Prenat Cardio 2020
DOI: https://doi.org/10.5114/pcard.2020.99686
Received: 7.08.2020
Accepted: 27.08.2020

Prenatal Cardiology
www.termedia.pl/Journal/Prenatal_Cardiology

Research paper

Interventions to improve fetal heart rate patterns during open myelomeningocele repair

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Abstract

Introduction: To access fetal heart rate (FHR) after multifactorial changes in the performance of open fetal myelomeningocele surgery.
Material and methods: A study with 37 fetuses submitted to intrauterine myelomeningocele repair between the 24th and 27th week of gestation was performed to evaluate FHR at specific periods: pre-anaesthesia, post-anaesthesia, during neurosurgery (early skin manipulation, spinal cord release, and synthesis), and at the end of surgery. Surgery room (SRT) and uterine surface (UST) temperatures were strictly controlled. A plastic cover was used to protect to protect uterine heat loss. We determined the mean ± standard deviation (SD) of FHR of each period, and we used analysis of variance (ANOVA) with repeated measures to assess differences among these periods. Tukey multiple comparation test was used to compare global surgery stages.
Results: The mean FHR in the specific time points were: 138.6, 138.4, 132.8, 127.7, 131.4, and 132.7 bpm, respectively ($p < 0.001$). In the comparisons between times two by two, the neurosurgery stage presents the lower frequencies, especially during release of the spinal cord, but episodes of bradycardia were no longer found. SRT and UST remained stable during the critical stages of the procedure.
Conclusions: It is known that many are the factors involved in fetal cardiovascular disorders. Possibly, these changes allowed for better haemodynamic control of the fetus, improving the safety of the procedure.

Key words: fetal heart rate, open fetal surgery, myelomeningocele repair.

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Introduction

In recent years, knowledge pertaining to neural tube defects has made great strides. Since the initial studies on their prevention, improvements in their detection and diagnosis have facilitated a new era in fetal therapy, significantly reducing the morbidity and mortality rates and improving the postnatal quality of life among patients with neural tube defects [1].

Myelomeningocele is responsible for orthopaedic, vesico-intestinal, and neurological sequelae, which are largely due to the high incidence of hydrocephalus associated with the Chiari II malformation [1]. It affects approximately 1 out of every 1000 to 2000 live births; approximately 80% of patients require surgery, and 46% experience complications in the first year of life [2].

Since the publication of the Management of Myelomeningocele Study (MOMS), fetal therapy centres around the world have broadened their research, and more centres have begun to perform open myelomeningocele repair [3]. Despite the increasing experience, there remain many challenges in the implementation of this highly complex procedure.

The frequent risk of fetal bradycardia is a major intraoperative concern; fetal heart rate (FHR) monitoring is essential for the identification of these changes and the rapid re-establishment of the haemodynamic state. As previously reported, the neurosurgical stage was shown to be a higher risk for fetal bradycardia, especially when nerve endings and the spinal cord were exposed [4].

Therefore, this study sought to evaluate FHR patterns after multifactorial changes to open fetal surgery and, in doing so, to contribute to improving the safety and quality of the procedure in addition to improving the understanding of fetal physiology.

Material and methods

A prospective, cross-sectional study was performed from July 2016 to July 2017. It included women who were pregnant with fetuses with myelomeningocele, who underwent open surgery. Patients were selected from the Centre for Fetal Medicine within the Department of Obstetrics of the Federal University of São Paulo (UNIFESP), the São Paulo Centre for Fetal Medicine, and Santa Joana Maternity Hospital in São Paulo, Brazil. The pregnant women who agreed to volunteer for the study signed an informed consent form, and this study was approved by the Research Ethics Committee of UNIFESP. The surgery was performed in operating rooms at UNIFESP's São Paulo Hospital and at Santa Joana Maternity Hospital.

Fetal heart rate was evaluated at specific time points during surgery: before the mother received anaesthesia (1), after the mother received anaesthesia (2), neurosurgery (beginning of skin manipulation) (3a), during neurosurgery at exposure of nerve endings and the spinal cord (3b), during neurosurgery at synthesis (3c), and at the end of the surgery (4). FHR was obtained by means of pulsatile Doppler wave velocimetry, with measurements at the closure of the mitral valve at an interval of at least three consecutive beats. The FHR range considered normal in this study was 110 to 160 bpm (range, 24 to 27 weeks). Measurements were performed within 3-4 min of each stage of the surgery.

