BMJ Open

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

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To cite: Xun L, Zhai L, Xu H. Comparison of conventional, doppler and contrast-enhanced ultrasonography in differential diagnosis of ovarian masses: a systematic review and meta-analysis. *BMJ Open* 2021;**11**:e052830. doi:10.1136/bmjopen-2021-052830

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-052830).

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Received 06 May 2021
Accepted 18 November 2021

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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.

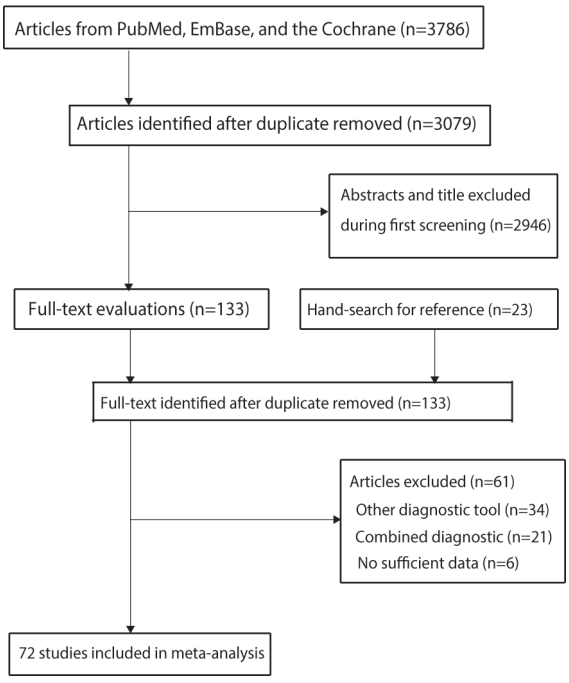


Figure 1 The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart for the study selection process.

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.

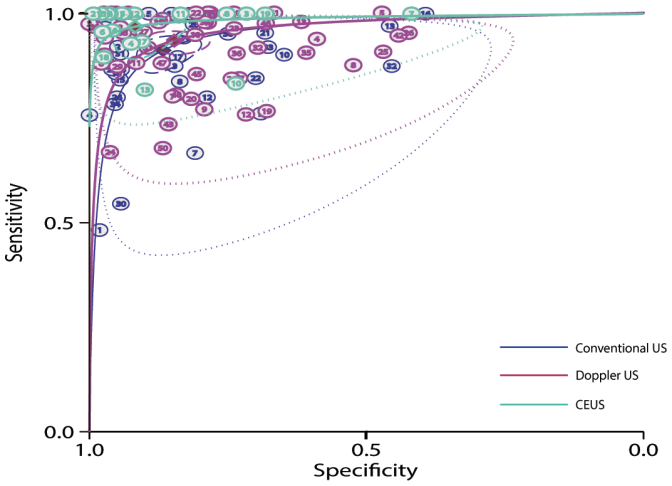


Figure 2 The area under the curve of conventional US, Doppler US and CEUS for differentiating between malignant and benign ovarian masses. CEUS, contrast-enhanced US; US, ultrasonography.

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

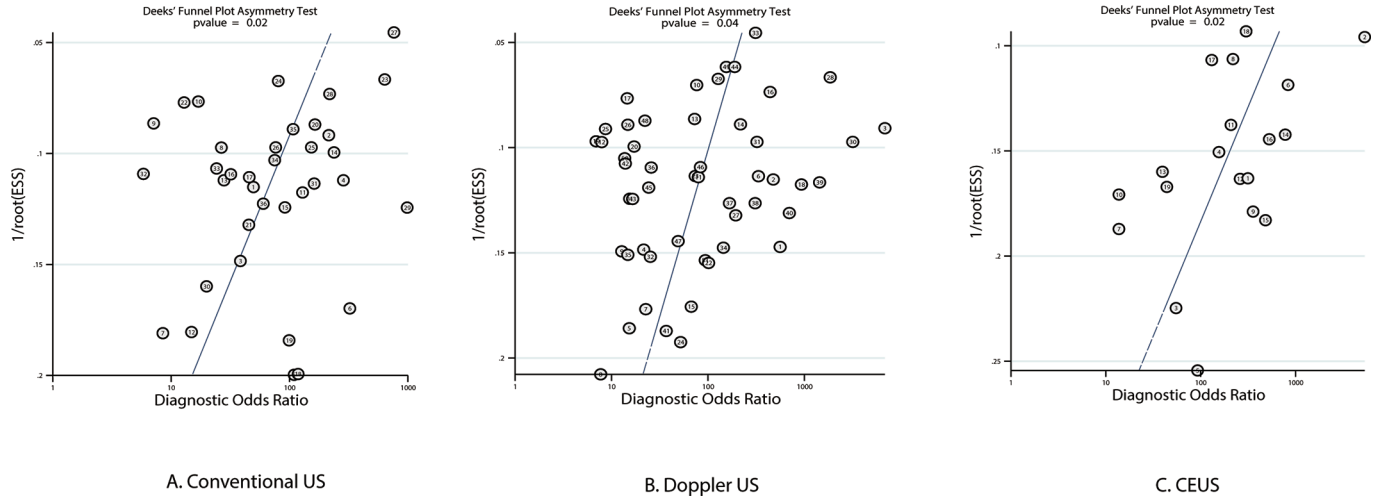
The AUC of conventional US, Doppler US and CEUS for differentiating between benign and malignant ovarian masses were 0.95 (95% CI: 0.93 to 0.97), 0.96 (95% CI: 0.94 to 0.97) and 0.99 (95% CI: 0.97 to 0.99), respectively (figure 2). Compared with CEUS, conventional US (ratio: 0.96; 95% CI: 0.94 to 0.98; 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.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. The data sets generated and analysed during the current study are all presented in the manuscript, and additional materials are available from the corresponding author on reasonable request.

