

P R A C E O R Y G I N A L N E
położnictwo

Comparison of fetal myocardial contractility before and after laser photocoagulation of communicating vessels in twin-to-twin transfusion syndrome

Porównanie zmian kurczliwości serca u płodów przed i po zabiegu laserowej okluzji naczyń łączących w zespole TTTS

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Abstract

Objectives: To evaluate changes in myocardial contractility that occur after selective laser photocoagulation of communicating vessels (SLPCV) in fetuses from pregnancies complicated with twin-to-twin transfusion syndrome (TTTS).

Methods: The study included 51 pregnant women between 16 and 26 weeks of gestation who underwent SLPCV due to TTTS. Ultrasonography was performed before SLPCV and on postoperative day 1, 3(4) and 7. Fetal heart contractility in both fetuses was evaluated by determining the shortening fractions of the left and right ventricles (FS LV and FS RV), and the myocardial performance index (Tei-Index).

Results: There was a significant increase in postoperative FS LV and FS RV in recipients (from 35.7% to 44%, $P=0.037$ and from 27.6% to 32.9%, $P=0.021$, respectively). Pre-operative Tei-Index values for both the left (0.55) and right ventricle (0.6) were above normal. The mean postoperative Tei-Index for the left ventricle decreased significantly to 0.49 ($P=0.011$), while no significant change was observed in the right ventricle (0.57). No significant differences between pre- and postoperative FS and Tei-Index values were noted in the donors.

Conclusions: SLPCV is reflected by a significantly increased myocardial contractility in recipients.

Key words: **gemi** / **pregnancy** / **fetoscopy** / **fetal myocardial contractility** /
/ **shortening fraction** / **Tei-Index** /

Streszczenie

Cel pracy: Celem pracy była ocena zmian kurczliwości mięśnia serca płodów dawcy i biorcy w ciąży wielopłodowej jednokosmówkowej powikłanej zespołem TTTS przed i po zabiegu selektywnej koagulacji naczyń łączących (SLPCV).

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Materiał i metoda: Badanie objęło 51 pacjentek, hospitalizowanych w Klinice Położnictwa Gdańskiego Uniwersytetu Medycznego, pomiędzy 16. a 26. tygodniem ciąży, u których przeprowadzono zabieg SLPCV. Badanie ultrasonograficzne wykonywano przed oraz w pierwszym, trzecim (czwartym) i siódmym dniu po zabiegu. Kurczliwość mięśnia serca u obu płodów była oceniana przez pomiar frakcji skracania lewej i prawej komory (FSLV i FSRV) i wskaźnika kurczliwości myocardiium (Tei-Index).

Wyniki: Zaobserwowano znamienne wzrost FSLV i FSRV u biorców po zabiegu SLPCV (odpowiednio z 35,7% do 44% ($P=0,037$) i z 27,6% do 32,9% ($P=0,021$)). Przedoperacyjne pomiary Tei-Index odbiegały od normy- dla lewej komory- 0,55, dla prawej komory- 0,6. Średni pooperacyjny wynik wskaźnika kurczliwości myocardiium dla lewej komory obniżył się znamienne do wartości 0,49 ($P=0,011$), w przypadku prawej komory Tei-Index również się obniżył do wartości 0,57, ale zmiana nie była statystycznie znamienne ($P=0,93$). Nie zaobserwowano istotnych zmian w wartościach FS i Tei-Index u dawców, przed i po zabiegu SLPCV.

Wnioski: Po zabiegu SLPCV znamienne poprawia się kurczliwość mięśnia serca biorców.

Słowa kluczowe: **cięża wielopłodowa / zespół TTTS / selektywna koagulacja naczyń łączących – SLPCV / Tei-Index /**

Introduction

Twin-to-twin transfusion syndrome (TTTS) is a severe condition occurring in monochorionic multiple pregnancies and diagnosed on the basis of ultrasonographic findings. Untreated TTTS leads to a mortality rate of 80% to 100% [1, 2].

Selective laser photocoagulation of communicating vessels (SLPCV) is a causative treatment. Occlusion of the vascular anastomoses has no direct impact on fetal hemodynamics [2]. The cardiac response depends on the myocardial status before surgery and the adaptive capacities of the fetus.

