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Fetal skeletal computed tomography: When? How? Why?

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KEYWORDS
Prenatal diagnosis; Constitutional bone diseases; 2D ultrasound; CT

Abstract

Purpose: To study the additional role of fetal skeletal computed tomography in suspected prenatal bone abnormalities.
Materials and methods: Two centers included in a retrospective study all fetuses who benefited from skeletal computed tomography for a suspected constitutional bone disease or focal dysostosis.
Results: A total of 198 patients were included. CT was performed in 112 patients (56%) for an isolated short femur below the third percentile (group A), in 15 patients (8%) for bowed or fractured femur (group B), in 23 patients (12%) for biometric discrepancy between a short femur and increased head circumference (group C) and in 48 patients (24%) for suspected focal dysostosis (group D). CT was interpreted as normal in 126 cases (64%), i.e. 87% in group A, 0% in group B, 65% in group C and 25% in group D. When including only cases with postnatal or postmortem clinical and/or radiological confirmation was available, CT provided additional and/or more accurate information than ultrasound in 20% of cases in group A, 66% in group B, 30% in group C and 72% in group D. Sixty-seven percent of patients in whom CT was interpreted as normal were lost to follow-up.

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Conclusion: In isolated short femur, fetal skeletal CT is normal in the great majority of cases although protocolized follow-up of these babies is absolutely compulsory, as a large proportion is lost to follow-up. Fetal skeletal CT can confirm or improve imaging for the suspected diagnosis in suspected focal dysostosis or constitutional bone disease.

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Fetal skeletal malformations are an extremely wide and heterogeneous group of disorders. They may be generalized, as in constitutional bone diseases (CBD), or affect one or more bony parts in focal dysostosis.

Prenatal diagnosis of most of these disorders is still very variable. Screening ultrasound with measurement of femoral length and assessment of femoral morphology can be used to screen for certain abnormalities. The French National Technical Prenatal Screening Ultrasound Committee guidelines also emphasize examination of the different limb segments, spine and cranium to diagnose skeletal dysostoses.

Investigation of the bony pelvis and assessment of the overall skeleton are the main limitations of two-dimensional and three-dimensional ultrasound, but several preliminary publications have shown these to be useful (computed tomography [CT] as well).

Our aim was to determine the additional role of fetal skeletal CT in the prenatal diagnosis of bone disorders in a large-scale study.

Materials and methods

Between September 2005 and October 2009, 198 patients referred to two university prenatal diagnostic centers in the same town for suspected bone disorders on two-dimensional ultrasound were included in the study. All of the patients included underwent “diagnostic” ultrasound, although because of the retrospective nature of the study and long inclusion period, not all measurements of all long bones other than the femur were found.

All had a fetal skeletal CT scan.

The ultrasound indications for the fetal CT were classified into four groups:

- group A: fetuses with isolated short femur below the 3rd percentile;
- group B: fetuses with a bowed or fractured femur;
- group C: cases of biometric discrepancy between a short femur below the 5th percentile and an increased head circumference over the 95th percentile;
- group D: ultrasound showed suspected focal dysostosis particularly of the vertebral or cranio-facial bones or extremities.

Fetal upper and lower poles were identified using a portable ultrasound instrument (VOLUSON I — GENERAL ELECTRICS), realizing an ultrasound scout view, and CT images were obtained using two devices (SIEMENS — definition 64 section and SIEMENS — definition double source —, SIEMENS MEDICAL SYSTEMS — ERLANGEN — GERMANY).

Collimation was 0.625 mm, with a kilovoltage of 100 and 120 kV depending on patient body morphology and 100 mAs was used in all cases.

The acquisition lasted an average of 10.2 seconds with the mother holding her breath and without any premedication.

CT results were formalized as a standard report also used for ultrasound in the reference centers in order to allow a strict comparison of the results.

