36. Screening Ultrasonography in Pregnancy

RECOMMENDATION

Routine third-trimester ultrasound examination of the fetus is not recommended. There is insufficient evidence to recommend for or against routine ultrasound examination in the second trimester in low-risk pregnant women (see ***Clinical Intervention***).

Burden of Suffering

Ultrasonography is widely used in pregnancy in the U.S. According to 1992 U.S. natality data, 58% of mothers who had live births received ultrasonography in pregnancy, compared to 48% in 1989.[1] The highest rates occurred in white women and those ages 25–39 years. For asymptomatic low-risk women, a single scan in the second trimester may be used to estimate gestational age in women with unreliable dates of last menses and to detect multiple gestation and fetal malformations. A third-trimester scan may be used to screen for intrauterine growth retardation (IUGR) and fetal malpresentation as well as previously undetected multiple gestations and malformations.[2]

These conditions may be associated with increased maternal or perinatal morbidity and mortality. Inaccurate estimation of gestational age may lead to repeated testing of fetal well-being and induction of labor in pregnancies erroneously thought to be postterm.[3,4] About 25–45% of women are unable to provide an accurate menstrual history;[3,5,6] the estimated date of confinement derived from the last menstrual period differs by more than 2 weeks from the actual date of birth in nearly one quarter of pregnancies.[5] Multiple gestation is associated with increased perinatal mortality, preterm delivery, and other obstetric complications,[7] and it is more likely to result in cesarean delivery (56% compared to a baseline rate of 23%).[8] The ratio of multiple gestation births to all births (currently 24/1,000 live births) has risen steadily since 1972 and is the highest reported in the past 50 years.[1] Congenital anomalies are the leading cause of death before 1 year of age in the U.S., with a mortality rate of 1.7/1,000

live births, and are also important contributors to childhood morbidity and shortened life expectancy.[10,11] Fetal growth retardation has been associated with poor pregnancy outcomes, including fetal and neonatal death, reduced intelligence, seizures, and cerebral palsy, although most term growth-retarded infants develop normally.[12] Breech and other malpresentations may be associated with poor outcome and result in cesarean delivery in 84% of cases.[8] Malpresentation occurs in 38/1,000 live births, with the risk increasing with increasing age of the mother.[1]

Accuracy of the Screening Test

Real-time ultrasound consists of high-frequency sound waves that allow two-dimensional imaging of both structural and functional characteristics of the fetus, as well as the location and morphology of the placenta.[2] (This chapter will not address the topic of umbilical Doppler ultrasound[13]). Ultrasound is the recommended test for determination of gestational age in women with uncertain menstrual dates because measurement of the biparietal diameter, when performed early in the second trimester, has been shown to be accurate in determining gestational age.[5,6] Ninety percent of patients deliver within 2 weeks of the due date when gestational age is determined by early second-trimester ultrasound.[5]

Ultrasound can also detect multiple gestations, which are missed by clinical examination in nearly one third of cases.[14] One center that provided the only maternity services in its community reported that 98% of all twins were detected antenatally when routine ultrasound screening was performed.[4,6] The average gestational age at detection fell from 27 weeks to 20 weeks. Randomized controlled trials of routine ultrasound before 20 weeks found higher rates of early detection of multiple gestation with screening (83–100%) compared to unscreened controls (60–76%).[15–19] False-positive ultrasound diagnoses also occur, however, primarily in the first trimester; over 20% of multiple fetuses identified in the first trimester are either artifacts or die early in pregnancy.[20]