In TTTS, myocardial changes, including cardiomegaly, myocardial hypertrophy, insufficiency of the tricuspid (and later, also mitral) valve, cardiac distention, and functional pulmonary atresia, are often observed in recipients rather than donors [3, 4, 5, 6, 7, 8]. Changes in the recipient heart are possibly related to hypervolemia and increased flow in the umbilical vein. They typically resolve after successful SLPCV [1, 9, 10, 11]. Prognostic factors that enable the selection of fetuses with good chances of survival to term, have not been established thus far. We hypothesized that preoperative assessment of myocardial contractility, as well as the changes following laser photocoagulation, might predict the outcome. In cases of poor adaptation, one might consider inotropic support. If effective, this might promote in utero recovery as well as prevent functional pulmonary atresia, or other persistent cardiac changes.

Whereas most donor fetuses do not display contractility changes, they are prone to postoperative circulatory overload, which in turn might lead to tricuspid insufficiency and decreased contractility.

The aim of our study was to evaluate changes in myocardial contractility that take place in recipients and donors after SLPCV.

Methods

This study included 51 consecutive pregnant women, patients of the Department of Obstetrics at the Medical University of Gdansk (Poland), who were subjected to SLPCV due to TTTS between 2007 and 2012. All women were between 16 and 26 weeks of gestation. The protocol of the study was approved by the Local Ethics Committee of the Medical University of Gdansk, and the patients gave their informed consent before the start of any procedure.

The diagnosis of TTTS was made on the basis of the following criteria: increased volume of the amniotic fluid in the amniotic sac of one fetus ($DVP > 8$ cm), and decreased volume of the amniotic fluid in the amniotic sac of the other fetus ($DVP < 2$ cm) [8].

Ultrasonography was performed within 24 hours before laser occlusion of anastomoses and one day after the procedure. The patients were followed-up for one week, with control examinations on postoperative days 1, 3(4), and 7. Laser surgeries were performed by two operators (MSF and KP) and perioperative ultrasound examinations were done by two obstetricians (MSF and KL).

Fetal heart contractility in both fetuses was evaluated using M-mode projection by determining the shortening fractions of the left and right ventricles (FS LV and FS RV, Figure 1). Measurements were repeated in triplicate, in subsequent cycles, and the mean was calculated [12]. We considered the following reference ranges of FS: normal values 25-45%, mild decrease 15-25%, severe cardiac dysfunction $< 15\%$ [13].

From 2009 onwards, also the myocardial performance index (Tei-Index) was measured (Figure 2). We considered the normal range of this parameter as defined by Huhta, i.e. 0.41 ± 0.05 and 0.38 ± 0.05 for the left and right ventricle, respectively [14]. There were also Polish attempts of defining the reference ranges for myocardial performance index. Specialists from the Department of Perinatology and Perinatal Cardiology, supervised by Prof. Joanna Szymkiewicz-Dangel, examined a group of 140 healthy patients and defined the normal values of Tei-Index for the left and right ventricle as 0.47 ± 0.07 and 0.48 ± 0.07 , respectively. However, the results of that study were published in 2011, and since our experiment had started earlier, we still used the reference ranges proposed by Huhta.

Only cases where both twins survived the surgery were included in further analyses. Continuous variables (shortening fractions and Tei-Index values) were presented as arithmetic means and their ranges. Their normal distribution was tested with the Shapiro-Wilk test. Mean pre- and post-operative values were compared using the paired Student *t*-test for dependent variables. Calculations were performed using Statistica 7 (StatSoft®, Poland) software, with statistical significance defined as $P \leq 0.05$.

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Results

The mean pre-operative value of FS LV in recipients was 35.7%, as compared to 42.8% in donors. Following SLPCV, the mean FS LV in the recipient group increased to 44%, as compared to 41% in donors. Compared to pre-operative values, there was a significant increase in postoperative FS LV in recipients ($P=0.037$), whereas there was no change in donors ($P=0.420$, Table 1). The shortening fraction increased postoperatively in all but one recipient. In the one aforementioned case, the postoperative shortening fraction value was lower than preoperatively due to an episode of supraventricular tachycardia, which developed prior to SLPCV and resolved after one day of digoxin therapy. This case was excluded from further analysis.

In recipients, the mean FS RV increased significantly from 27.6% before SLPCV to 32.9% ($P=0.021$) thereafter. No significant increase in FS RV was observed in donors (Table I).

