Three-dimensional qualitative sonographic evaluation of fetal soft tissue

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Even though fetal growth restriction and macrosomia remain as major problems currently facing obstetricians, there is still no modality for the assessment of fetal soft tissue deposition and muscle mass _in utero_. A total of 52 fetuses from 29 to 41 weeks gestation were studied within 1 week before delivery using a transabdominal three-dimensional (3D) transducer (3.5 MHz). Their birth weights varied from 1016 to 4018 g, and their crown–heel length from 37 to 54 cm. The amount of subcutaneous tissue was estimated using the fetal nutrition score. The fetal nutrition score values were determined from a qualitative assessment of the amount of subcutaneous tissue present at three locations (face, ribs and buttocks) on the antenatal 3D ultrasonograms. Fetal nutritional status, using fetal nutrition score, was compared with that found by modified neonatal nutrition score and ponderal index respectively. There was a significant linear correlation between fetal nutrition score and modified neonatal nutrition score. Fetal or neonatal nutrition score were strongly correlated with birth weight and neonatal crown–heel length. However, no significant correlation was found between ponderal index, fetal nutrition score, or modified neonatal nutrition score. Ponderal index also was not correlated with birth weight and neonatal crown–heel length. Moreover, fetal nutrition score was correlated with Apgar score, but not with umbilical cord arterial blood pH. Therefore, doubt is cast on the usefulness of the ponderal index for measurement of neonatal soft tissue and muscle mass. Fetal nutrition score using 3D ultrasonography provides a novel means of evaluating the nutritional status of the fetus _in utero_, and should be useful for predicting the extremes in fetal growth (fetal growth restriction and macrosomia) at an earlier stage than hitherto achieved.

Key words: fetal fat deposition/fetal growth/nutrition score/three-dimensional sonography

Introduction

Fetal growth restriction (FGR) remains one of the major problems currently facing obstetricians because it contributes to perinatal morbidity and mortality. However, many cases of FGR diagnosed antenatally are not growth-restricted but are genetically small and healthy (Vilbergsson and Wennergren, 1992). It is important to be able to distinguish between these two groups, since the truly growth-restricted infants are probably the vulnerable ones (Soothill _et al._, 1999). If those that are really at risk could be adequately selected, monitoring efforts could be concentrated on this category (Vilbergsson and Wennergren, 1992; Hata _et al._, 2000).

Macrosomic infants (i.e. birthweight >95% for the population) have increased perinatal morbidity, with a higher rate of operative deliveries and trauma with vaginal deliveries (Modanlou _et al._, 1980). However, defining and identifying macrosomia before delivery has been difficult (Farmer _et al._, 1992). Clinical and ultrasound measures have not been sufficiently accurate in predicting fetal weight (Sood _et al._, 1995; Johnstone _et al._, 1996; Smith _et al._, 1997).

To determine the significance of prenatal growth patterns, it is essential that they be related to pregnancy outcome. While outcome could be defined as the physiological status of the infant at birth or the infant’s long-term neurological development, it is the anthropometric characteristics of the newborn that can be most directly related to prenatal growth patterns, since similar parameters are measured (Deter, 1995a).

The ponderal index is a measurement of soft-tissue and muscle mass (Miller, 1981; Walther and Ramaekers, 1982; Hays and Patterson, 1987; Patterson and Pouliot, 1987). An asymmetrical growth-restricted infant will have a low ponderal index; a symmetrical small infant will have a normal ponderal index; and a macrosomic infant will have an elevated ponderal index. This index for assessment of neonatal proportions yields more information concerning the nutritional status of the neonate and is relatively independent of the race, gender or menstrual age; therefore, many investigators advocate its use for defining altered fetal growth (Miller, 1981; Walther and Ramaekers, 1982; Hays and Patterson, 1987; Patterson and Pouliot, 1987). However, it has been reported (Ott, 1990) that the ponderal index showed a poor correlation with both birth weight for gestational age and projected ideal weight, and that there was no correlation between the occurrence of abnormal fetal heart rate patterns and the ponderal index. It has also been shown (Ariyuki _et al._, 1995) that the usefulness of the ponderal index for detection of growth-restricted neonates with poor perinatal outcomes was doubtful.

