Who is a Poor Responder in IVF?

IVF'TE ZAYIF CEVAP VEREN OLGUNUN TANIMI NE OLMALIDIR?

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Abstract

Objective: There is no uniform definition for the poor ovarian response (POR) in IVF. There is also no consensus on the cutoff values for the suggested variables for the definition of the POR. In the present study, we aimed to compare the ovarian response parameters as well as the ovarian reserve tests with each other as a predictor of the IVF success, i.e. pregnancy, and to find a cutoff for these parameters in order to suggest a uniform and acceptable definition for the POR.

Material and Methods: In this retrospective analysis of 152 ICSI cycles, predictive powers of different ovarian reserve and response parameters, i.e. age, basal serum FSH level and antral follicle count, duration of gonadotropin stimulation, serum E_2 level, number of dominant (≥10 mm, #DF) and mature follicles on the day of hCG, number of oocytes and mature oocytes retrieved, for the clinical pregnancy were compared by using the lower or upper tenth percentiles as cutoffs. Different combinations of these parameters were further analyzed in an attempt to find an optimum combination for the definition of the POR.

Results: #DF on the day of hCG had the highest predictive value among the pre-OPU parameters. Tenth percentile for that parameter was 4. The group of poor responders as determined by the threshold of ≤4 for the #DF had good correlations with those as determined by using 10th percentiles for the number of oocytes or MII oocytes retrieved.

Conclusions: Poor ovarian response in IVF with a luteal down-regulation regimen may be defined as those with ≤ 4 dominant follicles on the day of hCG.

Key Words: Definition; IVF; Poor ovarian response; poor responder

Özet

Amaç: Uzun protokol uygulanan IVF olgularında zayıf over cevabının sabit ve kabul görmüş bir tanımı yoktur. Literatürde kullanılan değişik tanımlardaki sınır değerler de farklılıklar göstermektedir. Bu çalışmadaki amacımız over rezervini ve over cevabını gösteren değişik parametrelerin gebeliği belirlemedeki prediktif değerlerini karşılaştırmak ve uygun sınır değerleri analiz ederek overin zayıf cevabını tanımlamada kullanılabilecek sabit ve kabul görebilir bir tanımı araştırmaktır.

Gereç ve Yöntemler: 152 ICSI siklüsunun retrospektif olarak incelendiği bu çalışmada yaş, bazal serum FSH düzeyi ve antral folikül sayısı, stimulasyon süresi, hCG'nin uygulandığı günkü serum E_2 düzeyi, dominant (≥10 mm, #DF) ve matür folikül sayıları, aspirasyonda elde edilen oosit ve matür oosit sayıları gibi farklı over rezervi ve cevap parametrelerinin gebeliği belirlemedeki etkinlikleri, 10. ve 90. persentiller sınır değer alınarak karşılaştırıldı. Zayıf ovaryan cevabın uygun tanımını bulabilmek amacıyla bu parametrelerin farklı kombinasyonları da analiz edildi.

Bulgular: OPU öncesindeki parametreler içinde hCG'nin uygulandığı günkü #DF en yüksek prediktif değere sahipti. Bu parametre için 10. persentil 4 idi. Dominant folikül sayısı 4 veya altında olan olgular grubu ile oosit sayıları ve MII oosit sayıları 10. persentilin altında olan olgu grupları arasında iyi derecede korelasyon gözlendi.

Sonuç: Uzun protokol uygulanan IVF olgularında zayıf over cevabı, hCG'nin uygulandığı gün 4 veya daha az dominant folikül olması olarak tanımlanabilir.

