

Myocardial Contractile Dysfunction is Associated with Fetal Cardiac Bypass in a Sheep Model

Jodie Y. Duffy, PhD; R. Scott Baker, BS; Mitali Basu, MS; Danielle Everman; Casey Reed; Emily Heeb; Pirooz Eghtesady, MD, PhD
Cincinnati Children's Hospital Medical Center, Division of Cardiothoracic Surgery, Cincinnati, Ohio
University of Cincinnati College of Medicine, Department of Surgery, Cincinnati, Ohio

Abstract

Objective: Declining cardiac output and placental dysfunction are the key barriers to successful fetal cardiac bypass for *in utero* repair of congenital heart defects. Identifying myocardial dysfunction, especially in the RV that is considered the systemic ventricle in fetal life, may be important for success. We hypothesized that fetal cardiac bypass results in myocardial contractile dysfunction that reduces cardiac output and placental perfusion, leading to placental dysfunction and fetal demise.

Methods: Three fetuses from mid-term pregnant ewes were subjected to 30 min of cardiac bypass and followed for 120 min after bypass. Piezoelectric crystals (Sonometrics, Ontario, CA) were placed on three axes of the fetal heart and pressure catheters (Millar Instruments, Houston, TX) were inserted in the left ventricle (LV) and right ventricle (RV). Data were analyzed by repeated measures ANOVA with Fisher's PLSD post hoc analyses.

Results: Representative RV pressure-volume loops showed that preload increased after bypass, indicated by increased end-diastolic volume (mean 4.1±.7 vs. 4.4±1 mL) and pressure (mean 14.3±7 vs. 31.3±3 mmHg, P<.05). RV contractility decreased after bypass: pre-bypass dP/dt_{max} (mmHg/sec) - 880±93 vs. 731±102 at 120 min after bypass (P<.1) and dP/dt_{min} - 798±4 vs. 689±11 (P<.1). Preload recruitable stroke work (slope of regression line) also decreased from 28.5±7 pre-bypass to 22.1±5 at 120 min post-bypass.

Conclusions: Increased RV preload and RV contractile dysfunction are evident after fetal cardiac bypass. Minimizing the associated myocardial dysfunction is important for the success of fetal surgery to repair complex congenital heart defects.

Introduction

Preservation of myocardial function and fetal cardiac output are crucial for successful clinical translation of fetal cardiac surgery. Therefore, assessing the effects of fetal surgery and bypass on the fetal myocardium, especially the RV (the systemic ventricle in fetal life) would be of great significance. The purpose of the following experiment was to determine whether there is myocardial dysfunction of the right and left ventricles during and after fetal bypass and to determine the components that may contribute to this pathophysiology through the analysis of pressure-volume loops during each cardiac cycle.

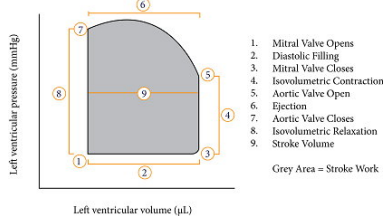


Figure 1. Schematic of Pressure-Volume Loop through One Cardiac Cycle.¹

Aim

We hypothesized that fetal cardiac bypass could result in myocardial contractile dysfunction that reduces cardiac output.

Methods

1. Singleton and twin pregnant ewes from 90-110 days of gestation were studied. Catheters were placed in the ewes' femoral artery and vein for measurement of blood gases and delivery of intravenous fluids, respectively.
2. After midline laparotomy and minor hysterotomy, catheters were placed in the fetal femoral artery for blood gas measurements, blood sampling, and pressure monitoring. Additionally, an umbilical flow probe, 4-6 mm (Transonic Systems, Ithaca, NY) was placed on the common umbilical artery to measure placental blood flow.
3. Through a fetal median sternotomy, the fetal heart was exposed and piezoelectric crystals (Sonometrics, Ontario, CA) were placed on three axes of the fetal heart to measure changes in ventricular dimensions. Pressure catheters (2F, Millar Instruments, Houston, TX) were then inserted into the RV and LV to develop pressure-volume loops.
4. The ovine fetuses (n=3) were subjected to 30 min of cardiac bypass with a target flow rate of 200-250 mL·kg⁻¹·min⁻¹ and followed for 120 min post-bypass.
5. Maternal and fetal arterial blood gases are collected immediately upon gaining arterial access at hysterotomy, immediately prior to bypass (pre-bypass), every 15 min during bypass, and every 30 min after bypass until completion of the study at 120 min post-bypass.
6. Fetal hemodynamic variables were monitored and recorded continuously on a PowerLab data acquisition system (ADInstruments, Colorado Springs, CO) during experiments. Complex hemodynamic and contractile parameters of cardiac function were analyzed using CardioSoft (Sonometrics, Ontario, CA).
7. Data were analyzed by repeated measures ANOVA with Fisher's PLSD post hoc analyses.

