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Comparison of conventional, doppler and contrast-enhanced ultrasonography in differential diagnosis of ovarian masses: a systematic review and meta-analysis

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ABSTRACT

Objectives To assess the value of conventional, Doppler and contrast-enhanced ultrasonography (CEUS) (conventional ultrasonography (US), Doppler US and CEUS) for diagnosing ovarian cancer.

Design Systematic review and meta-analysis.

Data sources PubMed, Embase and the Cochrane Library were conducted for studies published until October 2021.

Eligibility criteria Studies assessed the diagnostic value of conventional US, Doppler US or CEUS for detecting ovarian cancer, with no restrictions placed on published language and status.

Data extraction and synthesis The study selection and data extraction were performed by two independent authors. The sensitivity, specificity, positive and negative likelihood ratio (PLR and NLR), diagnostic OR (DOR) and area under the receiver operating characteristic curve (AUC) were pooled using the bivariate generalised linear mixed model and random effects model.

Results The meta-analysis included 72 studies and involved 9296 women who presented with ovarian masses. The pooled sensitivity, specificity, PLR, NLR, DOR and AUC for conventional US were 0.91 (95% CI: 0.87 to 0.94) and 0.87 (95% CI: 0.82 to 0.91), 6.87 (95% CI: 4.98 to 9.49) and 0.10 (95% CI: 0.07 to 0.15), 57.52 (95% CI: 36.64 to 90.28) and 0.95 (95% CI: 0.93 to 0.97), respectively. The sensitivity, specificity, PLR, NLR, DOR and AUC for Doppler US were 0.93 (95% CI: 0.91 to 0.95) and 0.85 (95% CI: 0.80 to 0.89), 6.10 (95% CI: 4.59 to 8.11) and 0.08 (95% CI: 0.06 to 0.11), 61.76 (95% CI: 39.99 to 95.37) and 0.96 (95% CI: 0.94 to 0.97), respectively. The pooled sensitivity, specificity, PLR, NLR, DOR and AUC for CEUS were 0.97 (95% CI: 0.92 to 0.99) and 0.92 (95% CI: 0.85 to 0.95), 11.47 (95% CI: 6.52 to 20.17) and 0.03 (95% CI: 0.01 to 0.09), 152.11 (95% CI: 77.77 to 297.51) and 0.99 (95% CI: 0.97 to 0.99), respectively. Moreover, the AUC values for conventional US (p=0.002) and Doppler US (p=0.005) were inferior to those of CEUS.

Conclusions Conventional US, Doppler US and CEUS have a relatively high differential diagnostic value for differentiating between benign and malignant ovarian masses. The diagnostic performance of CEUS was superior to that of conventional US and Doppler US.

Strengths and limitations of this study

- ► This study provides indirect comparison analyses among conventional ultrasonography, Doppler ultrasonography and contrast-enhanced ultrasonography for detecting ovarian cancer.
- ► This study included prospective, retrospective and cross-sectional studies; moreover, the results could be affected by uncontrolled selective and recall biases.
- ► Subgroup analyses according to country and route were performed.
- ► Inevitable publication bias and restricted detailed analyses are limitations.

INTRODUCTION

Annually, an estimated 60 000 women in the USA undergo surgical excisions for adnexal masses or suspected ovarian neoplasm; moreover, approximately 313 959 ovarian cancer cases were diagnosed in 2020 worldwide.[1 2] Adnexal masses are often incidentally observed given widespread diagnostic imaging use; further, most cases are diagnosed with benign masses.[3 4] Currently, most newly diagnosed ovarian cancer (OC) cases are at stages III and IV, with the survival rate ranging from 25% to 30%.[5] However, the survival rate for OC at stage I could be as high as 90%.[6] Therefore, early OC detection and accurate tumour property assessment remain important issues in clinical practice.[7]

Currently, there are no reliable approaches for early OC detection; however, early-stage differential diagnosis of benign and malignant ovarian masses is important. The use of ultrasonography (US) for determining benign or malignant ovarian masses is mainly based on subjective and qualitative diagnosis. The current overall diagnostic accuracy of US for OC could reach 80%.[8] Conventional

US can visualise the capsule and tumour shapes, which could allow differential diagnosis of benign or malignant tumours.[9] Angiogenesis could be involved in tumour growth and metastasis; additionally, it is significantly correlated with malignant tumours.[10] Moreover, spectral analysis of Doppler US could detect the blood flow status in tumours through the Doppler waveform.[11] Furthermore, contrast-enhanced US (CEUS) could improve imaging quality.[12] However, the diagnostic values of conventional US, Doppler US and CEUS for differentiating between benign and malignant ovarian masses have not been compared. Therefore, we aimed to perform a systematic review and meta-analysis to assess the value of conventional US, Doppler US and CEUS for differential diagnosis of benign and malignant ovarian masses. Moreover, we aimed to perform indirect comparison analysis to compare the diagnostic value among conventional US, Doppler US and CEUS.