Many fetal structural malformations, including cardiac, gastrointestinal, renal, limb, and neural tube defects, can also be detected by current ultrasound techniques (for detailed discussion of ultrasound screening to detect chromosomal abnormalities and neural tube defects, see Chapters 41 and 42, respectively). Detection rates depend on the quality of the equipment and the expertise of the ultrasonographer. In a trial in low-risk pregnant women, routine serial ultrasonography at 15–22 and 31–35 weeks of gestation had a sensitivity of 35% for detecting fetuses with at least one major anomaly before delivery but only 17% for detection before the typical gestational-age limit for legal abortion (<24 weeks).[21] Only 4% of missed cases occurred in women who did not comply with scheduled screening ultrasounds. The sensitivity of selective ultrasound, performed

only for obstetric or medical indications, was significantly lower than routine ultrasound: 11% before delivery and 5% before 24 weeks. In this study, the sensitivity of routine midtrimester ultrasound was significantly higher at tertiary compared to other scanning facilities (35% vs. 13%). False-positive diagnoses were reported for 7 cases, or 0.9/1,000 pregnant women scanned before 24 weeks, with most reported from other than tertiary facilities. In another trial, the rates of detection of major malformations by screening before 20 weeks (confirmed at abortion or delivery) were 36% and 77% at two hospitals.[19] Ten of the thirty cases with suspected major malformations were judged normal at follow-up ultrasound examinations at 20–36 weeks and an 11th was found to have only a minor anomaly at delivery; 2.7/1,000 pregnant women received a false diagnosis of a major fetal malformation. Large case series evaluating routine ultrasound in low-risk women have reported sensitivities ranging from 21% to 74% for detecting major fetal abnormalities prior to 22–24 weeks among women who were scanned in the second trimester.[22–24] False-positive rates of 0.2–1.0/1,000 women scanned were reported; in one study, 6 of 8 initially false-positive diagnoses were corrected on follow-up evaluation. Direct comparisons of the trials and series results are hampered by varying definitions of "fetal malformation."

The ultrasound examination is the most accurate means of detecting IUGR, although the lack of consensus on standards for the definition or diagnosis of IUGR[12] makes evaluating screening tests for this condition difficult. Measurements of the fetal abdomen and head, and indices that compare the relative sizes of these structures, are accurate in assessing fetal growth.[25–32] A small abdominal circumference, for example, the most commonly affected anatomic measurement,[3] has a sensitivity of 80–96% and a specificity of 80–90% in detecting growth-retarded fetuses in the third trimester.[3,26,33,34] The product of the crown-rump length and the trunk area has a sensitivity of 94% and a specificity of 90%.[35] Because of the relatively low risk of IUGR in the general population, however, the likelihood that an abnormal test indicates IUGR is relatively low. For example, an abnormal abdominal circumference at 34–36 weeks' gestation indicates IUGR in only 21–50% of cases.[26,33,36] The generalizability of these studies has also been questioned; many had small samples, used only expert ultrasonographers, and/or suffered from methodologic limitations.[26,37] In addition, the definitions commonly used in these studies may cause normal but constitutionally small fetuses to be labeled as IUGR.

Effectiveness of Early Detection

For routine ultrasonographic screening to be proven beneficial, evidence is needed that interventions in response to examination results lead to improved clinical outcome. Twelve randomized controlled trials have exam-

ined the effectiveness of routine ultrasound screening in improving maternal or neonatal outcomes. Four of these evaluated a single ultrasound before 20 weeks,[15–17,19] three trials assessed serial ultrasound at 18–20 weeks and 31–35 weeks,[18,21,38–40] three trials evaluated one or two ultrasounds between 32 and 37 weeks when all subjects received one ultrasound before 24 weeks,[35,41,42] and two tested multiple scans (plus Doppler flow studies in one trial) every 3–4 weeks beginning at 24–28 weeks, with all subjects receiving a single midtrimester scan.[43,44] In a 13th trial, all subjects received three ultrasounds, but the results of placental grading at 34–36 weeks were reported only for the experimental group.[45] In addition, four meta-analyses have been published, none of which included the U.S. RADIUS trial, the most recent and largest to date.[46–49] In most of the trials, large proportions of the controls also received ultrasound results, although not with the same timing or frequency as in the screened groups.

