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Control/Tracking Number: 2017-A-1912-ASRM
Activity: Abstract
Current Date/Time: 5/3/2017 11:33:36 AM

QUANTITY VERSUS QUALITY: DO PATIENTS WITH DIMINISHED OVARIAN RESERVE (DOR) AND POOR RESPONSE TO STIMULATION ALSO EXHIBIT POOR BLASTULATION AND INCREASED ANEUPLOIDY?

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Abstract:
OBJECTIVE: A vexing question in ovarian biology and clinical ART remains whether the DOR phenotype in younger patients represents solely a quantitative challenge or if there is an associated qualitative penalty after oocytes are retrieved. While quality is difficult to define, 2 reliable indicators associated with age-related decrease in oocyte efficiency are a decline in blastulation rate (BR) and an increase in aneuploidy rate (AR). With this in mind, a large database was utilized to explore the relationship between the pre-cycle (serum antimullerian hormone [AMH] level) and post-cycle (number of oocytes retrieved) determinants of DOR, and BR/AR.
DESIGN: Retrospective cohort.
MATERIALS AND METHODS: All autologous IVF cycles between 2012-2016 were reviewed for inclusion. Only cycles with female partner <38 years old were included as BR remains relatively high and AR relatively low at all ages in this range. Only the 1st cycle was included for each patient to eliminate previous failure bias. Cases involving surgical sperm retrieval or chromosomal translocations were excluded. Two analyses were performed: 1) To evaluate the effect of pre-cycle DOR diagnosis, all patients with AMH levels drawn within 6 months of cycle start were evaluated (n=3457). Patients with AMH levels <10th percentile (10%ile) were then compared patients in the 25th-75th %ile (IQR) with respect to BR and AR. 2) To determine the effect of post-cycle DOR diagnosis, all patients who proceeded to retrieval were included (including those with no pre-cycle AMH data; n=5372) and the 10%ile of oocyte yield was again compared to the IQR for both parameters. Mixed-effects logistic regression models were used to control for female age.
RESULTS: 1) The 10%ile threshold and the IQR for AMH were 0.5 and 1.1-4.5 ng/ml, respectively. Patients in the 10%ile group were more likely to be cancelled prior to retrieval (11.3% vs. 1.7%, p<0.01). However, the age adjusted BR was no different. Among patients pursuing PGS, AR was also not different. 2) The 10%ile threshold for oocyte yield was 5 oocytes and the IQR was 10-21 oocytes. Again, age adjusted AR was not different, while odds of blastulation were higher in the 10%ile group.
CONCLUSIONS: DOR as defined by <10%ile values for pre-cycle AMH or post-cycle oocyte yield is not associated with low BR or high AR in patients <38yo. Mechanisms governing ovarian reserve and response to stimulation appear to be different than those responsible for age-related decrease in embryo viability and increase in aneuploidy. Further studies are needed to elucidate these differences.

Blastulation rate and aneuploidy rate are no different between DOR patients and normal responders

Pre-Cycle DOR Comparison according to AMH within 6 months of cycle start					
	<10%ile (AMH ≤0.5 ng/mL)	IQR (AMH 1.1 - 4.5 ng/mL)	Adjusted OR	95% CI	p-value
Blastulation Rate	51.8% (667/1297)	51.5% (13413/25592)	0.99	(0.98 - 1.06)	0.46
Aneuploidy Rate	30% (108/360)	29% (1173/4051)	0.85	(0.6 - 1.2)	0.358
Post-Cycle DOR Comparison according to Oocyte Yield					
	10%ile (≤5 oocytes)	IQR (10 - 21 oocytes)	Adjusted OR	95% CI	p-value
Blastulation Rate	55.8% (718/1286)	52.4% (13413/25592)	1.15	(1.03 - 1.31)	0.045
Aneuploidy Rate	32.2% (127/394)	28.7% (1739/6053)	1.13	(0.88 - 1.45)	0.37

Financial Support & References:
Financial Support: None
References:

Category (Complete): Reproductive Endocrinology: Clinical
Topic (Complete): Ovarian Function
Presentation Preference (Complete): Either Oral or Poster
Questionnaire (Complete):
ABOG-Approved Fellowship Program: Yes
Separate Abstract & Video Consideration: No
IRB Approval
: The study material in this abstract has been approved or exempted by the appropriate Institutional Review Board (IRB) with jurisiction if any human subjects or any human material was utilized.
HIPAA Compliance : True
ACCME Disclosure: Slide
This abstract was not previously published, presented, or accepted for presentation. : True
I accept complete responsibility for the data at the time of submission. : True
Please consider this submission as newsworthy. : True

Awards (Complete):
In-Training Awards for Research : True
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Country of Residence: United States

Attached Files: CV Morin 2017 (MS-WORD, 30904 bytes)

Status: Complete

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