Besides the shortening fraction, heart contractility was evaluated using the Tei-Index ($n=37$). We considered the normal range of this parameter as defined by Huhta¹³, i.e. 0.41 ± 0.05 and 0.38 ± 0.05 for the left and right ventricle, respectively. Mean pre- and postoperative Tei-Index values for the left and right ventricles in donors were within the normal range. In the case of recipients, pre-operative Tei-Index values for both, the right and left ventricle were above normal, suggesting impaired myocardial function. Improvement in the performance of both ventricles was observed after surgery. The mean postoperative Tei-Index for the left ventricle decreased to 0.49 ($P=0.011$). No significant improvement was noted in right ventricle function (Table I).

Shortening fractions can be classified into four categories: markedly impaired contractility (<15%), mild decrease (15-25%), normal values (25-45%), and hyperkinetic values (>45%). We did not observe any abnormalities in the left ventricle of donors (although the left ventricular contractility was slightly impaired, it still remained within the normal range). Mild right ventricular contractility disorders (15-25%) were documented in 3 fetuses; they normalized after the surgery. In contrast, severe contractility disorders were observed in the left and right ventricle of recipients, in 2 and 7 fetuses, respectively. Additionally, there were 3 cases of mild left ventricular disorders and 5 cases of mild contractility decrease in the right ventricle. Following the surgery, a transition from severe hypokinesia to hyperkinesia (64-82%) was documented in the two fetuses with left ventricular contractility disorders; the left ventricular contractility decreased gradually during seven-day follow-up, and eventually the intrauterine death of the recipient was revealed in both cases. Myocardial contractility normalized in all fetuses from the

group with mild left ventricular decrease. Following the surgery, markedly impaired right ventricular contractility of 7 recipients normalized ($n=3$), improved to the mild decrease category ($n=3$), or remained unchanged ($n=1$). Additionally, the postoperative right ventricular function normalized in all recipients whose baseline contractility ranged between 15% and 25%.

Abnormal Tei-Index values for the left and right ventricle were documented in 5 and 6 donors, respectively. The right ventricular values of all fetuses normalized after the surgery; also the left ventricular values improved postoperatively, including 3 cases of normalization. Significantly poorer myocardial function was documented in the recipients. Abnormal Tei-Index values for the left ventricle were observed in 15 fetuses; following the surgery, they normalized ($n=9$), improved but did not reach the normal level ($n=4$), or worsened ($n=2$). Abnormal Tei-Index values for the right ventricle were documented in 17 fetuses; they improved in 14 patients (including seven cases of normalization), and worsened in 3 fetuses.

Intrauterine death of one fetus, recipient ($n=2$) or donor ($n=5$), was documented in 7 cases. Forty-four patients delivered two live neonates, each. Mean gestational age at delivery equaled 31.4 weeks, and mean birth weight of donors and recipients amounted to 1530 g and 1750 g, respectively.

Discussion

Selective laser coagulation of communicating vessels is currently the most effective and efficient method of TTTS management. However, it remains impossible to fully predict the outcome, which may depend on the ability of the fetus to adapt to the new hemodynamic situation after SLPCV.

Several studies have shown an improved cardiac function following laser photocoagulation [2, 12, 14]. In the present study, the prognosis was markedly worse in fetuses in whom myocardial function was already impaired before the surgery. Surprisingly, the results of cases where the recipient heart switched from hypo- to hyperkinesia shortly after the surgery were worse than cases where improvements in contractility were slower or virtually absent.

Currently, in our center digoxin is administered prior to SLPCV in all pregnant women with detected fetal recipient myocardial hypokinesia. However, low number of such cases does not allow for drawing any conclusions, and therefore they were not included in hereby presented analysis.

Compared to the whole cohort of patients operated at the Department of Obstetrics, Medical University Gdansk, in which two live newborns were delivered in 62% of the cases, our group

Table I. Fetal myocardial contractility before and after laser photocoagulation of communicating vessels in donors and recipients with TTTS.

