Maternal Age Related Issues

Background

1. Definition:
    - Advanced maternal age:
        - Pregnant woman who will be ≥35 years of age on the estimated date of confinement
    - Term becoming obsolete; some experts suggest definition should be more dynamic
    - Greatest risk occurs >40 yr
2. General info:
    - Patients of AMA have 2-3x higher rates of hospitalization, cesarean delivery, and pregnancy -related complications
    - Racial considerations:
        - African Americans have 2x risk of adverse perinatal outcomes

Pregnancy Risk for Complications

1. Fetal anomalies
    - Chromosomal anomalies
        - 1/66 risk in women >40 yo
    - Cardiac malformations
    - Clubfoot
    - Diaphragmatic hernia
2. Miscarriage
    - Increase in both trisomic and euploid losses
    - 2.0 adjusted odds ratio for age 35-39 yr
    - 2.4 adjusted odds ratio for age ≥40 yr
3. Ectopic pregnancy
    - 2-8x increased risk of ectopic pregnancy
4. Preterm labor & delivery
    - Women ≥40 yo have adjusted odds ratio 1.4 for preterm delivery
5. Hypertension related complications
    - Maternal age >40 years RR 1.96 (95% CI 1.34-2.87) for multiparous women
    - Also increased if >10 year interval since previous pregnancy
6. Gestational diabetes
    - Adjusted odd ratio 1.8 for women aged 35-39 years and 2.4 for women ≥40 years old
    - ACOG considers age >25 a risk factor for gestational diabetes and recommends screening
7. Stillbirth
    - Relative risks of 1.2-4.5
    - Strategy of antepartum testing at 38 weeks may be beneficial
8. Placenta previa
    - Nulliparous women ≥40 years of age have 10x increased risk of placenta previa compared to nulliparous women aged 20-29
    - Absolute risk still small (0.25 vs 0.03%)
9. Placental abruption

- Women aged 40 years and older had adjusted odds ratio 2.3 for abruption (when compared to women <35)

10. Caesarean section
    - Women ≥35 years of age are more likely to deliver by cesarean

Screening

1. First trimester options
    - Tests:
        - Fetal nuchal translucency
        - Serum markers of beta-hCG and pregnancy-associated plasma protein A (PAPP-A)
    - Combination results in higher Down syndrome detection rate than 2nd-trimester maternal serum triple screen and is comparable to quadruple screen
    - Detects 83% of cases of Down syndrome, with 5% FPR
    - Women found to have increased risk should be offered
        - Genetic counseling
        - Chorionic villus sampling (CVS) or 2nd trimester amniocentesis
2. Second trimester options
    - **Triple Screen**
        - Combination of maternal age and MSAFP, unconjugated estriol (MSuE3) and human chorionic gonadotropin (MS hCG) measured at 15-20 weeks gestation
        - Detects 65% of fetuses with Down syndrome with 5% FPR
        - Also detects neural tube defects, gastroschisis, omphalocele, placental dysfunction, Smith-Lemli-Opitz syndrome, and trisomy 18
    - **Quad screen**
        - Adds dimeric inhibin-A (DIA) to triple screen
        - Increases detection rate to 75-85%
    - Note: if patient received 1st trimester testing, subsequent 2nd trimester screening is not indicated
        - Unless performed as a component of integrated test, stepwise sequential, or contingent sequential test
3. Combined trimester options
    - **Integrated test**
        - Definition:
            - Measurement of serum markers with or without ultrasound, in 1st and 2nd trimesters
            - Nuchal translucency at 10-13 weeks
            - PAPP-A at 10-13 weeks
            - alpha fetoprotein (AFP), unconjugated estriol (uE3), hCG, and inhibin A obtained at 15-18 weeks
        - Sensitivity:
            - Greater with lower false-positive rates than 1st-trimester screening alone
    - **Stepwise sequential test**
        - Definition:
            - 1st trimester portion of integrated screen; offer CVS only to women at high risk of an affected fetus

