The accuracy of ultrasound scan in diagnosing retained products of conception: A systematic review and meta- analysis

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TITLE

The accuracy of ultrasound scan in diagnosing retained products of conception: A systematic review and meta- analysis

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Running title- The accuracy of ultrasonography in diagnosing RPOC.

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1) Dr Sundararajan- performed the systematic review, quality assessment, meta-analysis and the prepared the final manuscript
2) Dr Roy- performed the systematic review, quality assessment and reviewed the final manuscript
3) Dr Polanski- devised the study, resolved conflicts in the systematic review and quality assessment, reviewed the meta-analysis and made final changes to the manuscript.

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Condensation page

Tweetable statement- What is the best ultrasound predictor of retained pregnancy tissue? Our review concluded that the presence of bright tissue on ultrasound is a better indicator of retained pregnancy tissue compared with blood flow or thickened lining of uterus

Short version of the article title- Sonographic accuracy of detection of RPOC

AJOG at a glance-

Why was this study conducted?

The diagnosis of Retained products of conception (RPOC) is mainly based on clinical presentation along with ultrasound findings. The lack of accurate diagnostic predictors has influenced the incidence and the management. A reliable diagnosis of RPOC can avoid unnecessary surgical intervention and associated risks. We conducted the systematic review and meta-analysis to summarize the evidence on different sonographic markers used to diagnose RPOC.

Key findings

We found that echogenic mass had the highest sensitivity, specificity and Diagnostic Odds Ratio (DOR) for prediction of retained products of conception. The sensitivity, specificity and DOR are 0.915 (95% CI 0.844-0.955), 0.843 (95% CI 0.615-0.947) and 57.787 (95% CI 15.171-220.112), respectively. The diagnostic threshold for endometrial thickness was set as 10 mm with the sensitivity, specificity and DOR being 0.667(95% CI 0.072-0.981), 0.866(95% CI 0.375-0.986) and 12.927 (95% CI 0.23-726.582). The sensitivity, specificity and DOR of color Doppler flow are 0.850 (95% CI of 0.756-0.913), 0.406 (95% CI 0.198-0.655) and 3.893 (95% CI 1.005-15.081).

What does this add to what is known?

Our study has demonstrated that the presence of echogenic mass or a hyperechoic material on ultrasound scan is the best predictor of RPOC when compared with endometrial thickness and color Doppler studies.

ABSTRACT

Objective- To analyse and summarize the evidence on accuracy of different ultrasound methods in diagnosis of retained products of conception.

Data sources- We searched Ovid Sp, Cumulative Register to Nursing and Allied Health Literature (CINAHL) and EBSCO, Grey literature which included CORE, TRIP, NDLTD Global ETD search , BMJ best Practice, PubMed, GreyLit report website (http://www.greylit.org/), Cochrane Central register of controlled trials (CENTRAL) and Google scholar (https://scholar.google.com/).

Study eligibility criteria- We included prospective and retrospective cross sectional or Cohort studies that evaluated both ultrasound findings (prior to management of RPOC) and histopathological results of RPOC in all gestational ages.

Study appraisal and synthesis methods- We used COVIDENCE for data extraction of the studies and quality assessment. The meta-analysis was performed using RevMan 5.4 (Forest plot), MetaDTA version 2.01 and Meta-DiSc 2.0 online software.

Results- In total, eleven studies were eligible for data extraction and meta -analysis. The total number of study participants from these eleven studies were 1567. Out of these, nine studies were included to test the accuracy of echogenic mass, four studies analysed the endometrial thickness and five studies analysed color Doppler flow. We found that echogenic mass had the highest sensitivity, specificity and Diagnostic Odds Ratio (DOR) for prediction of retained products of conception. The sensitivity, specificity and DOR are 0.915 (95% CI 0.844-0.955), 0.843 (95% CI 0.615-0.947) and 57.787 (95% CI 15.171-220.112), respectively. The diagnostic threshold for endometrial thickness was set as 10 mm with the sensitivity, specificity and DOR being 0.667(95% CI 0.072-0.981), 0.866(95% CI 0.375-0.986) and 12.927 (95% CI 0.23-726.582). The sensitivity, specificity and DOR of color Doppler flow are 0.850(95% CI of 0.756-0.913), 0.406 (95% CI 0.198-0.655) and 3.893 (95% CI 1.005-15.081).

Conclusions- Our review concluded that echogenic mass is the most sensitive and specific predictor of retained products of conception after any pregnancy event. The most important limitation of our review is that the design of the studies included has resulted in significant statistical heterogeneity.

Keywords- Retained products of conception, transvaginal ultrasonography, miscarriage, termination, Cesarean, Doppler, endometrium

Acknowledgements -none

INTRODUCTION

Retained products of conception (RPOC) remains a diagnostic challenge following all pregnancy events, including miscarriage before viability (<24 weeks gestation; historical studies), termination, fetal demise, vaginal delivery (both preterm and full term), and Caesarean section. The incidence of RPOC ranges from 1% to 6% after term delivery [1], 6% following first or second trimester losses and up to 15% following medical terminations of pregnancy [2]. The diagnosis of RPOC is mainly based on clinical presentation along with ultrasound findings. The lack of accurate diagnostic predictors has influenced the incidence and the management. The management options for treatment of RPOC include conservative, medical or surgical interventions, depending on patient's severity of

haemorrhage and cardiovascular status, presence or absence of intrauterine infection and ultrasonographic features of RPOC [2]. Surgical intervention with suction evacuation to empty the uterine contents is the gold standard to treat RPOC [3], however they are associated with complications like uterine perforation, endometritis and development of intra-uterine adhesions. All of these, can impact future reproductive outcomes of the woman [2]. Hence, an accurate diagnosis of RPOC can avoid unnecessary surgical intervention and associated risks.

OBJECTIVE

We have conducted a systematic review of the literature to evaluate the best ultrasound features to describe RPOC and interpret the diagnostic accuracy of each modality and propose a sonographic definition of RPOC, based on the results.

METHODS

1) Eligibility criteria

The protocol of this review was registered on the International Prospective Register of Systematic Reviews (PROSPERO; https://www.crd.york.ac.uk/prospero/). The registration number is CRD42021254687.

Types of studies- We included prospective and retrospective cross sectional or Cohort studies that evaluated both ultrasound findings (prior to management of RPOC) and histopathological results of RPOC in all gestational ages. For the purpose of meta-analysis, we only included studies that published a 2X2 table (TP, TN, FP, FN) of disease prevalence; or if there were other variables like sensitivity, specificity or other statistical values that would help us derive the 2X2 table.

Case controlled studies and other types of review studies (systematic reviews, scoping review) were excluded. We also excluded case reports, case series and conference abstracts since it would not be possible to extract relevant data for meta-analysis. We also excluded studies that reported hysteroscopic evaluation of RPOC and other imaging modalities like MRI. We also excluded studies that reported outcomes of incomplete miscarriage. We have excluded studies that reported hysteroscopic appearance of retained product of conception only without prior reports of their sonographic appearance.

Types of participants- We have included studies with women who present with symptoms and signs of RPOC after a full term or preterm vaginal delivery or Caesarean section, miscarriage or termination of pregnancy (TOP).

Index test- The index test used was ultrasonographic evidence of RPOC. The ultrasonographic variables used in this review to describe RPOC included echogenic mass (EM; also called hyperechoic material), endometrial thickness (ET) and color Doppler flow (CDF). The target disease evaluated was RPOC after any pregnancy event (including term or preterm vaginal and caesarean deliveries, miscarriage or TOP). The gold reference standard considered for this review was the histopathological confirmation of RPOC.

2) Study selection

Search strategy- We searched Ovid Sp, Cumulative Register to Nursing and Allied Health Literature (CINAHL) and EBSCO, Grey literature which included CORE, TRIP, NDLTD Global ETD search , BMJ best Practice, PubMed, GreyLit report website (http://www.greylit.org/), Cochrane Central register of controlled trials (CENTRAL) and Google scholar

(https://scholar.google.com/). The database that was included in OvidSp were Journals@Ovid full text, Your Journal @Ovid, AMED, Embase, Ovid Emcare, HMIC, Ovid Medline ® ALL. We limited the search to years between 2001-2021 and the literature that were published in English language only.

The initial literature search was conducted on 30.04.2021 by S.S and S.R. independently. This yielded 2140 results of which 15 studies were included for data extraction. Due to the delay of over six months to complete the data extraction, a second search was carried out independently by the same researchers on 04.11.2022. Titles and abstracts were reviewed independently by S.S. and S.R. Any conflicts were resolved by the third author L.P.. S.S. and S.R. retrieved the full text of the articles that met inclusion criteria. The final decision to include in the full text screening was made by L.P.

3) Data extraction

The review was conducted using online software platform COVIDENCE (https://www.covidence.org/) [4]. The article titles that were found suitable for review were imported onto the website. The software system would automatically eliminate any duplicate articles that were imported. S.S. and S.R independently screened the titles and abstract of the articles and provide a decision to include or exclude in the review. The third author L.P. would independently resolve any conflicts at this stage. The full text of the included article would then be reviewed independently by S.S. and S.R. The full text of the articles was either accessed via the institutional open Athens account or through the aid of the departmental library. L.P. resolved any conflicts arising and gave a final decision to include or exclude from the review. Data was then extracted independently by the two authors S.S. and S.R. The third author (L.P.) assessed the data collected and provided consensus on both data extraction and quality assessment.

The study characteristic recorded were Study ID, Title, Authors, Country in which study conducted, Objectives, Study funding source, Conflict of interest, Type of study, Participants, Population description, Inclusion and Exclusion criteria, Year of study, Methodology, Ultrasound features of RPOC, Total number of participants, Participant characteristics - maternal age, parity , gestational age, type of delivery, duration between ultrasound assessment and surgical intervention, and clinical presentation, Statistical parameters- sensitivity, specificity, NPV, PPV of ultrasound features- Echogenic mass, Doppler findings, endometrial thickness , abdominal pain and bleeding, TP, TN, FP, FN Statistical test used, Results, Limitations and Conclusions.

Outcome- the primary outcome of our review was to measure the sensitivity and specificity of each of the ultrasonographic variables using the 2X2 table of TP (True positive), FP (false positive), TN (True negative) and FN (False negative). If we concluded that a study could be included but, further data was required to create a 2X2 table for meta-analysis, the authors of the study were contacted via the contact emails provided in their publication. If there was no reply within 2 weeks, the decision was made to exclude the study from meta-analysis.

4) Study risk of bias assessment

We used QUADAS 2 template to assess the quality of studies included in the review [5]. We assessed four domains in our study – patient selection index test, reference standard, flow and timing. We used quality assessment template available in COVIDENCE and formulated

questions to assess the quality in each domain [4]. S.S and S.R independently assessed the quality of description, signalling questions used to describe each of the above domains, risk of bias and concerns regarding applicability of the study to our review question. The final outcome was classified as being low, unclear or high. Any conflicts were resolved and consensus was provided by L.P.

5) Data Synthesis

We analysed the statistical data for three variables- Echogenic mass, endometrial thickness and color Doppler flow study. The measurement cut off for endometrial thickness was assigned as 10mm for the purpose of this review (majority of the studies included in our meta-analysis have used 10mm as a cut off). The studies that reported sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were considered eligible for the statistical analysis. We were able to complete statistical analysis only if studies provided information on TP, FP, TN and/or FN. In some studies, the authors had provided a 2X2 table.