METHODS

Data sources, search strategy and selection criteria

This systematic review and meta-analysis was performed and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.[13] There were no restrictions regarding publication language and status. Studies assessing the diagnostic value of conventional US, Doppler US or CEUS differentiating between benign and malignant ovarian masses were considered eligible for our analysis. We systematically searched PubMed, Embase and the Cochrane Library for eligible studies published until October 2021. The following search terms were used as text words or Medical Subject Heading terms: "ovarian neoplasms" AND ("ultrasonography" OR "Doppler ultrasonography" OR "contrast-enhanced ultrasonography") AND "diagnosis." In addition, we manually reviewed the reference lists of the retrieved studies to identify new eligible studies.

Two authors (LX and LZ) independently performed the literature search and study selection, with disagreements being resolved by group discussion after reading the full-text of available articles. The inclusion criteria were as follows: (1) Study design: no restrictions were placed on study design, including cross-sectional, retrospective and prospective design; (2) Participants: adult women experience ovarian masses; (3) Diagnostic tool: conventional US, Doppler US or CEUS; (4) Gold standard: pathological; and (5) Analysis data: true and false positive, as well as true and false negative for differentiating between benign and malignant ovarian masses.

Data collection and quality assessment

Two authors (LX and LZ) independently performed data collection and quality assessment. The following data were collected: first author's name, publication year, country, sample size (malignant/benign), age, type of OC, modality, route, agent, US machine, true and false positive and true and false negative. The Quality Assessment of Diagnostic Accuracy Studies was applied to assess the methodological bias for individual study based on patient selection, index test, reference standard, risk of bias and concerns regarding applicability.[14] Between-author inconsistencies concerning data collection and quality assessment were settled by an additional author (HX) who reviewed the full-text of the original article.

Statistical analysis

We applied true and false positive and negative in each study to calculate the sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic OR (DOR) and area under the receiver operating characteristic curve (AUC). Subsequently, the pooled diagnostic effect estimates for conventional US, Doppler US and CEUS were calculated using the bivariate generalised linear mixed model and random effects model.[15–17] Heterogeneity across the included studies was assessed using I^2 and Q statistic, with I^2 >50.0% or p<0.10 indicating significant heterogeneity.[18 19] Next, the diagnostic value for conventional US, Doppler US and CEUS was calculated using an indirect comparison approach.[20] We performed subgroup analysis for the diagnostic performance of conventional US, Doppler US and CEUS according to country and route; subsequently, between-subgroup differences were assessed using the interaction P test.[21] Moreover, publication biases for the diagnostic value of conventional US, Doppler US and CEUS were assessed using the funnel plot and Deeks' asymmetry test.[22] The inspection level for pooled results was two-sided, with p<0.05 being considered statistically significant. All statistical analyses were performed using the software Stata (V.10.0; Stata Corporation).

Patient and public involvement

No patient involved.

RESULTS

Literature search

The initial electronic searches identified 4028 articles; among them, 3192 were retained after removing duplicate articles. Subsequently, 3038 studies were excluded for reporting irrelevant topics. The remaining 154 studies were retrieved for further full-text evaluations, with 82 studies being excluded for the following reasons: other diagnostic tools (n=45), combined diagnostic strategies (n=31) and insufficient data (n=6). The remaining 72 studies were included in the final meta-analysis. No eligible study was identified from reviewing the reference lists of the included studies. Figure 1 presents the detailed results regarding the study selection.

Study characteristics

The characteristics of the identified studies and recruited patients are shown in online supplemental 1. The included studies involved 9296 women presenting ovarian masses, with the sample size ranging from 19 to 826.

