SYSTEMATIC REVIEW

Effectiveness and radiation dose of computerized tomography virtual hysterosalpingography in the evaluation of female infertility: Systematic review and meta-analysis

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Abstract

Objective: To build evidence about the effectiveness of computerized tomography virtual hysterosalpingography (CT-VHSG) in the evaluation of female infertility and to assess the estimated radiation dose imposed.

Methods: A systematic review method was utilized to evaluate relevant diagnostic studies. Electronic database was searched from July to October 2017. Hand search was also conducted when applicable. Study quality was assessed according to standardised criteria. Heterogeneity was assessed using subjective and statistical measures. Meta-analysis was judged appropriate and conducted using Open met-analyst software utilizing the random effect model.

Results: Based on the assessment of risk of bias of the eligible studies, five studies were included in the final review. Random effects models showed that CT-VHSG has high diagnostic performance (pooled sensitivity 0.992 and specificity 0.98, with negative and positive likelihood ratios of 14.671 and 0.04 respectively). CT-VHSG had comparatively lesser radiation dose than conventional HSG (pooled mean effective dose 4.14 mSV vs 6 mSV respectively).

Conclusion: CT-VHSG is a reliable procedure with high diagnostic performance in evaluation of the female reproductive tract. CT-VHSG can be regarded as generally safe imaging diagnostic technique in the infertility workup. In contrary to common belief, CT-VHSG has comparable or lower radiation dose than conventional HSG.

Keywords: Female; infertility; tomography; X-ray computed; hysterosalpingography. (JPMA 71: 114; 2021)

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Introduction

The computerized tomography-virtual hysterosalpingography (CT-VHSG) is a minimally invasive diagnostic modality which allows a complete evaluation of the gynaecological system that is to say uterus, cervix, fallopian tubes and ovaries in a single study, where the multidetector computerized tomography (MSCT) obtains volumetric acquisition in few seconds.[1]The idea arose first in a northern area of Greater Buenos Aires, Argentina and the procedure grows over the years with the technological advances. Patient preparation and contraindications for the CT-VHSG examination are similar to that of conventional hysterosalpingography (con. HSG).[2]

The overall risk of complications with this technique is low compared with conventional HSG. The risks of infection and haemorrhage are greatly minimized with less patient discomfort, however there is a concern about the potentially harmful effects of radiation even with the many techniques that have been developed to reduce the radiation hazard.[3,4]

The examination itself is still relatively new, not widely utilized in radiology diagnostic departments nor routinely requested in the evaluation of infertile women or current gynaecological assessment probably because of the lack of a systematic evidence for its validity and the concern about the associated radiation hazard. Therefore, this systematic review was conducted to build an empirical evidence on the value of CT-VHSG as a reliably effective imaging technique in the evaluation of female infertility. Secondarily, the review also aimed to assess the estimated radiation dose in the CT-VHSG and if this can justify the benefit relative to the con. HSG.

Material and methods

This systematic review of diagnostic studies was conducted between March to September2017, according to established methods and in line with recommendation by Cochrane Collaboration guidelines for systematic review and meta-analysis.[5,6]

Review questions. The following questions were formulated; 1) Is CT-VHSG a reliable imaging modality that can safely replace or add to the current imaging modalities in diagnosis of various uterine, cervical and fallopian tube lesions in infertile women?; 2) Is the radiation dose justifiable for the benefit relative to other diagnostic tests.

Inclusion and exclusion criteria: All prospective and retrospective diagnostic studies that investigated the

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diagnostic value, effectiveness or accuracy of CT-VHSG were selected considering pre-specified criteria (appendix 1).

Search strategy. The review team agreed on a search strategy for the relevant papers. Words used in the search included: [CT or computerized tomography] and [virtual, hysterosalpingography or CT-VHSG or CT-VHSG or VSG]).The search started on 10/2016-10/2017dates in the following databases; websites (PubMed.com, Google scholar.gov, Cochrane.net, Medline and Embase). Hand-search was conducted in the regional and institutional medical libraries. Reference lists search as well as personal contact for information on relevant published or unpublished studies were also done when necessary.

