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CONSENSUS STATEMENT

ISUOG consensus statement on the impact of non-invasive prenatal testing (NIPT) on prenatal ultrasound practice

The emergence of effective cell-free fetal DNA-based techniques to screen for trisomy 21 and other aneuploidies has greatly expanded the range of prenatal tests available over the last few years. Non-invasive prenatal testing (NIPT) is rapidly being incorporated into prenatal care, thus changing the traditional approach to prenatal screening and diagnosis. However, although NIPT techniques are highly efficient, their role and performance must be considered alongside and combined with other screening modalities. The role of prenatal ultrasound in particular needs to be reassessed as NIPT becomes more widely available.

It is important to emphasize that the main goal of prenatal screening is to provide accurate information that will facilitate the delivery of optimized antenatal care, with the best possible outcome for both mother and fetus. Women should be informed about prenatal screening performance by appropriately trained health professionals, allowing them to make an informed decision. It is the parent's choice to undergo such procedures, and their wishes should be determined and respected.

The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) has compiled the following Consensus Statement, which will be updated on a regular basis.

- All women should first be offered a first-trimester ultrasound scan according to ISUOG guidelines[1], regardless of their intention to undergo NIPT.
- Pre-test counseling is essential. Various options should be explained clearly to women, discussing the pros and cons of each, including the expected test performance and potential adverse effects.
- Following a normal early pregnancy scan, as defined by ISUOG guidelines[1], three options should be considered for women who wish to have a further risk assessment for trisomy 21 and, to a lesser extent, trisomies 13 and 18:

  (1) Screening strategies based on individual risk calculated from maternal age and nuchal translucency measurement and/or maternal serum markers and/or other ultrasound markers in the first trimester (defined by the conventional crown–rump length range of 45–84 mm).

  At the moment, ISUOG endorses this strategy. Following such screening, women can be offered a choice, according to their calculated individual risk, of having no further testing, undergoing NIPT, or undergoing invasive testing. Cut-offs should be defined on a local/national basis and will be affected by public health priorities and available resources.

  (2) Invasive testing based on background risk (including, for example, maternal age and history of aneuploidy), with no other individual risk calculation.

  (3) NIPT as a first-line screening test.

  Most current guidelines endorse NIPT only for high-risk populations for which adequate data exist. Using NIPT on intermediate- or low-risk patients might be endorsed as a widely available option only when new data emerge and NIPT costs decrease.

- NIPT is not a diagnostic test and confirmatory invasive testing is required in the presence of any abnormal results.
- NIPT has not been evaluated extensively in low-risk populations, in which its positive predictive value is lower than in high-risk populations.
- First-trimester risk estimates for trisomies 21, 18 and 13 based on nuchal translucency measurements and maternal biochemistry should not be computed in a woman who has already received a normal NIPT result for these trisomies.
- NIPT may be discussed as an alternative to invasive testing following an abnormal result on combined screening or offered to patients who are not sufficiently reassured by an 'intermediate risk' result.
- The role of NIPT as an alternative to standard invasive testing in women considered to be at very high risk (>1:10) after combined screening but with no

ultrasound anomaly should be evaluated in prospective studies. Expert opinion currently suggests that NIPT should not replace invasive testing in this group. This is based on the fact that only 70% of chromosomal abnormalities in this population are trisomy 21, 18 or 13. Furthermore, emerging microarray techniques may provide additional, clinically relevant information in some cases.

- In the presence of a fetal structural anomaly, the indications for fetal karyotyping and/or microarray testing should not be modified by a normal NIPT result obtained previously.
- Accuracy of NIPT in twin pregnancies should be investigated further.
- Variations in NIPT performance by different providers should be investigated further.
- The so-called 'genetic sonogram', which includes looking for soft markers of trisomy 21, should not be performed in women with a normal NIPT result due to its high false-positive rate and poor positive predictive value.
- It is becoming technically feasible to test non-invasively, not only for trisomies but also for other genetic syndromes. Both healthcare providers and women should therefore be clearly aware of the tests being performed and of their performance, as having multiple tests may increase the false-positive rate.
- Prospective, publicly-funded studies assessing the cost-effectiveness of various screening strategies should be performed as a matter of urgency.

Writing group

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[Correction added on 5 September 2014, after first online publication: author Dario Paladini was added].

Reference

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