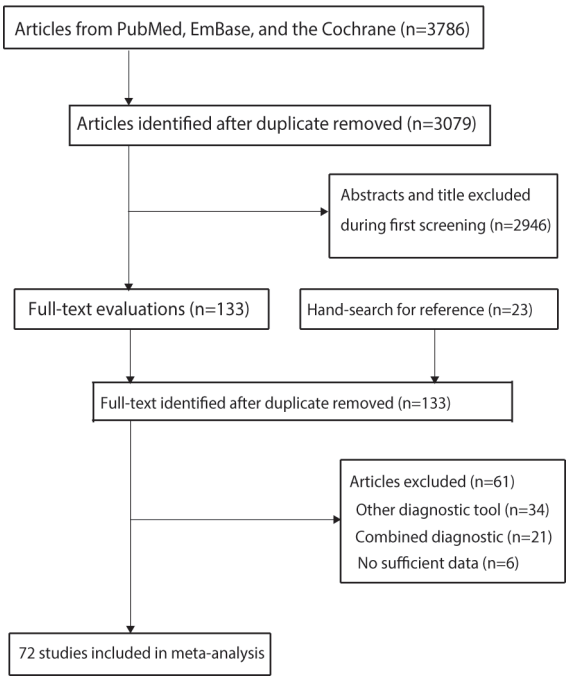


Figure 1 The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart for the study selection process.

Among the included studies, 24 were conducted in Asia with the remaining 48 studies being conducted in Europe or America. Further, 36, 51 and 29 cohorts assessed the diagnostic performance of conventional US, Doppler US and CEUS, respectively. Online supplemental 2 presents the details regarding the quality of each study with most of them having moderate-to-high quality.

Sensitivity and specificity

The pooled sensitivity and specificity for conventional US in the differential diagnosis of benign and malignant ovarian masses were 0.91 (95% CI: 0.87 to 0.94) and 0.87 (95% CI: 0.82 to 0.91), respectively. The values for pooled sensitivity and specificity in Doppler US were 0.93 (95% CI: 0.91 to 0.95) and 0.85 (95% CI: 0.80 to 0.89), respectively. Furthermore, the summary sensitivity and specificity for CEUS were 0.97 (95% CI: 0.92 to 0.99) and 0.92 (95% CI: 0.85 to 0.95), respectively (online supplemental 3). Conventional US had a lower sensitivity than CEUS for differentiating between benign and malignant ovarian masses (ratio: 0.94; 95% CI: 0.89 to 0.99; p=0.019). Doppler US had a lower specificity than CEUS for differentiating between benign and malignant ovarian masses (ratio: 0.92; 95% CI: 0.86 to 1.00; p=0.044) (table 1). Subgroup analysis revealed high sensitivity of conventional US and Doppler US in the transvaginal group (table 2).

PLR and NLR

The pooled PLR and NLR for conventional US differentiating between benign and malignant ovarian masses were 6.87 (95% CI: 4.98 to 9.49), and 0.10 (95% CI: 0.07 to 0.15), respectively. The corresponding values for Doppler

Table 1 Comparison the diagnostic value among conventional, Doppler and contrast-enhanced US

Diagnostic tool	Sensitivity	Specificity	PLR	NLR	DOR	AUC
US	0.91 (0.87 to 0.94)	0.87 (0.82 to 0.91)	6.87 (4.98 to 9.49)	0.10 (0.07 to 0.15)	57.52 (36.64 to 90.28)	0.95 (0.93 to 0.97)
Doppler US	0.93 (0.91 to 0.95)	0.85 (0.80 to 0.89)	6.10 (4.59 to 8.11)	0.08 (0.06 to 0.11)	61.76 (39.99 to 95.37)	0.96 (0.94 to 0.97)
CEUS	0.97 (0.92 to 0.99)	0.92 (0.85 to 0.95)	11.47 (6.52 to 20.17)	0.03 (0.01 to 0.09)	152.11 (77.77 to 297.51)	0.99 (0.97 to 0.99)
US vs Doppler US	0.98 (0.94 to 1.02)/0.336	1.02 (0.95 to 1.10)/0.541	1.13 (0.73 to 1.73)/0.588	1.25 (0.77 to 2.03)/0.369	0.93 (0.50 to 1.74)/0.824	0.99 (0.96 to 1.02)/0.435
US vs CEUS	0.94 (0.89 to 0.99)/0.019	0.95 (0.88 to 1.02)/0.151	0.60 (0.31 to 1.15)/0.122	3.33 (1.04 to 10.66)/0.042	0.38 (0.17 to 0.85)/0.018	0.96 (0.94 to 0.98)/0.002
Doppler US vs CEUS	0.96 (0.92 to 1.00)/0.052	0.92 (0.86 to 1.00)/0.044	0.53 (0.28 to 1.00)/0.050	2.67 (0.85 to 8.34)/0.092	0.41 (0.18 to 0.90)/0.027	0.97 (0.95 to 0.99)/0.005

AUC, area under the curve ; CEUS, contrast-enhanced US ; DOR, diganostic OR; NLR, negative likelihood ratio; PLR, positive likelihood ratio; US, ultrasonography.

