Effect of air bubbles localization and migration after embryo transfer on assisted reproductive technology outcome

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Objective: To evaluate the effect of embryo flash position and movement of the air bubbles at 1 and 60 minutes after ET on clinical pregnancy rates (PRs).
Design: Prospective clinical trial.
Setting: University fertility clinic.
Patient(s): A total of 230 fresh ultrasound-guided ETs performed by a single physician (C.F.) at the IVF center of Yeditepe University Hospital between September 2016 and February 2017 were included.
Intervention(s): Transabdominal ultrasonographic guidance at ET.
Main Outcome Measure(s): Clinical PRs.
Result(s): There was no significant difference in terms of clinical PRs between women with embryo flash located >15 mm and <15 mm from the fundus at 1 or 60 minutes ($P=.6$ and $P=.7$, respectively). The PRs in women with embryo flash located <15 mm and >15 mm from the fundus were 47% and 60%, respectively ($P=.6$). The clinical intrauterine PRs were 69.5%, 38.5%, and 19.1% in fundal, static, and cervical, respectively. The highest PR was in fundal when compared with others ($P<.01$). The clinical PR appears to be associated with the embryo flash movement/migration and the PR was dramatically reduced when the embryo migrated from its original position toward the cervix at 60 minutes.
Conclusion(s): We concluded that clinical PR appears to be associated with the embryo flash movement/migration at 60 minutes after ET and embryo flash movement toward the fundus is associated with higher clinical PRs. Further well-designed randomized controlled trials are required to optimize ET technique in the future. (Fertil Steril® 2018;109:310–4. ©2017 by American Society for Reproductive Medicine.)
Key Words: Embryo transfer, in vitro fertilization, air bubble, embryo flash position, assisted reproductive technology

There are many factors including female age, ovarian reserve, ET technique, embryo quality, and endometrial receptivity to influence the success of assisted reproductive technology (ART) and predictors of pregnancy outcome (1). The ET is the final and crucial step of ART. Despite high rate of success of ART with great advances in several factors, there is no consensus on the optimal ET technique. Therefore, studies recently focused on the importance of ET to achieve higher pregnancy rates (PRs).

After the introduction of ultrasound guidance for ET, publications recently moved on to assess the effect of various parameters related to ET on PR that are able to determine ART success and failure. Studies evaluated these technical parameters, such as transfer catheter type, catheter-loading technique, catheter placement, blood or mucus effects injection speed, catheter withdrawal, and ultrasonographic parameters, such as ET depth, fundal level of the uterine cavity, the

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optimal location for embryo deposition within the uterus, exact position of the catheter tip, and air bubble (2–9).

Monitoring the final position of air bubble at ET could be associated with PR. In our previous study (7), we demonstrated that the optimal position of embryos, as shown by the location of air bubbles at ET, is a distance of <10 mm from the fundal endometrial surface and placing air bubbles closer to the fundus is associated with higher PRs. But the position of the air bubble in the uterine cavity may change after ET. Therefore, after the initial assessment of the air bubbles at ET, the embryo can migrate toward the fundus or toward the cervix, or it may remain static. We then hypothesized that the change of the embryo flash position at 60 minutes after ET may have either a positive or negative influence for PR. The purpose of our current study is to evaluate the effect of embryo flash position and movement of the air bubbles at 1 and 60 minutes after ET on clinical PRs.

MATERIALS AND METHODS

Participants

A total of 230 fresh ultrasound-guided ETs, performed by a single physician (C.F.), at the IVF center of Yeditepe University Hospital between September 2016 and February 2017 were included. The prospective study protocol was approved by the Ethical Committee of the Medical Faculty of Yeditepe University. Written informed consent was obtained from all patients. Inclusion criterias were patients programmed for IVF, body mass index (BMI) $\leq$25 kg/m^2, between 18 and 41 years old, and with FSH levels on cycle day 3 of $\leq$12 mIU/mL. Exclusion criterias were patients with congenital or acquired uterine anomalies, repeated implantation failure, with blood present on the catheter during the transfer procedure, with a difficult transfer or with a suspicion of touching the fundus, presence of hydrosalpinx, and cycle cancelation.

