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The diagnostic efficiency of diffusion-weighted imaging in placenta accreta spectrum: a systematic review and meta-analysis

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Abstract. – OBJECTIVE: This study aims to evaluate the diagnostic efficiency of diffusion-weighted imaging (DWI) in patients with placenta accreta spectrum (PAS).

MATERIALS AND METHODS: The present study searched on PubMed, Embase, OVID, Cochrane, Scopus and CNKI, Chinese Bio-Medical Literature, VIP, Wanfang, Duxiu, databases for studies related to the diagnostic performance of DWI for PAS from inception to December 2022. The pooled sensitivity, the pooled specificity, positive likelihood ratio (LR+), negative likelihood ratio (LR-), and diagnosis odds ratios (DOR) were calculated by Meta-disc 1.4 and STATA 16.0.

RESULTS: A total of 11 studies met the criteria and were included in the meta-analysis. The effect indexes of DWI in combined PAS were as follows. The pooled sensitivity was 0.670 (0.619-0.719). The pooled specificity was 0.720 (0.661-0.773). The pooled LR+ was 2.161 (1.454-3.211). The pooled LR- was 0.413 (0.280-0.609). The pooled AUC was 0.7841, and Q* was 0.7221. The pooled diagnostic ratio DOR was 6.713 (2.981-15.118). Subgroup analysis showed that four studies used T2-weighted imaging (T2WI) + DWI to diagnose PAS, and the pooled AUC was 0.9822.

CONCLUSIONS: The results showed that DWI had high sensitivity and specificity in the diagnosis of PAS. Furthermore, T2WI+DWI has higher diagnostic efficacy than DWI alone in the diagnosis of PAS. Therefore, it is necessary to set T2WI+DWI as a routine sequence for PAS, and T2WI+DWI should be a routine method for the daily diagnosis of PAS.

Key Words:
Placenta accreta, Diffusion-weighted imaging, Diagnosis.

Introduction

Placenta accreta spectrum (PAS) is a serious clinical risk to the health of third-trimester pregnant women and fetuses. The state of the placenta is an important factor in deciding whether to have a cesarean section or a natural birth. Diffusion-weighted imaging (DWI) is an important functional imaging method of magnetic resonance imaging (MRI), which can provide more microscopic information. However, the clinical application of DWI in PAS is not well described. PAS is caused by the abnormal attachment of the placental trophoblastic villi to the myometrium[1]. PAS includes placenta accreta, placenta increta, and placenta percreta[2,3]. With the increase of advanced maternal age, the incidence of PAS also increases gradually, which seriously endangers the health of the pregnant woman and even the fetus. The risk of maternal and fetal death with placenta implantation has been reported[4-6] to be about 6-7% and 9-19%, respectively, which makes it crucial to clearly diagnose the occurrence of PAS.

MRI is commonly used in suspected cases of PAS and is a strong complement to ultrasound, especially when the placental tissue is located in the posterior wall of the uterus. T2-weighted imaging (T2WI) has been routinely used to assess placental invasion. However, diffusion-weighted imaging (DWI) has been shown[7] to perform better in depicting the placental myometrial interface because of the high contrast between the placenta and the myometrium on DWI. By detecting the diffusion of water molecules in biological tissues, DWI provides more microscopic information about the tissues and generates an apparent diffusion coefficient (ADC) value for quantitative assessment[8,9]. DWI is currently used in cancer diagnosis[10], tumor grading[11], and treatment response assessment[12]. DWI allows highly accurate differentiation of malignant and benign

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lesions and different histological types[13-16]. At the same time, these studies[13-16] differ significantly in the formulation of DWI parameters and the definition of areas of interest and lack systematic summary and analysis.

Therefore, a comprehensive and systematic review of the data available from the numerous existing DWI studies in PAS is valuable. In this study, we conducted a meta-analysis to evaluate the role of DWI as a diagnostic tool for PAS.

Materials and Methods

This meta-analysis is registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) and the registration number is INPLASY2022120110. This meta-analysis follows the guidelines provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) and proceeds based on the PICO principles for its study design. Because the present study is a systematic review and meta-analysis, Institutional Review Board approval and written informed consent are not required.

