Three-dimensional versus two-dimensional ultrasound-guided embryo transfer: a randomised control study (abridged secondary publication)

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KEY MESSAGES

1. There was no significant difference in the live birth rate after two- or three-dimensional ultrasound-guided embryo transfer.
2. Although three-dimensional ultrasonography is a newer tool for embryo transfer, it should not be recommended as a strategy to improve clinical outcomes.

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Introduction

The use of ultrasonography (US) in gynaecology enables diagnosing pathologies of the uterus, tubes, and ovaries. In reproductive medicine, it can be used to monitor endometrial thickness, follicular status and growth, and to guide retrieval of oocytes from the ovaries and transfer of fertilised embryos into the uterus.[1] These are critical procedures of artificial reproductive technology (ART). Three-dimensional (3D) US images can be acquired and analysed live or retrospectively. Its scanning procedure does not differ from the routine two-dimensional (2D) US, and acquisition of a 3D volume requires only a few seconds. As a result, 3D US is considered to be the most accurate non-invasive modality to diagnose uterine anomalies.[2,3] Furthermore, 3D US allows accurate volume calculations of structures such as the endometrium and follicles. Coupled with advanced software for automated measurements, 3D US may improve accuracy, reduce inter-observer variability, and increase efficiency of ART.[4] Therefore, we conducted a randomised controlled trial to compare 3D US with 2D US in guiding embryo transfer in terms of pregnancy outcomes.

Methods

This was a single-blind, single-centre prospective randomised controlled trial. The study was approved by the Institutional Review Board (reference number CREC 2014.650) and was registered online at Clinicaltrials.gov (registration number NCT02413697). All patients were fully counselled and completed a written informed consent prior to participation.

Consecutive women undergoing US-guided embryo transfer in our unit were included. Those aged 42 years or older or women whose endometrial cavity could not be visualised adequately were excluded.

On the morning of the embryo transfer procedure, women were randomised into the 3D or the 2D US guidance group in a 1:1 ratio using a computer-generated list and sealed opaque envelopes prepared by one of the research nurses. All patients were blinded to their allocation. All US examinations were performed by a single experienced operator using a General Electric Voluson Expert series US machine (E8 or V730) with a 3D/4D RAB6-D trans-abdominal probe (GE Medical Systems Kretztechnik, Austria). The technique and settings were kept standardised throughout the trial.

The primary outcome measure was the live birth rate. The secondary outcome measures included implantation rate, clinical pregnancy rate, ongoing pregnancy rate, multiple pregnancy rate, early miscarriage rate, and ectopic pregnancy rate.

Results

Of 546 women assessed for eligibility, 481 were recruited and 474 completed the study (Fig.). The 3D and 2D US groups were comparable in terms of baseline characteristics, except for the median level of oestradiol on the day of trigger (9216 pmol/L vs 10654 pmol/L, P<0.02, Table 1). However, this variable was not found to be predictive of any of the outcome measures. There was no significant difference between the two groups in terms of the live birth rate (32.1% vs 32.5%, P=0.92, Table 2), positive human chorionic gonadotropin

rate, implantation rate, biochemical pregnancy rate, clinical pregnancy rate, early miscarriage rate, ongoing pregnancy rate, ectopic pregnancy rate, or multiple pregnancy rate.

Discussion

To the best of our knowledge, this is the first randomised controlled trial to compare the use of 3D versus 2D US guidance during embryo transfer. There was no significant difference between the two groups; this contradicts the postulated benefits reported in the literature. In our experience, the echogenic tip embryo transfer catheter allows 2D US to provide a clear appreciation of its location within the uterine cavity in most cases, even without the benefit of the 3D coronal plane. In addition, in cases where the embryo transfer catheter was found along the lateral wall of the cavity on 3D US, it was not always possible to correct this as the catheter could only be adjusted in an 'in-out' motion and not a 'left-right' motion. Although 3D US may theoretically allow for a more accurate transfer of the embryo, whether the position of transfer translates into improved clinical outcomes remains unclear, as the embryo may migrate within the uterine cavity after transfer.[5]