Data collected included age, duration of infertility, type of infertility, BMI, serum FSH, E_2, and antimüllerian hormone (AMH) levels on cycle day 3, maximum E_2 levels, total number of oocytes retrieved, number of mature oocytes retrieved, number of embryos transferred, endometrial thickness on day of ET (in millimeters), and clinical PR. All ETs were classified into three groups according to the embryo flash movement/migration. It was evaluated by measuring the change of the embryo flash position at 60 minutes after ET. If it had remained within $\pm$15 mm from its original position, it was classified as static; if it had migrated <15 mm toward the fundus or >15 mm toward the cervix, it was classified as fundal and cervical, respectively (Supplemental Fig. 1, available on-line). The evaluation and management of the patients and ET are performed by one operator (C.F.).

Assisted Reproduction Procedures

A controlled ovarian stimulation protocol was used: antagonist (Cetrotide; Serono) protocol and stimulation with recombinant FSH (Gonal F; Serono) as previously described (7). A single dose of recombinant hCG (Ovitrelle, 250 mg; Serono) was administered to trigger when at least two follicles reached a mean diameter of 17 mm. Transvaginal uktrasound-guided oocyte retrieval was carried out 36 hours after recombinant hCG administration under general anesthesia. Fertilization of the oocytes was performed 4–6 hours after retrieval by using standard intracytoplasmic sperm injection (ICSI) techniques. According to maternal age, indication for IVF, and number and quality of embryos available, one or two embryos were transferred on day 5. As luteal phase support, vaginal crinone gel (Crinone 8%, 90 mg; Merck Serono, Central Pharma Ltd.) daily was started on the day of retrieval. Serum quantitative beta-hCG levels were obtained at 12 days after ET. A clinical pregnancy was defined as the presence of a fetal sac visualized by transvaginal ultrasound examination at 6–8 weeks of amenorrhea.

Embryo Selection and ET

All ETs were performed by one experienced operator (C.F.) with the Wallace catheter (Smiths Medical International Ltd.) using after-load transfer technique under transabdominal ultrasound guidance without any anesthesia or sedation. The highest quality embryos according to morphology and cleavage criteria were selected for transfer. After the women, with moderately full bladder, were placed in a lithotomy position, the cervix was exposed with a bivalve speculum. The mucus in the cervical canal was cleaned by using a sterile cotton swab soaked in culture medium. Embryos were loaded into a Wallace catheter (Smiths Medical International Ltd.) by using a "three-drop technique." First, an air bubble was loaded into the catheter. Then, 20 μL of medium was drawn up into the catheter, followed by the embryos in the smallest possible volume of medium. A second air bubble was then loaded into the catheter. Finally, enough medium was drawn up to bring the total volume to 30 μL. The outer catheter was first inserted into the cervical canal. Once the guide was positioned before or after the internal os, the inner catheter was placed through the outer catheter. The tip of the inner catheter was placed 1.5–2 cm from the fundal endometrial surface. The medium containing the embryos was gently released into the uterine cavity. The catheter was slowly withdrawn and examined by the same embryologist under a stereomicroscope to be sure that there were no retained embryos. After the procedure, the patient was kept supine for approximately 60 minutes. Ultrasonography were carried out at 1 and 60 minutes after ET. The embryo flash position at 1 and 60 minutes after ET and the embryo flash movement/migration were recorded for future analysis. The embryo flash position at 1 and 60 minutes after ET was assessed by measuring the distance between the air bubble and the uterine fundus in the coronal image. The embryo flash movement/migration was assessed by measuring the change of the embryo flash position at 60 minutes after ET. If embryo had migrated >15 mm toward the fundus, it was classified as fundal, or >15 mm toward the cervix, it was classified as cervical, and if the embryo flash had remained within $\pm$15 mm from its original position, it was classified as static (Supplemental Fig. 1). When more than one air bubble was seen, the closest one to uterine fundus was used for the measurements. We measured the distance from the lead portion of the air bubble to the uterine fundus.

Statistical Analysis

Analyses were done using the Statistical Package for the Social Sciences, version 24 (SPSS). Data were reported as mean ± SD or number and percentage. The variables were investigated using Kolmogorov Smirnov test to determine whether or not they are normally distributed. When the variables were normally distributed, two independent *t*-tests were used to compare. When the variables were not normally distributed, the Mann-Whitney *U* test was used to compare the patient and the control groups. The χ^2 and Fisher's exact tests, where appropriate, were used to compare the proportions of the groups. The χ^2 test was used to compare categorical variables in the form of frequency tables. A forward conditional multivariable logistic regression model was used to calculate the odds ratios and 95% confidence intervals for the likelihood of a clinical pregnancy between groups and age, the total number of oocytes retrieved, and the embryo flash movement/migration toward the fundus. $P<.05$ was considered significant.

