

A LIFE BIRTH PREDICTIVE MODEL AFTER IN VITRO FERTILIZATION (IVF) MAY HAVE A FAIR DISCRIMINATION: RESULTS OF A MULTICENTER EXTERNAL VALIDATION BASED ON 15039 IVF CYCLES. P. Arvis,^a A. Guivarc'h-Leveque,^a C. Colella,^b P. Leherc'h,^c ^aClinique La Sagesse, Rennes, Ille et Vilaine, France; ^bMerck Serono, Lyon, Rhone, France; ^cFaculty of Economics, Louvain, Leuven, Belgium.

OBJECTIVE: Because accuracy of previous predictive models remains insufficient for routine practice, and external validation questionable, we recently added new predictors to a modified Templeton model (FSH, Smoking habits, BMI), which significantly improved the accuracy and outperformed all other models (auROC=.71). We assessed here the external validation of our model.

DESIGN: Retrospective analysis based on 3 French centers.

MATERIALS AND METHODS: Our study was based on 15039 cycles from 3 IVF centers. The Intent to treat overall selection, and a generalized mixed model featuring logistic regression were used. External validity was assessed in modeling the main effect of the patient mix variables by a fixed and random component. Discrimination was evaluated by area under the ROC curve (auROC), calibration by comparing observed and predicted proportions.

RESULTS: A full factorial model demonstrated the high significance of the center effect (Random model, between center SD=3.5%, 95%CI [1.4,5.6], p<.001), followed by age(OR: .94[.92,.96] and (10[.92,.96]), infertility duration (.95 [.93,.97]), number of attempts(.69 [.66,.73]), tubal problems (.67 [.55,.83]), previous live birth (2.5 [2.1,2.9]), FSH>10 (.41 [.34,.48]), BMI (.76 [.68,.85]) and smoking (.59 [.52,.67]). For no one of these predictor, the random components was found significant (largest p value=.16). Compared with the initial model, a fair discrimination was found (AuRoc=.723), and calibration successfully tested in each centre.

CONCLUSION: The between-center variability is the most important predictor: any external validation not accounting for the center will prove bad predictions. As only small variations of the main Mix patient effects were found, we conjecture that Patient mix remains invariant among center, thus the constant term of the model may be assimilated to the performance of each center. The 6 mentioned predictors provide a fairly discriminant model, externally validated, based on common variables, thus applicable in routine practice.

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PREDICTING PREGNANCY POTENTIAL USING ANTI-MULLERIAN HORMONE (AMH) AND CALCULATING AN AMH REFERENCE POINT. C. E. Likes III,^a A. M. Craig,^b J. E. Johnson,^a H. L. Higdon III,^a W. E. Roudebush,^b W. R. Boone.^a ^aDepartment of Obstetrics and Gynecology, Greenville Health System University Medical Center, Greenville, SC; ^bDepartment of Biomedical Sciences, University of South Carolina School of Medicine - Greenville, Greenville, SC.

OBJECTIVE: Anti-Mullerian hormone (AMH), a member of the transforming growth factor- β family, is produced in small amounts by ovarian granulosa cells after birth until menopause, and then becomes undetectable. AMH levels during the reproductive years are representative of the ovarian reserve and are useful to help determine egg recovery potential for ART. Whereas, AMH levels can reflect egg quantity, said levels have not been well correlated with pregnancy outcomes following IVF-ET. Therefore, the study objective characterized pregnancy outcomes by AMH levels in patients undergoing ART for infertility.

DESIGN: Retrospective data analysis of patients undergoing IVF-ET at a tertiary fertility clinic.

MATERIALS AND METHODS: Patients diagnosed with polycystic ovarian syndrome (AMH > 5.0 ng/mL), ovarian insufficiency (AMH < 0.3 ng/mL), and male factor were excluded from the study. A receiver operator curve (ROC), and Student's t-test were used where appropriate and P was set at < 0.05.

RESULTS: A total of 45 patients were included in this study. An ROC demonstrated a definitive AMH cut-off value (i.e. criterion) for a viable pregnancy of 1.26 ng/mL: criterion >1.26, specificity 65.2, and sensitivity 68.2. Using this criterion, pregnancy rates between the "good" AMH group (> 1.26 ng/mL; 65.2% pregnancy rate) and the "poor" AMH group (< 1.26 ng/mL; 27.3% pregnancy rate) was significantly different (P < 0.001).

