Original Article
3D hysterosalpingo-contrast sonography (3D-HyCoSy) diagnoses of tubal patency in infertile patients: a meta-analysis

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Abstract: Objective: The present meta-analysis was conducted to get conclusive evidence about the diagnostic accuracy of 3D-HyCoSy for tubal patency. Methods: Potential articles were identified in PubMed, China National Knowledge Infrastructure (CNKI) and Chinese Wanfang database. Stata 12.0 software was used for meta-analysis. Pooled sensitivity and specificity were calculated to evaluate the diagnostic accuracy of 3D-HyCoSy. Also, area under curve (AUC) could demonstrate its detection accuracy. Significant heterogeneity was defined as I² > 50% and P < 0.05. If there was significant heterogeneity, the random effects model was used to pool data, otherwise, the fixed effect model was adopted. Results: 29 articles were included after the detailed search and selection. The pooled sensitivity and specificity of 3D-HyCoSy were 0.91 (0.89-0.94) and 0.92 (0.90-0.94), respectively. Similar results were also revealed in Asian population: sensitivity, 0.91 (0.88-0.93); specificity, 0.92 (0.89-0.94). When laparoscopy was used as gold standard, the detection sensitivity and specificity of 3D-HyCoSy were 0.92 (0.89-0.94) and 0.93 (0.90-0.95), while they were 0.88 (0.82-0.92) and 0.88 (0.82-0.93) compared with hysterosalpingography (HSG). AUC of SROC curve was 0.97 (0.95-0.98). Conclusion: 3D-HyCoSy could be an independent diagnostic biomarker for tubal patency.

Keywords: 3D-HyCoSy, tubal patency, diagnosis, meta-analysis

Introduction

About 30% cases of female infertility are caused by fallopian tubal problems [1]. Detection of tubal status is a crucial step in the diagnosis of infertile women. Hysterosalpingography (HSG) and laparoscopy are always used in the clinical detection of tubal patency [2-4]. Hysterosalpingo-contrast sonography (HyCoSy) is a newly developed technology for evaluating tubal patency. It has been proved to be a more reliable method compared to conventional methods (laparoscopy and HSG). In addition, it is rapid, non-invasive and inexpensive [5-7]. Moreover, it avoids an operation as in laparoscopy and usage of ionizing radiation as in HSG. Few side effects of HyCoSy were observed after the detection.

Both of 3D-HyCoSy and 2D-HyCoSy are extensively used to detect fallopian tubes [8-10]. However, traditional 2D-HyCoSy has several limitations [11]. First, the detection method strongly depends on operators and the interpretation of results is not straightforward. Second, the entire fallopian tube cannot be observed because of the tortuosity of tubes during the inspection. Moreover, it is difficult to distinguish surrounding bowel tissues from tubes, which is brought about by the spill of contrast medium from the fimbrial end of tubes. While 3D-HyCoSy could overcome the limitations of 2D-HyCoSy. It allows the flow of contrast through the full tubes and free spill of contrast to be visualized [12, 13]. Besides, less time is consumed with 3D-HyCoSy, compared to 2D-HyCoSy. Meanwhile, half a dose of contrast medium was required for 3D-HyCoSy. At present, 3D-HyCoSy has been extensively used to detect tubal patency [14-42]. However, no consistent opinion about the diagnostic role of 3D-HyCoSy was extracted due to the influences of ethnicity, district and gold standard.

We initiated the present meta-analysis to obtain more reliable results about the diagnostic role
3D-HyCoSy diagnoses tubal patency

of 3D-HyCoSy for tubal patency. The outcome will help for resolving the tubal problem and improving the treatments of infertile women.

Materials and methods

Articles search

The potential articles were searched in PubMed, China National Knowledge Infrastructure (CNKI) and Chinese Wanfang database with keywords: “three-dimensional hysterosalpingo-contrast sonography” or “3D-HyCoSy” and “tubal patency” or “tubal obstruction” or “tubal occlusion” or “tubal infertility”. The references of obtained articles were also checked during the search.

Inclusion criteria

The inclusion criteria were: (1) the articles explored the diagnostic role of 3D-HyCoSy on tubal patency; (2) the subjects were clinically diagnosed infertile patients; (3) the articles provided data of true positive (TP), false positive (FP), false negative (FN) and true negative (TN) or obtained these data after calculation; (4) the article used laparoscopy or HSG as gold standard.

