | 1               | 1              | NS  
| Age at admission, h            | 73±210          | 2.2±2.8        | <0.01 
| Mechanical ventilation         | 95 (38)         | 12 (17.6)      | <0.01 
| Metabolic acidosis±MOF         | 56 (8)          | <0.05          |     
| PGE, infusion                  | 95              | 32             | NS  
| BAS                            | 168             | 54             | NS  
| Preoperative mortality         | 15              | 0              | <0.05 
| Coronary artery pattern        | 233 ASO         | 68 ASO         |     
| Normal                         | 168             | 47             | NS  
| Abnormal                       | 65              | 21             | NS  
| Postoperative mortality        | 20              | 0              | <0.01 
| Hospital stay, d               | 30±17           | 24±11          | <0.01 

VSD indicates ventricular septal defect; CoA, coarctation; MOF, multiorgan failure; PGE, prostaglandin E1; BAS, balloon atrioseptostomy; and ASO, arterial switch operation. Values are n (%).

Results

Age at admission in our Pediatric Cardiology Unit was 2.2±2.8 hours (95% CI, 1.4 to 2.9 hours) in the prenatal group versus 73±210 hours (95% CI, 46 to 100 hours) in the neonatal group (P<0.01). Mechanical ventilation was more frequently required in the neonatal group (95 of 250 [38%] versus 12 of 68 [17.6%], P<0.01). Metabolic acidosis (pH<7.10) as well as multiorgan failure or neurological distress was significantly more frequent in the neonatal group (P=0.02). It is of note that in the prenatal group, 8 of 68 patients (12%) suffered acute hemodynamic distress within the first few minutes after birth. Five of 8 of these latter had to undergo a balloon atrioseptostomy in the delivery room. The absence of prenatal diagnosis was the only risk factor for hemodynamic compromise at admission (odds ratio, 4.1; 95% CI, 1.2 to 13.5). There was no difference in oxygen saturation or need for prostaglandin E1 infusion at admission. Once in the pediatric cardiology intensive care unit, the management of the patients of the 2 groups was not different with regard to balloon atrioseptostomy, prostaglandin E1 infusion, or delay between admission and surgery.

Preoperative mortality was 0 of 68 in the prenatal group versus 15 of 250 (6%; 95% CI, 3% to 9%) in the neonatal group (P<0.05). Eight infants born in our usual referring obstetric units died within 1 hour and 2 days after birth; the diagnosis of TGA was made at necropsy. These patients were identified by screening of the autopsy reports of the 3 major fetopathology units of the Paris area collected during the same period. Seven died within a few hours after admission with multiorgan failure. Fourteen of 15 deceased newborns had isolated TGA, and 1 had a TGA with ventricular septal defect and coarctation of the aorta. Age at admission (29±12 hours) was not different in the patients who died compared with the survivors.

All patients underwent an arterial switch operation with associated closure of the ventricular septal defect and/or coarctation repair when needed (mean age, 7±6 days). Four patients in the neonatal group underwent a Senning operation because of delayed diagnosis in 2 and severe preoperative complications contraindicating anatomic correction during the neonatal period in the other 2.

Postoperative mortality was significantly higher in the neonatal group (20 of 235, 8.5%; 95% CI, 4.9% to 12%) than in the prenatal group (0 of 68, P=0.01). The presence of associated lesions, the coronary artery distribution, perioperative coronary events, and postoperative nonspecific complications (infection, mechanical ventilation duration) were not different in the 2 groups. Postoperative mortality was randomly distributed throughout the study period, whereas the prevalence of prenatal diagnosis increased during the same period. Therefore, increased mortality in the postnatal group could not be attributed to a surgical learning curve. Multiple logistic regression of risk factors for postoperative mortality could not be performed because there was no death in the prenatal group. Finally, hospital stay in the neonatal group was longer (30±17 days versus 24±11 days, P<0.01).

Data are summarized in the Table.