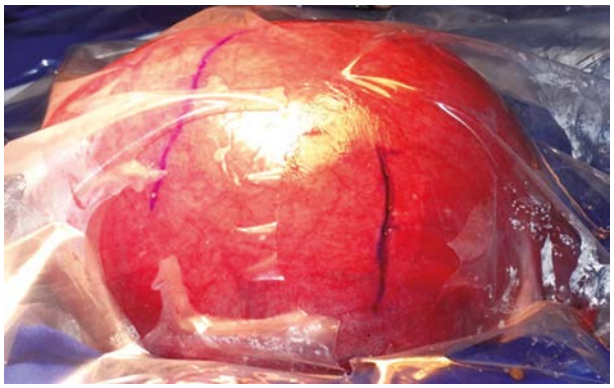

Figure 1. Image of the uterus lining with a plastic cover to minimise heat losses

The ultrasound machine used in the operating room was a Logiq P5 (GE, Medical Systems, Milwaukee, WI, USA) with a multifrequency convex probe (2-5 MHz). The ultrasound probe was wrapped in a sterile laparoscopic cover, and gel was then placed directly on its surface. The transducer was positioned such that an adequate image could be obtained without hindering the surgery. All the images were saved on the device's hard drive and printed in real time to be added to each patient's medical record.

The inclusion criteria of this study were a singleton pregnancy with a live fetus, myelomeningocele with a top margin between the first lumbar vertebra and the first sacral vertebra, evidence of brain stem herniation, gestational age between 24 and 27 weeks, and normal fetal karyotype. The exclusion criteria were fetuses with structural and/or chromosomal abnormalities, fetal kyphosis, increased risk of preterm labour (short uterine cervix < 25 mm, and/or prematurity in previous gestation), low-lying placenta, body mass index (BMI) > 35 kg/m^2, and hysterotomy of the anterior segment.

After a previous study by the authors, in which a reduction in fetal heart rate was observed during the neurosurgical stage, as were some instances of bradycardia, changes in the fetal surgery protocol were suggested to minimise the previous findings [4]. We decided against the use of intramuscular fentanyl for fetal anaesthesia because the surgical team initially experienced increases in cases of fetal bradycardia with no additional benefit to the surgical outcome or the well-being of the fetus.

Temperature control became more rigorous. Using a laser thermometer, the temperature of the uterus while exposed to the external environment was controlled by a team member present outside the operating field. To prevent the uterine temperature from reaching levels below 30°C, the uterine surface was irrigated with a saline solution heated to 37°C. The temperature marked on the thermometer in the operating room itself was also monitored.

The team then wrapped the exposed uterus in a sterile plastic cover (Figure 1), leaving only the region of the hysterotomy exposed, to further minimise heat loss (Figure 2).

Manual compression of the uterus (a subjective parameter) to display the operating field to the neurosurgeon has also become a focus in this procedure because it is associated with fetal chest compression, decreases in fetoplacental circulation, and fetal response to surgical stress.

In cases of maternal hypotension, ephedrine or metaraminol was administered if necessary, to preserve fetoplacental circulation. The plan for cases of fetal bradycardia included the infusion of atropine into the mother's circulatory system at a dose of 0.02 mg/kg in addition to epinephrine at 1 μg/kg.

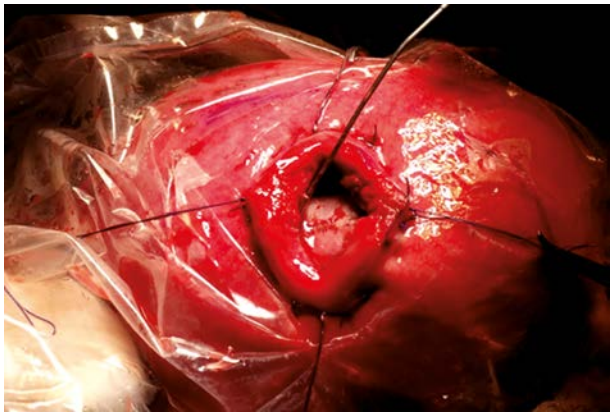

Figure 2. Image of the uterus lining with a plastic cover leaving only the hysterotomy region exposed

