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The Fetal Growth Velocity and Placental Weight/Birth Weight Ratio in Concordant and Discordant Twins at 20–36 Weeks of Gestation

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Abstract：Objectives：To establish fetal growth velocity curves in twin pregnancy and to investigate the relationship between growth patterns and the placental weight/birth weight ratio (PW–BWR). Methods：Fifty–one concordant and forty discordant twins had ultrasound examinations at weekly or biweekly intervals, from 20 weeks until delivery. The fetal growth velocity (FGV) was calculated for each fetus. Disparities in the FGV and the PW–BWR between larger (L) and smaller (S) fetuses of concordant and discordant twins were determined. Results：Concordant L and S and discordant L fetuses showed similar growth velocity patterns, reaching a maximum at 31 weeks. Discordant S fetuses were growth–retarded at 21－23 weeks, followed by "catch–up" growth until 31 weeks, and then were growth–restricted thereafter. In the concordant twins, no difference in the PW–BWR between L and S fetuses were shown at ＜31 weeks and ≥31 weeks. In the discordant L and S fetuses, the PW–BWR of S fetuses were higher than that of the L fetuses at ＜31 weeks ($P<0.05$), but not different between the L and S fetuses at ≥31 weeks. Conclusion：These findings may suggest an adaptive mechanism in discordant twin fetuses, which maximizes the fetal growth potential of both fetuses, by compensatory changes in the placental weight.

Key words：Twin pregnancy, Fetal growth velocity, Placenta, Ultrasonography

Introduction

The principal determinants of fetal growth are fetal genetic potential and intrauterine environmental factors.[1] The latter mainly include placental factors which modulate fetal growth by providing nutrition and oxygen, and by producing various hormones and growth factors. In singleton fetuses, the placental weight closely parallels the fetal body weight.[2)3)] Small–for–gestational age (SGA) fetuses have heavier placental weight for their body weight,[4)] which may protect against adverse intrauterine environments such as malnutrition or hypoxia.[5)6)]

In twin pregnancy, SGA infants frequently exist when evaluated by singleton standards. However many do not face a worse perinatal outcome than concordant twins.[7)] Therefore, this phenomenon may imply the supposition of an "adaptive mechanism", which enables the growth of twin fetuses to adapt to their intrauterine environment.[8)]

Previous ultrasonic studies focusing on fetal growth were mostly based on growth size curves.[9)] Recent research has demonstrated that the fetal growth velocity is superior to the fetal size in evaluating the dynamic changes of fetal intrauterine growth in singleton pregnancy,[10)] yet no such

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standard of growth velocity for twin fetuses has yet been established.

The focus of this study was to establish the fetal growth velocity curves in twin pregnancy, and furthermore, to investigate the relationship between fetal growth patterns and the placental weight/birth weight ratio to verify the adaptive mechanism in twin pregnancy.

Material and Methods

1. Fetal population

Ninety-six pregnant women who delivered twins at ≥22 weeks and ≤36 weeks of gestation at Fukuoka University Hospital from January 1996 to November 2002 met the following criteria : (1) The gestational age at delivery was calculated from the first day of the last menstrual period and confirmed by the crown-rump length at 9-11 weeks of gestation. (2) At least three ultrasound examinations were received from 20 weeks to delivery. (3) The absence of structural or chromosomal abnormalities in the individual fetuses. After excluding 2 cases with intrauterine death and 3 cases with incomplete data, 91 remaining cases were studied for subsequent analyses. Discordant and concordant twins were defined according to the criteria of whether the difference between the birth weights of the larger (L) and smaller (S) fetuses, divided by that of the L fetus, was >0.15 or not.[11] There were 51 concordant and 40 discordant twin pairs in our study.

2. Data acquisition

The following maternal variables were recorded : 1) maternal age, 2) smoking habit, 3) gravidity, 4) parity, and 5) types of twins (dichorionic diamnionic, monochorionic diamnionic or monochorionic monoamnionic). The neonatal outcome was evaluated as follows : 1) gestational age at delivery, 2) birth weight of each fetus, 3) sex, 4) 1-minute and 5-minute Apgar scores, and 5) neonatal death at 7 days after birth.

