Effect of embryo quality on pregnancy outcome following single embryo transfer in women with a diminished egg reserve

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Objective: To evaluate independently the effect of blastomere number and degree of fragmentation on pregnancy outcome following single ETs in women with a decreased egg reserve.

Design: Retrospective cohort analysis.

Setting: In vitro fertilization center of a university-based practice.

Patient(s): Women having a single ET related to a decreased egg reserve. A requirement for inclusion was a day 3 serum FSH >12 mIU/ml and ≤3 antral follicles on ultrasound.

Intervention(s): Patients received no or minimal stimulation with gonadotropins.

Main Outcome Measure(s): Pregnancy rates (PRs) following single ETs were evaluated according to blastomere number (group 1, ≤4 cells; group 2, 5 cells; group 3, 6 cells; group 4, 7 cells; and group 5, ≥8 cells) and fragmentation index (A, no fragmentation; B, 1–25% fragmentation; and C, >25% fragmentation). Embryo transfers and morphologic evaluation were performed on day 3.

Result(s): The clinical and delivered PRs according to blastomere number showed that 6–8-cell embryos were six times more likely to implant than 4–5-cell embryos (6.6% versus 40.4% clinical). Degree of fragmentation did not predict outcome nearly as well as blastomere number. The overall clinical and delivered PRs per transfer were 27.8% and 24.1%, respectively, and were 14.8% and 12.8% per retrieval, respectively, and were 9.0% and 7.3% per initiated cycle, respectively.

Conclusion(s): Six-, seven-, or eight-cell embryos have equal chances of implanting in women with day 3 elevated serum FSH. The key finding is that these embryos do better than those with ≤6 blastomeres. These data may be helpful in women with a diminished ovarian reserve in attempting IVF with their own eggs or when choosing donor oocytes. (Fertil Steril® 2007;87:749–56. ©2007 by American Society for Reproductive Medicine.)

Key Words: Blastomeres, fragmentation index, single embryo transfer

As a result of the high hospital costs involved with multiple gestations and the effects on the delivered infants, especially from prematurity, there have been recent debates about transferring only a single embryo (1–7). Even a twin gestation involves a perinatal outcome with a 15-fold increased risk of complications, compared to a singleton (8, 9).

Most IVF centers transferring one embryo still employ controlled ovarian hyperstimulation (COH) to provide multiple embryos from which to choose one with the best quality (7). Many IVF centers have the opportunity to allow all fertilized pronuclear embryos to cleave. The next objective is to select the best embryo in the group for transfer on day 2, 3, or 5 (blastocyst stage). However, some countries (e.g., Germany) are limited to allowing a maximum of three embryos to cleave (10, 11). Thus, pressure has been placed on these centers to find a means of selecting the best three pronuclear embryos for continued growth.

There are data suggesting that pronuclear morphology can help identify embryos with the highest implantation potential (12–14). Others suggested that isolating the fastest cleaving embryos would provide those with the best implantation potential (15–18). However, not all studies agree (19, 20). Previous studies found improved outcome when at least one embryo in a multiple embryo transfer had 6–8 blastomeres; our own studies found higher pregnancy rates (PRs) with increasing numbers of blastomeres of day 3 embryos (21, 22).

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However, the degree of fragmentation did not seem to predict PRs very well (21). Some data suggest that combining pronuclear morphology, cleavage speed, and morphology on day 3 (known as the graduated embryo score) may be the best way to select a single embryo (23, 24). Others think that transferring a single blastocyst is the best way to ensure optimal selection (25).

The best way to assess the importance of blastomere number and degree of fragmentation would be to evaluate these parameters in PRs following single ETs. Unfortunately, though we have a sizable population having single ETs, the women in our IVF program having single ETs are almost exclusively women with a markedly decreased egg reserve, as evidenced by elevated day 3 serum FSH levels. The theoretical problem with the evaluation of this group with a decreased egg reserve is that according to some studies, the PR per transfer would be expected to be extremely low (26–28). However, our own experience using minimal or no gonadotropins in this population has not been nearly so unpromising (29).

