Received:
30 November 2015

Revised:
24 March 2016

Accepted:
21 April 2016

<http://dx.doi.org/10.1259/bjr.20151013>

Cite this article as:

Wang Y, Qian L. Three- or four-dimensional hysterosalpingo contrast sonography for diagnosing tubal patency in infertile females: a systematic review with meta-analysis. *Br J Radiol* 2016; **89**: 20151013.

FULL PAPER

Three- or four-dimensional hysterosalpingo contrast sonography for diagnosing tubal patency in infertile females: a systematic review with meta-analysis

YUELONG WANG, MM and LINXUE QIAN, MD

Department of Ultrasound, Beijing Friendship Hospital affiliated to Capital Medical University, Beijing, China

Address correspondence to: Mrs Lin-xue Qian
E-mail: qianlinxue2002@163.com

Objective: To assess the diagnostic value of three-dimensional (3D) or four-dimensional (4D) hysterosalpingo contrast sonography (HyCoSy) for detecting tubal patency in infertile females.

Methods: A comprehensive search was conducted to identify related research. The pooled results were calculated by diagnostic meta-analysis with bivariate mixed-effects binary regression. Subgroup analyses and publication bias were further performed.

Results: 23 studies, including 1153 females with 2259 detected fallopian tubes, were identified. The pooled estimates of sensitivity and specificity were 0.92 [95%

confidence interval (CI): 0.90–0.94, $I^2 = 36.68$] and 0.91 (95% CI: 0.89–0.93, $I^2 = 38.99$), respectively. The area under the receiver-operating characteristic curve was 0.97 (95% CI: 0.95–0.98). No publication bias was observed.

Conclusion: 3D/4D HyCoSy is an accurate test for diagnosing tubal patency in infertile females.

Advances in knowledge: 3D/4D HyCoSy is an accurate test for diagnosing tubal patency in females suffering from infertility, whilst overcoming some main limitations of other methods. 3D/4D HyCoSy is recommended as a fundamental test for female infertility.

INTRODUCTION

A global research found that the global prevalence of infertility had hardly changed between 1990 and 2010, and estimated 48.5 million couples worldwide have difficulty in having a baby after 5 years in 2010.¹ Morphological and functional abnormalities of the fallopian tubes, such as obstruction, distortion, stiffness and peristaltic incongruity arising from various diseases, account for 25–30% of all cases of infertility.² Accurate evaluation of tubal patency can provide an important evidence for clinical targeted treatments. Therefore, the accurate evaluation of tubal patency is one of the fundamental steps in the diagnostic work-up of infertile females.

Laparoscopy and dye intubation (lap and dye) has long been regarded as the gold standard investigation for tubal patency; but, in the public sector, there are concerns about long time delay and expense as well as anaesthetic and operation risks.³ The more easily accessible hysterosalpingography involves X-ray exposure and the risk of a hypersensitivity reaction to the iodinated contrast medium.⁴ Compared with these procedures, transvaginal hysterosalpingo contrast sonography (HyCoSy) is a non-invasive, safe and cost-effective method, providing a rapid, easily conducted and reliable diagnosis for tubal patency.^{5–7}

So far, several research have made some attempts to evaluate the accuracy of HyCoSy in tubal patency diagnosis, compared with traditional techniques. A meta-analysis with most two-dimensional (2D) HyCoSy studies showed that HyCoSy was better than hysterosalpingography in diagnosing tubal occlusion and should be in the initial work-up of subfertile couples.⁸ In recent years, with the development of ultrasound imaging technology, three-dimensional (3D) or four-dimensional (4D) HyCoSy is widely studied in the diagnostic work-up of infertile females. However, the results of each study for 3D/4D HyCoSy were inconsistent^{9–12} and the inadequate sample size in the individual study could not attain the precise outcome.

Meta-analysis is a useful method to overcome the shortages of individual studies, analyze the reasons of inconsistent results and increase the statistical power and the precision of effect estimates. In this study, our objective was to determine the diagnostic accuracy of 3D/4D HyCoSy for detecting tubal patency in females suffering from infertility.

METHODS AND MATERIALS

This article was written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses.¹³

Figure 1. Flow diagram of study selection in meta-analysis. 3D/4D HyCoSy, three-dimensional or four-dimensional hysterosalpingo contrast sonography.

