

Doppler assessment of fetal aortic isthmus flow in twin

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Objective

The purpose of this study was to investigate the aortic isthmus (Aoi) flow difference between larger fetus and smaller fetus of twin; and to evaluate the predictive value of early diagnosis of hemodynamic change in twin growth.

Methods

This prospective study on 49 pairs of twin fetuses was performed to obtain Aoi blood flow data. Cases with structural or chromosomal abnormalities and co-twin death were excluded. The interval from examination to delivery was within 4 weeks and 3 cases over 4 weeks interval were re-examined. Assessment of fetal Aoi Doppler parameters were peak systolic velocity (PSV), end-diastolic velocity, times-averaged maximum velocities, pulsatility index (PI), and resistance index (RI). According to the direction of the diastolic flow in the Aoi, antegrade and retrograde flow were made and was used to analyze the perinatal outcomes of each fetus. The predictive value of Aoi Doppler parameters in predicting fetal growth was obtained by using ANOVA and logistic regression analysis of quantitative variables in each fetus of twins.

Results

There were significant differences in the gestational weeks at delivery, birth weight and the incidence of growth discordance over 20% or more between monochorionic twin and dichorionic twin. The Aoi PI and RI were significantly higher in smaller fetus than in larger regardless of chorionicity. Retrograde flow was noted in 8 of 98 cases (8.2%) and the only one case was of the larger fetus and the others were smaller fetuses of twin. Significant correlations were found between the Aoi PI and birthweight ($P=0.018$) and between the PSV and growth discordance ($P=0.032$). In monochorionic twin, linear correlation was shown between the Aoi PI and birthweight ($P=0.004$) and between Aoi PI and growth discordance ($P=0.031$). Also, the meaningful correlation between the PSV and birthweight ($P=0.036$) was found by using logistic regression analyses.

Conclusion

On the basis of our observation, Aoi PI has revealed their hemodynamic status and this result may improve the understanding of growth patterns in twins.

Keywords: Aortic isthmus; Chorionicity; Doppler; Growth discordance; Twins

Introduction

The aortic isthmus (Aoi) is the vascular segment located between the origin of the left subclavian artery and the aortic end of the ductus arteriosus. The Aoi has been suggested to be the only arterial connection between the right and left fetal vascular systems [1]. In placental insufficiency, the fetal circulation shows preferential redistribution of the arterial circulation of cardiac output toward the left ventricle, which maintains an adequate oxygen supply to both brain and the heart. Doppler examination of the umbilical artery and the middle cerebral artery (MCA) have proved to be good predictors of adverse perinatal outcomes. Venous Doppler patterns such as reversed flow in the ductus ve-

nous (DV) and atrial pulsations in the umbilical vein have been advocated as the best predictors of adverse perinatal outcome

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[2,3]. The Aol flow as an indicator of the progression of fetal hemodynamic deterioration in fetuses has been proposed [4].

Discordant twin growth made on serial ultrasound examinations can predict adverse pregnancy outcome. Especially in a smaller fetus of discordant twin, there is a much higher risk for adverse outcome than in an appropriate size of twin fetus [5,6]. Such this discordance usually results from unequal placentation, umbilical cord abnormalities and fetal malformation in dizygotic twins, and vascular anastomoses within the placenta in monozygotic twins [7]. Currently there are no reports on the study of Aol flow in the twin with discordant growth, where the discordant growth is caused by the hemodynamic imbalance.

The purpose of our study is to investigate the Aol blood flow difference between the larger fetus and smaller fetus in twin and the additionally showed the difference of Aol flow by chorionicity and finally to evaluate the clinical usefulness of hemodynamic change in twins.

Materials and methods

This prospective study on twin fetuses was performed between November 2008 and December 2009. The Aol data was obtained from 49 twin pairs (74.4%) out of 66 twins delivered at our hospital during this period. The remaining 17 twins were excluded due to several reasons. In some cases, the Aol images were inappropriate as it was available only to one twin fetus due to fetal position. In other cases, it was unable to measure the Aol blood flow due to the immediate deliveries transferred from another hospital.

The research protocol was approved by the local ethics committee and all subjects gave their informed consent to participate. Gestational age was confirmed by sonographic examination in the first trimester in all cases. There were no cases with structural or chromosomal abnormalities and co-twin death. And there were no twin-to-twin transfusion syndrome in our twins. The mean gestational age to perform Doppler examination was 29.4 weeks (range between 21 and 36 weeks of gestation). The interval from examination to delivery was within 4 weeks. Three cases of over 4 week's interval were re-examined Aol blood flow values and a last result was used for analysis. Image-directed pulsed and color Doppler equipment (ATL HDI 5000 Philips, USA) with a multifrequency sector array transabdominal transducer was used.

