Review

Accuracy of point-of-care ultrasound and radiology-performed ultrasound for intussusception: A systematic review and meta-analysis

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ABSTRACT

Objective: It is unclear whether point-of-care ultrasound (POCUS) by emergency medicine physicians is as accurate as radiology-performed ultrasound (RADUS). We aim to summarize the diagnostic accuracy of ultrasonography for intussusception and to compare the performance between POCUS and RADUS.
Methods: Databases were searched from inception through February 2018 using pre-defined index terms. Peer-reviewed primary studies that investigated the diagnostic accuracy of ultrasound for intussusception in children were included. The study is reported using Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA). Meta-analysis of the diagnostic accuracy of ultrasound for intussusception was conducted using the random-effects bivariate model. Subgroup analysis (POCUS vs RADUS) was also performed. Meta-regression was utilized to determine if the diagnostic accuracy between POCUS and RADUS was significantly different.
Results: Thirty studies ($n = 5249$) were included in the meta-analysis. Ultrasonography for intussusception has a sensitivity: 0.98 (95% CI: 0.96–0.98), specificity: 0.98 (95% CI: 0.95–0.99), positive likelihood ratio: 43.8 (95% CI: 18.0–106.7) and negative likelihood ratio: 0.03 (95% CI: 0.02–0.04), with an area under ROC (AUROC) curve of 0.99 (95% CI: 0.98–1.00). Meta-regression suggested no significant difference in the diagnostic accuracy for intussusception between POCUS and RADUS (AUROC: 0.95 vs 1.00, $p = 0.128$).
Conclusions: Current evidence suggested POCUS has a high diagnostic accuracy for intussusception not significantly different from that of RADUS.

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1. Introduction

Intussusception is a relatively common abdominal emergency in children between 6 and 36 months of age, affecting 26–38 per 100,000 live birth annually [1]. The classic triad of intussusception, including currant jelly stool, colicky abdominal pain and vomiting, is seen in <15% of cases at presentation [2,3]. Diagnosing intussusception can be challenging in children presenting with atypical symptoms and unable to provide a clear history. Traditionally, hydrostatic or pneumatic enema was the gold standard for both diagnostic and therapeutic purposes [4]. However, it is an invasive procedure that exposes children to radiation. Furthermore, it is a procedure performed by radiologists, who may not always be immediately available. Delayed diagnosis and treatment of intussusception can decrease the success rate of reduction and lead to significant morbidity and mortality [5].

Since the 1990s, ultrasonography conducted by radiologists has repeatedly proven to be a reliable and radiation-free method of screening for intussusception due to its high sensitivity (97.9%) and specificity (97.8%) [6,7]. It has become the first-line test to diagnose

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intussusception at many institutions [8]. Additionally, studies have reported that novice sonographers with limited training can perform as well as experienced sonographers [9]. There has a been a growing interest in using point-of-care ultrasound (POCUS) at the bedside to facilitate clinicians making a timely diagnosis in patients who present with suspicion for intussusception. Furthermore, the American College of Emergency Physicians (ACEP) ultrasound guidelines published in 2009 consider POCUS as an adjunct to help emergency physicians diagnose intussusception [10].

It is still unclear whether the diagnostic accuracy of POCUS for intussusception conducted by emergency medicine physicians is comparable with the accuracy of ultrasounds interpreted by radiologists. Current studies investigating the diagnostic accuracy of POCUS for intussusception were limited by their sample size and unstandardized POCUS training. Therefore, it is difficult to conclusively define the role of POCUS for intussusception [11,12]. The sensitivity and specificity reported in these studies are mixed due to non-standardized protocols and heterogeneous study populations. Individual results do not conclusively support the general use of POCUS. The objective of this systematic review and meta-analysis is to perform a quantitative and qualitative evaluation of the diagnostic accuracy of ultrasonography for intussusception, and, more importantly, to compare the diagnostic accuracy of POCUS with RADUS in diagnosing intussusception.

