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Three-dimensional ultrasound-guided embryo transfer: A preliminary study

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KEY WORDS
Three-dimensional ultrasound
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Objective: Embryo transfer techniques have emerged as 1 of the most important variables during in vitro fertilization. Two-dimensional ultrasound guidance is an integral part of this procedure and a method to monitor catheter passage through the cervix into the endometrial cavity. Catheter placement may better be achieved with 3-dimensional monitoring to assess the relationship of the catheter tip to the uterine cavity. The purpose of this study was to compare the precision of catheter placement and position by 2- and 3-dimensional ultrasound.

Study design: Twenty-four patients were studied. The cervix, uterus, and endometrial cavity were prescreened in 2 dimensions at the midline in the longitudinal plane of the uterus. Embryo transfers were then performed under 2-dimensional guidance. After satisfactory catheter placement and transfer of the embryos, the catheter was held in place for 60 to 120 seconds. During this interval, an automated, single sweep of the uterus and endometrial cavity was performed for net volume acquisition. All images were stored and retrospectively reviewed. Embryo transfer catheter placement with 2-dimensional ultrasound guidance was then compared with the images obtained in 3 simultaneous planes.

Results: Visualization of the embryo catheter tip with 2-dimensional ultrasound was achieved in all patients. These images suggested that the catheter was 2 cm from the uterine fundus and in the midline. Satisfactory 3-dimensional images for review and comparison were obtained in 21 of 24 patients. Three-dimensional ultrasound images confirmed placement and agreed with findings of 2-dimensional ultrasound images in 17 of 21 patients. In 4 patients, the catheter tip on 3-dimensional ultrasound was observed to be displaced either anteriorly or laterally from the ideal region as suggested by 2-dimensional ultrasound. In 1 case, the catheter tip on 3-dimensional ultrasound was observed to be far laterally in the region of the uterine cornua.

Conclusion: Two-dimensional ultrasound-guided embryo transfer continues to be the standard for image-guided transfers. Data of the present study suggest that the precision of catheter tip placement and consequently embryo transfer may be improved with 3-dimensional imaging. Four of 21 patients studied had catheter tip placement in a different and less-than-ideal area when studied with 3-dimensional ultrasound. Three-dimensional imaging may provide an improvement in embryo transfer technique and have a positive impact on overall pregnancy rates.

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The development of novel intraoperative navigational systems has improved surgical and interventional precision.[1-3] These image-guided systems yield simultaneous multiplanar visualization using 2- or 3-dimensional magnetic resonance or ultrasound technology. Contemporary 3-dimensional ultrasound systems provide a means of assessing 3 planes simultaneously and capturing volume data. Three-dimensional ultrasound databases are obtained by acquiring a series of conventional 2-dimensional ultrasound images and reconstructing them into a surface or volume rendering. These volume data sets can be displayed using planar images for any orientation within the volume, including planes that cannot be obtained using conventional 2-dimensional ultrasound. This technique provides a flexibility to view objects from perspectives that potentially can optimize visualization of target issues or instruments. These systems provide a platform for data and image storage and recall for review and retrospective analysis. This technology may have a role in enhancing the efficiency of embryo transfer techniques.

Two-dimensional ultrasound has been shown to be an excellent real-time modality for tracking needles, instruments and, and intraoperative monitoring for a variety of endoscopic procedures.[4-6] In infertility and reproductive endocrinology, the position of the embryo transfer catheter within the endometrial cavity may be monitored with this technique. However, 2-dimensional ultrasound provides only limited views and understanding of 3-dimensional spatial relationships, particularly when applied to narrow acoustic windows. The ability to view the catheter location within the uterine volume using 3 perpendicular views simultaneously could provide an enhanced method of tracking the embryo catheter during an embryo transfer.

Given our experience, with 2-dimensional ultrasound to monitor a variety of procedures, we postulated that 3-dimensional ultrasound might be useful to improve depiction and understanding of geometric relationships of the embryo transfer catheter within the endometrial cavity. This expanded visualization could potentially optimize placement of the embryos. The purpose of this study was to compare catheter placement by 2-dimensional and 3-dimensional ultrasound imaging.