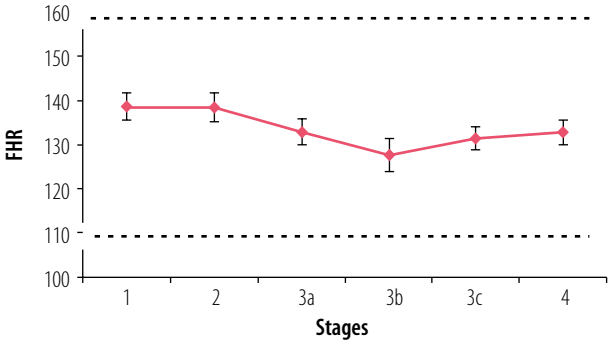

Figure 3. o heart rate (FHR) monitoring during open fetal myelomeningocele surgery. The mean values of the global stages are presented ($n = 37$)

All the data were processed in an Excel 2007 worksheet (Microsoft Corp., Redmond, WA, USA). We determined the mean ± standard deviation (SD) of the FHR of each stage and used analysis of variance (ANOVA) with repeated measures to assess differences between the surgical stages. To compare different stages of the fetal surgery, we used the mean difference with a 95% confidence interval (CI), and the differences were analysed using Tukey's multiple comparison test.

Results

In a total of 37 open fetal myelomeningocele surgeries, the descriptive statistics tests showed that the mean maternal age was 32.6 years, mean gestational age at the time of surgery was 25.9 weeks, mean body mass index was 28.0 kg/m^2, and mean fetal weight was estimated at 830.9 g. The mean surgical time was 127.3 min. Delivery occurred after an average of 235.5 days of pregnancy. Mean fetal birth weight was 2225 g, and delivery occurred, on average, 56.1 days after surgery (Table 1).

ANOVA with repeated measures was used to assess the differences between the following stages of surgery. The mean FHR before maternal anaesthesia (1), after maternal anaesthesia (2), during neurosurgery at the beginning of skin manipulation (3a), during neurosurgery at exposure of nerve endings and the spinal cord (3b), during neurosurgery at synthesis (3c), and at the end of the surgery was 138.6 ±9.1, 138.4 ±9.7, 132.8 ±9.1, 127.7 ±11.4, 131.4 ±8.1, and 132.7 ±8.5 bpm, respectively ($p < 0.001$) (Table 2).

Table 1. Characteristics of the cases undergoing open fetal myelomeningocele surgery ($N = 37$)

Parameter	Mean ± SD	Median (range)
Age (years)	32.6 ±4.7	33.0 (24-43)
Body mass index (kg/m^2)	27.1 ±4.4	26.4 (20.9-35.2)
Gestational age at surgery (weeks)	25.9 ±0.9	25.7 (25-27)
Estimated fetal weight (g)	830.9 ±126.7	816.0 (611-1086)
Surgical time (min)	127.3 ±18.3	126.0 (84-166)
Gestational age at delivery (days)	235.5 ±16.6	240.0 (188-261)
Gestational age at delivery (weeks)	33.8	34.4
Birth weight (g)	2225.0 ±560.7	2325.0 (1165-3225)
Days from surgery	56.1 ±183	56.0 (5-89

SD – standard deviation

Table 2. Means and standard deviations values of fetal heart rate (FHR) in each surgical stage ($N = 37$)

	1	2	3a	3b	3c	4
Mean	138.6	138.4	132.8	127.7	131.4	132.7
Standard deviation	9.1	9.7	9.1	11.4	8.1	8.5

ANOVA with repeated measures; $p < 0.001$; 1: pre-anaesthesia; 2: post-anaesthesia; 3a: neurosurgery (early skin manipulation); 3b: neurosurgery (spinal cord releasing); 3c: neurosurgery (synthesis); 4: end of surgery.

Table 3. Paired comparison of fetal heart rate (FHR) between each specific stage ($N = 37$)

	FHR 1	FHR 2	FHR 3a	FHR 3b	FHR 3c	FHR 4
FHR 1						
FHR 2	1.000					
FHR 3a	0.022	0.006				
FHR 3b	0.000	0.000	0.028			
FHR 3c	0.001	0.002	0.955	0.444		
FHR 4	0.006	0.022	1.000	0.131	0.823	

p values obtained by Tukey's multiple comparison test. For surgical stages, see Table 2.