Anahtar Kelimeler: Tanım; IVF; zayıf over cevabı

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A reasonable percentage (9-24%) of women undergoing infertility treatment respond poorly to the usual gonadotropin stimulation protocol applied.[1] The ideal approach to these women has not been well established.[2] Although the number of studies on the success of different regimens is increasing, critical evaluation of the many published protocols is extremely difficult. One of the main reasons, and probably the most basic, is the difference in inclusion criteria for characterizing subjects as poor responders. No

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Table 1. Criteria used to define the poor responder

	Values used as cutoffs
Age (years)	40
Basal serum FSH levels (mIU/mL)	>6.5; >9; >12; >15
Number of mature follicles	<2; <3; ≤4; <5
Maximal E_2 level (pg/mL)	<300; <400; <500; <660
Total gonadotropin dose (ampules)	>25; >44
Number of mature oocytes retrieved	≤3; ≤4; <6

more than a few sets of investigators have used any single definition (Table 1).[2] It is extremely difficult to compare outcomes in the absence of a uniform definition for the poor responder. Furthermore, there is no consensus on the cutoff values for the suggested variables for the definition of the poor ovarian response (Table 1).[2]

Therefore, we aimed to compare the ovarian response parameters as well as the ovarian reserve tests with each other as a predictor of the IVF success, i.e. pregnancy. We aimed also to find a cutoff for these parameters in order to suggest a uniform and acceptable definition for the poor ovarian response.

Material and Methods

Subjects

The present study is a retrospective analysis of 152 consecutive ICSI cycles of subjects with an indication for IVF/ICSI between November 2001 and August 2003. These were the first cycles of the subjects. All women underwent an ICSI cycle following a luteal phase down-regulation. Cycles of all patients, whose spontaneous cycle preceding the treatment cycle has been followed and who had two ovaries, were included in the study. Only cycles with sufficient number of motile spermatozoa available for all of the retrieved mature oocytes were included in the study. Cycles with ovum pick-up (OPU) cancellations due to poor ovarian response (n=10) were not included in this analysis. Institutional review board approval was obtained from the Marmara University School of Medicine.

Treatment protocol

In our center, treatment cycles were performed after a spontaneous cycle, during which a work-up, including basal ovarian reserve tests and office hysteroscopy or HSG, has been done. Basal serum FSH and E_2 levels were determined in this sponta-

Table 2. Characteristics of the unsuccessful cycles and those, that led to clinical pregnancies

	Not pregnant (n = 139)	Pregnant (n = 53)	P
Age (years)	33.6±5.2	30.2±5.1	<0.001
BMI (kg/m^2)	24.40±4.22	23.20±3.21	0.11
Basal serum FSH level (mIU/mL)	7.7±2.3	6.5±2.1	0.006
Basal serum E_2 level (pg/mL)	46.4±26.9	40.0±23.7	0.18
Antral follicle count	6.6±3.9	9.2±3.9	<0.001
Total rFSH dose (IU)	1717±848	1492±862	0.15
Total hMG dose (IU)	4035±1605	2925±1725	<0.001
Days of gonadotropin therapy	9.3±1.4	8.7±1.1	0.007
Serum E_2 level on the hCG day (pg/mL)	2177±2600	3299±3950	0.07
Number of follicles ³ 16 mm in diameter on the hCG day	3.2±1.7	4.4±1.9	<0.001
# DF on the hCG day	10.9±6.6	16.6±6.0	<0.001
Number of oocytes retrieved	8.9±7.7	12.7±6.3	0.002
Number of MII oocytes retrieved	6.6±5.4	10.1±5.2	<0.001
Number of embryos transferred	2.4±1.1	3.0±0.6	<0.001
Number of oocytes retrieved / # DF (%)	74.7±32.6	75.4±22.0	0.9
Number of MII oocytes retrieved / # DF (%)	57.5±25.9	60.8±19.4	0.4
Number of embryos transferred / # DF (%)	26.5±18.4	23.3±11.0	0.2

Note: # DF = number of dominant follicles (³ 10 mm in diameter).

neous cycle preceding the treatment cycle. For all patients, pituitary desensitization was performed with leuprolide acetate SC daily (Lucrin, Abbott, Istanbul, Turkey) starting one week before the expected menses. Luteal administration of 1.0 mg/d was given during the luteal phase of the cycle preceding treatment until the second day of the onset of menses, and decreased to 0.5 mg/d from day 2 till the day of hCG injection.