Search strategy

Studies were identified using a search standard in PubMed, Web of Science, Scopus, Cochrane Library, China National Knowledge Infrastructure, Wanfang database, Database of Chinese Scientific and Technical Periodicals from inception to 24 July 2015. Search items were listed as follows: (fallopian tube* OR uterine tube* OR oviduct OR ovarian duct* OR tubal occlusion OR tubal pathology OR tubal patency) AND (hysterosalpingosonography OR ((ultrasound OR ultrasonic OR ultrasonography OR echography OR sonography) AND (contrast OR angiography))). In addition, the references from potential articles were reviewed to find out other relevant research. If

some relevant articles were derived from a unique research project, only the article with more complete participants would be brought into this study.

Inclusion criteria

All identified studies were carefully reviewed to determine whether an individual study was eligible for the following pre-defined criteria:

- (1) population of interest: infertile females
- (2) index test: three-dimensional or four-dimensional HyCoSy
- (3) reference test: laparoscopy as gold standard
- (4) outcomes: the data of true positive (TP), false positive (FP), false negative (FN) and true negative (TN) fallopian tubes for each study could be directly or indirectly obtained
- (5) study design: diagnostic test study
- (6) the number of subjects participating in both index and reference test should be more than 20 in the included studies
- (7) there were no restrictions in publication date or language.

Data extraction and quality assessment

A data extraction sheet was developed which included the first authors, publication year, country where the study was performed, sample size, age, the number of fallopian tubes, 3D or 4D type, contrast agent, contrast resolution and the number of TP, FP, FN and TN of fallopian tubes. In published articles, the definition of a positive test alternated between the presence of an occluded tube and the presence of a patent tube. In our study, a positive test was uniformly defined as an occluded tube by way of summarizing the pooled data. The Quality Assessment of Diagnostic Accuracy Study 2 was used to estimate the quality of the included studies.¹⁴ Study inclusion, data extraction and quality assessment were performed by two independent investigators (YW and LQ). Any disagreement was settled by discussion.

Statistical analysis and data synthesis

Diagnostic meta-analysis was performed by computing the number of TP, FP, FN and TN of each study in bivariate mixed-effects binary regression using Stata v. 13.1 (Stata Corporation, College Station, TX). Pooled and individual estimates of sensitivity, specificity and 95% confidence intervals (CIs) were presented in paired

Figure 2. Risk of bias and applicability concerns based on the Quality Assessment of Diagnostic Accuracy Study 2 presented as percentages across included studies.

Figure 3. Forest plot of three-dimensional or four-dimensional hysterosalpingo contrast sonography (sensitivity and specificity) for diagnosing tubal patency. CI, confidence interval; df, degree of freedom; Ref, reference.

forest plots. The Q test and I^2 were used to assess the heterogeneity among included studies.¹⁵ The summary receiver-operating characteristic (SROC) curves with point estimates were generated to present the symmetrical summary curves and summary point estimates with their 95% CIs and 95% prediction intervals. The publication bias in diagnostic meta-analyses was assessed by linear regression of log odds ratios in the funnel plot asymmetry.¹⁶ A two-sided probability (p -value) <0.05 was regarded as statistically significant.

RESULTS

Study characteristics

The entire inclusion process of our study is demonstrated in Figure 1, and 23 eligible articles were included in this meta-analysis. Among them, 3 articles were published in English,^{9,11,12} 1 article in German,¹⁷ 1 article in Romanian¹⁸ and 18 articles in Chinese.^{10,19–35} 3 studies were conducted in Caucasians and^{10,19–18} 20 studies were performed in Chinese. 16 and 7 studies reported the diagnostic accuracy of 3D and 4D HyCoSy for detecting tubal patency in infertile females. The contrast agent was Echovist (Schering AG, Berlin, Germany) in 3 studies, saline solution in 1 study and SonoVue (Bracco, Milan, Italy) in 19 studies. General characteristics and data of these

studies included in this meta-analysis are shown in Table 1. Figure 2 summarizes the risk of bias and applicability concerns of the studies based on the Quality Assessment of Diagnostic Accuracy Study 2.

