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REVIEW ARTICLE

Diagnostic Accuracy of Ultrasonography for Detection of Intussusception in Children; a Systematic Review and Meta-Analysis

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Abstract: **Introduction:** The diagnosis of intussusception can be challenging in children due to the fact that the findings of clinical evaluations are nonspecific and most of the patients present with unclear history. Therefore, in this systematic review and meta-analysis, we aimed to investigate the diagnostic accuracy of ultrasonography for detection of intussusception and also compare the efficacy of point-of-care ultrasound (POCUS) with radiologist-performed ultrasound (RADUS). **Methods:** Two independent reviewers systematically searched different online electronic databases including MEDLINE, Scopus, Web of Science, Google Scholar, Embase, and Cochrane from inception to December 1, 2022 to identify published papers reporting accuracy of ultrasonography for diagnosis of intussusception. The quality assessment of the included studies was investigated using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool. **Results:** A total of 1446 records were retrieved in the initial search of databases. After screening the titles, a total of 344 studies were retrieved for the detailed assessment of full-text. Finally, 37 studies were included in qualitative and quantitative analysis. The pooled sensitivity and specificity of ultrasonography for diagnosis of intussusception were 0.96 (95% CI: 0.95-0.97) and 0.97 (95% CI: 0.97-0.98), respectively. The pooled positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were 24.57 (95% CI: 8.26-73.03) and 0.05 (95% CI: 0.04-0.08), respectively. The area under the hierarchical summary receiver operating characteristic (HSROC) curve was 0.989. Mete-regression showed that there is no significant difference between diagnostic performance of POCUS and RADUS (p = 0.06 and rDOR (diagnostic odds ratio) = 4.38 (95% CI: 0.92-20.89)). **Conclusion:** This meta-analysis shows that ultrasonography has excellent sensitivity, specificity, and accuracy for diagnosis of intussusception in pediatric patients. Moreover, we found that diagnostic performance of POCUS is similar to that of RADUS for diagnosis of intussusception.

Keywords: Intussusception; Ultrasonography; Point-of-Care Testing; Diagnostic Imaging; Meta-analysis

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1. Introduction

Intussusception is the most prevalent cause of intestinal obstruction among the pediatric population younger than 6 years old, occurring in 1.1 to 4.3 children per 1,000 live births in Europe and 0.5 to 2.3 children per 1,000 live births in United States with the male to female ratio between 1.4:1 to 4:1 (1). If this obstructive condition is left undiagnosed and untreated, it can potentially lead to fatal complications such as intestinal gangrene, necrosis, perforation, and death. Indeed, prompt and appropriate diagnosis and management of intussusception in children is crucial to achieve a successful reduction using air enema (2). The diagnosis of intussusception can be challenging in children due to the fact that the findings of clinical and physical evaluations are nonspecific and most of the patients are younger than two years old, presenting with unclear history and symptoms such as abdominal discomfort and crying. Previous studies have shown that the classic triad of colicky abdominal pain, vomiting, and "currant jelly" stool are found in less than 40% of cases on presentation to emergency departments, which means that more than 60% of cases are indistinguishable from acute gastroenteritis (3). Abdominal ultrasonography is gradually emerging as the standard criterion for diagnosis in the emergency department due to its advantage of being cost-effective, non-invasive, and radiation-free. Although barium enema is known as the gold standard for diagnosis of intussusception, this modality requires an experienced radiologist, is expensive and invasive, and exposes cases to radiation, making it impractical in outpatient setting and emergency departments. There is a growing body of literature suggesting ultrasonography as a rapid, safe, and reliable imaging modality for diagnosis of intussusception in children (4-7). Although multiple diagnostic studies have been recently published and ultrasound is suggested for the diagnosis of intussusception, their results were controversial with relatively wide confidence intervals. Moreover, previous investigations have proposed that sonographers with limited experience or pediatric physicians as well as experienced radiologists can perform point-of-care ultrasound (POCUS) (8-10). However, to the best of our knowledge, the comparison of diagnostic accuracy of POCUS and radiologist-performed ultrasound (RADUS) for detection of intussusception has not been carried out in a systematic review and meta-analysis. Therefore, in this systematic review and meta-analysis, we aimed to investigate the diagnostic accuracy of ultrasonography for detection of intussusception and also compare the efficacy of POCUS with RADUS in this regard.

2. Methods

2.1. Literature Search

This systematic review and meta-analysis was carried out according to the guidelines of Preferred Reporting Items for

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Systematic Reviews and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA). Two independent reviewers (MF and RAB) systematically searched different online electronic databases including MEDLINE, Scopus, Web of Science, Google Scholar, Embase, and Cochrane from inception to December 1, 2022 to identify published papers reporting accuracy of ultrasonography for diagnosis of intussusception. The following keywords and Medical Subject Heading (MeSH) Terms and also their combinations with Boolean operators ''AND" and ''OR" were used for systematic search of the databases: "ultrasonography" OR "ultrasound" OR "sonography" OR "ultrasonic" OR "US" OR "medical sonography" AND "intestinal invagination" OR "intussusception". The references of the identified papers were also screened to retrieve the relevant articles more comprehensively. The disagreements between two reviewers were resolved via a consensus meeting or by a third reviewer.

2.2. Eligibility Criteria

The eligible studies were included in our meta-analysis according to the following inclusion criteria: 1) diagnostic accuracy data including true positive (TP), false positive (FP), true negative (TN), and false negative (FN) can be extracted from a 2×2 table directly or data are available to calculate these items; 2) reported the diagnostic performance of ultrasonography for detection of intussusception; 3) the number of included cases was 10 or more; 4) the definite diagnosis came from the result of air or barium enema, surgical report, clinical follow-up, and finings of imaging by experienced radiologist or combination of them; 5) included cases <18 years old presenting with manifestations suggestive of intussusception. Meta-analysis, reviews, comments, case reports, case series with less than ten patients, animal and cadaveric studies, studies with incomplete data regarding diagnostic characteristics of ultrasonography for diagnosis of intussusception were excluded.

2.3. Data Extraction

The following variables were extracted from the included studies using the finalized data extraction excel sheet: first author, year of publication, country, study design, mean age, number of patients, prevalence of intussusception, TP, FP, TN, and FN. Data extraction was carried out by two independent researchers and any discrepancies were resolved through a consultation with a third researcher.

2.4. Quality Assessment

The quality assessment of the included studies was investigated using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool which evaluates the risk of bias and applicability of each study. Similarly, the quality assessment was performed by two independent researchers and their disagreements were resolved by a third party.