We used Tukey's multiple comparison test to show two-tailed comparisons (Table 3). Based on the 95% CI and 5% of level of significance, marked highlights were determined to be significant in the comparisons. There was a significant reduction in FHR between stages 2 and 3a and between stages 3a and 3b; it stayed at the same level until stage 4 (Figure 3). Unlike in previous protocols for fetal surgery, no episodes of fetal bradycardia were recorded in this series.

ANOVA with repeated measures showed that mean values for room temperature (in °C) during the different surgical stages (Table 4) were 23.2 (stage 1), 22.9 (stage 2), 22.9 (stage 3a), 22.9 (stage 3b), 22.9 (stage 3c), and 22.0 (stage 4). Therefore, the temperature of the room decreased only at the end of the surgery (between stages 3c and 4) (Figure 4). Mean uterine temperature (in °C) was 31.83 in stage 3a, 31.87 in stage 3b, and 31.26 in stage 3c (Table 4). There were no significant changes during the three neurosurgery stages (Figure 5).

Table 4. Means and standard deviations values of surgery room temperature and uterus temperature (in °C) for the global stages ($N = 37$)

Parameter	Mean	SD
SRT1	23.206	1.019
SRT2	22.967	1.022
SRT3a	22.950	0.25
SRT3b	22.997	0.916
SRT3c	22.919	0.954
SRT4	22.044	1.123
UST3a	31.836	1.498
UST3b		1.316
UST3c	31.267	3.528

SRT – surgery room temperature, UST – uterine surface temperature, SD – standard deviation. ANOVA with repeated measures; $p < 0.001$; 1: pre-anaesthesia; 2: post-anaesthesia; 3a: neurosurgery (early skin manipulation); 3b: neurosurgery (spinal cord releasing); 3c: neurosurgery (synthesis); 4: end of surgery.

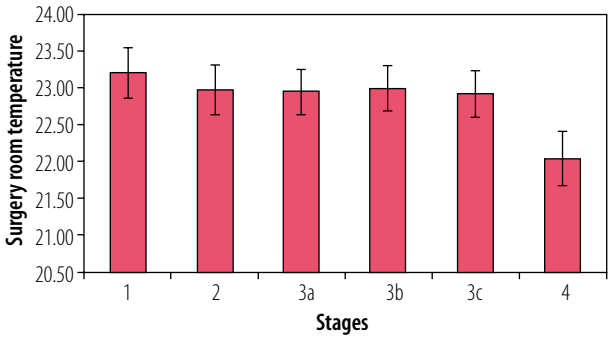

Figure 4. Surgery room temperature (SRT) in Celsius during open fetal myelomeningocele surgery. The mean values of the global stages are presented ($n = 37$)

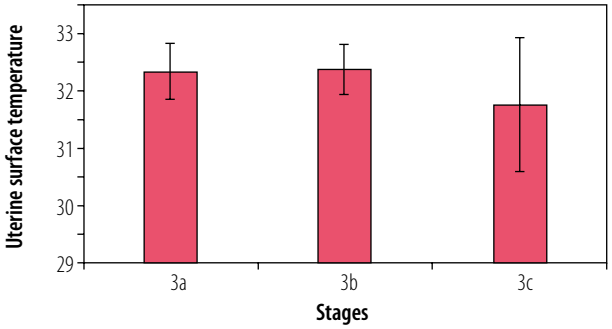

Figure 5. Uterine surface temperature (UST) in Celsius during open fetal myelomeningocele surgery. The mean values of the global stages are presented ($n = 37$)

Discussion

Maintaining the haemodynamic balance of the fetus during open surgery is complex and depends on multiple factors such as maternal anaesthesia, fetal anaesthesia, fetal response to surgical stress, uterine manipulation by fetal chest compression, possible decreases in fetoplacental circulation, and possible heat loss [4].

It is evident that the mother's haemodynamic state influences fetal circulation. Van de Velde et al. reported that the use of vasopressors in cases of maternal hypotension during fetal procedures may be necessary [5]. Therefore, the surgical team's monitoring should be as vigilant as possible.

