Original Article
http://mjiri.iums.ac.ir

Medical Journal of the Islamic Republic of Iran (MJIRI)
Iran University of Medical Sciences

Can combination of hysterosalpingography and ultrasound replace hysteroscopy in diagnosis of uterine malformations in infertile women?

Mansoureh Vahdat[1], ElahehSariri[2], Maryam Kashanian[3], Zahra Najmi[4]*
Alireza Mobasseri[5], Mahjabin Marashi[6], Behnaz Mohabbatian[7], Shideh Ariana[8]
Yousef Moradi[9]

Received: 20 May 2015 Accepted: 28 November 2015 Published: 10 April 2016

Abstract

Background: Müllerian anomalies are associated with infertility. Hysteroscopy as the gold standard for evaluating Müllerian anomalies is an invasive, expensive and risky procedure which requires enough experience. Transvaginal sonography (TVS) and hysterosalpingography (HSG) are less invasive procedures, but there is little known about the accuracy of these tests. The aim of this study was to evaluate the accuracy of the combination of TVS and HSG with hysteroscopy as the gold standard.

Methods: Medical records of infertile women who were undertaken all three diagnostic modalities were reviewed to analyze their sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Results: Ninety-nine infertile women were assessed with a mean±SD age of 29.1±6.47 years, mean±SD duration of themarriage of 8.9±10.28 years, and mean±SD duration of infertility of 5.6± 4.16 years. The sensitivity, specificity, PPV, and NPV of TVS were 98.55%, 30%, 76.4%, and 90%, respectively. HSG had a sensitivity of 95.6%, specificity of 60%, PPV of 84.62%, and NPV of 85.71%.When both modalities were combined, the sensitivity, specificity, PPV, and NPV were 94.2, 66.67, 86.67, and 83.33%, respectively. The diagnostic accuracy of single TVS, HSG or combined techniques was statistically similar that was equal to 77.7, 84.8 and 85.8 % respectively.

Conclusion: The accuracy of combination of two diagnostic modalities, 2D TVS and HSG is not higher than HSG alone for assessing uterine malformation in infertile women.

Keywords: Ultrasound, Hysterosalpingography, Hysteroscopy, Müllerian anomaly, Accuracy, Infertility.

Cite this article as: Vahdat M, Sariri E, Kashanian M, Najmi Z, Mobasseri A, Marashi M, Mohabbatian B, Ariana Sh, Moradi Y. Can combination of hysterosalpingography and ultrasound re-place hysteroscopy in diagnosis of uterine malformations in infertile women?. *Med J Islam Repub Iran* 2016 (10 April). Vol. 30:352.

Introduction

Müllerian anomalies are a group of female reproductive system malformations develop during early embryologic life (1). These congenital abnormalities might present with irregular menses, repeated abortions and infertility, and the diagnosis often delays until adulthood. Infertility af-

1. MD, Assistant Professor of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran. mansoureh_vahdat@yahoo.com
2. MD, Assistant Professor of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran. drelaheh_sariri@yahoo.com
3. MD, Professor of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Iran University of Medical Sciences, Tehran, Iran. maryamkashanian@yahoo.com
4. (**Corresponding author**) MD, Assistant Professor of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran. zahranaj@yahoo.com
5. MD, General Practitioner, Department of Obstetrics and Gynecology, Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran. dr.mobasseri@yahoo.com
6. MD, Obstetrician and Gynecologist, Department of Obstetrics and Gynecology, Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran. drmahjabin@yahoo.com
7. MD, Obstetrician and Gynecologist, Department of Obstetrics and Gynecology, Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran. dr.mohabatian@gmail.com
8. MD, Resident of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran. shideh.ryn@yahoo.com
9. MSc, Pars Advanced Minimally Invasive Manners Research Center, Iran University of Medical Sciences, Tehran, Iran. yousefmoradi211@yahoo.com

fects 9% of women of reproductive age (2). It is estimated that 3.5% of women with infertility have a congenital Mullerian uterine anomaly, a 21-fold incre ased prevalence compared to normal fertile women (1).

