Università degli Studi di Padova
Dipartimento di Scienze Ginecologiche e della Riproduzione Umana
Scuola di Specializzazione in Ginecologia e Ostetricia
Direttore Prof. Giovanni Battista Nardelli

MENSTRUAL CYCLE LENGHT:

AN UNEXPENSIVE TOOL TO BETTER ASSESS

OVARIAN AGE & ART SUCCESS RATE

Dott.ssa F. Esposito

Original Article

Ovarian Reserve Test: An Impartial Means to Resolve the Mismatch Between Chronological and Biological Age in the Assessment of Female Reproductive Chances

Salvatore Gizzo, MD[1], Alessandra Andrisani, MD, PhD[1],
Federica Esposito, MD[1], Alessandra Oliva, BS[1], Cecilia Zicchina, BS[1],
Denise Capuzzo, MD[1], Michele Gangemi, MD[1],
and Giovanni Battista Nardelli, MD[1]

Fig. 1.2 Chance of retrieval more than 6 oocytes
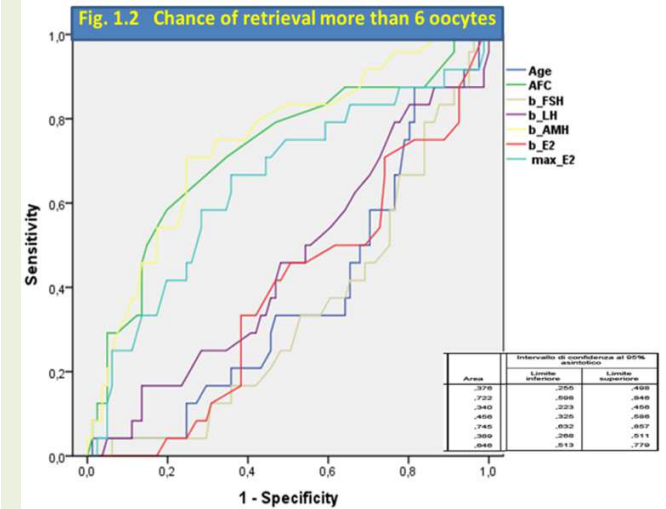
Table 3. Estimation of the Sensitivity, Specificity, Positive and Negative Predictive Values (PPV and NPV, Respectively), Positive and Negative Likelihood Ratio, and their 95% CIs for the Hypothetical Markers Cutoff in Detecting Pregnancy and Ongoing Pregnancy.

Pregnancy	AFC: 10 Antral Follicles		b_AMH: 0.5 µg/L		Max_17β-Estradiol: 5.5 nmol/L		Max_End-Thickness: 10 mm	
	Value	95% CI	Value	95% CI	Value	95% CI	Value	95% CI
Sensitivity	0.7	0.44-0.88	0.94	0.69-0.99	0.7	0.44-0.89	0.53	0.29-0.79
Specificity	0.48	0.38-0.6	0.22	0.14-0.32	0.56	0.45-0.66	0.64	0.54-0.74
PPV	0.21	0.11-0.34	0.19	0.11-0.29	0.24	0.13-0.38	0.23	0.11-0.39
NPV	0.9	0.76-0.96	0.95	0.73-0.99	0.91	0.79-0.97	0.87	0.77-0.94
LR+	1.38	0.95-1.99	1.20	1.02-1.41	1.59	1.08-2.34	1.5	0.89-2.55
LR−	0.6	0.28-1.28	0.3	0.04-1.97	0.52	0.24-1.13	0.72	0.43-1.21

VARIABLE OVARIAN AGE   FIXED OVARIAN AGE   NUMBER OF EMBRYOS   IMPLANTATION RATE
(clinical pregnancy)   (ongoing pregnancy)
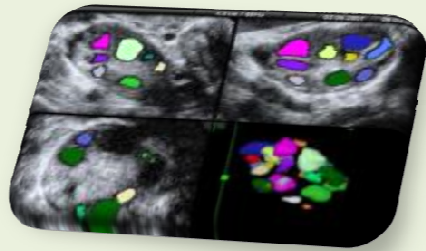
PRE-TREATMENT
ESTIMATION CHANCHES
(OOCYTES)