After down-regulation was achieved (serum E_2 <40 pg/mL), ovarian stimulation was commenced at day 3 with a daily dose of 150 – 300 IU recombinant FSH (rFSH), IM (Gonal-F, Serono, Istanbul, Turkey or Puregon, Organon, Istanbul, Turkey) in combination with 300 - 600 IU of hMG (Humegon, Organon, Istanbul, Turkey or Menogon, Ferring, Istanbul, Turkey; both hMG contain 75 IU FSH and 75 IU LH). At the same day, basal antral follicles, which were between 2-10 mm in diameter, were counted. Subjects, who had a basal follicle of >10 mm or evidence of an ovarian pathology, were cancelled. Starting dose was adjusted according to patient's age, basal serum FSH and E_2 values at the preceding cycle and basal antral follicle count (AFC).

The subjects returned on days 6 or 7 of stimulation for an assessment of follicular recruitment and growth by transvaginal ultrasound. The gonadotropin dose and timing of subsequent scans were determined by the subject's response to controlled ovarian stimulation. When there were at least three follicles that were ≥16 mm in diameter, hCG was administered, and transvaginal oocyte retrieval was performed 34 - 36 hours later. All subjects received 10,000 IU of hCG. Subjects, who did not have at least one follicle of >10 mm after 9 days of gonadotropin stimulation, had their cycles canceled before oocyte retrieval. Subjects, who had one or two follicles of ≥16 mm in conjunction with no follicles between 10 and 16 mm at any day, were informed about the success rate and offered intrauterine insemination. OPU was performed to subjects, who decided to go on with IVF.

Approximately 4 hours after the retrieval and just before sperm injection, oocytes were assessed for maturity by using the criteria described by Veeck (ref). All metaphase II oocytes were injected. Embryo transfer was performed 72 hours after oocyte retrieval. Up to four transferable embryos were transferred. The luteal phase was supported by using progesterone in oil, 50 mg/day IM starting on the day of OPU. A pregnancy test was performed 10 days after ET. A clinical pregnancy was defined as the presence of a gestational sac within the uterus in transvaginal ultrasonography (which excludes ectopic and biochemical pregnancies) associated with rising serum β-hCG.

Assays and ultrasonographic measurements

Serum FSH and E_2 concentrations were determined using the Immulite immunoassay system (Diagnostic Products Corporation, Los Angeles, CA, USA). This assay is standardized to the World Health Organization Second International Reference Preparation 78/549. The interassay and intraassay coefficients of variation were 6.6% and 5.4% for FSH, and 5.4% and 4.4% for E_2, respectively.

Transvaginal ultrasound was performed by using a GE Logiq 200 Pro (GE Medical Systems, Milwaukee, WI, USA) with a 6.5-MHz vaginal transducer. All ovarian follicles measuring 2 mm to 10 mm on both ovaries were counted on cycle day 3. The total number was expressed as the AFC. Ovarian follicles measuring ≥ 10 mm in diameter were accepted as dominant follicles, and those ≥ 16 mm as mature follicles. The total numbers were used for calculations.

Statistical analysis

Statistical analysis involved univariate comparisons between the unsuccessful cycles and those, that led to clinical pregnancies using student's t-test. Variables in Table 2 were compared between groups. All ovarian reserve and response parameters, which had a P value <0.1 in the univariate analysis were included in receiver operating characteristic (ROC) analysis. The dependent variable in the ROC analysis was the clinical pregnancy.

ROC analysis was performed to determine the predictive power of the significant prognostic variables. Diagnostic sensitivity and specificity were

Table 3. Results of the ROC analysis and cutoffs corresponding to the 10th or 90th percentiles for different parameters. Predicitve roles and pregnancy rates for these parameters also are shown, when these percentiles were used as cutoffs