The technique of Doppler blood flow of the fetal Aol was as follows: from a horizontal 4-chamber view of the fetal heart, a

90-degree rotation of the transducer provides a sagittal view of the fetus on which the aortic arch can be observed. The isthmus is then identified between the origin of the left subclavian artery and the aortic end of the ductus arteriosus. An angle of less than 30° between the vessel and the Doppler beam was accepted for analysis. Three consecutive Doppler velocity waveforms were analyzed and their mean values of were used for analysis (Fig 1). Assessment of fetal Aol Doppler parameters were peak systolic velocity (PSV), end-diastolic velocity (EDV), times-averaged maximum velocities (TAMXV), pulsatility index (PI), and resistance index (RI).

Recordings were performed during the absence of fetal movement. Furthermore, a qualitative assessment of Aol flow, according to the direction of the diastolic flow in the Aol (i.e., antegrade and retrograde flow) was made and used for analysis of perinatal outcomes of each fetus. We did not measure the isthmus flow index (IFI). One experienced operators have performed all the Doppler measurements.

The perinatal outcome included birth-weight, intertwin discordance, and the Apgar score at 5 minutes. Statistical analysis was performed using SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were computed for all variables considered

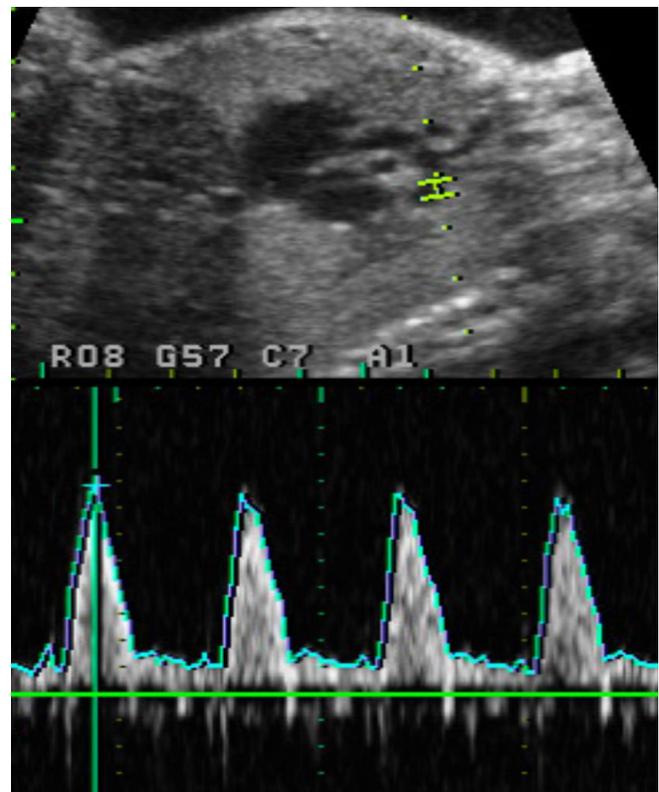


Fig. 1. Ultrasonographic images of aortic isthmus.

in this study. Doppler variables and perinatal outcome were analyzed by Student's *t*-test, Fisher's exact test and Mann-Whitney test as indicated. The Aol blood flow and other Doppler parameters in predicting adverse perinatal outcomes were assessed by two-way ANOVA test and logistic regression analysis. Statistical significance was assumed at $P < 0.05$.

Results

Reliable flow velocity waveforms of the Aol for optimal analysis were obtained in both twin fetuses. The mean maternal age in the study group was 31.7 ± 4.1 years old and the median gestational age was 29.4 weeks (range, 21.3 to 36.5 weeks) at the time of the scan. Gestational weeks at delivery, as well as birth weight were significantly lower in mono chorionic twins. The incidence of growth discordance over 20% or more was double

in mono chorionic twin than that of dichorionic twin. The number of lower Apgar scores at 5 minutes was also shown more commonly in mono chorionic twins (Table 1). The PSV, EDV, and TAMXV value did not differ between larger fetus and smaller fetus. However, the Aol PI and RI were significantly higher in smaller fetus than in larger fetus regardless of chorionicity (Table 2). Retrograde flow was noted in five of 55 cases (9.1%) in dichorionic twin and in three of 35 cases (8.6%) in mono chorionic twins. There were no significant differences between the chorionicity. The only one case out of total 8 cases was of the larger fetus, while the others were of smaller fetuses. In two-way ANOVA, two significant correlations were found between the Aol PI and birthweight ($P = 0.018$) and between the PSV and growth discordance ($P = 0.032$) (Table 3). In mono chorionic twin, a linear correlation between the Aol PI and birthweight ($P = 0.004$) and between Aol PI and growth discordance ($P = 0.031$). Also, there was a meaningful correla