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Table S1. The baseline characteristics of included studies and patients

Study	Country	Sample size (Malignant/Benign)	Age (years)	Type of ovarian cancer	Modality	Route/agent	US machine	TP	FP	FN	TN
Weiner 1992 [S1]	Israel	53 (17/36)	NA	NA	Doppler US	Transvaginal/none	SSD 680	16	1	1	35
Kurjak 1992 [S2]	Croatia	83 (29/54)	NA	NA	US	Transvaginal/none	SSD 680	14	1	15	53
					Doppler US	Transvaginal/none	SSD 680	28	3	1	51
Kurjak 1992 [S3]	Croatia	174 (38/136)	48.0	Pa (18), A (10), E (3), GrC (2), Me (5)	US	Transvaginal/none	SSD 680	35	7	3	129
					Doppler US	Transvaginal/none	SSD 680	37	0	1	136
Schneider 1993 [S4]	USA	55 (16/39)	67.0	NA	US	Both/none	Acuson 128	14	6	2	33
					Doppler US	Both/none	Acuson 128	15	16	1	23
Brown 1994 [S5]	USA	44 (8/36)	42.3	C (4), B (2), SCL (1), MMT (1)	Doppler US	Both/none	Acuson 128	8	19	0	17
Zanetta 1994 [S6]	Italy	80 (33/47)	NA	NA	US	Transvaginal/none	ATL Ultramark	25	0	8	47
					Doppler US	Transvaginal/none	ATL Ultramark	29	1	4	46
Levine 1994 [S7]	USA	35 (7/28)	42.0	NA	US	Transvaginal/none	Acuson 128	7	3	0	25
Jain 1994 [S8]	USA	50 (10/40)	43.0	NA	US	Transvaginal/none	Acuson 128	10	2	0	38
					Doppler US	Transvaginal/none	Acuson 128	8	6	2	34
Bromley 1994 [S9]	USA	33 (12/21)	NA	NA	US	Both/none	Acuson 128	8	4	4	17
					Doppler US	Both/none	Acuson 128	7	10	1	11
Salem 1994 [S10]	Canada	102 (13/89)	NA	P (10), Me (3)	Doppler US	Transvaginal/none	Acuson 128	10	17	3	65
Wu 1994 [S11]	China	228 (76/152)	41.3	Ep (34), GC (6), Me (18), B (6), others (4)	Doppler US	Transvaginal/none	SSD680	72	29	4	123
Chou 1994 [S12]	China	108 (25/83)	38.0	S (10), M (3), E (2), CC (1), ES (3), IT (1), Me (5)	Doppler US	Transvaginal/none	SSD680	22	7	3	76
Franchi 1995 [S13]	Italy	129 (37/92)	44.0	B (7), S (19), M (2), other (9)	US	Both/none	Au450	31	15	6	77
					Doppler US	Both/none	Au450	28	26	9	66
Stein 1995 [S14]	USA	169 (46/123)	39.4	NA	US	Both/none	NA	35	38	11	85
					Doppler US	Both/none	NA	45	47	1	76

Tepper 1995 [S15]	Israel	203 (38/165)	44.3	S (19), M (6), E (2), GrC (3), MT (2), SCS (1), U (3), stromal (1), GC (1)	Doppler US	Transvaginal/none	SSD680	38	43	0	122
Tailor 1996 [S16]	UK	51 (9/42)	44.5	M (1), S (2), E (1), CC (3), Pa (1), GrC (1)	Doppler US	Transvaginal/none	Acuson 128	9	9	0	33
Prompeler 1996 [S17]	Germany	212 (68/144)	60.5	P (50), T (2), Me (5), GrC (1), ES (1), LMP (9)	Doppler US	Transvaginal/none	ATL Ultramark	67	19	1	125
Rehn 1996 [S18]	Germany	310 (51/259)	43.5	P (45), Me (6)	US	Transvaginal/none	Acuson 128	46	91	5	168
					Doppler US	Transvaginal/none	Acuson 128	43	70	8	189
Caruso 1996 [S19]	Italy	122 (21/101)	38.4	A (13), S (4), M (1), Pa (3)	US	Transvaginal/none	Au570	21	25	0	76
					Doppler US	Transvaginal/none	Au570	21	4	0	97
Anandakumar 1996 [S20]	Singapore	156 (34/122)	36.7	NA	Doppler US	Transvaginal/none	Acuson 128	26	39	8	83
Matthes 1996 [S21]	Brazil	43 (10/33)	45.7	NA	US	NA	NA	8	7	2	26
Komatsu 1996 [S22]	Japan	82 (34/48)	45.9	NA	US	Transvaginal/none	Acuson 128	33	26	1	22
Buy 1996 [S23]	France	132 (34/98)	43.5	NA	US	Transvaginal/none	ATL Ultramark	30	3	4	95
					Doppler US	Transvaginal/none	ATL Ultramark	27	18	7	80
Strigini 1996 [S24]	Italy	128 (19/109)	43.0	NA	US	Transvaginal/none	Au590	16	6	3	103
					Doppler US	Transvaginal/none	Au590	16	28	3	81
Tailor 1997 [S25]	UK	64 (12/52)	45.3	NA	Doppler US	Transvaginal/none	Acuson 128	12	10	0	42
Valentin 1997 [S26]	Sweden	151 (24/127)	NA	NA	US	Transvaginal/none	Acuson 128	24	77	0	50
Reles 1997 [S27]	Germany	98 (29/69)	NA	B (4), P (18), other (7)	US	Transvaginal/none	Acuson 128	26	11	3	58
					Doppler US	Transvaginal/none	Acuson 128	26	18	1	51
Yang 1998 [S28]	China	69 (7/62)	39.0	B (6), E (1)	US	Transvaginal/none	HDI 3000	6	3	1	59
Buckshee 1998 [S29]	India	36 (9/27)	NA	Ep (8), IT (1)	US	Transvaginal/none	Sonoline Versa	9	4	0	23
					Doppler US	Transvaginal/none	Sonoline Versa	6	1	3	26