2. Methods

2.1. Data sources and searches

The meta-analysis was performed in accordance with Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) [13,14]. General bibliographic databases (PubMed and EMBASE) were searched from inception through February 2018. MeSH terms from PubMed and Emtree terms from Embase were combined with free text words. The "OR" connector was used for similar concepts; "AND" connector was used to combine concepts. The following search terms were used: "ultrasound" OR "medical sonography" OR "sonography" OR "ultrasonography" OR "echography" OR "echogram" AND "intussusception." The search was limited to human studies and pediatric populations. There was no restriction on publication date, language or country. In addition to the electronic search, reference lists in all known reviews and primary studies were checked manually.

Two authors (YH Wang and YK Ma) independently conducted the study selection and data extraction. A uniformed search strategy was developed through a consensus meeting. Discrepancies between the reviewers were resolved by a consensus meeting initially and using arbitration by a third reviewer (PY Tsou) if consensus could not be reached. Initial evaluation was based on screening of titles and abstracts. At the full-text screening stage, two authors reviewed each article and group consensus was used to resolve conflicts.

2.2. Selection criteria

2.2.1. Types of studies

We included any type of studies investigating the diagnostic accuracy of ultrasonography for intussusception, except for case reports, case series with sample sizes <10, comments, animal studies and studies without original data (e.g., editorials, commentaries, etc.)

2.2.2. Types of participants

We considered eligible studies that enrolled patients <21 years old presenting with symptoms suggestive of intussusception to the emergency department and inpatient settings.

2.2.3. Index test

The index test was ultrasound for intussusception when a patient presented with symptoms suggestive of intussusception. A test was considered positive if signs of intussusception (e.g. target or donut sign on cross-sectional view or pseudokidney or sandwich sign on longitudinal view) were present.

2.2.4. Reference test

Reference test was defined using the sole or combinational use of the following criteria: results of air or barium enema, results of ultrasonography by experienced radiologists, surgical findings, or clinical diagnosis

2.3. Data abstraction and quality assessment

Data were extracted for overall study characteristics, study design, study setting, patient characteristics, sonographer experience, type of ultrasound transducer, patient inclusion criteria, diagnostic criteria of sonography for intussusception, gold standard, and quantitative data required for construction of a 2×2 table. In studies that reported multiple pairs of sensitivity and specificity data, we consistently used the data with the highest Youden index (sensitivity + specificity − 1). We used the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool to assess the methodological quality of the select studies before meta-analyses [15]. That instrument evaluates the risk of bias and the applicability in four domains of the included studies: flow and timing, the objectivity of reference test and index test, and patient selection.

2.4. Quantitative data synthesis

We calculated the pooled sensitivity and specificity, and positive and negative likelihood ratios, along with the respective 95% confidence intervals (CIs) of ultrasound for diagnosing intussusception among children. To understand whether POCUS detects intussusception as well as RADUS, it was decided a priori to stratify studies into POCUS and RADUS groups and compare the diagnostic accuracies between the two groups. Ultrasound performed by sonographic technicians and interpreted by radiologists was also considered as RADUS. Studies that did not specify the training level of US performers ($n = 7$) were not included into the subgroup analyses (i.e. POCUS, RADUS). We used a bivariate model to derive summary effect estimates [16]. When 2×2 tables contained zero cells, we performed continuity correction by adding 0.5 to each cell. We constructed a hierarchical summary receiver operating characteristic (HSROC) curve that plots sensitivity versus specificity and calculated the area under the curve (AUROC) [17]. Fagan plot analyses were conducted using the presumed pre-test probabilities of intussusception of 25%, 50%, and 75%, and the corresponding positive and negative post-test probabilities of intussusception were further calculated. The degree of between-study heterogeneity was calculated using the I^2 test [18]. If I^2 was above 50%, subgroup analyses were conducted to explore the source of heterogeneity. Meta-regression was also conducted to determine if type of sonographer affects the diagnostic accuracy of ultrasound for intussusception (i.e. POCUS versus RADUS). To minimize risk of misclassification bias for not taking into account of studies unclear of US training ($n = 7$) conducted in the era when POCUS was uncommon, a sensitivity analysis was conducted to determine whether the inclusion of studies of unclear type of sonographer ($n = 7$) into the RADUS arm ($n = 16$) affects subgroup analysis for POCUS. Additionally, as part of the sensitivity analysis, we compare the RADUS that included 7 studies unclear of US performers ($n = 23$) against the POCUS group using meta-regression. The presence and effect of publication bias were examined using Deek's test [19]. If publication bias was present, the trim-and-fill method proposed by Duvall and Tweedie would be used to reach an symmetric funnel plot and imputed summary estimate [20]. Galbraith test was used to explore heterogeneity across studies [21]. The statistical analysis was

conducted using the statistical package STATA (Version 12.0, Stata Corp., College Station, TX). Meta-regression and the HSROC plot were made using the R Statistical Software (Foundation for Statistical Computing, Vienna, Austria). All statistical tests were two-sided and statistical significance was defined as a *p*-value < 0.05.