Table 1. Clinical characteristics of the twin fetuses by chorionicity

	DCDA (30)	MCDA (19)	P-value
Maternal age (yr)	31.7±4.1 (22–43)	31.6±4.2 (24–40)	0.857
GA at Aol exam (wk)	29.1±4.5 (21.3–36)	29.8±4.7 (21.5–36.5)	0.499
GA at delivery (wk)	35.2±2.4 (28–38)	33.8±3.2 (26.3–38.3)	0.014
Birth weight (g)	2,201.8±467.2 (1,140–3,010)	1,898.2±540.5 (660–2,740)	0.004
Discordance >20%	4	8	0.020
Apgar at 5 min (less than 7)	1	6	0.013

Values are presented as mean±standard deviation (range) or number.

DCDA, dichorionic diamnion; MCDA, mono chorionic diamnion; GA, gestational age; Aol, aortic isthmus.

Table 2. Doppler flow for PSV, EDV, TAMXV, Aol PI and RI between larger and smaller fetus by chorionicity

	DCDA (30)		MCDA (19)		P-value
	Larger fetus	Smaller fetus	Larger fetus	Smaller fetus	
No. of retrograde flow	1	4	0	3	
PSV (cm/sec)	68.6±17.1 (46.7–115)	68.6±19.5 (25.3–108.2)	69.0±17.9 (40.4–109.4)	74.7±21.2 (40.3–115)	DC=0.98 MC=0.37
EDV (cm/sec)	8.4±4.4 (0–18.6)	6.8±4.4 (0–19.3)	7.6±4.6 (0–15.6)	7.2±8.2 (4.5–36.8)	DC=0.19 MC=0.85
TAMXV (cm/sec)	38.5±9.7 (25.2–65.2)	37.8±10.8 (15.4–63.7)	38.3±10.4 (23.4–62.5)	41.0±13.3 (20.5–75.9)	DC=0.79 MC=0.50
Aol PI	2.01±0.36 (1.32–3.05)	2.53±0.38 (1.75–3.41)	2.17±0.34 (1.59–2.80)	2.65±0.65 (1.67–4.19)	DC=0.000 MC=0.005
Aol RI	0.88±0.06 (0.74–1.00)	0.96±0.10 (0.81–1.28)	0.90±0.05 (0.81–1.00)	0.96±0.09 (0.83–1.21)	DC=0.000 MC=0.010

Values are presented as number or mean±standard deviation (range).

PSV, peak systolic velocity; EDC, end diastolic velocity; TAMXV, time average maximum velocity; Aol PI, aortic isthmic pulsatile index; Aol RI, aortic isthmic resistance index; DCDA, dichorionic diamnion; MCDA, mono chorionic diamnion.

Table 3. The correlation between Aol Doppler parameters and clinical variables

	Peak systolic velocity	Aol PI	Aol RI
Parity	0.941	0.048	0.496
Chorionicity	0.481	0.614	0.496
Birthweight	0.072	0.018	0.800
Growth discordance	0.032	0.118	0.971

Aol, aortic isthmus; Aol PI, aortic isthmus pulsatile index; Aol RI, aortic isthmus resistance index.

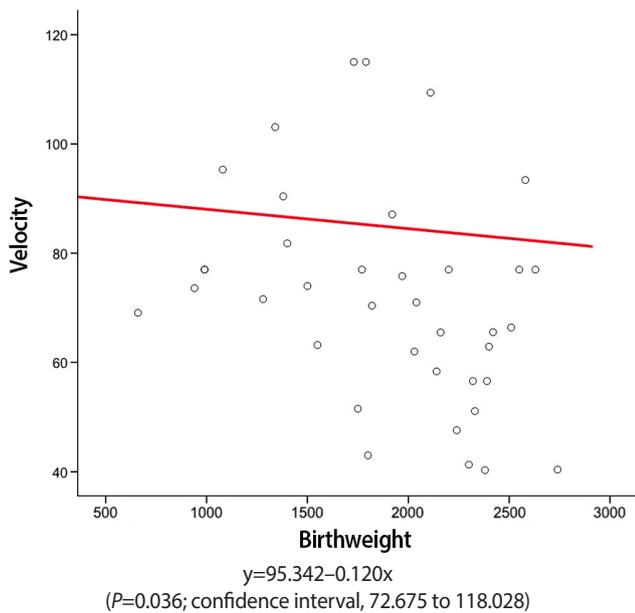


Fig. 2. The correlation between peak systolic velocity and birthweight in monozygotic twin.

