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Doppler Ultrasound Parameters for Predicting Adverse Perinatal Outcomes in Fetal Growth Restriction: A Rapid Systematic Review and Exploratory Diagnostic Meta-analysis

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Abstract

Background

Fetal growth restriction (FGR) is associated with increased risks of fetal death, neonatal morbidity and adverse long-term outcomes. Doppler ultrasound is central to antenatal surveillance, yet the comparative predictive performance of umbilical artery (UA), middle cerebral artery (MCA), cerebroplacental/umbilicocerebral ratio (CPR/UCR) and ductus venosus (DV) parameters remains clinically context-dependent.

Objective

To evaluate, using extractable two-by-two diagnostic data, the ability of Doppler ultrasound parameters to predict adverse perinatal outcomes in pregnancies affected by or at risk of FGR.

Methods

We performed a rapid systematic review with exploratory diagnostic synthesis. Original studies were eligible if they included singleton pregnancies with FGR, severe intrauterine growth restriction, or risk of late-preterm FGR; assessed at least one fetal Doppler parameter; reported adverse perinatal outcomes; and allowed extraction or reconstruction of true-positive, false-positive, false-negative and true-negative values. Reporting was structured according to PRISMA 2020 and PRISMA-DTA principles, and risk of bias was appraised using QUADAS-2. Sensitivity, specificity, likelihood ratios and diagnostic odds ratios (DORs) were calculated. Because of the small number of studies and substantial clinical heterogeneity, estimates were synthesized descriptively and by exploratory crude pooling rather than formal hierarchical modeling.

Results

Three studies comprising 1,011 singleton pregnancies were included. Bilardo et al. studied severe early-onset IUGR, Stampalija et al. studied late-preterm pregnancies at risk of FGR, and Li et al. studied early-onset FGR. In exploratory crude pooled analyses, DV abnormality showed the highest specificity (0.867) and DOR (5.661). UA abnormality showed higher sensitivity than the other parameter groups (0.621) but lower specificity (0.700). MCA abnormality showed modest sensitivity and specificity (0.456 and 0.696, respectively). CPR/UCR abnormality had low sensitivity (0.375) but relatively higher specificity (0.806).

Conclusions

Doppler ultrasound parameters have clinically meaningful but context-dependent predictive value for adverse perinatal outcomes in FGR. UA and DV abnormalities appear most informative in early-onset or severe FGR, whereas MCA and CPR/UCR abnormalities may contribute to risk stratification in late-preterm FGR. Current evidence based on directly extractable diagnostic data remains limited; future studies should report standardized FGR definitions, Doppler thresholds, time from scan to delivery and complete two-by-two diagnostic data.

Highlights

• Doppler parameters predict adverse outcomes in FGR in a clinically context-dependent manner.

• DV abnormality showed the highest specificity in the available extractable diagnostic data.

• UA abnormality was more sensitive but less specific than DV abnormality.

• MCA and CPR/UCR abnormalities may be more relevant to late-preterm risk stratification.

• Future FGR studies should report complete two-by-two diagnostic data to support robust meta-analysis.

1. Introduction

Fetal growth restriction (FGR) is a major obstetric condition in which the fetus fails to achieve its biological growth potential. It is associated with stillbirth, neonatal acidosis, admission to neonatal intensive care, respiratory morbidity and neurodevelopmental impairment. Although small-for-gestational-age fetuses may include constitutionally small but healthy fetuses, FGR implies pathological growth failure, most commonly related to placental insufficiency. International consensus definitions distinguish early-onset and late-onset FGR, often using 32 weeks of gestation as a clinically relevant boundary, and combine fetal biometry with placental or fetal Doppler evidence of compromise.

Antenatal Doppler ultrasound is central to the surveillance of pregnancies affected by FGR. UA Doppler reflects placental vascular resistance; absent or reversed end-diastolic flow indicates advanced placental vascular disease. MCA Doppler reflects cerebral blood flow redistribution, commonly interpreted as a fetal brain-sparing response. CPR and UCR integrate placental resistance and cerebral redistribution. DV Doppler reflects venous cardiac preload and myocardial function and is considered particularly relevant in severe early-onset FGR, when fetal cardiovascular decompensation may precede stillbirth or severe neonatal morbidity.

Despite extensive clinical use, Doppler parameters should not be interpreted as interchangeable predictors. The predictive meaning of a Doppler abnormality varies according to gestational age, FGR phenotype, Doppler threshold, scan-to-delivery interval and the outcome definition used. For example, a DV abnormality in severe early-onset FGR may indicate imminent decompensation, whereas an abnormal MCA or CPR/UCR in late-preterm FGR may identify a fetus with redistribution but not necessarily immediate deterioration. This heterogeneity has limited the comparability of individual studies and has made simple ranking of Doppler parameters clinically misleading.

The aim of this rapid systematic review and exploratory diagnostic meta-analysis was to synthesize the currently extractable two-by-two diagnostic data on Doppler ultrasound parameters for predicting adverse perinatal outcomes in FGR or pregnancies at risk of FGR. We focused on diagnostic transparency rather than broad narrative inclusion: only studies from which true-positive, false-positive, false-negative and true-negative values could be directly extracted or reconstructed were included in the quantitative synthesis.

2. Methods

2.1 Study design and reporting framework

This study was designed as a rapid systematic review with exploratory diagnostic synthesis. The manuscript was structured according to the PRISMA 2020 framework for systematic reviews and the PRISMA-DTA extension for diagnostic test accuracy reviews. Because the available number of studies with directly extractable two-by-two data was small, the quantitative synthesis was explicitly treated as exploratory. The review question, eligibility criteria, index tests, reference standards and outcomes were specified before data extraction.