For each of the ultrasonographic variables, we planned to calculate an estimate of sensitivity and specificity and their 95% confidence interval (CI). The estimate sensitivity, specificity and DOR were calculated in both bivariate and univariate models. We planned to graphically represent sensitivity and specificity on a Forest Plot. We used RevMan 5.4 to generate the Forest plot [6]. We also generated Forest plot to represent positive likelihood ratio, negative likelihood ratio and diagnostic odds ratio using Meta DiSc 1.4 application software [17]. We performed meta-analysis using both methods- the linear regression (summary operator receiver curve- SROC) and hierarchal method (HSROC) [7]. We performed meta-analysis using MetaDTA version 2.01 online software (https://crsu.shinyapps.io/dta_ma/) [5,8-15]. The online application was used to generate the SROC plot. The application also created a prevalence model based on sensitivity and specificity. The univariate statistical summary was generated using an online application called Meta-DiSc 2.0(https://ciberisciii.shinyapps.io/MetaDiSc2/) [16]. We have pooled sensitivity and specificity separately to obtain heterogeneity between studies and to obtain Cochran Q value and diagnostic threshold to analyse the source of heterogeneity. The pooled sensitivity and specificity are calculated using formulas that correspond to weighted averages in which the weight of each study is its sample size. We have used Random effects model (DerSimonian- Laird method) to demonstrate separate pooling using Meta DiSc 1.4 application software [17].

Heterogeneity- Individual heterogeneity score of inconsistency was generated using the MetaDiSc 1.4 application software. The heterogeneity was calculated using the DerSimonian- Laird method [17].

Additional analysis- We generated a table using GRADEproGDT software [18] to summarize the quality of evidence as:

a) High quality- further research is unlikely to change our confidence in the estimate of effect
b) Moderate quality- further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
c) Low quality- further research is very likely to have an important impact on our confidence in the estimate of the effect and may change the estimate
d) Very low quality- we are uncertain about the estimate [19].

We also generated a sample prevalence model for each of the ultrasonographic variable included in our meta-analysis. This model was generated using MetaBayes online software [5,8-15].

RESULTS-

a) Study selection - We have summarised the results of search conducted on 04.11.2022 (see Table 1). The databases that were included in OvidSp were Journals@Ovid full text, Your Journal @Ovid, AMED, Embase, Ovid Emcare, HMIC, Ovid Medline ® ALL. We performed multifield search in all fields. The search criteria used in OvidSp and CINAHL/EBSCO were

[Ultrasound or Sonograph* or Imaging or Doppler or Scan] (In one field)
AND [Retained placenta or Retained Tissue or Retained Trophoblast or Retained Products or Retained Conception] (in the next field). This yielded 3180 results in OvidSp and 114 results in CINAHL/EBSCO.
The CORE database was searched with terms Sonography and Retained Products of Conception and limited the search to English language. This gave 359 results.
The TRIP database was searched in 2 ways- We searched the advanced tab. This gave 2 options:
All of these words (tab)- we used Ultrasound and Retained Products of conception
Any of these words (tab) - we used [Ultrasound or Sonograph* or imaging or Doppler or Scan] AND [Retained placenta or retained tissue or retained trophoblast or retained products or retained conception]. We limited the clinical area search to Obstetrics and Gynaecology (231 results) and Women's Health (90 results).
The NDLTD Global ETD database was searched with words- Ultrasound and retained products of conception. The search was restricted to English and this gave 27 results.
The google scholar was searched with following terms:
[Ultrasound or sonograph* or Doppler or Scan or imaging] and [Retained products or retained tissue or retained placenta or retained trophoblast or retained conception] . This resulted in 1210 pages. The results of the search after page number 10 were less relevant and would be less beneficial for the review. So, we screened titles of 200 articles from first 10 pages.
The BMJ best practice and Greylit report websites yielded 0 results. SS and SR screened the titles from all database except Grey literature. SS screened the titles from greyliterature.

We screened the titles of 4201 articles, 52 of these were duplicates. Following title and abstract screening, 4111 studies were excluded as they did not meet the inclusion criteria. Detailed review of the full text article was carried out in 38 studies. Of these, 27 studies, though of good quality, were deemed not suitable for review and meta-analysis (see Table 2). The remaining 11 studies met our inclusion criteria and were included in the final review. In two, we have contacted the authors to obtain more data in order to include their studies in the meta- analysis [20,21](14,23), however we have not received any response. We have therefore, excluded these studies. Any conflicts to include in the review at any stage of the process, were resolved by LP on COVIDENCE [4]. Figure 1 represents the PRISMA flowchart explaining the process of article inclusion.

The inter -rater reliability was calculated using COVIDENCE software [4] (Table 3). The inter-rater reliability of full text review between S.S. and S.R. was calculated and the Cohen's Kappa co-efficient derived a value of 0.53894. This demonstrates a moderate agreement between the two reviewers. The title and abstract screening between S.S. and S.R. derived a Cohen's Kappa value of 0.26316 which demonstrates a fair agreement between the two reviewers [22].

b) Study characteristics

In total, 1567 participants were included in our review from eleven studies. Table 4 summarizes the demographic details of individual studies. The mean average age of the participants from the studies ranged between 28.1 to 31.8. Time interval between the ultrasound examination and surgical intervention was reported only by three studies [23-25] and this ranged from 0-8 days. Eight [23-30] out of eleven studies reported gestational age in their study population, with the mean gestational age ranging between 9.2 to 38.8 weeks. Eight studies reported the mode of delivery[23-31]. In total, 50 patients had Caesarean section, 429 had term or preterm vaginal delivery, 451 had miscarriage and 42 participants had termination of pregnancy. The highest number of study participants in miscarriage group was attributed to the design of the studies included in the review. Six studies were prospective [23,28-32] and four [24-27] were retrospective studies. Qazi et al. did not mention the type of study in their publication [33]. During the review process, the eleven studies that were included in meta-analysis described echogenic mass, endometrial thickness and/or color Doppler as the sonographic variables. Hence, we used the three sonographic descriptions in our review to perform the meta-analysis.

c) Risk of bias of included studies- Figure (4) demonstrates the risk of bias of each of the studies included in the review

d) Data synthesis

We assessed 3 important aspects of reporting ultrasonographic features of Retained products of conception in literature-

a) Echogenic mass- also described in various studies as hyperechoic material or irregular, mixed echogenic endometrium
b) Endometrial thickness (ET) – the measurement has been variable across different studies and we have included studies that have reported ET>= 10mm.
c) Color Doppler imaging

A) Echogenic mass- In total, nine studies [23-27,29,30,32,33] that reported echogenic mass were included in our review. The total number of participants from these studies were 1237. Figure 2(A) demonstrates the forest plot of nine studies used to evaluate the echogenic mass. The estimated (bivariate analysis) sensitivity and specificity of echogenic mass for detection of RPOC from meta-analysis was 0.915 (95% CI 0.844-0.955) and 0.843 (95% CI 0.615-0.947) (27-36). Of note, the diagnostics odds ratio (bivariate analysis) is reported as 57.787 (95% CI 15.171-220.112). Figure 3 (A) demonstrates the HSRoC (Hierarchal Summary Receiver Operator Curve) curve derived from a bivariate hierarchal model meta- analysis. The summary estimate of all the included studies demonstrates a high sensitivity and specificity. The univariate statistics summary has been tabulated in table5. The pooled sensitivity, specificity and DOR are 0.897 (95% CI 0.867-0.923), 0.868

(95% CI 0.841-0.891) and 50.954 (95% CI 13.424-193.42), respectively. The χ^2 heterogeneity value was calculated using the DerSimonian- Laird method and the χ^2 values for sensitivity, specificity and DOR are 37.01, 177.39 and 60.19, respectively [17]. The Cochran Q value for DOR to test heterogeneity is 60.19. This gave the final source of heterogeneity (I-Squared) for sensitivity, specificity and DOR as follows-78.4%,95.5% and 86.7%, respectively [17]. This high degree of heterogeneity was expected by the reviewers due to the nature of selection of studies included. The pooled positive and negative likelihood ratio of echogenic mass was 5.49 (95% CI 2.44-12.39) and 0.15 (95% CI 0.08-0.28), respectively. Supplementary Figure A, B and C shows the Forest plot of echogenic mass describing the positive likelihood ratio, negative likelihood ratio and DOR, respectively. Figure 5 (A) is an example of prevalence model of RPOC based on echogenic mass diagnosed on ultrasound [5,8-15]. Figure 6(A) demonstrates the diagnostic threshold calculations that provide values to calculate the heterogeneity of the studies. Table 6 summarises the assessment of the evidence produced from the meta-analysis of echogenic mass [18]. Our meta-analysis result concludes that the echogenic mass has a high sensitivity and specificity for diagnosing RPOC.

B) Endometrial thickness- Four studies [26,29,30,31]analysed the endometrial thickness as a predictor in diagnosing RPOC. The total number of participants from these studies was 504. All four studies that were of good quality used 10mm as a cut off and we set the diagnostic threshold as 10 mm for the purpose of our review. Ideally, a diagnostic threshold is set using the Receiver operator curve. However, generation of Receiver Operator Curve (RoC) for diagnostic threshold was not the objective of the study. Furthermore, many studies that described various endometrial thickness either demonstrated high selection bias or lacked the data to perform statistical analysis (Table 12). Four [26,29,30,31] studies described the endometrial thickness cut off as 10mm. We were unable to find good quality evidence in the literature to recommend a measurement cut off for endometrial thickness to diagnose RPOC.
Figure 2(B) demonstrates the Forest plot of the four studies that analysed endometrial thickness. Figure 3(B) represents the hierarchal SROC generated using bivariate hierarchal model. The summary estimate point on the HSROC plot is in the region of high sensitivity and specificity. However, the wide scatter of studies on the graph has led to limited application, both clinically and statistically. The summary estimate (bivariate analysis) sensitivity and specificity are 0.667(95% CI 0.072-0.981) and 0.866(95% CI 0.375-0.986). The wide range in the confidence interval implies that we are unable to confidently ascertain the sensitivity and specificity of RPOC using endometrial thickness. This is a result of high degrees of heterogeneity between studies and the limited number of studies that have been included in the meta-analysis of endometrial thickness. The diagnostic odds ratio (bivariate analysis) is 12.927 (95% CI 0.23-726.582). Table 7 tabulates the univariate statistical summary. The pooled sensitivity, specificity and DOR are 0.430 (95% CI 0.359-0.503), 0.807 (95% CI 0.759-0.849) and 7.256 (95% CI 0.171-308.21), respectively. The χ^2 values for sensitivity, specificity and DOR are 133.69, 74.94 and 48.75, respectively. The Cochran Q value for DOR to test heterogeneity is 48.75. This gave the final source of heterogeneity (I-Squared) for sensitivity, specificity and DOR as follows- 97.8%, 96% and 93.8%, respectively. Figure 6 (B) demonstrates the statistical diagnostic threshold analysis [17]. The statistical analysis thus summarises the poor corelation between endometrial thickness and RPOC. The pooled positive and negative likelihood ratio of endometrial thickness were 1.67 (95% CI 0.33-8.41) and 0.41 (95% CI

0.08-2.02), respectively. supplementary Figure D, E and F shows the Forest plot of Endometrial thickness describing the positive likelihood ratio, negative likelihood ratio and DOR, respectively.

Figure 5 (B) is an example of prevalence model of RPOC using endometrial thickness as a predictor. Table 8 summarises the GradePro classification of certainty of evidence from the studies included in meta-analysis. As expected, the analysis has resulted in low quality of evidence. The reviewers conclude that from the statistical analysis, due to wide range of heterogeneity between studies, endometrial thickness is a poor statistical predictor of RPOC.