Search Strategy

The present study conducted a computerized search of PubMed, Embase, OVID, Cochrane, Scopus and CNKI, Chinese Bio-Medical Literature, VIP, Wanfang, and Duxiu databases for studies reporting the diagnostic performance of DWI of placenta accreta from inception to December 9, 2022. The search criteria included variations of the following: placenta accreta (placenta increta or placenta percreta) and Diffusion-Weighted Imaging (diffusion MRI or diffusion-weighted MRI or DWI or ADC) and the sensitivity or specificity or predictive value or accuracy of the test.

Inclusion and Exclusion Criteria

DWI was applied in prenatal diagnostic studies of placenta accreta. Inclusion criteria: (1) published Chinese or English literature; (2) literature that evaluated the diagnostic value of DWI in PAS; (3) the subjects were patients with suspected placenta accreta or diagnosed with placenta accreta; (4) sample size ≥ 5 cases; (5) pathological examination was used as the 'gold standard', and all cases were confirmed by the 'gold standard'; (6) the original data of diagnostic tests, such as true positive value, false negative value, false positive value, and true negative value, could be obtained directly or indirectly. Exclusion criteria: (1) studies with no control group; (2) types of literature that were non-monographs or non-complete monographs such as reviews, letters, comments, meeting minutes and case reports; (3) sample size < 5 cases; (4) incomplete data; (5) if the article was repeatedly published, the most recently published literature or the most detailed data was selected.

Data Extraction and Study Quality Assessment

All data extraction was done independently by two authors. The extracted data included true positive value, false negative value, false positive rate, and true negative rate of DWI in the diagnosis of PAS. Study characteristics were extracted, including country of origin, study type, reference standard, patient age, sample size, and magnetic field strength. If there were subgroups, a secondary extraction was performed according to the above criteria. Quality assessment was conducted using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool[17].

Statistical Analysis

Meta-disc 1.4 (Cochrane Colloquium, Barcelona, Spain), StataCorp Stata (Stata) 16.0 (STATA Corp., University of Texas Station, Texas, USA), and Review Manager 5.3 (RevMan 5.3, Nordic Cochrane Centre, Cochrane, Copenhagen, Denmark) were used for meta-analysis. The random-effects model was used to calculate the pooled sensitivity and specificity. To determine whether threshold effect existed, the receiver operating characteristic (ROC) and summary receiver operating characteristic (sROC) were plotted to calculate Spearman's correlation value and p-value. If there was no threshold effect, the pooled sensitivity, pooled specificity, positive likelihood ratio (LR^+), negative likelihood ratio (LR^-), and diagnosis odds ratios (DOR) were calculated. Publication bias was assessed using Deeks' funnel plots. $p < 0.05$ suggested a statistically significant difference.

Results

Literature Search and Article Selection

A total of 337 articles met the search requirements (Figure 1). Then, duplicates were removed, and 149 articles were left. 20 articles were excluded because they were reviews, conferences, and