For this high prevalence, one of the first steps in the workup of female infertility is a radiologic evaluation for Müllerian anomalies. The optimal diagnostic test should be accurate, cost-effective, and minimally invasive. Hysterosalpingography (HSG) demonstrates fallopian tubal patency, submucosal fibroid, endometrial polyp, hypertonia, hyperkinesia, and intrauterine adhesions and septa. Abdominal ultrasound displays external anatomy of the uterus and fallopian tubes, even in patients with an imperforate hymen, artic vagina, and transverse vaginal septum, without the risk of radiation, contrast allergy, uterine perforation, and infection (3). Hysteroscopy is known as the gold standard method for the visualization of the Müllerian structures and simultaneous treatment. Although hysteroscopy is safe and efficient, this invasive procedure is associated with increased risk of uterine cavity perforation, fluid overloads, bleeding and infection (4-6).

HSG and ultrasound are routinely used in the evaluation of infertility, and the accuracy of each modality in comparison of hysteroscopy as the gold standard method have been evaluated. However, the accuracy of their combination is still indeterminate. So the aim of this study was to compare the diagnostic accuracy of combined transvaginal sonography (TVS) and HSG with that of hysteroscopy in the assessment of uterine anomalies.

Methods

After approval by Ethics Committee of Iran University of Medical Sciences, the study was performed on medical records of infertile women who had diagnostic or therapeutic hysteroscopy at the Department of Obstetrics and Gynecology of Rasoul e Akram Hospital, Tehran, Iran, between Januarys and March 2013. Our study population was infertile women with the report of Müllerian anomalies in their TVS or HSG evaluation that random elected. The analysis was performed on patient's records which had complete data of prior two-dimensional TVS, HSG and hysteroscopy all done in our center.

Data of a full medical history and complete gynecologic physical examination was extracted from clinical visits for all patients. Infertility was defined as the absence of conception in the at least past 12 months, despite unprotected intercourse. The age, duration of infertility, duration of the marriage, history of fertility or abortion, and menstrual characteristics of patients were recorded. Menstrual bleeding was categorized as irregular if each cycle lasted >35 days or the cycle length varied>10 days. Infertility was categorized as primary or secondary based on the presence of any previous conception. Abortion was defined as spontaneous loss of the fetus before 20 weeks of gestation.

All Participants had undergone TVS, HSG and hysteroscopy examination in our center. Hysteroscopy had performed by experienced gynecologists during the proliferative phase of menstrual cycle, with a 4.5-mm rigid hysteroscopy equipped with a 30 degree lens. Normal saline was used as the distension medium, and a cuff-mounted manometer controlled the pressure between 80 and 100 mmHg. All procedures were undertaken under general anesthesia and without prophylactic antibiotic.

TVS had performed at Radiology Department after proper preparation. HSG had performed and interpreted by gynecologists during the proliferative phase of menstrual cycle. HSG initiates with an injection of 10-ml contrast medium with a sterile cannula into the uterine cavity after placement of a vaginal speculum. Then three plain radiographs were taken to illustrate filled view of the uterine cavity, filled view of fallopian tubes, and contrast medium leak into the abdomen.

Data were analyzed using the SPSS version 19. Results are presented as numbers

Table 1. Demographic data of the patients who underwent hysteroscopy

Number of patients	99
Mean±SD Age (year)	29.10± 6.47
Mean±SD duration of Marriage (year)	8.93± 10.28
Mean±SD duration of Infertility (year)	5.59± 4.16
Menstrual bleeding Pattern	
Regular, N (%)	54 (54.6)
Irregular, N (%)	45 (45.4)
Infertility kind	
Primary, N (%)	55 (55.6)
Secondary, N (%)	44 (44.4)
History of abortion, N (%)	28 (28.3)

and percentages. The mean±SD duration of marriage and infertility were calculated separately. The sensitivity, specificity, and positive and negative predictive values of ultrasound and HSG were compared to hysteroscopy as the gold standard. Accuracy was calculated as:

(True Positive + True Negative)/ (True Positive +False Positive + True Negative +False Negative)

Also in the study used of LR to calculate the probability of disorder while adapting to varying prior probability of the chance of disease from different contexts.

