American Society for Reproductive Medicine 2017 Scientific Congress & Expo
October 28 to November 1, 2017 • San Antonio, TX, USA

Title:

A COMPARISON OF PREIMPLANTATION GENETIC TESTING PLATFORMS: TARGETED NEXT GENERATION SEQUENCING (NGS) RESULTS IN COMPARABLE CLINICAL OUTCOMES DESPITE IDENTIFYING FEWER SUITABLE EMBRYOS FOR TRANSFER

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Objective:

Targeted NGS provides unprecedented high-throughput and enhanced detection of whole chromosome abnormalities, partial or segmental aneuploidies, and mosaicism. Due to the relatively recent introduction of NGS for PGT, no study has compared to previously used platforms the rate at which NGS identifies embryos to be aneuploid or mosaic, and whether the choice of platform influences the likelihood of implantation. This study compared three major PGT platforms (array comparative genomic hybridization (aCGH), quantitative polymerase chain reaction (qPCR), and targeted NGS) and sought to determine whether the increased resolution of NGS impacted the rate of usable embryos and the implantation potential following transfer of screened embryos.

Design:

Retrospective, cohort study

Materials and Methods:

The study included all patients undergoing freeze-all autologous IVF cycles with embryonic aneuploidy screening by targeted NGS, qPCR and aCGH from January 2012 to February 2017.

Only patients with ≥1 euploid embryo available for subsequent single, euploid, frozen embryo transfer (FET) were included. Donor oocyte IVF cycles and translocation carriers were excluded. Trophectoderm cells, obtained via blastocyst biopsy, underwent comprehensive chromosomal screening. The proportions of tested embryos that were deemed suitable for transfer (euploid and not mosaic) were compared according to PGT platform. Clinical outcomes of FET cycles were compared according to the PGT platform used. Chi-square test and binary and linear logistic regression analysis were used.

Results:

A total of 1678 patients had blastocysts (n=9271) screened by targeted NGS (n=315), qPCR (n=1256) and aCGH (n=105). Regardless of age, there was a lower proportion of 'normal' embryos available for transfer (euploid and not mosaic) in the NGS cohort compared with PCR (<38 years: 60.2% vs. 68.1%, p<0.0001; ≥38 years: 41.4% vs. 47.0%, p=0.02) and aCGH (<38 years: 60.2% vs. 65.4%, p=0.04; ≥38 years: 41.4% vs. 49.6%, p=0.08) cohorts. Patient clinical outcomes were similar among all PGT platforms (Table 1). Controlling for oocyte age, BMI, endometrial thickness and the day of embryo biopsy, the odds of implantation (x^2=0.5, p=0.9), ongoing pregnancy (x^2=0.3, p=0.97) and biochemical (x^2=2.3, p=0.5) and clinical pregnancy loss (x^2=1.5, p=0.7) were not modified by the PGT platform used.

Conclusion:

While targeted NGS identified embryos as abnormal and unsuitable for transfer more frequently than aCGH and PCR, this increased stringency did not impact clinical outcome in patients with ≥1 euploid embryo available for transfer. This is the first large study to compare patient and embryo-level clinical outcomes among the three currently available PGT platforms. Future studies including patients whose cycles do not result in any 'normal' embryos available for subsequent transfer are necessary to quantify the clinical impact of the improved resolution of NGS-PGT on patient outcome.

Support:

None

Table 1:

Clinical outcomes after single, euploid FETs, according to PGT platform.

	NGS	qPCR	aCGH	P value
Implantation Rate	60.4% (226/374)	59.5% (953/1601)	57.4% (85/148)	NS
Ongoing pregnancy rate	54.8% (205/374)	55.4% (887/1601)	54.1% (80/148)	NS

Biochemical pregnancy loss rate	11.0% (41/374)	12.7% (203/1601)	16.9% (25/148)	NS
Clinical pregnancy loss rate	9.9% (37/374)	9.5% (152/1601)	6.1% (9/148)	NS