

Cardiovascular compromise in monochorionic twins Gijtenbeek, M.

Citation

Gijtenbeek, M. (2021, July 7). *Cardiovascular compromise in monochorionic twins*. Retrieved from https://hdl.handle.net/1887/3195073

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Title: Cardiovascular compromise in monochorionic twins

Issue Date: 2021-07-07





CHAPTE

SUMMARY





This thesis discusses cardiovascular compromise in complicated monochorionic twin pregnancy, with special emphasis on short- and long-term effects of hemodynamic adaptations.

Part I comprises the general introduction of this thesis. In **part II** we evaluated fetal hemodynamics and cardiac function in monochorionic twins with twin-twin transfusion syndrome (TTTS) in order to predict the outcomes of these pregnancies. **Part III** describes the postnatal effects of hemodynamic alterations in monochorionic twin pregnancies.

PART II: FETAL CIRCULATION

In **chapter 2** we assessed fetal cardiac function in healthy singletons and TTTS recipients by measurement of cardiac time intervals using color-coded Tissue Doppler Imaging (cTDI). We used linear mixed models to construct age-adjusted reference ranges for shortening time (St) and lengthening time (Lt) in three cardiac regions: global heart and right and left ventricular wall. St decreased and Lt increased with gestational age in all regions. We found a high feasibility (99.6%) and excellent intra/interobserver variability for St (0.96/0.94) and Lt (0.99/0.96) of the global heart. Left and right ventricle performance parameters were good. In TTTS recipients, St was prolonged (p < 0.01) and Lt was shortened (p < 0.01) in all regions as compared to healthy singletons, and the feasibility was excellent (96.6%). With the technique of cTDI it is possible to discriminate between healthy and compromised fetuses.

In **chapter 3** we present a prospective study in which monochorionic twins with an amniotic fluid discordance ≥ 4 cm underwent serial ultrasound examinations. Each examination consisted of evaluation of the amniotic fluid (deepest vertical pocket), fetal Dopplers and fetal cardiac function. We have found that intertwin discordance in myocardial performance index (MPI) of both the left and right ventricle of the heart may help to differentiate between future TTTS and pregnancies with discordant amniotic fluid volume without TTTS. Using cardiac time intervals measured by cTDI clinicians can furthermore identify future recipient twins and differentiate between future TTTS and selective fetal growth restriction (sFGR) and uncomplicated monochorionic twin pregnancies.

In **chapter 4** a systematic review and meta-analysis of the literature on the value of echocardiography and Doppler in the prediction of intrauterine fetal demise (IUFD) after laser coagulation for TTTS is presented. We found that absent or reversed end-diastolic flow (A/REDF) in the umbilical artery (UA), absent or reversed a-wave in the ductus

venosus and middle cerebral artery peak systolic velocity (MCA-PSV) > 1.5 multiples of the median (MoM) increases the risk of recipient-IUFD. In donors, only A/REDF in the UA and absent or reversed a-wave in the ductus venosus were found to be associated with donor-IUFD. The limited amount of available reports on the value of a detailed cardiovascular assessment in the prediction of fetal survival provided discordant results.

In **chapter 5** we investigated the possible relationship between perioperative hemodynamic changes and neurodevelopmental outcomes at two-years of age in 492 TTTS survivors. Neurodevelopmental impairment (NDI) was present in 5% of survivors. After adjustment for severe cerebral injury (detected in 4% of the children), the following parameters were associated with NDI: MCA-PSV > 1.5 MoM one day after surgery, a change from normal umbilical artery pulsatility index (UA-PI) pre-surgery to UA-PI > p95 post-surgery and change from normal to increased MCA-PSV. This study indicates that perioperative hemodynamic changes in TTTS twins treated with laser surgery may contribute to poor neurological outcome.

PART III: POSTNATAL CIRCULATION

In **chapter 6** the incidence of persistent pulmonary hypertension of the newborn (PPHN) in TTTS was described and risk factors for the development of PPHN in TTTS survivors were identified in a case-control study. Severe PPHN occurred in 26 of the 1,091 (2.4%) liveborn monochorionic twins. The incidence of severe PPHN was 10-fold increased in TTTS twins compared to monochorionic twins without TTTS (4% vs. 0.4%). Two risk factors were independently associated with severe PPHN: a younger gestational age (GA) at birth and a recipient status. In TTTS recipients, post-laser twin anemia polycythemia sequence (TAPS) (indicating incomplete fetoscopic laser surgery) contributed to a higher risk of PPHN in the univariate analysis, and an independent association with severe prematurity and anemia at birth was found. We propose a 'double hit theory' for anemic recipients after post-laser TAPS: the baseline increased risk of PPHN due to increased pulmonary vascular resistance is further increased by acute hypoxia as a result of anemia at birth.

In **chapter 7** an updated overview of congenital heart defects (CHD) in monochorionic twins is presented with a systematic review and meta-analysis. In this review 12 studies were included. Compared to the reference population, monochorionic twins were 6.3 times more likely to be born with a CHD (59.3 per 1,000 live born twins). TTTS twins had a 12-fold increased risk of having a CHD at birth (111.3 per 1,000 live births). The increased incidence of CHDs can mainly be attributed to the risk of right ventricular outflow tract obstruction (35/1,000 TTTS twin live births vs. 0.5/1,000 singleton live births).

In **chapter 8** we assessed cardiac function and postnatal CHD prevalence in 168 TTTS survivors. The main findings of the study were a high prevalence of structural CHD (11.3%) after fetoscopic laser coagulation and a low prenatal detection rate (21%). Both recipient and donor twins were at risk of a CHD, with a prevalence of 9.2% and 13.6% respectively. Pulmonary stenosis was the most frequently diagnosed defect in 4.2% of TTTS survivors (seven of 168), of whom five were recipients (five of 87, 5.7%) and two were donors (two of 81, 2.5%). In donors, also three ventricular septal defects, three atrial septal defects and three bicuspid aortic valves were detected. The only significant functional echocardiographic parameter was a lower peak aortic velocity in donor twins compared with recipient twins.

In **chapter 9** seven cases of coarctation of the aorta (CoA) in monochorionic twins are presented. All were the smaller twin of monochorionic pairs complicated by sFGR. In this study, one neonate underwent coarctectomy at the age of one month (2,330 g), six underwent stent implantation as bridging therapy to surgery. All seven developed normally, except for one child with neurodevelopmental delay. Three of the larger twins had pulmonary stenosis of whom one required balloon valvuloplasty. An additional systematic literature review revealed ten cases of monochorionic twins with discordant CoA, where the affected twin was the smaller baby. Six cases of critical CoA detected in the first weeks after birth were treated with prostaglandins alone, by repeated transcatheter angioplasty or by surgical repair, with good outcome in two out of six.