The most important potential benefit of ultrasound screening is reduced perinatal mortality. Among the seven trials that evaluated an ultrasound before 20 weeks (with or without additional late ultrasound), only the Helsinki trial[19] and a meta-analysis heavily influenced by that trial's results[47] were able to demonstrate a statistically significant benefit in lowering perinatal mortality. Two trials[17,40] showed nonsignificant reductions in mortality while the remaining four trials and another meta-analysis[48] showed no mortality benefit. In the Helsinki trial, the overall perinatal death rate was 4.6/1,000 deliveries (n = 18) in screened women versus 9.0/1,000 deliveries (n = 34) in unscreened women. In the experimental group, 11 induced abortions were performed because of ultrasound findings and two babies died with major anomalies, compared to no abortions and 10 deaths with anomalies in the control group. There was no difference in perinatal mortality when the induced abortions resulting from ultrasound detection of congenital anomalies were included as deaths in the analysis. The meta-analysis[47] that reported a significant mortality reduction included the four then-published trials[16–19] that compared routine to selective ultrasound scanning and that reported number of pregnancies, deliveries, and perinatal deaths. It also evaluated the live birth rate, which takes into account induced abortions for malformations, and found it to be identical in the screened and control groups. The largest trial to date, the RADIUS trial,[38] randomized 15,151 low-risk pregnant women to routine ultrasound scans at 15–22 and 31–35 weeks of gestation or to usual care, which included ultrasounds performed for indications that developed after randomization. The risk of fetal or neonatal death was the same in the screened (0.6%, n = 52) and control (0.5%, n = 41) groups. Including induced abortions for fetal anomalies (9 vs. 5 in the routinely and selectively screened groups, respectively) did not affect these estimates.

Effects on neonatal and maternal morbidity from a single second-trimester scan have also been evaluated. Most of the trials and meta-analy-

ses showed no statistically significant benefit of prenatal ultrasound on neonatal morbidity (including low birth weight, admission to special care nursery, neonatal seizures, mechanical ventilation, and Apgar scores), or on maternal outcomes such as antenatal hospitalization.[15,17–19,46,47] In one randomized controlled trial of early second-trimester ultrasound,[16] babies born to screened women had a significantly greater mean birth weight (3,521 g vs. 3,479 g) than did those born to controls, with most of the benefit accruing to smokers. The Cochrane Database meta-analysis reported significantly fewer low birth weight singleton births and reduced risk of admission to special care nurseries with routine early ultrasound, but no effect on Apgar scores.[48] The RADIUS trial reported a slightly lower rate of tocolysis in screened women (3.4% vs. 4.2%), but no other differences in maternal outcomes (e.g., amniocentesis, external version, cesarean delivery, or days of hospitalization)[39] or in overall or individual indicators of perinatal morbidity.[38]

Accurate dates determined by second-trimester ultrasound might help prevent routine tests of fetal well-being and the induction of labor for fetuses thought to be postterm on the basis of erroneous dating.[3,4,26] Rates of induced labor for postterm pregnancy were significantly reduced in three trials[16,39,40] but were unaffected in two others;[17,18] meta-analysis demonstrated significantly decreased inductions for postterm pregnancy.[48] These trials may have underestimated such effects by including women with reliable dates, who are less likely to benefit from ultrasound dating. Trials and meta-analyses have not established whether overall rates of induced labor are reduced by a second-trimester ultrasound.[15–18,39,40,47,48] In the RADIUS trial, the significant decreases in induced labor for postterm pregnancy were completely offset by significant increases in inductions for IUGR.[39] Two meta-analyses[46,47] reported significant heterogeneity among the trials, suggesting that other factors, such as differences in obstetric management between countries or over time, may also influence this outcome. In one community, the incidence of postterm inductions fell from 8% to 2.6% after ultrasound screening was instituted,[4] but it was not proved that this trend was due specifically to improved accuracy of estimating gestational age. Two trials of second-trimester ultrasound reported other outcomes potentially related to inaccurate dates. The RADIUS trial found no significant effect of ultrasound screening on adverse perinatal outcomes among postdate pregnancies[38] or on the number of tests performed to assess fetal well-being.[39] Another trial reported significantly fewer days of inpatient neonatal care after treatment for “overdue pregnancy” among screened cases.[40]

