J Ultrasound Med 3:193–197, May 1984

RESEARCH PAPERS

Fetal Ossification Centers as Predictors of Gestational Age in Normal and Abnormal Pregnancies

Paolo Gentili, MD, Alessandro Trasimeni, MD, Claudio Giorlandino, MD

The main fetal ossification centers appear ultrasonically as egg-shaped echo-rich areas. The calcaneal and talar ossification centers are seen at the level of the tarsus osseus, and the distal femoral epiphyseal and proximal tibial epiphyseal ossification centers are found at the level of the knee. Examination of 312 normal pregnancies between 20 and 40 weeks of gestation showed that the calcaneal ossification center was detectable from 24 weeks of gestation, the talar ossification center from 26 weeks, and the distal femoral epiphyseal and proximal tibial epiphyseal ossification centers, from 32 and 36 weeks, respectively. Corresponding figures found for 36 pregnancies showing intrauterine growth retardation (IUGR), examined between 34 and 40 weeks of gestation, were similar for the calcaneal and talar ossification centers but showed delays in the development of the epiphyseal ossification centers, which were particularly striking in cases of symmetrical IUGR. The amniotic fluid lecithin/sphingomyelin ratio was also evaluated in 51 normal pregnancies between 31 and 38 weeks of gestation and was found to be ≥2 in every case where the distal femoral epiphyseal ossification center was ≥6 mm in diameter. Evaluation of the fetal ossification centers may be another useful means to evaluate gestational age in late pregnancy. (Key words: fetus; gestational age; ossification centers)

Recent technological advances in real-time ultrasonography have greatly enhanced the discriminatory powers of studies of fetal anatomy. Great interest has been shown in fetal skeletal structures: various authors[1–4] have stressed the importance of correct identification and measurement of fetal long bones for analysis of fetal growth in both normal and abnormal conditions.

Particularly relevant to our study, a high-amplitude echo originating from the fetal epiphyseal regions has recently been described[5] and correlated with gestational age.[6]

Our studies in this field have enabled us to identify ultrasonographically in utero all the main ossification centers in the fetus: the calcaneal ossification center (fig. 1), the talar ossification center (fig. 2), the distal femoral epiphyseal ossification center (fig. 3), and the proximal tibial epiphyseal ossification center (fig. 4).

The purpose of this study has been to describe the method of identification of these structures, their sonographic characteristics in normal and abnormal pregnancies, and the possible practical applications in assessments of fetal maturity and gestational age.

MATERIALS AND METHODS

Subjects of the study were 312 white pregnant women undergoing sonographic examination between 22 and 40 weeks of pregnancy. All patients were sure of the dates of their last menstrual periods and had had regular cycles in the months preceding pregnancy.

Real-time ultrasound scans were carried out with

Received June 13, 1983, from the Department of Ultrasonography, Artemisia Medical Centre, Viale Liegi, 49, 00198 Roma, Italia. Accepted for publication November 21, 1983.

Address correspondence and reprint requests to Dr. Gentili.