Emoto 1998 [S30]	Japan	143 (43/100)	44.4	B (12), P (31)	Doppler US	Transvaginal/none	SSD 680	39	53	4	47
Alcazar 1999 [S31]	Spain	167 (42/125)	45.7	P (30), LMP (6), Me (6)	Doppler US	Transvaginal/none	Philips P-700 SE	40	72	2	53
Schelling 2000 [S32]	Germany	257 (39/218)	NA	LMP (4), S (23), M (5), E (2), GrC (2), other (3)	US	Transvaginal/none	Sonoline Elegra	38	41	1	177
		63 (22/41)	NA	LMP (4), S (11), M (1), U (2), CC (1), E (1), other (2)	US	Transvaginal/none	Sonoline Elegra	21	13	1	28
					Doppler US	Transvaginal/none	Sonoline Elegra	21	4	1	37
Kupesic 2000 [S33]	Croatia	45 (12/33)	49.7	NA	CEUS	Transvaginal/Levovist	Voluson 530	12	2	0	31
Wanapirak 2001 [S34]	Thailand	185 (65/120)	44.8	NA	US	Transabdominal/none	Aloka 5000	55	36	10	84
Guerriero 2001 [S35]	Italy	328 (71/257)	42.0	S (37), M (9), E (8), CC (2), U (4)	US	Transvaginal/none	Acuson 128	71	47	0	211
					Doppler US	Transvaginal/none	Acuson 128	71	18	0	239
	Spain	328 (70/258)	44.0	S (39), M (11), E (5), CC (1), U (6)	US	Transvaginal/none	SSA 370	66	44	4	214
					Doppler US	Transvaginal/none	SSA 370	61	13	9	245
Kurjak 2001 [S36]	Croatia	251 (30/221)	54.0	S (17), M (9), YS (1), GrC (1), FT (2)	CEUS	Transvaginal/Levovist	Voluson 530	30	2	0	219
					Doppler US	Transvaginal/none	Voluson 530/SSD 2000	56	8	4	434
					US	Transvaginal/none	SSD 2000	50	20	10	422
Marret 2002 [S37]	France	124 (12/112)	42.1	NA	Doppler US	Transvaginal/none	Catana 5	11	34	1	78
Guerriero 2002 [S38]	Italy	826 (147/679)	40.0	NA	US	Transvaginal/none	SSA 370	146	109	1	570
					Doppler US	Transvaginal/none	SSA 370	140	41	7	638
Alcazar 2003 [S39]	Spain	44 (21/23)	49.3	NA	Doppler US	Transvaginal/none	SSA 370	40	14	2	32
Ueland 2003 [S40]	USA	442 (53/389)	50.0	NA	US	Transvaginal/none	GE Logiq	52	75	1	314
Itakura 2003 [S41]	Japan	95 (31/64)	49.2	S (10), M (3), CC (4), E (2), U (2), Un (1), Me (1), GrC (2), S-B (3), tubal (3)	Doppler US	Transvaginal/none	Logiq 500	28	17	3	47
Gu 2003 [S42]	China	19 (12/7)	42.2	NA	CEUS	Transvaginal/Levovist	ATL Ultramark	12	2	0	5
Orden 2003 [S43]	Finland	66 (14/52)	49.4	U-solid (1), M-solid (7), solid (6)	CEUS	Transvaginal/Levovist	Sequoia 512	13	4	1	48
D'Arcy 2004 [S44]	UK	20 (4/16)	49.0	NA	CEUS	Transvaginal/Levovist	Sequoia 512	4	1	0	15
Marret 2004 [S45]	France	101 (23/78)	46.2	NA	CEUS	Transvaginal/Levovist	MPX	22	2	1	76

Alcazar 2005 [S46]	Spain	69 (45/24)	48.4	P (30), LMP (4), Me (11)	Doppler US	Transvaginal/none	SonoAce SA-9900	88	8	2	40
Marret 2005 [S47]	France	101 (23/78)	46.2	P (21), B (2)	Doppler US	Transvaginal/none	MPX	23	2	0	76
Erdogan 2005 [S48]	Turkey	63 (21/42)	48.2	NA	Doppler US	Transabdominal/none	PowerVision 6000	21	2	0	40
Testa 2007 [S49]	Belgium	33 (9/24)	41.0	NA	CEUS	Transvaginal/SonoVue	MPX	9	14	0	10
					Doppler US	Transvaginal/none	MPX	9	8	0	16
Testa 2009 [S50]	Italy	89 (37/52)	50.0	B (10), Ep (17), non-Ep (3), tubal (3), Me (4)	CEUS	Transvaginal/SonoVue	MPX	37	13	0	39
					Doppler US	Transvaginal/none	MPX	35	29	2	23
Fleischer 2009 [S51]	USA	36 (10/26)	48.3	S (5), E (2), Me (2), B-M (1)	CEUS	Transvaginal/Definity	iU22	10	1	0	25
Zhou 2009 [S52]	China	65 (30/35)	46.6	NA	US	Transabdominal/none	GE Logiq7	29	1	1	34
					Doppler US	Transabdominal/none	GE Logiq7	22	5	8	30
Veyer 2010 [S53]	France	42 (12/30)	49.7	S (3), CC (3), Me (2), E (2), ES (1), other (1)	CEUS	Transvaginal/SonoVue	MTX	10	8	2	22
Hassan 2011 [S54]	China	52 (22/30)	45.0	NA	CEUS	Transvaginal/SonoVue	GE Logiq	22	5	0	25
Zheng 2011 [S55]	China	36 (14/22)	41.0	NA	CEUS	Transabdominal/SonoVue	GE Logiq	14	2	0	22
Huchon 2012 [S56]	France	99 (11/88)	45.8	U (1), U-solid (2), M (2), M-solid (6)	US	Transvaginal/none	ATL HDI 5000	6	5	5	83
					CEUS	Transvaginal/Levovist	Voluson 730	9	9	2	79
Wang 2012 [S57]	China	49 (20/29)	NA	NA	CEUS	Transabdominal/SonoVue	Philips iU22	20	1	0	28
Hafeez 2013 [S58]	Pakistan	78 (42/36)	NA	NA	US	Transabdominal/none	NEMIO XG	38	2	4	34
Kalmantis 2013 [S59]	Greece	318 (93/225)	47.4	NA	Doppler US	Transvaginal/none	Voluson 730	87	16	6	209
Perez-Medina 2013 [S60]	Spain	72 (41/31)	53.2	NA	Doppler US	Transvaginal/none	Voluson 730	35	6	6	25
Shah 2013 [S61]	India	84 (40/44)	NA	NA	US	Transabdominal/none	NEMIO XG	35	24	5	20
					Doppler US	Transabdominal/none	NEMIO XG	39	14	1	30
Xiang 2013 [S62]	China	51 (8/43)	46.5	NA	CEUS	Transvaginal/SonoVue	MyLab90	8	1	0	42