TREATMENT
ESTIMATION CHANCHES
(PREGNANCY)

human
reproduction
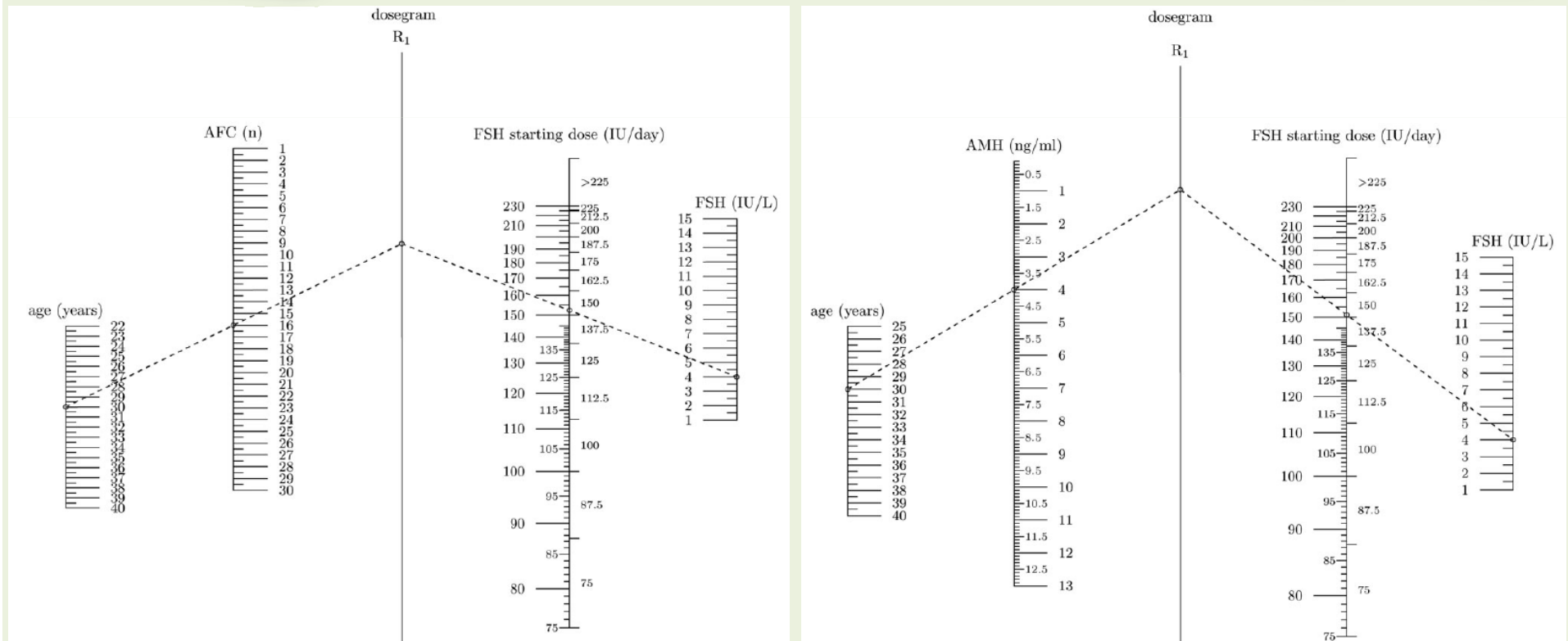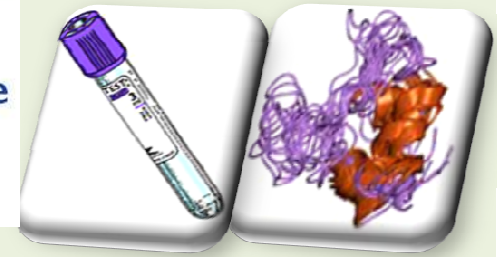update

Individualization of controlled ovarian stimulation in IVF using ovarian reserve markers: from theory to practice

Antonio La Marca[1,*] and Sesh Kamal Sunkara[2]

dosegram
R_1

AFC (n)

FSH starting dose (IU/day)

FSH (IU/L)

age (years)

dosegram
R_1

AMH (ng/ml)

FSH starting dose (IU/day)

FSH (IU/L)

age (years)

human reproduction   **ESHRE PAGES**

ESHRE consensus on the definition of 'poor response' to ovarian stimulation for *in vitro* fertilization: the Bologna criteria[†]

A.P. Ferraretti[1,*], A. La Marca[2], B.C.J.M. Fauser[3], B. Tarlatzis[4], G. Nargund[5], and L. Gianaroli[1] on behalf of the ESHRE working group on Poor Ovarian Response Definition[‡]

Results: POR definition

Following the same logical approach utilized for polycystic ovarian syndrome (PCOS) diagnostic criteria (The Rotterdam ESHRE/American Society for Reproductive Medicine (ASRM) Sponsored PCOS Consensus Workshop Group, 2004), a consensus was reached on the minimal criteria needed to define POR.

