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A comparative study on therapeutic outcomes and clinical implications of transvaginal and transabdominal guidance during embryo transfer

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Summary

Purpose: To comparatively assess the clinical features and therapeutic outcomes in patients that underwent embryo transfer (ET) under transvaginal (TV) and transabdominal (TA) ultrosonographic guidance. *Materials and Methods:* ET was performed under TV ultrasonography in 184 cases, whereas TA ultrasonography was used in 188 cases. These two groups were compared in terms of therapeutic outcome including rates of implantation and clinical pregnancy. *Results:* Two groups displayed similar results in terms of rates of implantation and clinical pregnancy. However, duration of ET procedure was significantly shorter ($p = 0.001$), but pain during the ET intervention was more prominent ($p < 0.001$) in TA group. Need for Foley catheterization of urinary bladder was more frequent in TV ultrasonography group ($p = 0.002$). *Conclusion:* Attributed to the notable differences with respect to ease of procedure, patient comfort, and duration, selection of the appropriate mode of guidance must be made on individualized basis for each case.

Key words: Embryo transfer; In vitro fertilization; Ultrasonography; Transvaginal; Transabdominal; Implantation rate;Clinical pregnancy.

Introduction

Embryo transfer (ET) is an important aspect of infertility treatment with assisted reproductive technology [1]. Contemporarily, there is increased awareness on this issue and technical aspects of ET procedure have been particularly under focus [2]. Ultrasound guidance is a significant parameter which may influence the therapeutic outcome [3]. Studies investigating the rates of clinical pregnancy after ET with ultrasound guidance indicated that outcomes were improved with the use of transabdominal (TA) ultrasound guidance. Similarly, rates of implantation and pregnancy were more favorable for ET under transvaginal (TV) ultrasound guidance [4]. Moreover, TV-guided ET was found to provide benefit for in vitro fertilization (IVF) patients with previous failed cycles [5].

Comparison of ultrasound guidance with TV and TA approaches in ET demonstrated comparable rates of pregnancy [6]. This circumstance was valid IVF patients [2, 6]. Actually, TV approach is supposed to offer additional advantages such as increased patient comfort and lack of need for sonographer [2].

The objective of the current study was to evaluate and compare the therapeutic outcomes in ET under TA and TV ultrasound guidance in IVF patients.

Materials and Methods

This prospective, randomized trial was performed in a single infertility clinic between April 2014 and August 2015. Approval of the local Institutional Review Board (2013/563) and written informed consents of all patients have been obtained before the study. All procedures have been carried out in accordance with principles included in the Helsinki Declaration.

Candidates for fresh ET with cleavage-stage and blastocyst were considered as eligible for the present study. Patients were randomly allocated into TA and TV ultrasound guidance groups before ET and randomization was made using a computer program. Data including age of patients, number of oocytes collected, number of mature oocytes (MII), fertilization status, date and duration of ET, administration of Foley catheter into the urinary bladder, patient comfort during procedure and rates of implantation and clinical pregnancy were recorded and compared in two groups. All procedures were performed by a single operator.

In the beginning, 747 patients were approved as eligible for the study. However, some patients were excluded due to age over 40 years (n=78), spouse with a history of azoospermia (n=62), uterine myoma or endometriosis (n=63), or unwillingness for participation in the study (n=98). Patients that necessitated the use of different catheters for ET due to technical difficulty in TV (n=23) and TA (n=19) groups were also eliminated. Patient recruitment with respect to the CONSORT statement flow diagram is shown in Figure 1.

Ovarian stimulation of patients was accomplished via a gonadotropin releasing hormone (GnRH) antagonist protocol coupled with recombinant human chorionic gonadotropin (hCG) trigger. Hysterosalpingography or hysteroscopy was used to eval-