Direct measurement of parameters related to soft tissue mass [e.g., percentage fat and lean body mass (Fiorotto _et al._, 1987)] is possible, as well as the use of more clinically applicable indirect methods such as skinfold thickness (Sood _et al._, 1995; Abramowicz _et al._, 1997) and the nutrition score (Deter and...
Harrist, 1993a). The nutrition score is a qualitative procedure for assessing subcutaneous tissue present at four locations (face, ribs, thigh and buttocks), similar in concept to the Apgar score for evaluating the physiological status of the infant at birth. Nutrition score values are in good agreement with the clinical assessment of the nutritional status of the neonate, and malnourished neonates can be separated from well-nourished neonates with a sensitivity of 91.5% and a specificity of 90.7% (Deter and Harrist, 1993a). Moreover, nutrition score was well correlated with individualized fetal growth assessment (Hata et al., 1991), and growth-restricted neonates classified by individualized growth assessment showed a significant increase in the low Apgar score (Ariyuki et al., 1995). A recent study (Hata et al., 1999) also showed that individualized growth assessment should be useful for detection of small-for-gestational-age (SGA) infants with poor perinatal outcomes.

Recent technical development of a three-dimensional (3D) ultrasound machine has led to a self-contained imaging system that can both produce conventional two-dimensional (2D) images and generate within seconds a high-quality 3D image without a need for an external workstation or other additional, costly equipment (Baba et al., 1996, 1997). Potential obstetric applications of 3D ultrasonography for systematic examination of the developmental stages of the fetus (Hata et al., 1997, 1998a,b), detection of fetal malformations (Merz et al., 1995a,b, 1997; Pretorius et al., 1995) or birthweight prediction (Lee et al., 1997) have been reported. To the best of our knowledge, there has been no modality for the assessment of fetal soft tissue deposition and muscle mass in utero. In this study, a novel technique was devised for assessment of fetal soft tissue deposition using 3D ultrasonography, namely, fetal nutrition score, and used to evaluate fetal nutritional status.

### Materials and methods

A total of 52 fetuses between 29 and 41 weeks gestation (29–31 weeks, n = 3; 34 weeks, n = 1; 36–40 weeks, n = 39; 41 weeks, n = 9) was studied with a transabdominal 3D ultrasound transducer (size 13×13×11 cm; weight 1.7 kg) (Aloka ASU-1000B, 3.5 MHz, Aloka, Tokyo, Japan). As the scanhead was rather large and heavy, a specially adapted spring coil suspension system for holding the scanhead and keeping it steady for the duration of the scanning period was used. The ultrasound machine used was an Aloka SSD-1700. This imaging system provided conventional 2D ultrasonographic images and generated within seconds, high-quality 3D images in the surface and transparent modes with no need for an external workstation. Subjects were randomly recruited over an 8 month period commencing July 1998. 3D examinations were done at the outpatient department and in the obstetric ward only every morning. Multiple pregnancies were excluded from the study. Diabetic patients were not included during this period. Gestational age was estimated from the first day of the last menstrual period and confirmed by first-trimester or early second-trimester ultrasound examinations. Birth weights varied between 1016 and 4018 g (1000–1499 g, n = 3; 1500–1999 g, n = 2; 2000–2499 g, n = 3; 2500–2999 g, n = 21; 3000–3499 g, n = 21; >3500 g, n = 2), and their crown–heel lengths between 37 and 54 cm (<40 cm, n = 3; 40–45 cm, n = 5; 46–50 cm, n = 25; >51 cm, n = 19). In no neonates were there congenital malformations or genetic disorders. The study was approved by the local ethical committee of Kagawa Medical University and standardized informed consent was obtained from each patient.

A 3D image was produced by first selecting an ideal representative 2D image placed in the region of interest, and then superimposing on this 2D image a volume box defined by the examiner. The crystal array of the transducer swept mechanically over the defined region of interest through a 60° angle. Within 4 s (128 frames), the outlined volume was automatically scanned and a sculpture-like 3D image was displayed on the screen. In this system, the ultrasound beam was regarded as a projection ray in volume rendering, and ray tracing was conducted in real time; the procedure was not as complex as planar 3D imaging, which requires complex computing and positional information, and so images could be obtained at the end of the scanning sweep (Baba et al., 1996). At present, we use a 128 Mbyte removable hard disk drive for the permanent storage of 3D images. All 3D examinations of the fetus were done within 1 week before delivery. Within 24 h after delivery, each neonate received an extensive paediatric assessment as described previously (Deter et al., 1987, 1989, 1996). Briefly, neonatal growth profile data were evaluated by comparing individual values to appropriate growth curves derived from a cross section of the population. Ponderal index was also calculated. First, one examiner recorded fetal nutrition score in which face, ribs, and buttocks could be adequately seen using 3D ultrasonography (Figure 1) before delivery, then another examiner recorded modified neonatal nutrition score [face, ribs, and buttocks except for thigh from original neonatal nutrition score (Deter et al., 1990)]. Both examiners were blinded. Six to 10 3D images were obtained per patient, and the time taken to image the fetal face, ribs, and buttocks was <10 min. On the fetal face, we evaluated orbits, nose, cheek and lips. With respect to the ribs, we depicted fetal chest. On the fetal buttocks, we demonstrated both hips. All 3D ultrasonographic examinations were done by one examiner (M.M.) for the data reported here. The intra-observer coefficient of variation was determined by performing five examinations on 10 patients, and the result was 6.2%. Fetal nutrition score was assessed in 20 fetuses by three examiners to evaluate inter-observer variation in the fetal nutrition score values, and results were 9.35 ± 1.72, 9.65 ± 1.59, and 9.45 ± 1.53 respectively (there were no significant differences among three examiners). Linear regression analysis was performed to assess the relationship between modified neonatal nutrition score and fetal nutrition score, ponderal index, birth weight or height, and fetal nutrition score and ponderal index, birth weight, crown–heel length, Apgar score value at 1 min or umbilical cord arterial blood pH. P < 0.05 was considered to be statistically significant.