2.2 Eligibility criteria

Studies were eligible if they met all of the following criteria: (1) original human research; (2) singleton pregnancies affected by FGR, severe IUGR, early-onset FGR, or late-preterm pregnancy at risk of FGR; (3) assessment of at least one fetal Doppler parameter, including UA, MCA, CPR/UCR, DV or uterine artery parameters; (4) reporting of adverse perinatal or neonatal outcomes; and (5) availability of data to construct a two-by-two table for at least one Doppler parameter. Studies were excluded if they were reviews, guidelines, editorials, case reports, animal studies, conference abstracts without usable data, multiple-pregnancy cohorts without separable singleton data, or studies in which the outcome or Doppler threshold was not interpretable.

2.3 Information sources and study identification

A targeted rapid-review search was performed using PubMed, publicly accessible full-text repositories and citation chaining from key FGR and Doppler studies. Search terms combined concepts for fetal growth restriction, Doppler ultrasound and adverse perinatal outcome. The search strategy included the following terms: “fetal growth restriction”, “intrauterine growth restriction”, “FGR”, “IUGR”, “small for gestational age”, “Doppler”, “umbilical artery”, “middle cerebral artery”, “cerebroplacental ratio”, “umbilicocerebral ratio”, “ductus venosus”, “adverse perinatal outcome”, “neonatal outcome”, “acidosis”, “Apgar”, “NICU” and “perinatal mortality”. For a conventional full systematic review, this strategy should be expanded to Embase, Web of Science, Cochrane Library and regional databases; the present manuscript therefore uses the term rapid systematic review.

2.4 Study selection

Titles, abstracts and full texts were screened for eligibility. Systematic reviews, guidelines and narrative reviews were used only for background and citation tracking and were not included in the quantitative synthesis. When a study reported multiple gestational-age strata or scan-to-delivery windows, one clinically interpretable dataset was selected for the main analysis to avoid double-counting the same participants.

2.5 Index tests and outcomes

The index tests were Doppler-defined abnormalities of UA, MCA, CPR/UCR and DV. UA abnormality included elevated UA pulsatility index (PI), absent end-diastolic flow or reversed end-diastolic flow, depending on the original study. MCA abnormality was primarily defined as MCA-PI below the fifth centile. CPR/UCR abnormality was defined according to the original study threshold, including abnormal CPR or gestational-age-specific UCR elevation. DV abnormality included elevated DV pulsatility index for veins or absent/reversed a-wave.

The primary outcome was composite adverse perinatal outcome as defined in each original study. Components included perinatal death, antenatal death, neonatal death, severe neonatal morbidity, intraventricular hemorrhage, bronchopulmonary dysplasia, low Apgar score, acidosis, NICU admission, mechanical ventilation, sepsis, pneumonia and necrotizing enterocolitis. Because outcome definitions differed across studies, outcome heterogeneity was considered in interpretation.

2.6 Data extraction and calculation of diagnostic metrics

For each eligible study, the following variables were extracted: first author, year, study design, population, gestational-age range, sample size, Doppler parameter, threshold, outcome definition and two-by-two table values. True positives were fetuses with an abnormal Doppler result who developed an adverse outcome; false positives were fetuses with an abnormal Doppler result who did not develop an adverse outcome; false negatives were fetuses with a normal Doppler result who developed an adverse outcome; and true negatives were fetuses with a normal Doppler result who did not develop an adverse outcome.

Sensitivity was calculated as TP/(TP + FN), specificity as TN/(TN + FP), positive likelihood ratio as sensitivity/(1-specificity), negative likelihood ratio as (1-sensitivity)/specificity, and DOR as (TP×TN)/(FP×FN). Wilson 95% confidence intervals were calculated for sensitivity and specificity. When a zero cell was present, a continuity correction of 0.5 was used for DOR estimation.

2.7 Risk of bias assessment

Risk of bias and applicability were assessed using QUADAS-2 across four domains: patient selection, index test, reference standard, and flow and timing. Given the rapid-review design and small number of studies, QUADAS-2 judgments were used primarily to support interpretation rather than to perform formal sensitivity analyses.

2.8 Statistical synthesis

Because each Doppler parameter was represented by only two extractable datasets and because the included studies differed in gestational age, population, index-test threshold and outcome definition, formal bivariate random-effects modeling and HSROC modeling were not performed. Instead, we present individual-study diagnostic estimates and exploratory crude pooled estimates by parameter group. The pooled estimates were calculated by summing TP, FP, FN and TN across studies within each parameter group. These pooled estimates are descriptive and should not be interpreted as definitive hierarchical diagnostic meta-analysis estimates.

3. Results

3.1 Study selection

Twelve candidate records were initially identified from targeted screening and citation chaining. Five records were excluded because they were systematic reviews, guidelines or meta-analyses and therefore not eligible as primary data sources. Four additional records were excluded because two-by-two diagnostic data could not be extracted from the available information. Three original studies were included in the qualitative and exploratory quantitative synthesis, comprising 1,011 singleton pregnancies. The study selection process is presented in Fig. 1.

[Insert Fig. 1 **here]**

3.2 Study characteristics

The three included studies represented clinically distinct FGR settings. Bilardo et al. evaluated severe early-onset IUGR between 26 and 33 weeks and reported relationships between arterial and venous Doppler parameters and perinatal outcome. Stampalija et al. analyzed late-preterm singleton pregnancies at risk of FGR between 32 + 0 and 36 + 6 weeks and evaluated fetal cerebral Doppler redistribution. Li et al. prospectively studied early-onset FGR and evaluated Doppler, umbilical venous flow and fetal cardiac parameters for prediction of composite adverse outcome. The key characteristics of the included studies are summarized in Table 1.