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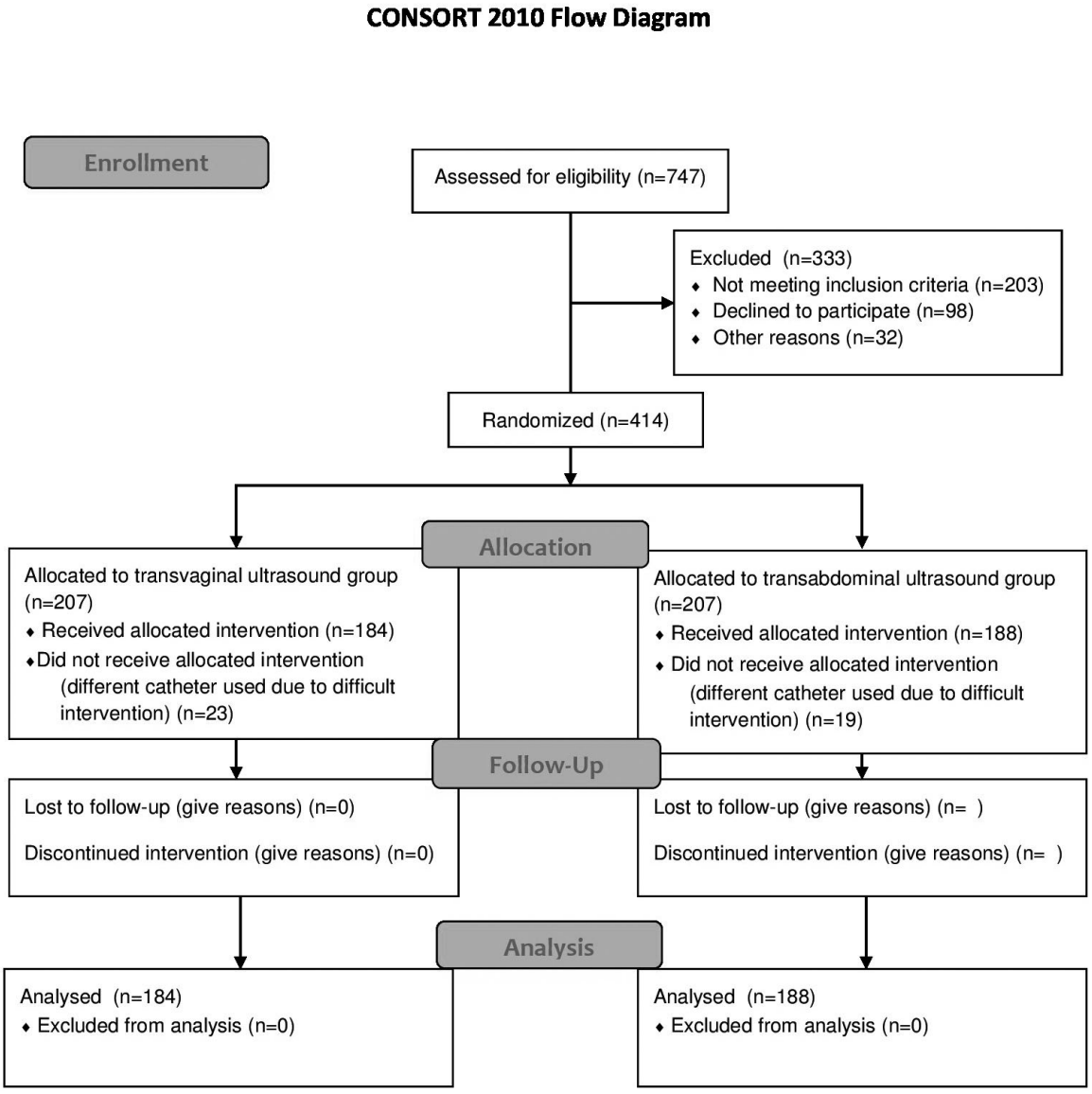

Figure 1. — CONSORT statement diagram for patient flow.

uate the uterine cavity. Mock transfer was not performed in this study. The duration of the treatment varied with respect to the availability of the oocytes. The laboratory procedures and combined embryo score used have been described in relevant literature [7]. If pregnancy occurred, luteal phase support with progesterone was carried on for 60 days after ET.