C) Color Doppler imaging or vascularity description – Five studies included color Doppler imaging in their description [24,26,27,30,35]. The total number of participants included from these five studies was 425. Figure 2C demonstrates the forest plot of the five studies that describe the Doppler flow and color Doppler imaging. The summary estimate (bivariate analysis) sensitivity, specificity and DOR of the color Doppler imaging are 0.850 (95% CI 0.756-0.913), 0.406 (95% CI 0.198-0.655) and 3.893 (95% CI 1.005-15.081), respectively. Figure 3 (C) demonstrates the HSROC plot of studies included in predicting the accuracy of color Doppler flow in diagnosing RPOC [5,8-15]. The HSROC plot in the graph is placed in the top right and this is due to the low specificity of the color Doppler analysis. Table 9 demonstrates the univariate statistical analysis of color Doppler flow [16]. The pooled sensitivity, specificity and DOR are 0.821 (95% CI 0.766-0.868), 0.442 (95% CI 0.37-0.516) and 3.963 (95% CI 0.907-17.326). Figure 6 (C) demonstrates the analysis of diagnostic threshold of color Doppler imaging [17]. The χ^2 heterogeneity value was calculated using the DerSimonian- Laird method and the χ^2 values for sensitivity, specificity and DOR are 12.09, 56.6 and 25.26, respectively. The Cochran Q value for DOR to test heterogeneity is 25.26. This gave the final source of heterogeneity (I-Squared) for sensitivity, specificity and DOR as follows- 66.9%, 92.9% and 84.2% [17]. The statistical analysis concludes that color Doppler imaging has low specificity in predicting RPOC. Figure 5 (C) is a sample prevalence model for the prediction of color Doppler flow in diagnosing RPOC. The pooled positive and negative likelihood ratio of color Doppler imaging are 1.59 (95% CI 0.91-2.77) and 0.41 (95% CI 0.51-1.11), respectively. Supplementary 1 Figure G, H and I shows the Forest plot of color Doppler imaging describing the positive likelihood ratio, negative likelihood ratio and Diagnostic Odds ratio, respectively.

Table 10 summarizes the GradePro classification of certainty of evidence from the studies included in meta-analysis of color Doppler flow. We conclude that the color Doppler flow is of some value in predicting RPOC but the statistical significance is complicated to summarize. The low specificity and high false positive rate from the statistical analysis has led to the limited application in diagnosing positive findings of RPOC. The heterogeneity of studies is quite significant and this could be due to the different descriptive methods used in these studies.

Atri et al.[24] conducted a retrospective analysis of endometrial based focal color vascularity and echogenic mass. Presence or absence of vascularity was evaluated using lowest pulse repetition frequency (PRF). In this study the PRF ranged between 2-9cm/sec. They concluded that focal vascularity showed a better trend toward sensitivity than an echogenic mass. Durfee et al.[26] reported on the presence or absence of flow in the endometrium or the endometrial mass. They concluded that endometrial mass is the most sensitive and specific

sonographic finding for diagnosing RPOC. Esmaeillou et al.[29] describe endometrial vascularity as the presence of color Doppler signal in the endometrium. They used Pulsed Doppler to obtain flow velocity waveform and calculated RI (Resistance Index). RPOC was suspected when RI <0.45. Ganer-Herman et al.[27] concluded that no variables (clinical, sonographic and intra-procedural) accurately predicted the presence of RPOC. They retrospectively recorded the sonographic findings of women who underwent operative hysteroscopy for suspected RPOC. Our review concluded that this study had a high risk of selection and index test bias (Figure 4). Komiya-Padilla et al. [30] reported the presence of color Doppler flow within the endometrium and designated subjective vascularity scores of the retained tissue with score ranging from 1 to 4. Their study showed that a larger proportion of subjects with endometrial mass on ultrasound had RPOC or were positive for histopathology (88.6%), compared with thickened endometrium of 10mm (71.4%) and color Doppler flow (85%) only. However, there was no statistically significant difference noted in the proportion when using color Doppler (P value of 1).

Proposed description of RPOC

In line with the findings of this review, we suggest RPOC be suspected following a pregnancy event, when on a sagittal and transverse sections of the endometrial cavity, a heterogenic mass is present with an endometrial thickness of at least 10 mm and with or without presence of multifocal Doppler signal. The mass can conform to the shape of the endometrial cavity or can be a distinct entity, however, a clear margin separating it from the endo-myometrial junction should be present. Presence of this clear boundary throughout the entire circumference of the content, may indicate presence of blood clots only. There can be particulate intracavitary fluid surrounding the mass representing blood. The heterogenic mass can have regular or irregular margins, can be lobulated and have calcifications, but the content of it has mixed echogenicity (figure 7). When pressure with the transducer is applied, the mass may or may not move freely along the endometrial layer, indicating it is free or adherent to the basal layer, respectively. In the context of an adherent mass, Doppler signal is more likely to be present.

COMMENT

Principal findings- Our review concludes that the presence of echogenic mass is the most sensitive and specific ultrasonographic variable to predict RPOC. Our review has also concluded that the endometrial thickness >10mm has a very poor statistical corelation in diagnosing RPOC. The Forest plots of positive likelihood ratio, negative likelihood ratio and DOR further strengthen our conclusion that echogenic mass is the best predictor of retained products of conception.

a) Comparison with existing literature- During our review, it was apparent that good value data on the topic is lacking. At present however, there is no consensus on the methods to describe an echogenic mass. Kamaya et al.[57] concluded that the lack of consensus on ultrasound features of RPOC may be due to changing technology in grey scale and Doppler imaging. Maslovitz et al.[43] reviewed the re-evacuation histopathology specimen in 69 women who presented with bleeding and clinical suspicion of RPOC. They found that the operator skills are an important factor in interpreting sonographic reports.

Matijevic et al.[44] performed a prospective audit of 93 women and their analysis showed that an endometrial mass is the most sensitive finding for RPOC. They defined RPOC as endometrial mass with hyperechoic or hypoechoic or mixed pattern in the uterine cavity measuring greater than 10mm, including both layers of endometrium at the medio-sagittal plane or a low RI (<0.45) detected by color or pulse flow in the same area. Mulic-Lutvica et al. performed a study on postpartum women and measured the maximum antero-posterior (AP) diameters of the uterus and uterine cavity in the longitudinal section. An echogenic mass was defined as well-circumscribed mass, often with a lobulated appearance and calcifications, without any fluid components [45]. Quantitative values of maximum antero-posterior diameter (in mm) were plotted on reference curves (denoted as 10^{th}, 50^{th} and 90^{th} percentile curves) generated from their previous study. The authors have found that echogenic mass in uterine cavity with a cavity diameter above 90^{th} percentile was the best predictor of RPOC. However, they also conclude that echogenic mass could be present in asymptomatic postpartum women with no RPOC [45].

There have been many studies that have tried to establish the accuracy of endometrial thickness in diagnosing RPOC. Ustunyurt et al.[53] have obtained very similar results from their analysis and recommend to avoid clinical decision making based on endometrial thickness alone. They have suggested considering conservative management in women with sonographic endometrial thickness of <13mm. Negm et al. [47] have analysed different endometrial thickness cut off points and, in their study, ROC (Receiver operator curve) showed a cut off value of >6mm.

The color Doppler flow is the least accurate to diagnose RPOC statistically. Van den Bosch et al. [54] specifically examined the vascularity within the entire myometrium up to the endometrial cavity. They found that enhanced vascularity along the whole thickness of myometrium was relatively common after pregnancy. The association between the occurrence of vascularity and the time interval of pregnancy and examination explain the transient nature of this ultrasound feature. Table 13 provides definition of color Doppler descriptors used in individual studies describing retained products of conception.

Strengths and Limitations- We have been successful in conducting a systematic statistical analysis of the ultrasound predictors. This enabled us to apply the statistical findings of the review to interpret the common sonographic appearances of retained products of conception. Our review also has provided a prevalence model which will enable sonographic Departments internationally to apply the findings to suit the individual needs.

Our study has multiple limitations. Some of the studies included were of very poor quality and hence the resultant statistical analysis is based on poor-quality evidence. The types of studies, participants and methodology, have all contributed to very high heterogeneity of observed values. We have shown that multiple definitions of RPOC and corresponding factors exist (see Tables 11, 12 and 13), and we have attempted to create a proposed description of sonographic appearance of RPOC based on the available descriptors. In order to focus only on sonographic descriptions, when designing the study, we have not taken into account the clinical aspects of RPOC, such as vaginal bleeding and its intensity, presence of pyrexia or pain.

CONCLUSION and IMPLICATIONS- In summary, our review concludes that presence of an echogenic mass within the endometrial cavity following a pregnancy episode is the best predictor of RPOC. Although endometrial thickness and color Doppler flow is widely used to predict RPOC, the lack of consensus on ET cut-off values and variable approach to Doppler imaging methodology makes their applicability of questionable importance. We found a wide variation in the techniques and methods used to describe the ultrasound appearance of retained products of conception. Though we have analysed each of the variables independently, additive effect of all their sonographic features (presence of echogenic mass with an endometrial thickness of >10 mm and presence of enhanced endo-myometrial vascularity) may be more diagnostic, than each variable individually. This has been seen in some of the studies reported [44]. We recommend a standardised definition of sonographic appearance of RPOC, and we recommend that this is followed by a prospective study assessing the predictive values of the sonographic descriptors of RPOC. This would assure good diagnostic accuracy, standardisation of future research and improved patient outcomes with minimisation of unnecessary medical or surgical interventions. We also conclude that clinical management should be guided by the clinical presentation, with intensity of haemorrhage as the main guide, and with respect to patient wishes.

Reference

1. Thangarajah F, Brunner M, Pahmeyer C, et al. Predictors of Postpartal Retained Products of Conception. *In Vivo*. Mar-Apr 2019;33(2):469-472. doi:10.21873/invivo.11496
2. Foreste V, Gallo A, Manzi A, Riccardi C, Carugno J, Sardo ADS. Hysteroscopy and Retained Products of Conception: An Update. *Gynecol Minim Invasive Ther*. Oct-Dec 2021;10(4):203-209. doi:10.4103/GMIT.GMIT_125_20
3. Tzur Y, Berkovitz-Shperling R, Goitein Inbar T, et al. Expectant vs medical management for retained products of conception after medical termination of pregnancy: a randomized controlled study. *Am J Obstet Gynecol*. Oct 2022;227(4):599 e1-599 e9. doi:10.1016/j.ajog.2022.06.025
4. *Covidence systematic review software*. https://www.covidence.org
5. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. Oct 18 2011;155(8):529-36. doi:10.7326/0003-4819-155-8-201110180-00009
6. *Review Manager (RevMan)*. Version 5.4. 2020.
7. Dinnes J, Mallett S, Hopewell S, Roderick PJ, Deeks JJ. The Moses-Littenberg meta-analytical method generates systematic differences in test accuracy compared to hierarchical meta-analytical models. *J Clin Epidemiol*. Dec 2016;80:77-87. doi:10.1016/j.jclinepi.2016.07.011
8. Patel A, Cooper N, Freeman S, Sutton A. Graphical enhancements to summary receiver operating characteristic plots to facilitate the analysis and reporting of meta-analysis of diagnostic test accuracy data. *Research Synthesis Methods*. 2021;12(1):34-44. doi:https://doi.org/10.1002/jrsm.1439
9. Freeman SC, Kerby CR, Patel A, Cooper NJ, Quinn T, Sutton AJ. Development of an interactive web-based tool to conduct and interrogate meta-analysis of diagnostic test accuracy studies: MetaDTA. *BMC Medical Research Methodology*. 2019/04/18 2019;19(1):81. doi:10.1186/s12874-019-0724-x
10. Burke DL, Ensor J, Snell KIE, van der Windt D, Riley RD. Guidance for deriving and presenting percentage study weights in meta-analysis of test accuracy studies. *Research Synthesis Methods*. 2018;9(2):163-178. doi:https://doi.org/10.1002/jrsm.1283
11. Chu H, Cole SR. Bivariate meta-analysis of sensitivity and specificity with sparse data: a generalized linear mixed model approach. *J Clin Epidemiol*. Dec 2006;59(12):1331-2; author reply 1332-3. doi:10.1016/j.jclinepi.2006.06.011
12. Harbord RM, Deeks JJ, Egger M, Whiting P, Sterne JA. A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics*. Apr 2007;8(2):239-51. doi:10.1093/biostatistics/kxl004
13. Harrison JK, Fearon P, Noel-Storr AH, McShane R, Stott DJ, Quinn TJ. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within a secondary care setting. *Cochrane Database Syst Rev*. Mar 10 2015;(3):Cd010772. doi:10.1002/14651858.CD010772.pub2
14. Rutter CM, Gatsonis CA. A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. *Stat Med*. Oct 15 2001;20(19):2865-84. doi:10.1002/sim.942
15. *LME4: Linear Mixed-Effects Models Using Eigen and S4. R Packageversion 1.1-4.* 2014. https://cran.r-project.org/web/packages/lme4/index.html
16. Plana MN, Arevalo-Rodriguez I, Fernandez-Garcia S, et al. Meta-DiSc 2.0: a web application for meta-analysis of diagnostic test accuracy data. *BMC Med Res Methodol*. Nov 28 2022;22(1):306. doi:10.1186/s12874-022-01788-2
17. Zamora J, Abraira V, Muriel A, Khan K, Coomarasamy A. Meta-DiSc: a software for meta-analysis of test accuracy data. *BMC Med Res Methodol*. Jul 12 2006;6:31. doi:10.1186/1471-2288-6-31
18. *GRADEpro GDT: GRADEpro Guideline Development Tool [Software]*. 2022. https://www.gradepro.org