RESULTS

A total of 220 ultrasound-guided ETs after ICSI treatment were analyzed. There was an exclusion of 10 women (6 with blood present on the catheter during the transfer procedure, 2 with a difficult transfer or with a suspicion of touching the fundus, and 2 cycle cancelations because of no viable embryos). Of all transfers, 47.2% (104/220) resulted in a clinical pregnancy. Pregnant and nonpregnant groups were significantly different from each other with regard to patient age, AMH, total number of oocytes retrieved, and number of mature oocytes retrieved. In women who did not conceive, mean age was 35.68 ± 5.40 years, which was significantly higher ($P<.01$). The serum AMH level, the total number of oocytes retrieved, and the number of mature oocytes retrieved were significantly lower compared with women who conceived ($P<.01$, $P<.01$, and $P<.01$, respectively) (Table 1). The pregnant and nonpregnant groups were similar in terms of duration of infertility, type of infertility, BMI, serum FSH, E_2 and AMH levels on cycle day 3, maximum E_2 levels, number of embryos transferred, and endometrial thickness on day of ET (in millimeters) (Table 1).

There was no significant difference in terms of clinical PRs between women with embryo flash located <15 mm from the fundus and women with embryo flash located >15 mm from the fundus at 1 or 60 minutes ($P=.6$ and $P=.7$, respectively). They did not reach statistical significance. It may result from the small sample size of women with embryo flash located >15 mm from the fundus at 1 or 60 minutes. Women with embryo flash located >15 mm from the fundus at 60 minutes (n = 215) and women with embryo flash located <15 mm from the fundus (n = 5) were similar with regard to patient age, serum FSH, E_2, and AMH levels on cycle day 3, maximum E_2 levels, total number of oocytes retrieved, number of mature oocytes retrieved, duration of infertility, type of infertility, and number of embryos transferred. Of clinical intrauterine pregnancy (IUP), 97.1% was in women with embryo flash located <15 from the fundus at 60 minutes. The PRs in women with embryo flash located <15 mm and >15 mm from the fundus were 47% and 60%, respectively ($P=.6$) (Table 2). It may not reach statistical significance, which could result from the small sample size of women with embryo flash located >15 mm from the fundus. The clinical intrauterine PRs were 69.5%, 38.5%, and 19.1%

TABLE 1

Characteristics of patients in pregnant and nonpregnant groups.

Variable	Pregnant group (n = 104)	Nonpregnant group (n = 116)	*P* value[a]
Age (y)	32.27 ± 4.9	35.68 ± 5.4	<.01
Duration of infertility (y)	4.88 ± 3.7	5.61 ± 4.1	.17
Type of infertility			.99
Primary	82.8 (86/104)	82.7 (96/116)	
Secondary	17.25 (18/104)	17.3 (20/116)	
Basal FSH level (IU/L)	7.93 ± 4.9	8.62 ± 4.5	.46
Basal E_2 level (pg/mL)	33.78 ± 13.6	39.98 ± 18.37	.05
Serum AMH level	4.32 ± 0.4	2.31 ± 2.4	<.01
Maximum E_2 level on day of hCG administration (pg/mL)	2,053.70 ± 908.2	1,771.94 ± 1,108.0	.14
Total number of oocytes retrieved	8.41 ± 3.5	5.56 ± 3.1	<.01
No. of mature oocytes retrieved	6.38 ± 3.12	4.24 ± 2.6	<.01
Endometrial thickness on day of embryo transfer (mm)	8.78 ± 2.8	8.90 ± 2.5	.74
No. of embryos transferred			.92
1	55.77 (58/104)	55.17 (64/116)	
2	44.23 (46/104)	44.82 (52/116)	
Embryo flash migration versus 60 min from transfer			<.01
Fundal	62.5 (65/104)	25.8 (30/116)	
Static	28.8 (30/104)	41.3 (48/116)	
Cervical	8.65 (9/104)	32.7 (38/116)	

Note: Values are expressed as mean ± standard deviation for continuous variables and percent (number) for categorical variables. AMH = antimüllerian hormone; FSH = follicle stimulating hormone; hCG = human chorionic gonadotropin.

[a] $P<.05$, significant difference.

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TABLE 2

Clinical pregnancy rates according to the position of the embryo flash relative to the fundus at 1 and 60 minutes after embryo transfer.