- **Contingent sequential test**
  - Definition:
    - 3 tiered approach with subsequent decisions based on 1st trimester results
      - Women at very high risk offered immediate invasive prenatal diagnosis
      - Women at very low risk provided with their risk estimate and require no additional testing
      - Women at intermediate risk receive 2nd trimester marker testing

4. Research
   - SEQureDx
     - Uses fetal nucleic acid technology
     - Non-invasive test
     - Still being studied

Pregnancy Monitoring

1. Early pregnancy:
   - No recommendations
2. Late pregnancy:
   - No randomized control trials to assess efficacy of a strategy of routine antepartum testing late in pregnancy
   - Weekly antepartum testing and labor induction may lower the risk of unexplained fetal death in women $\geq$35 yo
   - Consider weekly monitoring starting at 38 weeks

Current Recommendations

1. ACOG 2007 recommendations
   - All women be offered aneuploidy screening before 20 weeks of gestation
   - All women should have the option of invasive testing, regardless of maternal age
2. USPTSF 1996 recommendations
   - Offering screening for Down syndrome and neural tube defects by serum multiple-marker testing is recommended for all low-risk pregnant women
     - (This testing should be offered only to women who are seen for prenatal care in locations that have adequate counseling and follow-up services)
   - Offering amniocentesis or chorionic villus sampling (CVS) for chromosome studies is recommended for pregnant women at high risk for Down syndrome
   - Insufficient evidence to recommend for or against screening for Down syndrome by individual serum marker testing or ultrasound examination
   - Offering routine CVS or amniocentesis to women >35 should be done with discussion of the risks and benefits
   - Daily multivitamins with folic acid to reduce the risk of neural tube defects are recommended for all women who are planning or capable of pregnancy

Patient Education

1. http://www.acog.org/publications/patient_education/bp094.cfm
2. http://www.marchofdimes.com.offcampus.lib.washington.edu/pnhec/159_14008.asp (Pregnancy after age 35)

References

1. Cleary-Goldman J. Impact of maternal age on obstetric outcome. Obstet Gynecol 2005 May;105(5):983-990.
2. Duru UA. Indications for antepartum testing: making the case for antepartum surveillance or timed delivery for women of advanced maternal age. Semin Perinatol. 2008 Aug; 32(4):312-7.
3. Seidman DS, Ever-Hadani P, Gale R. Effect of maternal smoking and age on congenital anomalies.Obstet Gynecol 1990 Dec;76(6):1046-50.
4. Hassold T, Chiu D. Maternal age-specific rates of numerical chromosome abnormalities with special reference to trisomy.Hum Genet 1985;70(1):11-7.
5. Nybo Andersen AM et.al. Maternal age and fetal loss: population based register linkage study. BMJ 2000 Jun 24;320(7251):1708-12.
6. Conde-Agudelo A, Belizán JM. Maternal morbidity and mortality associated with interpregnancy interval: cross sectional study. BMJ 2000 Nov 18;321(7271):1255.
7. Huang L., et al. Maternal age and risk of stillbirth: a systematic review. CMAJ. 2008 Jan 15;178(2):165-72.
8. Reddy UM, Ko CW, Willinger M. Maternal age and the risk of stillbirth throughout pregnancy in the United States. Am J Obstet Gynecol. 2006 Sept; 195(3): 764-70.
9. Fretts RC, et.al. Should older women have antepartum testing to prevent unexplained stillbirth? Obstet Gynecol. 2004 Jul;104(1):56-64.
10. Bahtiyar MO, et.al. Stillbirth at term in women of advanced maternal age in the Unisted States: when could antenatal testing be initiated? Am J Perinatol. 2008 May;25(5):301-4.
11. Gilbert WM, Nesbitt TS, Danielsen B. Childbearing beyond age 40: pregnancy outcome in 24,032 cases. Obstet Gynecol 1999 Jan;93(1):9-14.
12. Summers AM, et.al. Maternal serum screening in Ontario using the triple marker test. J Med Screen 2003;10:107–11.
13. Puszyk WM, Crea F, Old RW. Noninvasive prenatal diagnosis of aneuploidy using cell-free nucleic acids in maternal blood: promises and unanswered questions. Prenat Diag. 2008 Jan 28 (1):1-6.

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