19. Group TGW. 5. Quality of evidence. In: Schünemann H BJ, Guyatt G, Oxman A., ed. *GRADE handbook for grading quality of evidence and strength of recommendations*. 2013.
20. McEwing RL, Anderson NG, Meates JB, Allen RB, Phillipson GT, Wells JE. Sonographic appearances of the endometrium after termination of pregnancy in asymptomatic versus symptomatic women. *J Ultrasound Med*. May 2009;28(5):579-86. doi:10.7863/jum.2009.28.5.579
21. van den Bosch T, Daemen A, Van Schoubroeck D, Pochet N, De Moor B, Timmerman D. Occurrence and outcome of residual trophoblastic tissue: a prospective study. *J Ultrasound Med*. Mar 2008;27(3):357-61. doi:10.7863/jum.2008.27.3.357
22. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med (Zagreb)*. 2012;22(3):276-82.
23. Cosmi E, Saccardi C, Litta P, Nardelli GB, Dessole S. Transvaginal ultrasound and sonohysterography for assessment of postpartum residual trophoblastic tissue. *Int J Gynaecol Obstet*. Sep 2010;110(3):262-4. doi:10.1016/j.ijgo.2010.03.036
24. Atri M, Rao A, Boylan C, Rasty G, Gerber D. Best predictors of grayscale ultrasound combined with color Doppler in the diagnosis of retained products of conception. *J Clin Ultrasound*. Mar-Apr 2011;39(3):122-7. doi:10.1002/jcu.20779
25. Abbasi S, Jamal A, Eslamian L, Marsousi V. Role of clinical and ultrasound findings in the diagnosis of retained products of conception. *Ultrasound Obstet Gynecol*. Oct 2008;32(5):704-7. doi:10.1002/uog.5391
26. Durfee SM, Frates MC, Luong A, Benson CB. The sonographic and color Doppler features of retained products of conception. *J Ultrasound Med*. Sep 2005;24(9):1181-6; quiz 1188-9. doi:10.7863/jum.2005.24.9.1181
27. Ganer Herman H, Kogan Z, Dabas A, et al. Clinical and Sonographic Findings in Suspected Retained Trophoblast: Correlation with Histological Findings. *Isr Med Assoc J*. Dec 2018;20(12):761-764.
28. Wong SF, Lam MH, Ho LC. Transvaginal sonography in the detection of retained products of conception after first-trimester spontaneous abortion. *J Clin Ultrasound*. Sep 2002;30(7):428-32. doi:10.1002/jcu.10086
29. Esmaeillou H, Jamal AS, Eslamian L, Marsousi V, Sarvi F, Kokab A. Accurate Detection of Retained Products of Conception after First- and Second-trimester Abortion by Color Doppler Sonography. *Journal of Medical Ultrasound*. 2015;23:34-38.
30. Komiya-Padilla J, Go-Suva L. Correlation of grayscale combined with color doppler sonography from histopathology in prediction of retained products of conception. . *PJOG*. 2019;43(3):22-30.
31. Abd EL Kareem MA, El Mantwe AN, Souidan EE, Rashwan HA. Diagnostic Accuracy of Ultrasonography in Women with Postabortive and Postpartum Hemorrhage. *Benha Journal of Applied Sciences*. 2021;6(4):267-272. doi:10.21608/bjas.2021.197756
32. Wolman I, Altman E, Faith G, et al. Combined clinical and ultrasonographic work-up for the diagnosis of retained products of conception. *Fertil Steril*. Sep 2009;92(3):1162-1164. doi:10.1016/j.fertnstert.2009.01.087
33. Qazi AS, Sabahat S. Devising New Management Protocol Based on Sonographic Sensitivity for the Detection of Retained Products of Conception. *Annals of King Edward Medical University*. 2009;15(3):123.
34. Alcazar JL, Ortiz CA. Transvaginal color Doppler ultrasonography in the management of first-trimester spontaneous abortion. *Eur J Obstet Gynecol Reprod Biol*. Apr 10 2002;102(1):83-7. doi:10.1016/s0301-2115(01)00573-5
35. Chopra N, Kaur M, Mohi MK. Correlation of ultrasound with histopathology for retained products of conception in medically managed abortions. *International Journal of Reproduction, Contraception, Obstetrics and Gynaecology*. 2017;6(8)doi:https://doi.org/10.18203/2320-1770.ijrcog20173373

36. de Vries JI, van der Linden RM, van der Linden HC. Predictive value of sonographic examination to visualize retained placenta directly after birth at 16 to 28 weeks. *Journal of Ultrasound in Medicine*. 2000;19(1):7-12. doi:https://doi.org/10.7863/jum.2000.19.1.7

37. Iqbal H, Khan MS, Muneeb A, Mirza WA. Diagnostic Accuracy of Ultrasound in Detecting Retained Products of Conception: A Study from a Tertiary Care Hospital in Karachi, Pakistan. *Cureus*. Nov 8 2018;10(11):e3564. doi:10.7759/cureus.3564

38. Iqbal K, Manzoor S, Butt R, Niazi M, Kulsoom U, Kalsoom U. Diagnostic Accuracy of Endovaginal Scan in Detection of Retained Products of Conception after Incomplete Abortion. *Journal of Rawalpindi Medical College*. 09/12 2019;23

39. Kamaya A, Petrovitch I, Chen B, Frederick CE, Jeffrey RB. Retained Products of Conception. *Journal of Ultrasound in Medicine*. 2009;28(8):1031-1041. doi:https://doi.org/10.7863/jum.2009.28.8.1031

40. Kido A, Togashi K, Koyama T, et al. Retained products of conception masquerading as acquired arteriovenous malformation. *J Comput Assist Tomogr*. Jan-Feb 2003;27(1):88-92. doi:10.1097/00004728-200301000-00016

41. Levin I, Almog B, Ata B, Ratan G, Many A. Clinical and sonographic findings in suspected retained trophoblast after pregnancy do not predict the disorder. *J Minim Invasive Gynecol*. Jan-Feb 2010;17(1):66-9. doi:10.1016/j.jmig.2009.11.002

42. Levinsohn-Tavor O, Feldman N, Svirsky R, Smorgick N, Nir-Yoffe A, Maymon R. Ultrasound criteria for managing postpartum patients with suspicion of retention of conception products. *Acta Radiol*. Feb 2020;61(2):276-281. doi:10.1177/0284185119855185

43. Maslovitz S, Almog B, Mimouni GS, Jaffa A, Lessing JB, Many A. Accuracy of diagnosis of retained products of conception after dilation and evacuation. *J Ultrasound Med*. Jun 2004;23(6):749-56; quiz 758-9. doi:10.7863/jum.2004.23.6.749

44. Matijevic R, Knezevic M, Grgic O, Zlodi-Hrsak L. Diagnostic accuracy of sonographic and clinical parameters in the prediction of retained products of conception. *J Ultrasound Med*. Mar 2009;28(3):295-9. doi:10.7863/jum.2009.28.3.295

45. Mulic-Lutvica A, Axelsson O. Ultrasound finding of an echogenic mass in women with secondary postpartum hemorrhage is associated with retained placental tissue. *Ultrasound Obstet Gynecol*. Sep 2006;28(3):312-9. doi:10.1002/uog.2849

46. Mungen E, Dundar O, Babacan A. Postabortion Doppler evaluation of the uterus: incidence and causes of myometrial hypervascularity. *J Ultrasound Med*. Aug 2009;28(8):1053-60. doi:10.7863/jum.2009.28.8.1053

47. Negm S, Al-Inany H, Omar H. Assessment of the accuracy of transvaginal ultrasonography in determining the presence of retained products of conception in patients presenting with spontaneous abortion. *Middle East Fertility Society Journal*. 01/01 2002;7:130-134.

48. Oba T, Hasegawa J, Sekizawa A. Postpartum ultrasound: postpartum assessment using ultrasonography. *J Matern Fetal Neonatal Med*. Jul 2017;30(14):1726-1729. doi:10.1080/14767058.2016.1223034

49. Sadan O, Golan A, Girtler O, et al. Role of sonography in the diagnosis of retained products of conception. *J Ultrasound Med*. Mar 2004;23(3):371-4. doi:10.7863/jum.2004.23.3.371

50. Sawyer E, Ofuasia E, Ofili-Yebovi D, Helmy S, Gonzalez J, Jurkovic D. The value of measuring endometrial thickness and volume on transvaginal ultrasound scan for the diagnosis of incomplete miscarriage. *Ultrasound Obstet Gynecol*. Feb 2007;29(2):205-9. doi:10.1002/uog.3914

51. Smorgick N, Krakov A, Maymon R, Betser M, Tovbin J, Pansky M. Postpartum Retained Products of Conception: A Novel Approach to Follow-Up and Early Diagnosis. *Ultraschall Med*. Dec 2018;39(6):643-649. Postpartal retinierte Schwangerschaftsprodukte: Ein neuer Ansatz fur die Nachverfolgung und fruhe Diagnosestellung. doi:10.1055/s-0043-113817

52. Shen O, Rabinowitz R, Eisenberg VH, Samueloff A. Transabdominal Sonography Before Uterine Exploration as a Predictor of Retained Placental Fragments. *Journal of Ultrasound in Medicine*. 2003;22(6):561-564. doi:https://doi.org/10.7863/jum.2003.22.6.561

53. Ustunyurt E, Kaymak O, Iskender C, Ustunyurt OB, Celik C, Danisman N. Role of transvaginal sonography in the diagnosis of retained products of conception. *Arch Gynecol Obstet*. Feb 2008;277(2):151-4. doi:10.1007/s00404-007-0436-z

54. Van den Bosch T, Van Schoubroeck D, Lu C, De Brabanter J, Van Huffel S, Timmerman D. Color Doppler and gray-scale ultrasound evaluation of the postpartum uterus. *Ultrasound Obstet Gynecol*. Dec 2002;20(6):586-91. doi:10.1046/j.1469-0705.2002.00851.x

55. Vyas S, Choi HH, Whetstone S, Jha P, Poder L, Shum DJ. Ultrasound features help identify patients who can undergo noninvasive management for suspected retained products of conception: a single institutional experience. *Abdom Radiol (NY)*. Jun 2021;46(6):2729-2739. doi:10.1007/s00261-020-02948-y

56. Zalel Y, Gamzu R, Lidor A, Goldenberg M, Achiron R. Color doppler imaging in the sonohysterographic diagnosis of residual trophoblastic tissue. *Journal of Clinical Ultrasound*. 2002;30(4):222-225. doi:https://doi.org/10.1002/jcu.10059

57. Kamaya A, Petrovitch I, Chen B, Frederick CE, Jeffrey RB. Retained products of conception: spectrum of color Doppler findings. *J Ultrasound Med*. Aug 2009;28(8):1031-41. doi:10.7863/jum.2009.28.8.1031

TABLES

Search engine	Database	Search words	Search limits	Results
Ovid Sp	Journals@Ovid full text, Your Journal @Ovid, AMED, Embase, Ovid Emcare, HMIC, Ovid Medline ® ALL	[Ultrasound or Sonograph* or Imaging or Doppler or Scan] (In one filed) AND [Retained placenta or Retained Tissue or Retained Trophoblast or Retained Products or Retained Conception] (in the next field).		3180
	CINAHL/EBSCO	[Ultrasound or Sonograph* or Imaging or Doppler or Scan] (In one filed) AND [Retained placenta or Retained Tissue or Retained Trophoblast or Retained Products or Retained Conception] (in the next field).		114
	CORE	Sonography and Retained Products of Conception	English language	359
	TRIP	All of these words (tab)- Ultrasound and Retained Products of conception, Any of these words (tab) - we used [Ultrasound or Sonograph* or imaging or Doppler or Scan] AND [Retained placenta or retained tissue or retained trophoblast or retained products or retained conception]	Obstetrics and Gyanecology and Women's Health	Obstetrics and Gyanecology-231, Women's health-90
	NDLTD Global ETD	Ultrasound and retained products of conception	English language	27

google scholar (1210 pages, but screened only 10 pages)		[Ultrasound or sonograph* or Doppler or Scan or imaging] and [Retained products or retained tissue or retained placenta or retained trophoblast or retained conception]		200
BMJ best practice		Ultrasound and retained products of conception		0
Greylit report		Ultrasound and retained products of conception		0

Table 1. The search criteria employed from each database, search limits applied and the number of studies that were screened from each database.