Embryo flash	< 15 mm	> 15 mm
1 min	100/213 (46.9)[a]	4/7 (57.1)[a]
60 min	101/215 (47)[b]	3/5 (60)[b]

Note: Values expresed as n (percent).
[a] $P = .6$.
[b] $P = .7$.

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TABLE 4

Multivariable analysis for likelihood of clinical pregnancy rates.

Variable	OR	*P* value	95% CI
The embryo flash movement/migration toward the fundus	13.7	< .01[a]	3.79–49.5
Total number of oocytes retrieved	0.88	.03[a]	1.01–1.31
Age (y)	1.15	< .01[a]	0.81–0.96

Note: CI = confidence interval; OR = odds ratio.
[a] $P < .05$, significant difference.

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in fundal, static, and cervical locations, respectively (Table 3). The highest PR was in fundal location when compared with others ($P < .01$). The clinical PR appears to be associated with the embryo flash movement/migration and the PR was dramatically reduced when the embryo migrated from its original position toward the cervix at 60 minutes. There were no ectopic pregnancies (EPs) in any group.

Multivariable logistic regression analysis was performed for clinical pregnancy (yes vs. no) against all relevant parameters listed in Table 1. It revealed that age, total number of oocytes retrieved, and migration of the embryo flash were related to PR (Table 4). Embryo flash located <15 mm from the fundus ($P < .01$) and high total number of oocytes retrieved ($P = .03$) increased the PR and advanced age ($P < .01$) decreased the PRs.

DISCUSSION

After several studies (8, 10, 11) focused on the importance of effect of ET on PRs in ART, it was recently demonstrated that the final position of the air bubble was an identifier of the position of the embryo and could determine PRs in ART, therefore monitoring the final position of the air bubble at ET is recommended to identify PR. The results of our previous study (7) were concordant with the literature. Furthermore, according to our previous study results, clinical PRs were higher in women with air bubbles closer to the fundus and the optimal position of the air bubble is <10 mm from the fundal endometrial surface. However, clinical PRs can be influenced by the change of the embryo flash position after ET, although the embryo was placed in the optimal position within the uterine cavity where the probability of implantation is the highest. There is not enough data in the literature regarding the effect of changing the embryo flash position after ET on clinical PRs of ART.

The fundal endometrium could be more suitable for implantation as a result of the increased expression of some factors (11–13) such as a lower endometrial wavelike activity and an increased endometrial tissue blood flow. The embryo flash movement from the fundus toward the cervix after ET may cause a tendency to decrease the PRs despite a successful fundal transfer. In a retrospective analysis of 7,489 ultrasound-guided ETs, Tıras et al. (9) evaluated the effect of embryo flash migration just after transfer on ART outcome. They showed that there is a strong positive relationship between clinical PRs with air bubbles moving toward the uterine fundus and increased PRs, whereas air bubbles moving toward the cervical canal after ET significantly decreased the PRs. In a retrospective cohort evaluating effect of ET depth on IVF and ET outcomes, Pope et al. (14) demonstrated that the odds ratio for the transfer distance from the fundus, as measured by ultrasound was 1.11 in regression analysis (95% confidence interval 1.07–1.14) and for every additional millimeter that the embryos are deposited away from the fundus, the odds of a clinical pregnancy increased by 11%. A recent prospective chort study (15) including 277 fresh cycle IVF/ICSI treatments assessed embryo flash position and migration at 1, 5, and 60 minutes after ET with three-dimensional ultrasound. They found that the PR and implantation rate in cases with embryo flashes located <15 mm from the fundus at 60 minutes was significantly higher than those with embryo flashes located >15 mm from the fundus. The embryo flash movement from fundus toward the cervix was also related to significantly lower PR and implantation rate. Based on previous study results (7), it seems that at least a 10-mm difference in ET depth may influence PR. Therefore, we preferred to evaluate a 15-mm difference in ET depth.

Because of the limited data regarding the effect of embryo flash position/movement after ET on clinical PRs, we designed a prospective study assessing the relationship between embryo flash movement/migration at 1 and 60 minutes after ET and clinical PR. According to our results, the clinical PR appears to be associated with the embryo flash movement/migration. Our results demonstrated most

TABLE 3

Clinical pregnancy rates according to embryo flash movement within 60 minutes of embryo transfer.