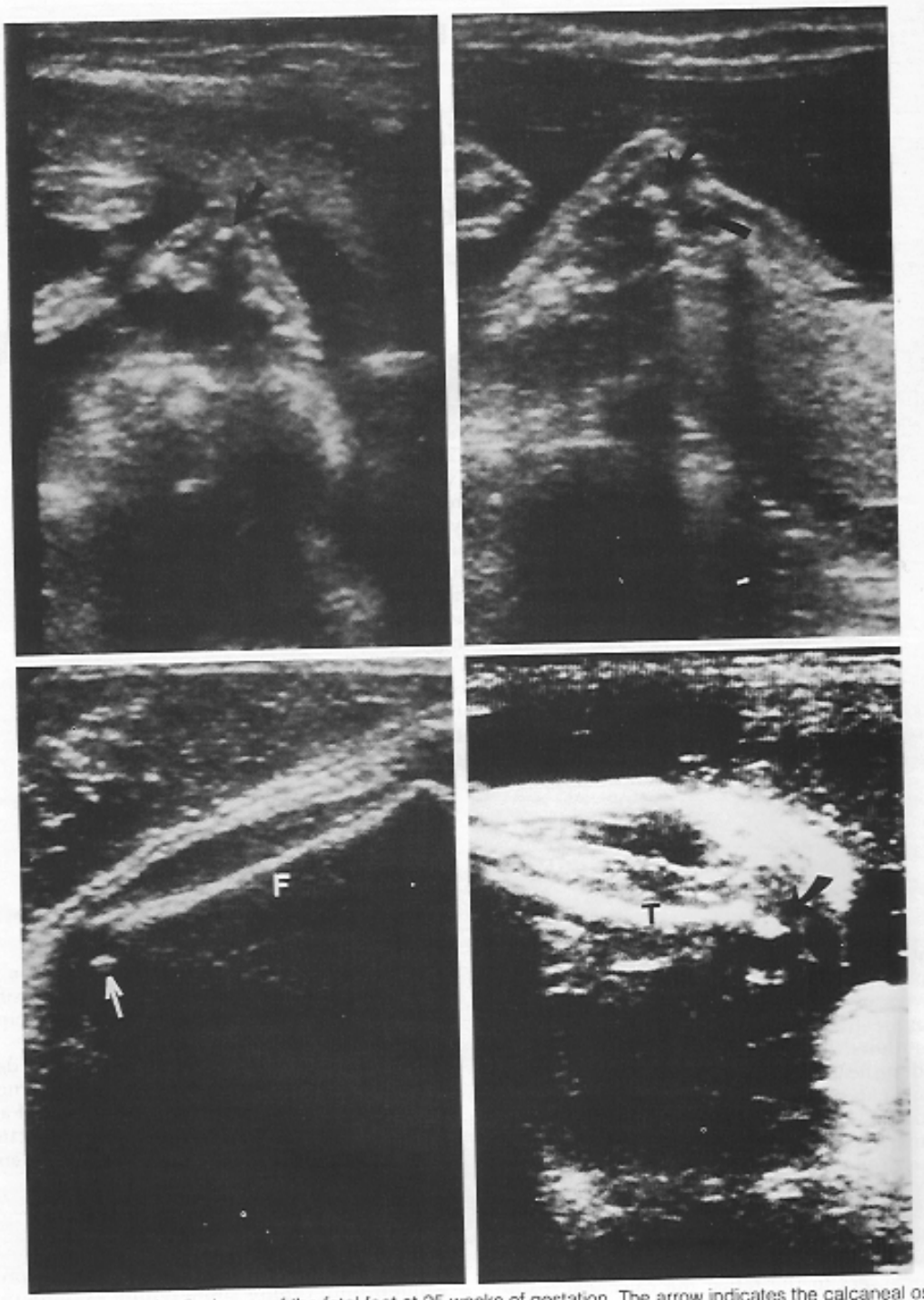

Figure 1 (*top left*). Longitudinal scan of the fetal foot at 25 weeks of gestation. The arrow indicates the calcaneal ossification center.

Figure 2 (*top right*). Longitudinal scan of the fetal foot at 27 weeks of gestation. The straight arrow indicates the calcaneal ossification center; the curved arrow indicates the talus ossification center.

Figure 3 (*bottom, left*). Fetal femur (F) at 38 weeks of gestation. The arrow indicates the distal femoral epiphyseal ossification center.

Figure 4 (*bottom, right*). Fetal tibia (T) at 39 weeks of gestation. The arrow indicates the proximal tibial epiphyseal ossification center.

Table 1. Detection of Fetal Ossification Centers by Weeks of Gestational Age

Gestational Age (Weeks)	Number of Fetuses Examined (n = 295)	Calcaneal	Talar	Distal Femoral Epiphyseal	Proximal Tibial Epiphyseal
22	12	—	—	—	—
23	14	—	—	—	—
24	9	4	—	—	—
25	10	9	—	—	—
26	8	8	2	—	—
27	12	12	10	—	—
28	9	9	9	—	—
29	10	10	10	—	—
30	15	15	15	—	—
31	14	14	14	—	—
32	17	17	17	5	—
33	19	19	19	10	—
34	15	15	15	14	—
35	21	21	21	19	—
36	29	29	29	27	8
37	25	25	25	23	19
38	22	22	22	22	20
39	18	18	18	17	16
40	16	16	16	16	16

an Aloka SSD 250 scanner equipped with a 3.5-MHz linear-array probe, freezing frame, and digital scan converter (sound speed 1,540 m/sec).