At least two of the following three features must be present:

(i) Advanced maternal age (≥40 years) or any other risk factor for POR;

(ii) A previous POR (≤3 oocytes with a conventional stimulation protocol);

(iii) An abnormal ovarian reserve test (i.e. AFC <5–7 follicles or AMH <0.5–1.1 ng/ml).

Despite the fact that the OR evaluation through the combination of biochemical and TVS assessment increase the ART cost of about €40 to 80,[8] it should be mandatory

MY FIRST IVF!

Menstrual cycle length is an age-independent marker of female fertility: results from 6271 treatment cycles of in vitro fertilization

Thomas Brodin, M.D.,[a,d] *Torbjörn Bergh, M.D., Ph.D.,*[b] *Lars Berg* ... *Nermin Hadziosmanovic, M.Sc.,*[b] *and Jan Holte, M.D., Ph.D.*[b,d]

[a] Department of Obstetrics and Gynaecology, Eskilstuna; [b] Carl von Linné C ... Akademiska sjukhuset; and [d] Department of Women's and Children's Health, Upp ...

ORIGINAL ARTICLE

Menstrual Cycle Characteristics

Associations With Fertility and Spontaneous Abortion

Chanley M. Small,* Amita K. Manatunga,† Mitchel Klein,‡ Heather S. Feigelson,§ Celia E. Dominguez,¶ Ruth McChesney,‖ and Michele Marcus*

Women with regular menstrual cycles and a poor response to ovarian hyperstimulation for in vitro fertilization exhibit follicular phase characteristics suggestive of ovarian aging

Menstrual cycle length in reproductive age women is an indicator of oocyte quality and a candidate marker of ovarian reserve

Rita Vassena [a,*], Ricard Vidal [a], Oriol Coll [a,b], Valérie Vernaeve [a,b]

[a] Department of Assisted Reproduction, Clínica EUGIN, Barcelona 08029, Spain
[b] Fundació EUGIN, Barcelona 08029, Spain

Do cycle disturbances explain the age-related decline of female fertility? Cycle characteristics of women aged over 40 years compared with a reference population of young women

P.van Zonneveld[1,6], G.J.Scheffer[1], F.J.M.Broekmans[1], M.A.Blankenstein[2,5], F.H.de Jong[3], C.W.N.Looman[4], J.D.F.Habbema[4] and E.R.te Velde[1]

RETROSPECTIVE STUDY
first fresh non-donor IVF/ICSI treatment
January 2011 and March 2014

personal menstrual diary for the six months before the ART treatment

MCL_class_1: >31 day
MCL_class_2: 30-31 day
MCL_class_3: 28-29 day
MCL_class_4: 26-27 day
MCL_class_5: <26 day

AGE_class_1: >40 yrs
AGE_class_2: 35-40 yrs
AGE_class_3: 26-34 yrs
AGE_class_4: <26 yrs

EXCLUSION CRITERIA
- smoking in the previous 12 months
- deep endometriosis
- BMI more than 30
- abnormalities of karyotype
- mutations of the cystic fibrosis gene
- acquired or inherited thrombophilia
- immunological disorders
- previous chemo and/or radio treatment
- untreated uterine diseases
- history of diabetes and thyroid disorders
- low-dose aspirin during treatment
- treatment ended before the pick-up for hyperstimulation syndrome or for failure of ovarian response