3. Results

3.1. Literature search

The flow of inclusion and exclusion is summarized in Fig. 1. Using our search criteria, we identified 1192 records from PubMed and 1995 records from EMBASE database. After removing 149 duplicated studies and excluding 2771 studies based on pre-defined criteria, a total of 267 articles were retrieved for detailed review. Further, one article was manually added, and 236 studies were excluded due to various reasons detailed in Fig. 1, leaving a total of 30 studies (4 abstracts and 26 full-text articles) for final analysis.

3.2. Study characteristics

The 30 studies included a total of 5249 patients with symptoms suggestive of intussusception. Table 1 details the characteristics of the 30

studies. There were 16 and 14 retrospective and prospective cohort studies, respectively. Thirteen studies were conducted in North America [4,6,7,12,22-30], seven in Europe [31-37], one in Africa [38], and nine in Asia [9,39-46]. Study subjects were mostly children younger than age six. There were seven studies evaluating the accuracy of POCUS conducted by emergency medicine physicians [4,12,22-24,42,45], 16 studies investigating the accuracy of RADUS conducted or interpreted by radiologists [6,7,9,27,29,32,34-36,38-41,43,44,47], and seven studies did not specify the training level of ultrasonographers [25,28,30,31,33,37,46]. Most of the emergency medicine physicians in the POCUS group received a certain level of training, including at least an hour monthly of didactics and one month of scanning training [4,12,45]. Fifteen studies were performed in the ED [4,6,9,12,22-24,28-30,42-45,47], and three in an inpatient setting [31,38,39]. Linear transducers of medium frequencies were most frequently utilized. Donut and target signs on cross-sectional view and pseudokidney and sandwich signs on longitudinal view visualized on sonography were most commonly used to define intussusception. To definitively ascertain intussusception, 11 studies used a combination of clinical judgment and imaging as the reference test [6,9,25,26,28,34,36,39,42,46,47], six studies used imaging studies (e.g. enema, CT scan) alone as the reference test [4,7,29,30,40,45], four studies used ultrasound conducted or interpreted by experienced radiologists as the reference test [12,22-
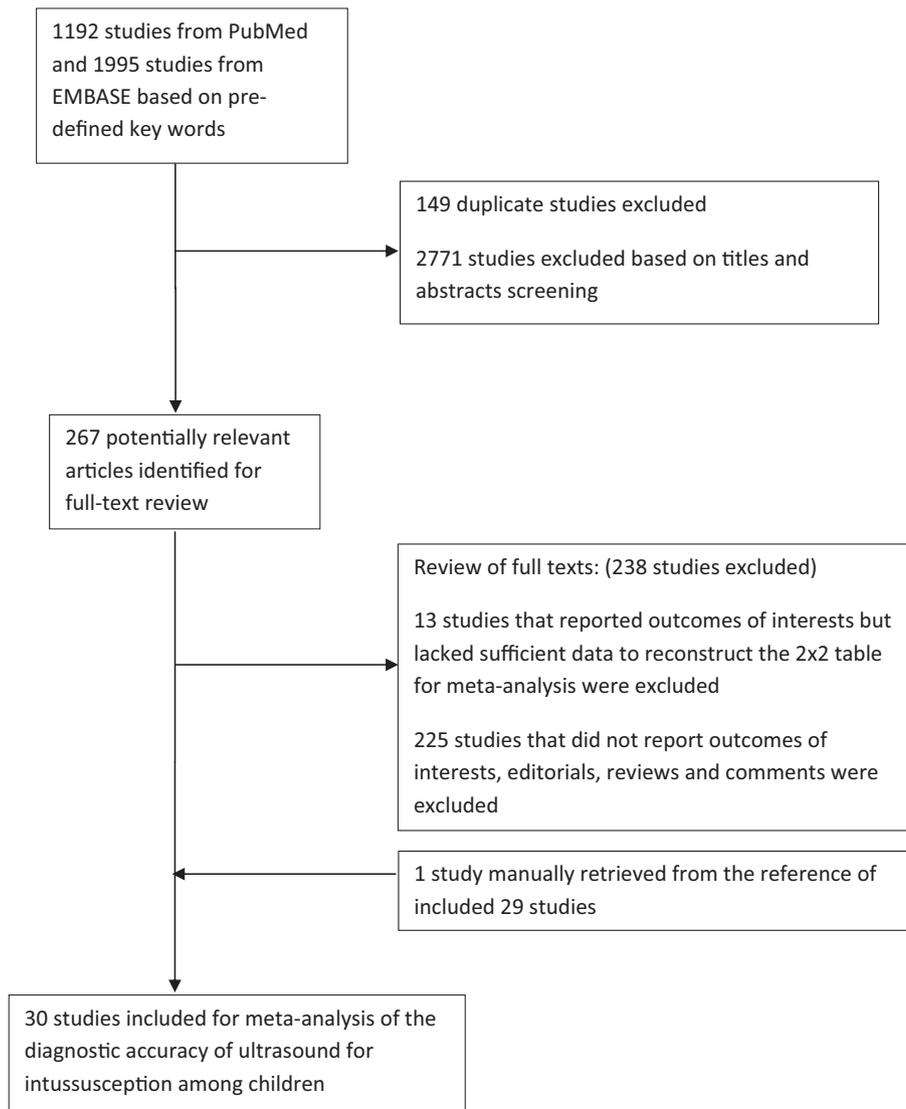


