Measurement of Pulse Wave Velocity in Fetal Descending Aorta with Dual Doppler Method: A Preliminary Study

ElJI Ryo (✉ yonchi@med.teikyo-u.ac.jp)

Teikyo University, School of Medicine <https://orcid.org/0000-0003-4626-5234>

Michiharu Seto

Teikyo University, School of Medicine

Keita Yatsuki

Teikyo University, School of medicine

Masayoshi Morita

Teikyo University, School of Medicine

Hideo Kamata

Teikyo University, School of Medicine

Original Paper

Keywords: Fetal blood pressure, Pulse pressure, Pulse wave velocity, Dual Doppler, Ritodrine hydrochloride

Posted Date: February 8th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-161088/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at SN Comprehensive Clinical Medicine on March 24th, 2021. See the published version at <https://doi.org/10.1007/s42399-021-00867-7>.

Abstract

Purpose: Pulse wave velocity (PWV) provides information regarding blood pulse pressure. This study examines the feasibility of using commercially marketed dual Doppler technology to measure PWV in the aorta of the human fetus.

Methods: Thirty-two singleton pregnant women participated. Eight women (tocolysis group) were given ritodrine hydrochloride and the other 24 women (normal group) were not. The descending aorta of the fetus was depicted in the longitudinal direction. Two distant sample volumes were set and two Doppler waveforms were simultaneously obtained. The distance between the two sample volumes was divided by the time interval between the start of the two waveforms, and a PWV value was obtained. 1) Scatter diagrams for the gestational week and PWV were made, and a linear regression analysis was determined. 2) The PWV for the normal group was compared with the PWV for a group described in a previous report, one measured using ultrasonic phased-tracking. 3) The PWV values in the tocolysis group were compared with those in the normal group.

Results: 1) Significant correlations between PWV and gestational weeks were not found. 2) The mean (SE) of the PWV was 2.1 (0.12) m/sec, which was similar to the PWV (2.2 (0.069) m/s) measured with ultrasonic phased-tracking. 3) The mean (SE) of the PWV (2.6 (0.25) m/s) in the tocolysis group was larger than that in the normal group ($p = 0.032$).

Conclusions: The PWV of the descending fetal aorta can be accurately and conveniently measured with a commercially marketed ultrasound machine.

Introduction

Information regarding blood pressure is very important in evaluating the cardio-vascular state in clinical settings; however, for fetuses, there has never been a non-invasive and practical way to do this evaluation.

Several studies have tried to evaluate the blood pressure of fetuses in utero. After doing animal experiments, Fujita et al. [1] reported that the aortic pressure and aortic wall distension waveforms were similar and that an analysis of the distension waveforms using an echo-tracking system could provide information regarding fetal aortic blood pressure. Mori et al. [2] measured human fetal aortic diameter waveforms using a phase-locked loop echo tracking system to obtain the arterial pressure waveform. Struijk et al. [3] estimated fetal blood pressure from two-dimensional color Doppler-derived aortic blood flow and diameter waveforms.

An arterial wall distension change is called a pulse. The pulse transmits distally, and the speed of this transmission is defined as pulse wave velocity (PWV). PWV depends on the blood pulse pressure. Miyashita et al. [4] measured PWV in the human fetal aorta using an ultrasonic phased-tracking method

and estimated pulse pressure. However, up to now, there has been no way to measure human fetal artery diameter waveforms or PWV using a device that is available for clinical use.

Recently, some ultrasonographic machines on the commercial market come equipped with dual Doppler technology, which allows simultaneous measurements of two independent Doppler signals from two different locations. In principle, PWV can be calculated by the time interval between the two different Doppler signals and the distance between the two locations in an artery. Wang Z et al. [5] reported that the PWV of the common carotid artery in a human adult could be measured using the dual Doppler method.

It follows that fetal PWV can also be measured with the dual Doppler technology; however, there have been no reports of PWV measurements in fetuses using this technology. The purpose of this study was to examine the feasibility of using commercially marketed dual Doppler technology to measure the PWV in the descending aorta of human fetuses.

Materials And Methods

Subjects

Thirty-two singleton pregnant women at 22–41 gestational weeks participated in the study. They delivered babies of an appropriate weight for their gestational weeks between February and October 2019 at Teikyo University Hospital. None of the babies had any anomalies. Twenty-four of the women (normal group) were given no medications. The other 8 women (tocolysis group) were diagnosed with threatened premature birth and were given ritodrine hydrochloride via infusion at a speed of between 50 and 200µg. For the tocolysis group, the PWV values were measured during the medication was given. None of the mothers had any other medical complications. Table 1 shows the characteristics of the mothers and newborns in both groups.