In every case we first evaluated fetal growth by measuring biparietal diameter, transverse thoracic diameter, transverse abdominal diameter, and femur and humerus lengths. The biometric values obtained were within the normal range in 94.5 per cent of pregnancies (295/312) that were considered normal; the remaining 5.5 per cent of such pregnancies were excluded from the study.

In all these normal pregnancies we carried out multiple scans at the level of the tarsus in order to identify calcaneal and talar ossification centers and at the level of the knee to identify distal femoral epiphyseal and proximal tibial epiphyseal ossification centers.

Table 2. Characteristics of Distal Femoral Epiphyseal Ossification Centers in 36 Cases of Intrauterine Growth Retardation (IUGR)

	Distal Femoral Epiphyseal Ossification Centers		
	Normal 41.6% (12)	Reduced 25% (9)	Absent 33.3% (15)
Symmetrical IUGR (n = 15)	6.6% (1)	20% (3)	73.3% (11)
Asymmetrical IUGR (n = 12)	25% (3)	41.6% (5)	33.3% (4)
Improving IUGR (n = 9)	88.9% (8)	11.1% (1)	—

We also studied 36 fetuses between 34 and 40 weeks of gestation whose biometric parameters indicated intrauterine growth retardation (IUGR)[7]: 1) 15 cases of symmetrical IUGR; 2) nine cases of improving IUGR; 3) 12 cases of asymmetrical IUGR. The ossification centers at the level of the knee were examinated to assess eventual appearance or growth delay.

Furthermore, the lecithin/sphingomeylin ratio (L/S) in the amniotic fluid was calculated for 51 normally pregnant women undergoing amniocentesis between 31 and 38 weeks of gestation. In these cases the diameter of the distal femoral epiphyseal ossification center determined before amniocentesis was compared with the L/S ratio and with the placental grade of maturity.[8]

RESULTS

We found that the fetal ossification centers become visible at different gestational ages: before 24 weeks they are not detectable; the calcaneal ossification center is detectable from 24 weeks; the talar ossification center, from 26 weeks; the distal femoral epiphyseal ossification center, from 32 weeks; and the proximal tibial epiphyseal ossification center, from 36 weeks. In table 1 we list, week by week, the numbers of cases observed and those in which the various ossification centers were detected.

In fetuses affected by IUGR (tables 2 and 3) we found that 1) the distal femoral epiphyseal ossification center was absent in 41.6 per cent, reduced 25 per cent, normal in only 33.3 per cent of cases;

Table 3. Characteristics of Proximal Tibial Epiphyseal Ossification Centers in 31 Cases of Intrauterine Growth Retardation (IUGR)

	Proximal Tibial Epiphyseal Ossification Centers		
	Normal 25.8% (8)	Reduced 22.5% (7)	Absent 51.6% (16)
Symmetrical IUGR (n = 13)	—	7.7% (1)	92.3% (12)
Asymmetrical IUGR (n = 10)	20% (2)	40% (4)	40% (4)
Improving IUGR (n = 8)	75% (6)	25% (2)	—

2) the proximal tibial epiphyseal ossification center was absent in 51.6 per cent, reduced in 22.5 per cent, and normal in only 25.8 per cent of cases; 3) the absences of both of these epiphyseal ossification centers were more frequent in symmetrical IUGR (73.3 per cent and 92.3 per cent of cases, respectively) while normal growth of these centers was more frequent in improving IUGR (88.9 per cent and 75 per cent of cases, respectively).

In the 51 cases of normal pregnancies in which the L/S ratio in the amniotic fluid was calculated and compared with the diameter of the distal femoral epiphyseal ossification center and with placental grade of maturity, we found a correlation between these parameters. There was a progressive increase in the percentage values of L/S ≥2 concomitant with the growth of the ossification center. When the diameter of the distal femoral epiphyseal ossification center was ≥6 mm, L/S was ≥2 in every case (table 4); in addition, when placental maturity was grade 3, L/S was ≥2 in every case (table 5).

DISCUSSION

The fetal ossification centers appear ultrasonographically as echo-rich, grossly egg-shaped areas well detectable in the femoral and tibial epiphyses and at the level of the tarsus (calcaneal and talar ossification centers). The median longitudinal scan is best for identifying the latter two ossification centers. In this scan these two ossification centers, although both are identifiable, cannot always be seen in their largest diameters. Therefore, to obtain a correct biometric evaluation, after these ossification centers are identified, it is necessary to do multiple scans to determine their largest diameters.