	AUC ± SE	*P* *	95% CI	Cutoff corresponding to the 10th or 90th percentile	Sn (%)	Sp (%)	PPV (%)	NPV (%)	PR per retrieval (100 - PPV)
Number of follicles ³ 10 mm in diameter on the hCG day	0.75 ± 0.04	<0.001	0.66 - 0.84	4	17.3	97.6	95.0	31.1	5.0
Number of MII oocytes retrieved	0.71 ± 0.04	<0.001	0.62 - 0.79	2	23.6	97.6	96.3	32.8	3.7
Number of oocytes retrieved	0.70 ± 0.05	<0.001	0.61 - 0.78	2	15.5	97.6	94.4	30.6	5.6
Basal AFC	0.71 ± 0.05	<0.001	0.62 - 0.81	2	11.8	95.2	86.7	29.2	13.3
Serum E_2 level on the hCG day	0.69 ± 0.05	<0.001	0.61 - 0.79	551 pg/mL	12.7	97.6	93.3	29.9	6.7
Number of follicles ³16 mm in diameter on the hCG day	0.69 ± 0.05	<0.001	0.60 - 0.78	1	13.6	97.6	93.8	30.1	6.2
Age	0.69 ± 0.05	<0.001	0.60 - 0.78	40 yrs	11.8	97.6	92.9	29.7	7.1
Basal serum FSH level	0.65 ± 0.05	0.005	0.55 - 0.75	10 mIU/mL	17.3	92.9	86.4	30.0	13.6
Days of gonadotropin stimulation	0.65 ± 0.04	0.005	0.55 - 0.75	11	14.5	95.2	88.9	29.9	11.1

Note: AUC=area under the curve, SE=standard error, CI=confidence interval, Sn=sensitivity, Sp=specificity, PPV=positive predictive value, PR=pregnancy rate, NPV=negative predictive value, AFC = antral follicle count.
* Significance of the difference from a coin test, which has an AUC of 0.5.

calculated, and the ROC curve was constructed by plotting the sensitivity against the false-positive rate (1-specificity) of various cutoff values for predicting pregnancy. Area under each ROC curve (AUC_{ROC}), which indicates the predictive power of the parameter, was calculated.

Cutoffs corresponding to 10^{th} or 90^{th} percentiles of the ovarian response parameters, depending on whether decreasing or increasing values indicate pregnancy, were determined. Predictive power and pregnancy rates in these percentiles were analyzed. To determine whether the ovarian response parameters could be used interchangably or in combination for the definition of the poor responder, correlations between the groups of poor responders as determined by these percentiles of different parameters, were analyzed. This analysis for correlations was performed between the ovarian response parameter, which had the highest AUC_{ROC} value among those parameters, which were obtained before the oocyte retrieval, and other parameters. The rationale was that any attempt to define the poor ovarian response according to the number of oocytes retrieved, would require an invasive procedure, i.e. OPU, for the diagnosis. Therefore, we analyzed the best parameter before the OPU as a possible diagnosis of the poor ovarian response. Spearman correlation test was used for the analysis. SPSS, Release 10.0 (SPSS, Inc, Chicago, IL, USA) was used for the statistical analysis and a P value of <0.05 was considered significant. Values were expressed as "mean ± SD"

Results

Univariate comparisons between the unsuccessful and successful cycles revealed that age, basal serum FSH level, basal AFC, total hMG dose, days of gonadotropin stimulation, number of dominant and mature follicles, number of oocytes retrieved, number of mature (MII) oocytes retrieved, and number of embryos transferred were significantly different ($P < 0.05$, Table 2). The predictive roles of these parameters as expressed by AUC_{ROC} are shown in Table 3. Number of dominant follicles on the day of hCG had the highest AUC_{ROC} value. It was also the best predictor among the ovarian response parameters before the retrieval, when the 10^{th} percentiles were chosen as cutoffs (Table 3). The numbers of oocytes, MII oocytes and embryos each divided by the number of dominant follicles were comparable between the pregnant and nonpregnant groups (Table 2).