Patients in TA ultrasound group were instructed to admit to the clinic with a full bladder, while TV group was instructed to void prior to the procedure. During the intervention, either filling or emptying the bladder was necessary for some patients in both groups. A portable ultrasound device having 9-4 MHz vaginal and 5-2 MHz abdominal transducers was utilized. The vaginal probe was covered with a sterile sheath during ET and meticulously cleaned between procedures. Patients in TA were allowed for getting up and voiding just after ET. All patients were maintained in a reclined position for 30 minutes before returning home and intense physical exercise was avoided.

A sterile Collin vaginal speculum was inserted for exposing the cervix. Following the cleansing of cervix gently, ET procedure was carried out by means of a two-stage technique in collaboration with the embryologist. The TA ultrasound scan was performed simultaneously by a trained nurse. An embryo replacement catheter has a teflon and soft echogenic (due to embedded small air bubbles) inner catheter. Initially, only the outer sheath was inserted into the cervix until reaching the internal cervical os. In order to facilitate access to the cervical canal, a similar outer sheath obturated with a rigid malleable stylet was used (*No. 1816ST*). Subsequent to confirmation of the position of the catheter on the TA ultrasound scan, the physician gave the signal to the embryologist to initiate the embryo loading. For this purpose, embryos were loaded into the echogenic inner soft catheter between two small air bubbles using Uterine Transfer Medium.

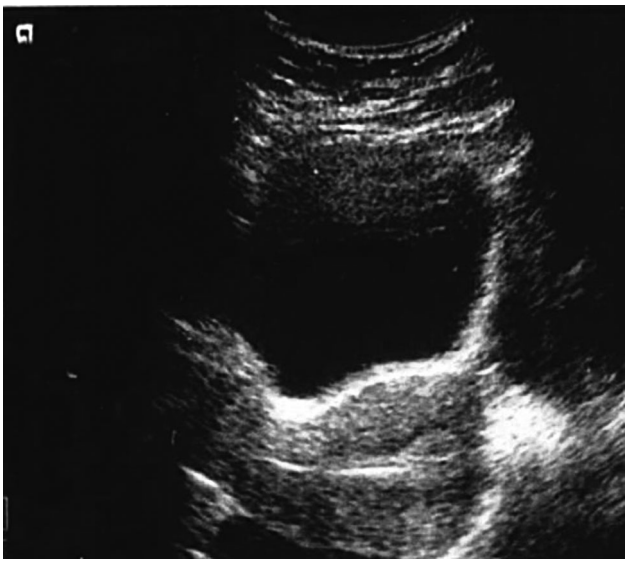

Figure 2. Transabdominal ultrasound image of the uterus after injection of embryos.

Figure 3. Transvaginal ultrasound image of the uterus after embryo injection.

The embryologist inserted the loaded inner catheter into the outer sheath, which was maintained in its position by the physician. Under ultrasound control, the inner echogenic catheter was advanced to a distance of 10 to 20 mm of the uterine fundus by the physician. Approximately 0.3 μL of media volume was injected by the embryologist in response to the signal of the physician. The appearance of echogenic spots generated by the air bubbles was visualized on the scan. The inner catheter was gently removed after ten seconds.

After identification of the position of the uterus, alignment of the cervical canal and thickness of the endometrium were assessed with TV ultrasound scan. A sterile Collin vaginal speculum was inserted for exposure of the cervix, and after the gentle cleansing of cervix with sterile gauze pads, ET was carried out using a two-stage technique with the aid of the embryologist. In this purpose, an embryo replacement catheter was utilized as described above. After verification of the correct position of the catheter, embryos were transferred into the echogenic inner soft catheter. The inner catheter was passed into the outer sheath and under TV ultrasound guidance, the inner catheter was placed at a distance of 10 to 20 mm of the uterine fundus. After the signal of the physician, a media volume of 0.2 μL was injected by the embryologist. Two echogenic spots formed by the two loaded air bubbles were observed on the scan. After noting the site of deposition for embryos, the inner catheter was withdrawn. In the present clinic, both TV and TA ultrasound guidance have been used for ET. The duration of ET was composed of catheterization time, embryo loading time and injection time. Figures 2 and 3 demonstrate the TA and TV ultrasound images of the uterus obtained after injection of embryos, respectively.