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│ and 1995 studies from         │
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│ 267 potentially relevant      │
│ articles identified for       │
│ full-text review              │
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              │          │ Review of full texts: (238 studies        │
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              │          │ reconstruct the 2x2 table for meta-        │
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│ 30 studies included for meta- │
│ analysis of the diagnostic    │
│ accuracy of ultrasound for    │
│ intussusception among children│
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Fig. 1. PRISMA flow diagram for inclusion of the studies investigating the diagnostic accuracy of ultrasonography for intussusception in pediatric population.

Table 1
Characteristics of included studies and patients eligible for meta-analysis.

Authors	Year	Country	Study design	Age (Mean ± SD), m	N	TP	FP	FN	TN	Prevalence
Eshed et al.	2004	Israel	Retrospective	13.8 (3–42) (mean, range)	151	37	7	3	104	0.26
Henrikson et al.	2003	USA	Prospective	<18 years old	19	11	1	0	7	0.58
John et al.	1998	USA	Retrospective	18 (0.5–84) (mean, range)	151	48	1	1	101	0.32
Harrington et al.	1998	Canada	Prospective	29.2	245	87	7	3	148	0.37
Stanely et al.	1997	Ireland	Prospective	11.4	25	7	2	0	16	0.29
Wright et al.	1996	Australia	Retrospective	0.5–72 (range)	50	7	2	0	41	0.14
Sarihan et al.	1996	Turkey	Prospective	38.8 (3–156) (mean, range)	27	21	0	2	4	0.85
Lim et al.	1994	South Korea	Prospective	<18 years old	176	64	0	0	112	0.36
Shanbhogue et al.	1994	Netherlands	Retrospective	3–60 (range)	163	128	0	2	33	0.80
Verschelden et al.	1992	USA	Prospective	18 (1.5–84) (mean, range)	83	34	6	0	43	0.41
Bhisitkul et al.	1991	USA	Prospective	84 (0.5–60) (mean, range)	65	20	3	0	42	0.31
Henderson et al.	2011	USA	Retrospective	16.1 ± 9.1	286	60	8	1	217	0.21
Riera et al.	2012	USA	Prospective	25 (3–127) (median, range)	82	11	2	2	67	0.16
Lin et al.	2012	Taiwan	Retrospective	72 ± 70	775	15	0	0	760	0.02
Usang et al.	2013	Nigeria	Retrospective	6.0 ± 5.57	25	20	1	3	1	0.92
Lam et al.	2014	USA	Retrospective	31	46	10	2	0	34	0.22
Chang et al.	2013	Taiwan	Retrospective	21 (median)	186	151	10	25	0	0.95
Lim et al.	2015	USA	Retrospective	23.0 ± 12.1	100	37	0	0	63	0.37
van Houwelingen et al.	2018	Germany	Retrospective	29 (median)	10	8	0	1	1	0.90
Hryhorczuk et al.	2009	USA	Retrospective	< 10 years old	812	97	15	2	698	0.12
Justice et al.	2006	Vietnam	Prospective	9.3 (3–24) (median, range)	585	466	1	12	106	0.82
Smoljanić et al.	2000	Serbia	Retrospective	21.4	35	26	0	0	9	0.74
Barzilai et al.	1994	Israel	Retrospective	3–24 (range)	14	5	1	0	8	0.36
Arnaud et al.	1986	France	Retrospective	3–72 (range)	32	8	1	0	23	0.25
Pracros J.P	1987	France	Prospective	0.75–156 (range)	426	145	0	0	281	0.34
Zerzan et al.*	2012	USA	Prospective	3–72 (range)	99	8	2	1	88	0.09
Trigylidas et al.*	2017	USA	Retrospective	22 (2–88) (mean, range)	105	75	2	3	25	0.74
Jones et al.	2012	UK	Retrospective	8 (3–152) (median, range)	197	79	5	0	113	0.40
Muniz et al.*	2010	USA	Prospective	12.3 ± 12.8	198	28	0	2	168	0.15
Wood et al.	1992	South Korea	Prospective	10 (2–48) (mean, range)	82	75	0	0	7	0.91