Other potential benefits of prenatal ultrasound, including the early detection of multiple gestations and congenital anomalies, are often cited in support of screening. The early detection of multiple gestation, a risk factor for intrapartum and neonatal complications,[3] might allow improved

antenatal surveillance and management, but direct evidence of clinical benefits from early detection, such as improved maternal or neonatal outcome, is lacking. No significant improvements in fetal, neonatal, or maternal outcomes in multiple gestations were reported in any of the screening trials, except for a small reduction in use of tocolytics in the RADIUS trial.[15–19,38,39] Numbers of multiple gestations were small in all trials, however, and power to detect improved outcomes from screening was generally inadequate. There is also no clear evidence that early intervention for identified multiple gestation, including routine hospital admission for bed rest, cervical cerclage, or prophylactic oral tocolysis, results in improved perinatal outcome.[50]

While ultrasound before 20 weeks allows earlier detection of fetal structural malformations, it is not clear that this results in improved outcome. In the Helsinki trial, early detection led to an increased rate of elective abortions (2.7/1,000 screened women vs. 0/1,000 control women) and therefore to reduced perinatal deaths (see above).[19] On the other hand, in the RADIUS trial,[38] screening had no statistically significant effect on the rate of induced abortion (n = 9 or 1.2/1,000 screened women compared to n = 4 or 0.5/1,000 controls). Although early detection might theoretically improve survival for infants with fetal anomalies if they could be delivered at tertiary care centers capable of immediate medical and surgical intervention, no significant effects of early detection on overall perinatal mortality, or on survival rates among infants born with acute life-threatening anomalies or with any major anomalies, were seen in the RADIUS trial.[21,38] Other trials of routine ultrasound before 20 weeks have detected too few (i.e., 0–2) malformations to allow meaningful comparisons of outcomes.[15–18,40] None of the trials has evaluated whether routine screening improves outcomes in newborns with nonlethal anomalies.

Eight randomized controlled trials and one meta-analysis have evaluated the effectiveness of routine third-trimester ultrasound focused on fetal anthropometry and morphology in improving outcomes.[18,35,38–44,49] Six trials involved low-risk patients or patients selected from the general population,[18,35,38–40,42,43] while two were restricted to women with suspected IUGR or at increased risk for IUGR or other complications (with results of the scan either released or withheld based on randomization).[41,44] Several of these trials had methodologic problems such as inadequate reporting of results,[40] use of hospital number for randomization,[35] and the revealing of test results for nearly one third of cases in the control group because of obstetrician requests.[41] These studies reported no significant reductions in low Apgar scores, admission to or length of stay in special care nursery, low birth weight or preterm delivery, perinatal morbidity, or perinatal mortality (excluding lethal malformations). There were also no consistent beneficial effects on antenatal hospitalization or induction of labor. The meta-analysis[49] reported that third-trimester ultra-

sound was associated with a significantly increased risk of antenatal hospital admission. One additional randomized controlled trial in unselected women, all of whom received ultrasounds at midtrimester and twice in the third trimester, evaluated whether reporting the result of placental grading by third-trimester ultrasound to the clinician responsible for care improved neonatal outcome.[45] Reporting the placental grading was associated with significant reductions in meconium staining in labor, low Apgar scores at 5 minutes, and perinatal mortality in normally formed babies. One previously cited trial[43] of serial third-trimester ultrasounds also assessed placental morphology and reported no beneficial effects of ultrasound on perinatal mortality or morbidity, but the method of assessing placental morphology was not described. Additional trials of third-trimester placental grading are needed to assess its effectiveness.