Accuracy of three-dimensional or four-dimensional hysterosalpingo contrast sonography for diagnosing tubal patency

23 studies, including 1153 females with detected 2259 fallopian tubes, served to estimate the global accuracy of 3D/4D HyCoSy for diagnosing tubal patency. From the forest plot in Figure 3, pooled estimates of sensitivity and specificity were 0.92 (95% CI: 0.90–0.94, with $I^2 = 36.68$) and 0.92 (95% CI: 0.89–0.93 with $I^2 = 38.99$), respectively. The corresponding SROC curve is presented in Figure 4 and the small prediction circle also reflects the weak heterogeneity between the studies. The area under the receiver-operating characteristic curve in the SROC plot was 0.97 (95% CI: 0.95–0.98).

Subgroup analyses and publication bias

Although the heterogeneity between the studies was not strong, subgroup analyses were also performed to analyze the inherent difference among these included studies. The results

Figure 4. Summary receiver-operating characteristic (SROC) curve for diagnosing tubal patency. The numbers in the circles are listed in Table 1. AUC, area under the curve; SENS, sensitivity; SPEC, specificity.

of subgroup analyses are shown in Table 2. The differences among the races (Caucasian and Chinese), number of tubes (<100 and ≥ 100), ultrasonic dimension (3D and 4D), agent

(SonoVue and others) and risk of bias (low and high) were not statistically significant. No publication bias was observed in this meta-analysis (p -value = 0.29 in Figure 5).

Figure 5. Funnel plot and Deek's funnel plot asymmetry test of this diagnostic meta-analysis. The numbers in circles are listed in Table 1. ESS, effective sample size.

Table 1. Characteristics of cross-sectional studies in the diagnostic meta-analysis

Number of studies	Authors	Years	Country	Subjects	Age (median/mean)	Tubes (excluded)	Contrast agent	Resolution (MHz)	3D/4D	TP ^a	FP ^a	FN ^a	TN ^a
1	Watermann et al ¹⁷	2004	Germany	21	NA	42 (0)	Echovist (Schering AG, Berlin, Germany)	5–8	3D	4	3	1	34
2	Chan et al ¹²	2005	Hongkong, China	21	33.6	34 (8)	Echovist	7	3D	6	0	3	25
3	Kupesic et al ¹¹	2007	Croatia	116	32	232 (0)	Echovist	5–7	3D	108	2	4	118
4	Socolov et al ¹⁸	2009	Romania	95	31	181 (9)	Saline	7	3D	35	17	8	121
5	Wang et al ¹⁹	2011	China	32	33	64 (0)	SonoVue (Bracco, Milan, Italy)	NA	3D	10	1	0	53
6	Wang et al ²⁰	2012	China	40	36	80 (0)	SonoVue	NA	3D	36	3	2	39
7	Zhang et al ²¹	2012	China	78	29	156 (0)	SonoVue	5.0–7.5	3D	106	7	8	35
8	Cai et al ²²	2013	China	95	28	190 (0)	SonoVue	3.75–9.25	3D	80	13	6	91
9	Liang et al ²³	2013	China	42	30	80 (4)	SonoVue	3.7–9.0	3D	55	5	3	17
10	Luo et al ¹⁰	2013	China	25	32	49 (1)	SonoVue	3.5–7.5	3D	18	4	2	25
11	Xiong et al ²⁴	2013	China	38	28.3	76 (0)	SonoVue	6–8	3D	31	4	1	40
12	Xu et al ²⁵	2013	China	20	29	40 (0)	SonoVue	NA	3D	15	1	0	24
13	Zhang et al ²⁶	2013	China	35	31.2	70 (0)	SonoVue	6–8	4D	14	3	2	51
14	Zhou et al ²⁷	2013	China	39	29	74 (4)	SonoVue	3.7–9.0	4D	29	7	4	34
15	Han et al ²⁸	2014	China	72	29.3	140 (4)	SonoVue	6–9	4D	73	7	5	55
16	Li et al ²⁹	2014	China	59	31	118 (0)	SonoVue	NA	4D	53	4	3	58
17	Wang et al ³⁰	2014	China	33	29.4	66 (0)	SonoVue	3.7–9.0	3D	40	2	3	21
18	Wu et al ³¹	2014	China	36	30.5	72 (0)	SonoVue	5–9	3D	29	4	4	35
19	Zhang et al ³²	2014	China	30	27.1	60 (0)	SonoVue	2–5	4D	32	3	4	21
20	Cheng et al ⁹	2015	China	39	29.6	77 (1)	SonoVue	5–9	3D	43	5	2	27