The ossification centers at the level of the knee are more easily detectable because of their location on the same plane where the measurement of the corresponding long bone is carried out. Even here, however, evaluation of the largest diameter requires multiple scans.

Considering the technical difficulties related to this kind of measurement, we believe it is preferable in the first weeks after the appearance of the ossification centers to report only their presence or absence; it is appropriate to make biometric evaluations in millimeters only when the centers are at least 3 mm in diameter.

We have demonstrated that the calcaneal is the first visible ossification center, appearing at the end of the twenty-fourth week of gestation; from 26 weeks we started to observe the talar ossification center. After 28 weeks both were detectable in every case in which the fetal position allowed correct visualization of the foot. These centers grow until term, often assuming a polyhedral aspect, the calcaneal ossification center being of greater dimension than the talar.

Until 32–33 weeks of gestational age no other ossification center appears; from that age on the distal femoral epiphyseal ossification center starts to become visible, and it is seen in 94.5 per cent of normal pregnancies (138/146) from 34 weeks till term. From 36 weeks the proximal tibial epiphyseal ossification center is detectable at the knee level. It can be seen from 37 weeks until term in 87.6 per cent of normal pregnancies (71/81).

These data obtained by ultrasonography do not substantially differ from those found by other investigators in radiographic[9–11] and sonographic[6] examinations.

Biometric evaluations of fetal ossification centers carried out at term have shown diameters of 13–16 mm for the calcaneal center, 9–12 mm for the talar, and 6–9 mm and 4–6 mm for the distal femoral and proximal tibial epiphyseal centers, respectively.

It is not difficult to identify the calcaneal and talar ossification centers until the last two months of pregnancy, when the fetal attitude, the reduction of amniotic fluid, and fetal movements often interfere with examination of the foot. Identification of the distal femoral and proximal tibial epiphyseal ossification centers is easier, because the fetal knee is nearly always detectable even in the last weeks of pregnancy.

Table 4. Correlation Between Diameters of Distal Femoral Epiphyseal Ossification Centers (DFE) and Lecithin/Sphingomyelin Ratios (L/S) in 51 Cases

Distal Femoral Epiphyseal Ossification Centers	L/S < 2	L/S ≥ 2
Undetectable (n = 12)	10 (83%)	2 (17%)
Diameter < 3 mm (n = 10)	5 (50%)	5 (50%)
Diameter ≥ 3 mm < 6 mm (n = 15)	1 (7%)	14 (93%)
Diameter ≥ 6 mm (n = 14)	—	14 (100%)

The finding of sonographic parameters that can be correlated with fetal pulmonic maturity is very interesting.

In 1979, Grannum et al. suggested that the grade of placental maturity could be used as an ultrasonographic predictor of fetal maturity, showing that a grade 3 placenta was always associated with L/S ≥ 2.[5] However, a grade 3 placenta is usually detectable only near or after term, and thus the clinical utility of this ultrasonic parameter is limited.

Instead, therefore, we examined the utility of the diameter of the distal femoral epiphyseal ossification center as an ultrasonographic predictor of fetal maturity, having noticed that all normal pregnancies in which this diameter was ≥6 mm had L/S ≥ 2.

In comparing the possibilities of fetal maturity evaluation offered by these two sonographic indicators, we found that: 1) the distal femoral epiphyseal ossification center measurement led to a greater number of correct diagnoses of maturity (14, compared with ten when grade of placental maturity was considered); and 2) the former allowed us to diagnose maturity earlier (from 33 weeks of pregnancy).

In IUGR fetuses we found a delay in the appearance or an absence of the distal femoral epiphyseal ossification center in 66.6 per cent of cases and of the proximal tibial epiphyseal ossification center in 74.1 per cent of cases. Although the number of cases of IUGR in this study was small, our preliminary data seem to provide evidence of a more marked delay in the appearance of the distal femoral and proximal tibial epiphyseal ossification centers according to the severity of IUGR. The greatest retardation of ossification center growth was observed in cases of symmetrical IUGR, with less marked growth compromise in asymmetrical IUGR, while in improving IUGR we found development of the ossification centers in the lower limits of the normal range.