Though the primary objective of this study was to evaluate the relative effect of blastomere number and fragmentation index on pregnancy outcomes, the use of this population of women with a markedly decreased egg reserve provided an opportunity to evaluate PRs in a larger group of women with elevated day 3 serum FSH with such low egg reserves that only a single ET was possible.

MATERIALS AND METHODS

A retrospective review was performed of all single fresh ETs from January 1, 1997 to November 30, 2005 in women aged ≤39 years, with elevated day 3 serum FSH (>12 mIU/mL) and an antral follicle count of ≤3 on day 2 or 3 of the menstrual cycle. Patients had, at most, one embryo transferred, and ≤3 mature oocytes retrieved.

Couples were evaluated by semen analysis and hysterosalpingogram (HSG). If detected, hydrosalpinges were surgically removed. The semen analysis included sperm concentration, percent motility subdivided in terms of percent forward linear motion versus fair motion, and versus poor motion, the presence or absence of antisperm antibodies determined by the direct immunobead assay, sperm morphology using strict criteria, and the hypoosmotic swelling test.

Women with regular or slightly irregular menses were evaluated by serial ultrasounds and serum E_2, LH, and P levels. If a mature follicle was found (average diameter of follicle, ≥18 mm; serum E_2, ≥200 pg/mL), a postcoital test was performed at least 8 hours after intercourse. Two days after developing a mature follicle, a repeat ultrasound was performed to see if the egg released from the follicle, as evidenced by a shrinkage of at least 5 mm and by frequent association with fluid in the cul de sac. Some women had a laparoscopy in addition to or instead of an HSG, and if endometriosis was present, it was treated by laser ablation. Adhesions were lysed, if possible.

Those women with severe tubal disease were treated with IVF-ET immediately, as were those whose male partner had severe oligoasthenozoospermia. Generally mild oligoasthenozoospermia or low morphology (<4% using strict morphology criteria) was treated first by intrauterine insemination. All women with a decreased egg reserve were treated with supplemental P in the luteal phase. Dosages were adjusted to attain a homogeneous hyperechogenic pattern in midluteal phase and an endometrial biopsy 12 days after ovulation and ≤2 days out of phase.

Failure to conceive after several cycles without IVF-ET led to the couples choosing IVF-ET. Some couples immediately chose IVF-ET because of the decreased egg reserve, even though it was not clear that conception could not take place through natural means or at least with just IUI.

Menstrual cycles varied from short intervals of 21 days, to regular menses of 28–30 days, to oligomenorrhea, to amenorrhea with normal estrogen (E) as evidenced by withdrawal menses because of P withdrawal, to amenorrhea with E deficiency. Some women with E deficiency failed to respond with a rise in E_2 despite high-dose gonadotropin therapy, yet they developed a mature follicle(s) and were able to undergo oocyte retrieval by lowering the elevated serum FSH with ethinyl E_2 (theoretically by possibly restoring down-regulated FSH receptors in granulosa and theca cells) (30, 31). The technique of using ethinyl E_2 either alone, or with a small boost of gonadotropins once a dominant follicle has been recruited, was previously described (32–34).

If a woman was being observed in a natural cycle but did not attain a minimum average 17-mm diameter follicle with a serum E_2 ≥200 pg/mL, oocyte retrieval was not attempted, but in the next cycle, 75 IU of exogenous FSH would be started once the follicle was about 10 mm in diameter with a serum E_2 of ≥80 pg/mL, or else would be started on day 5 if the FSH was not increased. Sometimes high FSH would be reduced by treating the women with 20 μg of ethinyl E_2 (which is not recorded in the serum E_2 assay), and gonadotropins would be started once the serum FSH approached normal, i.e., ≤10 mIU/mL. A woman showing three antral follicles on day 3 might be started with 75 IU gonadotropin by days 5–7 if the E_2 was spontaneously rising and the FSH dropped to ≤10 mIU/mL.

