In The Name of God

# *NIPT or First-Trimester NT scan?*

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The introduction of cell-free DNA screening for aneuploidy into obstetric practice in 2011 revolutionized the strategies utilized for prenatal testing.

The purpose of this document is to review the current data on the role of ultrasound in women who have undergone or are considering cell-free DNA screening.

Society for Maternal-Fetal Medicine
High-risk pregnancy experts

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# The role of ultrasound in women who undergo cell-free DNA screening

The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) both recommend that all women should be offered the option of aneuploidy screening or diagnostic testing for fetal genetic disorders

Summary of recommendations

| | Recommendations | GRADE |
|---|---|---|
| 1 | In women who have already received a negative cfDNA screening result, ultrasound at 11–14 weeks of gestation solely for the purpose of NT measurement (CPT code 76813) is not recommended. | 1B<br><br>Strong recommendation, moderate-quality evidence |
| 2 | Diagnostic testing should not be recommended to patients solely for the indication of an isolated soft marker in the setting of a negative cfDNA screen. | 1B<br><br>Strong recommendation, moderate-quality evidence |
| 3 | In women with an isolated soft marker that has no other clinical implications (ie, choroid plexus cyst or echogenic intracardiac focus) and a negative cfDNA screen, we recommend describing the finding as not clinically significant or as a normal variant. | 2B<br><br>Weak recommendation, moderate-quality evidence |
| 4 | In women with an isolated soft marker without other clinical implications (ie, choroid plexus cyst or echogenic intracardiac focus) and a negative first- or second-trimester screening result, we recommend describing the finding as not clinically significant or as a normal variant. | 2B<br><br>Weak recommendation, moderate-quality evidence |
| 5 | We recommend that all women in whom a structural abnormality is identified by ultrasound be offered diagnostic testing with chromosomal microarray. | 1A<br><br>Strong recommendation, high-quality evidence |
| 6 | Routine screening for microdeletions with cfDNA is not recommended. | 1B<br><br>Strong recommendation, moderate-quality evidence |

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# The role of ultrasound in women who undergo cell-free DNA screening

CrossMark

*What is the role of nuchal translucency measurement in women who plan to have, or have already had, cfDNA screening and received a negative or low-risk result?*

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# The role of ultrasound in women who undergo cell-free DNA screening

*An increased NT has been associated with*

- *structural anomalies,*
- *neuromuscular disorders,*
- *and a variety of other genetic conditions.*

*It has been noted that imaging the fetus at 11–14 weeks of gestation provides an early opportunity to evaluate the pregnancy and to potentially identify a fetus at risk for additional genetic or structural abnormalities*

*Ultrasound Obstet Gynecol* 2017; 49: 815–816
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.17483

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CONSENSUS STATEMENT

# ISUOG updated consensus statement on the impact of cfDNA aneuploidy testing on screening policies and prenatal ultrasound practice

*All women should be offered a first-trimester ultrasound scan according to ISUOG guidelines, regardless of their intention to undergo cfDNA testing*

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If the woman has had a negative cfDNA test result, nuchal translucency (NT) thickness should still be measured and reported as a raw value and centile.

However, it is not necessary to compute first-trimester risk estimates for trisomies 21, 18 and 13 based on NT measurements and maternal biochemistry in a woman known to have a normal cfDNA result.

cfDNA testing should not replace first-trimester ultrasound and should not be offered when an ultrasound anomaly or markedly increased NT is detected.

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CONSENSUS STATEMENT

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cfDNA test results should always be interpreted and explained individually in relation to the *a-priori* risk and the fetal fraction.

In the case of a failed cfDNA test, the patient should be informed about the increased risk of anomalies as well as alternative screening and testing strategies.

cfDNA testing is not diagnostic, and confirmatory invasive testing is required in the presence of an abnormal result. Whenever there is discordance between an abnormal cfDNA test result and a normal ultrasound examination, amniocentesis rather than chorionic villus sampling should be performed.

In the presence of a fetal structural anomaly, the indications for fetal karyotyping and/or microarray testing should not be modified by a previously normal cfDNA test result.

# The Use of Ultrasound as a Potential Adjunct to Cell-Free Fetal DNA Screening for Aneuploidy at Weill Cornell Medical College, New York, USA

Jessica Scholl, MD[1] Stephen Chasen, MD[1]

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Surg J 2018;4:e1–e6.

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*Using cfDNA screening as the primary evaluation strategy, the residual risk of a significant chromosomal abnormality after a negative cfDNA screen result was 2.5%.*

*In contrast, using cfDNA screening alone for those with an NT <3.0 mm and CVS for women with an NT of 3.0 mm or higher resulted in a residual risk of a significant chromosome abnormality of 1% in this high-risk cohort.*

# The Use of Ultrasound as a Potential Adjunct to Cell-Free Fetal DNA Screening for Aneuploidy at Weill Cornell Medical College, New York, USA

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The current ACOG and SMFM guidance states that nuchal translucency measurement for aneuploidy risk is not necessary at the time of cfDNA screening in the first trimester.

However, ultrasound examination is useful to confirm viability, to confirm the number of fetuses and the presence of an empty gestational sac, to assign gestational age, and to identify some major fetal anomalies for patients who may choose to have cfDNA screening.

Guidelines have been unclear as to whether to perform nuchal translucency imaging in patients who have undergone cfDNA screening.