Data extraction. Three investigators (IH, HN and NH) performed the search according to the agreed strategy. All abstracts of the studies with relevant titles were separately screened by all three reviewers. Thereafter, all full texts of the studies that matched the inclusion criteria were thoroughly read and assessed also by the same three reviewers. One investigator (IH) abstracted the study design information, population characteristics, reference test's details, outcome and diagnostic contingency data as well as (sensitivity, specificity, PPV, and NPV when available) and any relevant data from all included studies into a standardized table. A second investigator (HN) checked these data for accuracy. Duplicates, studies that were E-posters and general review were excluded (figure 1).

Assessment of methodological quality. After initial assessment using criteria from the CASP (Critical Appraisal Skills Programme) of diagnostic studies,[7] two investigators (HN and NR) blindly and independently assessed each study regarding its quality as "good," "moderate," or "poor" using predefined criteria based on a widely used tool for examining diagnostic accuracy that is the QUADAS 2 (Quality Assessment of Diagnostic Accuracy Studies) tool.[8] Disagreement was resolved by consensus or by another reviewer (IH). Low quality studies were excluded. The risk of bias related to the patients, tests, reference standard, and execution of each study was assessed. Selection of population was regarded at risk if sample is very small or no clear method of selection was reported.

CT-VHSG and the reference tests were considered at risk of bias when either was carried out with knowledge of the other or when the blinding is not reported by the study, and when tests for establishing the final diagnoses were unreliable. Risk of bias was also considered when there is a lack or unclear reporting of blinding in the interpretation of CT-VHSG images, reference test was not done for all patients were subjected to the same final reference test, when description of the test procedures is incomplete or vague and when participants were excluded from analyses. Risk of bias was also considered when the outcome was not analyzed clearly in form of sensitivity and specificity and when the reference test was not reliable for establishing the final diagnosis. Any disagreement was resolved through discussion among reviewers (figure 2).

Data synthesis and statistical analysis. The review team discussed the clinical and methodological consistency among included studies, decided subjectively and after consensus if significant heterogeneity is present. The outcomes including the 2x2 tables data as well as sensitivity, specificity, positive and negative likelihood rations (+LR and -LR) were directly extracted from the studies or constructed according to the available data at the forest plots of all outcome parameters were built using Open metanalyst software. Publication bias was assessed using funnel plot.

Heterogeneity among studies was also examined statistically using I^2 index as it is more suitable for our study (small number of included studies and different parameters utilized) than the traditional Q test using dedicated meta-analysis software (Open metanalyst). For better interpretation, I2 index was classified into three levels of power for the presence of heterogeneity: up to 25%, low heterogeneity; up to 50%, medium heterogeneity and; 75% and more, high heterogeneity.[9]

Results

Qualitative synthesis: Study characteristics (table 1): This systematic review included five studies[10-14] based on the assessment of risk of bias and quality of the eligible studies. Overall, these five studies were conducted between 2008 and 2016. Populations were all females (age range: 22-44year) who were either infertile (primary or Secondary),

Table: Main characteristics of the included studies.

Study	Year	Sample size	Age (years)	Comparison	Dose of Contrast (ml)	Duration of procedure (Second)	Radiation Dose (**mSv)
Carrascosa P et al. [1,10]	2008	22	35.76±3.96	*CON-HSG	10	2.33-2.43	5.13±0.24
Carrascosa P et al. [2,10]	2008	60	33.5±5.2	CON-HSG	10-20	24.49-25.21	5.08±0.21
Shaaban MM et al.[12]	2013	34	2.7.7±5.8	CON-HSG Laparoscopy	10-20	14.99-15.00	3.2±0.15
Abdelrahman A et al. [13]	2014	25	29.12±5.5	CON-HSG	10-20	3.33-3.37	3.54±0.6
Hasan D et al. [14]	2016	48	32.5±2.5	CON-HSG Hysteroscopy	15	3.27-3.63	3.54±0.6