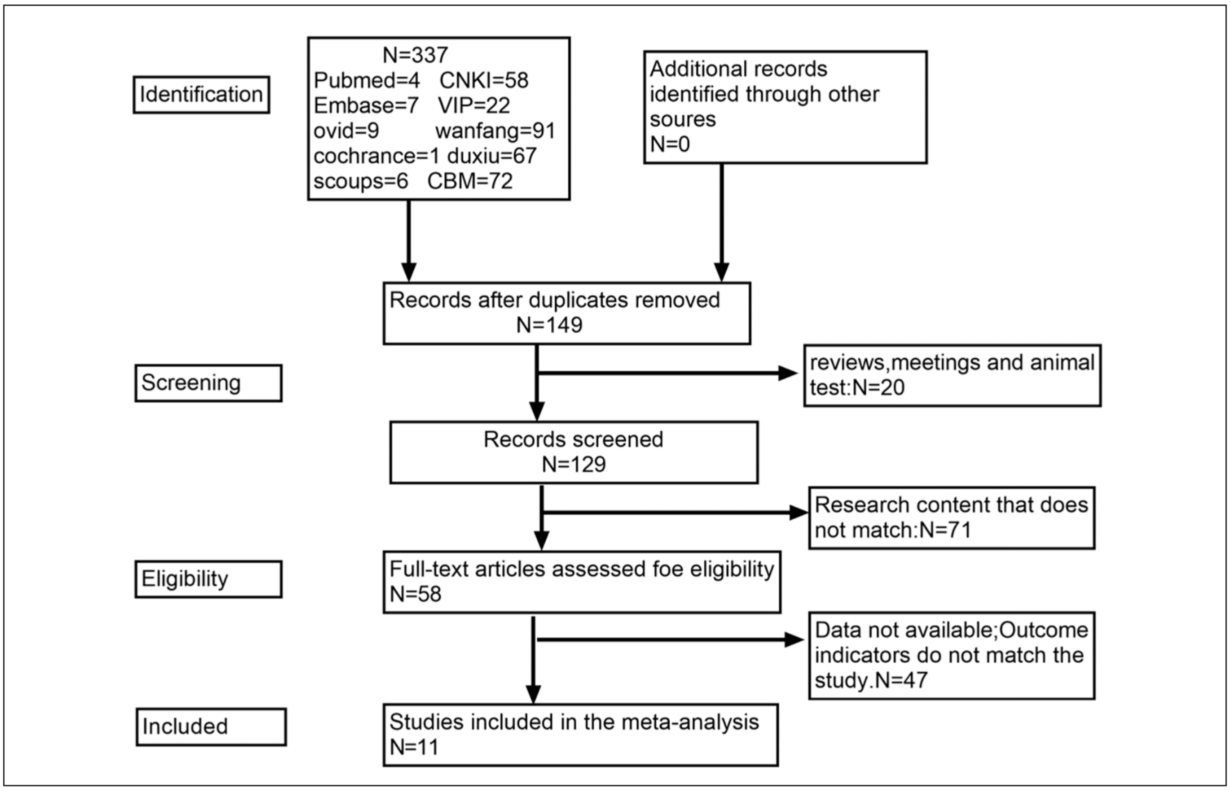

Figure 1. Flow chart of literature screening.

animal experiments. 71 articles were removed from the full-text review due to inconsistent study content. 47 articles did not have sufficient data to calculate or construct true positive value, false negative value, false positive value, and true negative value. Finally, a total of 11 studies[7,18-27] were included in the meta-analysis. All articles were managed by Note Express.

Basic Characteristics of the 11 Included Studies

11 articles[7,18-27] were included in this study (Table I), of which two[7,24] used a 3.0 T field strength and the rest 1.5 T. The use of b-values differed slightly among studies, with one not stating the choice of b-value[23], one study using a multiple b-value[20], and only the remaining articles using

Table I. Basic characteristics of the included 11 studies.

First author	Year	Country	Group (observation/ control)	Field strength	Study design	b-values (sec/mm^2)	Standard
Tao et al[18]	2015	China	18/16	1.5 T	Retrospective	0, 1,000	Surgically
Xiel[9]	2017	China	27/11	1.5 T	Retrospective	0, 800	Surgically
Wei[21]	2018	China	24/6	1.5 T	Retrospective	0, 600, 800	Surgically
Yang[22]	2020	China	15/2	1.5 T	Retrospective	50, 400, 800	Surgically
Lu et al[23]	2021	China	24/5	1.5 T	Retrospective	Unavailable	Surgically
Li et al[25]	2022	China	53/14	1.5 T	Retrospective	0, 1,000	Surgically
Li et al[26]	2022	China	48/60	1.5 T	Retrospective	0, 1,000	Surgically
Zheng et al[27]	2022	China	112/73	1.5 T	Retrospective	0, 1,000	Surgically
Li and Lu[24]	2022	China	22/36	3.0 T	Retrospective	0, 600	Surgically
Sannananja et al[20]	2018	USA	8/9	1.5 T	Retrospective	0, 50, 600, 800, 1,000	Surgically
Prakash et al[7]	2023	India	10/32	3.0 T	Retrospective	50, 400, 800	Surgically

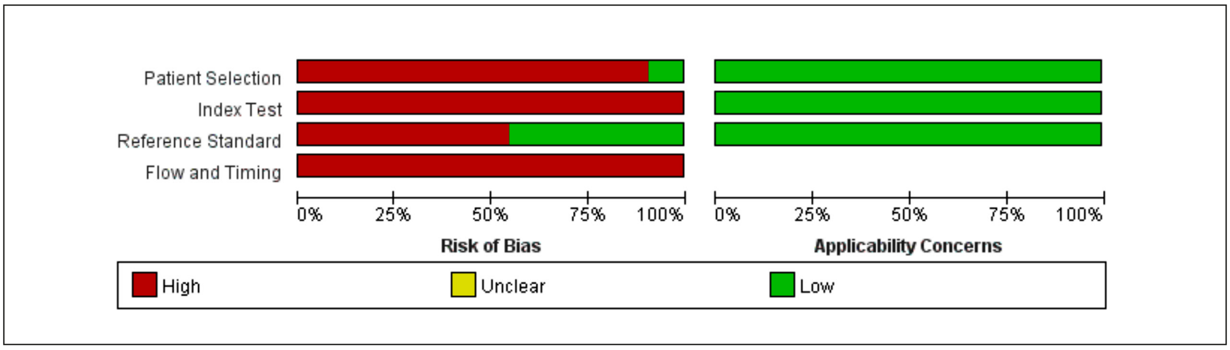

Figure 2. The literature quality evaluation of all studies.

the conventional double or triple b-values. The results of all studies were confirmed by surgical pathology.