Likelihood ratio calculated with:

Positive likelihood ratio: Sensitivity / 1-specificity and negative likelihood ratio: 1-sensitivity / specificity

Results

Data collected from 99 patients who underwent all three diagnostic modalities. The mean±SD age, mean±SD duration of marriage, and mean±SD duration of infertility were 29.1± 6.47 years, 8.9±10.28 years, and 5.6±4.16 years, respectively. Of the enrolled patients, 32.4% had, at least, one previous conception. Forty-five patients (45.4%) had an irregular menstrual bleeding history. Only 28 women (28.3%) had the history of abortion. Table 1 shows the demographic data of infertile population who underwent hysteroscopy.

The diagnostic accuracy parameters of TVS, HSG, and the combination of both modalities are shown in Table 2. TVS reported 10 (11.3%) patients as abnormal while only 30 (30.3%) of them were confirmed using hysteroscopy (sensitivity=98.55%, specificity=30%, PPV=76.4%, NPP=90%). HSG detected abnormality in 21 (22%) patients while only 78 (78%) were normal with this test (sensitivity=95.6%, specificity=60%, PPV=84.62%, NPP=85.71%). When both modalities were combined, the sensitivity, specificity, PPV, and NPV were 94.2%, 66.67%, 86.67%, and 83.33%, respectively. Positive likelihood ratios for TVS, HSG, and combined modalities were 1.41, 2.39, and 2.83, respectively. The diagnostic accuracy of single TVS, HSG or combined techniques was statistically similar that was equal to 77.7, 84.8 and 85.8 % respectively.

Table 2. Diagnostic accuracy parameters of TVS, HSG, and combination of both modalities for uterine malformations (n=99)

	Sensitivity (%)	Specificity (%)	PPV (%)	NPP (%)	LR+	LR-	Accuracy
TVS	98.55 (92.19 – 99.9)	30 (14.7 – 49.4)	76.4 (66.22 – 84.22)	90.0 (55.5 – 99.7)	1.41 (1.11 - 1.78)	0.05 (0.01 – 0.36)	77.7 (68.3 – 85.5)
HSG	95.6 (87.8 – 99.09)	60 (40.6 – 77.3)	84.62 (74.67 – 91.79)	85.71 (63.66 – 96.95)	2.39 (1.54 – 3.72)	0.07 (0.02 – 0.23)	84.8 (76.2 – 91.2)
TVS+ HSG	94.2 (85.8 – 98.4)	66.67 (47.19 - 82.71)	86.67 (76.84 – 93.42)	83.33 (62.62 – 95.26)	2.83 (1.70 – 4.70)	0.09 (0.03 – 0.23)	85.8 (77.4 – 92.0)

Note: Prevalence=48.5%, the numbers in parentheses are the limits of the 95% confidence interval.
TVS: Transvaginalsonography, HSG: Hysterosalpingography, PPV: Positive predictive value, NPV; Negative predictive value
LR+: Positive likelihood ration, LR-: Negative likelihood ratio.

Discussion

We found that when both modalities (TVS ad HSG) were combined, the sensitivity, specificity, PPV, and NPV were 94.2, 66.67, 86.67, and 83.33%, respectively. So HSG and the combination of both diagnostic modalities are accurate enough and are not different for assessing uterine malformation in infertile women. The accuracy of both is higher than TVS alone.