2.5. Data Analysis

Statistical analysis was performed using meta-Disc software version 1.4 (Ramona Cajal Hospital, Madrid, Spain) and Stata statistical software package (Stata Corp., College Station, TX, USA) (version 17.0). The heterogeneity between the included studies was assessed using I2 and Cochran-Q test. If the value of I2 was higher than 50% or P-value of Q-test was less than 0.10, DerSimonian-Laird random effect was used. Alternatively, if the value of I2 was less than 50% and P-value of Q-test was higher than 0.10, the data were pooled using Mantel-Haenzsel model. Funnel plot, Egger's test, and Begg's test were used to investigate the publication bias.

3. Results

3.1. Search Results

A total of 1446 records were retrieved in the initial search of databases. Seventeen studies were identified through manual search and citation tracking. After screening the titles, we removed 96 duplicated records and excluded 1023 articles based on the pre-defined criteria and a total of 344 studies were retrieved for the detailed assessment of full-text. Finally, 37 studies were included in qualitative and quantitative analysis. The flow of the relevant studies is summarized in Figure 1.

3.2. Main Characteristics

Thirty-seven studies with 6453 patients from 17 countries were included in this meta-analysis. These studies were published between 1986 and 2021. The mean age of the studied cases ranged from 6 to 72 months. The sensitivity and specificity of the studies ranged from 84.6 to 100 and 0 to 100, respectively. In this meta-analysis, we included 20 retrospective and 17 prospective cohort studies. Ultrasonography by an experienced radiologist, clinical follow-up, surgical report, and air or barium enema were the most common gold standards reported in the included studies. True positive (TP), false positive (FP), true negative (TN), and false negative (FN) were also extracted from the studies. The main characteristics of the included studies are summarized in Table 1.

3.3. Quality Assessment

The quality assessment of the included studies was carried out using QUADAS-2 tool. The detailed results of this assessment are shown in table 2. Taken together, the overall results of quality assessment suggest good quality. Some items of QUADAS-2 were not well-described in conference abstracts, which led to high risk of bias.

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Table 1: Characteristics of the included studies

Authors	Year	Country	Study Design	Age (months)	Number	TP	TN	FP	FN	Sensitivity	Specificity	Prevalence
Arnaud et al. (19)	1986	France	Retrospective	-	32	8	23	1	0	100	96	25%
Pracros J.P et al. (20)	1990	France	Prospective	-	426	145	281	0	0	100	100	34%
Bhisitkul et al. (21)	1992	USA	Prospective	17	65	20	42	3	0	100	93	31%
Verschelden et al. (22)	1992	USA	Prospective	18	83	34	43	6	0	100	88	41%
Woo et al. (23)	1992	South Korea	Prospective	10	82	75	7	0	0	100	100	91%
Lim et al. (24)	1994	South Korea	Prospective	<18 y	176	64	112	0	0	100	100	36%
Shanbhogue et al. (25)	1994	Netherlands	Retrospective	-	163	128	33	0	2	98.5	100	80%
Barzilai et al. (26)	1994	Israel	Retrospective	-	14	5	8	1	0	100	89	36%
Wright et al. (27)	1996	Australia	Retrospective	-	50	7	41	2	0	100	95	14%
Sarihan et al. (28)	1997	Turkey	Prospective	38.8	27	21	4	0	2	91	100	85%
Stanely et al. (29)	1997	Ireland	Prospective	11.4	25	7	16	2	0	100	89	29%
John et al. (30)	1998	USA	Retrospective	18	151	48	101	1	1	99	98	32%
Harrington et al. (31)	1998	Canada	Prospective	29.2	245	87	148	7	3	97	95	37%
Smoljanić et al. (32)	2000	Serbia	Retrospective	21.4	35	26	9	0	0	100	100	74%
Henrikson et al. (33)	2003	USA	Prospective	<18 y	19	11	7	1	0	100	88	58%
Eshed et al. (34)	2004	Israel	Retrospective	13.8	151	37	104	7	3	93	94	26%
Justice et al. (35)	2007	Vietnam	Prospective	9.3	585	466	106	1	12	97.5	99	82%
Hryhorczuk et al. (36)	2009	USA	Retrospective	<10 y	812	97	698	15	2	97.9	97.8	12%
Muniz et al. (37)	2010	USA	Prospective	12.3	198	28	168	0	2	93.3	100	15%
Henderson et al. (38)	2011	USA	Retrospective	16	286	60	217	8	1	98.4	96.4	21%
Riera et al. (10)	2012	USA	Prospective	25	82	11	67	2	2	84.6	97.1	16%
Lin et al. (39)	2012	Taiwan	Retrospective	72	775	15	760	0	0	100	100	2%
Zerzan et al. (40)	2012	USA	Prospective	-	99	8	88	2	1	88.9	97.8	9%
Jones et al. (41)	2012	UK	Retrospective	8	197	79	113	5	0	100	100	40%
Mwango et al. (42)	2012	Kenya	Prospective	17	56	18	38	0	0	100	100	32%
Kim et al. (43)	2012	South Korea	Retrospective	26	38	13	22	2	1	92.9	91.7	37%
Usang et al. (44)	2013	Nigeria	Retrospective	6	25	20	1	1	3	87	50	92%
Chang et al. (8)	2013	Taiwan	Retrospective	21	186	151	0	10	25	86	0	95%
Lam et al. (9)	2014	USA	Retrospective	31	46	10	34	2	0	100	94.1	22%
Lim et al. (45)	2015	USA	Retrospective	23	100	37	63	0	0	100	100	37%
Trigylidas et al. (13)	2017	USA	Retrospective	22	105	75	25	2	3	96	92.6	74%
Al-Ani et al. (46)	2017	Iraq	Retrospective	13	47	34	8	0	5	87	100	72%
Van Houwelingen et al. (47)	2018	Germany	Retrospective	29	10	8	1	0	1	89	100	90%
Lee et al. (7)	2020	South Korea	Retrospective	25.5	575	70	483	22	0	100	95.6	13%
Arroyo et al. (4)	2021	USA	Prospective	24	100	8	89	1	2	88.9	97.8	8%
Bergmann et al. (5)	2021	Multi-national	Prospective	21.1	256	55	193	5	3	96.6	98	23%
La Tour et al. (6)	2021	Canada	Prospective	18	131	39	83	3	6	86.7	96.5	34%

TN: true negative; TP: true positive; FN: false negative; FP: false positive.

3.4. Meta-analysis

Typical "shoulder arm shape" of SROC and spearman correlation coefficient between the log of sensitivity and the log of 1 specificity (0.353 with P = 0.03) showed statistically significant threshold effect. The evaluation of the heterogeneity of the diagnostic characteristics revealed a significant heterogeneity for sensitivity (I2=68.7% and P<0.01), specificity (I2=81.7% and P<0.01), positive likelihood ratio (PLR) (I2=98.2% and P<0.01), negative likelihood ratio (NLR) (I2=54.7% and P<0.01), and diagnostic odds ratio (DOR) (I2=61.6% and P<0.01).