Quality Evaluation

Quality evaluation of the included studies (Review Manager 5.3) showed that flow index and timing index were high risk, which we suspected was caused by the differences in the region of interest (ROI) selection at DWI. Other evaluation metrics were acceptable (Figure 2).

Main Statistical Analysis Results

Threshold effect

The data were imported into Meta-disc 1.4 for analysis, and Spearman's correlation between the sensitivity log and (1-specificity) log was -0.109 (p = 0.75), implying that no threshold effect existed in this study. In addition, by plotting the symmetric sROC curve, there was no "shoulder arm shape", which further indicated that there was no threshold effect in the study (Figure 3).

Non-threshold effect heterogeneity

The Cochran-Q was 29.85 ($p < 0.01$), indicating the heterogeneity of non-threshold effects in this study. Furthermore, the sensitivity, the specificity, LR^+, LR^-, and I^2 of DOR were ≥ 50%. The random-effects model was used for the combination of the above five pooled indexes.

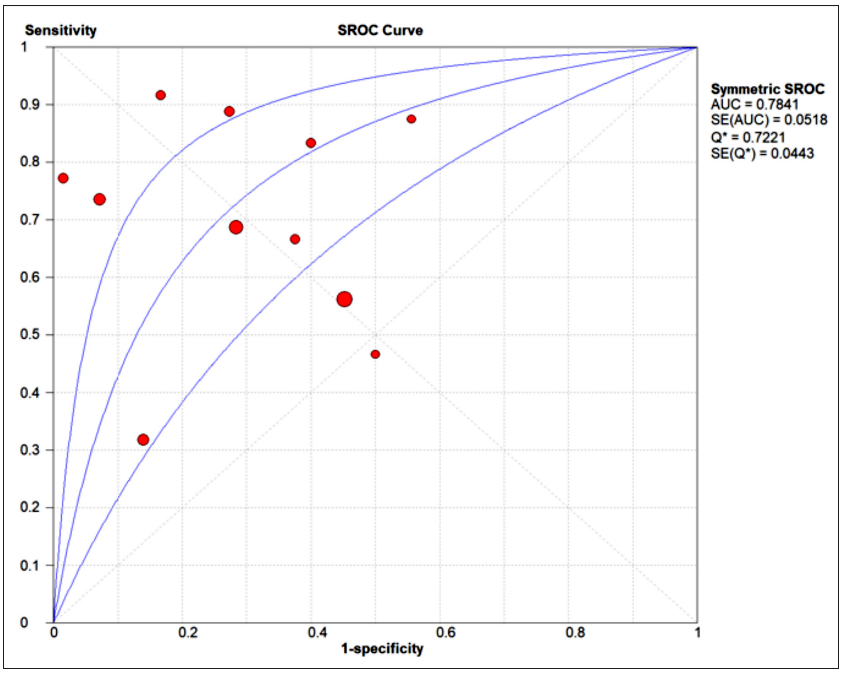

Figure 3. The symmetric sROC curve.