Excluded studies

Author name and reference	Reason for exclusion
Alcazar et al.2002 23	Data extraction not possible
Chopra et al. 2017 24	Data extraction not possible
De Vries et al. 2000 25	Irrelevant study- study designed to scan immediately after delivery
Iqbal et al. 2018 26	Wrong study design- results do not define features of RPOC. The discussion section mentions both endometrial thickness and echogenic mass whereas the histogram provides results for endometrial thickness.
Iqbal et al. 2019 27	Wrong study design- methodology states patient with ongoing bleeding and positive pregnancy test, includes ongoing threatened miscarriage.
Kamaya et al. 2009 28	Data extraction not possible
Kido et al. 2003 29	Wrong study design- mainly case report and includes various other imaging modalities like MRI.
Levin et al. 2010 30	Wrong index test used – used hysteroscopy for removal of suspected RPOC. Case control study that primarily analysed surgeons' opinion of RPOC during hysteroscopic procedure.
Levinsohn-Tavor et al. 2019 31	Data extraction not possible
Maslovitz et al. 2004 32	Data extraction not possible
Matijevic et al. 2009 33	Data extraction not possible
McEwing et al. 2009 20	Data extraction not possible
Mulic-Lutvica et al. 2006 34	Data extraction not possible
Müngen et al. 2009 35	Data extraction not possible
Negm et al. 2002 36	Data extraction not possible
Oba et al. 2017 37	Irrelevant article- published article describing various sonographic appearances in the postpartum period.
Qazi et al. 2013 38	Duplicate
Sadan et al. 2004 39	Data extraction not possible or Insufficient data- study reports incidence and prevalence of RPOC, not designed to calculate sensitivity, specificity, NPV (negative predictive value) or PPV (positive predictive value)
Sawyer et al. 2007 40	Wrong study design- not all women recruited underwent surgical management to confirm RPOC. Hence histopathology was not available in all participants.
Smorgick et al. 2017 41	No data to extract
Shen et al. 2003 42	wrong intervention- patients evaluated using transabdominal sonography.
Thangarajah et al. 1	Data extraction not possible
Ustunyurt et al. 2008 43	No data to extract

Van den Bosch et al. 2002 44	No data to extract
Van den Bosch et al. 2008 21	Data extraction not possible
Vyas et al. 2021 45	Wrong study design- evaluates ultrasound predictor of successful management of RPOC.
Zalel et al. 2002 46	Wrong study design- evaluates the role of color Doppler imaging during sonohysterography in diagnosis of RPOC.

Table 2. Excluded full text articles with corresponding reasons for exclusion from quantitative meta-analysis.

Inter-rater reliability

Full text review						
Reviewer A	Reviewer B	Proportionate Agreement	Yes Probability	No Probability	Random Agreement Probability	Cohen's Kappa
S.S.	S.R.	0.78378	0.41417	0.11687	0.53104	0.53894
Title and abstract screening						
Reviewer A	Reviewer B	Proportionate Agreement	Yes Probability	No Probability	Random Agreement Probability	Cohen's Kappa
S.S.	S.R.	0.6	0.28571	0.17143	0.45714	0.26316

Table 3- The inter-rater reliability calculation between the two reviewers (Sri Sundararajan- S.S. and Subhadeep Roy- S.R.) who screened the titles and abstract.

INDIVIDUAL STUDY CHARACTERISTICS

Study ID	Maternal age column	Parity column	Time duration between USS and surgery	Gestational age column	Cesarean	VD	misca rriage	Termination	Type of study
Komiya-Padilla 2019	29.44 +_7.02 (Pos), 31.31+_5.68(neg) (Mean+_ SD)	2+_2	no data	11.64+_3.32 (pos), 13.08+_4.02 (neg) (mean+_ SD)	no data	no data	no data	no data	cross sectional prospective study
Qazi 2009	29.45+_7.89(mean+_ SD)	no data	no data	no data	no data	no data	no data	no data	not stated
AbdEL Kareem 2021	Group 1- 22-44, Group 2- 20-43	Group 1- 13-primi, 20-multip, Group 2 .53-primi, 64-multip	no data	no data	no data	150	no data	no data	Prospective cohort analysis
Wolman 2009	no data	no data	no data	no data	no data	no data	no data	no data	Prospective study
Ganer Herman 2018	30.5+_5.6 (pos) , 31.2+_7.1 (neg) (mean+_SD)	2(0-7)(RPOC) , 1(0-5) (No RPOC) (meadian,range)	no data	delivery-38.8+_2.8 (pos), 37.1+_4.5 (neg), abortion-10+_4.3(pos), 11.2+_5(neg), (mean+_SD),	11	73	93	42	Retrospective cohort analysis

Table 4- Demographic characteristics of the included individual studies including the maternal age, gestational age, parity, type of delivery, the duration between ultrasonographic diagnosis of

Study ID	Maternal age column	Parity column	Time duration between USS and surgery	Gestational age column	Cesarean	VD	miscarriage	Termination	Type of study
Cosmi 2010	median-32(range 28-35years)	no data	2days (within)	35-40 weeks	no data	84	no data	no data	Prospective cohort
Durfee 2005	14-44 years(mean , 31years)	no data	no data	14-43 weeks (mean, 37 weeks)	39, 31.96%	122, 74.84%	no data	no data	Retrospective cohort
Abbasi 2008	28.3(+_6.1) (mean)	1(median) , 0-5	1 day (max)	11.1(+_2.7) (mean+_SD)	no data	no data	91	no data	Retrospective cohort
Atri 2011	17-48years(range), 31.8+_6.8 (mean)	no data	0-8days(mean 1.4+_2.1day SD)	5-24 weeks (range), 9.2+_3.8 (mean+_SD)	no data	no data	91	no data	Retrospective study
Esmaeillou 2015	RPOC- 28.1 ,4.8, no RPOC-28.1, 4.7(Mean, SD)	no data	no data	13.3 weeks (median) (RPOC) , 14.4 weeks (median)(no RPOC)	no data	no data	77	no data	Prospective interventional study
Wong 2002	no data	no data	no data	9(5-13)(median and range)	no data	no data			Prospective cohort

retained products and the surgical intervention to obtain histopathological diagnosis and the type of study. VD= Vaginal delivery

Univariate analysis of echogenic mass

Parameter	Estimate	95% LCI (2.5% CI)	95% UCI (97.5% CI)
Sensitivity	0.915	0.845	0.956
Specificity	0.842	0.616	0.946
Diagnostic Odds Ratio	57.613	14.452	229.684
Positive Likelihood Ratio	5.787	2.103	15.923
Negative Likelihood Ratio	0.1	0.052	0.194
False Positive Rate	0.158	0.054	0.384

Table 5- Univariate statistical values of the meta-analysis on echogenic mass.

Gradepro assessment of studies describing echogenic mass

		True positives (patients with retained products of conception)	False negatives (patients incorrectly classified as not having retained products of conception)	True negatives (patients without retained products of conception)	False positives (patients incorrectly classified as having retained products of conception)
Test accuracy CoE		⊕⊕⊕⊕ High		⊕⊕◯◯ Low[e]	
Effect per 1,000 patients tested	pre-test probability	732 (675 to 764)	68 (36 to 125)	169 (123 to 189)	31 (11 to 77)
	pre-test probability	458 (422 to 478)	42 (22 to 78)	422 (308 to 474)	78 (26 to 192)
	pre-test probability	92 (84 to 96)	8 (4 to 16)	759 (554 to 852)	141 (48 to 346)
Factors that may decrease certainty of evidence	Publication bias	none		none	
	Imprecision	not serious[12,18,8,1,25,7,4,9,6]		not serious	
	Inconsistency	not serious[12,4,1,25,7]		Serious[12,4,6,d]	
	Indirectness	not serious[12,18,8,125,7,4,2]		not serious[9,6,c]	
	Risk of bias	not serious[48,12,18,8,1,,a]		serious[7,4,10,6,b]	
Study design		cohort & case-control type studies		cross-sectional (cohort type accuracy study)	
№ of studies (№ of patients)		9 studies 498 patients		9 studies 734 patients	
Outcome		**True positives** (patients with retained products of conception)	**False negatives** (patients incorrectly classified as not having retained products of conception)	**True negatives** (patients without retained products of conception)	**False positives** (patients incorrectly classified as having retained products of conception)

Table 6- Assessment of quality of evidence for the diagnostic accuracy of echogenic mass.

Explanations:

a. Komiya Padilla et al. - little description about patient selection , Qazi et al- very little information regarding recruiting and inclusion criteria of patients, Esmaeillou et al- no mention regarding enrolment of consecutive patients

b. Cosmi et al. compared USS findings with HSG and used ergometrine prior to evacuation that might have resulted in spontaneous expulsion of products, Atri et al.- population description was clear but patient selection for D&C was less desribed, Ganer Herman et al.- high risk of bias because study seems to be weighted towards establishing hysteroscopy as better modality,

c. Cosmi et al. used HSG and implied HSG is a superior test, Ganer Herman et al. used hysteroscopy in their study alongside USS to confirm findings of USS.

d. Atri, Cosmi and Koniya Padilla conclude that Doppler or SHG studies are superior to echogenic mass

e. 2 studies reported inconsistent Sensitivity and specificity and hence the evidence downgrades to low for these 2 studies

Univariate analysis of endometrial thickness

Parameter	Estimate	95% LCI (2.5% CI)	95% UCI (97.5% CI)
Sensitivity	0.667	0.072	0.981
Specificity	0.866	0.375	0.986
Diagnostic Odds Ratio	12.936	0.231	725.043
Positive Likelihood Ratio	4.974	0.486	50.878
Negative Likelihood Ratio	0.385	0.043	3.44
False Positive Rate	0.134	0.014	0.625

Table 7- Univariate statistical analysis of meta-analysis on endometrial thickness.