Zhang 2013 [S63]	China	48 (25/23)	48.3	NA	CEUS	Transabdominal/SonoVue	GE Logiq	24	1	1	22
					Doppler US	Transvaginal/none	GE Logiq	22	3	3	20
Yang 2013 [S64]	China	106 (75/31)	44.4	NA	US	Transabdominal/none	Philips iU22	69	10	6	21
					CEUS	Transabdominal/SonoVue	Philips iU22	70	3	5	28
Abbas 2014 [S65]	Egypt	161 (46/115)	35.2	NA	Doppler US	Both/none	SonoAce X8	37	18	9	97
Zhang 2014 [S66]	China	120 (48/72)	39.6	C (27), Me (4), IT (4), CC (2), E (2), SC (1), ES (1), B (7)	CEUS	Transabdominal/SonoVue	Sequoia 512	43	2	5	70
Hu 2014 [S67]	China	57 (10/47)	NA	GrC (2), A (1), B-S (1), Re (2), SLC (1), tubal S (3)	CEUS	Transvaginal/SonoVue	MyLab90	10	15	0	32
Utrilla-Layna 2015 [S68]	Spain	367 (86/281)	45.8	B (4), P-Ep (61), P non-Ep (4), Me (16), R (1)	Doppler US	Transvaginal/none	Voluson 730	84	60	2	221
Zhang 2015 [S69]	China	102 (37/65)	37.2	NA	US	Transvaginal/none	Acuson 512	29	3	8	62
					Doppler US	Transvaginal/none	Acuson 512	23	9	11	59
Tongsong 2016 [S70]	Thailand	150 (45/105)	43.0	B (9), CC (8), M (6), E (7), S (5), Me (3), SCS (2), other (5)	US	Both	NA	39	6	6	99
Paul 2017 [S71]	Bangladesh	43 (24/19)	37.7	NA	Doppler US	NA	NA	22	2	2	17
Al-Asadi 2018 [S72]	Iraq	101 (21/80)	41.4	M (6), S (5), K (3), L (2), CC (2), GC (2), E (1)	US	Transabdominal/none	NA	20	20	1	60

*A: adenocarcinoma; B: borderline; P: primary; GC: Germ cell; GrC: Granular cell; E: endometrial; CC: clear cell; M: mucinous; Me: metastatic; S: serous; K: Krukenberg; L: Leiomyosarcoma; SCS: sex cord stromal; R: retroperitoneal; SLC: Sertoli-Leydig cell; Re: recurrence; C: Cystadenocarcinoma; IT: immature teratoma; SC: squamous cell; ES: endodermal sinus; U: Unilocular; M: multilocular; Ep: epithelial; LMP: low malignant potential; U: undifferentiated; Un: unclassified; YS: Yolk sac; FT: fallopian tube; Pa: papillary; MT: malignant teratoma; MMT: mullerian mixed tumor; TP: true positive; FP:false positive; FN: false negative; TN: true negative

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Table S1. QUADAS-2 Scoring of Included Studies

	PATIENT SELECTION		INDEX TEST		REFERENCE STANDARD	RISK OF BIAS			APPLICABILITY
AUTHORS	Consecutive patient enrollment?	Appropriate exclusion criteria?	Inter- or intra-rater reliability?	US training prior to study?	Always same reference standard?	Selection bias?	Bias from index test?	Bias from reference test?	Risk of inappropriate reference test?
Weiner 1992 [S1]	Yes	Yes	No	Unclear	Yes	Inter	Low	Low	Low
Kurjak 1992 [S2]	Yes	Yes	No	Unclear	Yes	Low	Low	Low	Low
Kurjak 1992 [S3]	Yes	Yes	No	Unclear	Yes	Low	Low	Low	Low
Schneider 1993 [S4]	Yes	Yes	No	Unclear	Yes	Inter	Low	Low	Low
Brown 1994 [S5]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Zanetta 1994 [S6]	Yes	Yes	No	Yes	Yes	Low	Low	Low	Low
Levine 1994 [S7]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Jain 1994 [S8]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Bromley 1994 [S9]	Yes	Yes	No	Unclear	Yes	High	Low	Low	Low
Salem 1994 [S10]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Wu 1994 [S11]	Yes	Yes	No	Unclear	Yes	Low	Low	Low	Low
Chou 1994 [S12]	Yes	Yes	No	Unclear	Yes	Inter	Low	Low	Low
Franchi 1995 [S13]	Yes	Yes	No	Yes	Yes	Inter	Low	Low	Low
Stein 1995 [S14]	Yes	Yes	No	No	Yes	Low	Low	Low	Low
Tepper 1995 [S15]	Yes	Yes	No	No	Yes	Low	Low	Low	Low
Tailor 1996 [S16]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Prompeler 1996 [S17]	Yes	Yes	No	Yes	Yes	Low	Low	Low	Low
Rehn 1996 [S18]	Yes	Yes	No	No	Yes	Low	Low	Low	Low
Caruso 1996 [S19]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low

