Early Human Development (2007) **83**, 263–267

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Noninvasive measurement of isovolumetric contraction time by Doppler cardiography can be substituted for fetal cardiac contractility: Evaluation of a fetal lamb study

Shoji Satoh [a,*], **Yasuo Yumoto** [b], **Yasuyuki Fujita** [b], **Naoko Kinukawa** [c], **Hitoo Nakano** [b]

[a] *Maternity and Perinatal Care Center, Oita Prefectural Hospital, Bunyo 476, Oita 870-8511, Oita, Japan*
[b] *Department of Obstetrics and Gynecology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan*
[c] *Department of Medical Information Science, Kyushu University Hospital, Fukuoka, Japan*

Accepted 15 June 2006

KEYWORDS
Isovolumetric contraction time;
Fetal cardiac contractility;
Pre-ejection period;
Doppler cardiography

Abstract

Objective: The objective of this study is to clarify whether the isovolumetric contraction time obtained from Doppler cardiography (Doppler ICT) can be an index substituted for fetal cardiac contractility.
Materials and methods: In 10 pregnant ewes, fetal hypoxemia was induced by giving a variable mixture of gases. Through experiment, the Doppler ICT, pre-ejection period (PEP), and the maximum first derivative of the left ventricular pressure waveform (Max d*p*/d*t*) were simultaneously recorded every 10 min. The relationship between both the Doppler ICT and PEP, and the Max d*p*/d*t* were analyzed.
Results: A significant negative linear regression was founded between the Doppler ICT and the Max d*p*/d*t*. A significant negative linear regression was also shown between PEP and the Max d*p*/d*t*. Moreover, the regression of Max d*p*/d*t* on ICT had significantly less residual variance than the regression of Max d*p*/d*t* on PEP ($p=0.0004$).
Conclusion: In contrast to PEP, Doppler ICT is a reliable, and non-invasive index which can be substituted or fetal cardiac contractility.

1. Introduction

External measurement of the pre-ejection period (PEP) or is volumetric contraction time (ICT), in cardiac systolic time interval (STI) analysis, has been described to assess ventric-

* Corresponding author. Tel.: +81 97 546 7111; fax: +81 97 546 0725.
E-mail address: satohs@oitakenbyo.jp (S. Satoh).

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doi:10.1016/j.earlhumdev.2006.06.001

ular performance [1,2]. Even in the fetus, PEP is defined as the interval between the onset of the Q wave in fetal electrocardiogram (ECG), which can be detected by using scalp electrode, and the opening of the aortic valve in Doppler cardiogram [3,4]. It has been reported that PEP is a useful indicator of myocardial function in the fetus, provided that the fetal ECG can be clearly traced [5].

On the other hand, some investigators have attempted non-invasive ICT measurement, which is defined as the interval from the signal of mitral valve closure to aortic valve opening (Ao) based on Doppler cardiac signal in the antenatal period [6,7]. However, this method has not been widely used in clinical practice because of the difficulty in differentiating mitral valve closing (Mc) from atrio-ventricular flow signals. We reassessed the significance of fetal ICT and found a band-pass filter setting, narrower than previously reported, enabling us to detect both Mc and Ao signals for calculating the Doppler ICT accurately [8]. The fact that a prolonged Doppler ICT clinically predicted adverse outcome in the human fetus [9] implies that impaired cardiac function could be sensitively detected by Doppler ICT. Through the animal experiment to validate Doppler ICT for fetal cardiac performance, external Doppler ICT values coincided well with the true ICT, measured by intracardiac catheterization, and reflected left ventricular contractility in the fetal lamb study [10]. Although the question of the superiority between PEP and Doppler ICT remains, there has yet to be any report on the comparison of these two parameters in STIs for evaluating fetal cardiac function. Hence, the purpose of this study is to clarify whether Doppler ICT can be an index substituted for fetal cardiac contractility.