One limitation of the present study is that it included an unselected population of women undergoing ART. However, US guidance during embryo transfer has traditionally concerned unselected populations of women undergoing ART, as reflected in the methodology of previous studies comparing 2D US guidance versus clinical touch embryo transfer. Another limitation is the degree of heterogeneity in the characteristics of the recruited women. Nonetheless, randomisation along with serial logistic regression and subgroup analyses were applied to control for this. In addition, there were limited prospective data recorded regarding the exact timing and difficulty of each transfer, which may have been informative. A single experienced operator performed both 2D and 3D US in this trial; it remains unknown whether the results would be similar with different operators or those early on in their learning curve.

Conclusion

There was no significant difference in the pregnancy rate after 3D or 2D US-guided embryo transfer. Although 3D US is a newer tool for embryo transfer, it should not be recommended as a strategy to improve clinical outcomes.

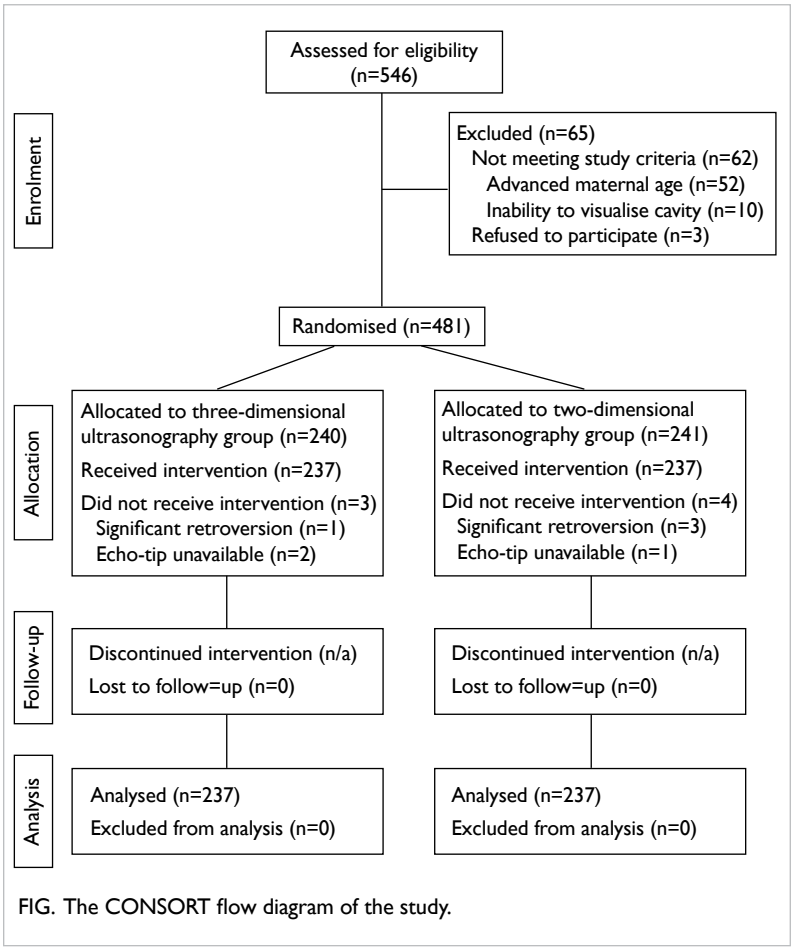

FIG. The CONSORT flow diagram of the study.

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Disclosure

The results of this research have been previously published in:

1. Saravelos SH, Kong GW, Chung JP, et al. A prospective randomized controlled trial of 3D versus 2D ultrasound-guided embryo transfer in women undergoing ART treatment. Hum Reprod 2016;31:2255-60.

2. Saravelos SH, Jayaprakasan K, Ojha K, Li TC. Assessment of the uterus with three-dimensional ultrasound in women undergoing ART. Hum Reprod Update 2017;23:188-210.