Anandakumar 1996 [S20]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Matthes 1996 [S21]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Komatsu 1996 [S22]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Buy 1996 [S23]	Yes	Yes	No	Yes	Yes	Inter	Low	Low	Low
Strigini 1996 [S24]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Tailor 1997 [S25]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Valentin 1997 [S26]	Yes	Yes	No	No	Yes	Low	Low	Low	Low
Reles 1997 [S27]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Yang 1998 [S28]	Yes	Yes	No	Unclear	Yes	Inter	Low	Low	Low
Buckshee 1998 [S29]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Emoto 1998 [S30]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Alcazar 1999 [S31]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Schelling 2000 [S32]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Kupesic 2000 [S33]	Yes	Yes	No	Yes	Yes	High	Low	Low	Low
Wanapirak 2001 [S34]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Guerriero 2001 [S35]	Yes	Yes	No	No	Yes	Low	Low	Low	Low
Kurjak 2001 [S36]	Yes	Yes	No	No	Yes	Low	Low	Low	Low
Marret 2002 [S37]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Guerriero 2002 [S38]	Yes	Yes	No	Unclear	Yes	Low	Low	Low	Low
Alcazar 2003 [S39]	Yes	Yes	No	Unclear	Yes	Inter	Low	Low	Low
Ueland 2003 [S40]	Yes	Yes	No	No	Yes	Low	Low	Low	Low
Itakura 2003 [S41]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Gu 2003 [S42]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Orden 2003 [S43]	Yes	Yes	No	No	Yes	Low	Low	Low	Low
D'Arcy 2004 [S44]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low

Marret 2004 [S45]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Alcazar 2005 [S46]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Marret 2005 [S47]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Erdogan 2005 [S48]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Testa 2007 [S49]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Testa 2009 [S50]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Fleischer 2009 [S51]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Zhou 2009 [S52]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Veyer 2010 [S53]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Hassan 2011 [S54]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Zheng 2011 [S55]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Huchon 2012 [S56]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Wang 2012 [S57]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Hafeez 2013 [S58]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Kalmantis 2013 [S59]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Perez-Medina 2013 [S60]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Shah 2013 [S61]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Xiang 2013 [S62]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Zhang 2013 [S63]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Yang 2013 [S64]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Abbas 2014 [S65]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Zhang 2014 [S66]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Hu 2014 [S67]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Utrilla-Layna 2015 [S68]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Zhang 2015 [S69]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low

Tongsong 2016 [S70]	Yes	Yes	No	No	Yes	Inter	Low	Low	Low
Paul 2017 [S71]	Yes	Yes	No	No	Yes	High	Low	Low	Low
Al-Asadi 2018 [S72]	Yes	Yes	No	No	Yes	High	Low	Low	Low

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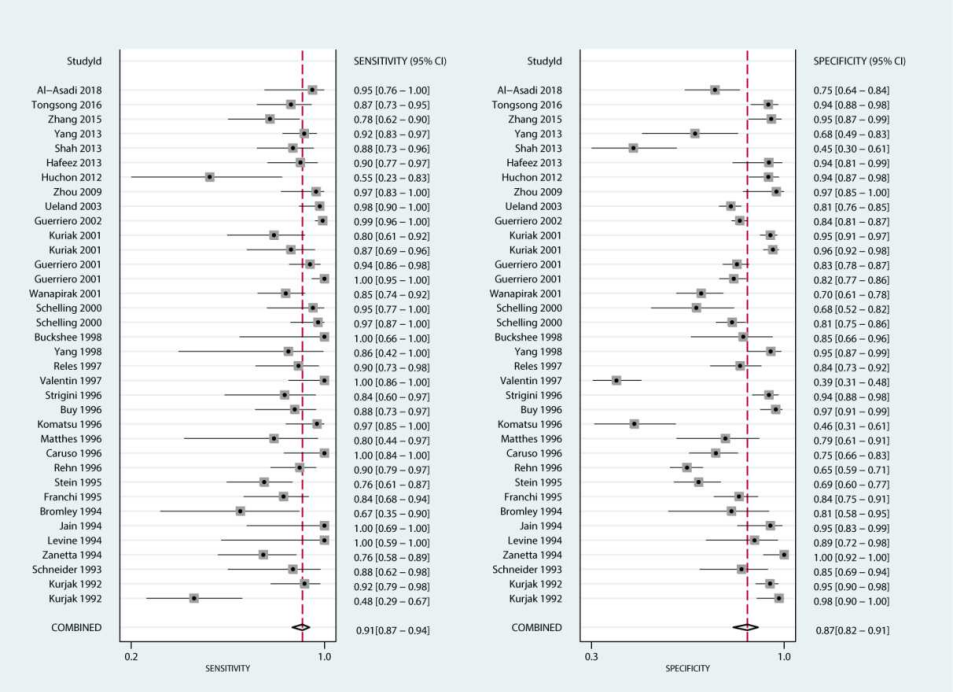

Figure S1. The pooled sensitivity and specificity for US differentiate the benign and malignant ovarian masses

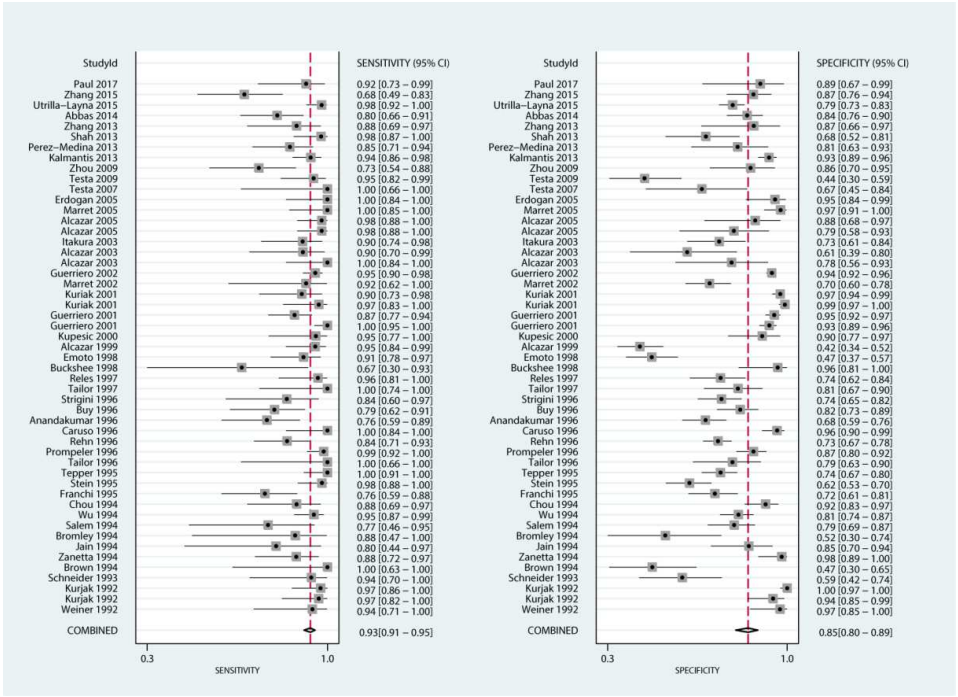

Figure S2. The pooled sensitivity and specificity for Doppler US differentiate the benign and malignant ovarian masses