(Continued)

Table 1. (Continued)

Number of studies	Authors	Years	Country	Subjects	Age (median/mean)	Tubes (excluded)	Contrast agent	Resolution (MHz)	3D/4D	TP ^a	FP ^a	FN ^a	TN ^a
21	Li et al ³³	2015	China	88	29.4	169 (7)	SonoVue	5–9	4D	41	8	9	111
22	Lin et al ³⁴	2015	China	42	30.1	84 (0)	SonoVue	5–9	3D	39	3	4	38
23	Zhang et al ³⁵	2015	China	57	32.2	105 (9)	SonoVue	4–9	4D	45	5	6	49

3D, three-dimensional; 4D, four-dimensional; FN, false negative; FP, false positive; NA, not available; No., the number of study; TN, true negative; TP, true positive.

^aThe number of included fallopian tubes.

DISCUSSION

The timely and accurate evaluation of tubal patency is essential for the diagnosis and treatment of female infertility. At present, this systematic review showed a high diagnostic accuracy of 3D/4D HyCoSy for tubal patency with an overall sensitivity of 0.92 (95% CI: 0.90–0.94) and specificity of 0.91 (95% CI: 0.89–0.93). The results had a good stability among these included studies.

A previous meta-analysis with most 2D HyCoSy studies showed that the sensitivity and specificity of 2D HyCoSy were, 0.88 (95% CI: 0.80–0.94) and 0.92 (95% CI: 0.86–0.96), respectively.⁸ For the sensitivity and specificity of 2D HyCoSy significantly overlapped with 3D/4D HyCoSy, the variation of sensitivity and specificity among different dimensional HyCoSy has not yet been determined. However, some limitations and difficulties of conventional 2D HyCoSy are often encountered in clinical operation. For instance, the tubal structure cannot be observed entirely in any scanning window because of its tortuosity and different visualized images relied on specific occasions.⁷ Compared with 2D HyCoSy, 3D HyCoSy requires less time,³⁶ avoids difficult probe movements and is less dependent on operator skill.^{4,7,37} Automated 3D volume acquisition of the entire fallopian tube easily shows the course of the tube and image acquisition also permits storage and later analyses of captures.^{7,38} However, because the 3D HyCoSy is a static imaging method, it cannot display the real-time process of contrast agent flow in fallopian tubes. Moreover, it is difficult to identify the morphology of the fallopian tubes by 3D HyCoSy among patients with myometrium venous reflux. These disadvantages can be overcome by the 4D HyCoSy, a real-time 3D HyCoSy.^{32,35}

The newer ultrasound contrast agents and imaging technology progress have made 3D/4D HyCoSy images clearer and more intuitive. The included studies used a newer generation of ultrasound contrast agent SonoVue (sulfur hexafluoride microbubbles), which has been widely applied in heart and blood vessel angiography.^{39,40} Moreover, 3D/4D HyCoSy also provides an adequate evaluation for the uterine cavity.⁵ But, the cost of both the new machine and contrast medium is considerable in clinical practice.³⁷

This study systematically assessed the diagnostic accuracy of 3D/4D HyCoSy for detecting tubal patency in females suffering from infertility. No strong heterogeneity between studies and publication bias was observed. However, some limitations of the present meta-analysis should be taken into consideration when interpreting the results. First, the present meta-analysis was based on original data and the potential confounding factors were not adjusted. Second, because it was very difficult to retrieve entire databases in various languages, we only searched the mainstream English and Chinese databases. The final results might not be applicable for other countries since most studies were conducted in China. Third, the distinction between distal and proximal tubal patency could not be analyzed in this study. It might be significant to differentiate the tubal location in future research diagnosing tubal patency by 3D/4D HyCoSy. Finally, the safety and pain of 3D/4D HyCoSy was not summarized