Parameter	Donors			Recipients		
	preoperatively	postoperatively	P	preoperatively	postoperatively	P
FS LV	42.8±8.4	40.7±9.1	0.420	35.7±12.1	44.0±12.8	0.037
FS RV	38.0±9.6	40.6±9.5	0.178	27.6±14.5	32.9±14.5	0.021
Tei Index LV	0.43±0.09	0.39±0.08	0.054	0.55±0.14	0.49±0.09	0.011
Tei Index RV	0.38±0.09	0.39±0.09	0.818	0.60±0.23	0.57±0.20	0.093

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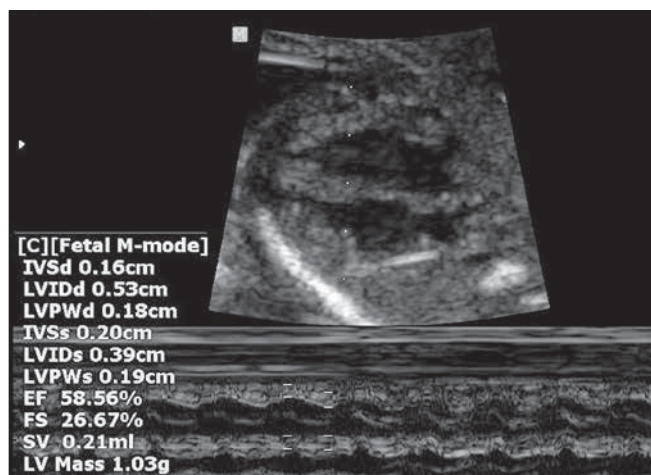


Figure 1. Example measurement of shortening fractions.

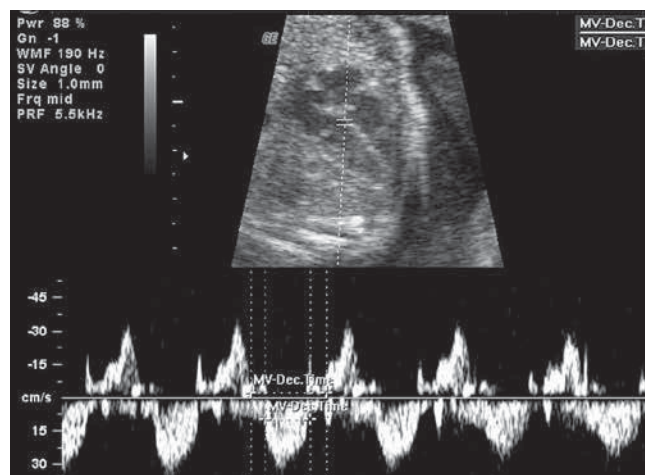


Figure 2. Example measurement of myocardial performance index.

included as many as 86% of the patients who gave birth to two live twins [15]. Most fetal deaths occurred within one week after SLPCV (these cases were excluded from the study). Hopefully, careful observation of operated patients, including comprehensive evaluation of the cardiac function, will enable early identification of cases at risk and proper intervention, namely administration of preparations improving fetal myocardial contractility.

Changes in the heart contractility of the fetuses after SLPCV are still the subject of research, and as such, relevant literature is sparse. There are some studies pertaining to echocardiography in pregnancies complicated with TTTS, however they mostly refer to cardiovascular complications in recipients and donors [3, 4, 5, 6, 7, 8]. It is plausible that an increase in our knowledge will enable the implementation of clinical algorithms of management before and after SLPCV, depending on echocardiographic findings.

In conclusion, this study revealed that SLPCV induces a significant increase in myocardial contractility in recipients. One can speculate that too large of an increase in cardiac contractility in recipients in whom impaired contractility was previously detected, may be associated with an elevated risk for compensation ability depletion and thus may result in cardiovascular insufficiency. Therefore, pharmacological treatment of myocardial contractility in recipients seems advisable prior to SLPCV. At present, it is hard to distinguish which method, shortening fraction determination or Tei-Index measurement, is more accurate for the assessment of myocardial contractility. These two methods give comparable results. We speculate that the measurement of the shortening fraction seems to be more useful during the observation of fetuses immediately after surgery, while Tei-Index is helpful in determining the moment of result normalization and for further control until pregnancy completion.

In conclusion, SLPCV is reflected by a significantly increased myocardial contractility in recipients and a slightly decreased contractility in donors.

Oświadczenie autorów

1. Katarzyna Leszczyńska – pomysł pracy, gromadzenie i analiza danych, redakcja, wykonywanie badań ultrasonograficznych przed i po zabiegach SLPCV - autor zgłaszający i odpowiedzialny za manuskrypt.
2. Krzysztof Preis – przeprowadzanie zabiegów SLPCV, gromadzenie i analiza danych.

3. Małgorzata Świątkowska-Freund – przeprowadzanie zabiegów SLPCV, wykonywanie badań ultrasonograficznych, gromadzenie i analiza danych.
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