*Con-HSG=conventional hysterosalpingography; **mSv = MilliSevert

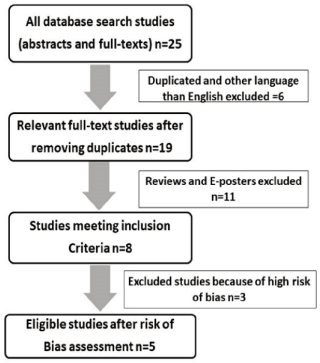

Figure-1: Flowchart detailing identification and selection of studies for inclusion in the review.

with suspected uterine anomaly or having recurrent miscarriages. All studies evaluated the same diagnostic test that is CT-VHSG but the comparisons were variable (including con. HSG, histopathology and laparoscopy). The outcomes were diagnostic accuracy as represented by sensitivity and specificity. All included studies had estimated the radiation dose associated with CT-VHSG and ranged between (3.2-5.13 mSv). Summary of individualized studies was also described (appendix 2).

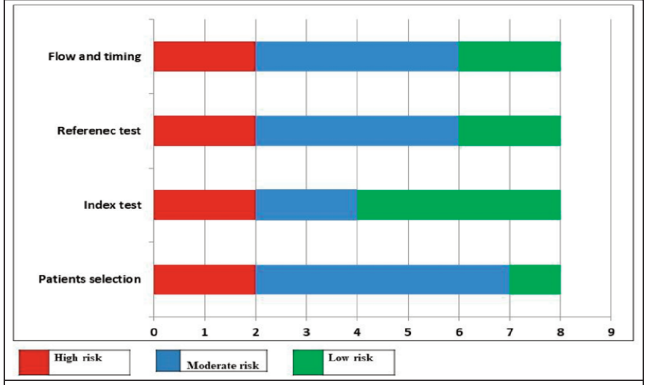

Figure-2: Summary risk of bias and concerns about applicability (based on adapted QUADAS-2).

Heterogeneity between studies: There was generally good consistency between all included studies regarding the diagnostic test used (CT-VHSG) with accepted similarities in the technique as well as the dose and dilution of the contrast material. However they used different comparisons (according to the nature and location of the main pathology or abnormality to be diagnosed). Furthermore, there was some inconsistency in regard to the method of presenting the outcome (diagnostic accuracy). I2 index was used to test the heterogeneity and there was significantly high heterogeneity among studies regarding

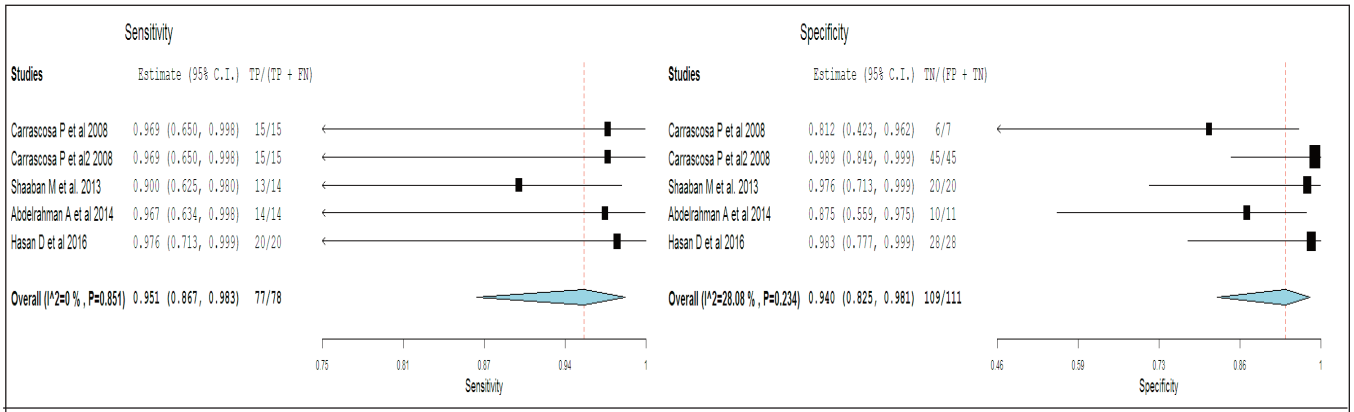

Figure-3: Forest plot of the sensitivity and specificity of CT-VHSG.