As demonstrated by Boat et al., the administration of desflurane along with intravenous anaesthetics is beneficial in reducing bradycardia, left ventricular dysfunction, and the need for fetal resuscitation during open surgery when compared with that of only high doses of desflurane. The protocol included propofol (150-250 μg/kg/min) and remifentanil (0.2-0.5 μg/kg/min) during the beginning of procedure, and then administration of desflurane (1-1.5 MAC) for uterine relaxation. At the time the uterus was exposed, propofol infusion rates were decreased (50-75 μg/kg/min) and the concentration of desflurane was gradually increased (2-2.5 MAC) until appropriate uterine relaxation was provided [6]. This finding was also described by Nguyen et al., who reported fetal bradycardia during surgery after the inhalation of high doses of anaesthetics [7]. In our patients, a 3% sevoflurane concentration was elevated to 5% when the uterus was removed from the abdominal cavity, and in this series, no similar episodes were observed.

It is known that the fetal response to stress and pain involves the activation of the hypothalamic–pituitary–adrenal axis and the release of stress-related hormones, such as noradrenaline, cortisol, beta-endorphin, and corticotropin [8]. As Anand et al. describe, this theory is limited, and often these stress responses cannot be interpreted as a painful sensation and do not present cortical involvement [9].

The viability of an intact system to transmit pain from the peripheral receptor to the cerebral cortex must be complete for the fetus to experience pain. The development of these peripheral receptors begins at the 17th week of gestation and is complete by the 20th week. This mechanism makes the sensation of pain possible; however, the serotonin-releasing downstream inhibitory system does not develop completely until after birth [10, 11].

Although the MOMS trial protocol [3] consisted of the use of intramuscular fentanyl in the fetus, in our experience in recent years, we have observed an increase in the incidence of fetal bradycardia associated with the use of this drug, and atropine is much more commonly used for vagolysis. This finding differs from those reported by Richick et al., who found that fentanyl and vecuronium increased FHR and decreased cardiac output [12]. Bellieni et al. also believed that because anaesthetic levels are lower in fetal circulation than in maternal circulation, analgesics and anaesthesia should be administered directly to the fetus [13].

Volatile anaesthetics are, in fact, known to pass through the placenta. This is due to the properties of these drugs, which include low-molecular-weight, high-fat solubility, and a non-ionic nature. Although it is believed that the use of fentanyl may reduce the fetal response to surgical stress, the confirmation of this effect and a full understanding of fetal physiology still require further studies [14].

Adequate control of body temperature during surgical procedures is essential [15]. It is known that hypothermia increases cardiac morbidity, increases oxygen consumption, is associated with coagulation disorders, and is also related to a high incidence of operative wound infection [16]. Mann et al. also

note their concern over cases of maternal hypothermia even after fetal surgery [17]. In our practice, the patient is covered with upper-body blankets to minimise heat loss. The operating room remains at a stable temperature during critical periods, and after the uterus is removed from the abdominal cavity, it is protected with a plastic cover, further minimising heat loss and thus protecting maternal–fetal haemodynamics. The continued use of uterine irrigation with heated saline during neurosurgery is an important step for maintaining a safe thermal balance. We observed that the uterine surface temperature did not change significantly during the three neurosurgical stages, and the room temperature decreased only during the final stage of the surgery after the uterus had already been returned to the abdominal cavity.

Although a reduction in the fetal heart rate was observed during the neurosurgical stage (when the nerve endings and spinal cord are exposed), there were no episodes of fetal bradycardia, which previously had been more frequent.

Conclusions

Although several factors are involved in the pathogenesis of fetal cardiovascular disorders, we believe that these changes allow for better haemodynamic control of the fetus and, in doing so, increase the safety of the procedure.

Of course, further studies are needed to improve our understanding of fetal behaviour during open surgery as well as that of the physiological aspects involved in this complex scenario. Maybe the assessment of FHR variability would be important in this context.

Acknowledgments

We would like to thank the Department of Obstetrics of the Federal University of São Paulo (UNIFESP) and the Association for the Improvement of Higher Education Personnel (CAPES) for enabling this study. We would also like to thank Santa Joana Maternity Hospital for supporting our team and the growth of open fetal surgery in Brazil.

Conflict of interest

The authors declare no conflict of interest.