[Insert Table 1 **here]**

Table 1
Characteristics of included studies

Study	Year	Design	Population	Sample size	Gestational age	Index tests	Outcome
Bilardo et al.	2004	Multicenter prospective longitudinal observational study	Severe early IUGR	70	26–33 weeks	UA-PI, DV-PIV, fetal heart-rate short-term variation	Perinatal death and severe neonatal morbidity
Stampalija et al.	2020	Prospective multicenter cohort study	Late-preterm singleton pregnancies at risk of FGR	856	32 + 0 to 36 + 6 weeks	MCA-PI, UCR	Composite adverse perinatal outcome
Li et al.	2026	Single-center prospective study	Early-onset FGR	85	Antenatal scans in eoFGR pregnancies	UA, MCA, CPR, DV, UtA, UVF and fetal cardiac parameters	Composite adverse perinatal outcome

3.3 Extracted two-by-two diagnostic data

Eight extractable two-by-two datasets were available across the three included studies: two for UA, two for MCA, two for CPR/UCR and two for DV. The extracted values are shown in Table 2.

Table 2
Extracted two-by-two diagnostic data

Study	Parameter	TP	FP	FN	TN	Notes
Li et al. 2026	UA abnormality	21	3	22	39	Early-onset FGR; composite adverse outcome
Bilardo et al. 2004	UA-PI ≥ 2 SD	15	15	0	3	26–29 weeks; 0–1 day before delivery
Li et al. 2026	MCA abnormality	13	7	30	35	MCA-PI below study threshold
Stampalija et al. 2020	MCA-PI <5th centile	49	238	44	525	Late-preterm FGR-risk cohort
Li et al. 2026	CPR abnormality	21	11	22	31	Study-defined CPR abnormality
Stampalija et al. 2020	Gestational-age-specific UCR elevation	30	132	63	562	Late-preterm FGR-risk cohort
Li et al. 2026	DV abnormality	14	2	29	40	DV-PI elevation or a-wave abnormality
Bilardo et al. 2004	DV-PIV ≥ 3 SD	13	6	2	12	26–29 weeks; 0–1 day before delivery

3.4 Individual-study diagnostic performance

Individual-study estimates are shown in Table 3. UA abnormality in Li et al. showed moderate sensitivity (0.488) and high specificity (0.929), whereas UA-PI ≥ 2 SD in the selected Bilardo dataset showed very high sensitivity but low specificity. DV abnormality showed high specificity in Li et al. and relatively high sensitivity in Bilardo et al. MCA and CPR/UCR abnormalities showed modest diagnostic performance, with generally higher specificity than sensitivity for CPR/UCR. Sensitivity and specificity estimates are displayed in Figs. 2 and 3, respectively, and diagnostic odds ratios are displayed in Fig. 4.

[Insert Fig. 2 **here]**

[Insert Fig. 3 **here]**

[Insert Fig. 4 **here]**

Table 3
Diagnostic performance of individual extracted datasets

Study	Parameter	Sensitivity	Specificity	PLR	NLR	DOR
Li et al. 2026	UA abnormality	0.488	0.929	6.837	0.551	12.409
Bilardo et al. 2004	UA-PI ≥ 2 SD	1.000	0.167	1.200	0.000	7.000*
Li et al. 2026	MCA abnormality	0.302	0.833	1.814	0.837	2.167
Stampalija et al. 2020	MCA-PI <5th centile	0.527	0.688	1.684	0.688	2.457
Li et al. 2026	CPR abnormality	0.488	0.738	1.864	0.693	2.690
Stampalija et al. 2020	UCR elevation	0.323	0.810	1.698	0.837	2.027
Li et al. 2026	DV abnormality	0.326	0.952	6.837	0.708	9.655
Bilardo et al. 2004	DV-PIV ≥ 3 SD	0.867	0.667	2.600	0.200	13.000

*DOR estimated with continuity correction because of a zero cell.

3.5 Exploratory crude pooled diagnostic estimates

Exploratory crude pooled estimates by parameter group are presented in Table 4. DV abnormality showed the highest pooled specificity (0.867) and highest DOR (5.661). UA abnormality showed the highest pooled sensitivity (0.621) but lower specificity (0.700). MCA abnormality showed moderate sensitivity and specificity. CPR/UCR abnormality showed low sensitivity (0.375) and relatively higher specificity (0.806). The distribution of diagnostic estimates in ROC space is shown in Fig. 5, and exploratory pooled sensitivity and specificity by Doppler parameter group are shown in Fig. 6.

[Insert Fig. 5 **here]**

[Insert Fig. 6 **here]**

Table 4
Exploratory crude pooled estimates by Doppler parameter group

Parameter group	TP	FP	FN	TN	Sensitivity	Specificity	DOR
UA abnormality	36	18	22	42	0.621	0.700	3.818
MCA abnormality	62	245	74	560	0.456	0.696	1.915
CPR/UCR abnormality	51	143	85	593	0.375	0.806	2.488
DV abnormality	27	8	31	52	0.466	0.867	5.661

3.6 Risk of bias

Risk-of-bias judgments are summarized in Table 5. All three studies used clinically relevant populations and outcomes. However, applicability differed because the populations represented severe early IUGR, early-onset FGR and late-preterm FGR-risk pregnancies. Index-test bias was considered unclear in studies that did not

explicitly state whether Doppler interpretation was blinded to subsequent outcome. Flow and timing concerns were greatest where data were extracted from selected scan-to-delivery windows.