There is no clear evidence of important adverse effects related to screening ultrasonography reported from the published randomized controlled trials, although such effects might be difficult to detect given the small number of ultrasounds (usually one or two per patient) and the fact that the controls in many trials were also scanned, with results concealed. One randomized controlled trial compared routine multiple ultrasound scans plus Doppler flow studies to selective ultrasound for indications, with four or more scans being done in 91% of screened vs. 8% of control women.[43] The screened group had a significantly higher percentage of infants with birth weight below the 3rd and 10th percentiles. Although this was not a primary endpoint of the study, it suggests a possible adverse effect of frequent ultrasound examinations with Doppler studies on fetal growth, which is supported by several studies in mice and monkeys.[51–53] Long-term follow-up of singleton live births to age 8–9 years from the two Norwegian trials (in which only 19% of controls received ultrasound) was performed to evaluate possible adverse effects of ultrasound on neurologic development.[54,55] These two studies, with 83–89% response rates, found no differences between the two groups in school performance; deficits in attention, motor control, or perception (by parent questionnaire); development in infancy; or prevalence of dyslexia. Although false-positive diagnoses of major fetal malformations occurred in both the Helsinki trial (2.7/1,000 women in the screened group) and in the RADIUS trial (0.9/1,000), none of these pregnancies was electively aborted as a result.[19,21] Case reports have suggested adverse psychological effects of early and false-positive diagnoses of fetal abnormalities,[56–58] but no controlled studies that evaluated adverse effects of ultrasound diagnosis of fetal anomalies were found.

Recommendations of Other Groups

A National Institutes of Health consensus development conference recommended that ultrasound imaging during pregnancy be performed only

for a specific medical indication and not for routine screening.[59] This is also the position of the American College of Obstetricians and Gynecologists.[2] The Canadian Task Force on the Periodic Health Examination found fair evidence to recommend a single second-trimester ultrasound examination in women with normal pregnancies, but concluded that there was insufficient evidence to recommend the inclusion or exclusion of routine serial ultrasound screening for IUGR in normal pregnancies.[60]

Discussion

Neither early, late, nor serial ultrasound in normal pregnancy has been proven to improve perinatal morbidity or mortality. Clinical trials show that a single midtrimester ultrasound examination detects multiple gestations and congenital malformations earlier in pregnancy, but there is currently insufficient evidence that early detection results in improved outcomes. In the U.S., it is not clear whether early detection of fetal anomalies by routine ultrasound leads to increased rates of induced abortion. In addition, many of the major fetal anomalies discoverable by routine ultrasound might be detected anyway during screening for Down syndrome (see Chapter 41) or neural tube defects (see Chapter 42). Routine second-trimester ultrasound can lower the rate of induction for presumed postterm pregnancy, a benefit likely to accrue primarily to women with unreliable dates, among whom ultrasound is more accurate than dates for predicting actual date of delivery. Early ultrasound has not been proven to reduce overall rates of induction, however, due to increases in inductions for other indications. It is also unclear whether the likeliest potential benefits of routine second-trimester ultrasound (reduced induction of labor for postterm pregnancy and increased induced abortions for fetal anomalies) would justify the significant economic implications of widespread testing. No benefits of routine ultrasound examination of the fetus in the third trimester have been demonstrated despite multiple randomized controlled trials. Additional trials of third-trimester placental grading are needed to adequately evaluate the potential benefits of screening for placental appearance. Further research to evaluate possible adverse effects of ultrasound and the cost-effectiveness of routine screening is also needed.

CLINICAL INTERVENTION

Routine ultrasound examination of the fetus in the third trimester is not recommended, based on multiple trials and meta-analyses showing no benefit for either the pregnant woman or her fetus (“D” recommendation). There is currently insufficient evidence to recommend for or against a single routine midtrimester ultrasound in low-risk pregnant women (“C” recommendation). These recommendations apply to routine screening

ultrasonography and not to diagnostic ultrasonography for specific clinical indications (e.g., follow-up evaluation of elevated maternal serum α-fetoprotein). Recommendations regarding screening for Down syndrome appear in Chapter 41, and those for neural tube defects appear in Chapter 42.