CONCLUSION: AMH has been shown to be a valid predictor of ovarian reserve, ovarian insufficiency and response to gonadotropin stimulation. Little information is available on the power of AMH to determine or predict pregnancy potential. While our initial data permit a calculated "cut-off value" or reference point, to achieve a viable pregnancy, this value does not exclude patients with low AMH a chance of obtaining a viable pregnancy. The AMH reference point may indicate that more aggressive means of fertility treatment would be warranted to obtain a viable pregnancy.

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ANTIMULLERIAN HORMONE VERSUS THE CLOMIPHENE CITRATE CHALLENGE TEST FOR EVALUATION OF OVARIAN RESERVE PRIOR TO IN VITRO FERTILIZATION. A. C. Eblen, M. Freeman, G. Hill, C. Whitworth, G. Weitzman. Nashville Fertility Center, Nashville, TN.

OBJECTIVE: The purpose of this study was to determine whether an anti-müllerian hormone (AMH) level or a clomiphene citrate challenge test (CCCT), is the best predictor of In vitro fertilization (IVF) pregnancy outcome prior to stimulation in women ≥ 35 years of age.

DESIGN: Women who underwent their first cycle of IVF in 2011-12 and were ≥ 35 , were included (n=50). Prior to IVF, ovarian reserve was evaluated with both a clomiphene citrate challenge test and an antimüllerian hormone level. Pregnancy was then evaluated to determine if an AMH level or the CCCT was more predictive of outcome.

MATERIALS AND METHODS: A chart review was done. Women in their first cycle of IVF who ≥ 35 years of age and had a CCCT and AMH level prior to the start of the cycle were included. Positive and negative predictive values were evaluated for AMH and CCCT. A sign test was used to determine significance.

RESULTS: Using an AMH level of ≥ 1 ng/ml as normal, positive and negative predictive values for pregnancy were 53% and 62%, respectively. Positive and negative predictive values using the CCCT were 51% and 65%, respectively. There was not a statistically significant difference for positive or negative predictive values regardless of which test was used. This study suggests that an AMH is just as useful in predicting pregnancy outcome prior to stimulation in women ≥ 35 years of age, as compared to the gold standard which is the CCCT. Furthermore the AMH is an easier test to obtain since the result is not cycle dependent. AMH testing is more cost effective and minimizes trips to the office and to the pharmacy. The cost of an AMH test is \$115. The total cost of a CCCT is \$271, including serum testing and the cost of the medication.

CONCLUSION: The AMH serum level alone has similar positive and negative predictive values as compared to the CCCT, with a cost savings of \$156. Due to the cost and ease of testing, the AMH should be used for ovarian reserve testing in women ≥ 35 years of age who are planning to do IVF.

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VITAMIN-D TREATMENT DOES NOT IMPROVE PREGNANCY RATES IN PATIENTS UNDERGOING ART: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL. E. Polak de Fried,^a N. M. Bossi,^a J. A. Notrica,^a M. H. Vazquez Levin.^{a,b} ^aReproductive Medicine, CER Medical Institute - Affiliated to the School of Medicine - Buenos Aires University, C.A.B.A., Buenos Aires, Argentina; ^bReproductive Medicine, IBYME Institute of Biology and Experimental Medicine, C.A.B.A., Buenos Aires, Argentina.

OBJECTIVE: To evaluate the effect of Vitamin-D (VD) to improve pregnancy rates in ART. Recent evidence shows that low VD is associated with infertility and low pregnancy rates in IVF.

DESIGN: Prospective, randomized, double-blind placebo-controlled trial.

MATERIALS AND METHODS: Fifty two patients were computer randomized during 5 consecutive months into Group A = at least one monthly oral VD dose (100.000 IU) and Group B = placebo. Basal and post treatment VD was evaluated. VD ranges (ng/ml): deficiency (<20), insufficiency (20-30) and sufficient (>30). ICSI cycles: 34 (A=17, B=17) and oocyte donation (OD)/ICSI cycles: 18 (A=9, B=9) were evaluated.

Statistics: Man-Whitney rank-sum test and Fisher exact test. P<0.5 = significant.

RESULTS: There were no significant differences between the groups in ICSI for age (A=39.2 \pm 1.1, B=38.4 \pm 0.9), basal VD (A=22 \pm 2.5, B=20.1 \pm 1.3), endometrial thickness (A=11.1 \pm 0.7, B=10 \pm 0.6), number

of oocytes retrieved (A=5.9±1.2, B=7.3±1.0), cancellation rate (A=23.5%, B=23.5%), number of embryos transferred (A=2.2±0.2, B=2.8±0.1), implantation rate (A=14.28%, B=15.15%), and clinical pregnancy rate (A=23%, B=33%). There was a significant difference of VD (ng/ml) post treatment (A=42.9±1.9, B=23.9±1.7, P<0.001).