Abbreviation: SD = standard deviation; m = month; N = sample size; TP = true positive; FP = false positive; FN = false negative; TN = true negative.
* These studies contained abstract only.

24], one used surgical confirmation as the reference test [31], and eight studies used either enema or surgical confirmation as the reference test [27,32,33,35,37,38,41,44]. For studies using combinational methods as the reference test (i.e. gold standard) to ascertain intussusception, the diagnoses of intussusception were definitively made based on findings of enema and surgery for patients with symptoms highly suggestive of intussusception, while clinical judgment and observation were used for those with symptoms less suggestive of intussusception.

3.3. Quality assessment

Quality assessment results of the diagnostic accuracy of the included studies are summarized in Fig. 2. Overall, the methodological quality of the studies was acceptable. Study types included prospective and retrospective cohort studies. The index test and criteria for patient inclusion were well described across studies except for conference abstracts. It is worth noting that many studies used a combination of reference tests as the gold standard for diagnosis of intussusception: patients with symptoms highly suggestive of intussusception would receive enema or surgery for definitive diagnoses, while patients with symptoms less suggestive of intussusception would be clinically observed. Although this is a reasonable clinical practice as this would potentially prevent the children from unnecessary radiation exposure and invasive procedures, this could potentially introduce misclassification bias as intussusception may be undiagnosed in individuals clinically observed.
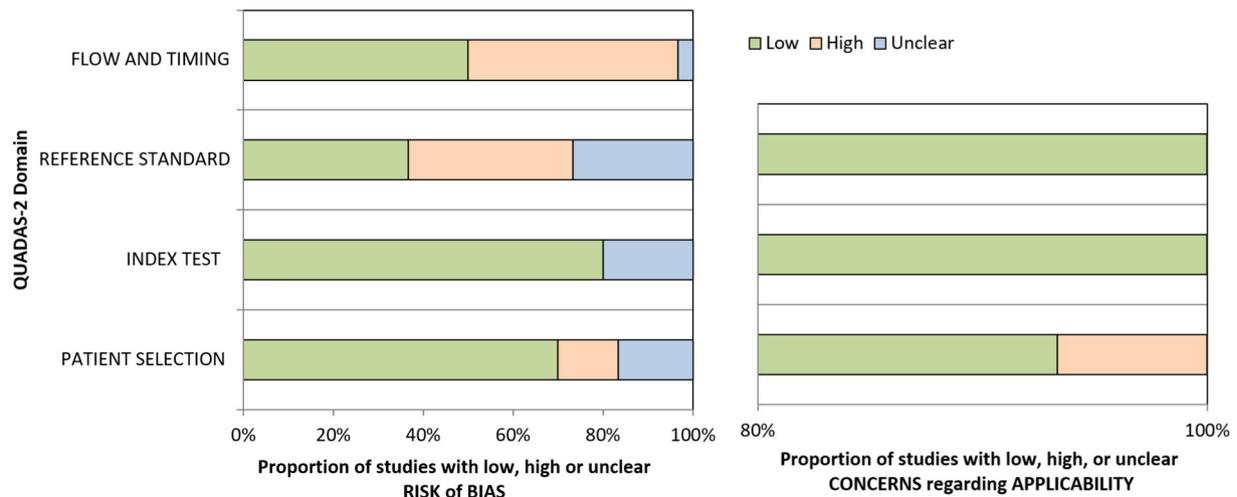

