Gestational age at abortion: The impact of first-trimester risk assessment for aneuploidy

Stephen T. Chasen, MD,* Robin B. Kalish, MD, Frank A. Chervenak, MD

Objective: The purpose of this study was to determine the impact of first-trimester risk assessment on gestational age at abortion for abnormal fetal karyotype.

Study design: Women who had abortion for trisomies 21, 18, and 13, 45X, and Triploidy in our hospital from 1999 to 2005 were included. Data collected included gestational age at abortion, method of prenatal diagnosis, and whether or not first-trimester risk assessment was performed. Analysis was performed using Spearman Correlation, Chi-square for trend, Fisher exact test, and Mann-Whitney U test.

Results: One hundred forty-nine patients were included. There was an inverse correlation between year of abortion and gestational age (rho = −0.31; P < .001) coinciding with significant increases in the rates of first-trimester risk assessment and prenatal diagnosis by chronic villus sampling.

Conclusion: First-trimester risk assessment is associated with earlier diagnosis of aneuploidy. In our institution, this has led to earlier abortions. Availability of quality first-trimester risk assessment can decrease the need for abortion later in pregnancy.

Fetal aneuploidy is most often detected in the second trimester following amniocentesis. Recent advances in prenatal risk assessment now allow pregnancies at high risk to be identified in the first trimester.8,7 The use of first-trimester risk assessment with nuchal translucency (NT) and biochemistry has been expanding.7 Early risk assessment, which is associated with higher detection rates compared to second-trimester biochemical testing, provides women with precise information regarding risk of trisomy 21, trisomy 18, and trisomy 13 in the first-trimester. Ultrasound will be abnormal in most cases of Turner syndrome and triploidy as well.8,9

Most women undergoing first-trimester risk assessment will receive early reassurance that the risk is quite low. When testing indicates increased risk, women have
the option to undergo prenatal diagnosis with chorionic villus sampling (CVS). Our objective was to determine whether the increasing rate of first-trimester risk assessment for aneuploidy is associated with earlier gestational age at abortion in affected pregnancies.

**Material and Methods**

We identified women who had abortion for aneuploidy in our hospital from 1999 to 2005. Those with aneuploidy associated with high detection rates with first-trimester risk assessment (trisomy 21, trisomy 18, trisomy 13, triploidy, and Turner syndrome) were included. To minimize the variation in the patient population over time, only those patients referred by obstetricians who deliver patients at our hospital were included. All first-trimester risk assessment was done in our department.

Throughout the entire study period, amniocentesis, CVS, and second-trimester abortion have been available. First-trimester risk assessment has been available since 2000, when we began combining NT with maternal age. Results were available at the time NT was measured, and on-site counseling by a member of the division of Maternal-Fetal Medicine was available.

Biochemistry was added in 2003, and risk assessment is now based on age, NT, free β-human chorionic gonadotropin (β-hCG), and pregnancy-associated plasma protein-A (PAPP-A). Written information describing the process and implications of risk assessment is given to all women. Women provide a blood sample when they present for NT measurement, and results are forwarded to the referring obstetrician after biochemical testing is completed in 2 to 3 days. Patients are then counseled by their obstetricians, though consultation is also available in our unit. Because biochemistry can be performed as early as 9 weeks’ gestation, women have the option of providing blood before presenting for NT measurement. In these cases, women can receive results and on-site counseling when NT is measured.

In our hospital, fetal karyotype from cell culture is available within 2 weeks following amniocentesis. In high-risk cases, fluorescent in situ hybridization (FISH) is offered to look for abnormalities in chromosomes 13, 18, 21, X, and Y, and these results are available in 2 days. Following CVS, the karyotype from chorionic villus culture is available within 10 days. Direct chromosome preparation of uncultured cells is performed in high-risk cases, with results available within 2 days.

Data collected included gestational age at abortion, method of prenatal diagnosis, and whether or not first-trimester risk assessment was performed. Institutional Review Board approval was obtained. Continuous data were analyzed with Spearman correlation and Mann-Whitney U. Categorical data were analyzed with Fisher exact test and Chi-square analysis.

**Results**

One hundred forty-nine pregnancies met inclusion criteria. The abnormal karyotypes included 88 cases of trisomy 21 (59%), 33 cases of trisomy 18 (22%), 12 cases of trisomy 13 (8%), 9 cases of Turner syndrome (6%), and 7 cases of triploidy (5%). The median maternal age was 37 years (interquartile range 34-39) and the median gestational age at abortion was 18 weeks (interquartile range 14-19 weeks).