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Prenat Cardio 2020
DOI: https://doi.org/10.5114/pcard.2020.98347
Received: 25.06.2020
Accepted: 02.08.2020

Prenatal Cardiology
www.termedia.pl/Journal/Prenatal_Cardiology

Research paper

Cardiac function in TTTS twins after laser coagulation

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Abstract

Introduction: Cardiac function in twin pregnancies complicated by twin-to-twin transfusion syndrome (TTTS) is an important issue in order to understand the modifications that any intervention aimed to solve the blood transfusion can determine on the surviving fetuses. Many studies have shown that in the long term, after laser coagulation (LC) of severe TTTS syndrome, cardiac function and blood pressure return to normal in the majority of surviving twins. This indicates that the preceding cardiac dysfunction regresses once LC has removed the underlying cause. However, a reported increased in the prevalence of pulmonary stenosis despite successful LC justifies the need for prenatal and postnatal cardiac surveillance.
Material and methods: In our data of 28 pairs of twins complicated by TTTS and undergoing LC, we observed abnormal prenatal cardiac findings before treatment and the postnatal occurrence of some structural heart defects. One twin recipient with hydrops and functional pulmonary atresia had the same features at postnatal follow-up; another twin recipient with fetal hydrops, and mitral and tricuspid valve regurgitation presented with moderate pulmonary stenosis postnatally.
Results: One fifth of all TTTS recipient twins show congenital and/or acquired diseases, i.e. right ventricle outflow tract obstruction (RVOTO), PA, or PS. Laser coagulation in severe stages can solve the blood transfusion but does not solve the acquired CHD (such as right ventricular outflow obstruction and pulmonary valve atresia).
Conclusions: Laser coagulation should always be performed before cardiac function deteriorates, if possible.

Key words: laser coagulation, TTTS, RVOTO, pulmonary atresia, pulmonary stenosis, twins.

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Introduction

In recent years multiple pregnancies have increased globally, in keeping with lifestyle changes, an increase in maternal age, and the use of assisted reproductive techniques (ART). However, multiple pregnancies contribute disproportionately to prematurity and perinatal mortality and morbidity [1].

Whereas in the past multiple pregnancies often went undiagnosed until delivery, today improved antenatal management, including ultrasound and monitoring, allow a comprehensive

Table 1. Ultrasound findings in the recipient twin TTTS before and after LC (recipients $n = 28$)

Abnormal findings	Prenatally present	CHD	Prenatally not present	CHD
Hydrops	4	1	24	3
MV regurgitation	3	1	25	3
TV regurgitation	9	1	19	3
DV absent/reverse	10	1	18	3
Functional pulmonary atresia	2	1	27	3

TTTS – twin-to-twin transfusion syndrome, LC – laser coagulation, CHD – congenital heart defects

and individualised plan for the mode and timing of each pregnancy care and outcome. Twin pregnancies are at increased risk for preterm birth, intrauterine growth restriction (IUGR), and other conditions such as hypertensive disorders and gestational diabetes. Monochorionic twins have additional risks for death and morbidity, primarily because of so called the twin-to-twin transfusion syndrome (TTTS), and for increased congenital abnormalities [1]. TTTS is a serious complication that affects 10-15% of monochorionic multiple pregnancies [2]. Communicating placental vessels on the chorionic plate between the donor and recipient twin are responsible for the imbalance of blood flow dynamics. There is evidence for the superiority of foetoscopic laser ablation-coagulation in solving this haemodynamic disorder.

Survival rates after fetoscopic laser surgery have significantly increased over the last 25 years. High-volume centres report up to 70% double survival rate, and at least one survivor in > 90% of cases. Long-term neurodevelopmental impairment occurs in about 10% of children after laser coagulation (LC) [3].

Congenital heart defects (CHDs) represent the most common human birth defect, having a prevalence at birth of 7-9 per 1000 singleton live births. CHDs are more common in twin pregnancies with a prevalence of 13 per 1000 total births. Monochorionic (MC) twins are at even higher risk (20 per 1000 total births) compared to dichorionic twins (11 per 1000 total births). In MC twins, all types of congenital heart defects have been reported. Furthermore, the development of acquired structural heart disease can be encountered also in association with TTTS [4].