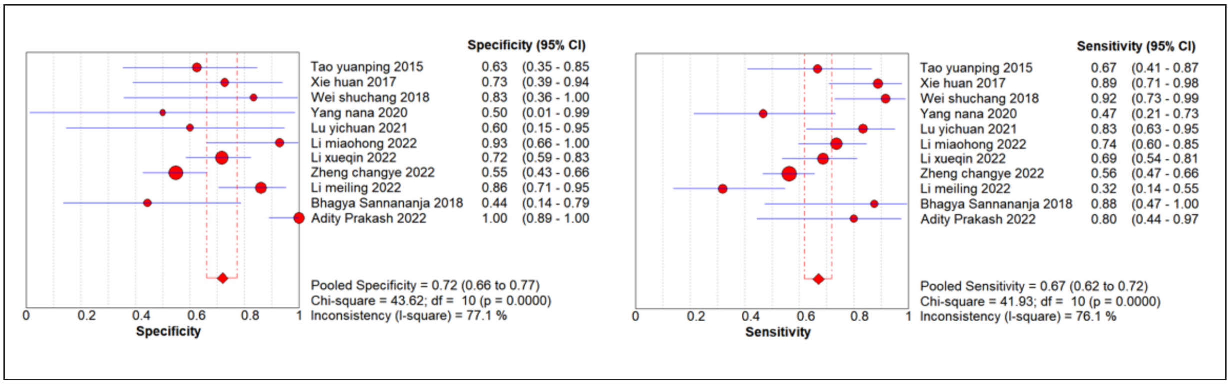

Figure 4. The pooled index.

The pooled index (Meta-disc 1.4)

The pooled sensitivity was 0.670 (0.619-0.719). The pooled specificity was 0.720 (0.661-0.773). The pooled LR^+ was 2.161 (1.454-3.211). The pooled LR^- was 0.413 (0.280-0.609). The pooled AUC was 0.7841, and Q* was 0.7221. The pooled diagnostic ratio DOR was 6.713 (2.981-15.118) (Figure 4).

Sensitivity analysis

STATA 16.0 was selected for sensitivity analysis of the data from this study. It can be observed from Figure 5 that the two original studies[7,24] have strong sensitivity, while the other original studies do not cause sensitivity with arithmetic results. So, the results of this study are relatively stable.