The majority of cycles did not use a GnRH antagonist, but if the LH doubled from baseline, either cetrorelix or ganirelix was added SC at 250 μg/day. If a GnRH antagonist was used, 75 IU of gonadotropin (all brands) were added if it was a natural cycle, or an extra 75 IU were added if the woman was already taking gonadotropins.

If the baseline serum FSH was increased and remained increased despite the serum E_2 rising as the follicle matured, frequently the retrieval would be performed completely naturally without gonadotropins. When evaluating a natural

cycle, if the follicle never reached maturity, the retrieval would be cancelled, but for the next cycle, a minimal boost of gonadotropin would be given. If a woman was started on ethinyl E_2 to lower FSH, and the FSH dropped to ≤6 mIU/mL, 75 IU gonadotropin would usually be started.

The fertilization method included conventional insemination and intracytoplasmic sperm injection (ICSI). Oocytes were inseminated in fertilization medium (Sage Bio9Pharma, Pasadena, CA). Embryos were cultured in cleavage medium (Sage BioPharma). Insemination and culture took place in organ-culture dishes (Falcon 3037; Thomas Scientific, Swedesboro, NJ) containing 1 mL of medium in the center, and 3 mL in the moat, at 37°C, in an atmosphere of 5% CO_2 and 95% air, with high humidity.

Embryo morphology was measured in terms of blastomere number and fragmentation level. Blastomere number was evaluated in terms of five groups: 1, ≤4 blastomeres; 2, 5 blastomeres; 3, 6 blastomeres; 4, 7 blastomeres; and 5, ≥8 blastomeres. These groups were selected because of our experience with blastomere number with transfer of multiple embryos (21, 22).

Fragmentation was evaluated according to three groups: A, no fragmentation; B, 1%–25% fragmentation; and C, >25% fragmentation. These groups were chosen based on the routine use of this grading system in our clinic for over 10 years (21).

Human chorionic gonadotropin (10,000 units) was given once a follicle reached a ≥17-mm average diameter with a serum E_2 ≥180 pg/mL. The eggs were removed generally 33–34 hours after hCG injection, but sometimes as early as 30 hours if LH was spontaneously rising prior to the hCG injection.

The embryos were 3 days old when transferred. Assisted embryo-hatching was usually performed before the embryos were transferred. All embryos with ≥4 blastomeres were transferred, regardless of degree of fragmentation. The exception was for multinucleated embryos.

Clinical (i.e., ultrasound evidence of pregnancy at 8 weeks) and delivered PRs were determined according to the five blastomere groups and the three fragmentation groups. Clinical and delivered PRs per retrieval and transfer were also provided for the type of protocol, irrespective of blastomere number. The three treatment protocols were [1] natural, where no FSH was given at all; [2] natural with a boost of FSH, where 75 IU were added once the follicle approached maturity and the FSH was <10 mIU/mL; and [3] minimal stimulation, where FSH was given at 75 IU per day when follicles were still at the antral stage. In addition, the clinical and delivered PRs per initiated cycle, despite the use of ethinyl E_2 and/or minimal gonadotropins, were also analyzed. Thus this latter category included women who did not attain a mature follicle, and so oocyte retrieval was not performed. The mean blastomere number and degree of fragmentation were also analyzed according to these three treatment options, i.e., [1] completely natural, [2] natural with a boost of gonadotropin when close to follicular maturation, or [3] low-dose gonadotropins from the antral stage. Ethinyl E_2 to lower serum FSH or increase the length of the follicular phase could be used in all three treatment regimens. Chi-square analysis and Fisher's exact test were used. There was an insufficient number of cycles to evaluate combinations of blastomere number and fragmentation index. This study received institutional review board approval from Cooper Hospital/University Medical Center.

RESULTS

One hundred and twenty-nine IVF-ET cycles were evaluated. Of these, 21 had been reported in a previous study, but they had not been previously evaluated for the efficacy of embryo morphology (29). There were 51 cycles in women with primary infertility (40.3%), and 77 (59.7%) with secondary infertility. The duration of infertility varied from as short as 3 months (in a woman aged 38 who had amenorrhea for 2 years who discovered a high day 3 FSH upon initial workup) to 19.6 years. The median number of years of infertility was 5.