Trends in maternal age, gestational age at abortion, and rate of first-trimester risk assessment are seen in Table I for the entire study cohort (n = 149), and in Table II for those pregnancies with Trisomy 21 (n = 88). There were significant correlations between year of abortion and lower gestational age at time of abortion in the entire cohort (rho = -.31; P < .001) and in Trisomy 21 pregnancies (rho = -.29; P = .006). There were significant trends towards a higher proportion of abortions occurring before 16 weeks’ gestation as well.

These changes in gestational age at abortion coincided with increasing rates of first-trimester risk assessment. Those who underwent first-trimester risk assessment were more likely to undergo CVS (44.3% vs 11.4%; P < .001) compared to those who did not undergo early risk assessment. Of women who underwent risk assessment, those who subsequently underwent CVS had risk assessment slightly earlier compared with those who did not undergo CVS. In those who underwent CVS, the mean crown-rump length at risk assessment was 53.8 ± 7.6 mm, corresponding to 12 0/7 weeks, versus 58.6 ± 7.4 mm, corresponding to 12 3/7 weeks, in those who did not (P = .01). First-trimester risk assessment was also associated with significantly earlier median gestational age at abortion (15 weeks, interquartile range 13-18 weeks vs 19 weeks! interquartile range 18-20 weeks; P < .001).

Of 70 patients who underwent early risk assessment, 34 (48.6%) underwent CVS, and 5 (7.1%) had abortion at ≤14 weeks based on sonographic findings, with fetal karyotype obtained from tissue. The remaining 31 patients (44.3%) who underwent early risk assessment had an abnormal fetal karyotype identified by amniocentesis, and underwent abortion at ≥16 weeks. Of these patients, 14 (45.2%) had an adjusted first-trimester risk of trisomy 21 or trisomy 18 of 1 in ≤25, and 19 (64.5%) had an adjusted first-trimester risk of 1 in ≤50.

**Comment**

In our hospital, we have observed a decrease in the gestational age at abortion for abnormal fetal karyotypes associated with high detection rates in the first trimester. This has coincided with increasing rates of first-trimester risk assessment and CVS. Though we cannot be certain based on a retrospective study that the earlier gestational age at abortion is attributable to
the use of first-trimester risk assessment, this is the most plausible explanation. To our knowledge, this is the first study documenting this association.

A limitation of this study is that it only includes abortions performed in our hospital, and may not reflect the general population. Based on our data, we cannot conclude that higher rates of earlier risk assessment would be associated with earlier abortion for fetal aneuploidy in a different population. A multicenter study, including all regional centers performing prenatal diagnosis, could provide such information.

Before the recognition of first-trimester sonographic and biochemical markers of fetal aneuploidy, the decision to undergo CVS was based almost exclusively on maternal age. Because risks associated with CVS may be higher than those associated with amniocentesis, relatively few patients undergo CVS. Our ability to adjust age-related risk based on nuchal translucency and biochemical markers has enabled us to provide much more precise risk estimates in the first trimester. This can lead to more selective use of CVS, with more abnormalities identified while fewer procedures are performed. Indeed, we and others have noted lower rates of CVS as well as overall invasive testing in women 35 and over as first-trimester risk assessment has become more common.12,13

Table I Trends in prenatal diagnosis and gestational age at abortion for trisomy 21, trisomy 18, trisomy 13, Turner syndrome, and triploidy from 1999 to 2005

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</thead>
<tbody>
<tr>
<td>Maternal age (median [interquartile range])</td>
<td>39 (36-42)</td>
<td>36 (31-37)</td>
<td>37 (34-39)</td>
<td>37 (32-39)</td>
<td>37 (35-39)</td>
<td>37 (35-40)</td>
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<tr>
<td>Weeks’ gestation at abortion (median [interquartile range])</td>
<td>19 (18-20)</td>
<td>18.5 (15-20)</td>
<td>18 (14-20)</td>
<td>18 (16-19)</td>
<td>17 (14-19)</td>
<td>17 (14-19)</td>
<td>15 (13-18)</td>
<td>&lt; .001*</td>
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<td>Abortion at &lt; 16 weeks’ gestation (%)</td>
<td>6.2%</td>
<td>25%</td>
<td>29.4%</td>
<td>16.7%</td>
<td>34.6%</td>
<td>48%</td>
<td>56%</td>
<td>&lt; .001†</td>
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<td>First-trimester risk assessment (%)</td>
<td>0%</td>
<td>18.8%</td>
<td>29.4%</td>
<td>33.3%</td>
<td>57.7%</td>
<td>72%</td>
<td>84%</td>
<td>&lt; .001†</td>
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<tr>
<td>Chorionic villus sampling (%)</td>
<td>6.2%</td>
<td>18.8%</td>
<td>29.4%</td>
<td>16.7%</td>
<td>26.9%</td>
<td>40%</td>
<td>40%</td>
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* Spearman correlation.
† Chi-square for trend.