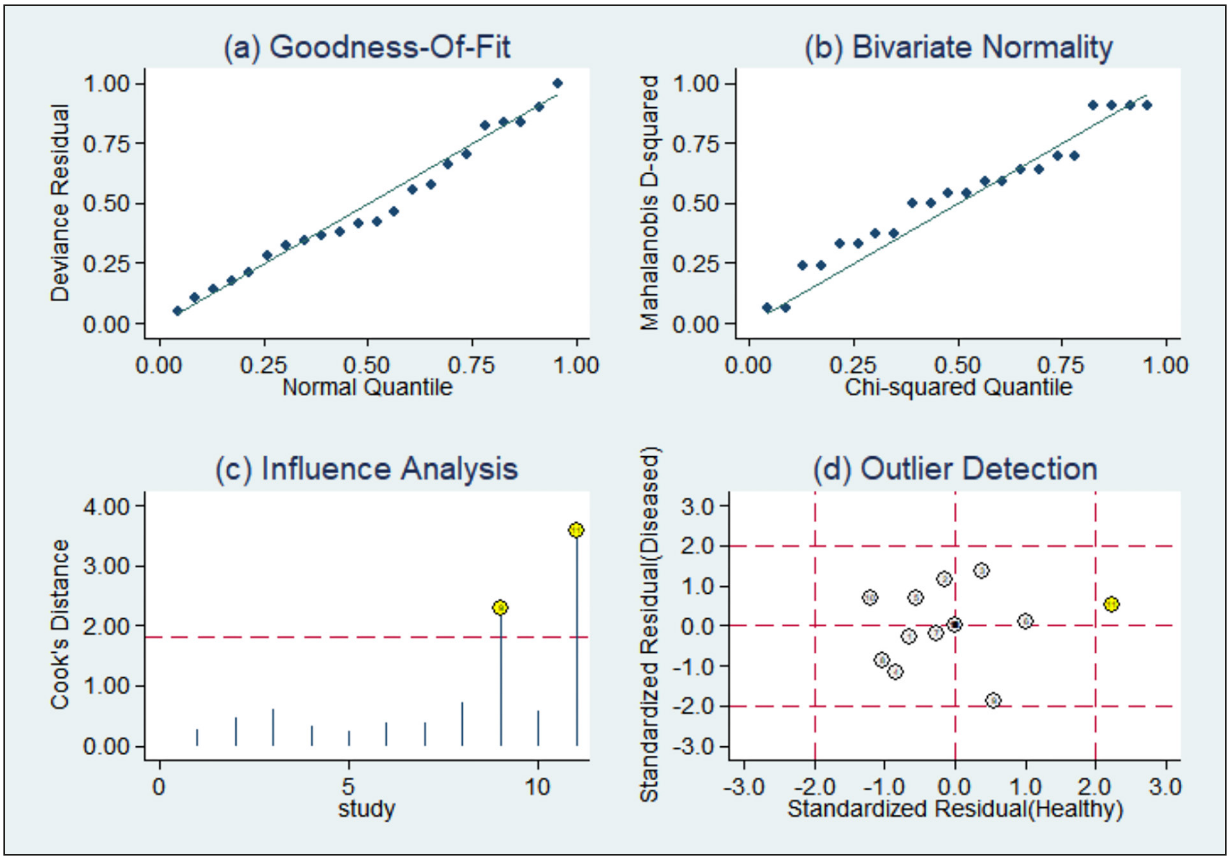

Figure 5. STATA 16.0 was selected for sensitivity analysis of the data from this study. **a**, Goodness-Of-Fit; **b**, Bivariate Normality; **c**, Influence Analysis; **d**, Outlier Detection.

Deek's funnel

STATA 16.0 was selected to test the data of this study for publication bias. It can be seen from the above results that $p = 0.13$, the funnel plot is asymmetric, and there is no publication bias in this study (Figure 6).

Subgroup analysis (Meta-disc 1.4)

A total of four studies[18,25-27] used pooled T2WI + DWI for the diagnosis of placenta accreta, with the pooled sensitivity of 0.93 (0.89-0.96), the pooled specificity of 0.86 (0.80-0.91), the pooled LR^+ of 6.41 (2.60-15.79), the pooled LR^- of 0.08 (0.05-0.15), the pooled AUC of 0.9822, Q* of 0.9414, and the pooled diagnostic ratio DOR of 100.32 (25.75-390.85). The above data suggest that T2WI + DWI is more effective in diagnosing placenta accreta than DWI alone (Figure 7).

Discussion

In this study, we evaluated the diagnostic efficiency of DWI in patients with the placenta accreta spectrum. Our study showed that DWI had high sensitivity and specificity in the diagnosis of PAS. Furthermore, T2WI + DWI has higher diagnostic efficacy than DWI alone in the diagnosis of PAS.

DWI is currently the only non-innovative functional imaging technique that can detect the diffusion motion of water molecules *in vivo*, and it is more widely used in the diagnosis of PAS[28,29]. With the occurrence of diseases, affected by various pathological and physiological factors, intracellular water molecules and tissue density change[30]. The diffusion motion of water also changes, resulting in a change in DWI. The apparent diffusion coefficient (ADC) can quantify the degree of restricted diffusion of water molecules[31]. In this meta-analysis, a total of 11 articles[7,18-27] on the application of DWI in PAS were studied, and a total of 625 patients were enrolled. QUADAS2 was used to evaluate the quality of the literature. The results showed that the influence of the case-control study type was not avoided when the included studies were selected, but all cases were selected continuously. None of