Ninety women contributed to the 129 IVF cycles. Forty-seven women were refused IVF with their own eggs at other IVF centers and were advised to consider donor oocytes, 23 were given COH at other IVF centers but the retrievals were cancelled because of inadequate response, 9 women went to oocyte retrieval (5 of them had ETs without pregnancy, and 4 retrievals resulted in no embryos), and 11 came to the Cooper Center for IVF first, and were advised to try the minimal stimulation protocol.

Thirty-four (37.8%) of the women had primary infertility, and 56 (62.2) had secondary infertility. There were 28 (31.1%) with tubal factor infertility, and 31 (34.4%) with male factor infertility. Eighteen (20%) proceeded to IVF because they failed many treatment cycles with follicle-maturing drugs, IUI, or P support in the luteal phase. Thirteen (14.4%) learned in their initial workup that they probably had a decreased egg reserve based on elevated day 3 serum FSH, and wanted to proceed to IVF-ET immediately (two requested this procedure at other IVF centers and were turned down).

Sixty-seven (74.4%) were still having menstrual cycles, and 38 of these (42.2%) were approximately once a month. Amenorrhea was present in 23 (25.6%), and 16 (17.7%) failed to have menses following P withdrawal.

If one evaluates all women during the same time period receiving minimal or no gonadotropin stimulation for high day 3 serum FSH with low antral follicle counts, there were 396 initiated cycles. One hundred and fifty-four IVF cycles did not lead to oocyte retrieval, because the follicle did not attain maturity, or the egg released before the retrieval. Thus there were 242 oocyte retrievals.

TABLE 1

Pregnancy rates per cycle, retrieval, and transfer, and embryo morphology according to type of stimulation protocol.

	Natural	Natural with boost of FSH	Minimal FSH stimulation
No. of cycles initiated	92.0	116.0	188.0
No. of retrievals	60.0	80.0	102.0
No. of transfers	19.0	59.0	51.0
No. of clinical	4.0	17.0	15.0
Percent clinical per initiated cycle	4.3	14.7	8.0
Percent clinical per retrieval	6.7	21.3	14.7
Percent clinical per transfer	21.1	28.8	29.4
No. ectopic	1.0	2.0	0.0
No. delivered	3.0	14.0	12.0
Percent delivered per initiated cycle	3.3	12.1	6.4
Percent delivered per retrieval	5.0	17.5	11.8
Percent delivered per transfer	15.8	23.7	23.5
Embryo morphology blastomere number (mean ± SD)	5.6 ± 1.3	6.2 ± 1.4	6.2 ± 1.5
No. with 6–8 cells (%)	11 (57.8%)	37 (62.7%)	32 (62.7%)
Fragmentation			
≤25%	31.6%	17.5%	28.6%
25%–50%	63.2%	78.7%	67.3%
>50%	4.1%	8.8%	4.1%

Check. Embryo morphology and single ET. Fertil Steril 2007.

Failure to retrieve an egg occurred in 33 cycles, failed fertilization occurred in 72 cycles, and failure to cleave to day 3 occurred in 8 cycles, resulting in 129 single ETs. There were no fresh transfers deferred, because the embryos were cryopreserved.

Overall, clinical pregnancies occurred in 36 ETs (27.8%/transfer), and delivered pregnancies (viable past 12 weeks) occurred in 31 (24.1%/transfer). The clinical and delivered PRs per retrieval were 14.8% and 12.8%, respectively, and were 9.0% and 7.3% per initiated cycle (Table 1). There were 19 cycles using a completely natural protocol, 59 cycles using a natural cycle with a minimal boost once the follicle approached maturity, and 51 cycles where low-dose stimulation (75 IU) was used earlier in the follicular phase. Clinical pregnancies occurred in 4 (21.0%), 17 (28.8%), and 15 (29.4%) of these cycles, respectively (Table 1). Delivered pregnancies occurred in 3 (15.8%), 14 (23.7%), and 14 (27.4%) of these cycles, respectively (Table 1).