*ACOG states that while a nuchal measurement for aneuploidy risk is not necessary, ultrasound is useful to confirm viability and number of fetuses, assign gestational age, and identify some major fetal anomalies.*

*(ISUOG) recommends that among women with a negative cfDNA test result, first-trimester ultrasound should be offered and nuchal translucency thickness should be measured and reported as a raw value and centile. However, computing the first-trimester risk assessments for trisomy 21, trisomy 18, and trisomy 13 based on both nuchal translucency measurements and maternal biochemistry is not necessary*

*Society of Maternal–Fetal Medicine has recently stated that in women who have had a negative cfDNA screen, first-trimester nuchal translucency screening may slightly reduce the residual risk of significant chromosomal abnormalities; however, further research is needed to determine the optimal approach*

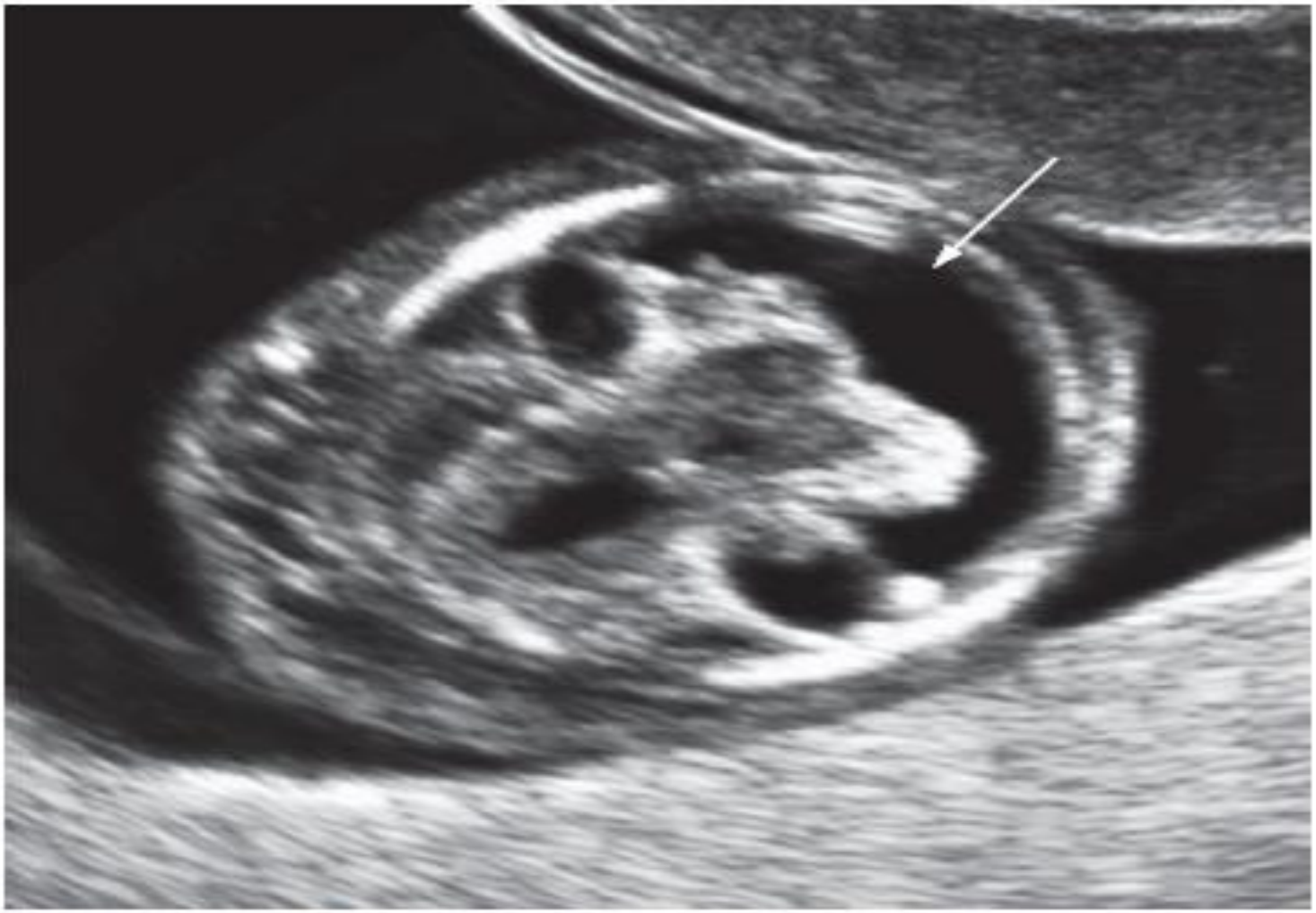

**Figure 29-5 Alobar holoprosencephaly.** Transverse image of a fetal head at 12 weeks demonstrating the monoventricle of alobar holoprosencephaly *(arrow)*.