Table 1
Characteristics of the mothers and newborns

Characteristics	Normal group (n = 24)	Tocolysis group (n = 8)	p
Maternal age	34.4 (4.7)	32.0(6.0)	0.32
Nulpara/Multipara	13/11	5/3	1.00
Preterm/Term delivery	7/17	3/5	0.68
Vaginal/Cesarean delivery	14/10	5/3	0.42
Newborn's body weight	2831(436)	2820(577)	0.90
Umbilical artery pH	7.28(0.08)	7.32(0.07)	0.29
Data are expressed as median (S.D.) or number.			
Statistical analyses were done using Fisher's exact or Wilcoxon's signed rank test.			

Pulse wave velocity

First, when there were neither fetal movements nor respiratory movements, the descending aorta of the fetus was depicted in the longitudinal direction with a transabdominal B-mode scan (HIVISION Preirus with a C715 5 – 1 R50 probe, Hitachi, Tokyo, Japan). Next, two sample volumes that covered the entire diameter of the aorta were set using the dual Doppler. The distance between the two sample volumes was made as long as possible. Then, the two Doppler waveforms at the two sample volumes were simultaneously obtained. The time interval between the start of the two waveforms was measured. Finally, the distance between the two sample volumes was measured in the B mode image. Figure 1 shows these procedures. The distance between the two sample volumes was divided by the time interval and a PWV value was obtained.

Analysis

From the obtained PWV values, the following examinations were done.

- 1) Scatter diagrams for the gestational week and PWV in the normal and tocolysis groups were made, and a linear regression analysis was applied in each group.
- 2) The PWV values for the normal group was compared with the PWV values measured with the ultrasonic phased-tracking method described by Miyashita et al. [4].
- 3) The PWV values for the normal group were compared with the values for the tocolysis group using Wilcoxon's method.

All data were analyzed with JMP Pro version 13 (SAS Institute Japan Ltd., Tokyo, Japan). The statistically significant level was set at a p-value of less than 0.05.

This study was approved by the ethics committee of Teikyo University. All women gave written informed consent before participating in the study.

Results

Thirty data points from the normal group and 19 data points from the tocolysis group were obtained. The dual Doppler procedure is an established technique and it was not difficult to measure PWV. The measurements took only a couple of minutes, and a PWV could be obtained from almost all fetuses.

1) Figure 2 shows the scatter diagram for gestational weeks and PWV. No significant correlation was found in the normal and tocolysis group ($p = 0.17, 0.55$, respectively).

2) The mean (SE) of the PWV in the normal group was 2.1 (0.12) m/s, which was similar to the PWV (2.2 (0.068) m/s) reported by Miyashita et al. [4].

3) The mean (SE) of the PWV (2.6 (0.25) m/s) in the tocolysis group was larger than that in the normal group ($p = 0.032$) (Figure 3).

Discussion

This study showed for the first time that the PWV in the descending fetal aorta can be measured with a commercially marketed ultrasound machine.

The artery's pulse is the diameter change caused by blood pressure change, i.e. pulse pressure. PWV is widely used as an index of atherosclerosis in adults because PWV depends on the elasticity of the arterial wall. However, PWV depends not only on this elasticity but also on the pulse pressure, because PWV is influenced by the speed of change in arterial diameter which is influenced by pulse pressure. Accordingly, PWV can provide information regarding blood pulse pressure.

In clinical practice, PWV in adults is commonly determined by arterial tonometry. However, Jiang B et al. [6] has reported that there is no difference between PWV values measured by tonometry and Doppler ultrasound. Using dual Doppler technology, Wang Z et al. [5] measured PWV and demonstrated that the measurement was accurate and reproducible, not only in vitro but also in vivo. The results of the present study showed that the PWV values from the fetal descending aorta obtained with the dual Doppler method were similar to those measured with the ultrasonic phased-tracking method. These results support the idea that the dual Doppler method is accurate for measuring PWV in the fetal descending aorta.

There seemed to be a slight positive correlation between PWV and gestational weeks in both groups, but significant correlations were found in neither group. Miyashita et al. [4] reported a weak correlation

between PWV and gestational weeks. The number of participants in the present study was small, and more study is needed before drawing conclusions.

In this study, the fetal PWV of descending aorta was increased when the mothers were given ritodrine infusion. Ritodrine is known to have cardio-vascular side effects, not only for the mother but also for the fetus. Gokay Z et al. [7] reported that ritodrine infusion caused an increase in the left cardiac output in human fetuses. Räsänen J reported that both the volumetric flow and the time-averaged systolic peak, mean, and end-diastolic velocities in the fetal descending aorta were increased by maternal ritodrine infusions. Though further studies are needed before drawing conclusions, the increased PWV shown in this study might indicate increased pulse pressure due to ritodrine's β stimulant effects. The results obtained in this study are reasonable and suggest that measuring PWV with the dual Doppler technology is promising for evaluating the fetal cardio-vascular state.

