Title: INTRACYTOPLASMIC SPERM INJECTION (ICSI) DOES NOT CAUSE AN INCREASE OF ANEUPLOIDY IN PATIENTS WITHOUT MALE FACTOR INFERTILITY (MFI) UNDERGOING IN VITRO FERTILIZATION (IVF).

Authors: Cailey Brogan, BS (1), Alexandra Peyser, MD (1), Disha Prakash Shahani, MPH (2), and Susan M. Maxwell, MD (3)

Institutions: (1) Northwell Health Fertility, Zucker School of Medicine at Hofstra Northwell, Manhasset, NY, USA, (2) Biostatistics Division, Office of Academic Affairs at Northwell Health, Manhasset, NY, USA, (3) Southern California Reproductive Center, Santa Barbara, CA, USA

Background
ICSI is typically used for patients with MFI. However, the utilization of ICSI in the absence of MFI has increased over time.

Objective
To determine the rates of embryonic aneuploidy and euploidy in patients with or without MFI using ICSI or standard insemination (SI).

Materials and Methods
All patients undergoing IVF and preimplantation genetic diagnosis for aneuploidy (PGT-A) using Next Generation Sequencing from November 2019-April 2022 at a large health system were reviewed. Patients were stratified into 3 groups: MFI where fertilization was performed with ICSI (MF ICSI), absence of MFI where fertilization was performed with ICSI (NMF ICSI), and absence of MFI where fertilization was performed with SI (NMF SI). Cases where both ICSI and SI were performed were excluded. Chi square and t-test were used to compare demographic data. The rates of aneuploidy and euploidy were compared between the 3 groups using Poisson regression model adjusting for age, BMI, and AMH.

Results
A total of 1,120 IVF cycles were analyzed, 262 with MFI and 856 without MFI. Of those without MFI, 666 utilized ICSI and 159 utilized SI. The patients in the NMF ICSI group were significantly older, and the NMF SI group had a lower BMI. There was no difference in the AMH, partners' age at start, the number of eggs retrieved, number of 2pn, the number of embryos biopsied, and the average number of aneuploid embryos among the groups (table 1). The NMF SI group had significantly more euploid embryos obtained (p=0.008). When controlling for age, BMI, and AMH, there was no difference in the rate of aneuploidy between the groups (NMF ICSI group adjusted RR 1.00 (95% CI: 0.87 – 1.16) compared to MF ICSI, NMF SI group adjusted RR 0.82 (95% CI: 0.67 – 1.08) compared to MF ICSI). There was no difference in the euploidy rate between the NMF ICSI group and the MF ICSI group (adjusted RR 1.00 (95% CI: 0.91 – 1.09). The NMF SI group, however, had a significantly higher euploidy rate than the MF ICSI group with RR 1.21 (95% CI: 1.07 – 1.36).

Table 1. Patient demographics and cycle outcomes

	MF ICSI	NMF ICSI	NMF SI	P-value
Patient Age (y)	36.09 ± 4.27	37.11 ±4.24	36.29 ± 3.76	0.002*
BMI (kg/m2)	27.38 ±5.84	27.06 ± 5.87	24.87 ± 4.48	<0.001*
AMH	3.33 ± 2.85	3.22 ± 3.35	3.60 ± 3.45	0.11
Partners Age (y)	38.60 ± 8.06	37.02 ± 9.86	37.21 ± 6.34	0.30

Eggs retrieved	14.57 ± 8.35	13.91 ± 8.38	15.81 ± 9.36	0.06
2pn	8.80 ± 6.01	8.45 ± 5.51	9.07 ± 5.99	0.60
Embryos biopsied	4.66 ± 3.97	4.56 ± 3.68	4.65 ± 3.94	0.90
Euploid	2.96 ± 2.76	2.52 ± 2.51	3.18 ± 2.73	0.008*
Aneuploid	1.41 ± 1.44	1.39 ± 1.43	1.17 ± 1.21	0.40

Conclusions
There was no difference in the rate of embryonic aneuploidy when ICSI was performed in non-MFI cases compared to MFI cases. NMF SI patients obtained more euploid embryos compared to MF ICSI. This difference could be attributed to a difference in the rate of mosaicism reported between the groups. Future studies looking at mosaicism are required to determine if there are differences in the rates between groups.

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