Müllerian anomalies are associated with infertility, so an accurate diagnosis of these defects would result in proper management of infertility (7). Although the gold standard for diagnosis is hysteroscopy, there is a need for a noninvasive, easy and accurate method for evaluating infertile patients with suspected malformations. The aim of this study was to compare the accuracy of the combination of two other methods with hysteroscopy in infertile population.

Ultrasound is the preferred diagnostic test of Müllerian anomalies in some centers because of its several advantages. It is an easy, economical, quick, non-invasive method for visualizing the external contour of uterine and myometrium simultaneously. This radiation-free test is widely available and needs no special preparation. However, the quality of its image easily degraded by bowel gas or abdominal fat pad. TVS can reveal more detailed information (3).

In the present study, ultrasound only identified uterine abnormalities in 19 of 48 defects, missing almost 60%. In a similar study, Caliskan et al. (8) reported the sensitivity and specificity of two-dimensional sonography as 30.2 and 78.1% in the follicular phase (42.1 and 81.2% in the luteal phase, respectively). Soares et al. (9) have reported a sensitivity of 44.4%, specificity of 100%, PPV of 100%, and NPV of 91.8% for TVS in the diagnosis of uterine malformations. On the contrary, TVS has demonstrated 100% sensitivity and 80% specificity in detecting Müllerian anomalies in a study by Pillerito et al. (10). Although the operator's experience and the type of transducer might result in different test accuracy, owning to its poor sensitivity in this series, 2D TVS does not seem like a suitable tool for screening uterine anomalies.

In our study HSG had not similar diagnostic sensitivity to TVS. The overall accuracy of HSG for identifying uterine malformations was almost 84.8 %. In a study by Acholonu et al. (11) the HSG had the sensitivity of 58.2% and specificity of 25.6% (accuracy, 50.3%) for detecting Müllerian anomalies in infertile population. Sakar et al. (12) compared the HSG with laparoscopy and reported the sensitivity of 63%, specificity of 89.3%, PPV of 92%, NPV of 55%, and total accuracy of 72% in diagnosing peritoneal factors of infertility. Another study of 216 infertile women presented the sensitivity of 80.3%, specificity of 70.1%, PPV of 84.5%, NPV of 64.5%, and accuracy of 76.4% for HSG in detecting intrauterine abnormalities (13). Brown et al. (14) estimated 60% accuracy of HSG for detecting Müllerian anomalies. Reuter et al. (15) reported the accuracy of differential diagnosis of septate and bicornate uterine HSG interpreted by a radiologist, a gynecologic, and combined with ultrasound examination as 55, 62.5 and 90% respectively. Others have reported the accuracy of 22.2% for HSG (10).

There are reports of more accurate diagnostic methods. Bocca et al. (16) analyzed the accuracy, costs, risks and benefits of 3D TVS and HSG among an infertile population with confirmed congenital Müllerian anomalies and reported the 3D TVS a more accurate, cost-effective, and safer method. Other investigators have also recommended 3D TVS for detecting Müllerian anomalies (8,17). In a study by Faivre et al. (18), 3D TVS was compared with hysteroscopy and MRI in differential diagnosis of bicornate and septate uterus and the reported accuracy was 100, 90 and 77% for each diagnostic method respectively; they concluded that the 3D TVS is a mandatory step in the assessment of patients with suspected anomalies.

The main limitation of our study was its retrospective design. Hysteroscopy is not usually performed in patients with normal ultrasound or HSG findings, so the diagnostic accuracy of these methods could be easily affected. Because both diagnostic tests are interpreted by physicians, the experience of the clinician influences the results.