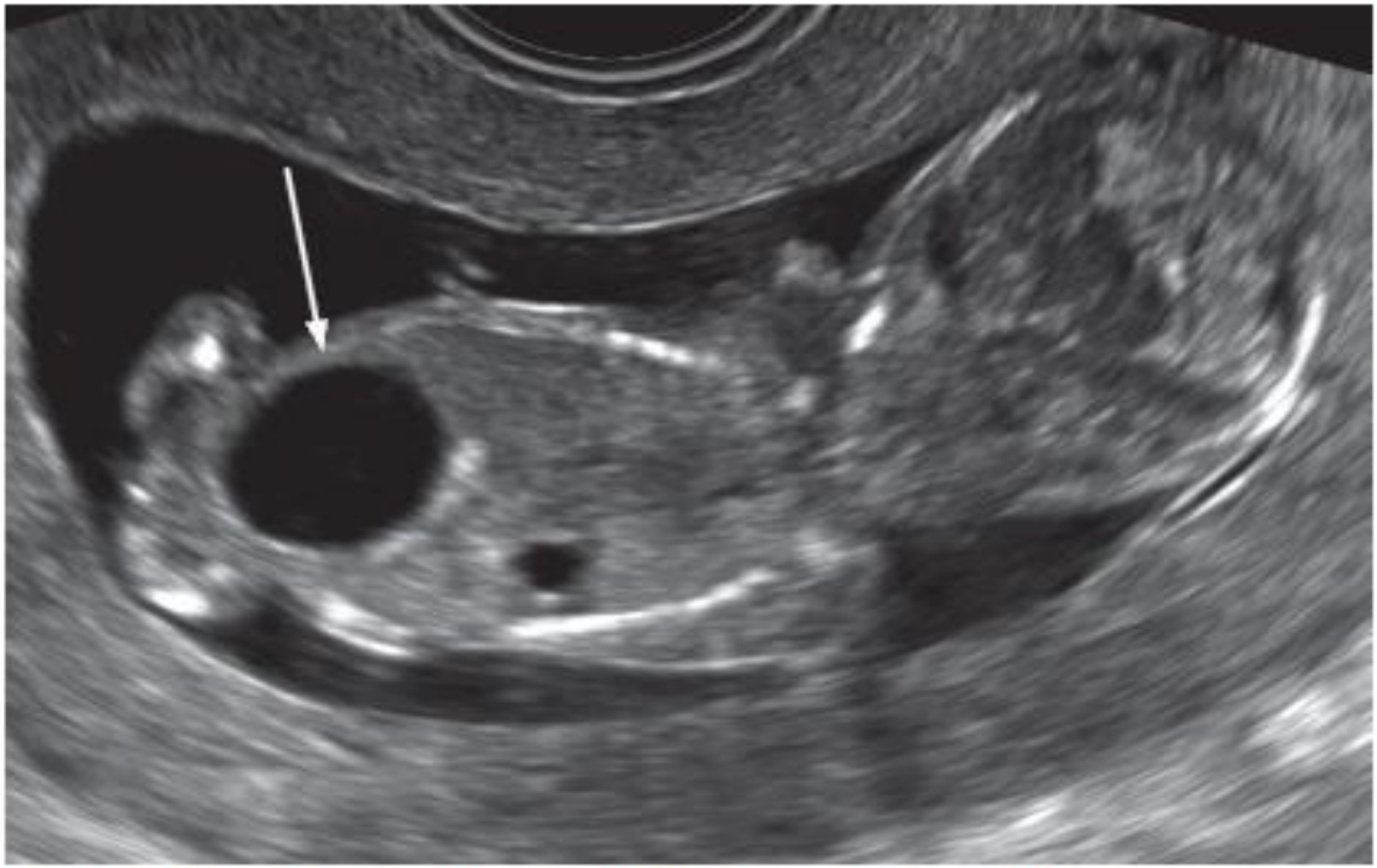

**Figure 29-7 Megacystis.** Oblique image of an 11-week fetus with megacystis *(arrow)*.

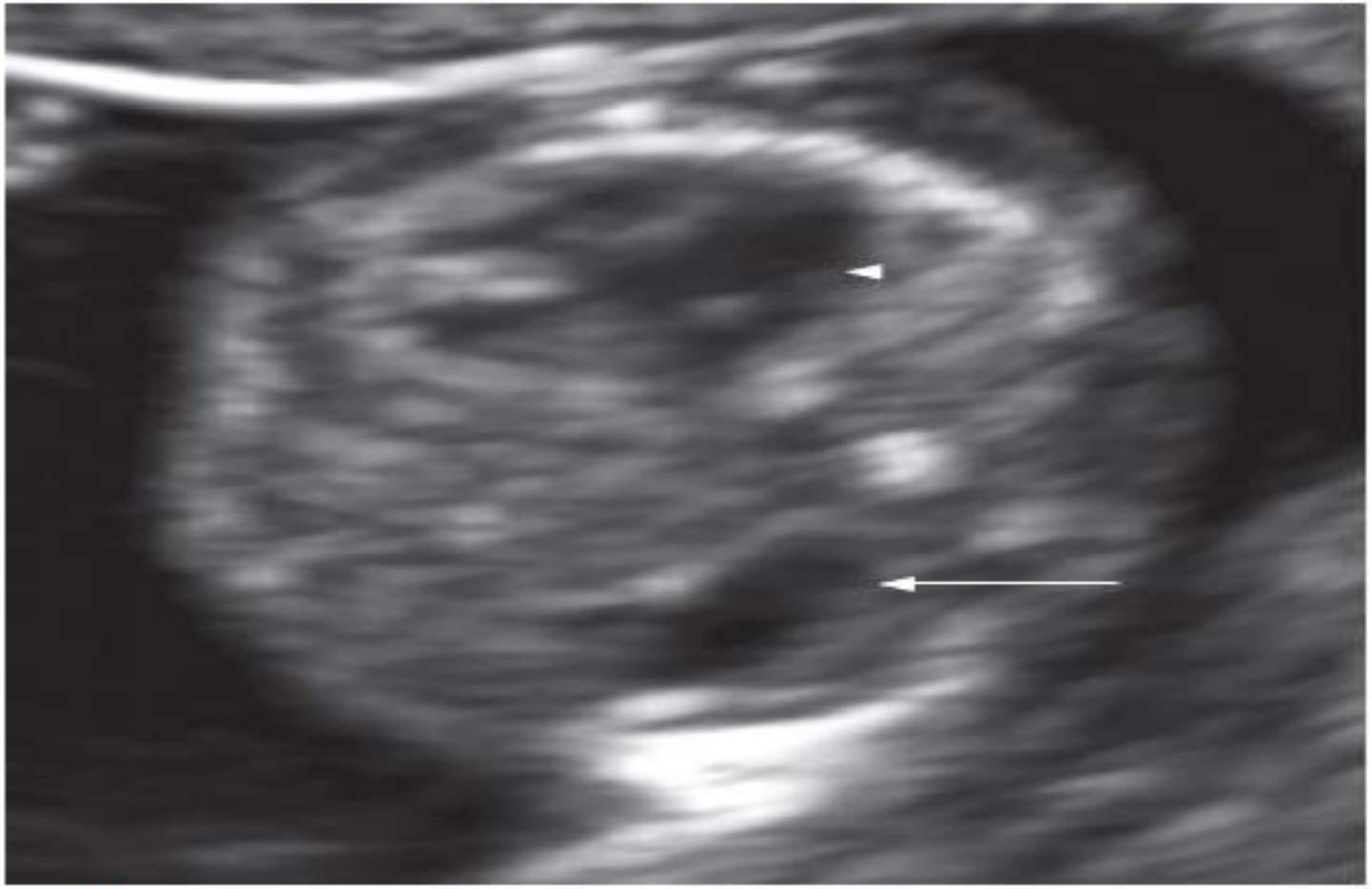

**Figure 29-6 Congenital diaphragmatic hernia.** Transverse image of the fetal chest at 12 weeks demonstrating a congenital diaphragmatic hernia. *Arrow*, stomach; *arrowhead*, heart.