Protocollo corto con antagonista GnRH
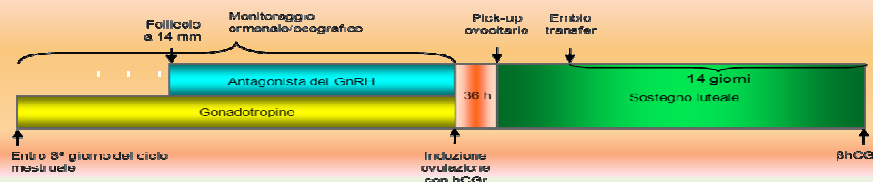
Protocollo lungo

SAMPLE DESCRIPTION

VARIABLES	ALL PATIENTS [MEAN(±STANDARD DEVIATION)]	AGE CLASS [MEAN(±STANDARD DEVIATION)]
PATIENT'S AGE (years)	455 [36.42 (7.25)]	CLASS_1 157 [44.3 (2.4)] CLASS_2 115 [37.9 (1.5)] CLASS_3 155 [29.4 (2.6)] CLASS_4 28 [24.4 (0.7)]
BMI	455 [22.1 (2.1)]	CLASS_1 157 [22.7 (1.6)] CLASS_2 115 [22.4 (2.1)] CLASS_3 155 [21.5 (2.4)] CLASS_4 28 [22.1 (2.1)]
bFSH	455 [9,8 (4.3)]	CLASS_1 157 [12.5 (4.3)] CLASS_2 115 [10.7 (4.3)] CLASS_3 155 [6.9 (1.8)] CLASS_4 28 [6.5 (2.0)]
bAMH	455 [2.0(1.7)]	CLASS_1 157 [0.7 (0.8)] CLASS_2 115 [1.7 (1.1)] CLASS_3 155 [3.3 (1.7)] CLASS_4 28 [3.6 (1.7)]
bAFC	455 [9.9(6.4)]	CLASS_1 157 [5.2 (3.3)] CLASS_2 115 [8.5 (3.9)] CLASS_3 155 [14.6 (5.9)] CLASS_4 28 [15.9 (7.7)]

455 eligible patients aged from 23 and 48
(mean value 36.42±7.25)

	ALL PATIENTS	AGE CLASS
mean MCL	455 [28.1(2.4)]	CLASS_1 157 [26.4 (1.9)] CLASS_2 115 [28.2 (1.7)] CLASS_3 155 [29.4 (2.1)] CLASS_4 28 [29.7 (2.7)]
FSH total dose	455 [2983.9(856.5)]	CLASS_1 157 [3596.8 (520.1)] CLASS_2 115 [3100.0 (511.1)] CLASS_3 155 [2405.3 (848.5)] CLASS_4 28 [2271.4 (933.6)]
E2 max	455 [5.7(3.2)]	CLASS_1 157 [3.4 (1.9)] CLASS_2 115 [5.1 (2.7)] CLASS_3 155 [8.1 (2.5)] CLASS_4 28 [8.1 (2.9)]
EE max	455 [10.9(2.1)]	CLASS_1 157 [9.7 (1.5)] CLASS_2 115 [10.6 (2.1)] CLASS_3 155 [11.9 (2.1)] CLASS_4 28 [12.3 (1.9)]
Total oocytes	455 [7.4 (4.7)]	CLASS_1 157 [3.9 (3.1)] CLASS_2 115 [6.6 (2.8)] CLASS_3 155 [10.9 (4.1)] CLASS_4 28 [11.4 (4.9)]
MII oocytes	448 [5.1 (3.3)]	CLASS_1 157 [2.5(2.3)] CLASS_2 115 [4.7 (1.6)] CLASS_3 155 [7.5(3.1)] CLASS_4 28 [7.7 (2.9)]
OSI	448 [3.5 (4.2)]	CLASS_1 157 [1.2 (1.2)] CLASS_2 115 [2.2 (1.1)] CLASS_3 155 [6.2 (5.4)] CLASS_4 28 [7.1 (5.6)]
Fertilization ratio	402 [0.74 (0.22)]	CLASS_1 157 [0.64 (0.34)] CLASS_2 115 [0.79 (0.15)] CLASS_3 155 [0.78 (0.08)] CLASS_4 28 [0.75 (0.52)]

53 patients NO embryo-transfer

7 patients (1.6%) NO oocyte
24 patients (5.3%) NO MII
22 patients (4.8%) NO embryo

110 clinical pregnancy (27.4%)