The draft update of this chapter was prepared for the U.S. Preventive Services Task Force by Carolyn DiGuiseppi, MD, MPH, based in part on materials prepared for the Canadian Task Force on the Periodic Health Examination by Geoffrey Anderson, MD, PhD.

REFERENCES

1. Ventura SJ, Martin JA, Taffel SM, et al. Advance report of final natality statistics, 1992. Monthly vital statistics report; vol 43 no 5 (suppl). Hyattsville, MD: National Center for Health Statistics, 1994.
2. American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. Technical Bulletin no. 187. Washington, DC: American College of Obstetricians and Gynecologists, 1993.
3. Warsof SL, Pearce JM, Campbell S. The present place of routine ultrasound screening. Clin Obstet Gynecol 1983;10:445–457.
4. Persson PH, Kullander S. Long-term experience of general ultrasound screening in pregnancy. Am J Obstet Gynecol 1983;146:942–947.
5. Campbell S, Warsof SL, Little D, et al. Routine ultrasound screening for the prediction of gestational age. Obstet Gynecol 1985;65:613–620.
6. Grennert L, Persson PH, Gennser G. Benefits of ultrasonic screening of a pregnant population. Acta Obstet Gynecol 1978;78:5–14.
7. Klein L, Goldenberg RL. Prenatal care and its effect on preterm birth and low birth weight. In: Merkatz IR, Thompson JE, eds. New perspectives on prenatal care. New York: Elsevier, 1990:501–529.
8. Taffel SM. Cesarean delivery in the United States, 1990. National Center for Health Statistics. Vital Health Statistics, Series 21, no. 51. Washington, DC: Government Printing Office, 1994. (Publication no. DHHS (PHS) 94-1929.)
9. *Deleted in proof.*
10. National Center for Health Statistics. Annual summary of births, marriages, divorces, and deaths: United States, 1993. Monthly vital statistics report; vol 42 no 13. Hyattsville, MD: Public Health Service, 1994.
11. Powell-Griner E, Woolbright A. Trends in infant deaths from congenital anomalies: results from England and Wales, Scotland, Sweden and the United States. Int J Epidemiol 1990;19:391–398.
12. Goldenberg RL, Davis RO, Nelson KG. Intrauterine growth retardation. In: Merkatz IR, Thompson JE, eds. New perspectives on prenatal care. New York: Elsevier, 1990:461–478.
13. Giles W, Bisits A. Clinical use of Doppler ultrasound in pregnancy: information from six randomised trials. Fetal Diagn Ther 1993;8:247–255.
14. Farooqui MD, Grossman JH 3d, Shannon RA. A review of twin pregnancy and perinatal mortality. Obstet Gynecol Surv 1973;28(suppl):144–152.
15. Bennett MJ, Little G, Dewhurst J, et al. Predictive value of ultrasound measurement in early pregnancy: a randomized controlled trial. Br J Obstet Gynaecol 1982;89:338–341.
16. Waldenstrom U, Axelsson O, Nilsson S, et al. Effects of routine one-stage ultrasound screening in pregnancy: a randomised controlled trial. Lancet 1988;2:585–588.
17. Ewigman B, LeFevre M, Hesser J. A randomized trial of routine prenatal ultrasound. Obstet Gynecol 1990;76: 189–194.
18. Bakketeig LS, Eik-Nes SH, Jacobsen G, et al. Randomised controlled trial of ultrasonographic screening in pregnancy. Lancet 1984;2:207–211.
19. Saari-Kemppainen A, Karjalainen O, Ylostalo P, et al. Ultrasound screening and perinatal mortality: controlled trial of systematic one-stage screening in pregnancy. The Helsinki Ultrasound Trial. Lancet 1990;336:387–391.
20. Landy HJ, Weiner S, Corson SL, et al. The "vanishing twin": ultrasonographic assessment of fetal disappearance in the first trimester. Am J Obstet Gynecol 1986;155:14–19.
21. Crane JP, LeFevre ML, Winborn RC, et al. A randomized trial of prenatal ultrasonographic screening: impact on the detection, management and outcome of anomalous fetuses. The RADIUS Study Group. Am J Obstet Gynecol 1994;171:392–399.