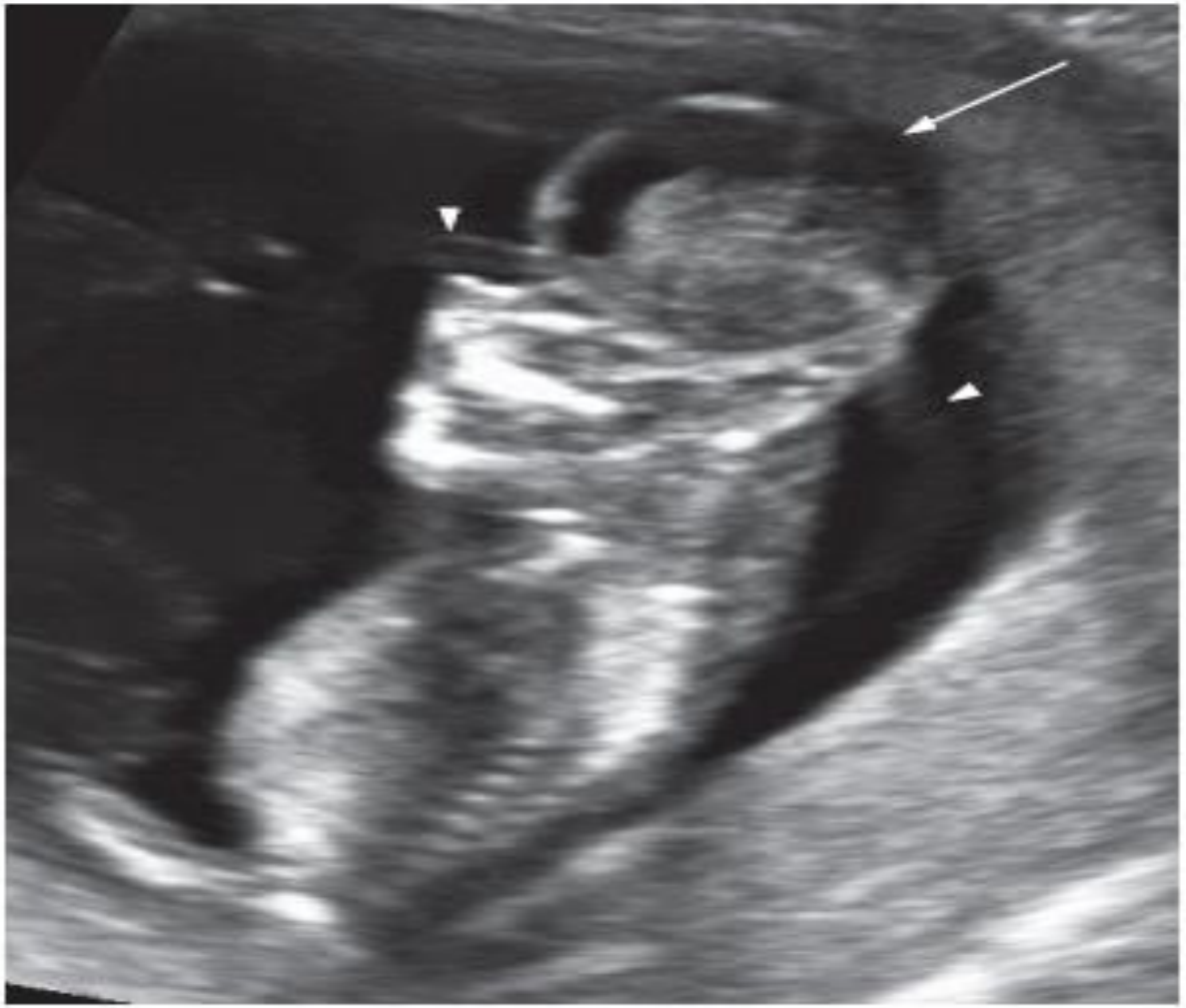

**Figure 29-3 Acrania.** Sagittal image of a 12-week fetus with acrania *(arrow). Arrowheads* show amniotic bands.

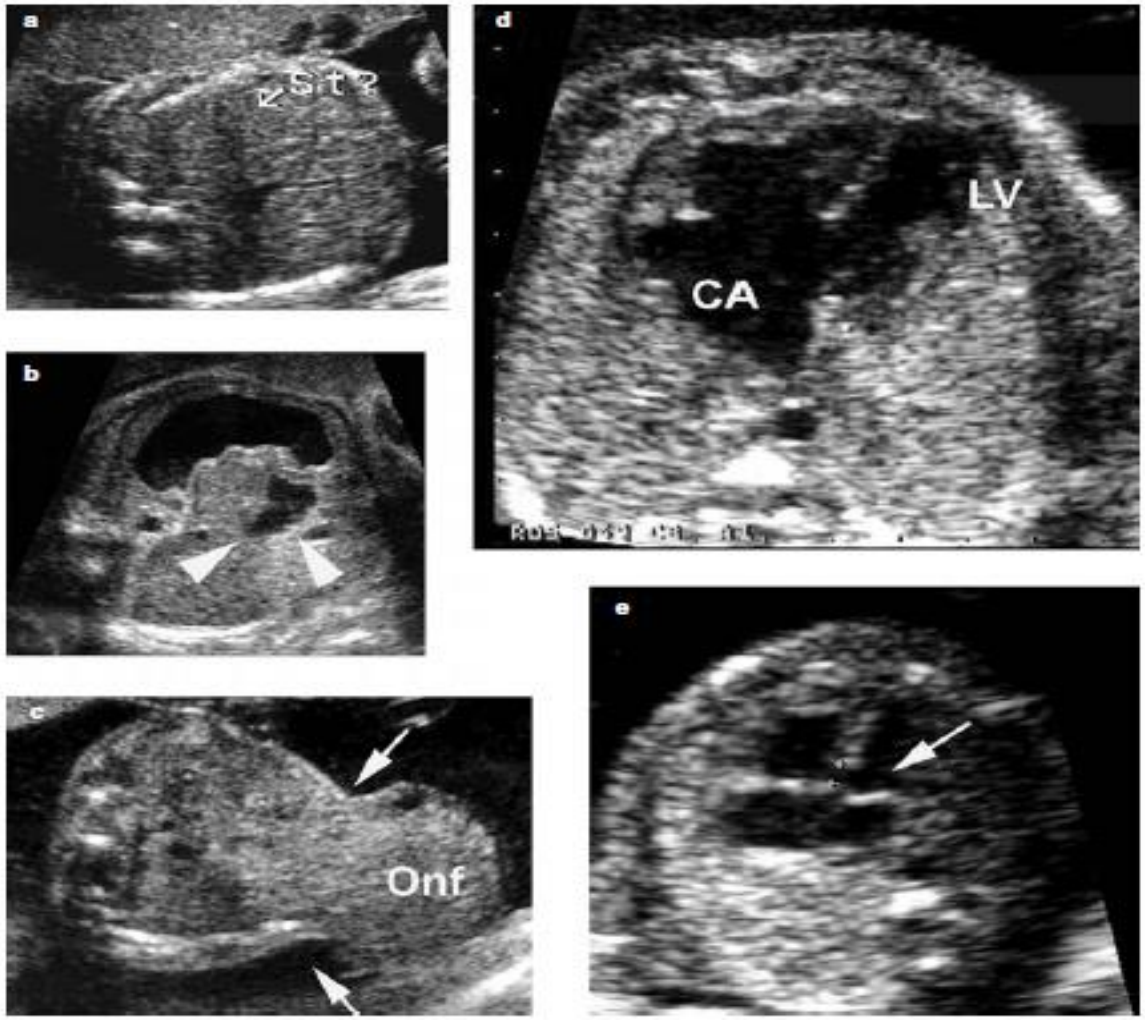


**Figure 10.1** Down syndrome: major signs. Axial view of the upper abdomen. (a) Esophageal atresia: the stomach (ST?) cannot be seen. (b) Duodenal atresia: the typical double bubble (arrowhead) is evident. (c) Omphalocele: the mass departing from the anterior abdominal wall (Onf) can be seen. The arrows indicate the abdominal defect. (d) Complete, balanced AVSD: a common atrium (CA) and a single atrioventricular valve are seen (LV, left ventricle). (e) Inlet VSD: small defect of the septum below the atrioventricular plane (arrow).