Embryo flash movement	Pregnancy rate
Fundal migration group	65/95 (68.4)[a]
Statik group	30/78 (38.5)
Cervical migration group	9/47 (19.1)

Note: Values expresed as n (percent).
[a] $P < .01$ for fundal migration group in comparison with the static group and the cervical migration group.

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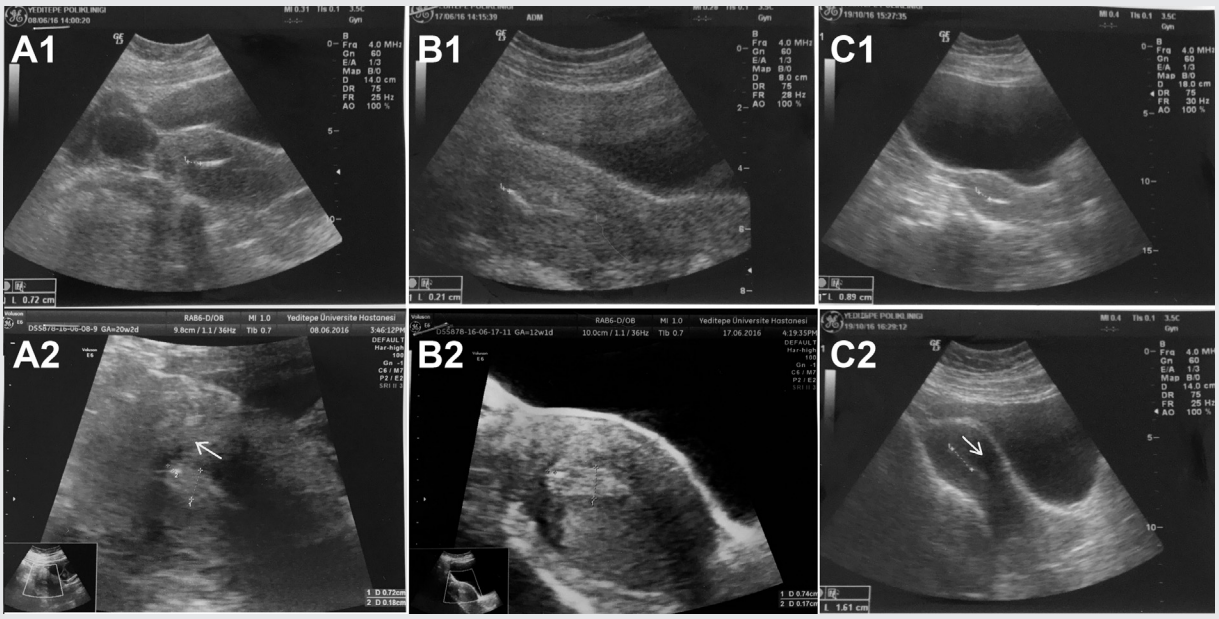
pregnancies occurred with the embryo flash located <15 mm from the fundus at 1 and 60 minutes. There is no statistical significance between embryo flash located <15 and >15 mm from the fundus in terms of clinical PRs. This may be the result of a small sample size of women with embryo flash located >15 mm from the fundus. Most air bubbles migrated toward the fundus after ET. Furthermore, PRs dramatically reduced when the embryo migrated from its original position toward the cervix at 60 minutes, whereas air bubbles moving toward the fundus were associated with higher clinical PRs. In our previous study, we also analyzed other variables that are able to influence the probability of pregnancy. We indicated that women who conceived were younger, with embryos migrating from the original position toward the fundus, and had more total number of oocytes retrieved. Based on the results of regression analysis, clinical PR could be predicted on the basis of a combination of total number of oocytes retrieved, the woman's age, and the embryo flash movement/migration from its original position toward the fundus at 60 minutes after ET. The strength of our study is that one experienced reproductive endocrinologist performed all the transfers. The limitation of our study is that only clinical PR was evaluated.