CT results were classified as normal or abnormal, and if an abnormality was present, the reviewers (GG-MP) established whether the scan provided additional information and/or provided greater diagnostic accuracy as a result of improved image quality compared to two-dimensional ultrasound. Only cases in which follow-up provided postnatal or postmortem confirmation of the prenatal findings were included in this comparison. Postnatal follow-up ranged from 3 to 8 years in the babies who were born.

Results

Of the 198 patients included, 112 (56%) were in group A, 15 (8%) in group B, 23 (12%) in group C and 48 (24%) in group D.

CT was interpreted as normal in 126 cases (64%): postnatal follow-up was only available in 41 cases, i.e. 67% of babies were lost to follow-up. Seventy-two CTs were interpreted as abnormal (34%) with postnatal or post-medical termination of pregnancy follow-up in 50 cases (70%). Thirty percent of patients were lost to follow-up.

The average gestational age when fetal CT was performed was 31.5 weeks (range 20–38). Only four CTs were performed before 26 weeks of pregnancy given a possible decision for medical termination of pregnancy.

The average CTDI dose received was 5.9 mGy.

Group A

Eighty-seven percent of CTs in this group were interpreted as normal and 71% of patients were lost to follow-up. In 14 fetuses the scan was interpreted as abnormal: follow-up was only available in 7 cases, which included 4 fetuses with Ellis Van Creveld’s disease (Figs. 1 and 2), 2 fetuses with chondrodysplasia punctata (Fig. 3) and 1 fetus with metaphyseal dysplasia (Fig. 4).
Fetal skeletal computed tomography: When? How? Why?

Figures 1 and 2. Maximum Intensity Projection (MIP) reconstructions of ¾ whole body (1) and posterolateral view centered on the pelvis (2) at 28 weeks of pregnancy in 2 cases of Ellis Van Creveld’s disease: note the short ribs and pelvic abnormalities with square shaped iliac wings, horizontal acetabular roofs with convex downward median shift and 2 lateral spurs.

Figure 3. Lateral volume rendering (VR) whole body reconstructions at 35 weeks of pregnancy in one of the 2 fetuses with chondrodysplasia punctata without Binder facies. Note the epiphyseal calcifications (arrow).

Group B
CT was interpreted as abnormal in all cases (15). Follow-up after medical termination of pregnancy was available in 13 cases (87%).
Six fetuses had osteogenesis imperfecta (Fig. 5), 2 had thanatophoric dysplasia, 2 others had campomelic dysplasia, 1 was a case of Stuve-Wiedemann syndrome and 1 had isolated femoral hypoplasia (Fig. 6).

Group C
CT was interpreted as normal in 15 of the 23 patients in this group. Sixty-six percent were lost to follow-up.
CT was deemed to be abnormal in 8 fetuses (3 lost to follow-up).
The 5 cases, which were followed-up after medical terminal of pregnancy, were all suffering from achondroplasia (Fig. 7).

Group D
Twelve of the CTs in this group of 48 patients were interpreted as normal (25%). Postnatal confirmation was available in 58% of cases.
The abnormality was confirmed on CT in 36 patients, 70% of which were followed-up postnatally. These involved vertebral abnormalities in 8 fetuses (Figs. 8–10), limb abnormalities in 8 fetuses (Figs. 11 and 12), 4 cases of spondylocostal dysplasia (Fig. 13), 4 cases of Binder phenotype (Fig. 14) and 1 case of craniostenosis (Fig. 15).

Discussion
Prenatal screening and diagnosis of fetal skeletal disorders is still a daily challenge for all fetal medicine practitioners.
Three-quarter MIP reconstructions centered on the trunk (a), spine (b) and lower limbs (c) at 31 weeks of pregnancy in a fetus with metaphyseal dysplasia.

Whole body MIP reconstructions at 28 weeks of pregnancy in a fetus with osteogenesis imperfecta. The bones are poorly mineralized (particularly the cranial vault), and the diaphyses are thin and curved. The ribs are spindly, the chest is narrow and the vertebral bodies are flattened.