Table 2 Subgroup analyses according to country and route

Diagnostic tool	Variables	Subgroup	Sensitivity	Specificity	PLR	NLR	DOR	AUC
US	Country	Asia	0.89 (0.85 to 0.93)	0.84 (0.71 to 0.92)	5.76 (3.00 to 11.07)	0.12 (0.09 to 0.18)	46.71 (20.69 to 105.41)	0.92 (0.89 to 0.94)
		Europe or America	0.92 (0.86 to 0.95)	0.88 (0.82 to 0.92)	7.37 (5.16 to 10.53)	0.09 (0.06 to 0.16)	63.54 (36.63 to 110.23)	0.95 (0.93 to 0.97)
		Difference between subgroups	0.333	0.520	0.516	0.348	0.540	0.068
	Route	Transvaginal	0.94 (0.88 to 0.97)	0.89 (0.83 to 0.93)	8.40 (5.52 to 12.77)	0.07 (0.04 to 0.13)	86.75 (56.93 to 132.20)	0.97 (0.95 to 0.98)
		Transabdominal	0.91 (0.86 to 0.94)	0.80 (0.60 to 0.91)	4.46 (2.03 to 9.78)	0.12 (0.07 to 0.20)	34.48 (11.10 to 107.05)	0.93 (0.90 to 0.95)
		Both	0.82 (0.74 to 0.88)	0.84 (0.74 to 0.91)	5.10 (2.90 to 8.99)	0.22 (0.14 to 0.34)	22.55 (7.70 to 66.05)	0.88 (0.85 to 0.90)
		Difference between subgroups	0.027	0.438	0.221	0.008	0.035	<0.001
Doppler US	Country	Asia	0.89 (0.82 to 0.93)	0.82 (0.74 to 0.89)	5.06 (3.37 to 7.59)	0.13 (0.08 to 0.22)	33.72 (17.44 to 65.22)	0.93 (0.90 to 0.95)
		Europe or America	0.94 (0.92 to 0.96)	0.85 (0.79 to 0.90)	6.41 (4.50 to 9.13)	0.07 (0.04 to 0.10)	76.07 (44.70 to 129.46)	0.97 (0.95 to 0.98)
		Difference between subgroups	0.107	0.533	0.389	0.075	0.060	0.008
	Route	Transvaginal	0.94 (0.91 to 0.95)	0.87 (0.82 to 0.90)	6.98 (5.02 to 9.70)	0.07 (0.05 to 0.10)	74.55 (45.34 to 122.60)	0.96 (0.94 to 0.98)
		Transabdominal	0.94 (0.77 to 0.99)	0.86 (0.72 to 0.94)	6.87 (3.19 to 14.82)	0.07 (0.02 to 0.31)	66.82 (15.41 to 289.83)	0.95 (0.93 to 0.97)
		Both	0.92 (0.80 to 0.97)	0.65 (0.54 to 0.75)	2.66 (2.02 to 3.51)	0.12 (0.05 to 0.30)	15.56 (8.20 to 29.52)	0.85 (0.82 to 0.88)
		Difference between subgroups	0.913	0.004	<0.001	0.544	0.001	<0.001
CEUS	Country	Asia	0.97 (0.90 to 0.99)	0.91 (0.83 to 0.96)	11.15 (5.76 to 21.61)	0.03 (0.01 to 0.12)	201.55 (90.19 to 450.41)	0.99 (0.97 to 0.99)
		Europe or America	0.97 (0.90 to 0.99)	0.91 (0.81 to 0.96)	11.32 (4.77 to 26.87)	0.03 (0.01 to 0.12)	133.64 (41.55 to 429.78)	0.99 (0.97 to 0.99)
		Difference between subgroups	1.000	1.000	0.978	1.000	0.570	1.000
	Route	Transvaginal	0.98 (0.92 to 1.00)	0.90 (0.81 to 0.95)	9.74 (4.93 to 19.24)	0.02 (0.00 to 0.10)	123.98 (50.61 to 303.71)	0.99 (0.98 to 1.00)
		Transabdominal	0.94 (0.89 to 0.97)	0.95 (0.91 to 0.97)	18.69 (9.88 to 35.36)	0.06 (0.04 to 0.11)	245.86 (95.66 to 631.92)	0.98 (0.97 to 0.99)
		Difference between subgroups	0.173	0.217	0.171	0.361	0.303	0.166