There were no significant differences between the groups in OD/ICSI for age (A=42.3±2.2, B=42.3±3.2), basal VD (A=20.8±2.4, B=24.7±3.2), endometrial thickness (A=9.8±0.7, B=9.1±0.6), number of embryos transferred (A=2.1±0.2, B=2.4±0.1), implantation rate (A=31.57%, B=22.72%) and clinical pregnancy rate (A=44.4%, B=44.4%). There was a significant difference of VD (ng/ml) post treatment (A=39.3±3.7, B=23.9±2.0, P<0.01).

CONCLUSION: No significant differences were found in pregnancy rates between patients who underwent ART and received VD, although these patients showed sufficient VD levels. To our understanding, this is the first prospective, randomized double blind preliminary trial using VD replacement in infertile women who underwent ART. Current studies are underway to expand the trial.

P-1200 Thursday, October 17, 2013

A SOLE PROGESTERONE VALUE ON DAY OF HCG DOES NOT PREDICT PREGNANCY AFTER IVF, REGARDLESS OF PROTOCOL OR TYPE OF RESPONSE. F. Martinez, F. Mancini, R. Tur, B. Coroleu, I. Rodriguez, P. N. Barri. Obstetrics, Gynecology and Reproduction, Institut Universitari Dexeus, Barcelona, Spain.

OBJECTIVE: To identify if a value of Progesterone on the day of hCG (P-hCG) could predict pregnancy in patients undergoing an IVF cycle.

DESIGN: A retrospective study of all IVF cycles achieving embryo transfer between January 2011 and June 2012.

MATERIALS AND METHODS: All patients were treated with GnRH analogue and rFSH or rFSH+hMG. Statistics: ROC analysis, area under the curve, trend analysis, Spearman correlation coefficient.

RESULTS: In total, 892 IVF cycles were analyzed: 605 antagonist cycles (67.8%) and 287 long agonist cycles (32.2%). Patients age: 36.87± 4.13 yo; P-hCG=1.02±0.56 ng/ml; num of retrieved oocytes 9.18± 5.33; num of transferred embryos 1.91±0.59; clinical pregnancy rate 38.7%. No differences were observed in P-hCG between pregnant and not pregnant cycles, both in antagonist (0.99±0.51ng/ml vs 0.95±0.40ng/ml) or long agonist cycles (1.18±0.50 ng/ml vs 1.15±0.79ng/ml). There was a positive correlation (p<0.001) with age (r=-0.132), estradiol on day of hCG (r=0.340) and number of retrieved oocytes (r=0.315). After adjusting for these variables, P-hCG was related with the stimulation protocol and the type of gonadotropin: P-hCG in agonist cycles were higher than in antagonist cycles (1.16±0.72 vs 0.96±0.47 ng/ml, p<.05) and in rFSH cycles compared to rFSH+ HMG cycles (1.14±0.63 vs 0.94±0.50 ng/ml, p<.05), without interaction between gonadotropin and protocol. When comparing P-hCG and their Confidence Intervals between pregnant and not-pregnant cycles, according to age group, stimulation and type of ovarian response, there were no differences. When analyzing the results according to type of response (low < 4 oocytes, normal=5-19 oocytes, high ≥ 20 oocytes) no P-hCG cut-off discriminating pregnancy was identified.

CONCLUSION: P levels on the day of hCG do not predict pregnancy. Therefore a sole P-hCG value should not be used as the only criteria for clinical decision making. Clinical management of IVF cycles should be based upon other safety criteria and keeping in mind the best patient's interest.

P-1201 Thursday, October 17, 2013

FORTY YEARS AND BEYOND: OUTCOME OF 1,939 IN VITRO FERTILIZATION CYCLES INITIATED IN WOMEN 40 YEARS AND OLDER WHO USED AUTOLOGOUS OOCYTES. P. J. Buzzi, L. Auge, A. Valcarcel, R. Quintana, E. T. Young, A. Bello. Instituto de Ginecología y Fertilidad (IFER), Buenos Aires, Argentina.

OBJECTIVE: Although fecundity decreases with age more women in the fifth decade of life seek fertility treatments. The aim of this study is to describe the reproductive outcome and predictors of success in 1-year age increments for women ≥ 40 years when initiating assisted reproductive technologies (ART).