Material and methods

Patients

Twenty-four patients were studied. All patients had undergone ovarian hyperstimulation using a protocol of luteal suppression with a gonadotropin-releasing hormone agonist and stimulation with a combination of recombinant follicle-stimulating hormone and urinary gonadotrophins. Oocytes were retrieved with transvaginal ultrasound guidance under intravenous sedation. Patients ranged in age from 28 to 39 years. All patients had normal uterine architecture as demonstrated on previous hysterosalpingography and sonohysterography. Two to four embryos were transferred, depending on age of patient and embryo quality. All transfers were performed by 2 clinicians under 2-dimensional transabdominal ultrasound guidance with a Medison 256 (model SA 8000 LV, Medison, Cypress, CA) channel system and 2-dimensional abdominal probe. The 2-dimensional transabdominal probe has frequency capabilities of 3 to 7 MHz. The 3-dimensional transabdominal and transvaginal probes have frequencies of 4 to 7 MHz and 5 to 8 MHz, respectively. Patients were studied sequentially and without regard to body mass index.

Two-dimensional ultrasound-guided embryo transfer

The cervix, uterus, and endometrial cavity were prescreened in 2 dimensions in the midline in the longitudinal plane of the uterus transvesically. A bivalve speculum was inserted into the vagina and the vaginal vault and the cervical canal carefully swabbed using sterile culture media. The cervical canal was gently irrigated using a syringe and catheter to clear any mucus. After irrigation, the outer sheath of the embryo catheter was brought into the field and advanced through the endocervical canal under transabdominal ultrasound guidance. Once in place, the inner sheath loaded with the embryos was then advanced through the endocervical canal into the lower uterine segment. Passage of the catheter tip by 2-dimensional ultrasound imaging was tracked through the endocervical canal and lower uterine segment. The transfer catheter was advanced to a distance 2 cm from the uterine fundus. The embryos were transferred and the catheter held in place for 60 to 120 seconds.

Three-dimensional ultrasound monitoring

After the transfer of the embryos and during the interval when the inner catheter was held in place, a volume box was centered on the uterus. A single automated sweep of the uterus and endometrial cavity was performed with the transducer held stationery for net volume acquisition. Five patients were studied with transvaginal and 19 with transabdominal ultrasound imaging. In patients monitored with 3-dimensional transvaginal imaging, the speculum was removed and transfer catheter held in place. The transvaginal probe was then inserted. During this transition, the catheter tip was monitored continuously with transabdominal imaging to assure the catheter tip did not move from the site of transfer. Image contrast and brightness were similar for both

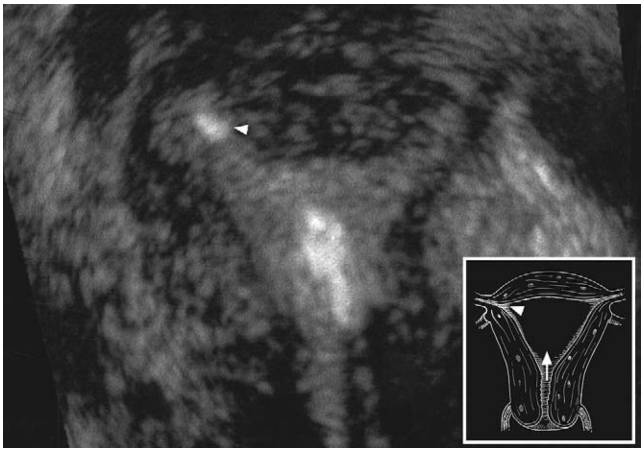

Figure 1 Three-dimensional transvaginal coronal image of catheter tip to right of midline. Diagram of catheter tip within endometrial cavity (*inset*).

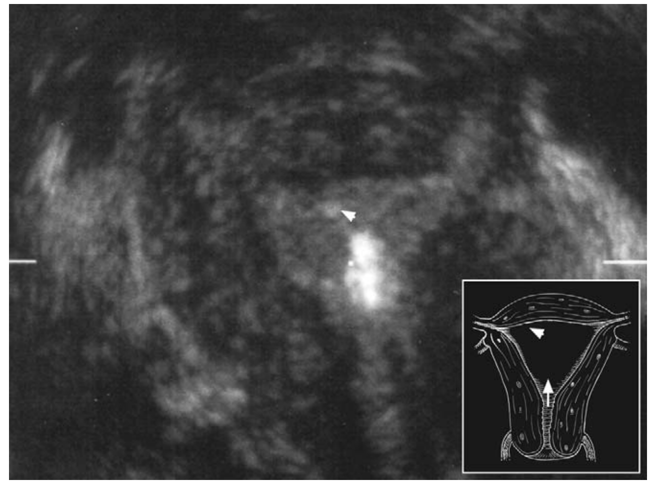

Figure 2 Three-dimensional transvaginal coronal image demonstrating catheter tip in right cornual region. Diagram of catheter tip within endometrial cavity (*inset*).

techniques. Transvaginal imaging was more cumbersome than transabdominal.