Table 5
QUADAS-2 risk-of-bias and applicability summary

Study	Patient selection	Index test	Reference standard	Flow and timing	Applicability concern
Bilardo et al. 2004	Low/unclear	Unclear	Low	High/unclear	Population limited to severe early IUGR
Stampalija et al. 2020	Low	Low/unclear	Low	Low	Late-preterm FGR-risk cohort rather than confirmed FGR only
Li et al. 2026	Low	Unclear	Low	Low	Single-center early-onset FGR cohort

4. Discussion

4.1 Principal findings

This rapid systematic review and exploratory diagnostic synthesis suggests that Doppler ultrasound parameters have clinically meaningful but phenotype-dependent value for predicting adverse perinatal outcomes in FGR. DV abnormality showed the highest specificity and DOR in the available extractable data, supporting its role as a marker of advanced fetal compromise in severe early-onset disease. UA abnormality showed comparatively higher sensitivity, consistent with its role as a marker of placental resistance. MCA and CPR/UCR abnormalities showed modest diagnostic performance, which may reflect their greater relevance for risk stratification rather than immediate prediction of severe outcome.

4.2 Clinical interpretation by Doppler parameter

UA Doppler is pathophysiologically linked to placental vascular resistance. In early-onset FGR, abnormal UA Doppler is expected to identify a substantial proportion of compromised fetuses, although its specificity may vary according to threshold and disease severity. In the current synthesis, UA abnormality had the highest pooled sensitivity, but specificity varied markedly between studies. This heterogeneity is clinically plausible because UA-PI elevation and absent or reversed end-diastolic flow represent different degrees of placental disease.

DV Doppler showed the highest specificity in this analysis. This is consistent with the concept that DV abnormality occurs later in the sequence of fetal deterioration and may therefore be more specific for severe compromise. However, high specificity should not be confused with screening sensitivity. A normal DV result does not necessarily exclude risk, particularly if the fetus has already demonstrated significant placental or cerebral Doppler abnormality.

MCA and CPR/UCR abnormalities reflect cerebral redistribution. In late-preterm or late-onset FGR, UA Doppler may remain normal despite clinically relevant risk, and cerebral Doppler changes may therefore add information. However, the present data suggest limited standalone diagnostic accuracy. This supports a

clinical approach in which MCA and CPR/UCR are interpreted alongside fetal size, growth trajectory, gestational age, maternal disease and other Doppler parameters rather than as isolated triggers for intervention.

4.3 Early-onset versus late-onset FGR

The most important source of clinical heterogeneity in this review is the distinction between early-onset and late-onset FGR. Severe early-onset FGR is more often associated with marked placental vascular disease, UA deterioration and eventual venous compromise. Late-onset FGR may present with subtler placental dysfunction, preserved UA flow and cerebral redistribution. Therefore, a pooled estimate across all FGR phenotypes should be interpreted cautiously. The current analysis supports phenotype-specific interpretation: UA and DV appear more informative in early-onset or severe disease, whereas MCA and CPR/UCR appear more relevant to risk stratification in late-preterm FGR-risk pregnancies.

4.4 Strengths

The principal strength of this study is its emphasis on extractable diagnostic transparency. Instead of mixing incompatible effect measures without a clear analytic plan, this review separated extractable two-by-two diagnostic data and calculated clinically interpretable diagnostic metrics. The manuscript also explicitly acknowledges that the current evidence is not sufficient for formal hierarchical modeling. This transparent positioning may make the work suitable for journals that accept rapid reviews or preliminary evidence syntheses.

4.5 Limitations

This study has important limitations. First, the number of included studies is small, and each Doppler parameter is represented by only two datasets. Second, the study populations differed substantially, including severe early IUGR, early-onset FGR and late-preterm pregnancies at risk of FGR. Third, Doppler thresholds and outcome definitions differed across studies. Fourth, the crude pooled estimates are not substitutes for bivariate random-effects or HSROC models. Fifth, because this was a rapid systematic review, the search strategy was not as exhaustive as a conventional systematic review across all major bibliographic databases. These limitations mean that the results should be interpreted as hypothesis-generating rather than definitive.

4.6 Implications for future research

Future studies should report standardized FGR definitions, specify whether early-onset and late-onset phenotypes were analyzed separately, define the scan-to-delivery interval, and provide complete two-by-two diagnostic data for each Doppler threshold. Future systematic reviews should expand the search to Embase, Web of Science, Cochrane Library and regional databases and should perform bivariate or HSROC modeling when sufficient studies are available. Prediction research should also evaluate combined models incorporating fetal biometry, UA, MCA, CPR/UCR, DV, maternal disease and fetal cardiac or venous-flow parameters.

5. Conclusions

In pregnancies affected by or at risk of FGR, Doppler ultrasound parameters show clinically relevant but context-dependent ability to predict adverse perinatal outcomes. UA abnormality may be useful for detecting placental vascular compromise, DV abnormality appears highly specific for severe early-onset compromise, and MCA or CPR/UCR abnormalities may contribute to late-preterm risk stratification. The current evidence

based on extractable two-by-two data remains limited. A larger conventional diagnostic test accuracy meta-analysis is warranted before firm comparative conclusions can be drawn.

Declarations

Ethics approval and consent to participate:

Not applicable. This study used data from previously published studies.

Consent for publication:

Not applicable.

Competing interests:

The authors declare no competing interests.

Funding:

No specific funding was received for this work.

Author Contribution

This replaces any statement written within the manuscript and is the one that we will publish.

Data Availability

Data availability: The extracted dataset and exploratory diagnostic estimates are included in the manuscript tables and can be provided as supplementary material upon reasonable request.Competing interests: The authors declare no competing interests.