GradePro assessment of studies describing Endometrial thickness

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence: Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Effect per 1,000 patients tested: pre-test probability	pre-test probability	pre-test probability	Test accuracy CoE
True positives (patients with retained products of conception)	4 studies 193 patients	cohort & case-control type studies	very serious	very serious	very serious	very serious	strong association all plausible residual confounding would suggest spurious effect, while	344 (287 to 402)	215 (180 to 252)	43 (36 to 50)	⊕◯◯◯ Very low[1,2,3,4,a]
False negatives (patients incorrectly classified as not having retained								456 (398 to 513)	285 (248 to 320)	57 (50 to 64)	
True negatives (patients without retained products of conception)	4 studies 311 patients	cohort & case-control type studies	serious	very serious	very serious	extremely serious	very strong association all plausible residual confounding would suggest spurious effect, while	161 (152 to 170)	404 (380 to 425)	726 (683 to 764)	⊕◯◯◯ Very low[1,2,3,4,b]
False positives (patients incorrectly classified as having retained								39 (30 to 48)	96 (75 to 120)	174 (136 to 217)	

Table 8- Assessment of quality of evidence for the diagnostic accuracy of endometrial thickness

Evidence

a. All studies have different study designs and included different population. By this we refer to the methodology and the variation in sonographic practice. The high risk of bias is also due to the use of

different definition of endometrial thickness- the method of measurements also varies across the studies.

b. The lack of consensus in definition of an endometrial thickness in RPOC setting has made this variable controversial and hence it's clinical application is limited

Univariate analysis of color Doppler flow

Parameter	Estimate	95% LCI (2.5% CI)	95% UCI (97.5% CI)
Sensitivity	0.846	0.752	0.908
Specificity	0.414	0.205	0.66
Diagnostic Odds Ratio	3.868	1.201	12.454
Positive Likelihood Ratio	1.443	0.941	2.213
Negative Likelihood Ratio	0.373	0.172	0.809
False Positive Rate	0.586	0.34	0.795

Table 9- Univariate statistical analysis of the meta-analysis on color Doppler imaging

Gradepro assessment of studies describing color Doppler flow

Outcome	**True positives** (patients with retained products of conception)	**False negatives** (patients incorrectly classified as not having retained products of conception)	**True negatives** (patients without retained products of conception)	**False positives** (patients incorrectly classified as having retained products of conception)
№ of studies (№ of patients)	5 studies 235 patients		5 studies 190 patients	
Study design	cohort & case-control type studies		cohort & case-control type studies	
Factors that may decrease certainty of evidence: Risk of bias	serious		serious	
Indirectness	not serious		serious	
Inconsistency	serious		not serious	
Imprecision	not serious		not serious	
Publication bias	none		strong association	
Effect per 1,000 patients tested: pre-test probability of10%	85 (76 to 91)	15 (9 to 24)	365 (178 to 590)	535 (310 to 722)
pre-test probability of50%	425 (378 to 457)	75 (43 to 122)	203 (99 to 328)	297 (172 to 401)
pre-test probability of80%	680 (605 to 730)	120 (70 to 195)	81 (40 to 131)	119 (69 to 160)
Test accuracy CoE	⊕⊕◯◯ Low[12,9,8,7,4,a]		⊕⊕⊕◯ Moderate[12,9,8,7,4]	

Table 10- GradePro summary of analysis of certainty of evidence for color Doppler flow.

Explanations

a. 2 out of 5 studies are of good quality

Echogenic mass description of individual studies

Authors	Description of Echogenic mass
Abbasi et al. 2008 49	Hyperechoic material
Chopra et al. 2019 24	Intrauterine mass distinct from the rest of the endometrium, measurable in 3 dimensions in 2 orthogonal planes.
Durfee et al. 2005 50	Focal echogenic or heterogenous lesion
Esmaeillou et al. 2015 53	Hyperechoic material
Ganer Herman et al. 2018 51	Irregular endometrial shape
Kamaya et al. 2009 28, 57	Intrauterine mass distinct from the rest of the endometrium, measurable in 3 dimensions in 2 orthogonal planes.
Komiya-Padilla et al. 2019 54	Intra uterine mass distinct from the endometrium
Matijevic et al. 2009 33	Endometrial mass with hyperechoic, hypoechoic or mixed echogenic pattern in the uterine cavity.
Mulic-Lutvica et al. 2006 34	Echogenic mass defined as well-circumscribed mass, often with lobulated appearance and calcifications, without any fluid component. Fluid in the cavity defined as a space separating anterior from posterior wall. A mixed echo pattern defined as echogenic material mixed with fluid components
Sawyer et al. 2007 40	Well defined hyperechoic tissue which appeared adherent to uterine wall
Smorgick et al. 2017 41	Discrete echogenic uterine mass
Van den Bosch et al. 2008 21	Echogenic well-defined mass inside the uterine cavity with or without distinct vascular pedicle.

Table 11- Common ultrasonographic definitions of RPOC in the literature.

Endometrial thickness description of individual studies

Authors	Endometrial thickness measurement
Abbasi et al. 2008 49	8mm
Abd El Kareem et al. 2021 55	10mm
Atri et al. 2011 48	8mm
Chopra et al. 2019 24	10mm
Durfee et al. 2005 50	10mm
Esmaeillou et al. 2015 53	10mm
Iqbal et al. 2019 27	12mm
Komiya-Padill et al. a 2019 54	10mm
Levinsohn-Tavor et al. 2019 31	10mm
Maslovitz et al. 2004 32	10mm
Matijevic et al. 2009 33	10mm
Negm et al. 2002 36	6mm
Sadan et al. 2004 39	8mm
Sawyer et al. 2007 40	5,8,12,15,25mm
Smorgick et al. 2017 41	10mm
Ustunyurt et al. 2008 43	13mm
Wong et al. 2002 52	8mm

Table 12- Endometrial thickness values used by various authors when considering RPOC.

Color Doppler flow description of individual studies

Authors	Doppler flow description
Alcazar et al. 2002 23	Vascular impedence was estimated by calculating the RI (RI <0.45 diagnostic)
Durfee et al. 2005 50	presence or absence of flow in the endometrium or in the endometrial mass
Esmaeillou et al. 2015 53	Colour Doppler signal of the endometrium. Pulsed Doppler was used to obtain a flow velocity waveform (RI <0.45 diagnostic)
Ganer Herman et al. 2018 51	Hypervascularity
Kamaya et al. 2009 28	The presence of color Doppler signal and amount of endometrial vascularity was assessed as none, minimal, moderate or marked. Avascular defined as undetectable vascularity in the endometrium, minimal vascularity defined as some detectable vascular flow in the endometrium but less than in the myometrium, moderate vascularity defined as vascularity equal to or near equal to that in the myometrium in the same image section, marked vascularity defined as endometrial vascularity greater than that in the myometrium in the same image section. The highest PSV for arterial and venous waveforms were recorded and the RIs were calculated.
Komiya-Padilla et al. 2019 54	degree of vascularity of the endometrial component compared with the myometrial vascularity in the same image section, We designated subjective vascularity score similar to IOTA classification Type 1 was defined as no detectable flow Type 2 was defined as certain detectable color flow in the endometrium but less than that of myometrium Type 3 was defined as vascularity nearly equal or same in the myometrium Type 4 was defined as greater than that of myometrium If arterial waveforms were present, RI <0.45 diagnostic
McEwing et al. 2009 20	Colour flow was defined as absent, minimal (1 or 2 areas with poor color signal), moderate (1 or 2 areas with prominent color) or marked (intense and generalized color flow) after optimization for low velocity
Matijevic et al. 2009 33	Blood flow signals detected by color or Pulsed Doppler imaging in the same area and low RI <0.45.
Mungen et al. 2009 35	Enhanced myometrial vascularity defiend as presence of high-velocity, low-impedance, and turbulent flow over the full or nearly full thickness of the myometrium. Spectral analysis

	of blood flow was also performed at 3 different sites within the area of enhanced myometrial vascularity (EMV), and the highest peak systolic velocity was recorded, PI also recorded.
Van den Bosch et al. 2002 44	Enhanced vascularity defined as presence of marked flow over full thickness of the myometrium reaching the endometrial cavity. Doppler flow signals in the outer and middle myometrium were normal.
Van den Bosch et al. 2008 21	Enhanced myometrial vascularity was defined as the presence on color Doppler imaging of an area of marked flow over the full thickness of the myometrium and reaching the uterine cavity.
Vyas et al. 2021 45	Focus of increased vascularity in the myometrium which extends into the endometrium, vascularity was categorised as Types 0–3, denoting avascular, mild, moderate, or marked. Inner myometrial peak systolic velocity (PSV) and resistive index (RI)

Table 13- Doppler blood flow descriptors used in various studies describing RPOC. The Doppler is applied to the content of the endometrial cavity, with the Doppler gate also including the sub endometrium.