The pooled sensitivity and specificity of ultrasonography for diagnosis of intussusception were 0.96 (95% CI: 0.95-0.97)

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Table 2: Quality assessment of the included studies using QUADAS-2 tool

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Arnaud et al.	?	☺	☺	?	☺	☺	☺
Pracros J.P	?	☺	☺	?	?	☺	☺
Bhisitkul et al.	☺	☺	☺	☺	☺	☺	☺
Verschelden et al.	☺	☺	☺	☺	☺	☺	☺
Woo et al.	☺	☺	☺	☺	☺	☺	☺
Lim et al.	☺	☺	☺	☹	☺	☺	☺
Shanbhogue et al.	☺	☺	☺	☺	☺	☺	☺
Barzilai et al.	☺	☺	☺	☺	☺	☺	☺
Wright et al.	☺	☺	☺	☹	☺	☺	☺
Sarihan et al.	?	☺	?	?	☺	☺	?
Stanely et al.	☺	☺	☺	?	☺	☺	☺
John et al.	?	☺	☺	☹	☺	☺	☺
Harrington et al.	☺	☺	☺	☺	☺	☺	☺
Smoljanić et al.	☺	☺	?	?	☺	☺	?
Henrikson et al.	?	☺	☺	☺	☺	☺	☺
Eshed et al.	☺	☺	☺	☹	☺	☺	☺
Justice et al.	☺	☺	☺	☺	☺	☺	☺
Hryhorczuk et al.	☺	☺	☺	☹	☺	☺	☺
Muniz et al.	?	☺	☺	?	?	☺	☺
Henderson et al.	☺	☺	☺	☺	☺	☺	☺
Riera et al.	☺	☺	☺	☺	☺	☺	☺
Lin et al.	☺	☺	☺	☺	☺	☺	☺
Zerzan et al.	?	☺	?	?	☺	☺	?
Jones et al.	☺	☺	☺	?	☺	☺	☺
Mwango et al.	☺	☺	☺	☹	☺	☺	☺
Kim et al.	☺	☺	☺	☹	☺	☺	☺
Usang et al.	☺	☺	☺	☺	☺	☺	☺
Chang et al.	☹	☺	☺	☺	☹	☺	☺
Lam et al.	☺	☺	☺	☺	☺	☺	☺
Lim et al.	☺	☺	☺	☹	☺	☺	☺
Trigylidas et al.	☺	☺	☺	☺	☺	☺	☺
Al-Ani et al.	☺	☺	☺	☹	☺	☺	☺
Van Houwelingen et al.	☺	☺	☺	☺	☺	☺	☺
Lee et al.	☺	☺	☺	☺	☺	☺	☺
Arroyo et al.	☹	☺	☺	☺	☺	☺	☺
Bergmann et al.	☹	☺	☺	☺	☺	☺	☺
La Tour et al.	☺	☺	☹	☹	☺	☺	☹

☺: Low Risk; ☹: High Risk; ?: Unclear Risk.

and 0.97 (95% CI: 0.97-0.98), respectively (Figure 2 and Figure 3). The PLR and NLR were 24.57 (95% CI: 8.26-73.03) and 0.05 (95% CI: 0.04-0.08), respectively (Figure 4 and Figure 5). The pooled DOR for ultrasonography was 517.45 (95% CI: 260.47-1027.97; Figure 6). The area under the hierarchical summary receiver operating characteristic (HSROC) curve was 0.989, suggesting that ultrasonography has an acceptable diagnostic performance (Figure 7).

Meta-regression showed that there was no significant difference between diagnostic performance of POCUS and RADUS for diagnosis of intussusception (P=0.06 and rDOR=4.38 (95% CI: 0.92-20.89)).

3.5. Publication Bias

Evaluation of the studies using Egger's test (P=0.30) and Begg's test (P=0.50) showed no significant publication bias. Furthermore, funnel plot of the included studies revealed no significant publication bias (Figure 8).

4. Discussion

This systematic review and meta-analysis was carried out to investigate the diagnostic accuracy of ultrasonography for intussusception and also compare the efficacy of POCUS with RADUS for diagnosis of intussusception. Our analysis showed that the sensitivity and specificity of ultrasonography

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for diagnosis of intussusception are 0.96 and 0.97, respectively. The accuracy of ultrasonography was 0.98 according to HSROC. Furthermore, meta-regression revealed that there was no significant difference between POCUS and RADUS for diagnosis of intussusception.

Previous studies have shown that the use of POCUS has a pivotal role in the management of life-threatening diseases by providing prompt diagnosis of the diseases (11, 12). In this regard, if not detected and managed early, intussusception can cause life threating complications such as intestinal gangrene, necrosis, perforation, and death. To reduce the risk of these complications, early diagnosis of intussusception in emergency departments would be crucial particularly in medical centers with no access to experienced pediatric radiologist (9, 10, 13). Our findings showed that ultrasonography and particularly POCUS can improve resource utilization by reducing time to diagnosis and prioritize the management of patients by providing early definitive treatment. Therefore, our results are in line with increasing popularity of POCUS for screening and diagnosis of pediatric emergencies (9, 10, 13).

In a similar study, Li et al. (14) investigated the performance accuracy of POCUS and RADUS for diagnosis of intussusception. They included 14 studies with 2367 patients in their analysis. Their study showed that the sensitivity and specificity of ultrasonography for diagnosis of intussusception are 0.94 and 0.96, respectively. The reported sensitivity and specificity of ultrasonography in their study were lower than ours (sensitivity: 0.96 and specificity: 0.97). However, similar to the results of our meta-regression, they found that there was no significant difference between RADUS and POCUS for diagnosis of intussusception. The difference between the accuracy found in our study and this meta-analysis may in part be clarified by the fact that our study included more studies (37 vs. 14), particularly those published before 2000 and after 2017; therefore, our meta-analysis is more comprehensive and updated. Similarly, in their meta-analysis, they found high heterogeneity among the included studies. One possible explanation for this high heterogeneity may be the fact that included studies had different sample sizes, gold standards for confirmation of the diagnosis, duration of follow-up of the patients, designs of the studies, and device types.

Traditionally, clinical evaluation and follow-up, X-ray, contrast enema, CT-scan, and Magnetic resonance imaging (MRI) are used for the diagnosis of pediatric intussusception. X-ray, computed tomography (CT)-scan, and contrast enema are not the first choice for the diagnosis of pediatric intussusception as they expose the patient to ionizing radiation and are expensive. Contrast enema is known as the gold standard for detection and management of intussusception in pediatric patients, but it should be performed by an experienced pediatric radiologist (15-17). On the other hand, during the last years, ultrasonography has evolved to achieve more popularity as the first choice for the diagnosis of pediatric intussusception. Although the use of ultrasonography for pediatric patients is accompanied with distinct advantages such as being safe, noninvasive, and inexpensive, providing real-time evaluation of the changes, and lacking ionizing radiation, this modality of imaging also has some critical limitations. Ultrasonography cannot adequately detect pathological lead points and discriminate ileo-colic from ileo-ileal intussusception, which have a pivotal role in prompt and appropriate diagnosis and management of intussusception in children (18).