Exclusion criteria

Studies were excluded if one of the following existed: (1) reviews and repeated literatures; (2) not offering the source of cases and controls and other essential information; (3) not designed as diagnostic studies.

Data extraction

Data was extracted from every study by two independent authors. The data were name of first author, publication year, country, number of patients, number of tubes, gold standard, TP, FP, FN and TN. The discrepancies were resolved by discussion.

Statistical analysis

Pooled sensitivity and specificity represented the diagnostic accuracy of 3D-HyCoSy for evaluating tubal patency. During the analysis, the summary receiver operating characteristic (SROC) curve was plotted and corresponded, the area under curve (AUC) was obtained. $P$ and $P$ values were used to evaluate the heterogeneity across the studies. $I^2 > 50\%$ or $P < 0.05$ indicated significant heterogeneity, then the ran-
Table 1. Characteristics of included studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Patients</th>
<th>Tubes</th>
<th>Patent</th>
<th>Occluded</th>
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</table>

Note: HSG, hysterosalpingography.

Table 2. Results of meta-analysis

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>P, P, heterogeneity between studies</th>
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<td>Asian</td>
<td>0.91 (0.88-0.93)</td>
<td>0.92 (0.89-0.94)</td>
<td>0.00</td>
</tr>
<tr>
<td>Caucasian</td>
<td>0.98 (0.94-1.00)</td>
<td>0.96 (0.91-0.99)</td>
<td>-</td>
</tr>
<tr>
<td>Comparison standard</td>
<td>0.92 (0.89-0.94)</td>
<td>0.93 (0.90-0.95)</td>
<td>0.00</td>
</tr>
<tr>
<td>HSG</td>
<td>0.88 (0.82-0.92)</td>
<td>0.88 (0.82-0.93)</td>
<td>0.93</td>
</tr>
<tr>
<td>Overall</td>
<td>0.91 (0.89-0.94)</td>
<td>0.92 (0.90-0.94)</td>
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</table>

Note: HSG, hysterosalpingography. P, heterogeneity between studies.

Results

Articles selection

After the detailed search, 305 articles were identified from PubMed, CNKI and Wanfang databases (Figure 1). Then, 243 articles were excluded for investigating 2D-HyCoSy, 4D-HyCoSy, HSG and laparoscopy. As for the remaining articles, 23 articles were removed for review studies, pain evaluation after inspection by 3D-HyCoSy, 3D-HyCoSy and pregnancy conducted in Stata 12.0. P < 0.05 indicated statistically significance.
3D-HyCoSy diagnoses tubal patency

Figure 2. Overall analysis of sensitivity and specificity.
3D-HyCoSy diagnoses tubal patency

Figure 3. Detection sensitivity and specificity of 3-D in Asian population.
3D-HyCoSy diagnoses tubal patency

Figure 4. SROC results.

results. Eventually, 29 articles were selected after removing 10 articles for without available data [14-42].

Characteristics of included studies

As shown in Table 1, most studies were based on Chinese population, except studies of Kupesic [14] and Kiyokawa [17]. The present meta-analysis studied 1440 infertile patients and 2817 tubes. The studies confirmed the patency of tubes with laparoscopy or HSG technology.

Detection sensitivity and specificity of 3D-HyCoSy on tubal patency

The sensitivity and specificity of 3D-HyCoSy were calculated based on the comparison with laparoscopy or HSG technology. Overall analysis showed that 3D-HyCoSy served as an accurate detection technology for tubal patency (Table 2; Figure 2). Detection sensitivity and specificity of 3D-HyCoSy were 0.91 (0.89-0.94) and 0.92 (0.90-0.94), respectively. Due to the significant heterogeneity, we conducted subgroup analyses based on Asian and comparison standard (Table 2; Figure 3). In Asian population, high detection accuracy of 3D-HyCoSy was also observed and the corresponding sensitivity and specificity were 0.91 (0.88-0.93) and 0.92 (0.89-0.94). Compared with laparoscopy technology, the detection sensitivity and specificity of 3D-HyCoSy were 0.92 (0.89-0.94) and 0.93 (0.90-0.95), while these index were 0.88 (0.82-0.92) and 0.88 (0.82-0.93) in comparison with HSG. The high detection accuracy of 3D-HyCoSy on tubal patency was also revealed in SROC analysis (Figure 4), in which AUC was presented as 0.97 (0.95-0.98).