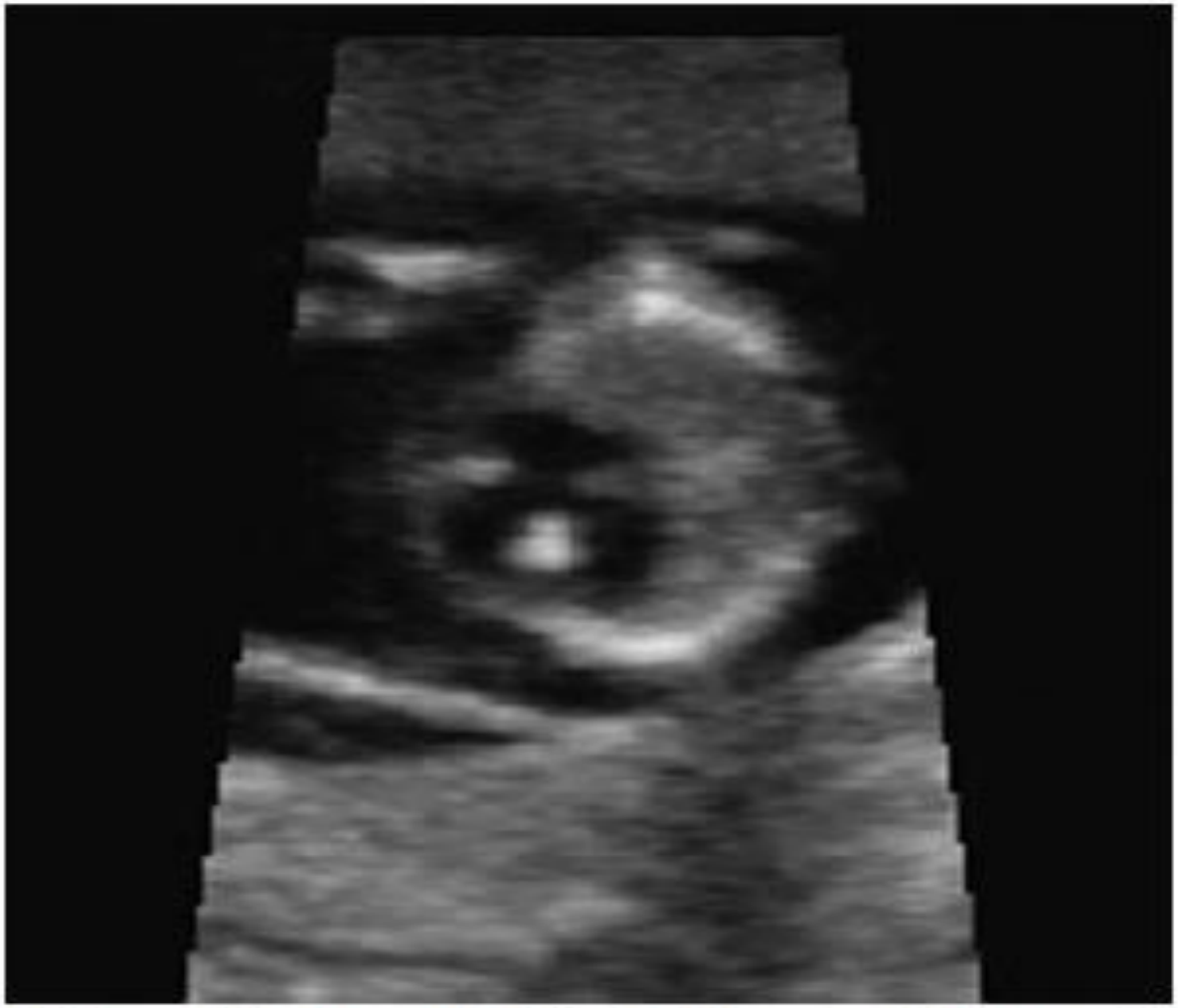

**FIG 5-23** Atrioventricular canal defect detected at 10 weeks' gestation in a fetus with a cystic hygroma. Cell-free fetal DNA test is positive for trisomy 13. Patient opted for termination of pregnancy.

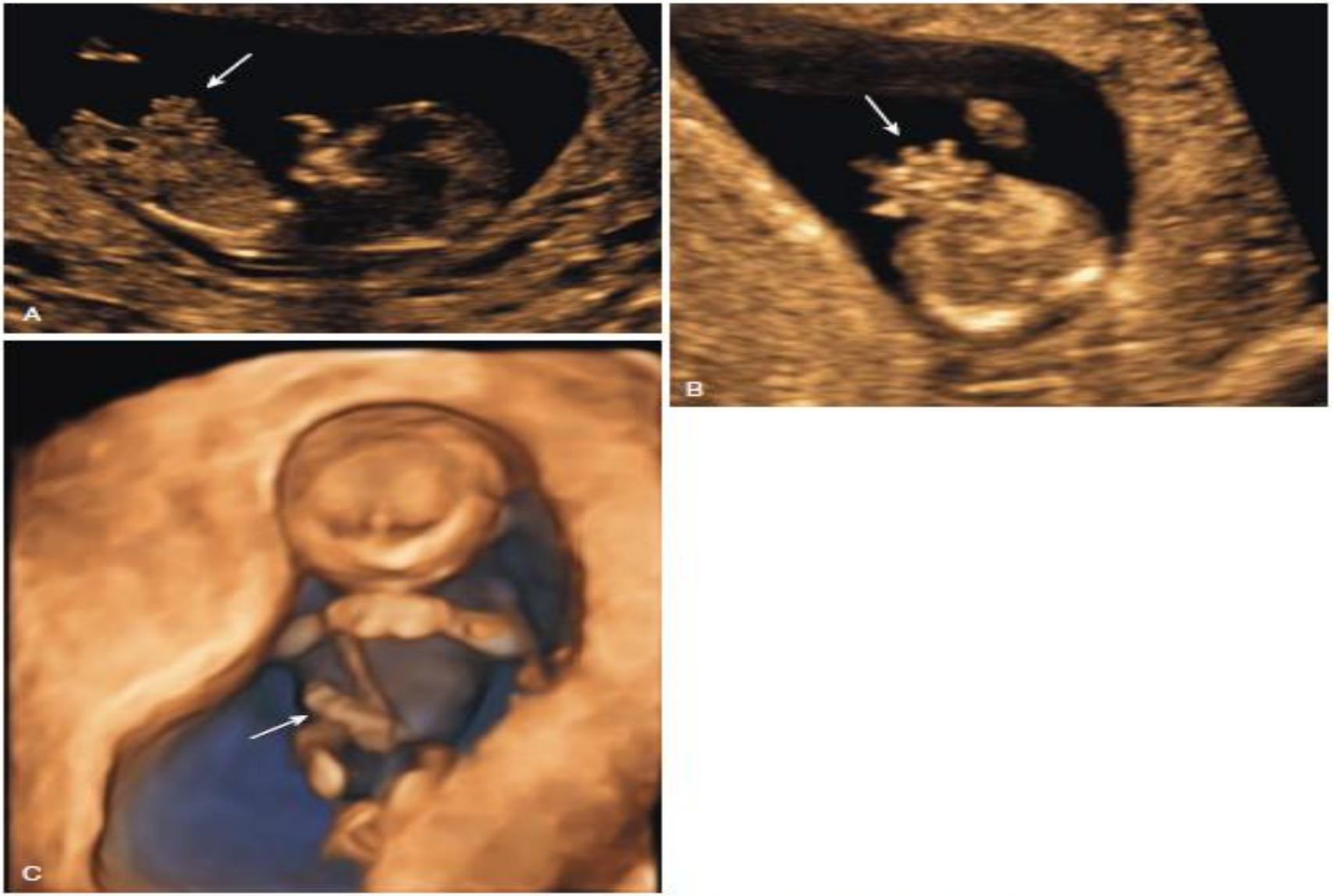


**FIG 5-24** Fetal gastroschisis (*arrows*) at 12 weeks' gestation in sagittal (**A**), axial (**B**), and three-dimensional (3D) (**C**) images. The 3D image clearly demonstrates the typical defect with extruded bowel to the right of the umbilical cord insertion. (Courtesy of Barbora Mrazek-Pugh.)

