LIKELIHOOD OF OBTAINING A USABLE EMBRYO FOR TRANSFER AMONG PATIENTS UNDERGOING IVF WITH PGT-A + PGT-M COMPARED WITH PATIENTS UNDERGOING IVF WITH PGT-A ALONE

Authors: Rachel A Martel (1), Mabel B Lee (1), Alessia Schadwell (2), Mehrnaz Siavoshi (3), Lorna Kwan (3), Jenna Miller (2), Chelsea Leonard (2), Robert A Roman (1), Abigail Armstrong (4), Lindsay Kroener (1)

Affiliations:
1) Department of Obstetrics and Gynecology, University of California, Los Angeles, CA
2) Cooper Genomics, Livingston, NJ
3) Department of Urology, University of California, Los Angeles, CA
4) Kindbody, Los Angeles, CA

Background:
Patients utilizing PGT-M for single gene testing may have fewer embryos available for transfer, as 25% to 50% of embryos will be affected by a pathogenic variant. Prior studies assessing number of transferrable embryos obtained from PGT-M compared with PGT-A cycles have been inconclusive. The likelihood of having at least one unaffected, euploid embryo for transfer in patients undergoing PGT-M, stratified by disease inheritance pattern, is unknown.

Objective:
To determine the likelihood of obtaining at least one usable embryo for transfer in patients undergoing IVF with PGT-A+PGT-M compared with patients using PGT-A alone.

Methods:
All IVF cycles for patients aged 18-45 undergoing PGT-A using next generation sequencing from trophectoderm biopsies with or without concurrent PGT-M at a single genetics laboratory were analyzed from 11/2019 to 3/2023. Cycles were stratified by SART age category and disease inheritance pattern: autosomal recessive (AR), autosomal dominant (AD), X-linked recessive (XLR), and X-linked dominant (XLD). Usable embryos were defined as euploid and unaffected by a single gene disorder, but could carry an AR condition or be a female carrier of an XLR condition. Non-usable embryos were aneuploid, mosaic (40-80% mosaicism), and/or affected by a single gene disorder. Comparative analyses were performed using median and Chi-square tests.

Results:
A total of 72,522 IVF cycles were included; 4,255 cycles (5.9%) using PGT-M and 68,267 cycles (94.1%) using PGT-A alone. The PGT-M group was younger, with 56.1% of cycles in patients <35 compared with 30.5% of cycles in the PGT-A only group ($p<0.001$). The median number of embryos biopsied was higher in the PGT-A only compared to PGT-M group for patients <35 (5 versus 4, $p<0.001$), but was equivant in all other age groups. After stratifying PGT-M cycles by inheritance pattern, the majority were AD (42.4%), followed by AR (36.5%), XLD (13.3%), and XLR (7.8%). The probability of having a useable embryo declined with increasing age across all inheritance patterns. Compared with PGT-A alone, PGT-M cycles for patients ≤40 across all inheritance patterns (with the exception of XLD diseases in the 38-40 group) were significantly less likely to yield a usable embryo ($p<0.01$). There was no consistent difference seen between groups in patients over 40. Cycles for patients with AD diseases had the lowest likelihood of yielding at least one embryo for transfer for patients aged <43 (Table 1).

Conclusions: Cycles for patients ≤ 40 using PGT-M are significantly less likely to yield a useable embryo compared to those using PGT-A alone. A significant difference between groups was not consistently seen in patients >40, which may be due to lower PGT-M utilization in older patients. This is important for counseling, as patients using PGT-M may require more cycles to obtain a useable embryo.

Financial Support: None

References: None

	N= Number of cycles Mean probability of at least one usable embryo (95% CI)								
	PGT-A alone N = 68,267	**PGT-A + PGT-M N = 4,255**				**p-value comparing to PGT-A**			
Age (years)		**AR N=1,551**	**AD N=1,805**	**XLD N=565**	**XLR N=334**	**AR**	**AD**	**XLD**	**XLR**
<35	N = 20823 0.642 (0.638 – 0.646)	N = 815 0.529 (0.507 – 0.551)	N = 1080 0.418 (0.398 – 0.438)	N = 314 0.494 (0.457 – 0.531)	N = 176 0.466 (0.523 – 0.510)	<0.001	<0.001	<0.001	<0.001
35-37	N = 10679 0.561 (0.555 – 0.567)	N = 288 0.447 (0.409 – 0.484)	N = 319 0.351 (0.315 – 0.387)	N = 84 0.391 (0.313 – 0.469)	N = 66 0.452 (0.367 – 0.537)	<0.001	<0.001	<0.001	0.006
38-40	N = 16947 0.451 (0.446 – 0.456)	N = 297 0.376 (0.339 – 0.412)	N = 293 0.282 (0.245 – 0.319)	N = 117 0.391 (0.325 – 0.457)	N = 74 0.309 (0.237 – 0.380)	0.007	<0.001	0.111	0.002
41-42	N = 10680 0.308 (0.302 – 0.315)	N = 95 0.253 (0.192 – 0.315)	N = 80 0.197 (0.132 – 0.263)	N = 40 0.328 (0.213 – 0.444)	N = 14 0.225 (0.051 – 0.399)	0.101	0.001	0.890	0.236
43-45	N = 9138 0.209 (0.203 – 0.216)	N = 56 0.092 (0.033 – 0.152)	N = 33 0.146 (0.044 – 0.248)	N = 10 0.267 (0.002 – 0.531)	N = 4 0 (0)	0.021	0.284	0.806	-

Table 1. Mean probability of having at least one usable embryo stratified by SART age and inheritance pattern per cycle. AR=autoromal recessive, AD=autosomal dominant, XLR=X-linked recessive, XLD=X-linked dominant.