The results of our meta-analysis support the increasing acceptance of ultrasonography for diagnosis of intussusception, but particular attention must be paid to some studies included in our analysis where ultrasonography showed weak diagnostic properties for identification of intussusception. In this regard, Chang et al. (8) reported that ultrasonography for intussusception has sensitivity of 0.86 and specificity of 0, which differed considerably from other included studies. This inconsistency might be explained by the mixed use of sonographers with different levels of experience, lack of appropriate patient selection criteria, and the retrospective design of the study. Ultrasonography is considered an operator-dependent modality of imaging in which lack of training and experience of sonographer can lead to misclassification bias and low diagnostic accuracy.

Our meta-analysis had some limitations such as heterogeneity in the design of the included studies, difference in experience level of sonographers, use of different gold standards for definite diagnosis of intussusception, and selection bias of the majority of included studies due to the retrospective design. Since the included studies did not control possible confounders, the diagnostic performance of POCUS cannot be easily generalized to all settings. Furthermore, some studies did not report the experience level of sonographer who assessed the suspected patients. Finally, it should be noted that we only included studies assessing suspected pediatric cases and our findings are not generalizable to other age groups.

5. Conclusions

This meta-analysis shows that ultrasonography has excellent sensitivity, specificity, and accuracy for diagnosis of intussusception in pediatric patients. Moreover, we found that diagnostic performance of POCUS is similar to that of RADUS for diagnosis of intussusception. However, further prospective studies with larger sample size are still required to establish these findings.

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6. Declarations

6.1. Acknowledgments

The authors thank all those who contributed to this study.

6.2. Conflict of interest

None.

6.3. Fundings and supports

None.

6.4. Authors' contribution

All authors contributed to study design, data collection, writing the draft of the study, and read and approve of final version.

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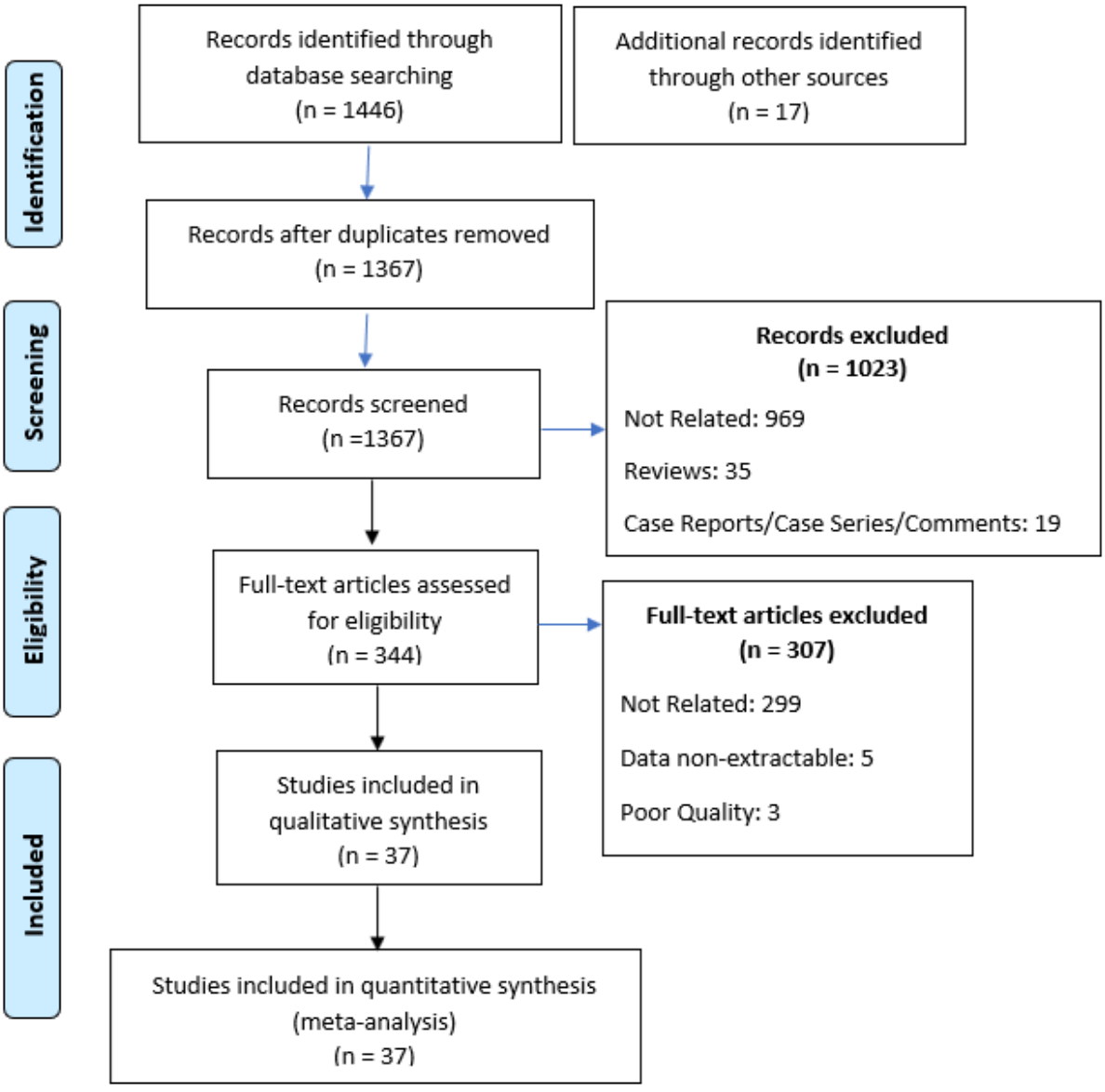

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) flowchart of the literature search and selection of studies that reported accuracy of ultrasonography for diagnosis of intussusception.