AUC, area under the curve; CEUS, contrast-enhanced US ; DOR, diagnostic OR; NLR, negative likelihood ratio; PLR, positive likelihood ratio; US, ultrasonography.

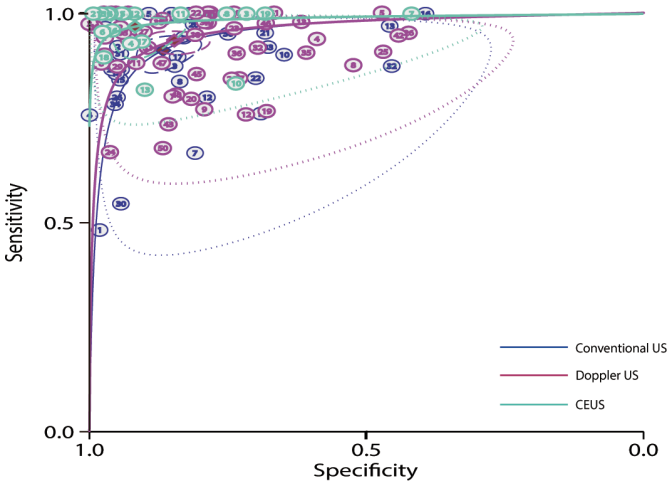


Figure 2 The area under the curve of conventional US, Doppler US and CEUS for differentiating between malignant and benign ovarian masses. CEUS, contrast-enhanced US; US, ultrasonography.

US were 6.10 (95% CI: 4.59 to 8.11) and 0.08 (95% CI: 0.06 to 0.11) for pooled PLR and NLR, respectively. Furthermore, the summary PLR and NLR for CEUS were 11.47 (95% CI: 6.52 to 20.17) and 0.03 (95% CI: 0.01 to 0.09), respectively (online supplemental 4). Conventional US versus CEUS showed higher NLR (ratio: 3.33; 95% CI: 1.04 to 10.66; p=0.042), while Doppler US versus CEUS showed lower PLR (ratio: 0.53; 95% CI: 0.28 to 1.00; p=0.050) (table 1). Subgroup analyses suggested that the NLR for conventional US and PLR for Doppler US were lower and higher in the transvaginal group, respectively (table 2).

DOR

The pooled DOR of conventional US, Doppler US and CEUS for differentiating between benign and malignant ovarian masses were 57.52 (95% CI: 36.64 to 90.28), 61.76 (95% CI: 39.99 to 95.37) and 152.11 (95% CI: 77.77 to 297.51), respectively (online supplemental 5). There was significant heterogeneity across the included studies for conventional US (I^2=66.5%; p<0.001) and Doppler US (I^2=73.9%; p<0.001) but not for CEUS (I^2=25.7%; p=0.147). The DOR of conventional US (ratio: 0.38; 95% CI: 0.17 to 0.85; p=0.018) and Doppler US (ratio: 0.41; 95% CI: 0.18 to 0.90; p=0.027) were significantly lower than that of CEUS for differentiating between benign and malignant ovarian masses (table 1). Subgroup analysis revealed that the DOR was high for conventional US and Doppler US in the transvaginal group (table 2).