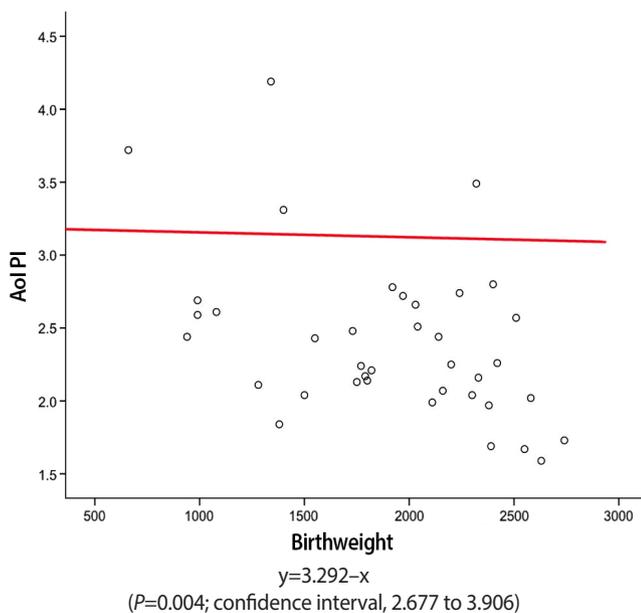


Fig. 3. The correlation between aortic isthmus pulsatility index (Aol PI) and birthweight in monozygotic twin.

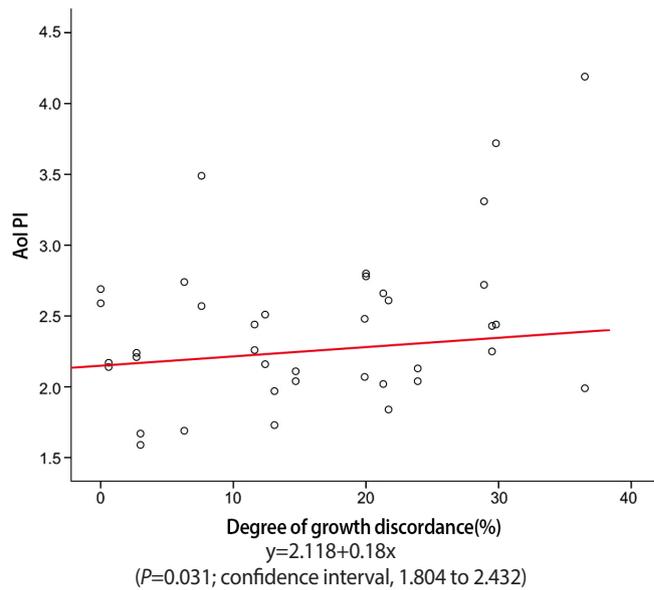


Fig. 4. The correlation between aortic isthmus pulsatility index (Aol PI) and growth discordance in monozygotic twin.

tion between the PSV and birthweight ($P=0.036$); identified by the logistic regression analyses (Figs. 2–4).

Discussion

The Aol is the only arterial connection between the right ventricle and the left ventricle. This means that the Aol blood flow pattern reflects the balance between ventricular outputs and provides the evidence for the differences in vascular impedance in either placental or cerebral vascular system [1,8,9]. Therefore, the Aol blood pattern may act as a reliable indicator of the progression of fetal hemodynamic deterioration in fetus. Intrauterine growth restriction (IUGR), especially when it includes the smaller twin fetus of discordant growth, increases the risk of adverse pregnancy outcome. Since there is no effective fetal therapy for IUGR, the timing of delivery is the key issue in the management of affected fetuses.

With the necessity of valuable monitoring of the optimal time for delivery, Doppler parameter was introduced. Umbilical (UmA) and MCA Doppler findings seem to become abnormal in early stages of placental insufficiency. In contrast, DV flow abnormalities have been described as a late marker, since this occurs within the last week before delivery reflecting adverse perinatal outcome and neurological damage [10–13]. However, there is a gap of some weeks between early and late signs, during which new parameters are needed

for better documentation of fetal deterioration. Specifically, Figueras et al. [14] reported that abnormal UmA PI and MCA PI (i.e., outside the 5th to 95th centile range) showed an almost linear deterioration throughout monitoring of IUGR fetus. Such correlation was shown on average 20 days before delivery. Further, the Aol PI became abnormal on average 13 days before delivery, and 7 days for the DV PI.