Conclusion

In conclusion, 2D TVS, HSG, and the combination of both diagnostic modalities are not accurate enough for detecting uterine malformations. Further studies are needed to evaluate the accuracy of 3D TVS and its combinations in the diagnosis of different uterine anomalies

References

1. Reichman DE, Laufer MR. Congenital uterine anomalies affecting reproduction. Best Pract Res Clin Obstet Gynaecol 2010 Apr;24(2):193-208.
2. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod 2007 Jun; 22(6):1506-12.
3. Pui MH. Imaging diagnosis of congenital uterine malformation. Comput Med Imaging Graph. 2004 Oct;28(7):425-33.
4. Jansen FW, Vredevoogd CB, van Ulzen K, Hermans J, Trimbos JB, Trimbos-Kemper TC. Complications of hysteroscopy: a prospective, multicenter study. Obstet Gynecol 2000 Aug; 96(2):266-70.
5. Izetbegovic S. [Early and late complications in patients treated with hysteroscopic surgery]. Med Arh 2002;56(4):217-9.
6. Shveiky D, Rojansky N, Revel A, Benshushan A, Laufer N, Shushan A. Complications of hysteroscopic surgery: "Beyond the learning curve". J Minim Invasive Gynecol 2007 Mar-Apr; 14(2):218-22.
7. Taylor E, Gomel V. The uterus and fertility. Fertil Steril 2008 Jan;89(1):1-16.
8. Caliskan E, Ozkan S, Cakiroglu Y, Sarisoy HT, Corakci A, Ozeren S. Diagnostic accuracy of real-time 3D sonography in the diagnosis of congenital Mullerian anomalies in high-risk patients with respect to the phase of the menstrual cycle. J Clin Ultrasound 2010 Mar-Apr;38(3):123-7.
9. Soares SR, Barbosa dos Reis MM, Camargos AF. Diagnostic accuracy of sonohysterography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases. Fertil Steril 2000 Feb;73(2):406-11.
10. Pellerito JS, McCarthy SM, Doyle MB, Glickman MG, DeCherney AH. Diagnosis of uterine anomalies: relative accuracy of MR imaging, endovaginal sonography, and hysterosalpingography. Radiology 1992 Jun; 183(3):795-800.
11. Acholonu UC, Silberzweig J, Stein DE, Keltz M. Hysterosalpingography versus sono-hysterography for intrauterine abnormalities. JSLS 2011 Oct-Dec;15(4):471-4.
12. Sakar MN, Gul T, Atay AE, Celik Y. Comparison of hysterosalpingography and laparoscopy in the evaluation of infertile women. Saudi Med J 2008 Sep;29(9):1315-8.
13. Wang CW, Lee CL, Lai YM, Tsai CC, Chang MY, Soong YK. Comparison of hysterosalpingography and hysteroscopy in female infertility. J Am Assoc Gynecol Laparosc 1996 Aug;3(4):581-4.
14. Brown SE, Coddington CC, Schnorr J, Toner JP, Gibbons W, Oehninger S. Evaluation of outpatient hysteroscopy, saline infusion hysterosonography, and hysterosalpingography in infertile women: a prospective, randomized study. Fertil Steril 2000 Nov;74(5):1029-34.
15. Reuter KL, Daly DC, Cohen SM. Septate versus bicornuate uteri: errors in imaging diagnosis. Radiology. 1989 Sep;172(3):749-52.
16. Bocca SM, Oehninger S, Stadtmauer L, Agard J, Duran EH, Sarhan A, et al. A study of the cost, accuracy, and benefits of 3-dimensional sonography compared with hysterosalpingography in women with uterine abnormalities. J Ultrasound Med 2012 Jan;31(1):81-5.
17. Ghi T, Casadio P, Kuleva M, Perrone AM, Savelli L, Giunchi S, et al. Accuracy of three-dimensional ultrasound in diagnosis and classification of congenital uterine anomalies. Fertil Steril 2009 Aug;92(2):808-13.
18. Faivre E, Fernandez H, Deffieux X, Gervaise A, Frydman R, Levaillant JM. Accuracy of three-dimensional ultrasonography in differential diagnosis of septate and bicornuate uterus compared with office hysteroscopy and pelvic magnetic resonance imaging. J Minim Invasive Gynecol 2012 Jan-Feb;19(1):101-6.