The biparietal diameter, anterioposterior trunk diameter, transverse trunk diameter, and femur length were measured for each fetus every week or two, from 20 weeks to delivery. All examinations were performed by experienced obstetricians using transabdominal ultrasonography (Aloka SSD-1700, SSD-5000, Tokyo, Japan) with curvilinear transducers of 3.5 and 5 MHz. Estimated fetal weight (EFW) was calculated according to the Japanese standard formula.[12] A total of 311 and 239 ultrasound examinations were made for concordant and discordant twins, respectively (Table 1). To test how accurate the EFWs were for predicting the actual fetal body weight, 22 twins who were delivered within 1 day of the final EFW measurement were sampled and the differences between the final EFW and actual birth weight were calculated. The difference ratios, defined as (Final EFW-Birth weight)/Birth weight×100%, were 2.6 ±0.3 (mean ± SEM) %.

3. Parameter definition

The FGV was defined as shown in the following formula : $FGV = (EFW_2 - EFW_1)$/number of days between measurements, where EFW_1 represented the value obtained at any given measurement and EFW_2 represented that obtained at the very next measurement of EFW_1. The value of FGV at each gestational week was compared for concordant L and S fetuses as well as for discordant L and S fetuses. The disparity in FGV (DFGV), between L and S fetuses, was determined by subtracting the FGV of the S fetus from that of the L fetus, in the

Table 1. Number of measurements each gestational age

Gestational age (weeks)	Concordant twins (n=51)	Discordant twins (n=40)
20	6	6
21	7	6
22	9	8
23	12	11
24	17	14
25	22	16
26	28	19
27	30	21
28	31	23
29	32	24
30	25	17
31	23	15
32	21	14
33	14	13
34	13	12
35	11	11
36	10	9
Total	311	239

pair.

Furthermore, to elucidate the ideal intrauterine growth model, the FGV of 116 singleton appropriate-for-gestational age fetuses (S-AGA) delivered at 22－36 weeks, meeting the same criteria as twin fetuses, were studied. The FGV constantly increased from 16.3±0.4 grams/day at 20 weeks to reach the maximum of 32.1±0.6 grams/day at 33 weeks of gestation, and then decreased thereafter (Fig. 1).

The placental weight was measured for each fetus after removing blood clots. In the monochorionic or fused dichorionic placenta, the proportion of placenta belonging to each twin was determined by measuring the width, length and T zone of the placental disk. Seven dichorionic and fifteen monochorionic twins were excluded because of our inability to reasonably distinguish the placental regions between the pairs. The placental weight/birth weight ratio (PW-BWR) was defined as the value of the placental weight divided by the birth weight, for each twin.

4. Statistical analyses

The Student t-test, Mann-Whitney U-test, one-way ANOVA and χ^2 test analyses were used, where appropriate, using the statistical analysis software program SPSS 10.0 (Version 10.0 ; SPSS Inc, Chicago, Ill). Data were presented as the mean±SEM. All tests were two sided, and the exact P values were considered to be significant at $P<0.05$.

Results

1. Clinical background parameters

The clinical characteristics of maternal and neonatal parameters are summarized (Tables 2 and 3). There were no significant differences observed in the maternal age, smoking habit, gravidity, parity, twin types, or gestational age at delivery between the concordant and discordant twins. The birth weight was significantly different between discordant L and S fetuses, but not between concordant L and S fetuses. No significant difference of fetal sex, 1-minute and 5-minute Apgar scores, or neonatal mortality were