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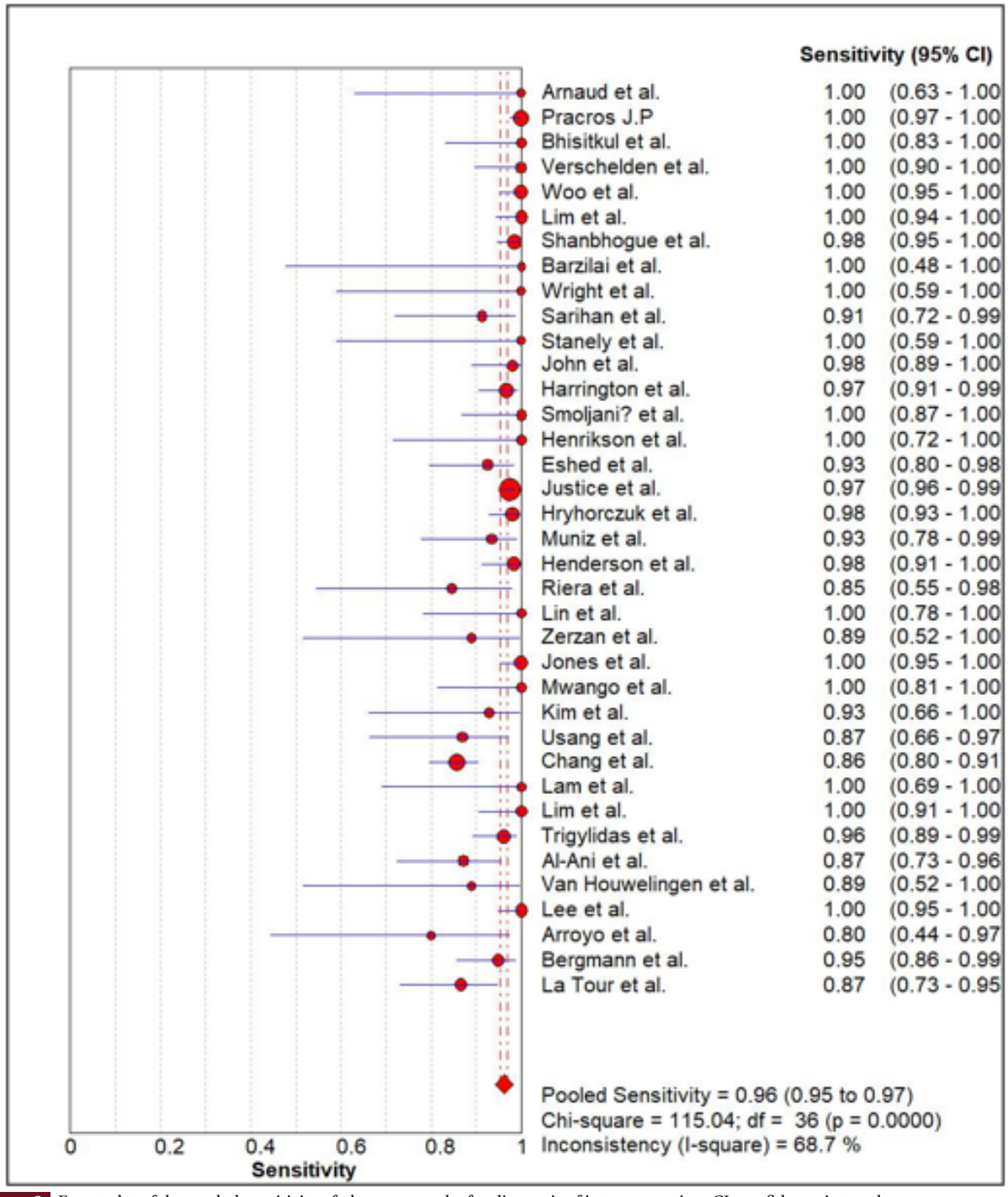

Figure 2: Forest plot of the pooled sensitivity of ultrasonography for diagnosis of intussusception. CI: confidence interval.

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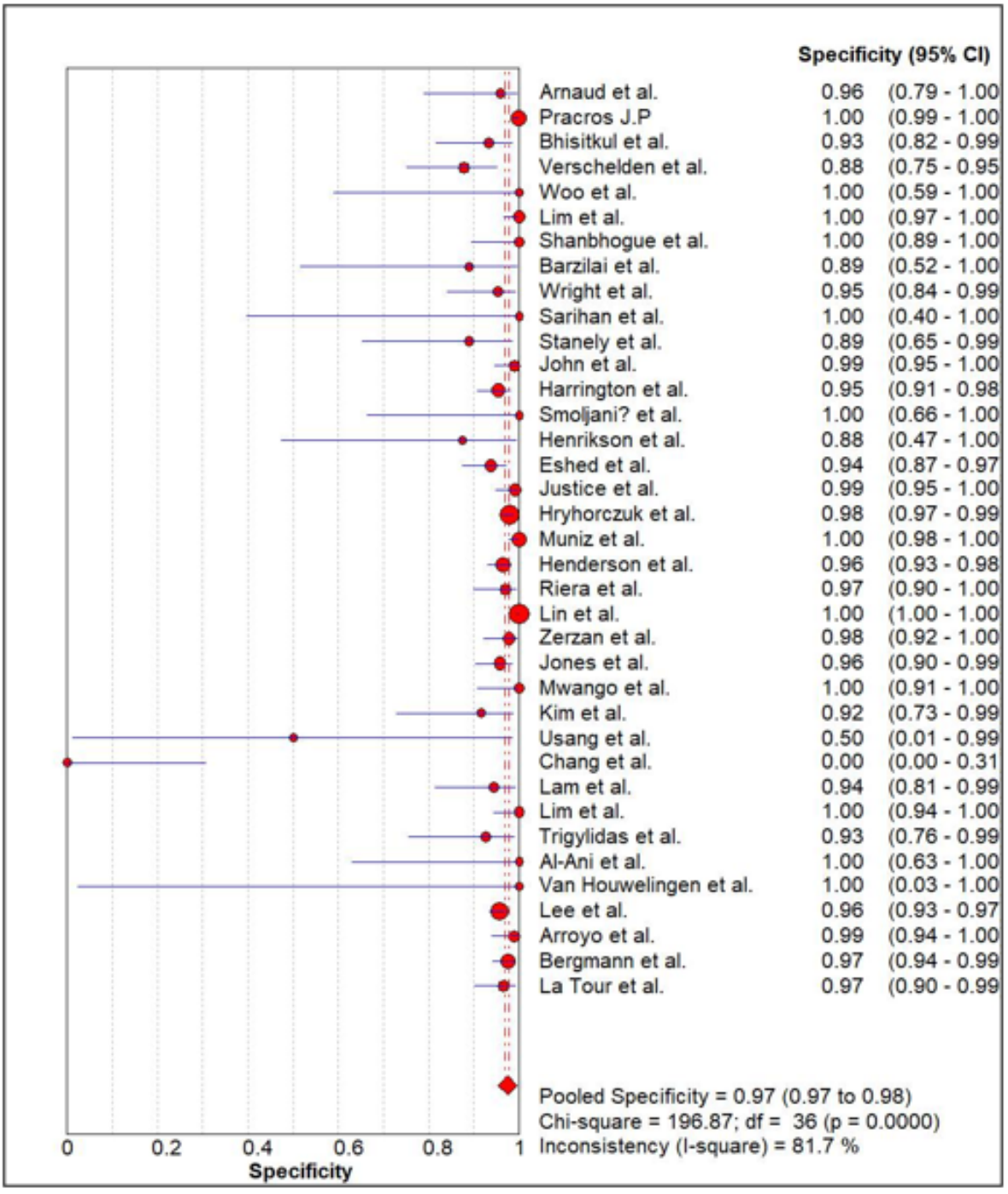

Figure 3: Forest plot of the pooled specificity of ultrasonography for diagnosis of intussusception. CI: confidence interval.