The volume data set for transabdominal images was acquired with an abdominal 5.0 MHz mechanical curved array volume transducer. The 3-dimensional ultrasound software (SonoView, Medison) compressed the images into a solitary volume data set. The volume data set was then stored within the computer memory for later recall and reconstruction.

With this system, images of the endometrial cavity were displayed on the console simultaneously in 3 orthogonal planes after the embryo transfer. These images enabled simultaneous viewing of a longitudinal, coronal, and sagittal view of the endometrial cavity. Simultaneous display of 3 orthogonal 2-dimensional images on the console was also available within 1 second of acquisition. Each of the 3 imaging planes could be manipulated to display any desired orientation at any location within the volume data set. During manipulation of any 1 plane, the orientation of the 2 nonmanipulated planes maintained an orthogonal relationship to the manipulated plane.

Outcome analysis

All images were stored and retrospectively reviewed by 2 individuals. The simultaneous display of 3 2-dimensional images was used to locate the catheter and compare with the 2-dimensional images obtained during the actual realtime transfer. All clinical decisions with regard to embryo placement were made using 2-dimensional real-time images. Three-dimensional imaging did not influence clinical decision making or alter clinical care. Placement of the catheter was assessed by visualizing the relationship of the catheter tip to the walls of endometrial cavity. No measurements or calculations to localize the tip in 3 dimensions were made.

Results

Visualization of the embryo catheter tip with 2-dimensional ultrasound was achieved in all patients. These images showed that the catheter was 2 cm from the uterine fundus and located in the midline. Satisfactory 3-dimensional images for review and comparison were obtained in 21 of 24 patients. In 3 patients, the image quality and identification of the catheter tip were of inadequate quality for any meaningful visual comparisons. Three-dimensional ultrasound verified catheter placement in 17 of 21 patients. In 4 patients, the catheter tip was observed to be displaced either anteriorly or posteriorly or laterally from the ideal region as suggested by 2-dimensional ultrasound (Figure 1). In 1 case, the catheter tip was observed to be far laterally in the region of the uterine cornua (Figure 2). Three-dimensional transabdominal images in 3 simultaneous planes captured the catheter tip but were not as useful as transvaginal coronal views of the endometrial cavity.

Comment

Embryo transfer has emerged as a significant aspect impacting the success of in vitro fertilization. Considerable attention is paid to atraumatic passage of the catheter through the endometrial cavity and precise location of the catheter tip and site of transfer of the embryos. Ease and precision are the hallmarks of a successful transfer. Contamination of the catheter tip suggests endometrial trauma and is associated with lower success rates.[7] A variety of techniques, catheters, and monitoring has been evaluated to enhance and refine this process.[8,9] In most clinics, 2-dimensional transabdominal ultrasound guidance is the standard of care. This technique enables tracking of the catheter tip and avoidance of endometrial damage. This imaging, however, provides a restricted view of the endometrial cavity.

Three-dimensional ultrasound has been shown to expand the field of view and enhance the efficiency and precision of a variety of other procedures.[10,11] Applications include intraoperative monitoring for a variety of neurosurgical procedures, the placement of transvenous intrahepatic catheters, and optimizing guidance for ablating focal liver tumors.[1,2,12,13] In these settings, 3-dimensional ultrasound has provided image detail that was unique, not captured in 2-dimensional imaging and enhanced the efficiency and precision of the procedure. The purpose of the present preliminary study was to evaluate the potential role of 3-dimensional ultrasound for ultrasound-guided embryo transfer. In this study, the precision of 2-dimensional ultrasound placement was compared with the more detailed 3-dimensional ultrasound imaging. In this study, 3 simultaneous orthogonal planes were viewed for catheter placement and compared with data obtained with 2-dimensional transabdominal imaging. In 4 of these patients, the catheter was noted to be in a position other than suggested by 2-dimensional techniques. These observations suggest that the placement of the catheter by 2-dimensional guidance may be misleading in as many as 20% of the cases.