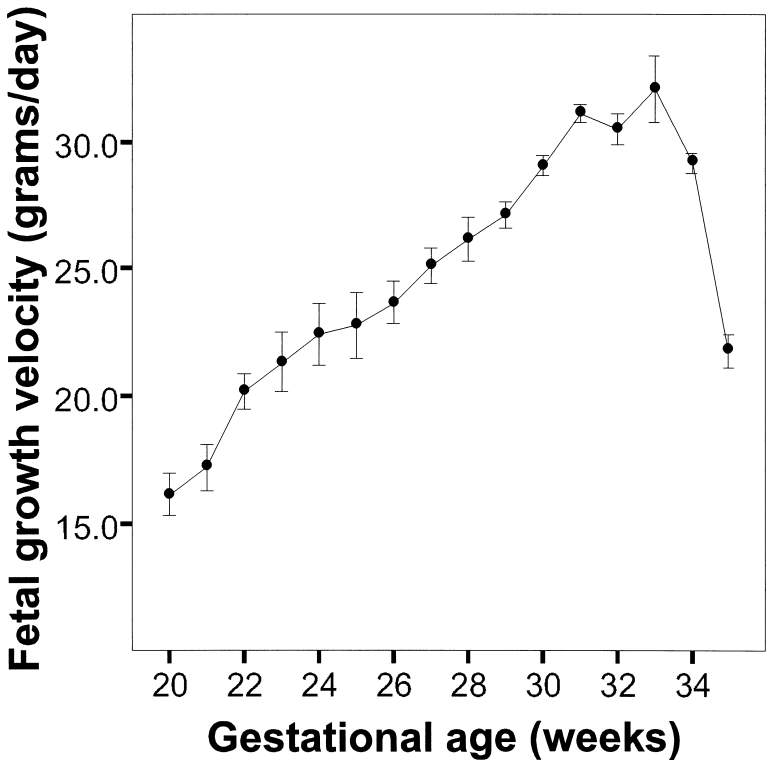

Fig. 1. Fetal growth velocity curve of singleton, appropriate-for-gestational age fetuses. Data presented as the mean±SEM.

Table 2. Maternal characteristics of concordant and discordant twin pregnancy

Characteristic	Concordant twins (n=51)	Discordant twins (n=40)	*P*
Maternal age (y)*	29.5±0.5	28.7±0.5	>0.05
Smoking habit †			
Not currently	40 (78.4)	31 (77.5)	>0.05
Currently	11 (21.6)	9 (22.5)	>0.05
Gravidity*	1.8±0.7	1.7±0.2	>0.05
Parity*	1.5±0.2	1.6±0.1	>0.05
Gestational age (wk)*	29.5±0.5	28.7±0.4	>0.05
Twin type †			
DD	27 (52.9)	21 (52.5)	>0.05
MD	24 (47.1)	19 (47.5)	>0.05
MM	—	—	

* Data are presented as the mean±SEM.
† Data are presented as the number (%). DD:dichorionic diamnionic, MD:monochorionic diamnionic, MM : monochorionic monoamnionic.

Table 3. Neonatal characteristics of concordant as well as discordant twin pregnancy

Type of fetuses	Case No.	Birth weight (g) †	Sex ‡		Apgar scores †		Neonatal death ‡
			Male	Female	1-minute	5-minute	
Concordant L	51	2,031±96	27 (52.9)	24 (47.1)	7.1±0.5	7.9±0.2	3 (5.9)
Concordant S	51	1,901±82	25 (49.0)	26 (51.0)	6.9±0.2	7.5±0.1	1 (2.0)
Discordant L	40	1,916±75*	22 (55.0)	18 (45.0)	7.0±0.6	7.7±0.3	1 (2.5)
Discordant S	40	1,595±78*	19 (47.5)	21 (52.5)	6.8±0.3	7.6±0.4	1 (2.5)

* Comparison between L and S fetuses in concordant or discordant pregnancy, $P<0.05$.
† Data are presented as the mean±SEM.
‡ Data are presented as the number (%).

found between concordant L and S fetuses, or between discordant L and S fetuses.

2. Fetal growth velocity

In concordant twins, both L and S fetuses showed similar growth velocity patterns, thus indicating a gradual increase from 15.9±0.7 (mean ± SEM) and 14.3±0.1 grams/day at 20 weeks, up to 30.5±0.2 and 29.4±0.1 grams/day at 31 weeks, with a gradual decrease thereafter, respectively (Fig. 2). The mean growth velocity of concordant S fetuses was consistently lower than that of the concordant L fetuses, at each gestational age. In the discordant twins, L fetuses had a growth velocity pattern similar to concordant twins, thus indicating a gradual increase from 13.3±0.5 grams/day at 20 weeks to 27.2±0.3 grams/day at 31 weeks, and a gradual decrease thereafter. On the other hand, the growth velocity of S fetuses demonstrated a gradual decrease from 9.3±0.3 grams/day at 20 weeks to 7.5±0.4 grams/day at 23 weeks, and a "catch-up" tendency to 23.3±0.2 grams/day at 31 weeks, with a rapid decrease thereafter.