Material and methods

Our experience of TTTS at Almazov National Medical Research Centre Ministry of Health Russian Federation between April 2019 and March 2020, is related to 28 twin pregnancies in which we performed a careful echocardiographic examination before and after the LC procedure. Our perinatal centre receives the majority of complicated pregnancies from the whole country. Right ventricular outflow tract obstruction was diagnosed or excluded by review of perinatal records, obstetrical ultrasounds, fetal echocardiograms, postnatal echocardiograms, and postnatal clinical assessments. In the cases with RVOTO, the clinical course and postnatal outcome were documented by a review of prenatal and postnatal medical records.

Results

From our data we observed a series of abnormal prenatal cardiac findings before LC and the postnatal occurrence of structural heart defects in recipients. Donors did not show significant changes in cardiac function, and the Doppler changes were related mainly to the high vascular resistance and occurred in umbilical arteries (high pulsatility index [PI], low diastolic flow, and absent/reversed flow in the umbilical artery). One twin recipient with hydrops and functional pulmonary atresia had the same features at postnatal follow-up; another twin recipient with fetal hydrops, and mitral and tricuspid valve regurgitation presented with moderate pulmonary stenosis postnatally (Table 1).

Discussion

The increased incidence of CHDs in twins with TTTS can be mainly attributed to the right ventricular outflow tract obstruction (RVOTO) (35/1000 TTTS twin live births vs. 0.5/1000 singleton live births) [5].

Therefore, it is important to understand how the pathophysiological process of TTTS may affect the fetal heart dynamics. It has been demonstrated that in the surface of the twin placenta there can be different types of anastomoses: arterio-venous, which are unidirectional and may cause haemodynamic imbalance, whereas arterio-arterial and the veno-venous anastomoses are bidirectional, and the circulation may remain balanced [6]. In the case of arterio-venous anastomoses, the predominant feature is that blood is mainly going from one fetus to the other. A fetus who is losing its blood volume and becomes hypovolaemic is referred to as the donor. In order to maintain an adequate blood pressure, the twin produces a greater amount of hormonal mediators (renin and angiotensin II), the vascular resistance therefore increases and aggravates the oligo-/anuria as vasopressin and hypoosmolality increase as well. The other fetus, the so-called recipient, becomes hypervolaemic because it receives not only an extra volume of blood but also some of the donor's hormones, which may cause a paradoxical reaction. The recipient has high natriuretic protein and endothelin, which contribute to heart failure. Vasopressin decreases, blood viscosity is high, urine production rises, and there is polyhydramnios [6, 7].

The consequence of an unequal circulatory volume defines the pathophysiology of this condition and determines the physiological responses to the volume imbalance. Moreover, this can lead to functional cardiac changes, usually in the recipient twin. Nevertheless, after the LC procedure, all this is expected to be solved. However, if TTTS progresses, there is the potential for 'acquired' structural congenital heart disease, particularly right ventricular outflow tract obstruction in the recipient and coarctation of the aorta in the donor.

The recipient twin usually has an increased preload. The increase in circulating volume is combined with the donor's hormonal mediators and there is a resulting release of natriuretic peptides, atrial natriuretic protein (ANP), and brain natriuretic protein (BNP), with increasing diuresis and polyhydramnios. Furthermore, the afterload increases as a result of high resis-

tance. There is an increased production of endothelin, which leads to ventricular hypertrophy, hypertension, and inappropriate stimulation of the renin-angiotensin system [6, 7].

The evolution of the functional changes in the recipient twin include ventricular dilatation at the beginning with mild hypertrophy and mild atrioventricular regurgitation [8]; at this time Doppler evaluation in the umbilical artery may still give a normal result. As the disease progresses, there is increasing ventricular thickening and compromised diastolic function. In the ductus venosus, we can observe absent or reversed flow, which is a marker of decreased atrial contraction, and umbilical vein pulsation [9].

As the diastolic function is compromised, the systolic function also deteriorates; there is decreased ventricular short fraction and atrioventricular regurgitation. These alterations usually start in the right side, followed by the left [10]: these modifications may lead to atrioventricular insufficiency and severe ventricular dysfunction, low cardiac output, hydrops, and finally fetal death [11]. The ventricular pressure becomes high before we can observe any outflow obstruction.