Table II Trends in prenatal diagnosis and gestational age at abortion for trisomy 21 from 1999 to 2005

<table>
<thead>
<tr>
<th></th>
<th>1999 (n = 12)</th>
<th>2000 (n = 11)</th>
<th>2001 (n = 7)</th>
<th>2002 (n = 14)</th>
<th>2003 (n = 17)</th>
<th>2004 (n = 14)</th>
<th>2005 (n = 14)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Maternal age (median [interquartile range])</td>
<td>39.5 (36-42)</td>
<td>35 (31-38)</td>
<td>35 (33-38)</td>
<td>38 (37-40)</td>
<td>37 (36-39)</td>
<td>38 (36-40)</td>
<td>36.5 (34-40)</td>
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<td>Weeks’ gestation at abortion (median [interquartile range])</td>
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<td>16 (14-18)</td>
<td>18 (15-19)</td>
<td>17 (14-20)</td>
<td>.006*</td>
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<tr>
<td>Abortion at &lt; 16 weeks’ gestation (%)</td>
<td>0%</td>
<td>18.2%</td>
<td>14.3%</td>
<td>28.6%</td>
<td>47.1%</td>
<td>28.6%</td>
<td>42.9%</td>
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<tr>
<td>First-trimester risk assessment (%)</td>
<td>0%</td>
<td>27.3%</td>
<td>14.3%</td>
<td>42.9%</td>
<td>70.6%</td>
<td>71.4%</td>
<td>78.9%</td>
<td>&lt; .001†</td>
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<tr>
<td>Chorionic villus sampling (%)</td>
<td>0%</td>
<td>18.2%</td>
<td>14.3%</td>
<td>28.6%</td>
<td>35.3%</td>
<td>28.6%</td>
<td>35.7%</td>
<td>.02†</td>
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* Spearman correlation.
† Chi-square for trend.
Thus, it is likely that early risk assessment is leading to earlier prenatal diagnosis and abortion of some pregnancies that would otherwise have been terminated later in pregnancy.

There is clearly the potential for more cases of fetal aneuploidy to be detected earlier in pregnancy, as a significant proportion of those with high adjusted risk in the first-trimester did not undergo CVS. This may be related to variation in how patients receive information regarding risk. Because biochemistry results are not available for at least 2 days, most patients receive risk assessment results from their obstetricians. There are likely to be significant differences in how individual physicians perceive these results as well as how they perceive the relative risks and benefits of CVS and amniocentesis. This is likely to be reflected in how patients are counseled.

Nicolaiades et al have shown that when patients receive standardized counseling, choices regarding invasive testing are more likely to appropriately reflect risk. When the ability to rapidly measure biochemical markers at the time NT is measured becomes available in the United States, results can be provided on-site and standardized counseling will be more feasible. In addition, as obstetricians and their patients become more aware of the reliability of early risk assessment, CVS may be utilized in more of these cases. Those women intent on undergoing amniocentesis should also be offered early risk assessment, as they might decide that CVS is the more appropriate procedure if adjusted risk is high.

Prenatal diagnosis in the second trimester has several disadvantages, aside from real concerns about safety and privacy. Some women are clearly less comfortable with second-trimester abortion, and might be willing to only consider abortion earlier in pregnancy. Access to second-trimester abortion is also limited in the second trimester in many regions. A concerted effort to detect most fetuses with an abnormal karyotype in the first trimester can lessen the impact of the lack of availability of second-trimester abortion.

In summary, our data demonstrate that the availability of quality first-trimester risk assessment is associated with earlier gestational age at abortion for the most common abnormal karyotypes. When CVS is available, early risk assessment can identify the most appropriate candidates for this procedure, and minimize the number of abortions performed later in pregnancy.

References