Biochemical and ultrasound markers of fetal cardiac dysfunction in twin-to-twin transfusion syndrome

Department of Obstetrics, Fetal Therapy Unit, Children’s Hospital V. Buzzi, Milan, Italy

Objective
To compare echocardiographic and biochemical parameters of cardiac function in recipient twins of monochorionic pregnancies complicated by twin-to-twin transfusion syndrome (TTTS), with uncomplicated monochorionic twins, analyzing association of those parameters with short-term (48 hours) recipient twin survival after fetoscopic laser coagulation (FLC), and monitoring them until delivery.

Methods
Amniotic fluid samples from recipient sacs were obtained in 57 TTTS cases during FLC, and in 40 controls. Samples were assayed for cardiac Troponin I (cTnI) and N-terminal pro-B-type natriuretic peptide (NT-proBNP). Echocardiographic parameters were evaluated in all 57 recipient twins before FLC and in 40 controls. Recipient survival was evaluated 48 hours after the procedure. Cardiac ultrasound parameters in recipients were re-evaluated at 1 and 4 weeks after laser. Follow-up was scheduled weekly to rule out postoperative complications, defined as recurrence or reversal of TTTS, and anemia-polycythemia sequence. Biochemical markers were assayed in umbilical cord blood at delivery in TTTS cases and controls.

Results
No differences in cTnI levels were found between cases and controls. NT-proBNP amniotic fluid levels were higher in TTTS than in controls both in absolute (median 5073 vs 2719 pg/L, p=0.002) and relative terms (ratio with total protein concentration, median 3.8 vs 11, p<0.001). Elevated NT-proBNP levels were associated with a worse myocardial performance index, abnormal atrioventricular valve inflow pattern and regurgitation, poor right ventricle systolic function, and elevated cardiothoracic circumference ratio. In the TTTS cases, there was a significant negative association between pulmonary artery peak systolic velocity (PA-PSV) and gestational age (p-value 0.03) while in controls a positive association was noted (p-value < 0.001). In TTTS cases, PA-PSV >100 cm/sec was found in 6 cases all detected at an earlier GA compared to TTTS cases with PA-PSV<100 cm/sec (p=0.004). Among all the cardiac parameters studied just the PA-PSV was positively correlated with short-term mortality of recipient twin after FLC (p=0.009, Odds ratio 1.46). In cases without postoperative complications a significant improvement was observed in cardiac functional parameters as myocardial performance index, mitral valve monophasic inflow pattern and thickness of left ventricular wall but no improvements were noted in atrioventricular valves insufficiency and worsening appeared in pulmonary stenosis (decrease of pulmonary valve diameter zeta score, p<0.001). In the TTTS group without complications after FLC, NT-proBNP at delivery became similar (median 1640 pg/L) to that of controls (median 2341 pg/L) (p=0.53), while in cases with postoperative complications, umbilical cord NT-proBNP at delivery was higher (median 14107 pg/L).

Conclusion
In TTTS cases biochemical and ultrasound parameters related with cardiac function improve after FLC while parameters related with organic damage to the cardiac valves especially to the pulmonary valve occurred at an early gestational age do not improve after FLC and increase recipient short term mortality after laser.