3. Disparity in fetal growth velocity

There was no significant change in the disparity in the growth velocity between L and S fetuses, in concordant twins, from 20 to 35 weeks. However, in discordant twins, a significant change in the disparity in growth velocity was detected with two critical points at 23 and 31 weeks. The value of disparity increased from 3.1±0.5 grams/day at 20 weeks to 11.3±0.4 grams/day at 23 weeks, then decreased to 3.2±0.1 grams/day at 31 weeks and finally increased again thereafter (Fig. 3).

4. Placental weight/birth weight ratio

In concordant L and S fetuses, the PW-BWR between L and S fetuses (23 pairs) at <31 were not significantly different to that between L and

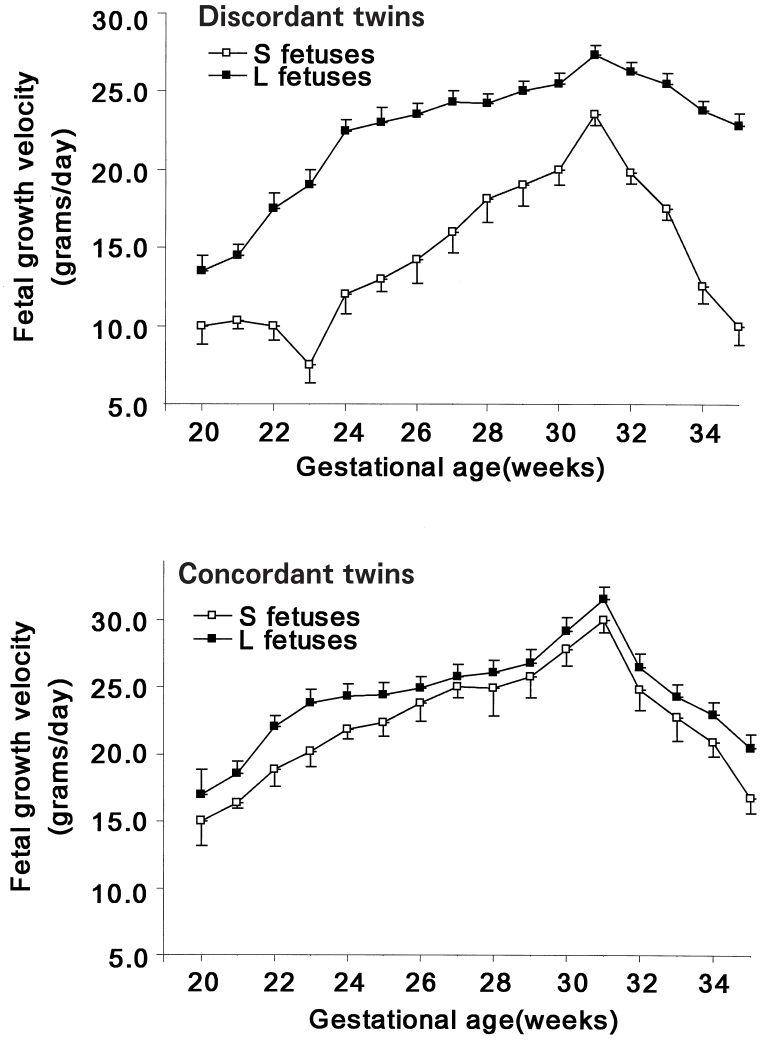

Fig. 2. Fetal growth velocity curves of discordant L and S fetuses, as well as concordant L and S fetuses. Data presented as the mean±SEM.