One of the limitations of PWV measurements is that pulse pressure values depend not only on PWV. Here is an equation from the study by Miyashita et al. [4]

$$\text{Pulse pressure} = 2\rho\Delta d \div d \times \text{PWV}^2$$

(ρ is the blood density, d is the internal diameter of the artery)

Pulse pressure depends also on the elasticity of the artery and the density of the blood; however, little is known about these factors in fetuses, and we cannot yet estimate their influence. More studies are needed to clarify how best to use PWV values in the clinical settings. One possibility, however, would be to follow PWV values in compromised fetuses. This might be a useful way to avoid missing the optimal timing of pregnancy termination, since PWV is presumed to fluctuate more than other factors. Acute prolongation of PWV in a compromised fetus could indicate a menacing drop in blood pressure.

Conclusion

In conclusion, measuring PWV in the fetal descending aorta can be done accurately and conveniently with a commercially marketed ultrasound machine.

Declarations

Acknowledgement

We thank Professor Takuya Ayabe for his support, and we appreciate language help by Mr. Howard Stacey.

- 1) This work was not supported by any funds.
- 2) All authors have no conflicts of interest to declare.

- 3) This study was approved by the ethics committee of Teikyo University.
- 4) All women gave written informed consent before participating in the study.
- 5) All authors consent to publication.
- 6) The corresponding author is ready to show the data when required.
- 7) Code availability:

Not applicable.
- 8) Contributions:

ER; planning the study, writing the manuscript, MS; collecting and interpreting the data, KY; collecting the data, MM; collecting the data, HK; collecting the data.

Conflict of interest

The authors declare no conflict of interest.

References

1. Fujita Y, Satoh S, Yumoto Y, Koga T, Kinukawa N, Nakano H. Fetal aortic distention waveforms for evaluating cardiac function and changes in blood pressure: Fetal lamb validation. *J Obstet Gynecol Res* 2006; **32**: 155-161.
2. Mori A, Trudinger B, Mori R, Reed V, Takeda Y. The fetal aortic pressure waveform in normal and compromised pregnancy. *Br J Obstet Gynaecol* 1997; **104**, 1255-1261.
3. Struijk PC, Mathews VJ, Loupas T, Stewart PA, Clark EB, Steegers EAP, Wladimiroff JW. Blood pressure estimation in the human fetal descending aorta. *Ultrasound Obstet Gynecol* 2008; **32**. DOI: [org/10.1002/uog.6137](https://doi.org/10.1002/uog.6137)
4. Miyashita S, Murotsuki J, Muromoto J, Ozawa K, Yaegashi N, Hasegawa H, Kanai H. Measurement of internal diameter changes and pulse wave velocity in fetal descending aorta using the ultrasonic phased-tracking method in normal and growth-restricted fetuses. *Ultrasound Med Biol* 2015; **41**: 1311-1319.
5. Wang Z, Yang Y, Yuan L, Liu J, Duan Y, Cao T. Noninvasive method for measuring local pulse wave velocity by dual pulse wave Doppler: in vitro and in vivo studies. *PLoS ONE* 2015; **10**, e0120482.
6. Jiang B, Liu B, Mcneill KL, Chowienckz PJ. Measurement of pulse wave velocity using pulse wave Doppler ultrasound: Comparison with arterial tonometry. *Ultrasound Med Biol* 2008; **34**: 509-512.
7. Gokay Z, Ozcan T, Copel JA. Changes in fetal hemodynamics with Ritodrine tocolysis. *Ultrasound Obstet Gynecol* 2001; **18**: 44-46.

8. Räsänen J. The effect of ritodrine infusion on fetal myocardial function and fetal hemodynamics. Acta Obstet Gynecol Scand 1990; **69**: 487-492.

Figures

Figure 1

The descending aorta of a fetus is shown in the left B mode image. The distance between sites 1 and 2 is measured. The image on the right shows the Doppler signals at sites 1 and 2. The time interval (Δt) between the start of the two signals was measured. Pulse wave velocity is calculated as the distance divided by the time interval.

Figure 2

Scatter diagram for gestational weeks and pulse wave velocity. The equations for the linear regression analysis are shown for the normal and tocolysis groups. No significant correlations were found in either group.

Figure 3

Box plot showing pulse wave velocity (median, 25%, 75%, minimum, and maximum) for the normal and tocolysis groups. The values were compared using Wilcoxon's method.