Fig. 2. Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2). Each domain is represented in a bar with the proportion of studies considered high risk, low risk, or unclear.

3.4. Overall meta-analysis of the diagnostic accuracy of ultrasonography for intussusception

Thirty studies evaluated the diagnostic accuracy of ultrasonography for intussusception (Table 2). The pooled sensitivity and specificity were 0.98 (95% CI: 0.96–0.98) and 0.98 (95% CI: 0.95–0.99), respectively. The pooled positive likelihood ratio was 43.8 (95% CI: 18.0–106.7) and the negative likelihood ratio was 0.03 (95% CI: 0.02–0.04). The area under the ROC curve was 0.99 (95% CI: 0.98–1.00), suggesting an excellent discrimination (Table 3, Fig. 3 and Supplemental Fig. 1). High heterogeneity (I^2 = 92%, 95% CI: 86–99) was present across the included studies. After outliers were excluded using Gailbraith test, sensitivity analysis was performed which showed that the heterogeneity across studies decreased (I^2 = 8%; 95% CI, 0 to 100) and that ultrasonography continues to demonstrate excellent diagnostic accuracy in detecting intussusception with an AUROC of 1.00 (95% CI, 0.99 to 1.00). This supports the subgroup analyses to explore sources of heterogeneity. Of note, we also conducted a sensitivity analysis by excluding the study by van Houwelingen et al. given its distinct population (i.e. cancer patients status post surgery), the pooled results (sensitivity = 0.97, specificity = 0.98, AUROC = 0.99) of 29 studies showed the diagnostic accuracies remained similar to the original pooled analysis.

3.5. Subgroup analyses: meta-analysis of the diagnostic accuracy of POCUS and RADUS for intussusception

Subgroup analyses based on type of sonographer (POCUS vs RADUS) were further conducted to assess if it affected the diagnostic accuracy of ultrasound for intussusception. Seven studies evaluating POCUS for intussusception demonstrated a pooled sensitivity and specificity of 0.94 (95% CI: 0.88–0.97) and 0.98 (95% CI: 0.62–1.00), respectively. The pooled positive likelihood ratio was 45.0 (95% CI: 1.7–1209.0) and the negative likelihood ratio was 0.06 (95% CI: 0.03–0.13). The area under the ROC curve was 0.95 (95% CI: 0.94–0.97), suggesting an excellent discrimination. Sixteen studies evaluating RADUS for intussusception revealed a pooled sensitivity and specificity of 0.98 (95% CI: 0.96–0.99) and 0.97 (95%CI: 0.95–0.99), respectively. The pooled positive likelihood ratio was 35.9 (95% CI: 19.6–65.6) and the negative likelihood ratio was 0.02 (95% CI: 0.01–0.04). The area under the ROC curve was 1.00 (95% CI: 0.98–1.00), demonstrating an excellent discrimination. Meta-regression was performed to compare the diagnostic accuracy for intussusception between POCUS and RADUS which suggested no statistic difference between the two groups (Fig. 3, p = 0.128). The sensitivity analysis that includes 7 studies unclear of ultrasonographers into the RADUS arm also showed no significant difference in diagnostic accuracy between POCUS and RADUS ($p > 0.05$).

3.6. Publication bias

Deek's funnel plot asymmetry test was used to explore potential publication bias and suggested significant publication bias ($p < 0.01$). Thus, the trim-and-fill method proposed by Duvall and Tweedie was used, and two missing studies were imputed and added to the left of the funnel plot to make it symmetric. The summary log-transformed diagnostic odds ratio (DOR) went from 6.31 (95% CI, 5.48–7.13) to 6.05 (95% CI, 5.20–6.90) after addition of these missing studies.