22. Chitty LS, Hunt GH, Moore J, et al. Effectiveness of routine ultrasonography in detecting fetal structural abnormalities in a low-risk population. BMJ 1991;303:1165–1169.
23. Shirley IM, Bottomley F, Robinson VP. Routine radiographer screening for fetal abnormalities by ultrasound in an unselected low risk population. Br J Radiol 1992;65:564–569.
24. Levi S, Hyjazi Y, Schaaps J-P, et al. Sensitivity and specificity of routine antenatal screening for congenital anomalies by ultrasound: the Belgian Multicentric Study. Ultrasound Obstet Gynecol 1991;1:102–110.
25. Mintz MC, Landon MB. Sonographic diagnosis of fetal growth disorders. Clin Obstet Gynecol 1988; 31:44–52.
26. Geirsson RT, Persson PH. Diagnosis of intrauterine growth retardation using ultrasound. Clin Obstet Gynecol 1984; 11:457–479.
27. Pearce JM, Campbell S. A comparison of symphysis-fundal height and ultrasound as screening tests for light-for-gestational-age infants. Br J Obstet Gynaecol 1987;94:100–104.
28. Eik-Nes SH, Persson PH, Grottum P, et al. Prediction of fetal growth deviation by ultrasonic biometry. II. Clinical application. Acta Obstet Gynecol 1983;62:117–123.
29. Campbell S, Kurjak A. Comparison between urinary oestrogen assay and serial ultrasonic cephalometry in assessment of fetal growth retardation. BMJ 1972;2:336–340.
30. Campbell S, Dewhurst CJ. Diagnosis of the small-for-dates fetus by serial ultrasonic cephalometry. Lancet 1971; 2:1002–1006.
31. Persson PH, Grennert L, Gennser G. Diagnosis of intrauterine growth retardation by serial ultrasonic cephalometry. Acta Obstet Gynecol Scand [Suppl] 1978;78:40–48.
32. Secher NJ, Hansen PK, Lenstrup C, et al. On the evaluation of routine ultrasound screening in the third trimester for detection of light for gestation age (LGA) infants. Acta Obstet Gynecol Scand 1987; 66:463–471.
33. Brown HL, Miller JM, Gabert HA, et al. Ultrasonic recognition of the small-for-gestational-age fetus. Obstet Gynecol 1987;69:631–635.
34. Neilson JP, Whitfield CR, Aitchison TC. Screening for the small-for-dates fetus: a two-stage ultrasonic examination schedule. BMJ 1980;280:1203–1206.
35. Neilson JP, Munjanja SP, Whitfield CR. Screening for small-for-dates fetuses: a controlled trial. BMJ 1984;289: 1179–1182.
36. Warsof SL, Cooper DJ, Little D, et al. Routine ultrasound screening for antenatal detection of intrauterine growth retardation. Obstet Gynecol 1986;67:33–39.
37. Deter RL, Harrist RB, Hadlock FP, et al. The use of ultrasound in the detection of intrauterine growth retardation: a review. J Clin Ultrasound 1982;10:9–16.
38. Ewigman BG, Crane JP, Frigoletto FD, et al. Effect of prenatal ultrasound screening on perinatal outcome. The RADIUS Study Group. N Engl J Med 1993;329:821–827.
39. LeFevre ML, Bain RP, Ewigman BG, et al. A randomized trial of prenatal ultrasonographic screening: impact on maternal management and outcome. The RADIUS Study Group. Am J Obstet Gynecol 1993; 169:483–489.
40. Eik-Nes SH, Okland O, Aure JC, et al. Ultrasound screening in pregnancy: a randomised controlled trial. Lancet 1984;1:1347.
41. Secher NJ, Hansen PK, Lenstrup C, et al. A randomized study of fetal abdominal diameter and fetal weight estimation for detection of light-for-gestation infants in low-risk pregnancies. Br J Obstet Gynaecol 1987;94:105–109.
42. Duff GB. A randomized controlled trial in a hospital population of ultrasound measurement screening for the small-for-dates baby. Aust NZ J Obstet Gynaecol 1993;33:374–378.
43. Newnham JP, Evans SF, Michael CA, et al. Effects of frequent ultrasound during pregnancy: a randomised controlled trial. Lancet 1993;342:887–891.
44. Larsen T, Larsen JF, Petersen S, et al. Detection of small-for-gestational-age fetuses by ultrasound screening in a high-risk population: a randomized controlled study. Br J Obstet Gynaecol 1992;99:469–474.
45. Proud J, Grant AM. Third trimester placental grading by ultrasonography as a test of fetal wellbeing. BMJ 1987;294: 1641–1647.
46. Thacker SB. Quality of controlled clinical trials. The case of imaging ultrasound in obstetrics: a review. Br J Obstet Gynaecol 1985;92:437–444.
47. Bucher HC, Schmidt JG. Does routine ultrasound scanning improve outcome in pregnancy? Meta-analysis of various outcome measures. BMJ 1993;307:13–17.