62 patients (56.4%) ongoing pregnancy

CORRELATION AMONG

DIFFERENT CLASS OF MEAN MCL

**number of MII oocytes
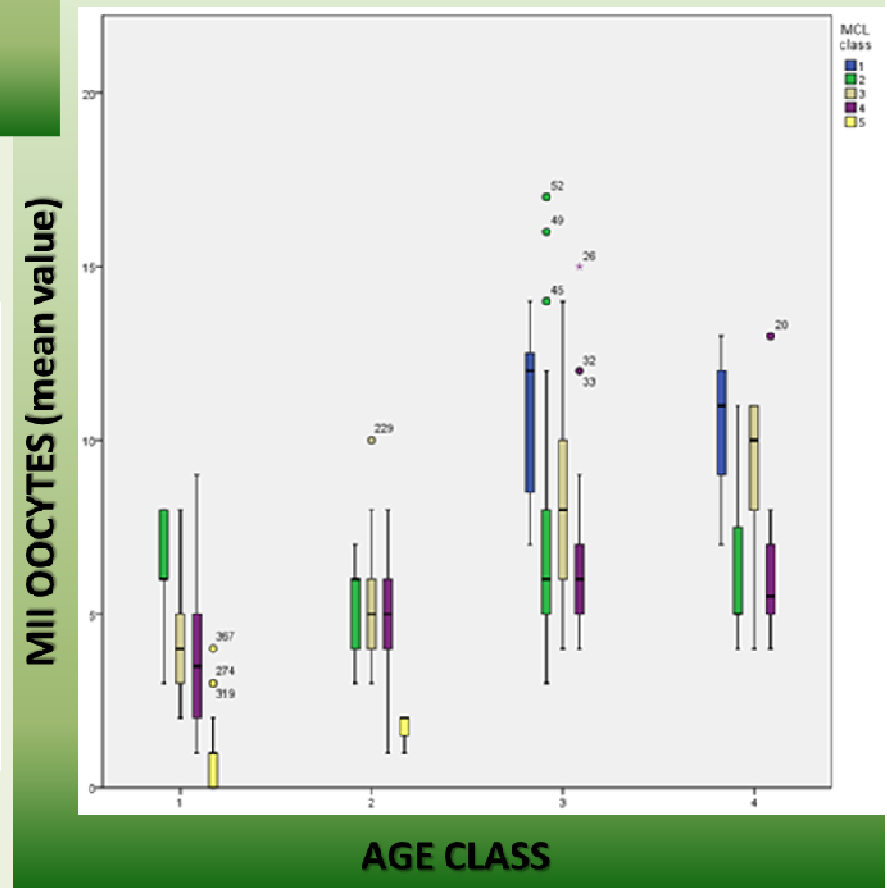MII oocytes fertilization ratio
Ovarian Sensitivity Index (OSI)**

IN ANY CONSIDERED CLASS OF AGE

Stratification data of patient's class of age, mean MCL class and number of MII oocytes showed that a statistical significant differences exists among different MCL class in patients older than 40 years (mean MII oocytes: 6.1 in MCL_2, 4.6 in MCL_3, 4.3 in MCL_4 and 1.3 in MCL_5 respectively) **[p<0.001].**