Data was analyzed by means of SPSS Statistics 20 program. Normal distribution of variables was tested with Kolmogorov Smirnov test. Variables with normal distribution were evaluated with parametric tests, while non-parametric tests were utilized for variables without normal distribution. Two independent groups were compared by means of Independent-Samples *t*-test and Mann-Whitney U test. For comparison of more than two groups, One-way ANOVA, a parametric test, was used, and homogeneous subsets were constituted by means of Tukey test. For the same purpose, Kruskal-Wallis test, a non-parametric test, was used, while Mann-Whitney U test was utilized. Assessment of categorical variables was carried out by Pearson Chi Square test. Quantitative variables are expressed as mean, standard deviation, median, interquartile range, minimum, and maximum. Confidence interval was 95% and level of significance was set at $p < 0.05$.

Results

TV and TA ultrasound guidance groups consisted of 184 and 188 patients, respectively. Comparison of two groups in terms of descriptive, clinical, and embryologic features yielded that duration of ET procedure was significantly shorter ($p < 0.001$) in TA ultrasound group. Two groups presented similar results with respect to number of previous ET procedures, number of oocytes and metaphase II (MII) oocytes collected, days of fertilization and ET, as well as number of embryos transferred and duration of ET (Table 1). Pain during ET procedure was more pronounced ($p < 0.001$) in TA group, whereas need for Foley catheterization was more frequent in TV group ($p = 0.002$). No significant differences were detected between two groups regarding rates of implantation ($p = 0.955$) and clinical pregnancy ($p = 0.592$) (Table 2).

In both TV and TA ultrasound groups, need for Foley catheterization and pain during ET procedure did not differ ,among groups with different numbers of implantation (Table 3).

In patients treated under TA ultrasound guidance, number

Table 1. — *Comparison of characteristics of patients receiving ET under TV and TA guidance.*

Variable	Group		*p*-value
	Transvaginal	Transabdominal	
Age	31.3±5.2	30.5±5.3	0.142
No. of ET procedures	2.0-2.0	2.0-1.0	0.583
No. of oocytes	8.0-7.0	7.0-6.0	0.453
No. of MII oocytes	6.0-6.0	6.0-5.0	0.579
Fertilization	5.0-5.8	5.0-5.0	0.747
Day of ET	5.0-2.0	5.0-2.0	0.846
No. of embryos transferred	1.0-1.0	1.0-1.0	0.724
Duration of ET	95.0-218.8	85.0-40.0	0.001*

*ET: embryo transfer; MII: metaphase II; TV: transvaginal; TA: transabdominal; * statistically significant.*

Table 2. — *Comparison of TV and TA ultrasound guidance groups with respect to need for Foley catheterization of the bladder, pain during ET, rates of implantation, and clinical pregnancy.*

Variable		Group		*p*-value
		Transvaginal n (%)	Transabdominal n (%)	
Need for Foley catheterization	No	133 (72.3)	160 (85.1)	0.002*
	Yes	51 (27.7)	28 (14.9)	
Pain during ET	None/mild	158 (85.9)	105 (55.9)	<0.001
	Moderate	22 (12.0)	65 (34.6)	
	Severe	4 (2.2)	8 (9.6)	
Implantation	0	92 (50)	96 (51.1)	0.955
	1	80 (43.5)	81 (43.1)	
	2	12 (6.5)	11 (5.9)	
Clinical pregnancy	0	92 (50)	96 (51.1)	0.592
	1	92 (50)	92 (48.9)	

** statistically significant; ET: embryo transfer.*

of procedures ($p = 0.027$), day of ET ($p = 0.017$) and number of embryos transferred ($p < 0.001$) displayed remarkable differences between various implantation groups.

For 51 cases in TV ultrasound guided ET group, the procedure was performed following adjustment of the amount of urine in the bladder by catheterization. Number of patients reporting discomfort during procedure and due to urinary distension were 29 and 79, respectively.

