

FREQUENCY AND CHARACTERIZATION OF ANEUPLOIDIES IN ART CYCLES USING SURGICALLY EXTRACTED SPERM

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Background:

Between 10-15% of infertile men are diagnosed with azoospermia and based on etiology can be divided into obstructive azoospermia (OA) and nonobstructive azoospermia (NOA). Surgical sperm extraction is the most common treatment for those seeking fertility with the help of IVF together with ICSI. Previous studies have demonstrated a higher proportion of aneuploid sperm in ejaculate (1) and increased sex chromosome aneuploidies after ICSI (2) from men with abnormal semen parameters. Additionally, increased specific chromosomal aneuploidies and mosaicism have been observed from testicular sperm even when controlled for partner or oocyte donor age (3).

One study evaluating the interaction between azoospermic men and embryo aneuploidy using FISH found increased rates of aneuploidy compared to normal controls, but no difference between obstructive and nonobstructive causes (4). Our study sought to evaluate the relationship between obstructive and nonobstructive azoospermia and embryo aneuploidies using next-generation sequencing platforms. Characterizing any differences in azoospermia etiology and embryo aneuploidy is important for robust patient counseling regarding utilization of preimplantation genetic testing for aneuploidy (PGT-A).

Objective:

To characterize the type and frequency of embryo aneuploidies in individuals with either nonobstructive or obstructive azoospermia.

Materials and Methods:

We performed a retrospective cohort study at a large multi-center fertility network between 2014-2023 studying embryos that were created from patients with a diagnosis of azoospermia. All embryos were created using surgically extracted sperm and ICSI. Additionally, all embryos were tested with PGT-A with next-generation sequencing platforms. The primary outcome was aneuploidy rate. Categorical variables were analyzed using chi-square analysis, Fisher's exact test, or z-test for proportion and two-tailed t-tests for continuous variables. All analyses were performed using R (v4.3.3).

Results:

359 IVF cycles were included (183 NOA and 176 OA) which produced 742 and 668 PGT-A tested embryos respectively. There was no difference in characteristics between the cohorts in

respect to maternal age. The aneuploidy rates were not different between the cohorts [NOA 376 (50.7%); OA 327 (49.0%); $p = 0.74$]. A subgroup analysis looking at patients with maternal age under 35 yielded similar results [NOA 135 (38.8%); OA 105 (39.3%); $p = 0.99$]. The only significant difference in chromosomal aneuploidies was the proportion of total Chromosome 5 aneuploidies between NOA and OA ($p = 0.042$). No other differences were noted including any sex chromosome aneuploidies individually or together ($p = 0.78$).

Conclusions:

Embryo aneuploidy rates were not different between IVF/ICSI cycles using nonobstructive or obstructive azoospermia surgical sperm samples and rates were ultimately similar to other etiologies of infertility. Only one individual chromosomal aneuploidy was different between nonobstructive and obstructive cohorts, however the clinical impact, if any, of this is unclear. Therefore, the type of azoospermia should not impact the decision to use PGT-A in couples undergoing IVF/ICSI with surgically extracted sperm.

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