Embryo morphology according to type of stimulation is shown in Table 2. Overall, the PR per retrieval was 14.8% (30/342), and the delivered PR per retrieval was 12.8% (31/242).

Fertilization rates and PRs in these 129 cycles according to blastomere number are shown in Table 2. There were 3 clinical and 3 delivered pregnancies in 47 ETs using 4-cell or 5-cell embryos (6.2% PR/transfer), versus 33 clinical pregnancies and 28 ongoing pregnancies in 82 ETs (40.4% and 34.1%, respectively) following transfer of 6–8-cell embryos, as shown in Table 2 ($P<.01$, Fisher's exact test). A study with 40 transfer cycles in one group and 80 in the second group would have 83% power to detect an absolute difference of ≥25% between the PRs in the two groups.

Fertilization rates and PRs according to fragmentation index are shown in Table 3. There were no significant differences when comparing the three groups. However, only a very small percentage of these embryos showed >25% fragmentation (8/129, 6.2%).

The mean ages (in years) of the five blastomere groups from lowest to highest number of cells, and the three fragmentation groups from least to most fragmentation, did not differ among the groups (five blastomere groups, from lowest to highest number of cells: 36.1 ± 3.29 (SD) years, 35.5 ± 4.09 years, 35.6 ± 3.35 years, 35.3 ± 3.23 years, and 36.7 ± 1.57 years; three fragmentation groups, from least to most fragmentation: 36.6 ± 2.98 years, 35.7 ± 3.06 years, and 35.1 ± 3.90 years). For age, the 95% confidence interval is 35.1–36.4. The mean (SE of the mean) was 35.7 (0.3). The mean day 3 serum FSH levels (in mIU/mL, with 95% confidence intervals) for the five blastomere groups were 19.7 ± 8.11 (16.4–23), 26.4 ± 16.4 (14.4–38.4), 25.3 ± 16.8 (19.2–31.4), 23.3 ± 9.7 (18.7–27.8), and 18.0 ± 6.9 (15.6–20.5), and for the three fragmentation groups were 22.9 ± 11.05 (18.9–27.0) for the no-fragmentation group, 22.2 ± 16.25 (18.8–25.6) for 1%–25%, and 19.1 ± 6.33 (13.8–24.4) for the

TABLE 2

Fertilization rates and PRs according to blastomere number in single ETs in women aged ≤39 years with a decreased ovarian egg reserve.

	4-cell only	5-cell	6-cell	7-cell	8-cell only
No. of cycles	102.0	87.0	78.0	70.0	59.0
No. of retrievals	64.0	58.0	49.0	35.0	36.0
No. of transfers	26.0	21.0	29.0	20.0	33.0
No. of follicles	49.0	38.0	52.0	39.0	46.0
No. of eggs retrieved	33.0	29.0	37.0	31.0	38.0
No. of mature retrieved	30.0	23.0	33.0	27.0	36.0
No. of insemination	32.0	26.0	33.0	29.0	37.0
No. fertilized	28.0	23.0	29.0	21.0	33.0
Percent fertilized	87.5	88.5	87.9	72.4	89.2
No. clinical	1.0	2.0	11.0	8.0	14.0
Percent clinical per cycle	1.0	2.3	14.1	11.4	23.7
Percent clinical per retrieval	1.6	3.4	22.4	22.9	38.9
Percent clinical per transfer	3.8	9.5	37.9	40.0	42.4
No. delivered	1.0	2.0	9.0	5.0	12.0
Percent delivered per cycle	1.0	2.3	11.5	7.1	20.3
Percent delivered per retrieval	1.6	3.4	18.4	14.3	33.3
Percent delivered per transfer	3.8	9.5	31.0	25.0	36.4

Check. Embryo morphology and single ET. Fertil Steril 2007.

>25% group. For day 3 serum FSH, the 95% confidence interval was 19.3–25.0. The mean serum (SE of the mean) for FSH was 22.2 ± 1.5 mIU/mL.