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Figures

Figure 1. PRISMA-style flow diagram for the current exploratory version

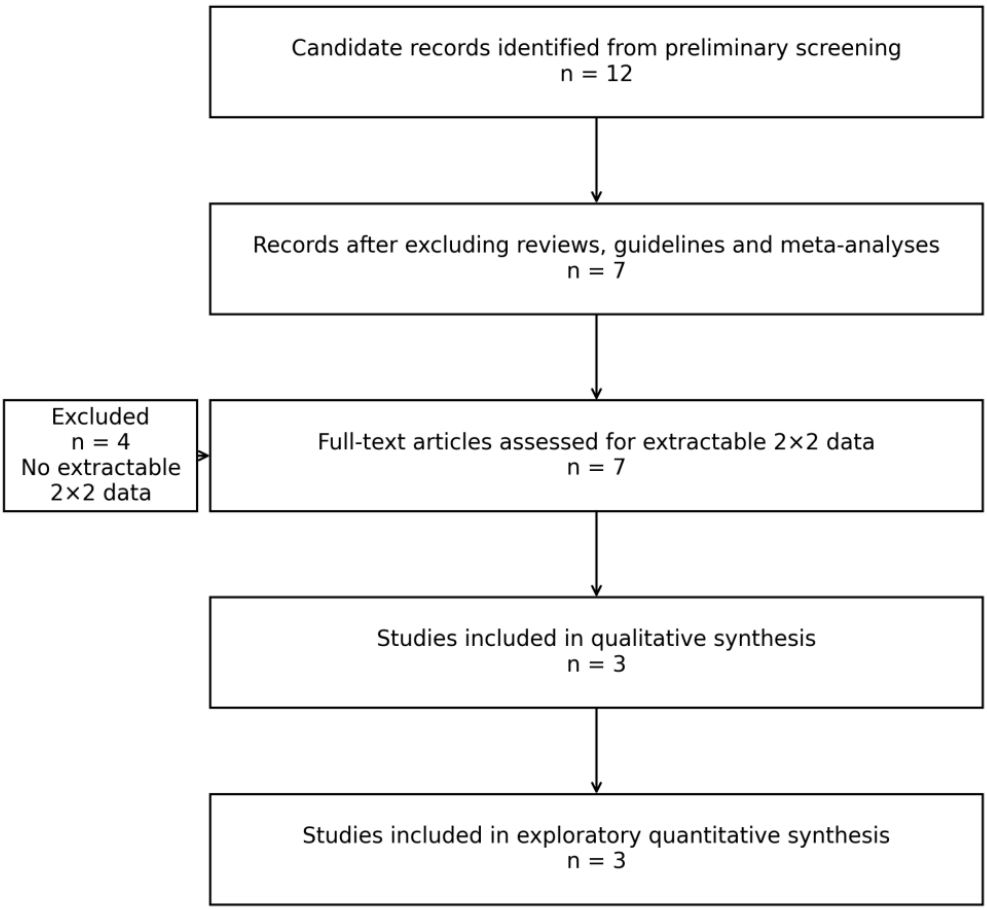


Figure 1

PRISMA-style flow diagram of study identification and selection for the rapid systematic review.