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: All patients (n= 1749) ≥ 40 years of age (40-48 years) who underwent ART with autologous oocytes between January 2004 and December 2012 were included. The primary outcome

was live birth. Secondary outcomes were cancellation rate, number of oocytes retrieved, mature oocytes, oocytes fertilized, implantation rate, pregnancy rates per cycle (PRC) and per transfer (PRT). A clinical pregnancy was defined by ultrasound visualization of an intrauterine sac with fetal heartbeat (FHT). Predictors of success such as number of embryos transferred, number of fetal heartbeats, availability of embryos for cryopreservation and cycle Day 3 FSH levels, were analyzed. Kruskal-Wallis and chi square test were used in analysis. Significance was defined at a level of P<.05.

RESULTS: The mean age of the patients was 41.9 years. The overall live birth rate per cycle start was 12, 9%. Cancellation rate was 22,5%. The mean number of mature oocytes per transferred cycle was 5.6. and the number of embryos replaced was 3.3. PRT was 20,86% (312/1495). Overall pregnancy loss was 33,3%. Higher pregnancy rates were predicted by greater number of good quality embryos available for transfer and by the presence of more than one FHT on ultrasound. Higher day 3 FSH levels were associated to higher cancellation rates when adjusting for age at cycle start.

CONCLUSION: For many older women oocyte donation is not an option. ART has reasonable chances of success in achieving a live birth up to the age of 43. Identifying factors associated with success in this group is significant at the time of considering more attempts.

P-1202 Thursday, October 17, 2013

THE EFFECT OF LOW BODY MASS INDEX (BMI) ON OOCYTE QUALITY IN IVF CYCLES. M. Brower,^{a,b} E. Wang,^{b,a} D. Hill,^c M. Surrey,^c H. Danzer,^c M. D. Pisarska.^{b,a} ^aDivision of Reproductive Endocrinology and Infertility, University of California Los Angeles, Los Angeles, CA; ^bDivision of Reproductive Endocrinology and Infertility, Cedars-Sinai Medical Center, Los Angeles, CA; ^cSouthern California Reproductive Center, Beverly Hills, CA.

OBJECTIVE: The impact of low BMI on oocyte quality and IVF outcomes has not been clearly established. The aim of this study was to determine if women with a low BMI produce oocytes of lesser quality and have poorer outcomes with IVF compared to normal weight women.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Data for 256 women undergoing their first ICSI or oocyte cryopreservation cycles at a single center between 2011-2012 were analyzed. Participants were classified into two groups based on BMI, ≤ 19 kg/m² (n=51) and 19.1-25 kg/m² (n=205). The primary outcome was oocyte quality as determined by qualitative descriptors provided by the embryologist at the time of oocyte retrieval. Oocytes described as being granular or having vacuoles, dark cytoplasm, debris or inclusions were considered poor quality. Secondary outcomes included fertilization, day 5 blastulation rate, implantation rate, clinical and ongoing pregnancy rate. Logistic regression analyses adjusted for age were used to determine the association between BMI and outcomes of interest.

RESULTS: Underweight women had a higher prevalence of poor quality oocytes compared to normal weight women (31% vs. 19%, p = 0.055). When controlling for age the multivariate model found that being underweight was associated with an almost 2 fold increased odds of poor oocyte quality (OR 1.93, 95% CI 0.95 - 3.82). The blastulation rate was significantly lower in underweight women than normal weight women (19% vs. 35%, p < 0.05). There were no differences in the number of oocytes retrieved, fertilization rate, clinical or ongoing pregnancy rates between the two groups.

CONCLUSION: Underweight women have a strong trend toward a higher prevalence of poor quality oocytes compared to normal weight women. Although no differences in pregnancy rates were observed, the significantly lower blastulation rate in underweight women could suggest underlying poor oocyte quality. These findings warrant further investigation with a larger study population.

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TOTAL AND GOOD QUALITY BLASTOCYST CONVERSION RATES FROM NORMAL AND MULTI-NUCLEATED EMBRYOS IDENTIFIED ON DAY 2 AND 3 OF CULTURE. M. T. Zavy, L. B. Craig, M. B. Zavy, N. M. Budrys, K. R. Hansen. Dept. of Ob-GYN, Division of Reprod. Endo. & Inf., Oklahoma University Health Sciences Center, Oklahoma City, OK.

OBJECTIVE: Multinucleation (MN) in 2PN embryos was identified on day 2 and 3 of culture to evaluate the total blastocyst conversion rate (TBCR) and good quality blastocyst conversion rate (GQBCR) in patients