Sensitivity analysis of meta-analysis

We extract one study at a time to evaluate its influence on pooled results of meta-analysis. Fortunately, no obvious changes of pooled results were observed during the analysis process.

Heterogeneity and publication bias analysis

In the meta-analysis, there existed significant heterogeneity ($P=0.00$). The subgroup analysis indicated that the heterogeneity might result from the differences in district, studied population and experimental process. As shown in Figure 5, the Deeks’ funnel plot seemed to be symmetry, indicating no publication bias ($P=0.243$).

Discussion

Laparoscopy method is still adopted as the gold standard for tubal assessment, which always brings about false positives with tubal spasm or spill due to imbalanced tubal resistance. The detection with laparoscopy is time consuming and costly, also, it involves the anesthetic and surgical risks [43]. As for HSG, the genital organs experience exposure to ionizing radiation. It causes hypersensitivity reaction due to the usage of contrast medium [44-46].
3D-HyCoSy diagnoses tubal patency

Presently, HyCoSy has become an alternative, non-invasive way for tubal detection. The infertile patients benefit a lot for its invasiveness, inexpensive and avoidance of ionizing radiation. Moreover, it could assess ovarian pathology simultaneously, which is not observed with HSG method [47, 48]. It has been widely accepted that HyCoSy could replace laparoscopy and accelerate the entire detection process. However, the existing problems involved in its performance and interpretation retard the promotion progress, which are reflected in 2D-HyCoSy. Fortunately, a new technique, called 3D-HyCoSy, was developed, which retains the superiority of 2D-HyCoSy technique and simultaneously overcomes disadvantages.

To date, there have been many researches investigating the diagnostic role of 3D-HyCoSy for tubal patency. One study in 25 subfertile women compared 3D-HyCoSy to HSG. The sensitivity and specificity of 3D-HyCoSy were 84% and 100%, respectively [17]. The study based on Chinese population arranged 59 cases with 3D-HyCoSy with laparoscopy as standard method and found that sensitivity and specificity of 3D-HyCoSy were 94% and 95%, respectively [22]. Another study recruited 75 infertile patients and conducted 3D-HyCoSy test before laparoscopy with chromotubation. This technique exhibited a sensitivity of 93.5%, specificity of 86.3%, negative and positive predictive values of 92.6% and 87.8%. There were no significant differences in detection positive rates of 3D-HyCoSy with laparoscopy (82/150 vs. 77/150, P > 0.05) [15]. The study by Wang W et al. detected 33 cases of infertile women with 3D-HyCoSy, compared the results of laparoscopy. The correspondence rare of 3D-HyCoSy was 86.4% (57/66) and sensitivity and specificity were 74% (17/23) and 93% (40/43) [26]. The varied results may be brought about by the influences of ethnicity, district and experimental performance.

In our meta-analysis based on 29 articles, the overall detection sensitivity and specificity of 3D-HyCoSy were 0.91 and 0.92. At the same time, SROC displayed high detection accuracy (0.97). In the analysis process, obvious heterogeneity was observed. So the subgroup analyses were conducted. First, comparisons of 3D-HyCoSy with laparoscopy and 3D-HyCoSy with HSG were performed. Sensitivity and specificity of 3D-HyCoSy were 0.92 and 0.93 for laparoscopy, while 0.88 and 0.88, respectively, for HSG. In the Asian population, 3D-HyCoSy exhibited relatively low sensitivity and specificity, compared to Caucasian population. We speculated that the heterogeneity might result from the differences in adopted gold standard and population races.

However, there are several potential risk factors that may affect the credibility of our results. Only one study was included for Caucasian population. The result about Caucasian population might not be reliable. Meanwhile, HSG was adopted as one of comparison standard, which may not fully explain the differences in detection accuracy of 3D-HyCoSy and HSG. The future analysis should avoid the problems as much as possible.

In a conclusion, 3D-HyCoSy could serve as an independent detection biomarker for tubal patency.
Disclosure of conflict of interest
None.

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