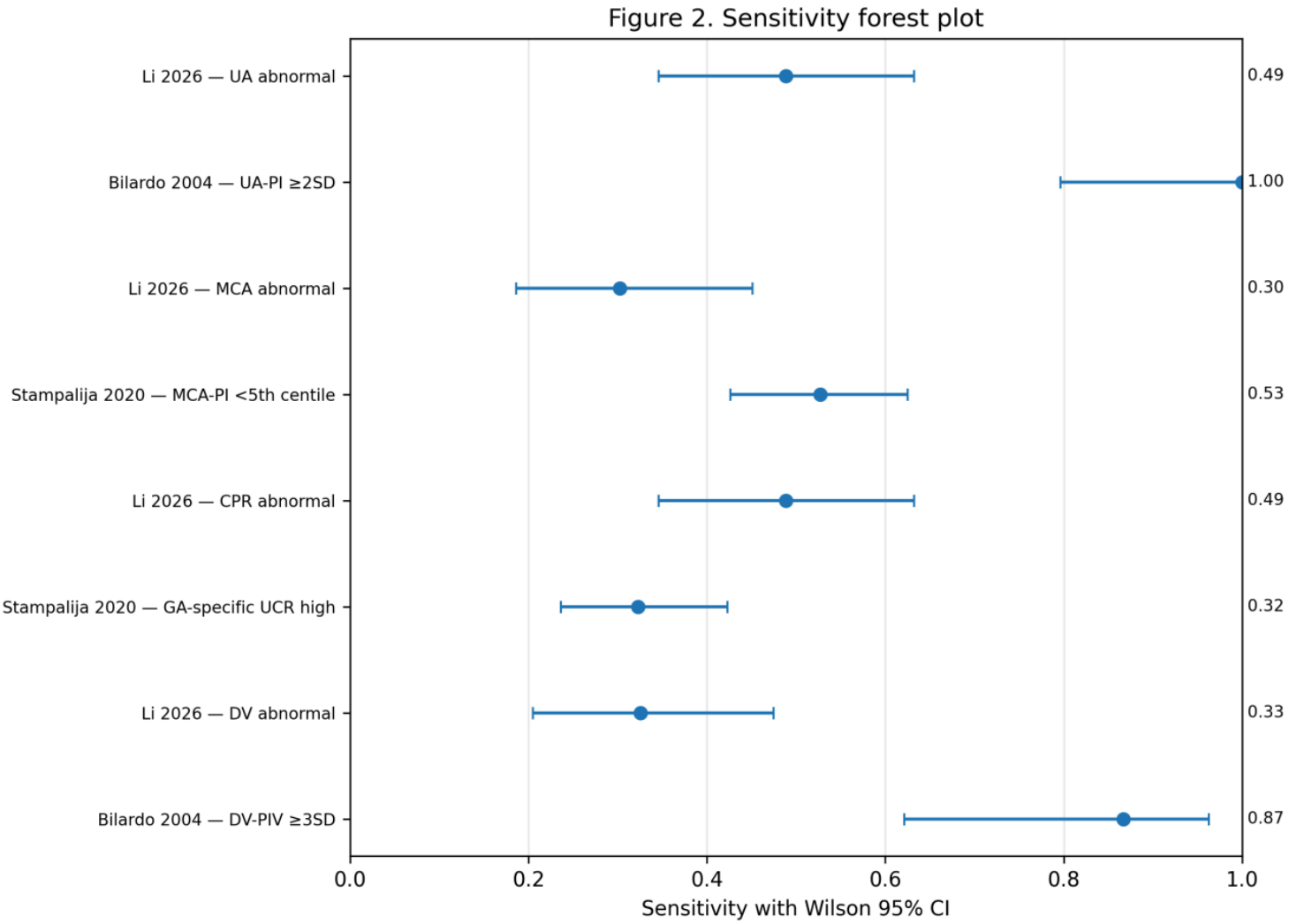


Figure 2

Sensitivity forest plot for extractable Doppler datasets. Wilson 95% confidence intervals are shown.

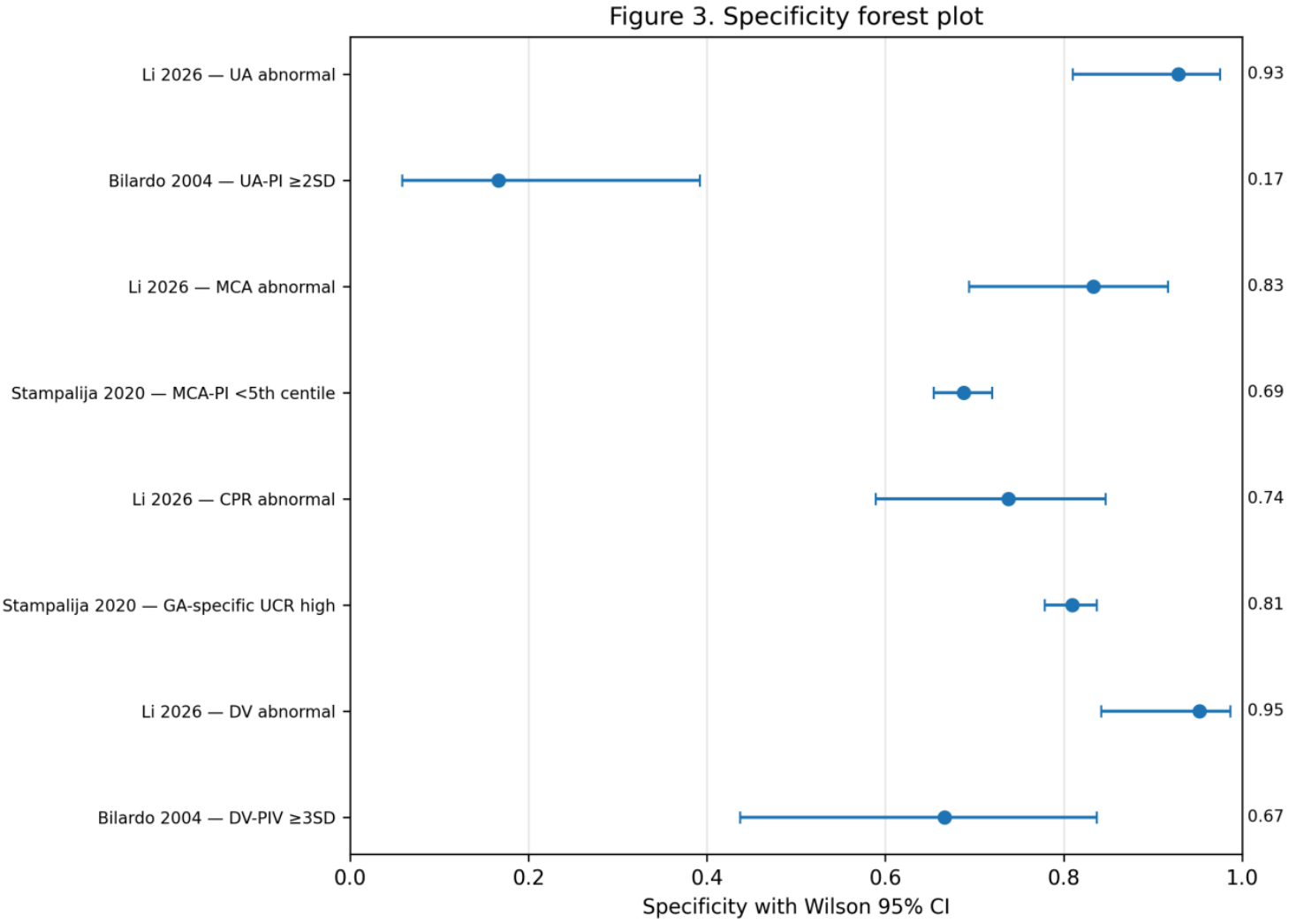


Figure 3

Specificity forest plot for extractable Doppler datasets. Wilson 95% confidence intervals are shown.