Table 2. Subgroup analyses to explore the potential difference among studies

Variables	Number of studies	Number of females	Number of tubes	Sensitivity (95% CI)	Specificity (95% CI)	<i>p</i> -values
Race						
Caucasian	3	232	455	0.91 (0.85–0.97)	0.93 (0.89–0.97)	0.49
Chinese	20	921	1804	0.92 (0.90–0.94)	0.91 (0.89–0.93)	
Tubes						
<100	15	493	968	0.92 (0.89–0.95)	0.91 (0.88–0.94)	0.94
≥100	8	660	1291	0.92 (0.89–0.94)	0.91 (0.88–0.94)	
Ultrasonic dimension						
3D	16	773	1523	0.93 (0.91–0.95)	0.91 (0.89–0.94)	0.33
4D	7	380	736	0.90 (0.86–0.93)	0.91 (0.88–0.95)	
Contrast agent						
SonoVue (Bracco, Milan, Italy)	19	995	308	0.92 (0.90–0.95)	0.91 (0.89–0.93)	0.12
Others	3	158	1951	0.89 (0.83–0.96)	0.94 (0.90–0.98)	
Risk of bias ^a						
Low bias	10	502	1277	0.92 (0.89–0.95)	0.91 (0.88–0.94)	0.99
High bias	13	651	982	0.92 (0.89–0.95)	0.91 (0.89–0.94)	

3D, three-dimensional; 4D, four-dimensional; CI, confidence interval.

^aGlobal appreciation for risk of bias and applicability concerns based on the Quality Assessment of Diagnostic Accuracy Study 2.

because most included studies did not report the corresponding information.

In conclusion, 3D/4D HyCoSy is an accurate test for diagnosing tubal patency in females suffering from infertility, whilst overcoming some main limitations of other methods. In fact, it does

not require radiation exposure, anaesthesia and operation risk and does not involve the use of iodinated contrast media. 3D/4D HyCoSy is recommended as a fundamental test for female infertility. In addition, an economic study comparing the cost-utility of 3D/4D HyCoSy and other methods would be an interesting perspective for clinical application.

REFERENCES

- Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. *PLoS Med* 2012; **9**: e1001356. doi: <http://dx.doi.org/10.1371/journal.pmed.1001356>
- Shalev J, Krissi H, Blankstein J, Meizner I, Ben-Rafael Z, Dicker D. Modified hysterosalpingography during infertility work-up: use of contrast medium and saline to investigate mechanical factors. *Fertil Steril* 2000; **74**: 372–75. doi: [http://dx.doi.org/10.1016/S0015-0282\(00\)00632-4](http://dx.doi.org/10.1016/S0015-0282(00)00632-4)
- Jansen FW, Kapiteyn K, Trimbos-Kemper T, Hermans J, Trimbos JB. Complications of laparoscopy: a prospective multicentre observational study. *Br J Obstet Gynaecol* 1997; **104**: 595–600. doi: <http://dx.doi.org/10.1111/j.1471-0528.1997.tb11539.x>
- Watrelet A, Hamilton J, Grudzinskas JG. Advances in the assessment of the uterus and fallopian tube function. *Best Pract Res Clin Obstet Gynaecol* 2003; **17**: 187–209.
- Lo Monte G, Capobianco G, Piva I, Caserta D, Dessole S, Marci R. Hysterosalpingo contrast sonography (HyCoSy): let's make the point! *Arch Gynecol Obstet* 2015; **291**: 19–30. doi: <http://dx.doi.org/10.1007/s00404-014-3465-4>
- Panchal S, Nagori C. Imaging techniques for assessment of tubal status. *J Hum Reprod Sci* 2014; **7**: 2–12. doi: <http://dx.doi.org/10.4103/0974-1208.130797>
- Exacoustos C, Di Giovanni A, Szabolcs B, Binder-Reisinger H, Gabardi C, Arduini D. Automated sonographic tubal patency evaluation with three-dimensional coded contrast imaging (CCI) during hysterosalpingo-contrast sonography (HyCoSy). *Ultrasound Obstet Gynecol* 2009; **34**: 609–12. doi: <http://dx.doi.org/10.1002/uog.7442>
- Maheux-Lacroix S, Boutin A, Moore L, Bergeron ME, Bujold E, Laberge P, et al. Hysterosalpingosonography for diagnosing tubal occlusion in subfertile women: a systematic review with meta-analysis. *Hum Reprod* 2014; **29**: 953–63. doi: <http://dx.doi.org/10.1093/humrep/deu024>
- Cheng Q, Wang SS, Zhu XS, Li F. Evaluation of tubal patency with transvaginal three-dimensional hysterosalpingo-contrast sonography. *Chin Med Sci J* 2015; **30**: 70–5.