Due to its closeness to the heart, the Doppler pattern of the Aol was very pulsatile and showed high systolic and low diastolic velocities than that of the MCA and UmA [15]. With advancing gestation, there were significant increase in the PSV, TAMXV, and the PI of the Aol; whereas the RI and EDV of the Aol remained constant during the second half of pregnancy [16].

Our study did not follow the measure of the Aol Doppler flow throughout the entire gestation of twins. Instead, we have measured the Aol PI and RI at on average of 29.4 weeks and the high Aol RI value was observed in smaller twin fetus than in larger twin fetus. Given the 9% average weight difference between the twin fetuses from our results, the high value of Aol PI on smaller fetus could be seen as the effect of the placental vascular resistance, rather than the gestational age.

Ruskamp et al. [17] has described a semiquantitative parameter called the IFI, which is particularly sensitive to the change in both amount and direction of diastolic flow. The IFI is an improved yet still an imperfect index as it involves the manual calculations. For this reason, we did not apply the IFI in our study. Doppler blood flow measurements across the fetal Aol can be reliably obtained from both three vessels view and the traditional long-axis view [18]. In our study, the Aol values have been taken according to the traditional long-axis method. The small diameter of the Aol precludes measurement of actual blood flow volume and so using PI, which is likely to be the best index to assess blood flow through fetal vessels. Indeed, the PI is angle-independent and analyzes blood flow over time taking into account downstream impedance during the whole cardiac cycles. These characteristics suggest that the PI is a useful dictator of fetal hemodynamic changes throughout pregnancy [19,20]. In our results, the birthweight was significantly correlated with Aol PI but not with Aol RI. Since our study is to investigate the characteristics Aol flow of both twin fetuses, we did not perform to measure the umbilical artery and MCA Doppler flow in all cases. We also did not used clinical decision for intervention of smaller fetus of twin by Aol flow. In 7 cases of our study, the absent and reversed

flow in umbilical artery was not shown in the retrograde Aol flow of smaller twin.

In placental insufficiency, an increase in placental vascular resistance may change the fetal Aol blood flow profile prior to any significant change in umbilical artery blood pattern [20,21]. The cerebral vasodilatation together with the increase in downstream vascular impedance appears to be the main factors accounting for the decrease of absolute velocities in the Aol.

Decreased blood flow velocity in the Aol was observed in virtually all cases with IUGR. This suggests that this is an early event in the fetal response to placental insufficiency, rather than a late event in the hemodynamic deterioration of such fetuses. Moreover, this low blood flow velocity was often associated with increased afterload of the fetal heart leading to a rise in ventricular pressure and wall tension. This may further increase oxygen demand of the myocardium. This is supported by the fact that fetuses with retrograde net blood flow of the Aol were delivered more frequently by cesarean section due to fetal distress [22]. But in our twin data, we did not have to classify to IUGR in twins. We had divided to larger fetus and smaller one in twins. And we investigated Aol values to predict growth discordance between fetuses. Our results were revealed that birthweight were negatively correlated with both the PSV in Aol flow and the Aol PI. We also observed a positive correlation between Aol PI and the growth discordance ratio in both fetuses. This relationship between the Aol PI and growth discordance possibly explains the effects of Aol PI in smaller fetus [23]. And such relationship between Aol PI and the growth discordance is limited to smaller fetus of monochorionic twin. In monochorionic twin, there are more abundant systemic blood volumes than those in singleton and well develop intertwin vascular anastomoses. There are some presumptions in the case where one of the twins has a normal growth, its blood shifts to the other fetus and maintains the Aol blood stream. As the twins share the placenta, pregnant woman's absolute blood volume is greater than the fetal weight and allows maintaining the Aol blood stream. Further study using data collection and follow up will be needed.

On the basis of our observation, Aol PI in twin was revealed their hemodynamic status and this result may improve the understanding of the growth discordance development. There were revealed the smaller fetus had high Aol PI values regardless to chorionicity and the effects of Aol flow were reflected more prominent in monochorion. These findings might be

explained twin hemodynamics and fetal growth in utero.

In conclusion, Aol flow might be meaningful to predict growth discordance in twin at least 4 weeks before delivery.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

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