The mean serum E_2 levels (pg/mL) on day of hCG injection (with confidence intervals) for the five blastomere groups were 265.7 ± 15.5 (233.6–297.8), 319.3 ± 28.0 (259.0–377.7), 406.1 ± 48.6 (305.1–507.1), 394.8 ± 44.2 (302.3–388.6), and 335.9 ± 35.2 (263.8–408.1); and for the three fragmentation groups, 356.6 ± 33.1 (288.7–424.5), 345.9 ± 21.4 (303.3–388.6), and 270.9 ± 30.4 (199.1–342.6). The mean (SE of the mean) for peak serum E_2 was 343 ± 16.8 (309.8–376.6) pg/mL.

Ethinyl E_2 was used in 4 of the 19 transfers using the natural protocol, 29 of the 59 transfers using an FSH boost, and 20 of the 51 transfers using the minimal stimulation protocol. Clinical pregnancies in those using ethinyl E_2 were achieved in 1 of 4 (25%) using the natural protocol, in 9 of 29 (31%) using a boost of FSH, and in 6 of 29 (30%) using minimal stimulation with FSH, versus 3 of 15 (20%), 8 of 30 (26.6%), and 9 of 31 (29.0%) not using ethinyl E_2. The comparative delivered PRs were 1 of 4 (25%), 7 of 29 (24.1%), and 5 of 20 (25%) with ethinyl E_2, versus 2 of 15 (13.3%), 7 of 30 (23.3%), and 7 of 31 (22.5%) without ethinyl E_2 in the three groups.

DISCUSSION

This retrospective study of single ETs in infertile women with a decreased egg reserve showed significantly higher clinical and viable PRs with the transfer of a single embryo with 6–8 blastomeres, versus a single embryo with only 4 or 5 blastomeres. According to the data presented here, different degrees of fragmentation had no significant impact on PR.

Despite the description of other selection methods, e.g., pronuclear morphology and embryo cleavage rates, the most common method currently used by most IVF centers performing elective single ET is day 3 blastomere number and fragmentation index. However, the value of assessing day 3 blastomere number and fragmentation was recently questioned in studies evaluating stimulated cycles (35, 36).

Various methods are used to determine embryo morphology. We designed the particular system used in this study, and in 1995 presented data showing that blastomere number could predict IVF outcome to a certain degree, following the transfer of multiple embryos (21). We confirmed our findings in a study 6 years later (22). However, only with single ET could one determine how much better embryos are with increasing cell number, and determine if there is a point where the implantation potential is the same. Indeed, the present study found a big difference between 4–5-cell embryos versus 6–8 cell embryos, but there is no difference within the 6–8-cell mark. Fortunately, the majority of embryos had at least 6 blastomeres (82/129, 63.5%) which had a good prognosis. The study also suggests that fragmentation may not be that predictive of pregnancy and implantation rates. However, only 25 of 396 embryos transferred (6.3%) had >25% fragmentation. This seems to be lower than in

TABLE 3

Fertilization rates and PRs according to fragmentation following single ETs in women aged ≤39 years with a decreased ovarian egg reserve.

	A	B	C
No. of cycles	134.0	237.0	25.0
No. of retrievals	88.0	138.0	16.0
No. of transfers	81.0	90.0	8.0
No. of follicles	49.0	163.0	12.0
No. of eggs retrieved	38.0	121.0	9.0
No. of mature retrieved	37.0	105.0	7.0
No. of insemination	37.0	112.0	8.0
No. fertilized	33.0	93.0	8.0
Percent fertilized	89.2	83.0	100.0
No. clinical	11.0	23.0	2.0
Percent clinical per cycle	8.2	9.7	8.0
Percent clinical per retrieval	12.5	16.7	12.5
Percent clinical per transfer	35.5	25.6	25.0
No. delivered	8.0	19.0	2.0
Percent delivered per cycle	6.0	8.0	8.0
Percent delivered per retrieval	9.1	13.8	12.5
Percent delivered per transfer	25.8	21.1	25.0

Check. Embryo morphology and single ET. Fertil Steril 2007.

other studies of a decreased egg reserve (37). Possibly COH is more likely to produce fragmented embryos in women with a limited egg reserve.