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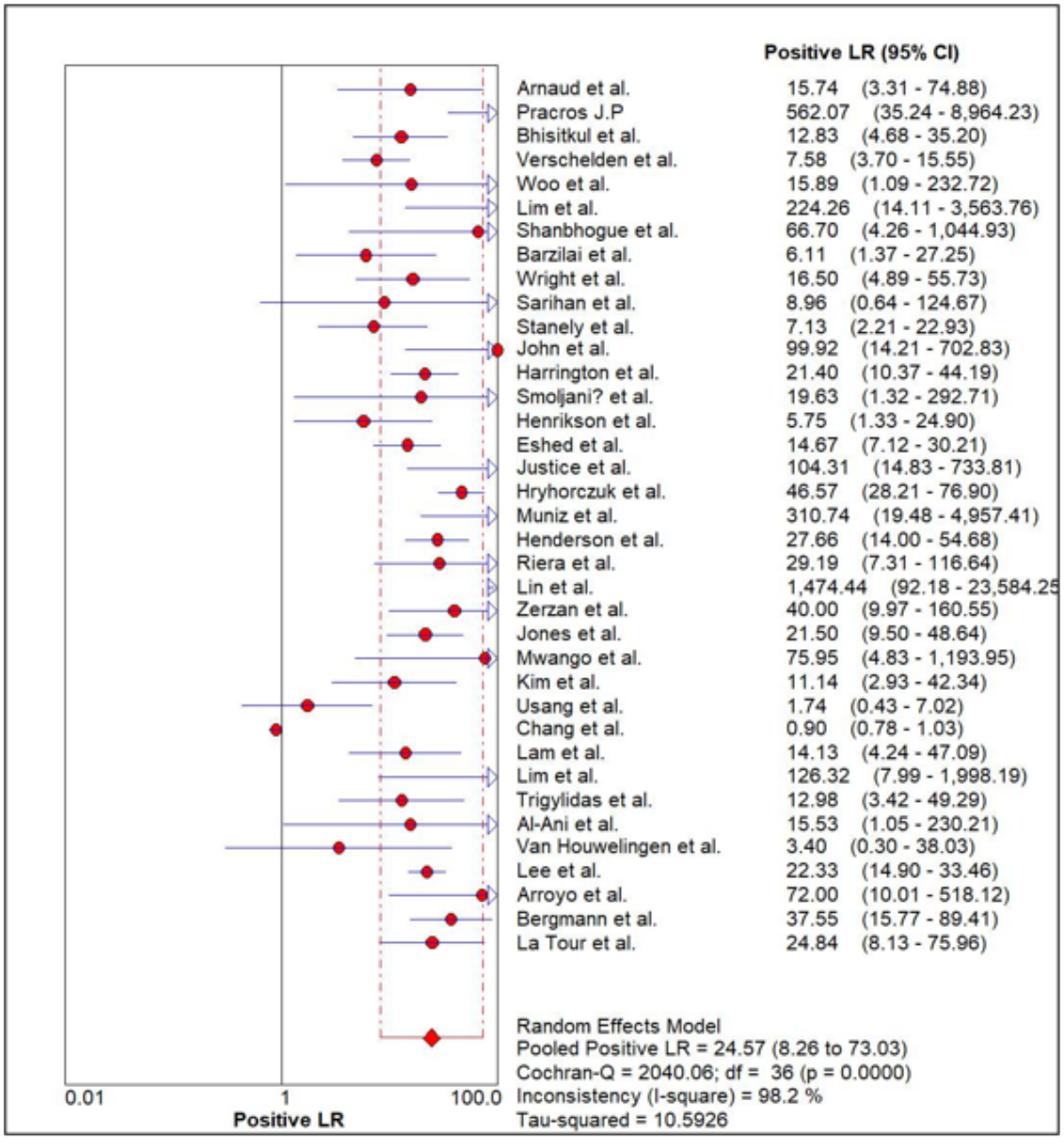

Figure 4: Forest plot of the pooled positive likelihood ratio (PLR) of ultrasonography for diagnosis of intussusception. CI: confidence interval.

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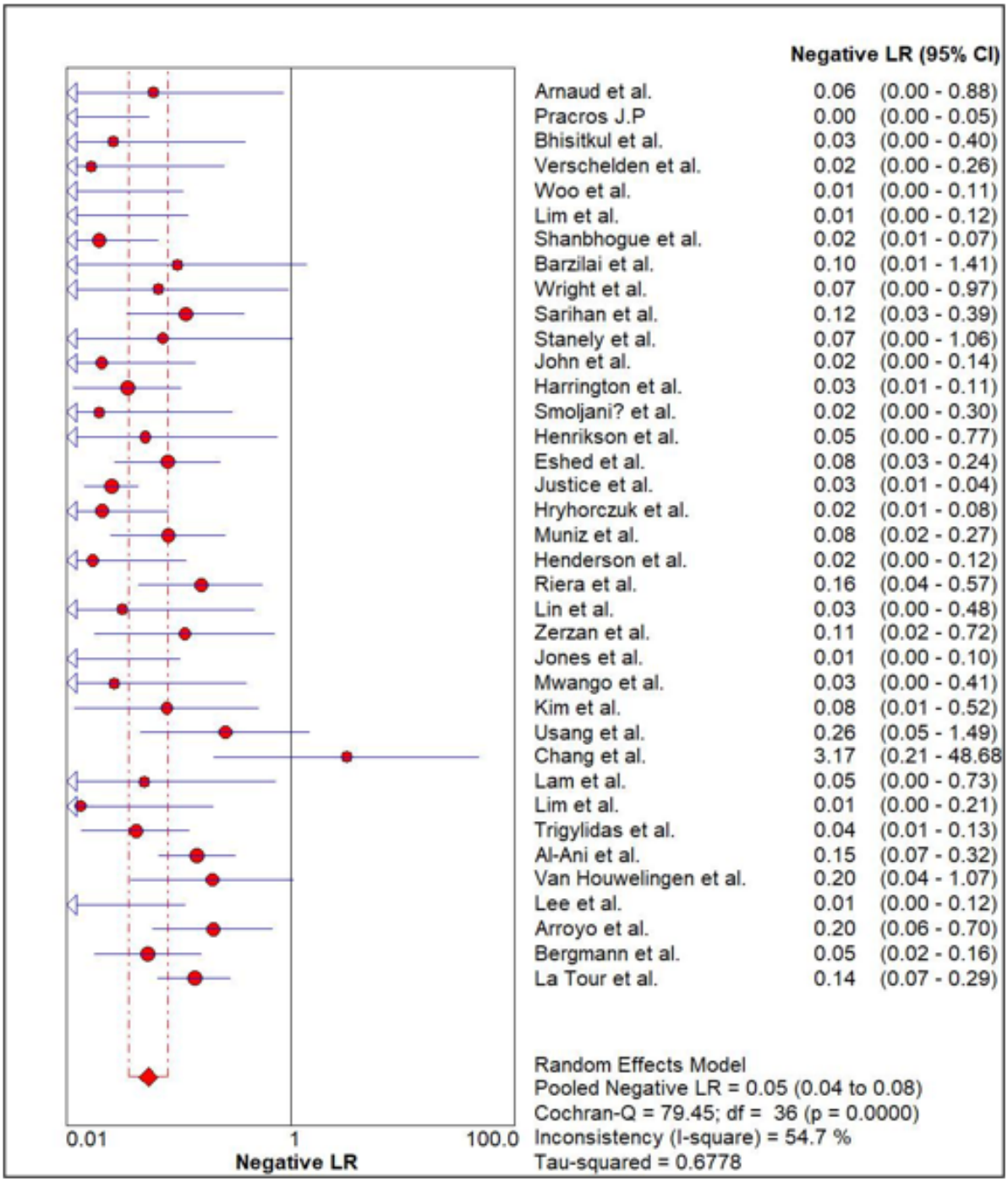