Statistical significant differences were also found in patients with MCL_1 respect to MCL_2, MCL_3 and MCL_4 in patients aged less than 35 years (both Age_class 3 and 4) **[p<0.05].** In Age_class_2 only patients with class MCL_5 showed significant differences respect to the other (1.9 versus 5.2, respectively) [p<0.01]. Instead, the comparison between MCL class 2,3 and 4 in Age_class 2, 3 and 4 did not show any statistical significant differences, despite a better results were found in MCL_class_3.
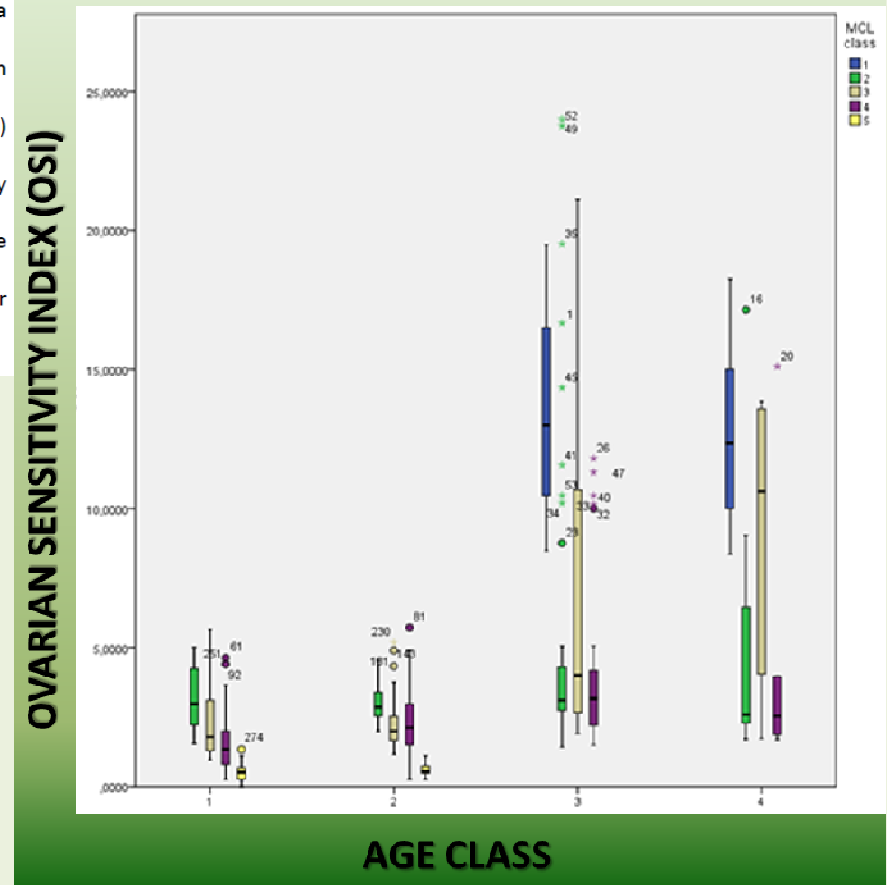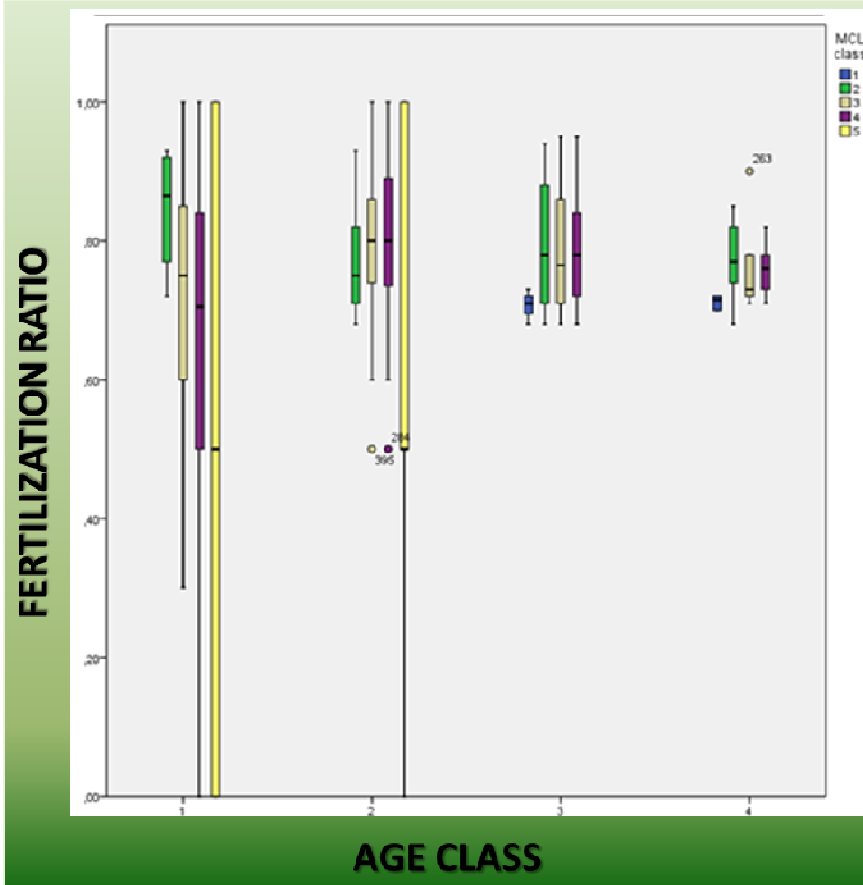
Stratification data of patient's class of age, mean MCL class and MII oocytes fertilization ratio showed that a statistical significant differences exists among different MCL class in patients older than 40 years (mean fertilization ratio: 86% in MCL_2, 77.5% in MCL_3, 71% in MCL_4 and 50.5% in MCL_5 respectively) [p<0.01]. Regarding patients aged between 35 and 40 years old, statistical differences were found only between MCL class_5 (50.8%) and MCL class_2, 3 and 4 (mean value 79.2%) **[p<0.01]**. No differences were found comparing different MCL classes in both Age class 3 and 4 despite MCL class_1 showed a lower fertilization rate than MCL classes 2, 3 and 4.