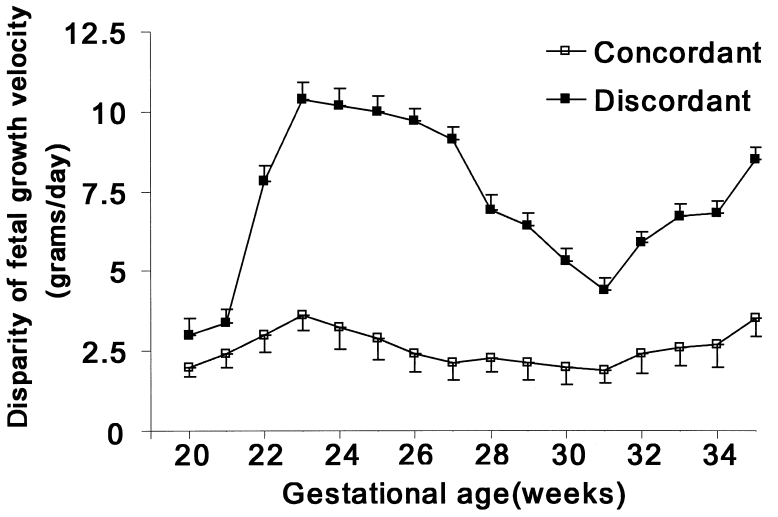

Fig. 3. The disparity of fetal growth velocity represented between L and S fetuses, in concordant and discordant twins. Data presented as the mean±SEM.

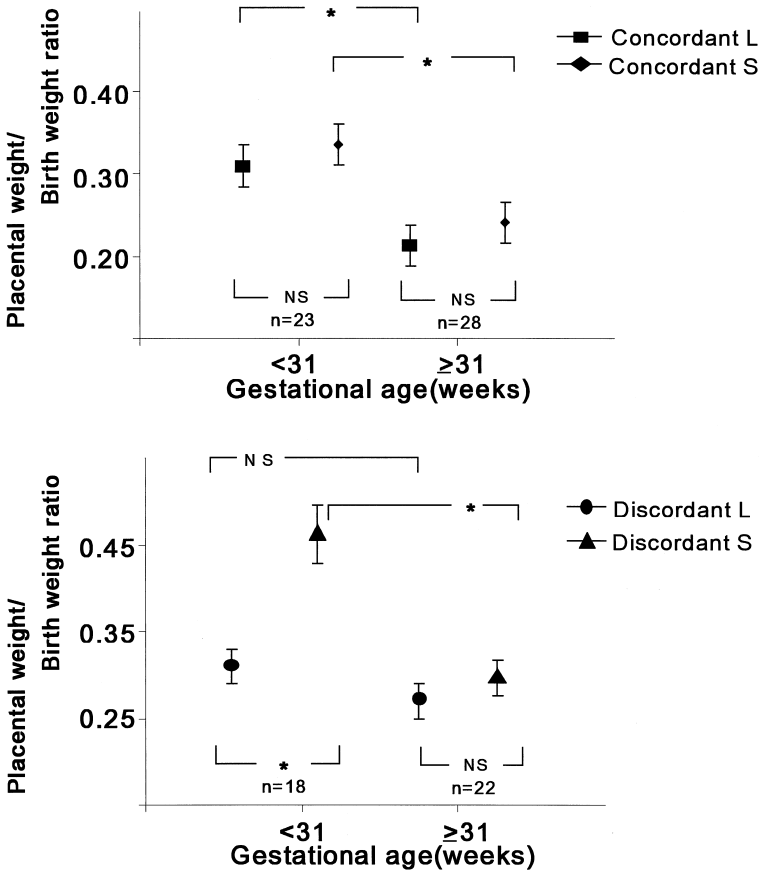

Fig. 4. Placental weight/birth weight ratio in concordant and discordant twins. Data presented as the mean±SEM. *: $P<0.05$. NS: not significant.

S fetuses (28 pairs) at ≥31weeks (Fig. 4). In discordant twins, the PW-BWR between L and S fetuses (18 pairs) was significantly different at <31 weeks (L:0.31±0.05 vs. S:0.45±0.04) ($P<0.05$), however, the PW-BWR between L and S fetuses (22 pairs) was not significantly different at ≥31 weeks. No significant difference was shown in this ratio for L fetuses between <31 weeks and ≥31 weeks. The ratio in S fetuses significantly decreased from 0.45±0.04 at <31 weeks to 0.30 ±0.02 at ≥31 weeks of gestation.

Discussion

This study is an extension of previous reports[13)-15)] which demonstrated the fetal growth velocity of twin fetuses to be restricted as early as 30 weeks by revealing in both concordant and discordant twin fetuses the maximum fetal growth velocity to appear at 31 weeks of gestation. Together with the finding that in singleton fetuses the growth velocity has the peak value at 33 weeks, the overall fetal growth process is accelerated in concordant as well as discordant twins, in comparison to singleton fetuses.

