

NIPT good clinical practice guidelines

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Introduction

To assist women and their partners in making reproductive choices, prenatal screening for Down syndrome and other common autosomal aneuploidies is offered to pregnant women in Belgium. Non-invasive testing (NIPT) for Down syndrome (trisomy 21) and other common autosomal aneuploidies (trisomy 18 and 13) based on sequencing of cell-free DNA (cfDNA) in maternal plasma is a valuable technique for prenatal screening of high and low risk populations.^{1,2,3}

Application of NIPT

The use of NIPT for prenatal screening in a general Belgian obstetric population results in the smallest number of missed diagnoses of fetal trisomy 21.^{4,5} Moreover, the number of invasive tests that are performed as a result of a positive screening test is much lower than using the combined first trimester screening (cFTS) as the primary screening instrument.

Therefore, NIPT is currently the best choice as a first tier prenatal screening tool for trisomy 13, 18 and 21.

Good clinical practice with NIPT as a screening tool

- NIPT is the first tier screening tool for prenatal screening for fetal trisomy 13, 18 and 21.
- Pre-test counselling with information about the different screening options and their possibilities and limitations is required.
- Informed consent has to be obtained.
- NIPT does not replace the first trimester fetal ultrasound for measurement of the nuchal translucency (NT) and identification of fetal malformations; fetal ultrasound should be performed before NIPT screening to ascertain whether there is an indication for another prenatal test or for additional genetic counselling.
- In case of ultrasound abnormalities, including NT >95 percentile, invasive techniques (chorionic villus sampling or amniocentesis) are indicated.
- Acquiring pre-NIPT family history by means of pedigree information is standard practice to make sure that no other prenatal test is indicated.
- Referral of a patient with a positive NIPT for invasive prenatal diagnosis by amniocentesis is necessary.
- Accreditation of genetic labs offering NIPT and regular peer review on a national level (Prenatal Working group of the Belgian Society of Human Genetics) is required.
- If NIPT is used beyond the scope of trisomy 13, 18 and 21, appropriate genetic counselling is required.

- The validity and clinical utility of NIPT as a screening tool for fetal sex chromosome abnormalities is not established, therefore they are not included in the report.
- NIPT should be performed with caution:
 - in case of a multiple pregnancy or a pregnancy with a vanishing twin
 - if the patient has (had) cancer
 - if the patient recently had heparin therapy or a blood transfusion
 - if the patient has had immunotherapy, a stem cell transplant or an organ transplantation
- Incidental findings (= findings which are not directly related to the indication for which the NIPT was performed, e.g. an fetal aneuploidy of a chromosome other than 13, 18 and 21 or a genetic anomaly in the mother) should be handled according to the “Belgian guidelines for managing incidental findings detected by NIPT”.⁶ In case of incidental findings that are likely to be valid and have obvious clinical utility, referral for genetic counselling is required.
- The fetal fraction (= proportion of fetal cell-free DNA) is determined as a standard quality control parameter that is taken into account while interpreting all NIPT results.

References

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5. PUBLICATIE VAN DE HOGE GEZONDHEIDSRAAD nr. 8912 Implementatie van niet-invasieve prenatale genetische screening van trisomie 21 (Syndroom van Down) in de Belgische zorgpraktijk 07.05.2014
6. Belgian guidelines for managing incidental findings detected by NIPT (BeSHG): <http://www.beshg.be/index.php?page=guidelines>