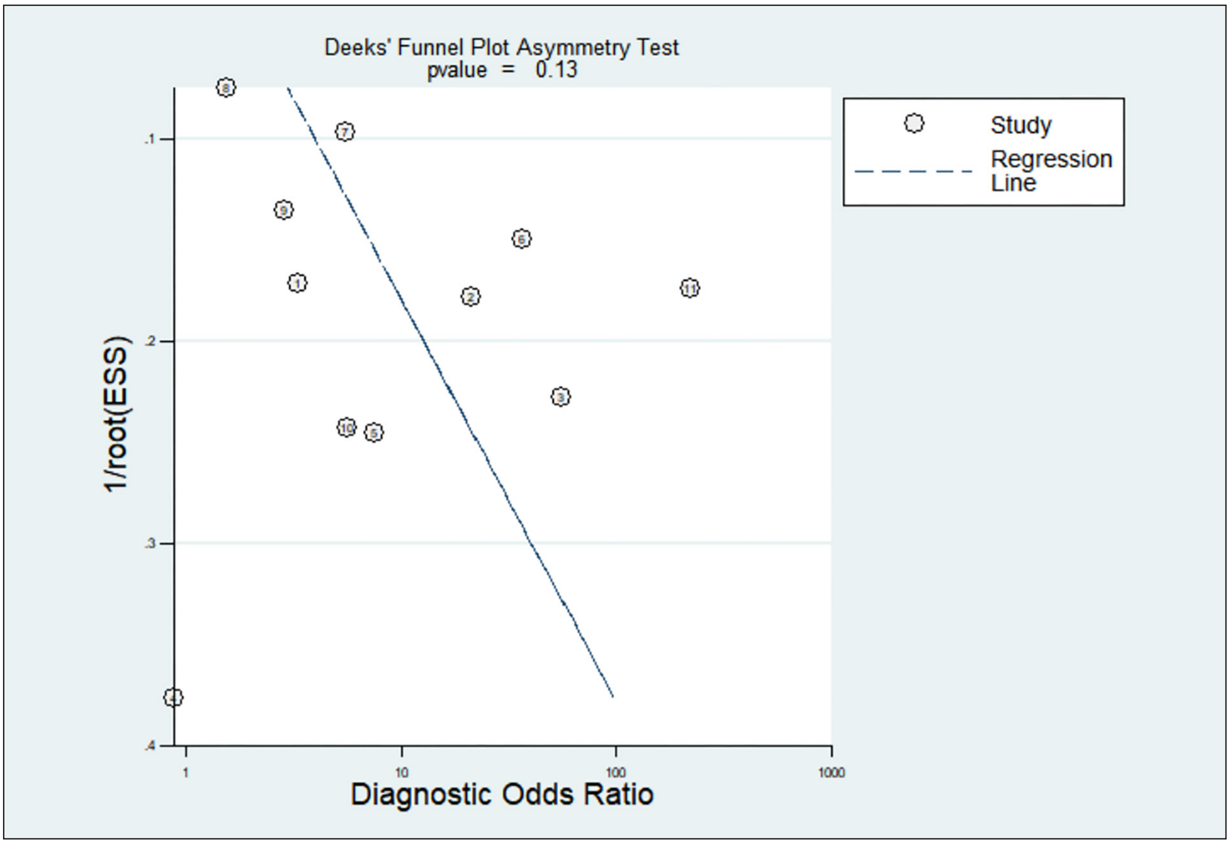

Figure 6. Publication bias.

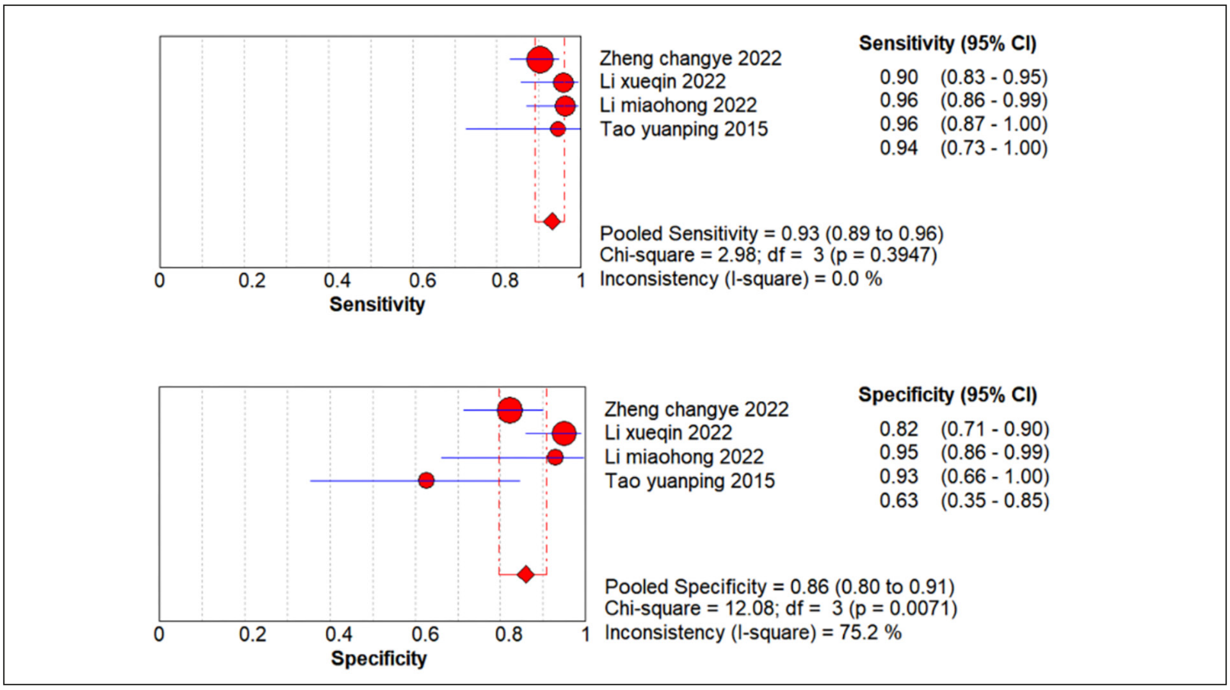

Figure 7. T2WI+DWI diagnosing placenta accreta.

the studies used a threshold because they qualitatively evaluated the use of DWI in the diagnosis of PAS. All studies used pathology as the gold standard of selection, but none of them stated the time interval between the gold standard and the experiment to be evaluated. Therefore, in future studies, it is recommended that diagnostic test reporting criteria be used to improve the accuracy of experiments[32,33].

