Managing chromosomal mosaicism in a PGT workflow

Recommendations for good practice

eshre
SCIENCE MOVING
PEOPLE
MOVING SCIENCE

✓ART/PGT centres should, regarding chromosomal mosaicism:
- develop and document their approach, including technical assessment, the transfer/cryopreservation strategy and the reporting policy.
- monitor data and adapt or refine their policy whenever new insights are available from emerging evidence.

✓If the *PGT technique used will not assess chromosomal mosaicism*: Discuss with the patients during genetic counselling and/or clearly mention in the preclinical work-up.

✓If *chromosomal mosaicism can be assessed*, the strategy for designating mosaicism, the reporting policy and the limitations should be discussed with the patients during genetic counselling and/or clearly mentioned in the preclinical work-up.

✓It is acceptable for a PGT centre not to report mosaicism provided the centre has a strategy for classifying embryos and acts on it. It is not acceptable to consider a 'mosaic' embryo per definition as aneuploid.

GENETIC COUNSELING

To be included:
- discussion of chromosomal mosaicism as an inherent biological phenomenon in human preimplantation embryos
- when appropriate, how it may affect diagnosis, embryo transfer and cycle outcomes.
- the centre's approach towards the management of mosaicism (also to be included in consent forms)
- technical and biological limitations of the detection of mosaicism, and the policy on mosaic embryo transfer and cryopreservation.

Further genetic counselling may be required prior to embryo transfer.

VALIDATION

It is recommended that:
- ✓ PGT centres participate on a regular basis in EQA schemes.
- ✓ include mosaic samples (i.e., a mixture of cells with known aneuploidies and euploid cells) in the validation study.
- ✓ validation experiments are performed, and validation data and specific criteria (e.g., quality control, cut-off) employed for the classification of mosaicism are clearly documented and available to the ART centre.

With regards to the limitations of the test, defining the threshold of mosaicism detection is recommended.

More information;

Visit the ESHRE website www.eshre.eu/guidelines

Please reference as: ESHRE Working group Chromosomal Mosaicism, et al.. ESHRE survey results and good practice recommendations on managing chromosomal mosaicism, Human Reproduction Open (2022) https://doi.org/10.1093/hropen/hoac044

Managing chromosomal mosaicism in a PGT workflow

Recommendations for good practice

eshre
SCIENCE MOVING PEOPLE MOVING SCIENCE

RISK ASSESSMENT

- ✓ Risk assessment should cover:
  - the risk of inconclusive or false positive/negative results due to technical and biological reasons. Detection of chromosomal mosaicism in a TE biopsy may not reflect the constitution of the entire embryo nor embryo viability.
  - the patient's risk of miscarriage, stillbirth, (viable) unbalanced offspring, mosaic offspring or offspring with a chromosomal imbalance that is below the resolution of the test.
- ✓ In case of PGT-M or PGT-SR, assessment of the risk of misdiagnosis related to the PGT-M or PGT-SR indication.

DESIGNATING AND REPORTING MOSAICISM

- ✓ Use stringent criteria for designating the range of mosaicism to avoid the risk of overcalling mosaicism.
- ✓ Findings consistent with mosaicism should be reported as "low-range" or "high-range". A cut off of 50% can be used to discriminate between low-range and high-range. Exact values (e.g. 60%, 65%) should be avoided.

For the PGT report:

- ✓ use "putative mosaic", "indicating mosaicism" or "suggestive of mosaicism" to reflect the fact that a TE biopsy cannot provide an absolute determination of mosaicism in the remainder of the embryo
- ✓ Include all technical and biological limitations associated with the detection of mosaicism
- ✓ Include technical information to allow careful interpretation of the data. (detailed technical information should be available upon request).

EMBRYO TRANSFER

- ✓ When selecting embryos for transfer among euploid and low-range mosaics, the PGT-A result should be co-evaluated with morphology.
- ✓ Not recommended:
  - A new stimulation cycle when with "low-range" mosaic embryos are available.
  - Discard low-range mosaic embryos.
  - Re-biopsy of embryos with a mosaic TE biopsy result for the purpose of confirming chromosomal/ploidy status.
- ✓ Specific recommendations relevant to the potential transfer of high-range mosaic embryos could not be formulated.

In case of PGT-M or PGT-SR:

- ✓ Chromosomal mosaic results should be considered with respect to their impact on the accuracy of the PGT-M/PGT-SR diagnostic results.
- ✓ A new stimulation cycle can be performed to allow for the transfer of embryos with an accurate PGT-M/PGT-SR diagnosis.

PRENATAL TESTING AND FOLLOW UP

- ✓ Genetic counselling on prenatal diagnosis should be offered to all women who become pregnant following PGT, even if no recommendations can be made at present with regards to the preferred prenatal follow up. A finding consistent with low-range mosaicism in a clinical TE biopsy does not represent an indication for invasive prenatal diagnosis.
- ✓ ART/PGT centres should be encouraged to obtain follow up data on babies born after treatment.