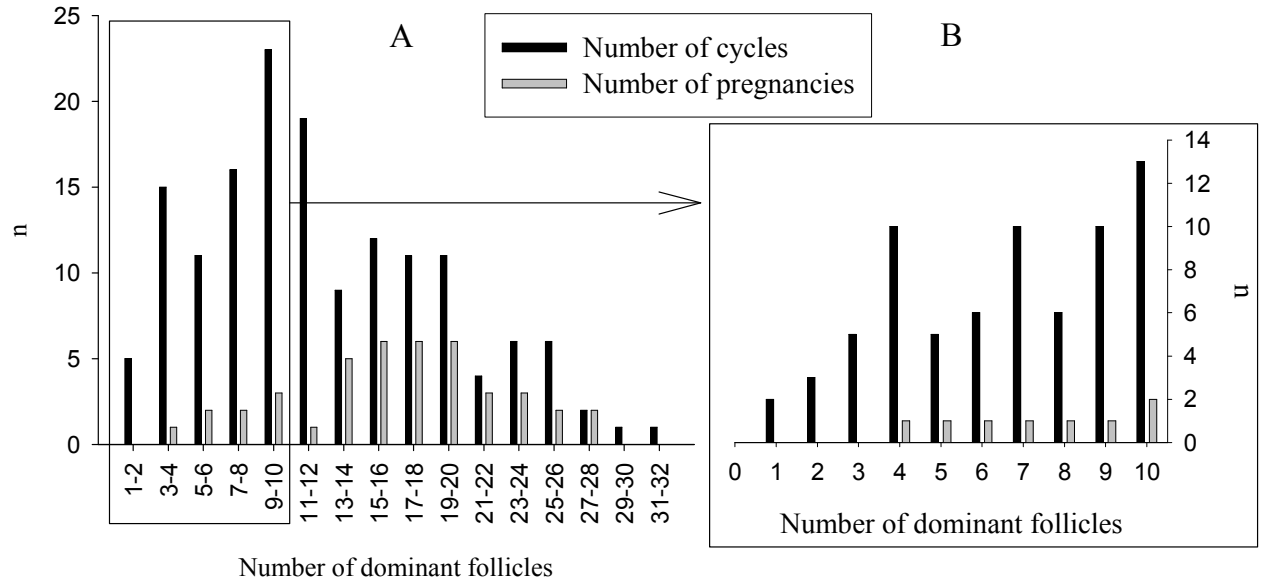

Figure 1. Pregnancy rates at different numbers of dominant follicles on the day of hCG.

Pregnancy rates at different numbers of dominant follicles on the day of hCG are shown in Figure 1. The cutoff corresponding to the 5th percentile was 3, and that corresponding to the 10th percentile was 4. When the number of dominant follicles was below the 5th percentile, the pregnancy rate was 0%, and when that was below the 10th percentile, it was 5.0%. The cutoffs corresponding to the lower or upper 10th percentiles for the other ovarian reserve and response parameters are shown in Table 3. Positive and negative predictive values for these parameters also are shown in the Table 3.

Analysis of correlations revealed that the group of poor responders as defined based on the number of dominant follicles had a good correlation ($r > 0.5$, Table 4) with both of the groups of poor responders as defined based on either number of oocytes or MII oocytes. Weak or no correlations ($r \leq 0.5$) were found between other parameters (Table 4).

After it was observed that there were weak correlations between these parameters, we analyzed the predictive power of binary combinations of the parameters. Since both of the components of an "and" type combination should be satisfied, these type of combinations decreased the number of subjects diagnosed as poor responder. Predictive values of these combinations (unpublished data) were not better than that of the number of dominant follicles on the day of hCG with the cutoff value of 3 (PPV=100%, NPV=29.6%), which decreased the number of subjects to a comparable percentile (5%). Upon analysis of the "or" type

Table 4. Correlations between the group of poor responders as determined by ≤4 dominant follicles on the day of hCG and other groups of poor responders as defined by their percentiles, which were shown in Table 3

	r	P
Number of MII oocytes retrieved	0.6	<0.001
Number of oocytes retrieved	0.6	<0.001
Serum E_2 level on the hCG day	0.5	<0.001
Antral follicle count	0.5	<0.001
Number of follicles ³16 mm in diameter on the hCG day	0.4	<0.001
Basal serum FSH level	0.3	<0.001
Age	0.2	0.009
Days of gonadotropin stimulation	0.1	0.2

combinations, that of the number of dominant and mature follicles resulted in slightly better predictive values than those of the number of dominant follicles alone, with the cutoff value of 5 (Table 5). This combination indicated 18% of subjects as poor responders.