The assumption that a catheter during embryo transfer may follow a direct line of migration to the desired midline position may be an oversimplification. The soft pliable consistency of the transfer catheter could theoretically follow a line of least resistance and migrate along the lateral wall of the endometrial cavity or into the endometrial lining anteriorly or posteriorly. This movement may be influenced by the contour of the cavity or the curvature of the outer sheath required for passing through the endocervical canal. These factors could result in movement of the catheter away from the desired midline location for embryo placement. Surface tensions of the endometrium may also contribute to a more anterior or posterior location.

Observations of the present study suggest that the catheter may migrate in unintended directions, resulting in misplacement of the embryos in spite of a reassuring image on 2-dimensional ultrasound. In 3 patients, the catheter tip was displaced laterally. In 1 patient, the tip appeared anterior. Two additional aspects of this series of observations are noteworthy. First, image quality in 3 of 24 patients was poor enough to compromise interpretation. This diminished quality may be secondary to technique, inexperience with the application in this setting, or a clinical task beyond the true sensitivity of technique. Second, determination of catheter position was qualitative and based on clinical assessment but nonetheless compelling. No measurements of exact location within this cavity in 3 dimensions were made. The intention of this preliminary study was to compare by inspection 2- and 3-dimensional images and determine whether our current techniques of monitoring can be improved. Future study of the technique will include a more specific and measurable assessment of position.

Evolving 3-dimensional real-time ultrasound technology may be another technique to enhance placement of embryos. Given the current technology and software, it is possible to perform live 3-dimensional imaging. In this technique, 3 simultaneous images are shown in each of 3 dimensions with an approximate 1-second lag. This modality may be applicable to embryo transfer techniques to further enhance precision of the embryo placement. It is open to question whether these techniques will ultimately improve pregnancy rates. Previous experience with enhanced materials, technologies, and techniques suggest that pregnancy rates increase as a result of careful, thoughtful, and precise embryo placement of the embryos.

Conclusion

In summary, observations from this preliminary study suggest that 3-dimensional ultrasound may have a role in ultrasound-guided embryo transfer. Improvements in image quality and a reduction in lag time for real-time imaging may enhance this technique for embryo transfer and possibly enhance pregnancy rates.

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Editor's note: This manuscript was revised after these discussions were presented.

Discussion

Dr Michael Kettel, San Diego, Calif. This is a prospective, preliminary report describing the use of 3-dimensional ultrasound to detect the placement of the embryo transfer catheter within the uterus after the actual embryo transfer had been done using standard 2-dimensional ultrasound. It is not a comparative trial between the 2 techniques but reports on the possible superiority of an extra dimension in determining the position of the catheter within the uterus.

Two-dimensional ultrasound has been used to aid in the placement of embryos during the transfer portion of in vitro fertilization. Before the advent of this technology, embryo transfer was done "blindly" and based on previously determined uterine measurements. The first technique reported using transabdominal ultrasound through a full or partially full bladder. This technique is still quite popular but does require an additional skilled provider to perform the ultrasound portion of the procedure while the physician performs the transfer itself. A full bladder may make the patient uncomfortable, and this can be amplified if a recommendation to remain at bed rest after the procedure is made. In addition, the visualization of the catheter can be difficult in some patients, particularly those of heavier body weight in whom the distance from the ultrasound transducer to the catheter is increased. Industry has helped by producing catheters that have design features that increase their visibility by ultrasound. A newer twist to this technique is the utilization of vaginal ultrasound to visualize the catheter. Vaginal ultrasound offers the advantage of allowing (encouraging) an empty bladder and better visualization of the catheter tip because of improved proximity to the transducer. Simultaneous placement of the catheter and vaginal transducer in the vagina requires the speculum be opened slightly more and may require increased dexterity of the physician performing the procedure because both right and left hands are used together.

In addition to using ultrasound to guide catheter placement, several other transfer techniques that improve pregnancy rates have been described. Avoiding the fundus while placing the embryos improves pregnancy rates as does keeping the catheter still within the uterine cavity for a minute or more.

In this report, the author used abdominal ultrasound to guide the transfer as is routinely done in their center. Once the transfer was done, a 3-dimensional ultrasound study was obtained while the catheter was maintained within the uterus. Some time later, the position of the catheter was compared by the information available from the 3-dimensional study and compared with the position determined by standard 2-dimensional ultrasound.