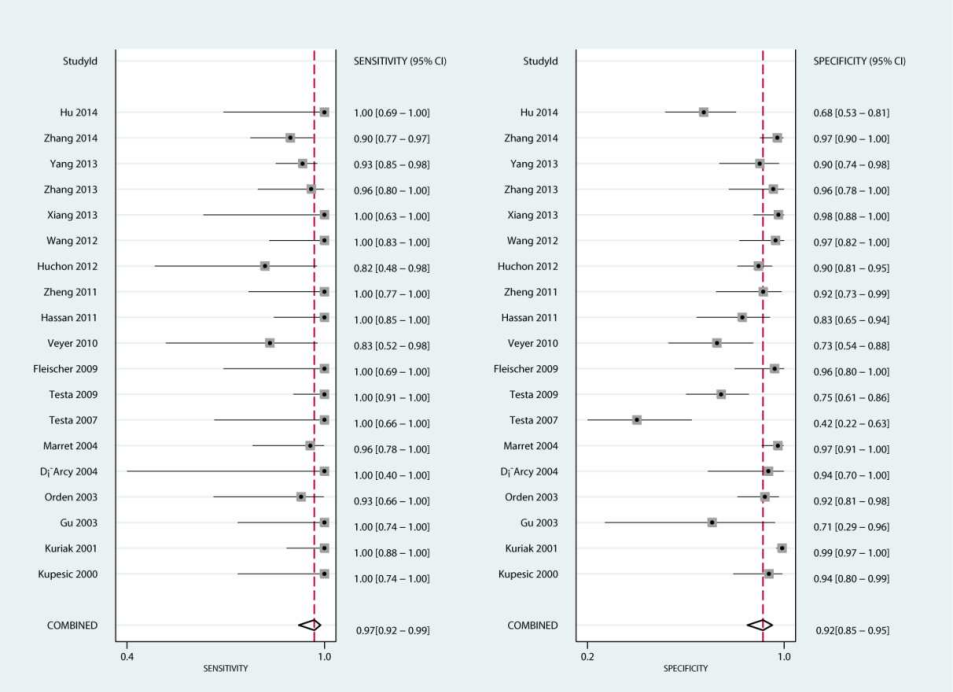

Figure S3. The pooled sensitivity and specificity for CEUS differentiate the benign and malignant ovarian masses

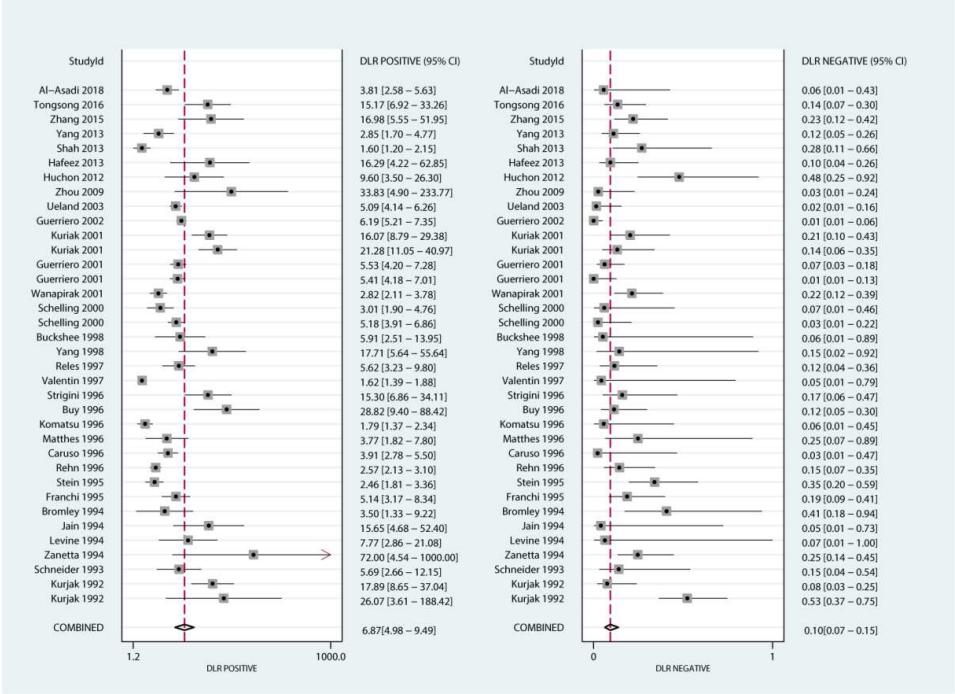

Figure S1. The pooled PLR and NLR for US differentiate the benign and malignant ovarian masses