Stratification data of patient's class of age, mean MCL class and OSI showed that a statistical significant differences exists among MCL class_1 and MCL classes 2,3 and 4 in patients younger than 35 years (both Age class_3 and 4) **[p<0.001]**. Considering Age class_3 and 4, MCL class_3 showed better OSI than MCL class_2 ad 4 **[Age class_3 p<0.05 and Age class_4 p<0.001, respectively]**.

Regarding Age class_1 and 2, OSI differed significantly in relation to the different MCL classes, with a trend in reduction from MCL class_2 to MCL class_5. **[p<0.05]**

TO DETECT IF
patients expected poor responders

SHOWED DIFFERENT OVARIAN RESPONSE
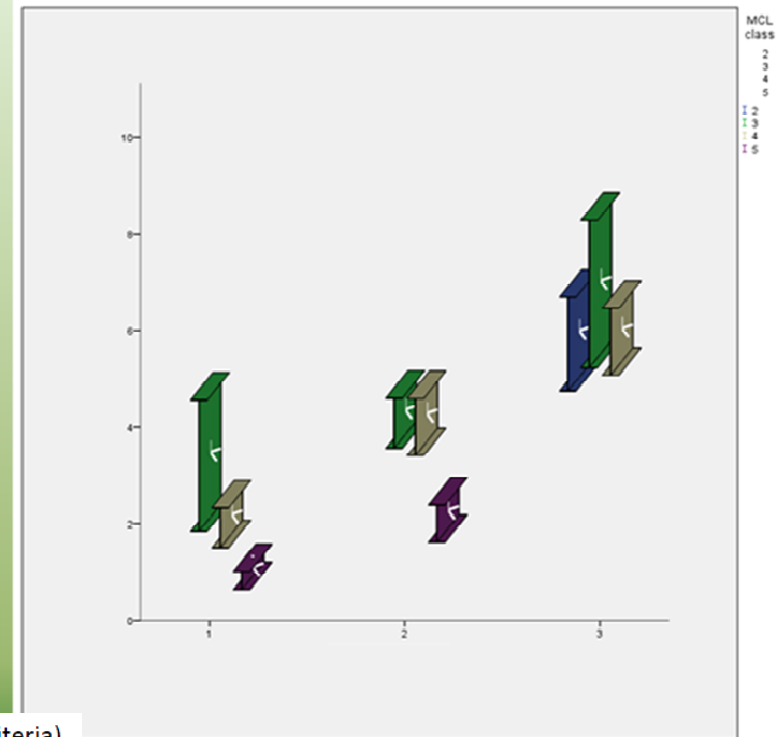(mean number of MII oocytes)

for cohort of AMH value
AMH cohort_1: 0.1-0.4 ng/ml;
AMH cohort_2: 0.5-1.1 ng/ml;
AMH cohort_3: >1.1 ng/ml