Diastolic function in the recipient twin is important for preserving fetal circulation. In the progression of the disease, the ventricular myocardium increases in thickness, therefore reducing the compliance, leading to inadequate relaxation and monophasic ventricular filling instead of the two active and passive phases [12]. Therefore, the so-called myocardial performance index, which describes systolic and diastolic dysfunction, increases.

The myocardial performance index (MPI) is the ratio between the combined isovolumetric times and the ejection time. As the global systolic and diastolic dysfunction worsens, MPI values increase. MPI is a reliable method to understand cardiac function in twins with TTTS using Doppler velocimetry [13, 14].

The twin donor haemodynamics further complicate with decreased preload and increased afterload. The donor rarely manifests cardiac anomalies at echocardiography. Systolic function remains preserved, and there is no effect on valvular function. When the systemic vascular resistance increases, we can find high pulsatility index (PI), low diastolic flow, and absent/reversed flow in the umbilical artery [15]. All of these changes in haemodynamics are aimed at preserving pressure and circulatory redistribution [16, 17].

We usually observe functional cardiac anomalies in the recipient as cardiomyopathy and valvular lesions (pulmonary, tricuspid). In the twin donor there is typically smooth muscle hypertrophy, increased blood pressure, and increased vascular stiffness. Nevertheless, during the progress of TTTS, the twin recipient can manifest acquired cardiac anomalies like right ventricular outflow obstruction or tricuspid valve dysplasia. Some reports show also coarctation of the aorta in the donor twin, but we cannot be sure that it is not congenital and is an underlying cause of the TTTS. All these alterations have long-term consequences [18].

Functional RVOTO may occur as a consequence of right ventricular hypertrophy, reduced RV function, in association with high systemic pressure, severe tricuspid and pulmonary regurgitation, and an inability of the RV to generate appropriate pressure to open the pulmonary valve.

The 'acquired' RV outflow tract obstruction is phenotypically identical to the congenital heart disease (CHD). Pulmonary atresia (PA) or pulmonary stenosis (PS) in the hypoplastic hypertrophic right ventricle [18, 19].

Accurate echocardiographic examination before intervention in TTTS revealed the following: 20% of recipients already had abnormal pulmonary valves before LC treatment, such as atresia or stenosis or regurgitation, and 9-12% showed persistent anomalies requiring surgical treatment at birth despite successful in-utero LC. We still do not know if LC always improves right ventricular function or if early LC reduces the risk of RVOTO [20].

During TTTS, we can observe tricuspid valve anomalies, such as regurgitation, which is one of the haemodynamic anomalies of TTTS, or it can appear after treatment and resolve in a short time. However, it is still unknown if this is a "primary" or "acquired" structural anomaly.

Cardiac anomalies of the twin donor are much less documented – there is a recent report of a series of four donor twins with coarctation and hypoplastic aortic arch [21]. The effect of treatment is unpredictable due to the limited number of cases. Moreover, it is again unknown if the anomalies were "primary" or "acquired" [22].

The purpose of LC is to separate the two twins' systems of circulation and the discharge of hormonal mediators that cause cardiovascular disfunction. However, not all cases of RVOTO can be eliminated by performing laser coagulation [10].

The key points are listed in Figure 1.

Conclusions

Before and after LC an accurate echocardiographic assessment of both twins should always be performed, with particular attention to the presence of the following:

- DV absent/reverse (atrial dysfunction/diminished contractility, stiff non-compliant RV),
- TV, MV regurgitation (dilatation, ventricular hypertrophy, diastolic dysfunction),
- one peak flow ventricular filling (poor compliant and stiff ventricle),
- MPI recipient > MPI donor,
- high gradient of pressure in RV (peak velocity regurgitant jet).

In this way the counselling and the expectations from LC in cases of TTTS will be more accurate and realistic.

Key points

1. Cardiac malformations are more common in twin pregnancies compared to singleton pregnancies. TTTS further increases the rate.
2. TTTS may contribute to the development of RVOTO, PS, and PA in the recipient and coarctation of the aorta in the donor twin, due to altered blood flow dynamics and hormonal mediators.
3. Cardiac evaluation for both twins (donor and recipient) is warranted.

Figure 1. The twin-to-twin transfusion syndrome – key points

Conflict of interest

The authors declare no conflict of interest.

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