We have demonstrated that the ossification centers are detectable at different specific gestational ages. This developmental feature can be useful in the assessment of fetal maturity in the last weeks of pregnancy, when biparietal diameter and measurements of long bones provide too wide a range of prediction for a feasible evaluation.[6]

For example, in a case of uncertain gestational age in which the biparietal diameter is 8.5 cm, femur length is 6.9 cm, and humerus length is 5.9 cm, fetal gestational age, considering the standard deviations of these parameters, could be 34 weeks ± 20 days (fig. 5). Examination of the ossification centers at the level of the knee to determine the presence or absence of the distal femoral and proximal tibial epiphyseal ossification centers, will lead us to the following considerations: 1) if both these ossification centers are absent, gestational age is less than 32 weeks; 2) if the former is present while the latter is still absent, gestational age is between 32 and 36 weeks; 3) if both are present gestational age is more than 36 weeks.

Table 5. Correlation Between Placental Maturity and Lecithin/Sphingomyelin Ratios (L/S) in 51 Cases

Placental Maturity	L/S < 2	L/S ≥ 2
Grade 1 (n = 14)	8 (57%)	6 (43%)
Grade 2 (n = 27)	8 (30%)	19 (70%)
Grade 3 (n = 10)	—	10 (100%)

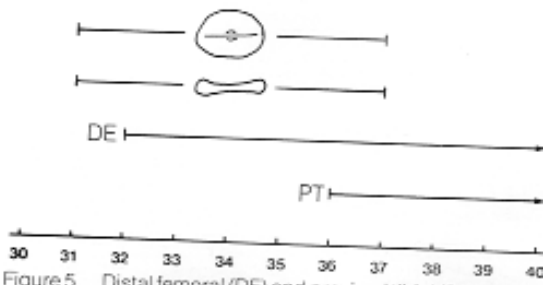

Figure 5. Distal femoral (DF) and proximal tibial (PT) epiphyseal ossification centers as an aid in the determination o uncertain gestational age in the last weeks of pregnancy.

In conclusion, we think that sonographic evaluation of fetal ossification centers not only provides further information about fetal anatomy, but also can fill a role of clinical importance: it can be used to evaluate fetal maturity, to identify IUGR, and, in the last weeks of pregnancy, to assess gestational age.

REFERENCES

1. Queenan JT, O'Brien GD, Campbell S: Ultrasound measurement of fetal limb bones. Am J Obstet Gynecol 138:297, 1980
2. Paparella P, Gentili P, Giorlandino C: Studio ecografico delle ossa lunghe fetali, *in:* Catizone FA, Ianniruberto A, Zulli P (eds): Atlante di ecografia Ostetrico Ginecologica. Roma, Edizioni Internazionali C.I.C., 1981, p 179
3. O'Brien GD, Queenan JT: Growth of the ultrasound fetal femur length during normal pregnancy. Am J Obstet Gynecol 141:833, 1981
4. Hohler CW, Quetal TA: Comparison of ultrasound fetal femur length and biparietal diameter in late pregnancy. Am J Obstet Gynecol 141:759, 1981
5. Filly RA, Golbus MS: Ultrasonography of the normal and pathologic fetal skeleton. Radiol Clin North Am 20:311, 1982
6. Chinn DH, Bolding DB, Callen PW, et al: Ultrasonographic identification of fetal lower extremity epiphyseal ossification centers. Radiology 147:815, 1983
7. Giorlandino C, Gentili P, Paparella P: Valutazione ecografica dei ritardi di accrescimento fetale, *in:* Catizone FA, Iannirubberto A, Zulli P (eds): Atlante di Ecografia Ostetrico Ginecologica. Roma, Edizioni Internazionali C.I.C., 1981, p 189
8. Grannum PAT, Berkowitz RL, Hobbins JC: The ultrasonic changes in the maturing placenta and their relation to fetal pulmonic maturity. Am J Obstet Gynecol 133:915, 1979
9. Hartley BJ: Radiological estimation of fetal maturity. Br J Radiol 30:561, 1957
10. Dee PM, Parkin JM, Simpson W: A study of some radiological criteria used in assessing the gestational age of the human infant. Clin Radiol 47:126, 1966
11. Russell JGB: Radiological assessment of fetal maturity. J Obstet Gynaecol Br Commonwlth 76:208, 1969