There are many independent technical and ultrasonographic parameters associated with ET success or failure such as trial transfer, ultrasound guidance, catheter-loading technique, transfer catheter type, catheter tip placement, blood or mucus effects, uterine cavity fluid, retained embryos, and physician's experience. Therefore, many trials are needed to evaluate the effects of these parameters on PRs. They must be designed to standardize these parameters, improve ET technique, and achieve maximum PRs by eliminating failure of ART resulting from ET technique. The one of main expectation for a successful ET is to facilitate deposition of the embryo in an optimal position within the uterine cavity where the probability of implantation is the highest. It is not always possible to standardize several variables for the ET technique such as ET depth or the position and migration of the air bubbles. The use of the syringe, the resistance of the plunger, the physician's experience, ease and nontraumatic transfer and patient-related determinants as a possible intrauterine resistance and uterine contractions may influence the final position and movement of the air bubbles. It would be better to know all relevant determinants with either positive or negative influence on ET success or failure and PRs. The misplacement or undesirable movement of air bubbles toward the cervical canal after ET may be associated with decreased PRs. This movement might be related to undesirable uterine contractions, a commonly accepted factor for ET failure. We concluded that clinical PR appears to be associated with the embryo flash movement/migration at 60 minutes after ET and embryo flash movement towards the fundus is associated with higher clinical PRs. Further well-designed randomized controlled trials are required to optimize ET technique in the future.

REFERENCES

1. Tıras B, Cenksoy PO. Practice of embryo transfer: recommendations during and after. Semin Reprod Med 2014;32:291–6.
2. Tıras B, Korucuoglu U, Polat M, Saltik A, Zeyneloglu HB, Yarali H. Effect of blood and mucus on the success rates of embryo transfers. Eur J Obstet Gynecol Reprod Biol 2012;165:239–42.
3. Singh N, Gupta P, Mittal S, Malhotra N. Correlation of technical difficulty during embryo transfer with rate of clinical pregnancy. J Hum Reprod Sci 2012;5:258–61.
4. Phillips JA, Martins WP, Nastri CO, Raine-Fenning NJ. Difficult embryo transfers or blood on catheter and assisted reproductive outcomes: a systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol 2013;168:121–8.
5. Moragianni VA, Cohen JD, Smith SE, Schinfeld JS, Somkuti SG, Lee A, et al. Effect of macroscopic or microscopic blood and mucus on the success rates of embryo transfers. Fertil Steril 2010;93:570–3.
6. Groeneveld E, de Leeuw B, Vergouw CG, Visser OW, Lambers MJ, Heymans MW, et al. Standardization of catheter load speed during embryo transfer: comparison of manual and pump-regulated embryo transfer. Reprod Biomed Online 2012;24:163–9.
7. Cenksoy PO, Fıcıcıoglu C, Yesiladali M, Akcin OA, Kaspar C. The importance of the length of uterine cavity, the position of the tip of the inner catheter and the distance between the fundal endometrial surface and the air bubbles as determinants of the pregnancy rate in IVF cycles. Eur J Obstet Gynecol Reprod Biol 2014;172:46–50.
8. Tıras B, Polat M, Korucuoglu U, Zeyneloglu HB, Yarali H. Impact of embryo replacement depth on in vitro fertilization and embryo transfer outcomes. Fertil Steril 2010;94:1341–5.
9. Tıras B, Korucuoglu U, Polat M, Saltik A, Zeyneloglu HB, Yarali H. Effect of air bubble localization after transfer on embryo transfer outcomes. Eur J Obstet Gynecol Reprod Biol 2012;164:52–4.
10. Friedman BL, Lathi RB, Henne MB, Fisher SL, Milki AA. The effect of air bubble position after blastocyst transfer on pregnancy rates in IVF cycles. Fertil Steril 2011;95:944–7.
11. Lambers MJ, Dogan E, Lens JW, Schats R, Hompes PG. The position of transferred air bubbles after embryo transfer is related to pregnancy rate. Fertil Steril 2007;88:68–73.
12. Van Gestel I, IJland MM, Hoogland HJ, Evers JL. Endometrial wave-like activity in the non-pregnant uterus. Hum Reprod Update 2003;9:131–8.
13. Jinno M, Ozaki T, Iwashita M, Nakamura Y, Kudo A, Hirano H. Measurement of endometrial tissue blood flow: a novel way to assess uterine receptivity for implantation. Fertil Steril 2001;76:1168–74.
14. Pope CS, Cook EK, Arny M, Novak A, Grow DR. Influence of embryo transfer depth on in vitro fertilization and embryo transfer outcomes. Fertil Steril 2004;81:51–8.
15. Saravelos SH, Wong AW, Chan CP, Kong GW, Cheung LP, Chung CH, et al. Assessment of the embryo flash position and migration with 3D ultrasound within 60 min of embryo transfer. Hum Reprod 2016;31:591–6.

SUPPLEMENTAL FIGURE 1



The embryo flash movement/migration. (**A**) Fundal, (**B**) static, (**C**) cervical.

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