Discussion

In this retrospective analysis, we observed that age, basal serum FSH level, basal AFC, total gonadotropin dose, number of dominant and mature follicles, number of oocytes retrieved, number of mature (MII) oocytes retrieved, and number of embryos transferred were predictors of pregnancy in IVF cycles following a luteal down-regulation. Gonadotropin protocols may not be uniform among IVF centers. Therefore, this was not analyzed as a possible definition of poor responder in the present study.

ROC analysis revealed that number of dominant follicles on the day of hCG had the highest value in the prediction of clinical pregnancy. This is in consistance with the facts that ovarian reserve tests are currently insufficient for the prediction of ovarian response, and ovarian response to stimulation remains the ultimate test. Therefore, if poor ovarian response in IVF is a diagnosis, then, the ovarian reserve tests should be regarded as screening tests. It may not be appropriate to define the poor responder according to the basal ovarian reserve tests. It should be mentioned that there cannot be any disagreement for a woman, who has a basal serum FSH level of 30 mIU/mL.

There is a lack of uniformity in the definition of the poor ovarian response in IVF among authors (Table 1).[2] Different parameters as well as different cutoffs for the same parameters have been used to define the poor responder (Table 1).[2] To our knowledge, the ovarian response parameters have not been evaluated previously to find the best definition for the poor ovarian response.

For defining abnormals in medicine, there are two common methods based on; (i) percentiles, or (ii) standard deviations. "Mean ± 2SD" is commonly used as the normal range for laboratory values. This range corresponds to the values between 2.5 and 97.5th percentiles. Tenth to 90th percentile range is also commonly used as normal in medicine, especially for growth charts. "Mean ± 2SD" approach may not be appropriate for the definition of the poor response since it estimates an incidence of 2.5% for the poor ovarian response, which is quite lower than the reported incidences of poor ovarian response in IVF.[1] Therefore, we chose the 10th percentile to analyze as the definition of the poor responder.

The 10th percentile corresponded to the cutoff value of 4 for the variable, which had the highest AUC_{ROC} in the present study, i.e. number of dominant follicles on the day of hCG. To our knowledge, this parameter has not been previously used for the definition of the poor responder. It has been suggested that basal AFC is a good predictor for the ovarian response.[3] We also recently have suggested that follicular counts during ovarian stimulation is a better predictor of ovarian response than the hormonal parameters, i.e. serum E_2 level.[4] The superiority of these ultrasonographic measurements over hormonal measurements throughout the whole period of ovarian stimulation, i.e. from the 3rd cycle day till the day of hCG, is important when the ease and availability of ultrasound, which is a prerequisite for IVF, and cost, time consumption and burden of blood samples are considered.

Below the 10th percentile for the number of dominant follicles on the day of hCG, the pregnancy rate (per retrieval) was 5.0%. ROC analysis in the present study revealed that this parameter had the highest AUC_{ROC} in the whole group of IVF cycles. However, the predictive value of a parameter may be lower than other parameters at a specific cutoff value, although it has the highest AUC_{ROC}. Therefore, we analyzed the predictive power of the parameters with the 10th or 90th percentiles used as cutoffs.

The aim in the attempt of defining the poor responder is to detect women with the least chance of pregnancy due to decreased oocyte number and/or quality. Therefore, it may be appropriate to interpret the pregnancy rates (1 minus PPV), instead of the combination of positive and negative predictive values, while comparing the parameters.

Table 5. Predicitve roles and pregnancy rates for the number of dominant follicles, single or combined with the serum E_2 level

	Rate of subjects diagnosed as poor responder (%)	Sn (%)	Sp (%)	PPV (%)	NPV (%)	PR per retrieval (100 - PPV)
Number of dominant follicles ≤4 or serum E_2 level < 551 pg/mL	16.4	20.9	95.2	92.0	31.5	8.0
Number of dominant follicles ≤5	16.4	20.9	95.2	92.0	31.5	8.0
Number of dominant follicles ≤4 or mature follicles ≤1	18.4	23.6	95.2	92.9	32.3	7.1
Number of dominant follicles ≤4 or days of stimulation ≤11	19.1	28.2	92.9	91.2	33.1	8.8

Note: Sn=sensitivity, Sp=specificity, PPV=positive predictive value, NPV=negative predictive value, PR=pregnancy rate.