To compare the disparity of growth velocity between L and S fetuses in concordant and discordant twins more distinctly, we created the disparity curves of fetal growth velocity. In concordant twins, there was no significant change in the disparity of fetal growth velocity from 20 to 35 week of gestation. This finding indicated that both L and S fetuses had similar growth patterns throughout the observed pregnancy. On the other hand, in discordant twins, there were three different stages in the change of fetal growth disparity. The discordant L fetuses had a growth pattern similar to that of the concordant L and S fetuses. In comparison to discordant L fetuses, discordant S fetuses showed retarded growth at 20-23 weeks, followed by catch-

up growth at 23–31 weeks and, finally, at 31–35 weeks, their growth potential was restricted again. Catch–up growth has been reported in rat fetuses[16] and in growth retarded human infants.[17] However, to the best of our knowledge, this is the first report to document the existence of intrauterine "catch–up" growth in human twin fetuses.

In singleton pregnancy, earlier studies have shown that malnutrition and chronic fetal hypoxia were the main causes of a subnormal fetal size.[18] The degree of malnutrition and hypoxia are not always equal between twin pairs because each fetus may not share available placental tissue evenly[19] and/or the smaller fetuses may not gain enough nutrients and oxygen from the placenta due to a relatively suboptimal implantation site.[20]

In concordant twins, the PW－BWR was similar between L and S fetuses at ＜31 and ≥ 31 weeks of gestation. This may thus suggest the existence of synchronous growth in twin pairs. The PW–BWR decreased after 31 weeks in concordant L and S fetuses. This corresponds to the growth velocity in concordant L and S fetuses. However, in discordant twins, the PW–BWR of the S fetuses was higher than that of L fetuses at ＜31 weeks, but not at ≥31 weeks of gestation. This finding may indicate that the capacity of placental transfer in S fetuses may be enhanced at ＜31 weeks, which may thus be a compensatory change for supplying more nutrients and oxygen to fetuses with relative hypertrophy of the placenta[5] and support the catch–up growth pattern of S fetuses until 31 weeks of gestation.[6][21]

The etiology of the initial growth retardation of discordant S fetuses remains unknown. The observed initial growth retardation was in line with the hypothesis that to promote whole maturity, the smaller fetus is selectively restricted early in gestation to cut down on the demand of nutrients and oxygen later in gestation. However, if given enough supply of nutrients and oxygen, the fetus will exhibit catch–up growth to achieve a normal growth potential.[22] This initial growth retardation may be a "physiological" adaptation before catch–up growth in the ensuing period.[23]

The PW–BWR decreased from ＜31 weeks to ≥ 31 weeks in concordant L and S fetuses. In concordant twins, a decreased ratio after 31 weeks correlated with the "physiological" growth restriction. In discordant S fetuses, the PW–BWR decreased the same as in concordant twins. However, in discordant L fetuses the ratio did not change significantly, from ＜31 weeks to ≥31 weeks of gestation. We speculate that their placenta may maintain a placental function to meet the demand of fetal growth. Therefore discordant L fetuses may thus maintain a growth pattern that is similar to concordant fetuses after 31 weeks. Discordant S fetuses, however, may lose this adaptive mechanism, and thus show a more rapid decrease in growth velocity. This may explain why the velocity disparity of discordant twins increased again.

The regulation of fetal growth is complex, and the adaptive changes of placental weight may only in part account for the adaptive growth pattern. The placental function has been also reported to play a key role in regulating fetal growth. In particular, placental growth promoting factors such as placental growth hormones[24] and leptin[25] are important for stimulating the functional maturation of the placenta, thereby influencing the fetal growth, both indirectly and directly.