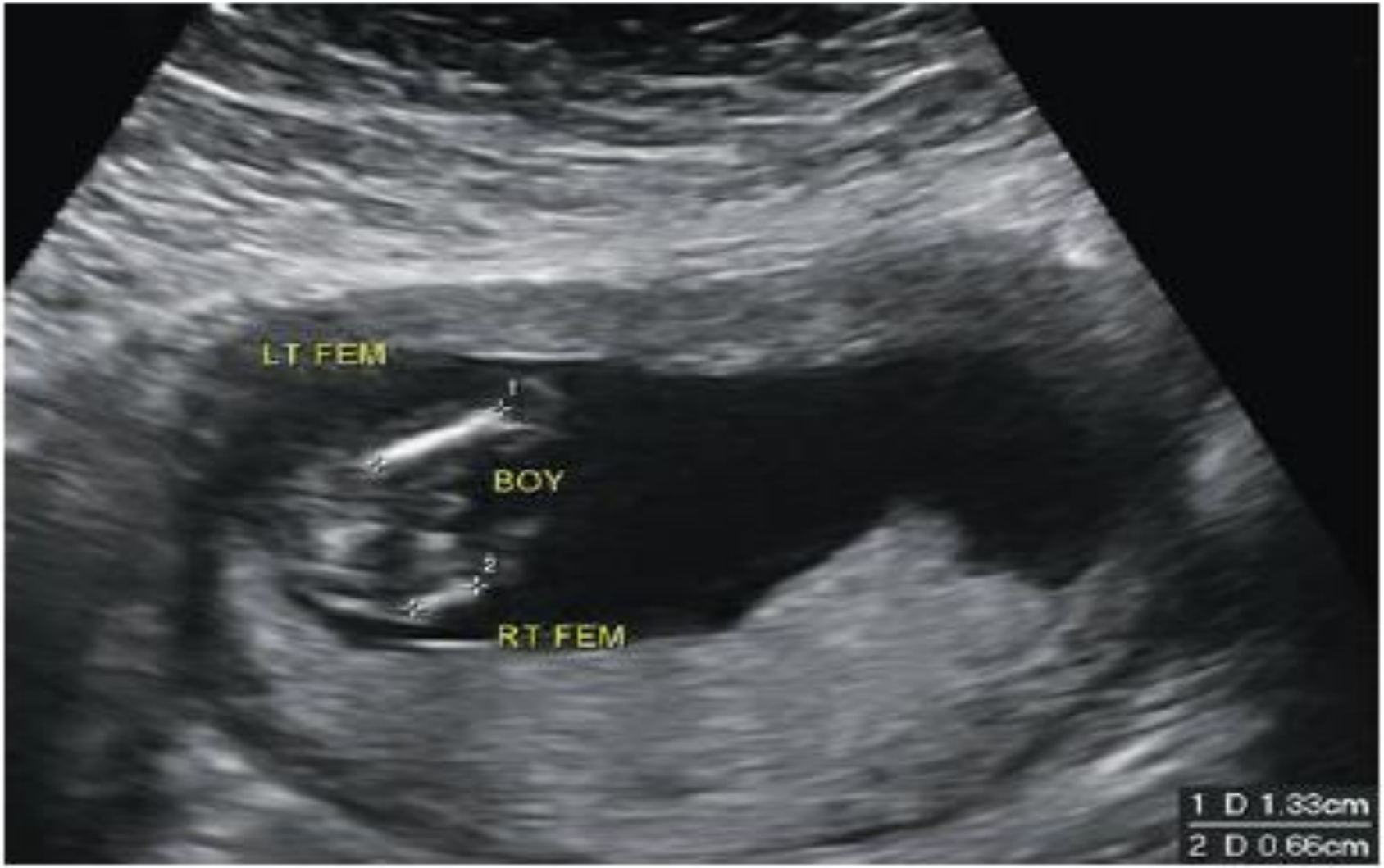


**FIG 5-25** Right focal femoral (RT FEM) deficiency detected at 13 weeks' gestation. LT FEM, left femoral.

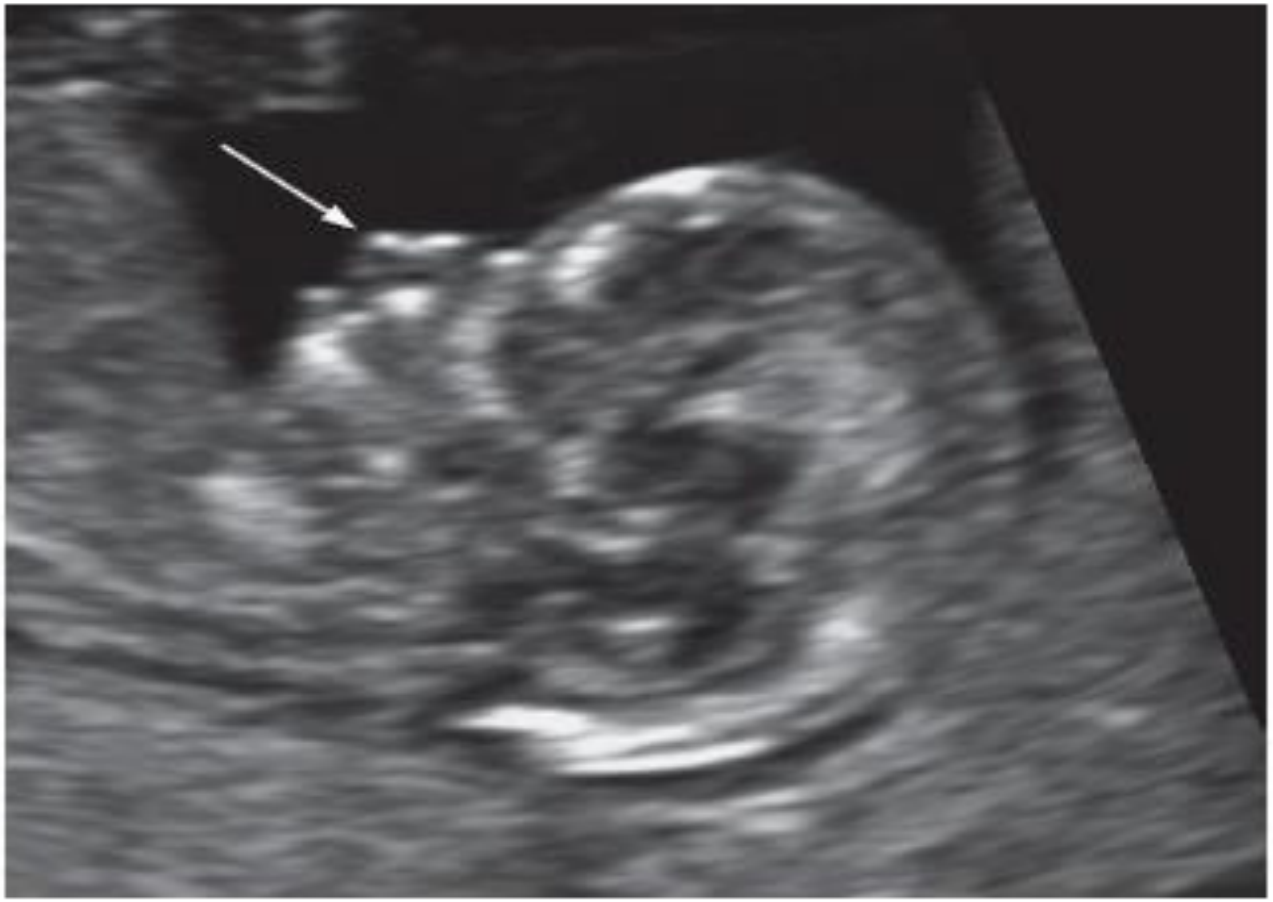

**Figure 29-2 Facial cleft.** Midsagittal view of the profile in a 12-week fetus showing a maxillary protruberance *(arrow)* characteristic of a large facial cleft.

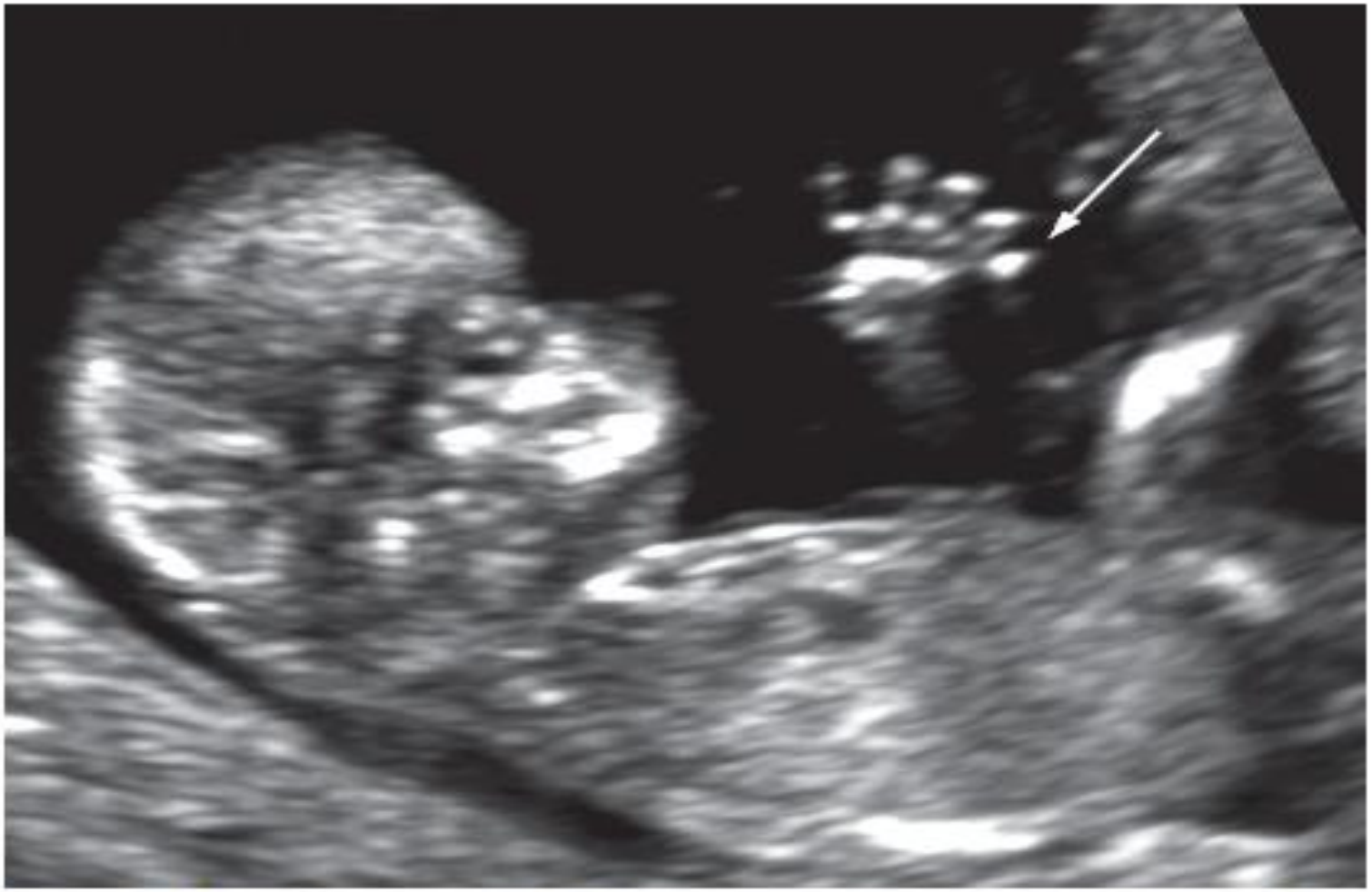

**Figure 29-8 Postaxial polydactyly.** Sagittal image of a 13-week fetus with upper extremity postaxial polydactyly. The *arrow* shows the extra digit. The thumb is not in the imaging plane.

## TABLE 5-4 First Trimester Detection Rate by Location of Fetal Anomaly

| Location of Anomaly | Detection Rate* |
|---|---|
| Neck | 92% |
| Abdomen | 88% |
| Brain and spine | 51% |
| Heart | 48% |
| Limbs | 34% |
| Genitourinary system | 34% |
| Face | 34% |

*Modified from Rossi AC, Prefumo F: Accuracy of ultrasonography at 11-14 weeks of gestation for detection of fetal structural anomalies: a systematic review. Obstet Gynecol 122(6):1160-1167, 2013.