Figure 5: Forest plot of the pooled negative likelihood ratio (NLR) of ultrasonography for diagnosis of intussusception. CI: confidence interval.

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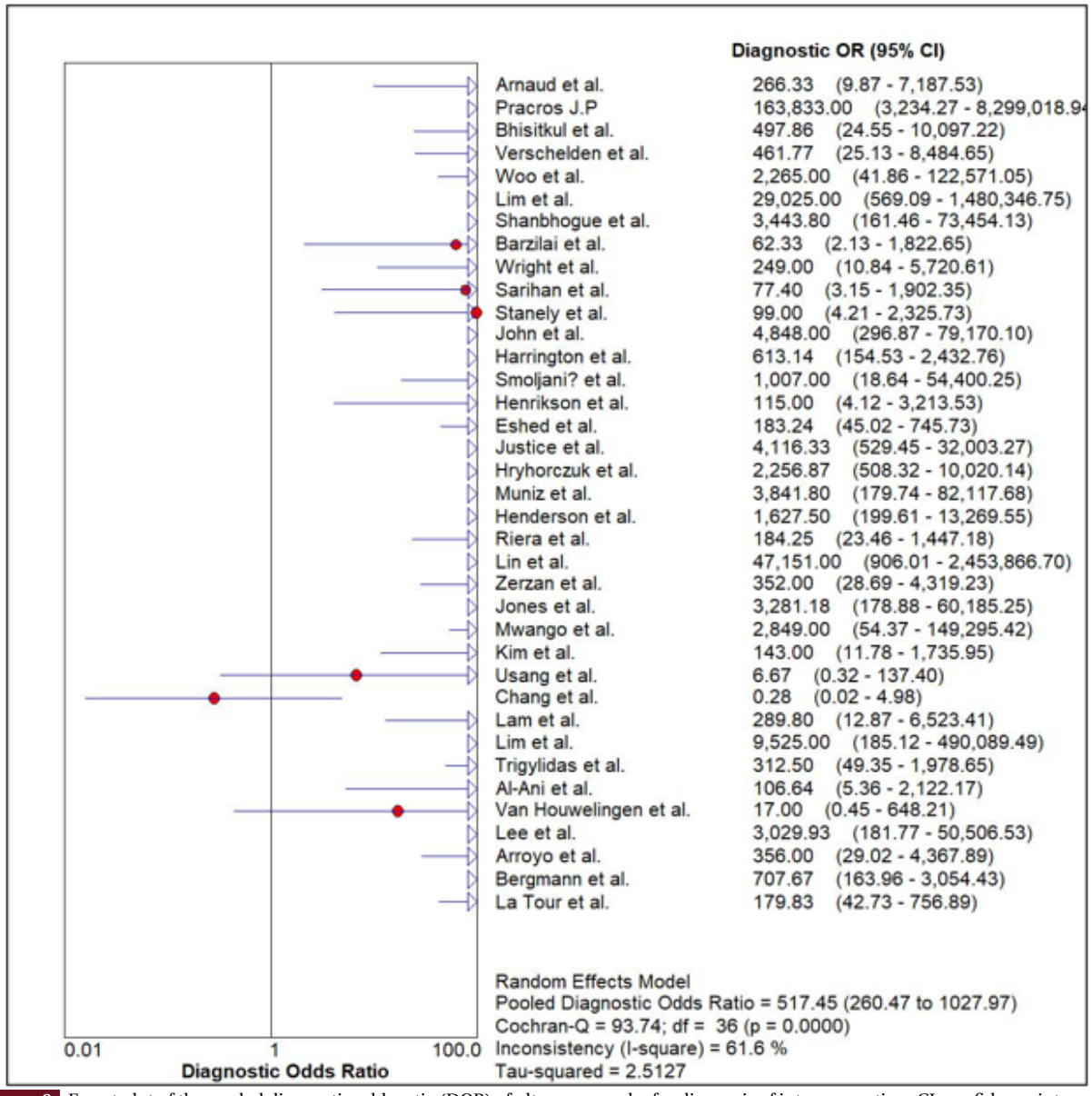

Figure 6: Forest plot of the pooled diagnostic odds ratio (DOR) of ultrasonography for diagnosis of intussusception. CI: confidence interval.