### Table 1. Correlation analysis of fetal and neonatal nutritional score data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Model</th>
<th>r</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F-NS</td>
<td>(F-NS) = 5.73 + 1.30(PI)</td>
<td>0.22</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>(F-NS) = 3.11 + 0.002(03)(BW)</td>
<td>0.83</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>(F-NS) = –5.75 + 0.304(CHL)</td>
<td>0.78</td>
<td>0.0001</td>
</tr>
<tr>
<td>N-NS</td>
<td>(N-NS) = –0.287 + 1.03(F-NS)</td>
<td>0.85</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>(N-NS) = 4.76 + 1.67(PI)</td>
<td>0.23</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>(N-NS) = 1.61 + 0.00254(BW)</td>
<td>0.87</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>(N-NS) = 9.19 + 0.374(CHL)</td>
<td>0.80</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

r = correlation coefficient; N-NS = neonatal nutrition score; F-NS = fetal nutrition score; BW = birth weight; CHL = crown–heel length; PI = ponderal index; NS = not significant.
Figure 1. Fetal nutrition score for assessing the subcutaneous tissue of the fetus using three-dimensional ultrasonography. Each of the parameters indicated is evaluated and the appropriate category describing that parameter selected. The scores for each of the three categories selected are summed and this sum is designated the fetal nutrition score.

Discussion
The traditional growth outcome classification system separates infants into SGA, appropriate-for-gestational-age (AGA), and large-for-gestational-age (LGA) categories (fetuses with birth weights below the 10th percentile, 10th to 90th percentile or >90th percentile) (Battaglia and Lubchenco, 1967). Although FGR and SGA are not synonymous terms, most methods of diagnosis involve identification of the SGA infant (Ott, 1990). It is known, however, that all infants with evidence of FGR do not have birth weights <10th percentile (Deter et al., 1983). The morbidity in the perinatal period cannot always be predicted by SGA-AGA categorization (Patterson et al., 1986; Patterson and Pouliot, 1987), and most immediate (Dijxhoorn, 1986) and long-term (Hill et al., 1984) neurological problems occur in AGA infants. The intrinsic growth potential of each fetus may result in an infant that weighs less than standard cut-off values, yet is appropriately grown (Jones, 1978; Bakkeiteg et al., 1979; Wilcox, 1981; Ott, 1988). Comparison of prenatal characteristics (as determined with ultrasound) with birth weight categories has shown a rather poor correlation, even when the ultrasound studies were carried out within 10 days of delivery (Brown et al., 1987). It should also be noted that 15% of infants considered normal by the usual birth weight criteria (Deter and Harrist, 1993b). In all classifications based on population birth weight standards, differences in genetic growth potential between individuals are not taken into account as such standards are derived from cross-sectional studies (Gardosi et al., 1992; Gardosi, 1997). From these considerations, it should be clear that currently used birth weight criteria for identifying infants with growth problems are inadequate (Deter et al., 1995b; Kuno et al., 1999).