Discussion

Routine fetal ultrasound screening for congenital heart diseases has been increasingly applied in developed countries.6,7 Controversies have emerged about the impact of prenatal diagnosis on the prevalence of congenital anomalies at birth in well-defined populations.8,9 In addition, the advantages of prenatal detection of cardiac anomalies in low-risk populations have not been clearly demonstrated.3 However, when specific congenital heart defects are detected, diagnosis in the fetus may have dramatic consequences. Allan et al10 demonstrated that the birth prevalence of hypoplastic left heart syndrome was reduced concurrently with an increased prenatal detection. Undoubtedly, many factors influence the outcome of fetuses with heart disease diagnosed in utero. Appropriate counseling is often biased in the current practice of prenatal diagnosis. Apart from ethical considerations about abortion, extracardiac malformations and chromosomal anomalies frequently result in termination of the pregnancy.11 The major concern after the diagnosis of an isolated congenital heart disease in utero is to inform the parents about the outcome after birth. A recent series demonstrated that prenatal diagnosis improved survival of newborn infants amenable to biventricular repair, whereas the prognosis of infants with univentricular heart was not influenced.12 Even these
encouraging results have to be interpreted with caution, because the outcome of congenital heart defects taken as a whole is meaningless.

For these reasons, we set out to assess the potential advantages of prenatal detection of TGA. The arguments for choosing this peculiar malformation were the following: no pregnancy termination in this defect in our practice, low prevalence of extracardiac malformations and chromosomal anomalies likely to modify postnatal outcome, severe malformation requiring intervention early in the neonatal period, potential influence of prenatal detection on neonatal care and planning of the birth conditions, and anatomic correction with low mortality in our institution. The diagnosis of TGA was always suspected by first-line fetal ultrasound screening in referring centers in which sonographers have been educated to use the standard 4-chamber view and the great-vessel view. Multidisciplinary counseling was always given after the diagnosis in the fetus (pediatric cardiologists [at least 2 interviews], neonatologist, obstetrician, and cardiac surgeon). We demonstrated in the present study that prenatal detection reduced the preoperative mortality of the neonates with TGA. Accordingly, since 1997, no fetus with TGA is delivered outside our institution, because a balloon atrioseptostomy might be required in the few minutes after birth. Indeed, even when a prenatal diagnosis was performed, urgent balloon atrioseptostomy was mandatory in 12% of our patients.

A common experience was recently reported describing early inadequate interatrial mixing as a major cause of preoperative attrition in neonates with D-transposition despite anatomy suitable for arterial switch operation. Predictive anatomic or hemodynamic factors for such a postdelivery course have not yet been evaluated. Improvement of postnatal care and even modifications of delivery conditions could follow from fetal assessment of the foramen ovale size or restrictive function in fetuses.

The impact of prenatal diagnosis on morbidity is also a major issue. Indeed, the risk for severe hemodynamic compromise was 4 times higher in the postnatal group, and the long-term consequences of profound metabolic acidosis or neurological distress have to be evaluated in the survivors. The arterial switch operation has now become the operation of choice in TGA. It is of note that 4 patients diagnosed postnatally have to undergo an atrial switch repair because of delayed admission or severe preoperative complications. Because this latter operation, ie, atrial repair, is considered to have a high rate of late complications compared with the arterial switch, these 4 patients could be included in the preoperative morbidity group.

The consequences of prenatal diagnosis on postoperative mortality in our series are more questionable. We could not identify any differences in the risk factors between the 2 groups. However, the absence of death in the group with prenatal diagnosis did not allow us to demonstrate that the diagnosis in the fetus was the only factor influencing this mortality in a multivariate model. Notwithstanding the absence of statistical evidence, the well-recognized risk factors for early mortality after the arterial switch, coronary pattern and postoperative coronary events, were not different in the 2 groups. We hypothesize that the worse preoperative condition of patients in the neonatal group influenced postoperative mortality without correlation to anatomic factors.

Efforts have to be made to increase prenatal detection of life-threatening cardiac malformations in neonates. Routine detailed fetal echocardiography is probably an immensely important task in many countries, for both technical and economic reasons. However, targeted education programs have to be developed to detect TGA in low-risk populations by including detection of parallel great vessels in the routine fetal ultrasound screening at 18 weeks of gestation. When a TGA is detected antenatally, delivery should take place in an institution able to provide adequate postnatal care, and this implies in utero transfers of fetuses with TGA.

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