TABLE 1. Baseline characteristics of the three-dimensional and two-dimensional ultrasound-guided embryo transfer groups

Parameter	Three-dimensional group (n=237)*	Two-dimensional group (n=237)*
Age, y	36 (34-38)	36 (33-38)
Body mass index, kg/m^2	22 (20-24)	22 (20-24)
Infertility duration, y	4 (2-7)	4 (2-7)
Type of infertility		
Primary	113 (47.7)	120 (50.6)
Secondary	124 (52.3)	117 (49.4)
Cause of infertility†		
Ovulatory	30 (12.7)	45 (19.0)
Tuberperitoneal	99 (41.8)	100 (42.2)
Male	96 (40.5)	101 (42.6)
Other/unexplained	48 (20.3)	40 (16.9)
Treatment protocol		
Agonist	140 (59.1)	139 (58.6)
Antagonist	97 (40.9)	98 (41.4)
Baseline follicle-stimulating hormone, IU/L	7.1 (6.2-8.3)	7.2 (6.2-8.4)
Baseline luteinising hormone, IU/L	3.6 (2.1-5.4)	3.5 (1.8-5.2)
Oestradiol on trigger day, pmol/L	9216 (6583-12832)	10654 (7133-15213)
Duration of stimulation, days	10 (10-12)	11 (10-12)
Total oocyte retrieved	9 (6-13)	10 (6-14)
Mature oocytes retrieved	7 (5-11)	8 (6-11)
Oocyte fertilised	6 (4-9)	6 (4-9)
Type of embryo transfer		
Fresh	118 (49.8)	119 (50.2)
Frozen	119 (50.2)	118 (49.8)
Stage of embryo		
Day 3	93 (39.2)	86 (36.3)
Day 5	144 (60.8)	151 (63.7)
Good quality	96 (40.5)	105 (44.3)
No. of embryo transferred		
1	158 (66.7)	161 (67.9)
2	79 (33.3)	76 (32.1)
Endometrial thickness, mm	11.1 (9.4-13.1)	10.7 (9.1-12.6)
Use of tenaculum	6 (2.5)	6 (2.5)

* Data are presented as median (interquartile range) or No. (%) of cases
† Some patients presented with more than one cause of infertility

TABLE 2. Pregnancy outcomes in the three-dimensional and two-dimensional ultrasound-guided embryo transfer groups

Parameter	Three-dimensional group (n=237)*	Two-dimensional group (n=237)*	P value	Rate ratio (95% confidence interval)
Positive human chorionic gonadotropin (hCG) rate	120 (50.6)	124 (52.3)	0.71	0.97 (0.81-1.15)
hCG day 14, IU/L	158 (76-262)	158 (74-243)	0.32	
hCG day 21, IU/L	2626 (757-4578)	2786 (1391-4595)	0.60	
Biochemical pregnancy rate	17 (7.2)	19 (8.0)	0.73	0.90 (0.48-1.68)
Implantation rate	37.1%±3%	38.0%±3%	0.84	
Clinical pregnancy rate	103 (43.5)	105 (44.3)	0.85	0.98 (0.80-1.20)
Ectopic pregnancy rate	3/103 (2.9)	3/105 (2.9)	0.98	1.02 (0.21-4.94)
Early miscarriage rate	16/100 (16.0)	14/102 (13.7)	0.65	1.17 (0.60-2.26)
Multiple pregnancy rate				
Twins	5/100 (5.0)	7/102 (6.9)	0.57	0.72 (0.24-2.20)
Triplets	1/100 (1.0)	1/102 (1.0)	0.99	1.02 (0.07-16.08)
Ongoing pregnancy rate	84 (35.4)	88 (37.1)	0.70	0.96 (0.75-1.21)
Live birth rate	76 (32.1)	77 (32.5)	0.92	0.99 (0.76-1.28)

* Data are presented as No. (%) of cases, median (interquartile range), or mean±standard error

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