It is interesting that the present study of single ETs in women with a decreased egg reserve reached the same conclusions that we reached with multiple ETs in women with an adequate egg reserve, i.e., that blastomere number predicts embryo implantation, whereas degree of fragmentation is less useful (21, 22). By using this grading system, we are not necessarily implying that it is the best one. The present study thus shows that blastomere number can predict pregnancy outcome following single ET in a group with decreased egg reserves. In addition, one could possibly enhance the choice of the best embryo by other methods, e.g., the graduated embryo score (23, 24). It would be interesting to determine if these parameters have the same influence in women with a normal egg reserve having single ET.

We believe these data are unique, because the majority of IVF centers use COH even when performing a single ET. Embryos with fewer blastomeres, or highly fragmented embryos, are generally not transferred in single ETs, and in fact are frequently discarded. However, women with a markedly decreased oocyte reserve, with only one embryo formed, have nothing to lose by transferring a lower-quality embryo.

The possibility exists that the data could have a different outcome if the study of blastomere number and fragmentation from single ETs came from a population with a normal oocyte reserve, if the women were given either minimal stimulation or were retrieved under natural conditions. Perhaps some IVF centers do single ETs using minimal or no gonadotropins in women with a normal oocyte reserve. These data may encourage them to evaluate their data in a similar manner, to either corroborate or refute our results.

Other IVF centers may use traditional COH regimens, but are limited by national law to transfer only one embryo. It would be interesting to see if the same prognosis would be seen with 6–8 blastomeres versus 4–5 blastomeres (as in the present study) in women undergoing traditional COH, or would the COH change the prognosticative potential of blastomere number?

The second objective of this study was to determine the likelihood of successful pregnancy in women aged ≤39 years following IVF-ET with a markedly decreased ovarian egg reserve. It should be noted that no one in this study wanted only one embryo transferred. We have treated women with high day 3 serum FSH levels and decreased antral follicle counts who have produced >1 embryo, and in these instances, usually all embryos (at least up to 3) would be transferred. These women were not included in this study. In total, only 168 eggs were retrieved in these 129 cycles, and of these, only 149 metaphase II eggs led to 129 day 3 embryos available for transfer.

Overall, there were 31 delivered pregnancies in 129 transfers. Thus the delivered PR/transfer, despite transferring only one embryo, was 24%. Our delivered PR per ET, including multiple embryos transferred in women aged 45–49 years during this same time period, was only 0.7% (1 of 130). This suggests that despite a marked decrease in egg reserve similar to women possibly closer to age 50 years in the younger group with a markedly decreased egg reserve that were the subjects in this present study, there is a qualitative difference in these fewer remaining oocytes in younger versus older women. There are studies showing that advanced age is a better predictor of a lower chance of pregnancy in women not undergoing IVF-ET and in women having IVF-ET (29, 38).

The process of IVF-ET has had a tremendous impact in terms of allowing couples to have babies, for whom this would have been impossible in the pre-IVF era. However, the downside of the procedure is the risk of multiple births and the tremendous increase in health costs that results from multiple births and complications to the babies because of prematurity. Thus there has been a new push toward limiting the number of embryos transferred (39–43). Hopefully, these data showing a reasonably good PR per ET in a group with diminished egg reserves will encourage other centers, including our own, to be more willing to try single ET in women with a normal egg reserve. Furthermore, these data

will hopefully encourage the use of much less ovarian hyperstimulation, to reduce the risk of ovarian hyperstimulation syndrome and to reduce the cost of IVF-ET.

Finally, it is hoped that these data will encourage other IVF centers to allow couples with elevated day 3 serum FSH levels the opportunity to try IVF-ET with their own gametes if that is the couple's wish, even if success with donor oocytes is potentially greater.

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