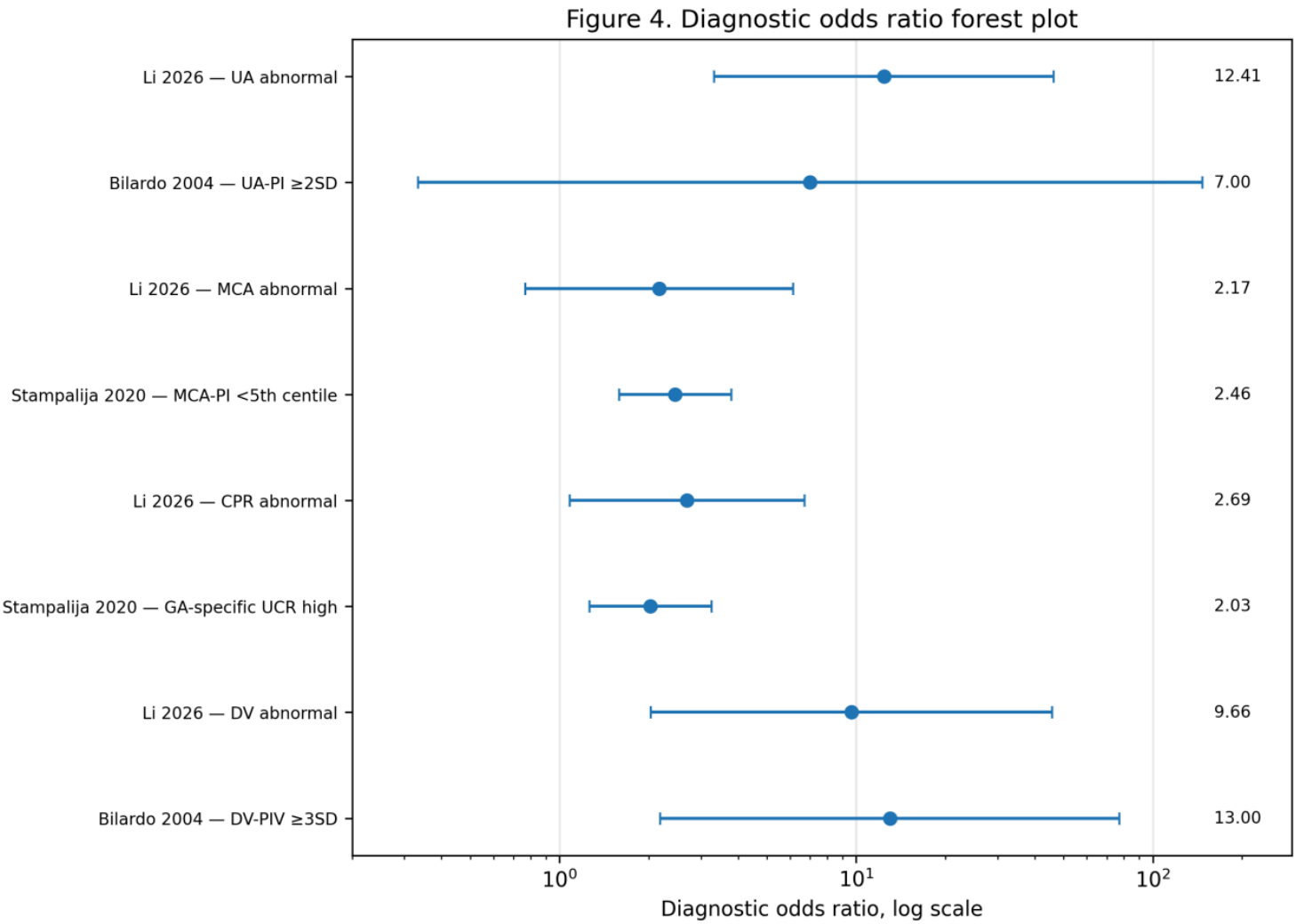


Figure 4

Diagnostic odds ratio forest plot. DOR values are displayed on a logarithmic scale; continuity correction was used when required.