10. Luo YJ, Gulinaer S, Xiang H, Feng YL. Value of vaginal three-dimensional ultrasound angiography in evaluation on the patency of fallopian tube. *Chin J Med Imaging Tech* 2013; **29**: 97–100.
11. Kupesic S, Plavsic BM. 2D and 3D hysterosalpingo-contrast-sonography in the assessment of uterine cavity and tubal patency. *Eur J Obstet Gynecol Reprod Biol* 2007; **133**: 64–9. doi: <http://dx.doi.org/10.1016/j.ejogrb.2006.10.010>
12. Chan CC, Ng EH, Tang OS, Chan KK, Ho PC. Comparison of three-dimensional hysterosalpingo-contrast-sonography and diagnostic laparoscopy with chromoperturbation in the assessment of tubal patency for the investigation of subfertility. *Acta Obstet Gynecol Scand* 2005; **84**: 909–13. doi: <http://dx.doi.org/10.1111/j.0001-6349.2005.00797.x>
13. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009; **339**: b2700. doi: <http://dx.doi.org/10.1136/bmj.b2700>
14. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; **155**: 529–36. doi: <http://dx.doi.org/10.7326/0003-4819-155-8-201110180-00009>
15. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002; **21**: 1539–58. doi: <http://dx.doi.org/10.1002/sim.1186>
16. Song FJ, Khan KS, Dinnes J, Sutton AJ. Asymmetric funnel plots and publication bias in meta-analyses of diagnostic accuracy. *Int J Epidemiol* 2002; **31**: 88–95. doi: <http://dx.doi.org/10.1093/ije/31.1.88>
17. Watermann D, Denschlag D, Hanjalic-Beck A, Keck C, Karck U, Prömpeler H. Hysterosalpingo-contrast-sonography with 3-d-ultrasound—a pilot study. [In German.] *Ultraschall Med* 2004; **25**: 367–72.
18. Socolov D, Lupaşcu IA, Danciu E, Doroftei B, Boian I, Boiculescu L, et al. Sonohysterosalpingography versus hysterosalpingography in the evaluation of uterine and tubal infertility. [In Romanian.] *Rev Med Chir Soc Med Nat Iasi* 2009; **113**: 803–8.
19. Wang H, Zhou Q, Jiang Y, Shang X, Li R, Liu T, et al. Diagnostic value of two-dimensional and three-dimensional hysterosalpingo-contrast sonography in tubal patency. *J Pract Obstetrics Gynecol* 2011; **27**: 824–7.
20. Wang Y, Zhang Y, Qu X, She Y. A comparison between 3D coded contrast imaging 2D hysterosalpingo-contrast-sonography. *J China Med Univ* 2012; **41**: 650–52.
21. Zhang YG, Shi H, Hao LD, Hu JQ. Three dimensional hysterosalpingo-contrast-sonography in diagnosis of fallopian tube infertility. *Chin J Gen Pract* 2012; **11**: 229–31.
22. Cai DM, Chen XL, Zhou LX, Zhang X, Zhou N, Zhou SL, et al. Clinical general evaluation of three-dimensional hysterosalpingo-contrast sonography with SonoVue in the assessment of tubal patency of infertility in 1043 cases. *New Med* 2013; **44**: 824–27.
23. Liang N, Wu QQ, Gao FY, Feng Y, Li JH. Three-dimensional hysterosalpingo-contrast-sonography evaluation of tubal patency. *Chin J Med Imaging Tech* 2013; **29**: 256–59.
24. Xiong X, Gao CY, Sun QL, Yan P. The safety and efficacy of three-dimensional ultrasound imaging in diagnosis of tubal infertility. *Chin J Interv Imaging* 2013; **10**: 163–66.
25. Xu H, Wang LX, Wang JY, Gao XW. The Comparative Study of 2D and 3D hysterosalpingography ultrasound imaging in the dianosis of infertility. *Chin Med J* 2013; **48**: 42–4.
26. Zhang XL, Gu J, Huang ZP, Mao YJ, Zheng RQ, Huang DM. A primary study of transvaginal real-time three-dimensional hysterosalpingo-contrast sonography in the assessment of tube patency. *Chin J Ultrasonogr* 2013; **22**: 970–73.