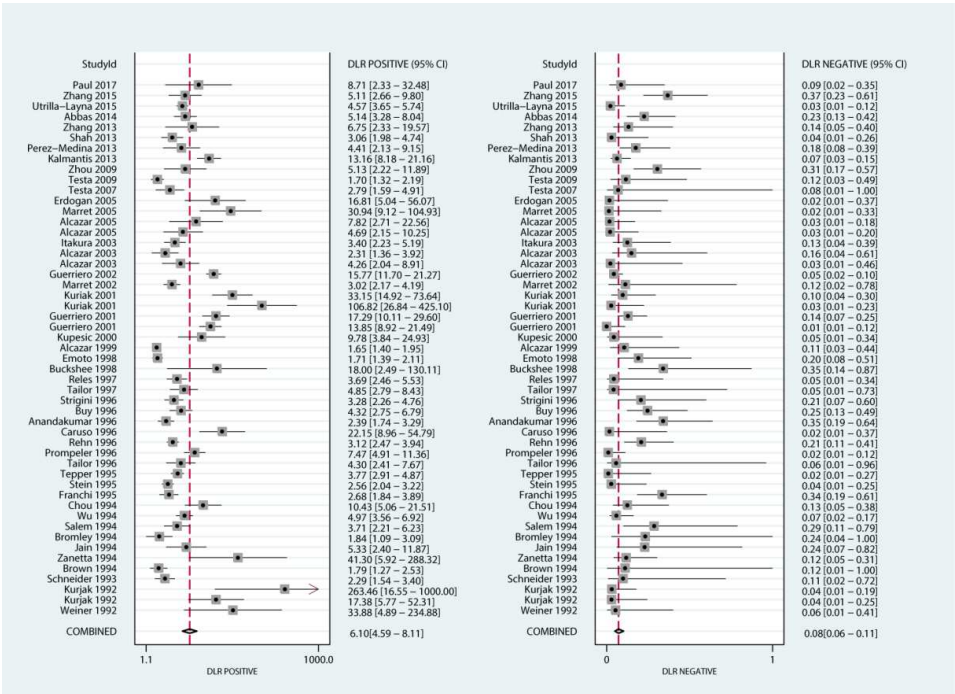

Figure S2. The pooled PLR and NLR for Doppler US differentiate the benign and malignant ovarian masses

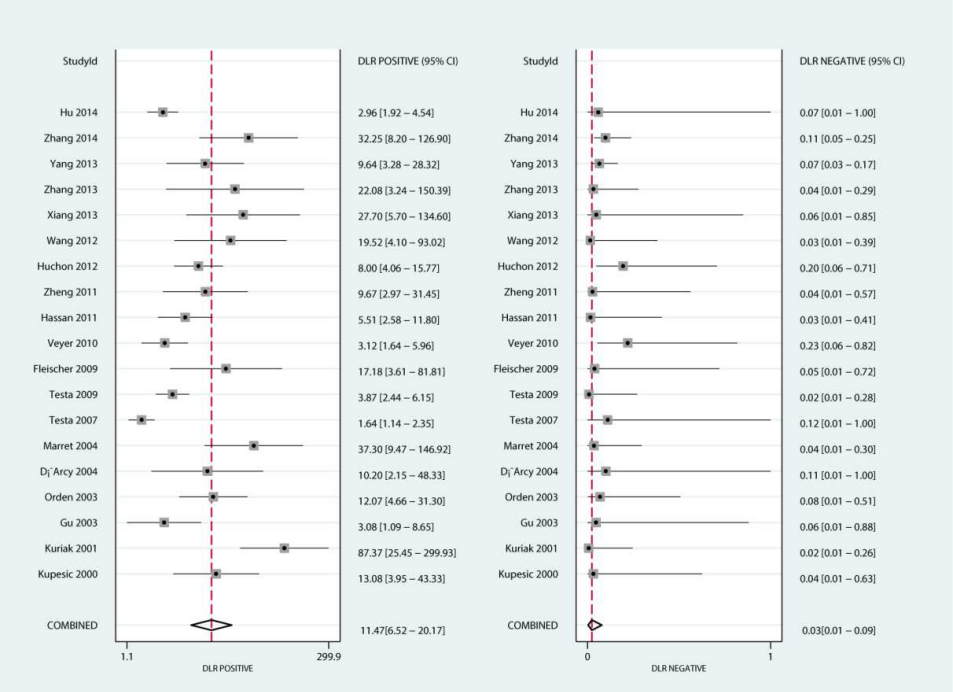

Figure S3. The pooled PLR and NLR for CEUS differentiate the benign and malignant ovarian masses

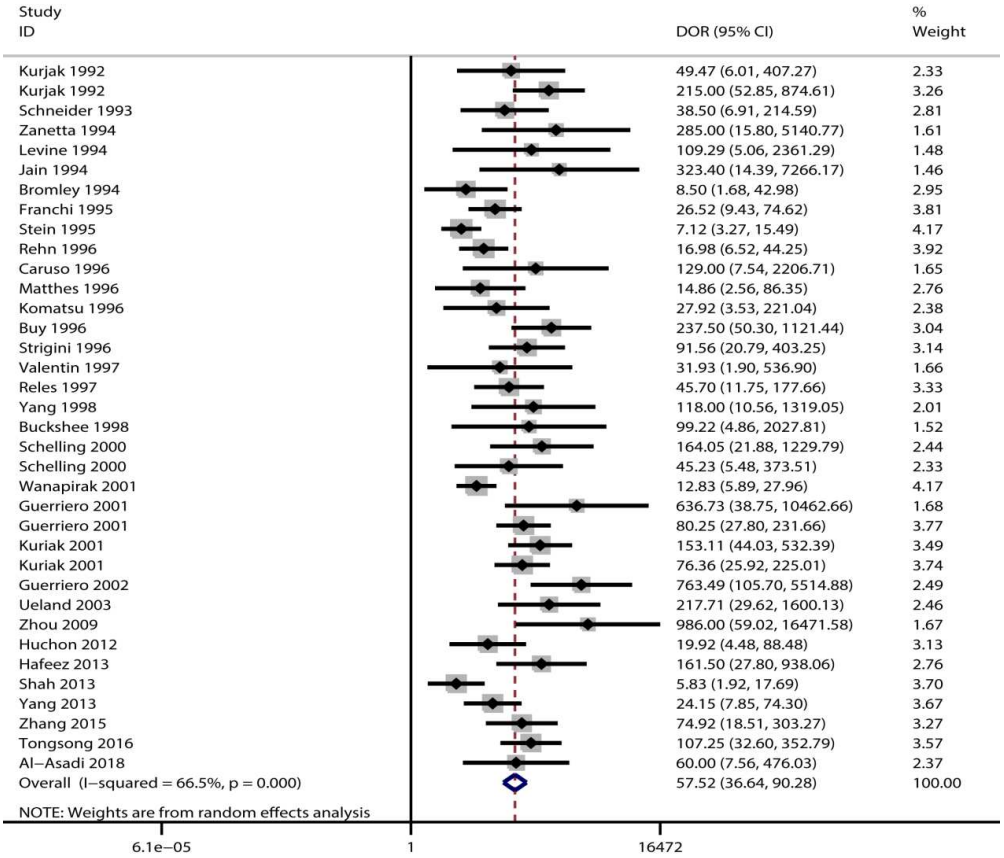

Figure S1. The pooled DOR for US differentiate the benign and malignant ovarian masses