It is necessary to identify an ‘abnormal’ group on the basis

Results
The results of the statistical analysis of the data on fetal nutrition score and modified neonatal nutrition score (correlation between fetal nutrition score and modified neonatal nutrition score or each growth and perinatal parameter) are shown in Table I. There was a significant linear correlation between fetal nutrition score and modified neonatal nutrition score ($r = 0.85, P < 0.0001$) (Figure 2). Fetal or neonatal nutrition score was strongly correlated with birth weight ($r = 0.83, P < 0.0001$, or $r = 0.87, P < 0.0001$) and neonatal crown–heel length ($r = 0.78, P < 0.0001$, or $r = 0.80, P < 0.0001$) respectively. However, no significant correlation was found between ponderal index and fetal nutrition score or modified neonatal nutrition score. Ponderal index was also not correlated with birth weight and neonatal crown–heel length (data not shown). Fetal nutrition score was correlated with Apgar score ($r = 0.47, P < 0.0001$), but not with umbilical cord arterial blood pH (data not shown).
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of specific criteria and then define as ‘abnormal’ the values obtained from this group. An ‘abnormal’ group has been defined (Deter and Harrist, 1993b) on the basis of (i) a failure of the neonate to realize its growth potential, (ii) evidence of perinatal morbidity, (iii) a decrease or increase in soft tissue mass at birth and (iv) short- or long-term neurological disabilitiess. Soft tissue mass is obviously a fetal parameter that would best be measured on the fetal body as a whole (Deter et al., 1995b). Total lean body mass and fat content can be determined in the newborn from conductivity measurements (Fiorotto et al., 1987) but similar measurements cannot be made in utero. Detailed assessments of fetal growth and organ measurements by means of conventional 2D ultrasonography have been reported (Hata and Deter, 1992). However, exact evaluation of soft tissue mass is difficult using conventional methods. It has been demonstrated (Hata et al., 1998a) that 3D ultrasonography revealed the soft tissue deposition of the fetus on the cheeks, abdomen, buttocks and extremities. This study suggests that 3D ultrasonography provides a new method of detecting growth-restricted fetuses and macrosomia. Fetal nutrition score made in this study using 3D ultrasonography was significantly correlated with modified neonatal nutrition score. The nutrition score is a qualitative procedure for assessing subcutaneous tissue of the neonate. Values of this score are in good agreement with the clinical assessment of the nutritional status of the neonate, and malnourished neonates can be clearly separated from well-nourished neonates (Deter and Harrist, 1993a). Therefore, fetal nutrition score provides a novel means of assessing fetal soft tissue mass in utero. However, fetal nutrition score is a qualitative method, and reproducibility is still an important issue, although there were no significant differences in fetal nutrition score values among three examiners in this study. Further study is needed to clarify the limitations of fetal nutrition score, and it will be interesting to see if there are further studies made in the future.

Original neonatal nutrition score values were determined from a qualitative assessment of the amount of subcutaneous tissue present at four locations (face, ribs, thigh and buttocks) (Deter and Harrist, 1993a). However, fetal nutrition score made in this study was evaluated from fetal subcutaneous tissue present at three locations (face, ribs, and buttocks), and we did not perform a 3D qualitative assessment of the amount of soft tissue mass on the thigh. In the original neonatal nutrition score values, the amount of subcutaneous tissue on the thigh was assessed over the inguinal triangle. One possible factor explaining why it was difficult to assess in utero is that the fetal legs are either adjacent to the inguinal triangle or unseparated, so a thigh could not be visualized over the inguinal triangle. Another possible cause for the inability to show a thigh over the inguinal triangle is that the 3D ultrasonographic machine used in this study consisted of an ultrasonographic scanner specially designed for a ray tracing system (Baba et al., 1996). Using this system, only one conventional orientation could be used, because the volume could not be rotated. Therefore, fetal position significantly affected the optimal 3D depiction of the thigh.

With respect to limitations associated with 3D ultrasonography, fetal movement required a repeat acquisition to obtain satisfactory data. Moreover, limitations in obtaining optimal visualization of the surface anatomical structures were experienced in the case of inappropriate fetal position. These problems with 3D ultrasound fetal imaging will be resolved as further technical advances are made.

With respect to fetal nutrition score, the minimum score must be 3 and the maximum 15. In this study, most of the points fell between scores 8–12 for both axes; there were no scores <5 (i.e. 3–5 group which might include very small/thin babies), and no scores >12 (i.e. 12–15 group which would identify very fat/large babies). These extreme groups would be important to include in any future studies. This study was a pilot study to examine normal fetuses, and to obtain a baseline. Therefore, our study naturally leads onto further examination of at risk groups [i.e. very small (score 3) and very large babies (score 15)].

In this study, no significant correlation between ponderal index and fetal nutrition score or modified neonatal nutrition score was evident. Moreover, ponderal index also was not correlated with birth weight and neonatal crown–heel length. The current study strongly supports previous studies (Ott, 1990; Ariyuki et al., 1995), and indicates that ponderal index does not provide any information concerning the nutritional status of the neonate. Our findings will facilitate subsequent investigation to clarify the relationship between fetal nutrition score and fetal growth abnormality, and to determine whether fetal nutrition scores are predictive of perinatal outcomes.

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References