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References

1) Holmes RP, Holly JMP, Soothill PW. A prospective study of maternal serum insulin–like growth factor–1 in pregnancies with appropriately grown or growth restricted fetuses. Br J Obstet Gynaecol 105：1273–8, 1998.
2) Molteni RA, Stys SJ, Battaglia FC. Relationship of fetal and placental weight in human being：fetal/placental weight ratios at various gestational ages and birth weight distributions. J Repro Med 21：327–34, 1978.
3) Robinson J, Chidzanja S, Kind K, Lok F, Owens P,

Owens J. Placental control of fetal growth. Reprod Fertil Dev 7：333–44, 1995.
4) Lao TT, Wong WM. The neonatal implications of a high placental ratio in small–for–gestational age infants. Placenta 20：723–6, 1999.
5) McCrabb GJ, Egan AR, Hosking BJ. Maternal undernutrition during mid–pregnancy in sheep. Placental size and its relationship to calcium transfer during late pregnancy. Br J Nutr 65：157–68, 1991.
6) Lynch AM, Bruce NW. Placental growth in rats exposed to carbon monoxide at selected stages of pregnancy. Biol Neonate 56：151–7, 1989.
7) Blickstein I, Smith－Levitin M. Twinning and twins. In：Chervenak FA, Kurjak A, editors. Current perspectives on the fetus as a patient, pp. 507–25, Parthenon (New York), 1996.
8) Blickstein I. Normal and abnormal growth of multiples. Semin Neonatol 7：177–85, 2002.
9) Rodis JF, Vintzileos AM, Campbell WA, Nochimson DJ. Intrauterine fetal growth in discordant twin gestations. J Ultrasound Med 9：443–8, 1990.
10) Owen P, Harrold AJ, Farrell T. Fetal size and growth velocity in the prediction of intrapartum caesarean section for fetal distress. Br J Obstet Gynaecol 104： 445–9, 1997.
11) Smih AP, Ong S, Smith NC, Campbell D. A prospective longitudinal study of growth velocity in twin pregnancy. Ultrasound Obstet Gynecol 18：485–7, 2001.
12) Shinozuka N, Okai T, Kohzuma S, Mukubo M, Shih CT, Maeda T, et al. Formulas for fetal weight estimation by ultrasound measurements based on neonatal specific gravities and volumes. Am J Obstet Gynecol 157：1140–5, 1987.
13) Ohel G, Granat M, Zeevi D, Golan A, Wexler SH, David MP. Advanced ultrasonic placental maturation in twin pregnancies. Am J Obstet Gynecol 156：76–8, 1987.
14) Loucopoulos A, Jewelewicz R. Management of multifetal pregnancies：Sixteen years' experiences at the Sloane Hospital. Am J Obstet Gynecol 143： 902–5, 1982.
15) Taylor GM, Owen P, Mires GJ. Fetal growth velocities in twin pregnancies. Twins Res 1：9–14, 1998.
16) Lynch AM, Bruce NW. Placental growth in rats exposed to carbon monoxide at selected stages of pregnancy. Biol Neonate 56：151–7, 1989.
17) Hack M, Schluchter M, Cartar L, Rahman M, Cutter L, Borawski E. Growth of very low birth weight infants to age 20 years. Pediatr 112：30–8, 2003.
18) Bajoria R, Hancock M, Ward S, D'Souza SW, Sooranna SR. Discordant amino acid profiles in monochorinic twins with twin－twin transfusion syndrome. Prediatr Res 48：821–8, 2000.
19) Richard LN, Kurt B, Jack WCH, Cril CM. Intrauterine growth of twins as estimated from liveborn birth–weight data. Pediatr 37：409–17, 1966.
20) Angela ME, Deborah L, Anthony MV, James FXE, Vassilios T, Carolyn MS. Placental pathology in discordant twins. Am J Obstet Gynecol 169：931–5, 1993.
21) Faichney GJ, White GA. Effects of maternal nutritional status on fetal and placental growth and on fetal urea synthesis in sheep. Aust J Biol Sci 40：365–77, 1987.
22) Phillips DIW. Mortality among twins (letter). Br Med J 310：1330–1, 1995.
23) Blickstein I, Goldman RD, Mazkereth R. Adaptive growth restriction as a pattern of birth discordance in twin gestations. Obstet Gynecol 96：986－90, 2000.
24) Mirlesse V, Frankenne F, Alsat E, Poncelet M, Hennen G, EvainBrion D. Placental growth hormone levels in normal pregnancy and in pregnancies with intrauterine growth retardation. Pediatr Res 34：439–42, 1993.
25) Schulz S, Hackel C, Weise W. Hormonal regulation of neonatal weight：placental leptin and leptin receptors. Br J Obstet Gynaecol 107：1486–91, 2000.

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