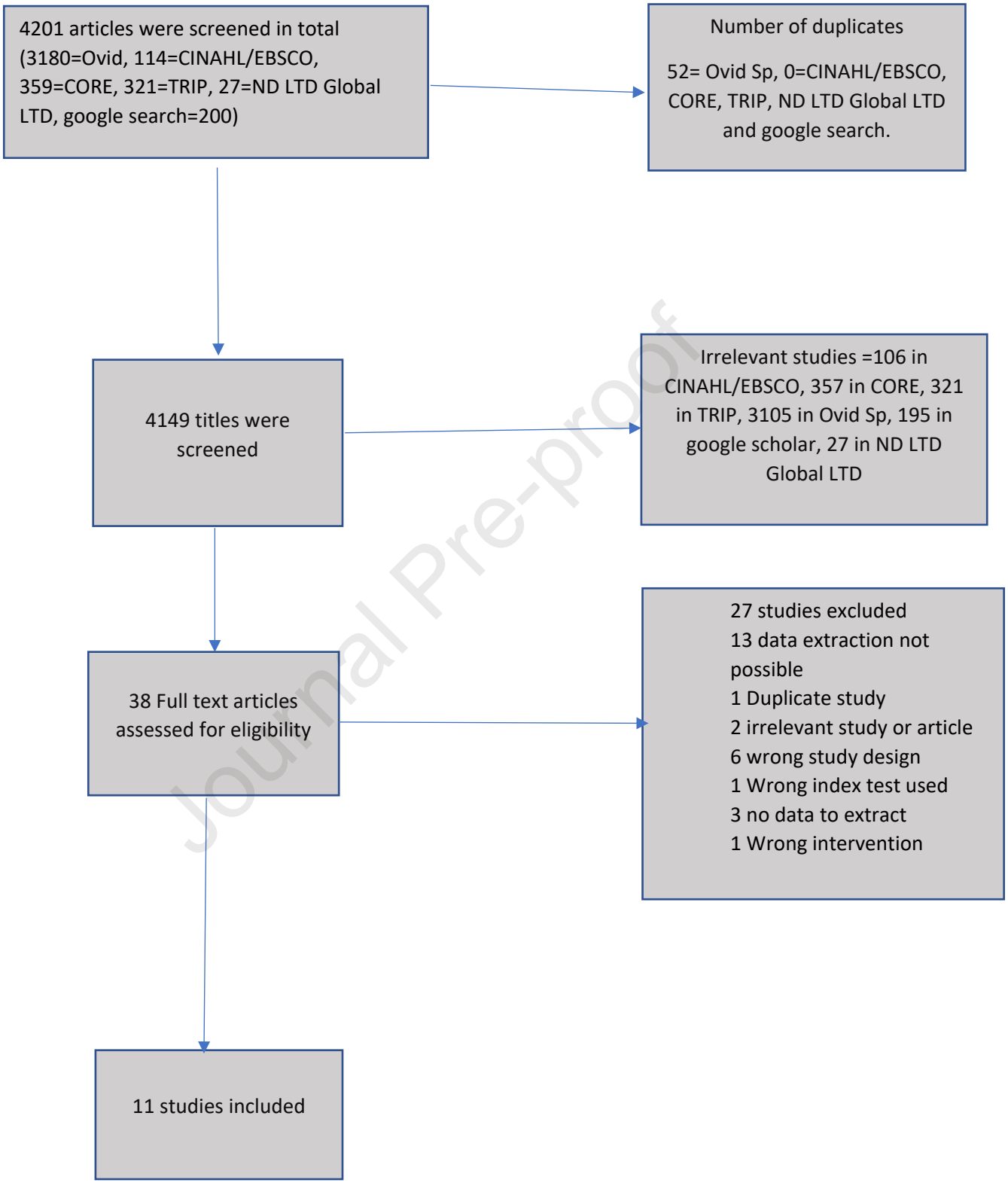


Figure (1) shows the PRISMA flow diagram of study selection

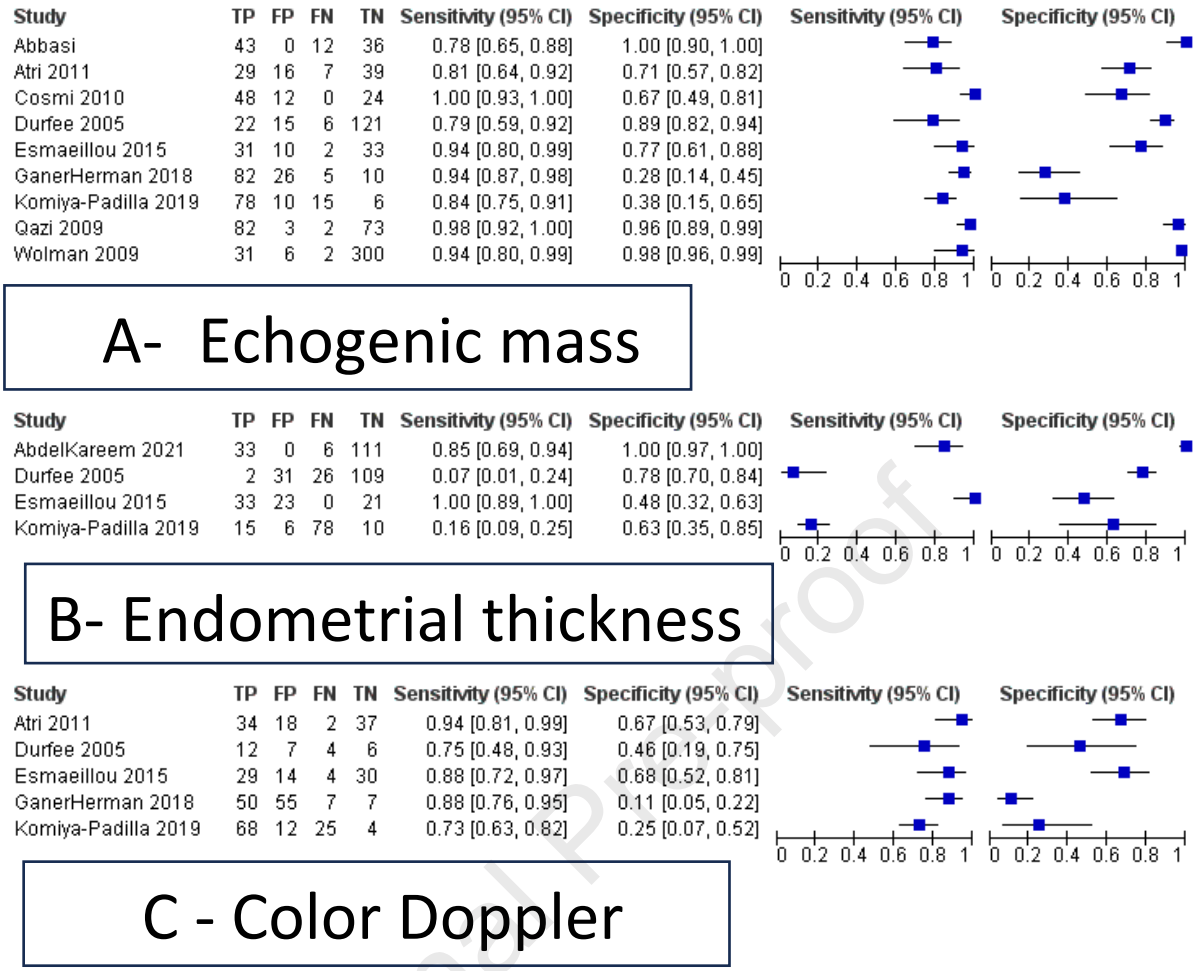
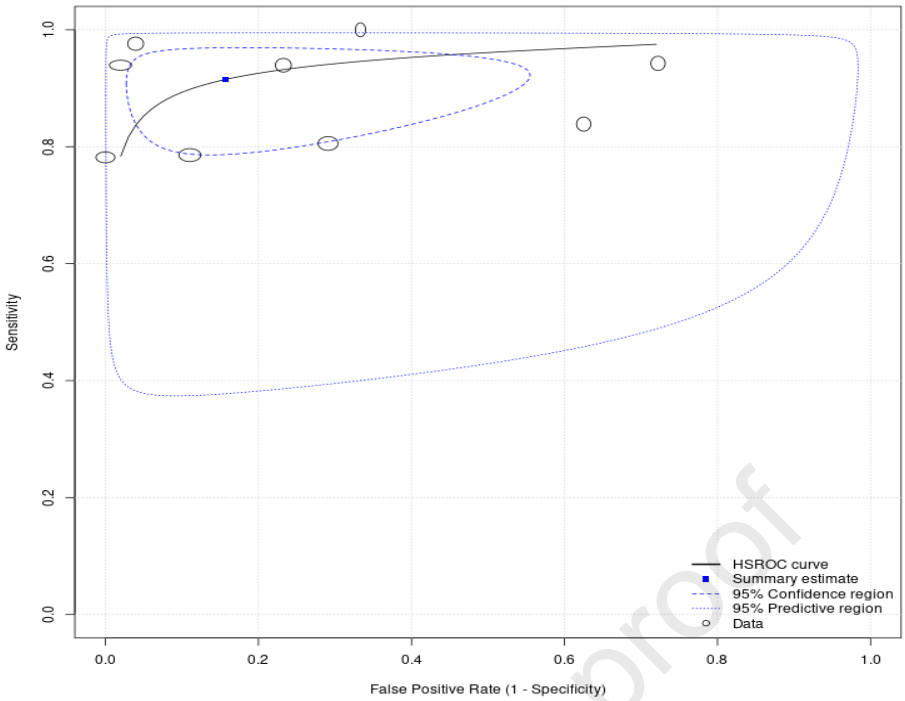
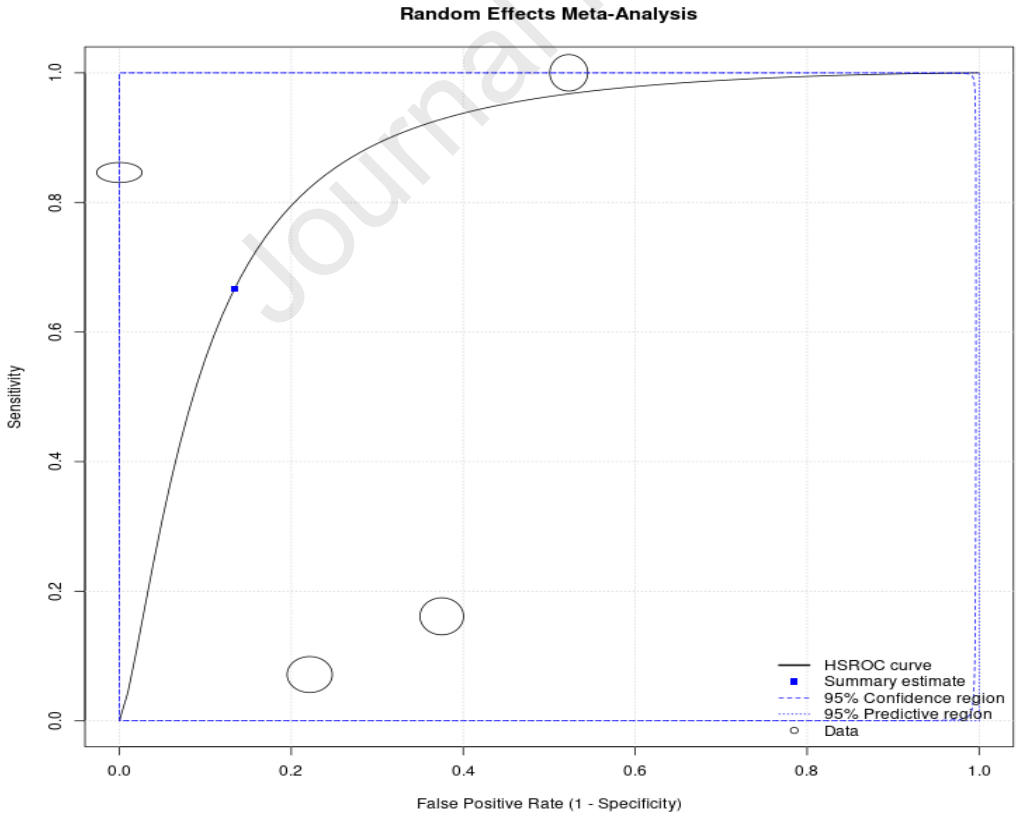


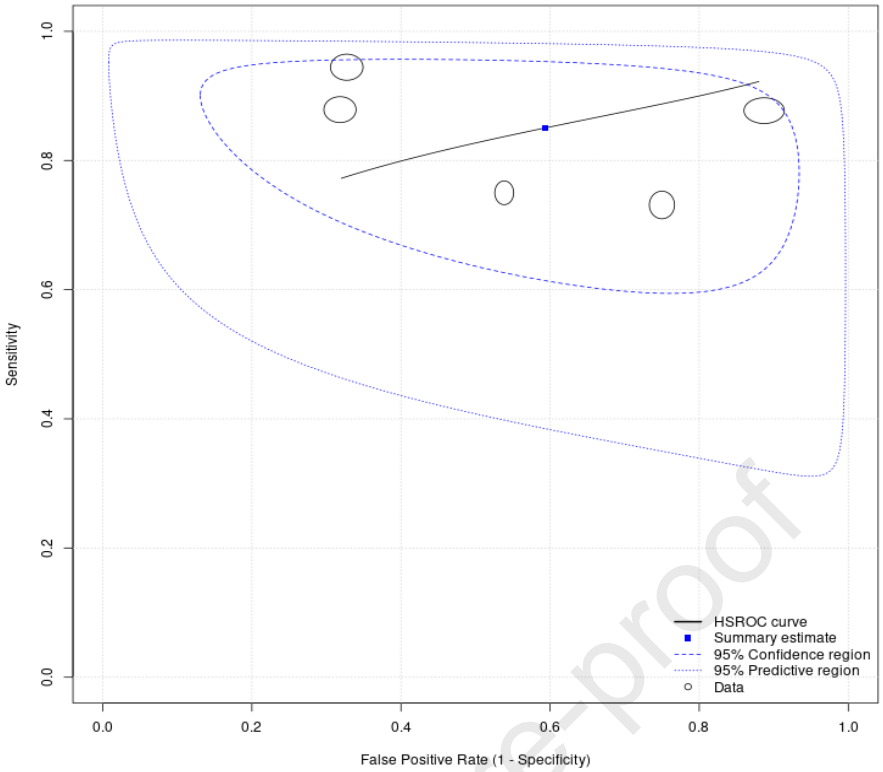
Figure (2) Forest plot of echogenic mass(A), Endometrial thickness (B) and Color Doppler imaging (C) and their individual accuracy in predicting Retained products of conception.TP=True positive, FP=False positive, FN=False negative, TN=True negative.