Results

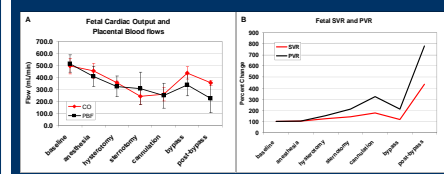


Figure 2. Changes in Fetal Hemodynamic Parameters with Cardiac Bypass. A: Fetal cardiac output and placental blood flow decline during the course of fetal surgery and fetal bypass. Cardiac output (CO) and placental blood flow (PBF) temporarily improve during bypass before declining post-bypass. B: A transient rise in systemic vascular resistance (SVR) and placental vascular resistance (PVR) are seen prior to bypass with a subsequent profound rise in afterload post-bypass. The animals are instrumented with flow probes and pressure monitors prior to surgery.

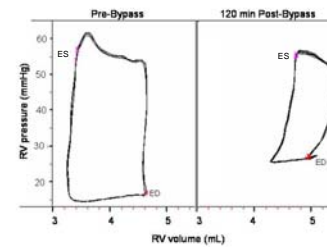


Figure 3. Representative Right Ventricle Pressure-Volume Loops from Fetal Sheep Prior to Fetal Cardiac Bypass and 120 min after Bypass. Increased preload after bypass is indicated by increased end-diastolic volume (mean 4.1 ± 0.7 vs. 4.4 ± 1 mL) and pressure (mean 14.3 ± 7 vs. 31.3 ± 3 mmHg, P<.05). Stroke work, the area within the loop, decreases after bypass. End-systole (ES) and end-diastole (ED) are marked for each cardiac cycle.

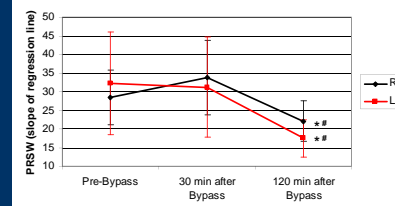


Figure 4. Preload Recrutable Stroke Work (PRSW) with Fetal Cardiac Bypass. PRSW, a measure of ventricular contractility, declines 120 min after fetal bypass in the RV and LV. * P<.0.10 vs. pre-bypass; # P<.0.10 vs. 30 min after bypass. Values are mean ± standard deviation (n=3).

Results (continued)

Fetal Parameters	Pre-Bypass	30 min after Bypass	120 min after Bypass
Heart Rate (beats/min)	167 ± 12	189 ± 27	193 ± 32
RV Output (mL/min)	220 ± 99	196 ± 29	75 ± 21 ^{b,c}
LV Output (mL/min)	315 ± 52	347 ± 13	351 ± 70
RV EDP (mmHg)	14.4 ± 7	26.3 ± 2 ^b	31.3 ± 4 ^b
LV EDP (mm Hg)	17.3 ± 2	14.8 ± 4	14 ± 2
RV dP/dt _{max} (mmHg/sec)	880 ± 93	975 ± 102	731 ± 102 ^c
LV dP/dt _{max} (mmHg/sec)	915 ± 169	1014 ± 113	772 ± 91 ^{a,c}
RV dP/dt _{min} (mmHg/sec)	798 ± 4	854 ± 113	688 ± 11 ^{a,c}
LV dP/dt _{min} (mmHg/sec)	851 ± 111	883 ± 30	708 ± 17
RV Tau (msec)	59.2 ± 3.7	51.1 ± 6.2	63.8 ± 7 ^a
LV Tau (msec)	34.1 ± 14.9	39.5 ± 12.5	48.5 ± 15

Table 1. Cardiac Hemodynamics and Parameters in Fetal Sheep Undergoing Cardiac Bypass. RV cardiac output declined and end diastolic pressure rose after fetal bypass. RV and LV dP/dt_{max} were depressed 120 min after bypass. RV dP/dt_{min} and Tau, indicators of diastolic function and relaxation, were worse by 120 min after bypass. There was less myocardial dysfunction evident in the LV compared with the RV. EDP, end-diastolic pressure; dP/dt: derivative of the change in pressure over the change in time; Tau: relaxation constant. a = P<.0.10 vs. pre-bypass, b = P<.0.05 vs. pre-bypass, c = P<.0.10 vs. 30 min after bypass. Values are mean ± standard deviation (n=3).

Conclusions

1. Increased RV preload and afterload occur after fetal cardiac bypass.
2. Complex functional parameters, PRSW and Tau, indicate that there are changes in cardiomyocyte function associated with fetal bypass.
3. Greater myocardial dysfunction is evident in the RV, the systemic ventricle in fetal life, compared with the LV.
4. Minimizing the associated myocardial dysfunction is important for the success of fetal surgery to repair congenital heart defects.

References:

¹Pressure-Volume Loop, 2008, ADInstruments. http://www.adinstruments.com/applications/image_new/bv01.jpg (Accessed on-line October 15, 2008).

No Financial or Regulatory Disclosures