Three-quarter MIP reconstructions centered on the femurs at 30 weeks of pregnancy illustrating unilateral femoral hypoplasia.

Screening two-dimensional ultrasound offers a sensitivity of around 60% [1,2] but is still the first line investigation, particularly if no family history of bone disorders is present. Three-dimensional ultrasound undoubtedly offers greater sensitivity [3–5] of around 80%, although this is a diagnostic rather than a screening investigation and is therefore carried out on a far more focused basis. The spine and pelvis are the two anatomical regions in which 3D ultrasound is an absolutely crucial help compared to conventional two-dimensional ultrasound.
Figure 7. Lateral MIP reconstructions centered on the lumbar, spine, pelvis and femurs in a fetus at 30 weeks of pregnancy clearly showing the features of achondroplasia: the pelvic height is reduced, the iliac wings are square and the roots of the acetabuli are horizontal with an internal spur.

Figure 8. Postero-anterior multiplanar reconstructions (MPR) reconstructions centered on the spine at 29 weeks of pregnancy confirming congenital spinal dislocation.

Until recently, fetal radiographs were occasionally performed after 30 weeks of pregnancy as two orthogonal views to help to visualize the fetal skeleton if a constitutional bony abnormality was suspected. This technique has never been properly assessed scientifically and has gradually been replaced in recent years by fetal skeletal CT [6,7].

Figure 9. Lateral MIP reconstructions centered on the lumbar spine at 32 weeks of pregnancy showing the vertebral mosaic.

Figure 10. Postero-anterior MIP reconstructions centered on the spine at 34 weeks of pregnancy illustrating stepwise posterior vertebral blocks.
Fetal skeletal CT, which was initially restricted because of dosimetry issues has also benefited from the revolution of multislice CT, both in terms of speed of image acquisition and spatial resolution but also in terms of a very considerable dose reduction.

The current literature only contains small series [5,8], which do not allow any conclusions to be drawn about the actual benefit of fetal skeletal CT in suspected bone diseases.

Our study is the largest cohort, which has assessed this technique.

The main advantages of fetal skeletal CT are:
• its excellent feasibility: all pediatric imaging departments have multislice CT devices, providing sectional images under a millimeter in size;
• the possibility for three-dimensional reconstruction either as volume-rendering or in multiplane reformatting of either the whole fetal skeleton, or segments of the skeleton depending on diagnostic needs;
• the far more detailed analysis of some regions (metaphyses), bone modeling, the pelvis, spine, ribs and facial bones (for example in mandibulo-facial dysostoses) and inner ear structures;
• a completely acceptable dosimetry, with an average CTDI of 5.9 mGy in our study, compared to an estimated average of approximately 3 mGy for one conventional radiograph of uterine contents [9], although of course there are acknowledged difficulties in comparing dosimetry values between these very different techniques;
• without being able to prove on the basis of strict scientific evidence, considerably greater amounts and better quality of information than previous standard two view radiographic techniques.

The main difficulties in performing and interpreting fetal skeletal CTs are:
• the examination of the cartilaginous epiphyses by CT is still difficult: for these regions ultrasound is still the reference investigation [10]. MR undoubtedly will play an increasing role [11];
• the need for collaboration on all aspects of the investigation: the indication for CT, the necessary detailed comparison with ultrasound findings and then the delivery of information to the patient. This collaboration is carried out closely with geneticists, ultrasonographers, obstetricians, psychologists and pediatrician colleagues;
• the knowledge of normal appearances and anatomical variants of the fetal skeleton, particularly the progressive nature of ossification during pregnancy [12];
• the knowledge of possible artifacts produced by the technique, particularly if the fetus moves during the image acquisition process. This can be partly compensated by the mother hyperventilating before CT, although the benefit of this approach has not been formally assessed;
• the assessment of the quality and quantity of global fetal skeletal mineralization is still a challenge, particularly the cranial vault, which may be particularly useful in diagnosing osteogenesis imperfecta. In the future, dual-source CT techniques may provide further information in this area;
Fetal skeletal computed tomography: When? How? Why?