A- Echogenic mass



B- Endometrial thickness



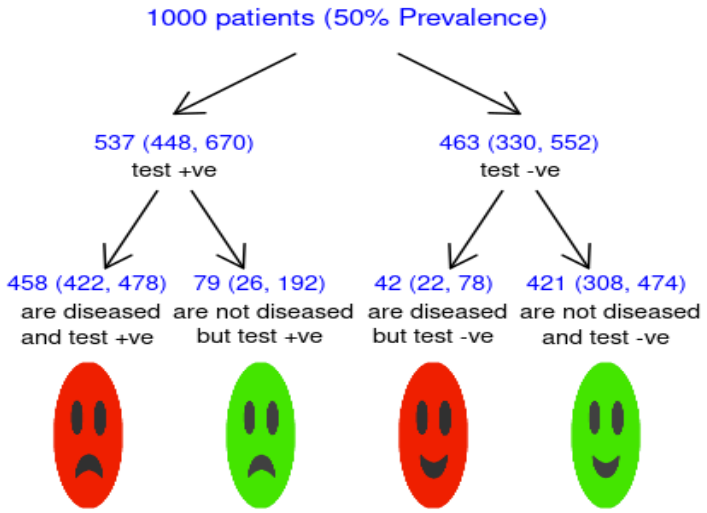
C- Color Doppler

Figure (3) Hierarchal Summary RoC (Receiver operator curve) plot of echogenic mass and its ability to predict retained products of conception. The circles represent individual studies and they are placed according to their sensitivity and specificity in the graph. The solid blue square represents summary estimate. The bigger blue dashed line represents 95% confidence interval and the smaller dashed line represents the 95% predictive region. The black solid line represents the hierarchal summary RoC line from the data input. Figure A represents the HSRoC curve of echogenic mass, Figure B represents the HSRoC curve of endometrial thickness and Figure C represents the HSRoC of color Doppler imaging.

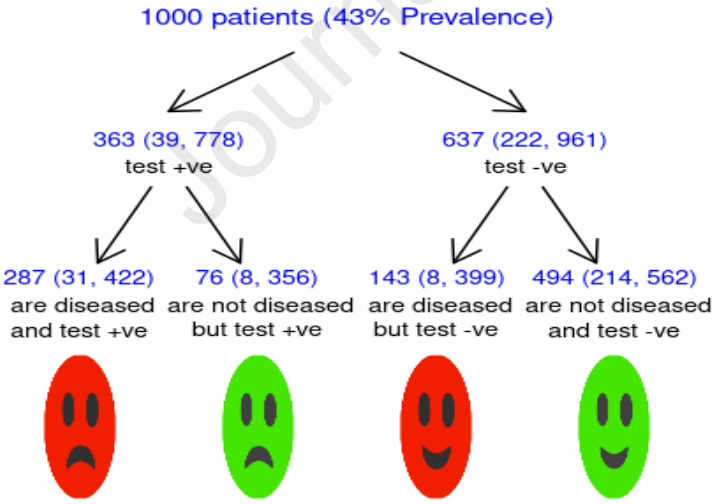
Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Abbasi 2008	☺	☺	☺	☺	☺	☺	☺
Abd El Kareem 2021	?	☹	?	?	☺	☺	☺
Atri 2011	☹	☺	☺	☹	?	☺	☺
Cosmi 2010	☺	☺	☺	☺	☺	☹	☺
Durfee 2005	?	☺	☺	☹	☹	☺	☺
Esmaeillou 2015	☺	☺	☺	☹	☺	☺	☺
Ganer Herman 2018	☺	☹	?	☺	☺	☹	☹
Komiya-Padilla 2019	☺	☺	☺	☺	☺	☺	☺
Qazi 2009	☺	☺	☺	☺	☺	☺	☺
Wolman 2009	☺	☺	☺	☺	☺	☺	☺
Wong 2002	☺	☺	☺	☺	☺	☺	☺

☺Low Risk ☹High Risk ? Unclear Risk

Figure (4) is a tabular summary of quality assessment of individual studies included in the meta-analysis



A



B

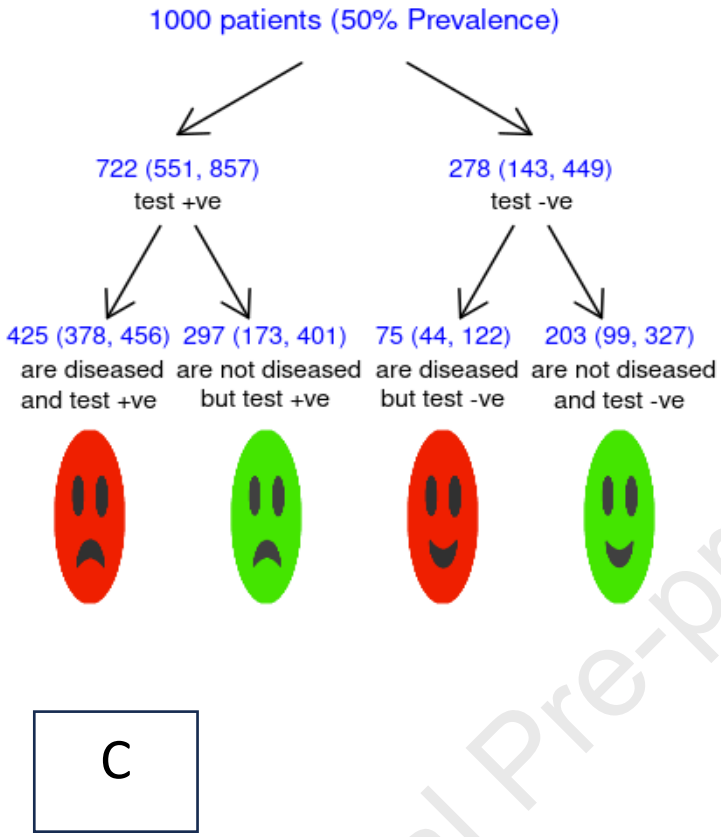


Figure 5A- Prevalence model of RPOC based on the presence of echogenic mass on transvaginal sonography. B- Prevalence model of RPOC using Endometrial thickness. C- Prevalence model of RPOC using color Doppler imaging as a predictor

Analysis of Diagnostic Threshold:

Spearman correlation coefficient: 0.377 p-value= 0.318
(Logit(TPR) vs Logit(FPR)
(Echogenic mass)

Moses' model (D = a + bS)
Weighted regression (Inverse Variance)

Var	Coeff.	Std. Error	T	p-value
a	4.329	0.724	5.978	0.0006
b(1)	-0.466	0.327	1.426	0.1969

Tau-squared estimate = 3.2361 (Convergence is achieved after 6 iterations)
Restricted Maximum Likelihood estimation (REML)

A

Spearman correlation coefficient: 0.400 p-value= 0.600
(Logit(TPR) vs Logit(FPR)
(Endometrial thickness)

Moses' model (D = a + bS)
Weighted regression (Inverse Variance)

Var	Coeff.	Std. Error	T	p-value
a	2.412	2.642	0.913	0.4577
b(1)	0.251	0.737	0.340	0.7661

Tau-squared estimate = 22.2839 (Convergence is achieved after 6 iterations)
Restricted Maximum Likelihood estimation (REML)

No. studies = 4
Filter OFF
Add 1/2 to all cells of the studies with zero

B

Spearman correlation coefficient: -0.600 p-value= 0.285
(Logit(TPR) vs Logit(FPR)
(Color Doppler imaging)

Moses' model (D = a + bS)
Weighted regression (Inverse Variance)

Var	Coeff.	Std. Error	T	p-value
a	2.935	1.708	1.718	0.1842
b(1)	-0.719	0.711	1.012	0.3861

Tau-squared estimate = 2.2461 (Convergence is achieved after 6 iterations)
Restricted Maximum Likelihood estimation (REML)

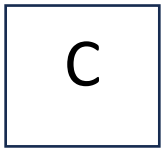


Figure 6- Analysis of diagnostic threshold for echogenic mass (A), endometrial thickness (B) and color Doppler imaging (C) as a predictor of retained products of conception.

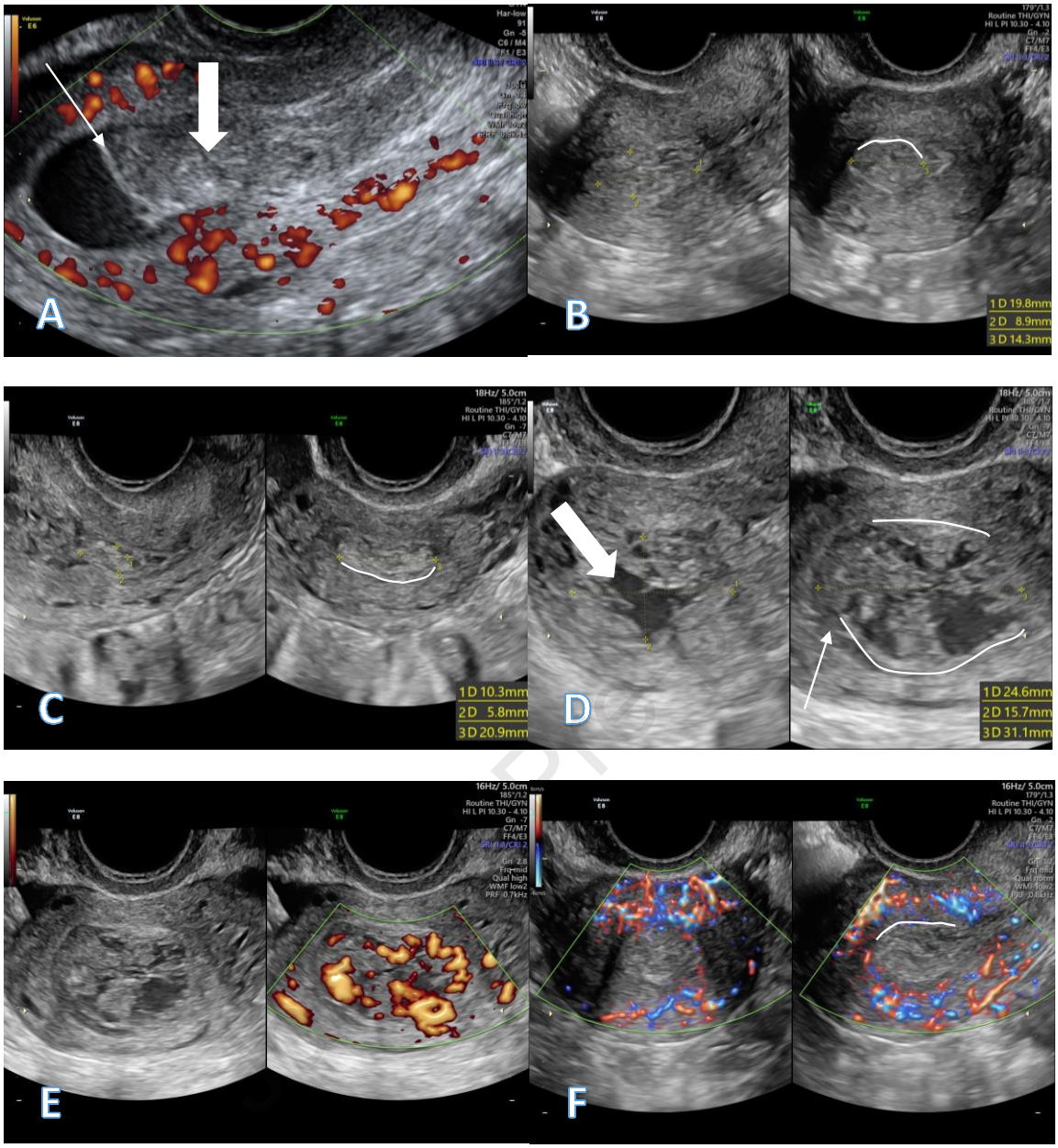


Figure 7– A- mixed echogenic fluid within the endometrial cavity, with a fluid level (thin arrow). Blood clot is below the fluid level (thick arrow). B- RPOC within the endometrial cavity between callipers, White line indicates the part conforming to the endometrial cavity shape, uninterrupted. C- small hyperechoic area of RPOC between callipers. D and E- large amount of RPOC with significant vascularity on power Doppler. White line indicates ha part conforming to the cavity shape, thick arrow indicates a very large blood vessel in keeping with enhanced endo-myometrial vascularity. F- colour Doppler image of RPOC with minimal vascularity. All images indicate the heterogenic appearance of the RPOC with various levels of vascularity within. The common feature is the clear division plane between the tissue and the endo- myometrial layer (white lines). RPOC- retained products of conception.