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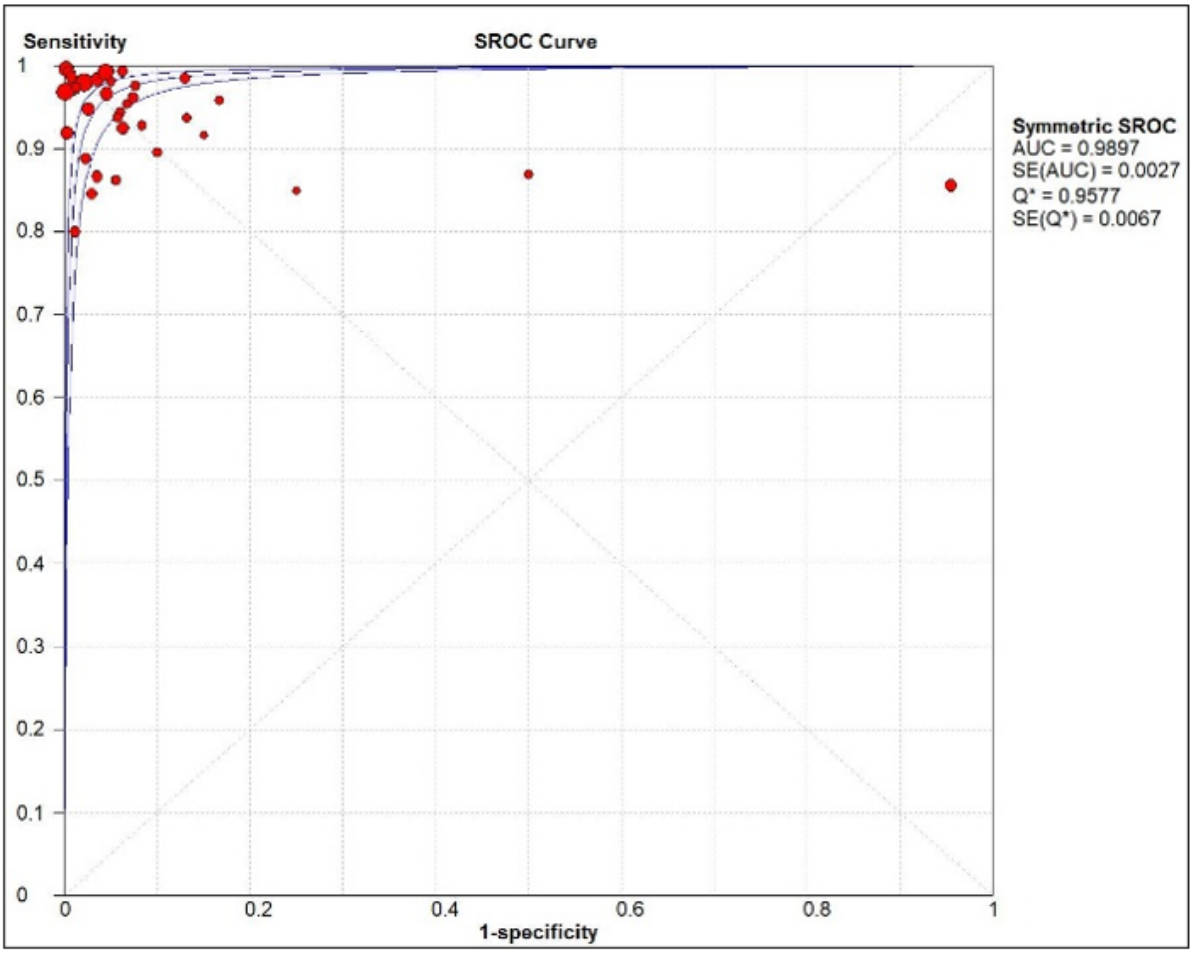

Figure 7: Hierarchical summary receiver-operating characteristic (HSROC) curve indicating accuracy of ultrasonography for diagnosis of intussusception.

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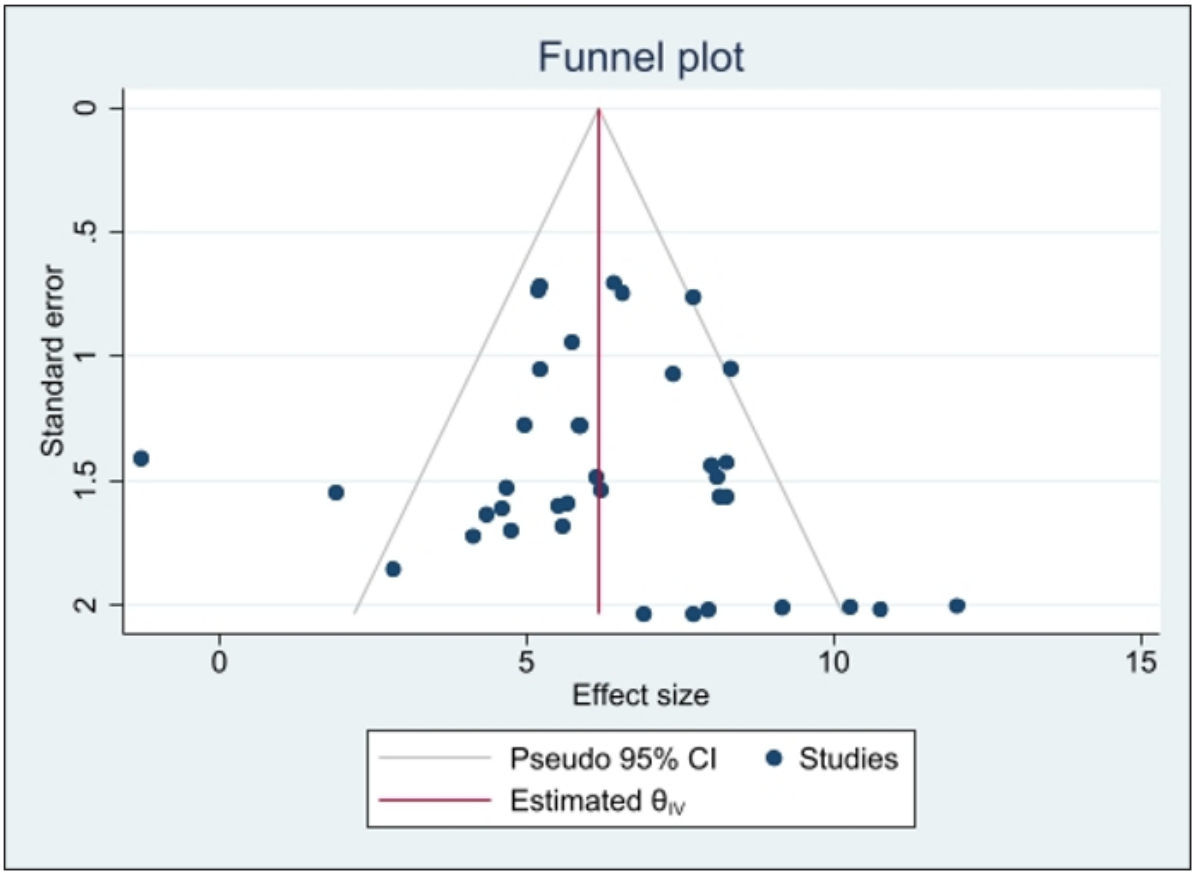

Figure 8: Funnel plot of publication bias on the pooled diagnostic odds ratio (DOR) of ultrasonography.

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