2. Materials and methods

2.1. Animal preparation

Ten pregnant ewes at 128—135 days of gestation were included in this study. They were fasted for 24 h before the operation. Anesthesia was induced with sodium thiopental (Pentothal 500 mg), and after intubation, maintained by artificial ventilation with oxygen and 2% isoflurane. The uterus was first exposed by a vertical midline incision. A small incision was made in the uterus and the hind limb was withdrawn. A polyvinyl catheter was inserted into the femoral artery and 15 cm into the descending aorta. This catheter was used to obtain samples for blood gas analysis. After closure of the uterine incision, another small incision was made to withdraw the fetal head, neck and chest. A catheter pressure transducer (Micro-Tip 3-F Model SPC-330, Millar, Tokyo, Japan) was inserted in the left ventricle (LV) after insertion into the right carotid artery. This catheter was used to record the LV pressure waveform. The position of pressure transducers was confirmed using ultrasonography. To record the fetal ECG, three silver electrodes were fixed in the subcutaneous tissue of the chest. After the position and axis of the heart were confirmed using ultrasonography, a continuous ultrasound transducer (FD-390, TOITU, Tokyo, Japan) was held manually against the upper right parasternal line, and the transmitting beam was directed along the axis of the heart. This equipment was used to record the Doppler cardiac signal necessary to measure the external ICT. The transmitted beam had a 2.5 MHz plane wave without focusing (ultrasound power 10 mW/cm^2) and the amplifier range was from 250 to 1500 Hz. When the high frequency Doppler sound of outflows following a sharp valvular sound was confirmed, the transducer was fixed. To maintain the body temperature of the fetus during the experiment, we used heat-retaining pads (TR-100 Temperature Controller, Fine Science Tools INC, North Vancouver, Canada). All surgery was done using aseptic techniques and the experiments were performed acutely. After the experiment, the ewes and the lambs were euthanized with intravenous sodium pentobarbital (50 mg/kg) infusion. All studies were approved by the Committee on Animal Research at Kyushu University.

2.2. Experimental procedure

After preparation, we confirmed that neither hypoxemia nor acidemia were present in the fetal lamb. Under artificial ventilation, the ewe was given a mixture of 10% oxygen, 4% carbon dioxide and 86% nitrogen. The endpoint of this acute experiment was the slowing of the fetal heart rate (FHR) to the 110 beats per minute (bpm). The experiment generally lasted between 40 and 70 min. All signals were monitored continuously throughout the experiment (Fig. 1).

The LV pressure waveform, fetal ECG and external Doppler cardiac signal were recorded at a sampling rate of 4 kHz, using a data recorder (PowerLab Chart/8s, AD Instruments, Tokyo, Japan) and stored in a personal computer after processing through a low-pass digital filter to remove noise signals.

(a) Max dp/dt: The LV pressure waveform was converted to the first derivative in order to detect the maximum first derivative (Max dp/dt) of the LV, as the representative parameter of myocardial contractility [11].
(b) Doppler ICT: The external Doppler cardiac signal was divided into three different frequency shift ranges through the band-pass digital filter (250—500, 500—1000 and 1000—1500 Hz), where both Mc and Ao signals, the atrioventricular flow signals, and the ventricular outflow signals were clearly detected in the range of 500—1000, 250—500 and 1000—1500 Hz, respectively [9]. We defined the external Doppler ICT as the interval between the end of the Mc signal and the beginning of the Ao signal, in the range of 500—1000 Hz.
(c) PEP: PEP was represented by the period between the onset of the Q wave of the ECG and the beginning of the Ao signal, from the combined fetal ECG- Doppler cardiac signal.
(d) FHR: Instantaneous FHR was measured using the R—R interval of the ECG.

Doppler ICT, PEP, the Max dp/dt of LV pressure waveform and FHR were measured manually as an average of the 5 consecutive cardiac cycles just before maternal hypoxic ventilation, and every 10 min thereafter.