Discussion

Results of the present randomized clinical trial demonstrated that there were no statistically significant differences in rates of clinical pregnancy or embryo implantation rates in IVF-ET groups that underwent ET with TV *vs.* TA ultrasound guidance. The authors found that ET procedure was shorter but linked with more patient discomfort under TA ultrasound guidance. On the other hand, need for Foley catheterization of urinary bladder was more frequent during the TV approach. Furthermore, compliance of the patients was better, quality of imaging was more clear, and less number of personnel was needed during TV ultrasound guided ET. Visualization was more problematic especially for overweight patients with retroposed uterus and urge incontinence in TA ultrasound guidance group.

Factors such as patient selection, uterine receptivity, quality of embryo, and ET technique can affect clinical pregnancy. ET is not only the last and most critical step, but also is the least effective part of the procedure [4].

Ultrasonography guidance provides the advantage of documentation of various conditions that occur before, during,

Table 3. — *Need for Foley catheterization and pain during ET in TV and TA ultrasound guidance groups with various implantation outcomes.*

Group	Variable		Implantation			p-value
			0 (n)	1 (n)	2 (n)	
Transvaginal	Need for Foley catheterization	No	69	57	7	0.461
		Yes	23	23	5	
	Pain during ET	None/mild	79	70	9	0.583
		Moderate	11	9	2	
		Severe	2	1	1	
Transabdominal	Need for Foley catheterization	No	85	67	8	0.274
		Yes	11	14	3	
	Pain during ET	None/mild	55	43	7	0.792
		Moderate	31	30	4	
		Severe	10	8	0	

(Abbreviations: ET: embryo transfer; TV: transvaginal; TA: transabdominal)

and after ET. Patient compliance for TV ultrasound as a component of the procedure was reported to be high [1]. Moreover, the patient and her partner may have the chance to be involved and directly visualize the transfer of embryo into the uterine cavity. Their involvement in the process may improve the adherence to the treatment cycle and enhance the psychological status. Notably, utilization of ultrasound in ET does not substantially add time to the procedure [1].

Similar to the present results, Bodri *et al.* suggested that TV approach offered noteworthy benefits [2]. Various degrees of bladder distension were reported by patients in the TA arm. Since the TV approach necessitated an empty urinary bladder, need for Foley catheterization may arise in this group. The degree of bladder distension is associated with pain or discomfort during ET [8]. Moreover, patient compliance for obtaining optimal bladder distension and extra waiting time for desired bladder distension may adversely affect the program of an already busy infertility clinic. Performance of TA ultrasound necessitates the presence of a well-trained nurse or sonographer. This is controversial to the TV approach where scanning can be readily performed by the operator.

Since TV ultrasound allows a better visualization of ET, it can be particularly of choice in obese patients or cases with retroverted uterus. Thus, TV ultrasound can optimize ET procedure and improved patient comfort. The prolongation of intervention during TV ultrasound can be attributed to procedures such as catheterization, injection, and positioning which necessitate additional time.

Since TV and TA arms yielded similar rates of implantation and pregnancy, selection of the approach must be made with respect to clinical features and preference of the physician [6]. Contrary to the present data, they observed no difference in pain between TV and TA groups and there was no difference in terms of duration of ET between groups [6]. However, some methodological differences must be remembered for interpretation of these differences. First, the present authors did not perform mock transfer; but they carried out a double mock transfer. Secondly, they used two different catheters (Wallace and Cook Echotip) for ET, but the present authors used only one type of catheter (Wallace).

TV ultrasound provided better resolution of details of pelvic anatomy and eliminated the need for a full bladder. Hurley *et al.* could not demonstrate improved results with TV ultrasound guidance [9]. Better outcomes have been reported with TA ultrasound guidance in ET, but Lindheim *et al.* reported better rates of clinical pregnancy for easy transfers only [4, 10].

Strengths of the present study include relatively large sample size and a homogeneous IVF-ET population. Nevertheless, role of inevitable confounding factors cannot be eliminated. Prognostic factors such as race, uterine anomalies, and genetic disorders may have affected the therapeutic outcomes. The weaknesses of the trial include bias effect and inability to blind the operator and patients for the technique used.

In conclusion, the present authors suggest that guidance by means of TV and TA ultrasonography during ET yielded similar therapeutic outcomes. Owing to the significant differences with respect to ease of procedure, patient comfort and duration, selection of the appropriate mode of guidance must be made on individualized basis for each case.

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