IN RELATION TO THE CLASS OF MEAN MCL

Considering the cohort of patients estimated poor responders (according to Bologna's Criteria), stratification data between MCL classes and AMH cohorts in relation to mean MII oocytes retrieved, showed that no differences exist among MCL class in AMH cohort_3. Instead, significant differences were found in AMH cohort 2 between MCL class_5 and MCL class_3 and 4 [p<0.01] as well as in AMH cohort_1 a statistical significant worsening trend was found comparing MCL class 3 versus MCL calss_4 versus MCL class_5. [p<0.05].
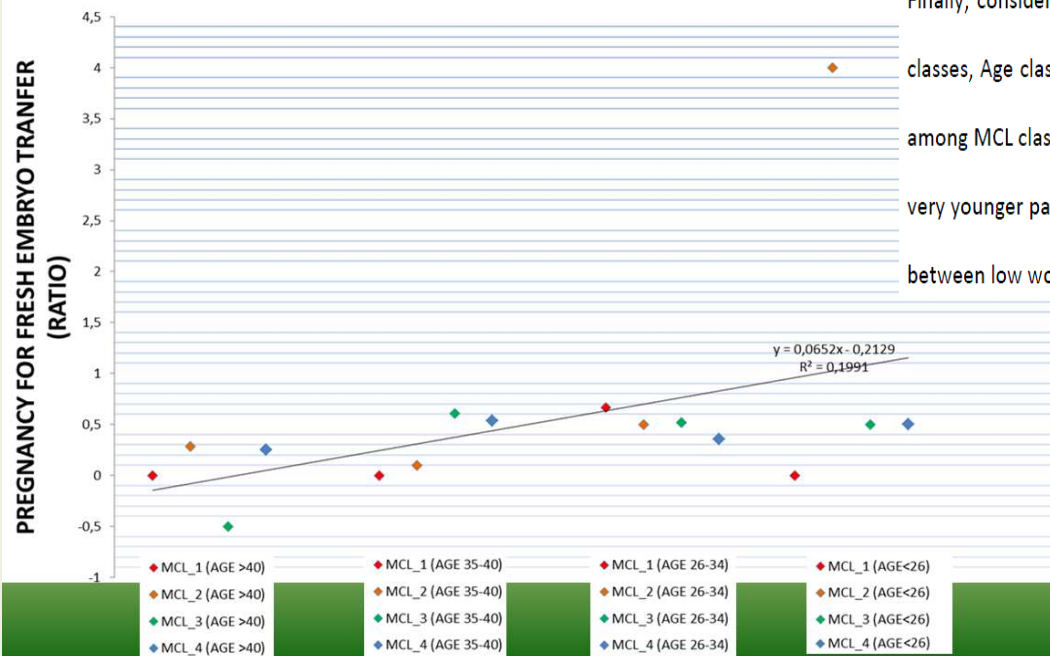
TO DETECT IF

"normo-responders" patients

SHOWED DIFFERENT
PREGNANCY RATE FOR FRESH EMBRYO TRASFERT

in different class of MCL
according to their class of age

COMPARISON AMONG subGROUPS IN TERM OF PREGNANCY RATE ACCORDING TO AGE CLASS AND MCL CLASS (NORMORESPONDERS PATIENTS)

y = 0,0652x - 0,2129
$R^2 = 0,1991$

Finally, considering the cohort of patients estimated normo responders, stratification data between MCL classes, Age classes and clinical pregnancy rate for fresh embryo transfer showed that no differences exist among MCL classes into any Age class except for MCL class_2 (better ratio) and MCL class_1 (worst ratio) in very younger patients (Age class_4). On the contrary, as expected, a significant linear correlation was found between low women age and pregnancy ratio independently from MCL classes. **[p<0.05]**

Legend:
- MCL_1 (AGE >40)
- MCL_2 (AGE >40)
- MCL_3 (AGE >40)
- MCL_4 (AGE >40)
- MCL_1 (AGE 35-40)
- MCL_2 (AGE 35-40)
- MCL_3 (AGE 35-40)
- MCL_4 (AGE 35-40)
- MCL_1 (AGE 26-34)
- MCL_2 (AGE 26-34)
- MCL_3 (AGE 26-34)
- MCL_4 (AGE 26-34)
- MCL_1 (AGE<26)
- MCL_2 (AGE<26)
- MCL_3 (AGE<26)
- MCL_4 (AGE<26)

MCL diary IS MORE PREDICTIVE THAN

CHRONOLOGICAL AGE
basal FSH value

IN PREDICTING

OVARIAN BIOLOGICAL AGE & RESPONSE TO COH

MCL diary IS MORE PREDICTIVE THAN

AMH & AFC

IN PREDICTING

OVARIAN BIOLOGICAL AGE & RESPONSE TO COH

In "ESTIMATED HIGH AND POOR RESPONDERS"