Figure 13. Lateral MIP reconstructions centered on the spine and ribs showing heterogeneous expression of spondylocostal dysplasia in 3 fetuses at 27 weeks of pregnancy (a), 34 weeks of pregnancy (b) and 30 weeks of pregnancy (c).

Figure 14. MIP reconstructions centered on the lumbar, spine and pelvis (at 30 weeks of pregnancy), the spine (b, 31 weeks of pregnancy) and femurs (c, 32 weeks of pregnancy) showing spinal and epiphyseal calcifications in 3 of 4 fetuses with the Binder chondrodysplasia punctata phenotypes.

- before 32 weeks of pregnancy, the analysis of the extremities (particularly the phalanges), is still also extremely challenging. Here again, ultrasound correlations are essential;
- the analysis of rib length in suspected narrow chest is still also difficult as no reference values are available in the literature;
- in particular, because of the very wide range of bone diseases, their extremely wide phenotypic variability and their progressive radiological appearances over time (both in the prenatal and postnatal phase) we need to be very cautious before stating that no signs of bone disease are present on CT.
For this reason, it is absolutely essential nationally to achieve protocolized postnatal and postmortem follow-up of fetuses who have had a prenatal CT, as our study shows that 67% of patients who had normal CT scans were lost to follow.

In terms of the additional benefit of CT itself, the different indications by group are summarized below. Table 1 summarizes the respective roles of each technique.

**Group A**

For an isolated short femur below the 3rd percentile, approximately 9 out of 10 scans were normal. A detailed retrospective analysis of the remaining 10% also shows that the related ultrasound signs should have been identified (polydactyly, cartilage calcification, etc.) which could not have been present in the other three groups. In conclusion, if short femur is strictly isolated and associated with shortening of the other long bones, CT is not necessary as this is essentially a growth retardation problem.

**Group B**

All of the suspected ultrasound findings were confirmed in this group. CT provided far more conclusive imaging of the suspected bone disease, both for the couple concerned and for the whole multidisciplinary prenatal diagnostic center team.

**Group C**

The condition in this case is mostly achondroplasia. All of the ultrasound findings were confirmed and imaging provided a greater level of certainty, particularly for pelvic abnormalities.

**Group D**

In a significant number of cases, CT excluded the suspected ultrasound diagnosis (7 out of 48 cases with postnatal confirmation, i.e. 14.5%), and in all of the other cases, CT confirmed far more clearly the extension of the abnormalities suspected on ultrasound, particularly in the spine and extremities.

Our study does of course have the limitations of all retrospective studies, i.e. the large number and the wide range of ultrasonographers, screeners and/or diagnosticians, in the absence of explicit guidelines during the study period (published in March 2010) from the national fetal ultrasound technical committee for diagnostic ultrasound in suspected constitutional bone disease. This range was particularly obvious and problematic for group A. Clearly this work has been continuing since on a prospective and far more standardized basis, although we believe it was important to share our initial experiences on such a large sample of patients.

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**Figure 15.** MIP reconstructions at 34 weeks of pregnancy with isolation of the cephalic pole and rotations around the pole — compensatory widening of the other sutures (a, b) because of asymmetrical partial closure of a coronal suture (c).

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CT: computed tomography. (−−−): very difficult; (−): difficult and/or does not visualize well; (+): easy and/or visualizes well; (++): visualizes very well.
Conclusion

In conclusion:
• if a completely isolated short femur below the 3rd percentile is found on ultrasound, a fetal CT is of no benefit and the indication threshold could probably be reduced to the first percentile;
• if a bowed or fractured femur is observed, if cephalic and femoral biometrics are discordant or if fetal focal dysplasia is suspected, fetal CT can confirm or improve imaging of the suspected bone condition.

This should only be considered on a close multidisciplinary basis in a multidisciplinary prenatal diagnostic center and requires appropriate protocolized follow-up of the fetuses investigated.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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