27. Zhou SF, Chen WW, Yi JB, Cao S. Application of real-time three-dimentioanl hysterosalpingo-contrast-sonography in the diagnosis of fallopian tube patency. *Med J Wuhan Uni* 2013; **5**: 765–69.
28. Han QF, Xie YH, Luo HB, Yuan LH, Liang JD, Liu FY, et al. Evaluation of the patency of fallopian tubes by transvaginal four-dimensional hysterosalpingo-contrast sonography. *J Reprod Med* 2014; **23**: 788–92.
29. Li H, Chen Y, Xue M, Wang Y, Qu X, Zhang Y. A comparative study between 3D coded contrast imaging and radiographic hysterosalpingography. *Chin J Ultrasound Med* 2014; **30**: 923–26.
30. Wang WQ, Chen ZY, Jiang L, He ZH, Cai K, Deng N. Three-dimensional hysterosalpingo-contrast-sonography in the assessment of fallopian tubal patency. *Chin J Med Imaging* 2014; **11**: 853–55.
31. Wu L, He J, Yan LM. Transvaginal three-dimensional ultrasonography diagnosis of infertility in the application of the source in the fallopian. *China Med Pharm* 2014; **4**: 99–101.
32. Zhang Y, Li R, Tian HY, Lv LH, Zhou YJ. Evaluation of tubal patency with transvaginal four-dimensional hysterosalpingo-contrast sonography. *Hebei Med J* 2014; **36**: 2654–56.
33. Li R, Wang Q, Zhang HW. Evaluation of the fallopian tubal patency with real-time three dimensional hysterosalpingo-contrast sonography and influence factors. *J Med Imaging* 2015; **25**: 127–30.
34. Lin Q, Guo QH, Xu R, Lin XQ, Hu FF, You T, et al. Comparison of two-dimensional and three-dimensional hysterosalpingo-contrast sonography in tubal patency. *Fujian Med J* 2015; **37**: 99–102.
35. Zhang XX, Chen JY, Zhang J, Li YX, Fan LX, Yang X, et al. Assessment of transvaginal four-dimensional hysterosalpingo-contrast sonography in evaluation of fallopian tube patency. *J Pract Obstetrics Gynecol* 2015; **31**: 198–201.
36. Sladkevicius P, Ojha K, Campbell S, Nargund G. Three-dimensional power doppler imaging in the assessment of fallopian tube patency. *Ultrasound Obstet Gynecol* 2000; **16**: 644–7. doi: <http://dx.doi.org/10.1046/j.1469-0705.2000.00302.x>
37. Exacoustos C, Di Giovanni A, Szabolcs B, Romeo V, Romanini ME, Luciano D, et al. Automated three-dimensional coded contrast imaging hysterosalpingo-contrast sonography: feasibility in office tubal patency testing. *Ultrasound Obstet Gynecol* 2013; **41**: 328–35. doi: <http://dx.doi.org/10.1002/uog.11200>
38. Kiyokawa K, Masuda H, Fuyuki T, Koseki M, Uchida N, Fukuda T, et al. Three-dimensional hysterosalpingo-contrast sonography (3D-HyCoSy) as an outpatient procedure to assess infertile women: a pilot study. *Ultrasound Obstet Gynecol* 2000; **16**: 648–54. doi: <http://dx.doi.org/10.1046/j.1469-0705.2000.00327.x>
39. Sidhu PS, Allan PL, Cattin F, Cosgrove DO, Davies AH, Do DD, et al. Diagnostic efficacy of SonoVue, a second generation contrast agent, in the assessment of extracranial carotid or peripheral arteries using colour and spectral Doppler ultrasound: a multicentre study. *Br J Radiol* 2006; **79**: 44–51.
40. Senior R, Moreo A, Gaibazzi N, Agati L, Tiemann K, Shivalkar B, et al. Comparison of sulfur hexafluoride microbubble (SonoVue)-enhanced myocardial contrast echocardiography with gated single-photon emission computed tomography for detection of significant coronary artery disease: a large European multicenter study. *J Am Coll Cardiol* 2013; **62**: 1353–61. doi: <http://dx.doi.org/10.1016/j.jacc.2013.04.082>