Screening and Testing in Multiples

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KEYWORDS

• Prenatal screening • Cell-free fetal DNA • Free β- hCG • Amniocentesis • CVS • Fetal reduction • Multiple pregnancy risks

KEY POINTS

- Both prenatal screening and testing are more complicated in multiples than in singletons.
- The risks of reproduction are directly related to chorionicity and for monochorionic twins (identical twins), the chromosomes and mendelian status of both twins are the same and the risk equals that of a singleton; for structural abnormalities the risks are considerably more than twice those for singletons.
- For dichorionic twins (fraternal) the risks of all are approximately additive.
- Screening is less effective in multiples than in singletons and it is difficult to distinguish which is which; diagnostic tests require more skill to determine which fetus is which.
- Fetal reduction, in experienced hands, has been shown to improve pregnancy outcomes in dichorionic twins but has high complication rates for monochorionic twins.

MULTIPLE PREGNANCIES

Over the past 35 years, infertility treatment has gone from fundamentally little more than providing encouragement to highly sophisticated pharmacologic and surgical interventions allowing millions of couples to have their own children.[1] However, of all babies born following in vitro fertilization (IVF), more than half are part of multiple pregnancies. In the United States the twin pregnancy rate, commonly quoted for decades to be 1 in 90, has more than doubled to nearly 1 in 30.[2] About 67% of all twins in the United States emanate from infertility treatments. Furthermore, the rate of monozygotic (MZ) twinning, per se, and as part of higher order multiples has continued

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to increase, with its associated dramatically increased risks of anomalies, loss, and prematurity.[1]

The increasing rate of multiple pregnancies that is associated with advanced maternal age has expanded the need for prenatal diagnosis in twins and higher order gestations.[2] The same principles for diagnosis and screening in singleton pregnancies apply to multiples. However, there can be significant differences in the safety and efficacy of all approaches.[3] Furthermore, screening for aneuploidy in multiple gestations with the possibility of discordant karyotypes bears significant clinical, technical, and ethical issues, such as:

1. Lower performance of serum screening protocols compared with singleton pregnancies[4]
2. Inability of cell-free DNA screening to distinguish which fetus is which
3. The complexity of invasive diagnostic procedures
4. The risk of loss of an unaffected twin caused by the sequelae of the invasive procedures

Risks of Anomalies

Certain structural abnormalities, such as neural tube defects and cardiac defects, are more commonly seen in twin gestations than in singletons.[5] Chromosomal risks are the same per fetus, but given that there are 2 chances per dizygotic (DZ) pregnancy, the effective rate seems double (**Table 1**). MZ twins are especially prone to defects of laterality, such as situs inversus, but they are identical for chromosomal or mendelian disorders.

For DZ twins the risk of either twin being aneuploid is an independent probability. For example, the risk of having a baby with a traditional chromosome abnormality at maternal age 35 years is approximately 1 in 190. If there are 2 fetuses, the risk is essentially doubled (ie, 2 in 190 or 1 in 95). A 1 in 95 risk corresponds with the risk of a singleton for a 38-year-old woman. Similarly, the risk for a 30-year-old woman with a singleton is 1 in 380. With twins the risk is approximately 2 in 380 (ie, 1 in 190), which is the risk for a 35-year-old woman. Overall, the risk of at least 1 DZ twin having a serious problem is about 7%, but for an MZ twin the number is about 10%. Monoamniotic twins have an even higher incidence of structural abnormalities than do monochorionic (MC)/diamniotic (DA) fetuses.

Counseling

Counseling for prenatal diagnosis should include appreciation of the differences between screening and diagnosis, including the risks and benefits of each. For multiple pregnancies, most of which are conceived after long-standing infertility and treatment, patients' attitudes and choices regarding invasive prenatal diagnosis might differ from

Table 1
Incidence of chromosomal abnormalities in at least 1 fetus in a multifetal gestation

Maternal Age (y)	Singleton	Twin	Triplet
20	1 in 526	1 in 263 ≈ age 34 y	1 in 175 ≈ age 36 y
25	1 in 476	1 in 238 ≈ age 34 y	1 in 150 ≈ age 36 y
30	1 in 385	1 in 192 ≈ age 35 y	1 in 128 ≈ age 37 y
35	1 in 192	1 in 96 ≈ age 38 y	1 in 64 ≈ age 40 y
40	1 in 66	1 in 33 ≈ age 43 y	1 in 22 ≈ age 45 y