AUC

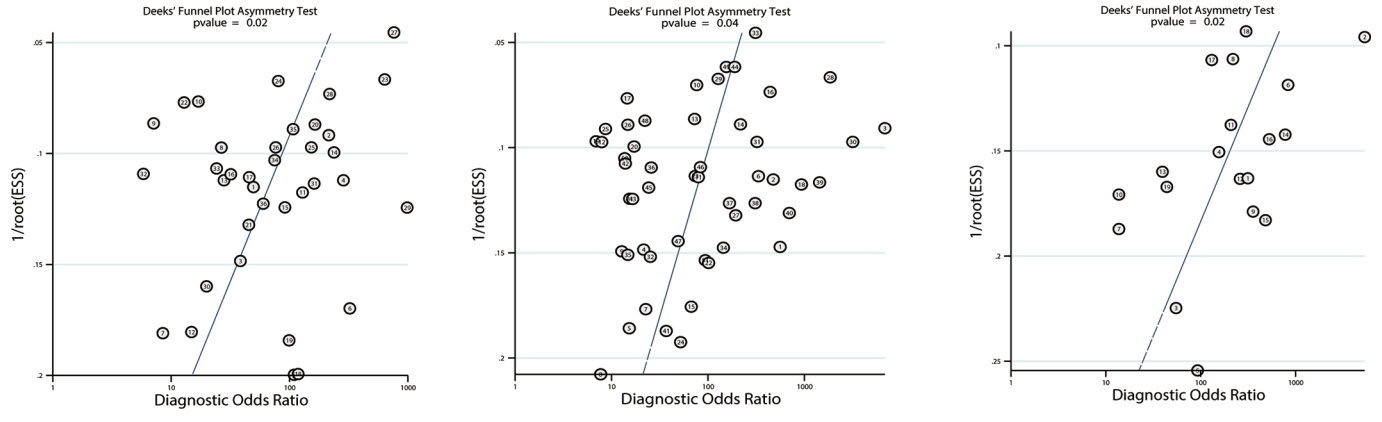
The AUC of conventional US, Doppler US and CEUS for differentiating between benign and malignant ovarian masses were 0.95 (95% CI: 0.93 to 0.97), 0.96 (95% CI: 0.94 to 0.97) and 0.99 (95% CI: 0.97 to 0.99), respectively (figure 2). Compared with CEUS, conventional US (ratio: 0.96; 95% CI: 0.94 to 0.98; p=0.002) and Doppler US (ratio: 0.97; 95% CI: 0.95 to 0.99; p=0.005) had significantly lower AUC values for detecting OC (table 1). Subgroup analysis suggested that the AUC of conventional US was affected by route and that the diagnostic value was high in the transvaginal group. Moreover, the AUC of Doppler US could be affected by country and route; further, the diagnostic value was high in the study groups from Europe or America, as well as in the transvaginal group (table 2).

Publication bias

Publication bias was also tested for in the diagnostic performance of conventional US, Doppler US and CEUS (figure 3). There were potentially significant publication biases for conventional US (p=0.02), Doppler US (p=0.04) and CEUS (p=0.02). However, after adjusting for potential publication bias, the diagnostic performance remained stable.[23]

DISCUSSION

The current systematic review and meta-analysis assessed the diagnostic performance of conventional US, Doppler



A. Conventional US B. Doppler US C. CEUS

Figure 3 Publication biases for conventional US, Doppler US and CEUS. CEUS, contrast-enhanced US; US, ultrasonography.

US and CEUS for differentiating between benign and malignant ovarian masses. This comprehensive, large-scale quantitative analysis included 9296 women with diverse individual characteristics assessed in 72 studies. There was a relatively high diagnostic value of conventional US, Doppler US and CEUS for differentiating between benign and malignant ovarian masses. Moreover, indirect comparison analysis revealed that the diagnostic value of CEUS was superior to that of conventional US and Doppler US. Moreover, there was a significant difference in the diagnostic performance between conventional US and Doppler US. Subgroup analysis suggested that the diagnostic value of conventional US could be affected by route, while country and route could affect the diagnostic performance of Doppler US.

There have been several systematic reviews and meta-analyses on the diagnostic performance of conventional US, Doppler US and CEUS for detecting OC. Medeiros *et al* found that the colour Doppler US could be a useful preoperative tool for diagnosing OC from pelvic masses.[24] Several studies also found CEUS had a high diagnostic value for differentiating between malignant and benign ovarian masses.[25–27] A meta-analysis conducted by Liu *et al* on 67 high-quality studies suggested that conventional US, Doppler US and CEUS had a relatively high diagnostic value for OC.[28] However, the aforementioned studies only reported the pooled diagnostic performance of conventional US, Doppler US and CEUS for differentiating between benign and malignant ovarian masses. Specifically, they did not compare among conventional US, Doppler US and CEUS; further, they did not illustrate the diagnostic performance of conventional US, Doppler US and CEUS based on country and route. Therefore, the current systematic review and meta-analysis assessed the diagnostic performance of conventional US, Doppler US and CEUS in differentiating between malignant and benign ovarian masses.