48. Neilson JP. Routine ultrasound in early pregnancy. In: Enkin MW, Keirse MJNC, Renfrew MJ, Neilson JP, eds. Pregnancy and childbirth module, Cochrane database of systematic reviews, review no. 03872, June 1993. Oxford: Update Software, 1994, Disk Issue 1.
49. Neilson JP. Routine fetal anthropometry in late pregnancy. In: Enkin MW, Keirse MJNC, Renfrew MJ, Neilson JP, eds. Pregnancy and childbirth module, Cochrane database of systematic reviews, review no. 03873, March 1993. Oxford: Update Software, 1994, Disk Issue 1.
50. Klein L, Goldenberg RL. Prenatal care and its effect on preterm birth and low birth weight. In: Merkatz IR, Thompson JE, eds. New perspectives on prenatal care. New York: Elsevier, 1990;501–529.
51. O'Brien WD Jr. Dose dependent effect of ultrasound on fetal weight in mice. J Ultrasound Med 1983; 2:1–8.
52. Tarantal AF, Hendrickx AG. Evaluation of the bioeffects of prenatal ultrasound exposure in the Cynomolgus Macaque (Macaca fascicularis): I. Neonatal/infant observations. Teratology 1989;39: 137–147.
53. Tarantal AF, O'Brien WD, Hendrickx AG. Evaluation of the bioeffects of prenatal ultrasound exposure in the Cynomolgus Macaque (Macaca fascicularis): III. Developmental and hematologic studies. Teratology 1993;47: 159–170.
54. Salvesen KA, Bakketeig LS, Eik-Nes SH, et al. Routine ultrasonography in utero and school performance at age 8–9 years. Lancet 1992;339:85–89.
55. Salvesen KA, Vatten LJ, Eik-Nes SH, et al. Routine ultrasonography in utero and subsequent handedness and neurological development. BMJ 1993;307:159–164.
56. Griffiths DM, Gough MH. Dilemmas after ultrasonic diagnosis of fetal abnormality. Lancet 1985;i: 623–624.
57. Brereton RJ. Importance of surgical consultation after ultrasonic diagnosis. BMJ 1984;289:1618–1619.
58. Murphy S, Das P, Grant DN, et al. Importance of neurosurgical consultation after ultrasonic diagnosis of fetal hydrocephalus. BMJ 1984;289:1212–1213.
59. National Institutes of Health Consensus Development Conference. The use of diagnostic ultrasound imaging during pregnancy. JAMA 1984;252:669–672.
60. Canadian Task Force on the Periodic Health Examination. Canadian guide to clinical preventive health care. Ottawa: Canada Communication Group, 1994:4–14.