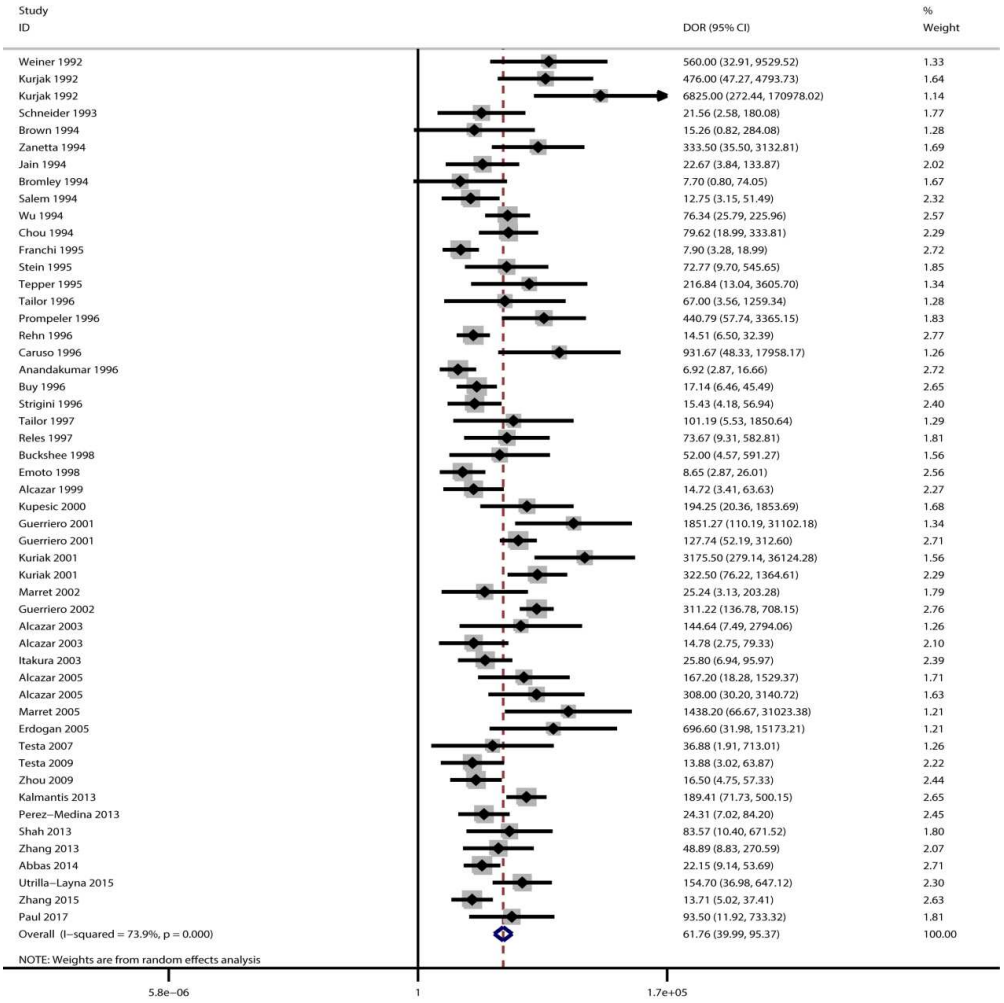

Figure S2. The pooled DOR for Doppler US differentiate the benign and malignant ovarian masses

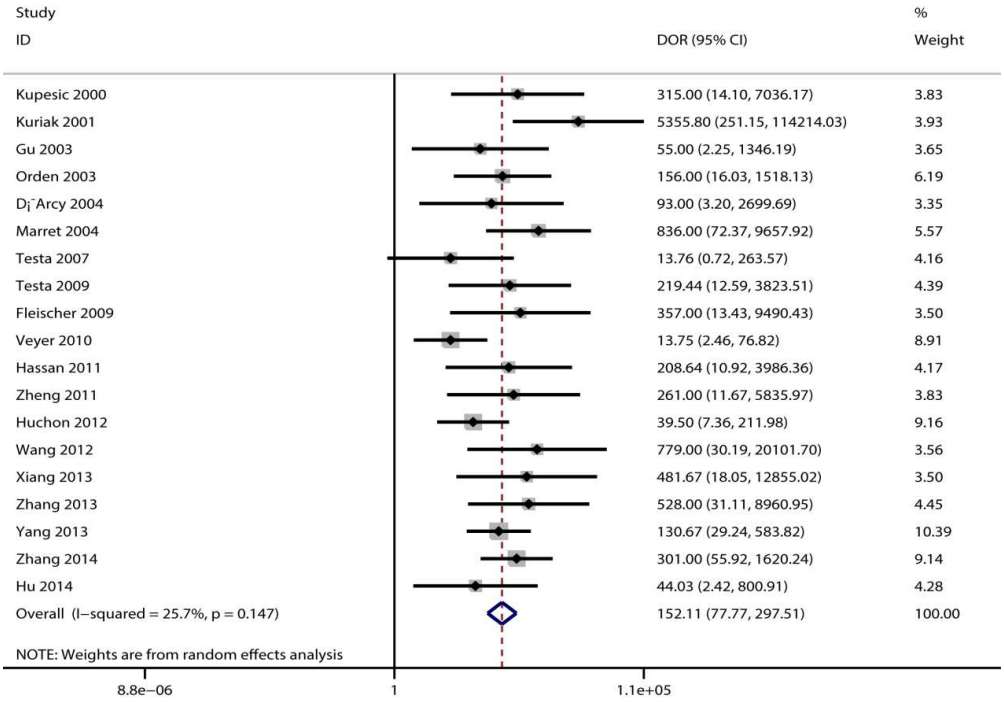

Figure S3. The pooled DOR for CEUS differentiate the benign and malignant ovarian masses