Ovarian reserve testing and prediction for natural and assisted conception

Juan A. Garcia-Velasco, MD
Ovarian reserve testing

- Indirect measure of reproductive age
- Used to define quantity (and quality?) of primordial ovarian follicles at a given age

screening  diagnosis
Ovarian reserve testing

*Why is it important?*

- Adequate counselling of ART outcome
- Tailor stimulation protocols (low, high resp)
- Predict cycle cancellation
- Donor oocytes?
- Previous to oncological treatments /ovarian surgery
- Fertility decline in women with age?
Prediction

- Essential tool for clinical decision-making
- To prevent unnecessary treatment
- Reliable counselling
What is a low response?

\[ n = 6349 \]

\[ \% \text{ pregnancy} = \frac{1}{1.8758 + \frac{4.0406}{n^0 \text{ eggs}}} \]

Muñoz et al. ASRM 2007
### How big is the problem?

<table>
<thead>
<tr>
<th>Fresh IVF</th>
<th>2047</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frozen cycles</td>
<td>1076</td>
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<tr>
<td>Egg donation</td>
<td>1005</td>
</tr>
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</table>

#### 412 LOW RESPONDERS

<table>
<thead>
<tr>
<th>Cycles</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>14 cycles</td>
</tr>
<tr>
<td>1</td>
<td>76 cycles</td>
</tr>
<tr>
<td>2</td>
<td>84 cycles</td>
</tr>
<tr>
<td>3</td>
<td>114 cycles</td>
</tr>
<tr>
<td>4</td>
<td>127 cycles</td>
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**20.1%**
How big is the problem?

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Age

1,404 > 34 y.o

68.6%
Ovarian reserve testing

- **Biochemical markers**
  - FSH
  - Estradiol
  - Inhibin B
  - AMH
  - FSH/LH ratio

- **Morphometric markers**
  - Ovarian volume
  - AFC
  - Mean ovarian diameter

- **Dynamic markers**
  - CCCT
  - Exogenous FSH ovarian reserve test
  - GnRH analogue stimulation test
Ovarian Aging: Mechanisms and Clinical Consequences

F. J. Broekmans, M. R. Soules, and B. C. Fauser

The variability of ovarian ageing among women is evident from the large variation in age at menopause. The identification of women who have severely decreased ovarian reserve for their age is clinically relevant. Ovarian reserve tests have appeared to be fairly accurate in predicting response to ovarian stimulation in the assisted reproductive technology (ART) setting. The capacity to predict the chances for spontaneous pregnancy or pregnancy after ART appears very limited.

(Endocrine Reviews 30: 465–493, 2009)
Basal FSH

Measuring day 3 FSH is a commonly used test to predict IVF response.
21 studies
Quality?
Extreme cut-offs
Limited sensitivity

Response – Non Pregnancy

Non Predictive

Moderate

www.ivi.es
Bancsi et al. Fertil Steril 2003
Useless to exclude patients

Ongoing Pregnancy Rate

FSH <10
FSH 10-15
FSH >15
All FSH

<30
31-36
>36
All ages

65%
47%
28%

N = 301

Van Rooij et al. Fertil Steril 2004
FSH vs AFC

Predictive performance of AFC vs FSH as ORT
11 studies on AFC and 32 on FSH

AFC performs better – easy, non invasive, essential

Hendriks et al. Fertil Steril 2005
- 1045 patients
- Both markers predicted quantitative ovarian response

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>FSH</th>
<th>Age + FSH</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 10 oocytes</td>
<td>0.688</td>
<td>0.703</td>
<td>0.718</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0.617</td>
<td>0.545</td>
<td>0.627</td>
</tr>
<tr>
<td>Cancellation</td>
<td>0.599</td>
<td>0.601</td>
<td>0.610</td>
</tr>
</tbody>
</table>

- Age was a better predictor of pregnancy rate in women undergoing IVF
Dynamic tests

- CCCT adds very little additional value to basal FSH (if any)

  Predictive accuracy not better than FSH + AFC

- GAST or EFFORT should not be advocated as a screening test as it performed similarly to inhibin B or AFC
Age influence

![Graph showing the influence of age on estradiol and oocytes]

- 56% below 30
- 32% between 30 and 40
- <6% above 40
Age influence
• Small in diameter (2-8mm)
• 2D and 3D similar accuracy
Ultrasound

Ovarian volume

- Limited prognostic value for IVF
- Simple tool: \((D1 + D2) / 2\)

Bowen et al 2007
AFC vs ovarian volume

- 10 studies on OV and 17 on AFC
- AFC better predictor of poor response

Clinical value in PR prediction only evident in AFC

For non-pregnancy absent for both
• Secreted by GC in primary and preantral fols

La Marca et al 2010
• Live birth rate according to AMH

![Bar chart showing live birth rate by AMH quintile with P<0.05](chart.png)
Multivariate models vs AFV as single test

11 studies of MVM

Sens 39-97%
Spec 50-96%
Cohort better than case-control

Similar accuracy of AFC to MVM

No data to predict Pregnancy

The use of more than 1 single test cannot be supported

# Simple predictors

**Age** = egg quality, **FSH** = egg quantity

*Toner J. Fertil Steril 2003*

<table>
<thead>
<tr>
<th>Young, high FSH</th>
<th>&gt; cancellation</th>
<th>&lt; oocytes</th>
<th>average IR / PR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older, normal FSH</td>
<td>good response</td>
<td>low IR / PR</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions

• We cannot recruit follicles that do not exist!

• Egg quality fundamentally cannot be altered
Conclusions

- Dynamic tests useless
- Basal FSH – high variability intercycle
- AMH more robust (during cycle, intercycle, OCP… and lower inter/intraassay variability)
- AFC highly reliable and reproducible, low cost
- Age: cheapest and only marker of egg quality
Thank you!

jgvelasco@ivi.es