I have several questions for Dr Letterie:

1. How were the patients selected and did body size influence the quality of the ultrasound images obtained? Was the bladder full?
2. Using real-time 2-dimensional ultrasound has become an integral part of the practice of obstetrics/gynecology. How "real time" is 3-dimenisonal ultrasound now, and when do you foresee real-time 3-dimenisonal being available?
3. The catheter was kept motionless during the acquisition of the 3-dimensional images. Some of these images were done by vaginal ultrasound, and one might think this would be quite difficult. How was this controlled?
4. What other uses do you see for 3-dimensional ultrasound in the assisted reproductive technologies?

Dr Gabriel Garzo, La Jolla, Calif. How do you know that the catheter was 2 cm from the fundus? In the patient that you showed, the catheter was actually in the cornua. Do you still think that the tip was 2 cm from the fundus, and why do you think you were wrong?

Dr Emmet Branigan, Bellingham, Wash. I was wondering whether a better way of studying this might be to do this imaging during a mock transfer. This would allow you more time for better imaging. Those that showed poor positioning of the catheter during the mock transfer might be the ones that would benefit from this imaging during the actual embryo transfer.

Dr David Adamson, Palo Alto, Calif. During your presentation you stated that it is not necessarily intuitive to look at the 3-dimensional picture. Could you discuss who did your scanning, and what do you think the usual training would be for an individual who would do this scanning? Can you also tell us the cost of this equipment?

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Dr Gerard Letterie (Closing statement), Seattle, Wash. In answer to Dr Kettel's question regarding selection criteria, the patients were selected sequentially. There were no inclusion or exclusion criteria. There was no attempt to select on the basis of body mass index or quality of the screening image at the time of transfer. The only criterion for participation was a willingness to cooperate for the minute or so that the scanning required.

Dr Kettel inquired about "real time" 3-dimensional ultrasound. Imaging techniques are available for the simultaneous display of 3 2-dimensional images in 3 orthogonal planes. Despite its very basic nature, we remarkably do have all dimensions captured in real time. The endometrial cavity and catheter are imaged in all 3 planes. This quality is not unlike the early video games that Nintendo marketed in the early 1990s or some of the early videos we would get on-line. There is a jerky quality to them, but I think we are going to see marked improvement in the software in the future enabling near-simultaneous transmission without the lag time that results in this jerkiness and a disparity between real time and image display.

In answer to the question regarding control of the catheter position, the coaxial system was held firmly in place by grasping both inner and outer sheaths simultaneously. For the 3-dimensional transvaginal scanning, the position of the catheter tip was continuously monitored to assure that there was no change in position during transition from transabdominal to transvaginal imaging. For 3-dimensional transabdominal imaging, there was continuous observation of the catheter tip during the 3-dimensional acquisition of data.

There are several potential uses for future use. I will mention 2. Software for image analysis that permits the reconstruction of volume data to more precisely study anatomy and in this case catheter position is available. The volume of the uterus may be rotated in 3 dimensions and, with the mouse, the anatomy shaved away from a lateral to medial point to visualize precisely where the catheter tip may be in the uterine cavity. Retrospectively we can review this dynamic and incorporate this information into an evaluation of the cycle. Future uses of 3-dimensional ultrasound include measuring follicles during hyperstimulation and evaluating antral follicle counts when the ovaries are measured in 3 dimensions. This latter application may more precisely evaluate ovarian reserve beyond the conventional techniques that we now use such as BA5A serum follicle-stimulating hormone on day 3.

Dr Garzo asked about the 2 cm location of the catheter tip from the uterine fundus. This distance was measured using the calipers in the midline. We did not make a qualitative assessment. This point highlights the potential role for 3-dimensional imaging in embryo transfer. There may be cases in which all due diligence is taken to ensure that the catheter is located in the midline, but because of variations in anatomy or imaging technique, it is in fact off to 1 side.

Dr Branigan asked about using this approach during a mock or trial transfer, and that is an excellent idea. This approach would identify patients at high risk for deviation of the catheter tip and who may benefit from the 3-dimensional technique.

Dr Adamson inquired about the personnel. The imaging was done initially with an instructor from the company who provided some hands-on instruction and manuals for instruction. We used the Medison scanner on several patients beforehand so we could gain a familiarity with the keyboard, technique, and software. Subsequent to that, we had an ultrasound technician in the room. The cost of the equipment is extremely variable. You can get an entry-level ultrasound system with 3-dimensional capability in the $50,000 to $60,000 range.