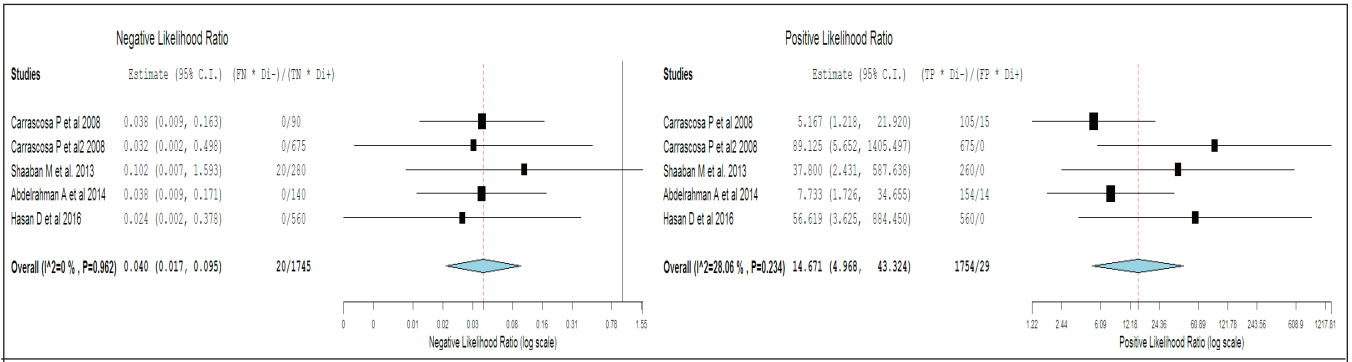

Figure-4: Forest plot of the negative and positive likelihood ratios (-LR and +LR) of CT-VHSG.

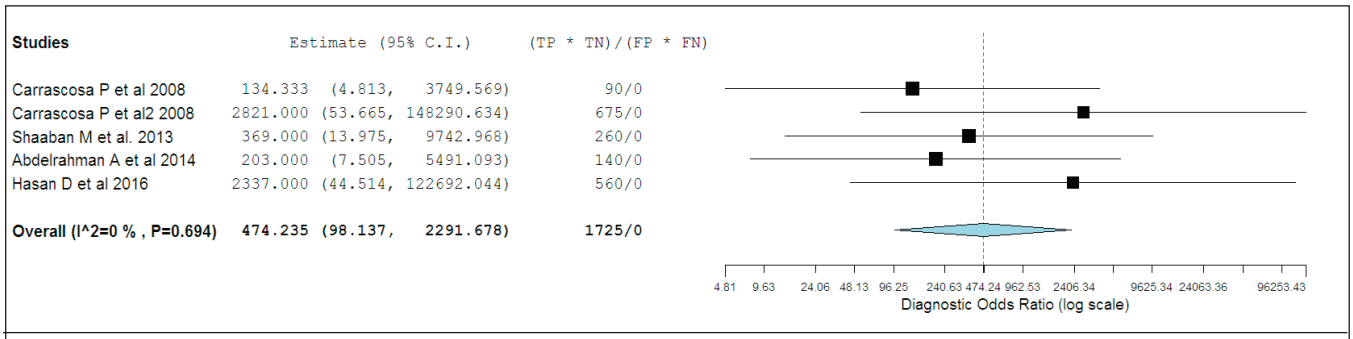

Figure-5: Forest plot of the sensitivity and specificity of CT-VHSG.

study sample size, duration of the procedure and radiation dose. Therefore, a random effect model was judged to be used in describing the variability in testing accuracy across studies.

Outcomes: Important characteristic of the included studies especially where heterogeneity noted, are demonstrated in table 1. The pooled sensitivity was 0.947 (95%CI 0.867-0.983) and specificity was of 0.940 (95% CI 0.825-0.981) (figure 3). Forest plots of the positive and negative likelihood ratios (+ive and –ve LR respectively), which provide a sense of how powerful a test in influencing the pretest probability of disease, showed pooled +ve LR estimate of 0.040 (0.40% having abnormality) and pooled –ve LR estimate of 14.671 (14% excluding abnormality) (figure 4).