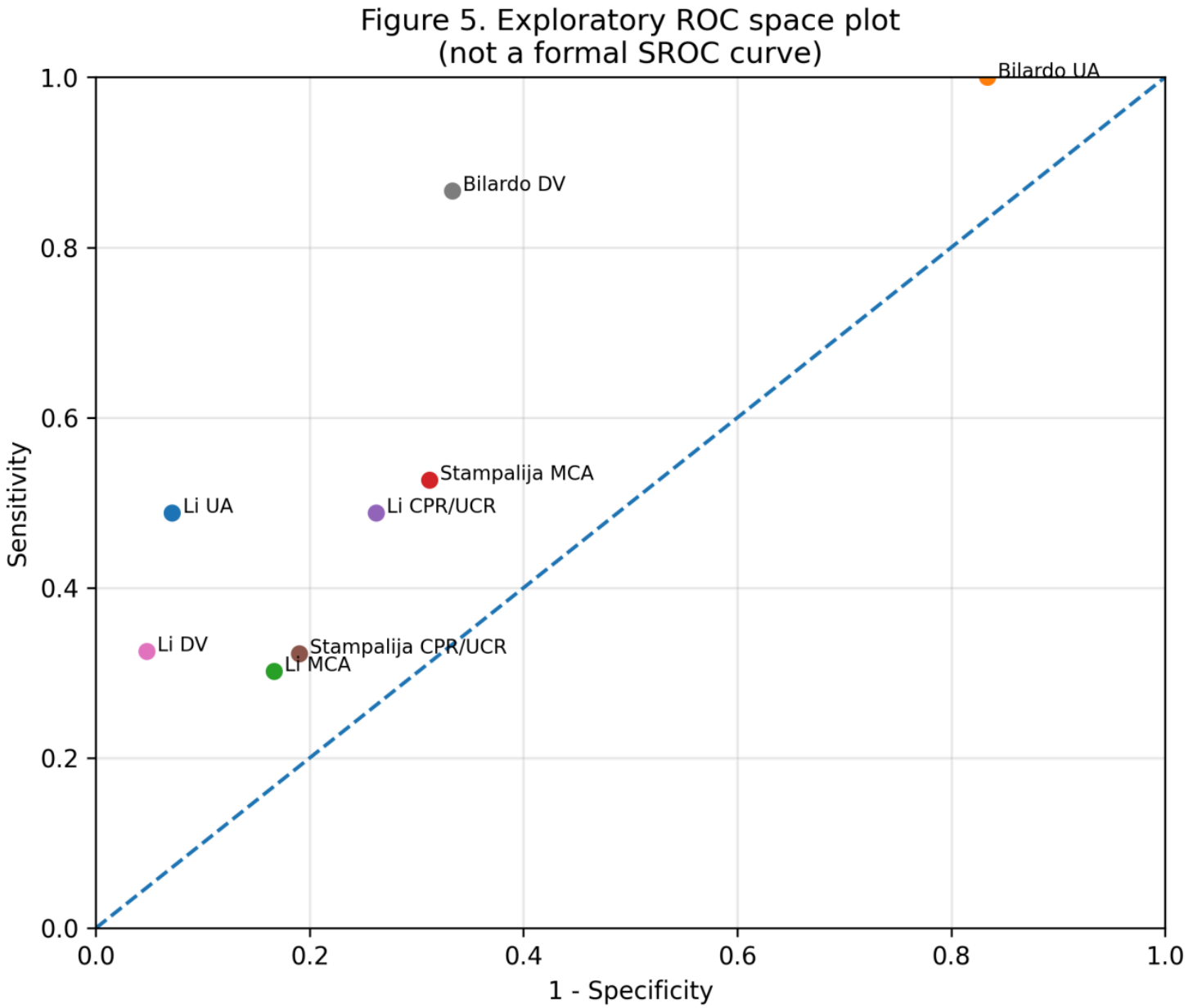


Figure 5

ROC space plot of extractable Doppler diagnostic datasets. This is not a formal SROC curve because the number of included datasets was insufficient for stable hierarchical modeling.

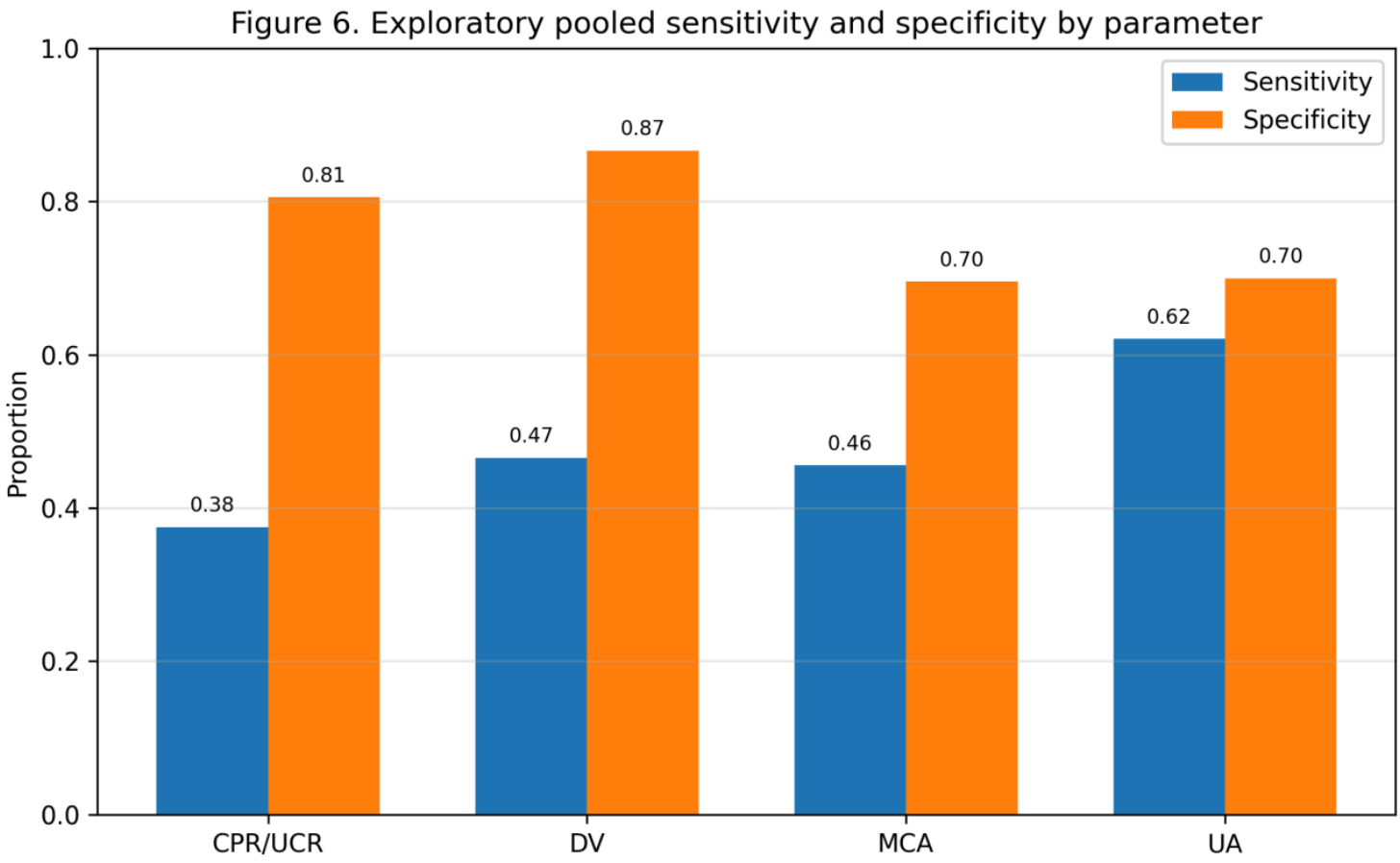


Figure 6

Exploratory crude pooled sensitivity and specificity by Doppler parameter group.