In the present study, there was a relatively high diagnostic performance of conventional US, Doppler US and CEUS for differentiating between benign and malignant ovarian masses, which is consistent with previous studies.[24–28] A meta-analysis performed by Liu *et al* found similar diagnostic value among US, CT and MRI.[8] Medeiros *et al* found the are under curve of MRI for detecting malignant OC was 0.9526,[29] which was similar compared with conventional US and Doppler US, but lower than CEUS from our study. Conventional US by placing a high frequency probe to scan the area adjacent to the sonic speed near field does not require a full bladder and is not affected by intestinal gas; moreover, it yields high-quality images.[30] Subjective evaluation of the colour content of ovarian tumours through Doppler US is simple with low colour content indicating benignity.[31] Moreover, the blood flow velocity in Doppler US could differentiate between benign and malignant pelvic masses.[28] We observed similar diagnostic performance between conventional US and Doppler US for differentiating between benign and malignant ovarian masses; furthermore, the role of Doppler US could be affected by the resistance index; the use of Doppler US to assess the grey-scale ultrasound morphology in an adnexal mass with high accurate for predicting its nature.[32] Moreover, CEUS had a higher diagnostic value than conventional US and Doppler US for differentiating between benign and malignant ovarian masses. This could be attributed to contrast agent injection improving the map of vascular anatomy, as well as the detection of signals from blood vessels with a diameter of <40 µm. Therefore, CEUS could effectively visualise a greater vessel number in malignant than in benign tumours.[33 34] Finally, the time-intensity curve parameters applied quantitatively assessed the kinetics of contrast agents in tumours, which was objective and reproducible and could be used for inexperienced examiners.[35]

In the present study, subgroup analyses revealed that route could affect the diagnostic performance of conventional US while country and route could affect the diagnostic performance of Doppler US for differentiating between benign and malignant ovarian masses. The aforementioned findings could be attributed to several reasons: (1) the number of studies in each subgroup was imbalanced and there were variable diagnostic performances of conventional US, Doppler US and CEUS; (2) there was between-study inconsistency in the prestudy US training, which could affect the diagnostic performance of conventional US, Doppler US and CEUS for differentiating between benign and malignant ovarian masses; and (3) most of the included studies performed transvaginal US with power stability, with fewer studies applying transabdominal US or both transvaginal and transabdominal US. Future large-scale prospective studies should verify these results.

This study has the following strengths: (1) the analysis was based on a large number of published studies and a large sample size, and therefore our findings are more robust than those of any individual study; (2) indirect comparison analyses were conducted to compare the diagnostic performance among conventional US, Doppler US and CEUS for differentiating between benign and malignant ovarian masses; and (3) stratified analyses for the diagnostic performance of conventional US, Doppler US and CEUS were conducted according to country and route, which allowed assessment of the diagnostic value in specific subpopulations.

Nonetheless, this study has several limitations. First, this study included prospective, retrospective and cross-sectional studies; moreover, the results could be affected by uncontrolled selective and recall biases. Second, the experience levels of clinicians in US could have differed, which could affect the diagnostic performance of conventional US, Doppler US and CEUS. Third, the agents used for CEUS differed across the included studies, which could induce heterogeneity in the diagnostic value of CEUS. Fourth, the type of ovarian mass could affect the diagnostic performance of conventional US, Doppler US and CEUS, while the stratified data according to ovarian

mass type were not available. Fifth, we performed an indirect comparison of diagnostic performance among conventional US, Doppler US and CEUS. Finally, there are inherent limitations of meta-analysis based on published articles, including the use of pooled data for analysis and the inevitable publication bias.

CONCLUSION

We observed a relatively high diagnostic performance of conventional US, Doppler US and CEUS for differentiating between malignant and benign ovarian masses. Moreover, the diagnostic value of CEUS was higher than that of conventional US and Doppler US. Furthermore, the diagnostic performance of conventional US could be affected by route, while country and route could affect the diagnostic value of Doppler US. Further large-scale prospective studies should directly compare the diagnostic performance of conventional US, Doppler US and CEUS for diagnosing OC.

Contributors LZ came up with the research idea and completed the study design. HX contributed to paper inclusion and data analysis. LX wrote the first draft of manuscript and finalised it with LZ. LX approved the submission of the final version of this paper. LX acts as a gaurantor for this study.

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Patient consent for publication Not applicable.

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Provenance and peer review Not commissioned; externally peer reviewed.

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