Analysis of the predictive power of the parameters with the 10th percentiles used as cutoffs revealed that the use of the number of dominant follicles on the day of hCG as the definition of the poor responder gave the highest PPV, and therefore, the lowest pregnancy rate, among the parameters which were obtained before the retrieval. The group of poor responders, as determined by the number of dominant follicles ≤4, had good correlations ($r > 0.5$) with those as determined by using the 10th percentiles of either the number of oocytes or MII oocytes. Therefore, the number of dominant follicles can be used as a definition for the poor responder instead of number of oocytes or MII oocytes retrieved. This removes the necessity of performing an invasive procedure, i.e. OPU, for the diagnosis of the poor responder.

The second best parameter was the number of mature follicles on the day of hCG with a PPV of 93.8%. However, the correlation between the number of dominant and mature follicles was weak ($r = 0.4$, Table 4). Therefore, it may not be appropriate to use these two different criteria interchangably for the definition of the poor responder.

After we observed that there were weak correlations between the pre-OPU parameters, we analyzed the predictive power of binary combinations of the parameters. Defining poor responders as subjects with either fewer dominant follicles (≤4) or fewer mature follicles (≤1) slightly improved the predictive values as compared to defining as those with fewer dominant follicles (≤5) alone (Table 5). During this comparison, 5 was chosen as the cutoff value for the latter group to make the percentiles comparable. Both definitions indicated an incidence of 16-18% for the poor responders. Otherwise, comparing definitions indicating different number of percentiles would be misleading. However, this indicated an incidence of 22% in started cycles including OPU cancellations (n=10).

In the present study, accepting pregnancy as the sign of a good ovarian response may have some limitations. Failure of pregnancy may have reasons other than a poor ovarian response. We aimed to exclude subjects with a sperm factor as the reason for failed pregnancy by including only ICSI cycles and excluding cycles with insufficient number of motile spermatozoa available for all of the retrieved mature oocytes. It should be mentioned that the only work-up for endometrial pathologies was office hysteroscopy or HSG, either of which was routinely performed to all subjects. In an attempt to exclude subjects with possible endometrial molecular pathologies, we did not exclude subjects with endometriosis, since endometriosis may also affect the ovarian response.[5,6]

The difference in the post-OPU parameters also may be other possible reasons for the failure

of pregnancy. To analyze that possibility, we determined the dependency between these parameters and the number of dominant follicles. The numbers of oocytes, MII oocytes and embryos each divided by the number of dominant follicles were comparable between groups ($P > 0.05$, Table 2). Therefore, the difference in the post-OPU parameters between groups may be due to the difference in the number of dominant follicles on the day of hCG, i.e. less embryos could be transferred to subjects in the nonpregnant group due to the less number of developed follicles, less number of retrieved oocytes, less number of MII oocytes, and finally, to the less number of transferable embryos.

To our knowledge, percentiles for ovarian reserve and response parameters in IVF have been analysed only for the serum E_2 level.[7] In that study, serum E_2 thresholds for the 10th percentile on the day of hCG were between 850 and 1000 pg/ml in different age groups.[7] These values seem higher than the threshold in the present study. This difference is probably due to the differences between the two studies. In that study, Papageorgiou et al. have analysed short protocols, and also, used a different assay kit.[7]

In conclusion, the best predictor of pregnancy among the ovarian response parameters before the retrieval is the number of dominant follicles on the day of hCG. The cutoff corresponding to the 10^{th} percentile of this parameter was 4. Poor ovarian response in IVF may be defined as those with ≤4 dominant follicles on the day of hCG following a long protocol (luteal down-regulation regimen). This definition has a good correlation with the post-OPU parameters, and therefore, can be used as a reliable indicator of the poor ovarian response instead of the number of oocytes or MII oocytes. This definition also estimates an incidence of 18% for the poor responders, and a pregnancy rate of 3.3 per started cycle in these subjects. However, the number of cycles is limited for a "percentile" approach in the present study, and larger analyses by using the percentiles may help to suggest a consensus for the definition of poor ovarian response.

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