Regarding the threshold effect, the sROC curves in this study did not show "shoulder-arm" changes, indicating that there was no consistency due to the threshold effect, but the pooled indexes were all greater than 50%, indicating that all articles in this study had heterogeneity due to the non-threshold effect. Combined with the 11 articles in this study, heterogeneity may be due to: (1) The ROI selection of DWI imaging ADC is inconsistent among all the included studies. Some studies state that the ROI from DWI imaging ADC is extracted in the preoperative implantation, while some studies state that the ROI is extracted in the preoperative non-implantation. However, some studies do not state this information. (2) Three types of placental implantation diseases: placental adhesion, placental implantation, and placental penetration. None of the studies showed differences between DWIs and ADCs of the three disease types. (3) Various studies were not consistent in b-value selection and field strength.

As for the sensitivity analysis of this meta-analysis, among the 11 articles[7,18-27], 2 were highly sensitive, which may be attributed to the fact that the FP of Prakash et al[7] was 0, while the overall sample of Li and Lu[24] was small. Overall, the stability of this study is relatively good. The asymmetry of Deeks' Funnel plot indicated that there was no publication bias in this study and that no publication bias caused fluctuation in the results of all articles of this study.

Despite the heterogeneity in this meta-analysis, a pooled sensitivity was 0.670 (0.619-0.719); the pooled specificity was 0.720 (0.661-0.773); the pooled LR^+ was 2.161 (1.454-3.211); the pooled LR^- was 0.413 (0.280-0.609); the pooled AUC was 0.7841, Q index was 0.7221, and the pooled diagnostic ratio DOR was 6.713 (2.981-15.118). All the above-pooled effects indicate that DWI has a high diagnostic value for PAS. This also indicates that DWI can not only identify benign and malignant tumors[13-16], but also play a certain role in the diagnosis of non-tumor diseases[34]. In routine prenatal diagnosis, especially when the state of PAS cannot be accurately determined by ultrasound, DWI sequences can be used to assist the diagnosis based on conventional MRI.

Among the 11 articles[7,18-27] of this meta-analysis, 4[18,25-27] used combined T2WI + DWI diagnosis, with a pooled sensitivity of 0.93 (0.89-0.96), a pooled specificity of 0.86 (0.80-0.91), and a pooled AUC of 0.9822, indicating that the efficacy of combined T2WI+DWI for the diagnosis of PAS is higher than that of DWI sequences alone. Although DWI can clearly show the continuity of the myometrium and the invasion of placental tissue into the myometrium, the signal-to-noise ratio and spatial resolution[35] of DWI are lower than T2WI, especially in patients in late pregnancy, as the thinning and aggravation of the myometrium make the display of the band more difficult. DWI can observe the direct signs of PAS, but the direct signs of PAS are inherently difficult to diagnose with certainty[29]. The combination of T2WI and DWI allows for the fusion of morphological and functional images, which can more clearly show the relationship between the placenta and the myometrium. The combination of T2WI and DWI can improve the diagnostic compliance rate of PAS.

Limitations

The shortcomings of this study are as follows (1) There is no specific threshold value regarding ADC values for PAS, resulting in inconsistent research results. (2) The language of this study only involves Chinese and English, which will affect the results of the study. (3) The number of included studies is small.

Conclusions

DWI is of high diagnostic value in the diagnosis of PAS and is valuable in guiding the clinical treatment of PAS. The combined T2WI+DWI is superior to DWI alone in the diagnosis and treatment of PAS, and it can provide more accurate and effective guidance information for clinical practice. In the future, we will conduct a multicenter clinical trial with a large sample size to explore the diagnostic value of combined T2WI+DWI in the diagnosis of PAS.

Conflict of Interest

The authors declare that they have no conflict of interests.

Ethics Approval

Not applicable.

Informed Consent

Not applicable.

Data Availability

The data presented in this study are available on request from the corresponding author.

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Authors' Contribution

Guo CY designed and conducted the study, Zhang XR designed and supervised the study, He Cand Xu BG designed the study and collected data.

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