The pooled estimate of DOR was 474.23, indicating that CT-VHSG is highly effective in discrimination between positive and negative case (figure 5).

Discussion

The infertile woman is usually subjected to a plenty of investigations to assess underlying cause of her fertility with consequent cost and both physical and psychological burden. Therefore, it is important for the physician to reduce these investigations to the possible minimum, provided diagnostic competency is not compromised. Both patient and physician prefer to have an investigation that carries the least discomfort, least cost with highest diagnostic information about the infertile reproductive system.[4,15]

Currently, gynaecological evaluation of the infertile women includes ultrasound (with or without hysterosonography), hysteroscopy and conventional HSG. CT-VHSG is proposed as a developing, minimally invasive diagnostic procedure that might be alternative for or complimentary to other more invasive, more costly and/or less informative procedures for evaluation of uterine, cervical and Fallopian pathologies.[10,16]

Among seven multicentric diagnostic studies conducted on the value of CT-VHSG, five studies with low-moderate risk of bias were included in this systematic review. Causes of bias were mainly related to the size of study sample, the referral way and the type of patients' collection.

All the five studies have deliberately explained the details of performing CT-VHSG, including the preparation of patients, duration of test, complications after the examination and the estimated radiation dose.

All studies have reported the outcome well in form of sensitivity, specificity, positive and negative productive values while only one study reported all results in details as 2x2 tables.

Review of diagnostic value and impact:

All CT-VHSG examinations in the included diagnostic studied have achieved high degree of accuracy with appropriate sensitivity, specificity and both positive and negative predictive values regarding uterine and tubal pathologies and tubal patency. This could be attributed to the much better delineation of the intramural portion of the submucosal myomas relative to the con. HSG. Intracavitary lesions like polyps or subendometrial myomas and synechiae could be more easily identified by viewing the reconstructed endoluminal images. Post-processing could add more for the interpretation by multiplanar visualization the uterine, cervical and tubal anatomy without significantly compromising image quality. Another advantage of the CT-VHSG over the con. HSG is the ability to evaluate parauterine pelvic structures[15-17]

Review of technique-related radiation dose:

Concerning the radiation exposure, an extremely important aspect in these childbearing aged women, there was an obvious reduction in the effective dose when using CT-VHSG in comparison to con. HSG by 2.59 ± 0.3 mSv (The pooled estimates of patient effective dose during CT- VHSG was 4.09 ± 0.36 mSv vs the 6.13 ± 0.3 mSv in the con. HSG). This significant reduction is due to technical improvement

like X-ray automatic tube current modulation and other new specially developed hardware and software algorithms.[18-20]

Strengths and limitations of the review: This was systematic review method used in the assessment of CT-VHSG gave a considerable strength to its validity. The authors are of opinion that the systematic search for diagnostic studies performed in this study using an adequate search strategy made it unlikely that any relevant information would have been missed. The pooled estimates of accuracy of CT-VHSG, compared to con. HSG, are plausible and reflect an improvement in DOR, sensitivity and specificity, as well as positive and negative LRs. The statistical tools were utilized so that most sources of bias and heterogeneity can be statistically examined. On the other hand, precision of the results might not be very high because of small sample size (relatively few studies). There was very little information from published studies comparing CT-VHSG to con. HSG and laparoscope. Despite heterogeneity was statistically assessed, the exact sources of heterogeneity might not be detectable from literature.

Conclusion

CT-VHSG is a valid imaging procedure in the assessment of female reproductive with high diagnostic performance and comparable or even lesser radiation dose than the conventional HSG. Considering results of our review, CT-VHSG could be recommended as an alternative and reasonably safe diagnostic technique in the infertility workup especially for those patients who are unfit for or refusing invasive and/or costly procedures. Nevertheless, the study suggested further diagnostic studies to be included in another systematic review with future update of the current systematic review.

Disclaimer: The authors state that study has not been presented or published in a conference, or published in an abstract book. We disclose that this work is a dissertation as a partial fulfilment for the requirement of high diploma in radiology, submitted to the Faculty of Medicine, University of Kufa.

Conflict of interest: The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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