3.7. Fagan plot analysis

The Fagan plot analysis suggested that the pre-test probabilities of 25%, 50%, and 75% for intussusception correspond to the positive post-test probabilities of 94%, 98%, and 99%, and the negative post-test probabilities of 1%, 2%, and 7%, respectively (Fig. 4).
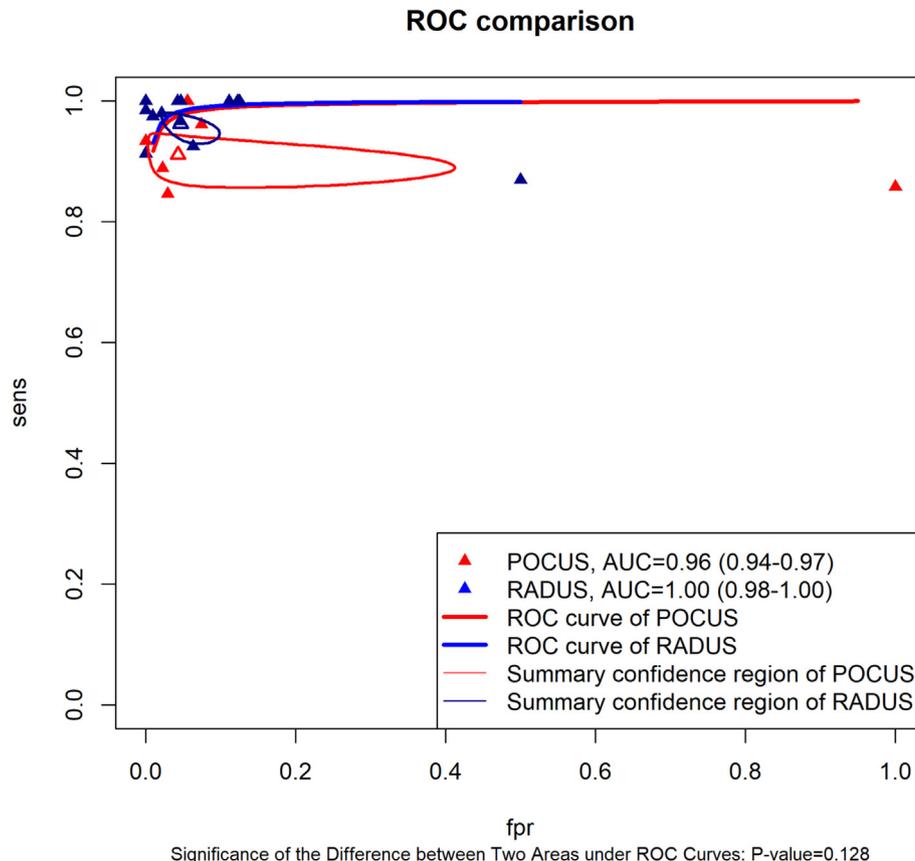
ROC comparison

Significance of the Difference between Two Areas under ROC Curves: P-value=0.128

Fig. 3. Hierarchical summary receiver operating characteristic graph for Point-of-Care Ultrasound (POCUS) and Radiology-performed Ultrasound (RADUS).

Table 2
Summary of the patient inclusion criteria and point-of-care ultrasound diagnostic criteria for intussusception

Authors	US setting	Performers	US brand	Inclusion criteria	Sonographic diagnostic criteria (index test)	Gold standard (reference test)
Eshed et al.	ED	Radiologist	Synergy (Diasonics)	Clinically suspected intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Air enema for US positive or highly suspected cases; follow-up for US negative cases
Henrikson et al.	Unclear	Scan by sonography technicians interpreted radiologist	GE or ATL	Clinically suspected intussusception	Doughnut/target sign (cross-section view)	Air or barium enema ± surgery
John et al.	Unclear	Unclear	Unclear	Clinically suspected intussusception referred to Radiology Department	Doughnut/target sign (cross-section view)	Barium or air enema for US positive or highly suspected cases; follow-up for US negative cases
Harrington et al.	ED	Radiologist	Acuson 128XP10 (Acuson)	Clinically suspected intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Air enema
Stanely et al.	Unclear	Radiologist	Ultramark 4 Scanner (ATL)	Clinically suspected intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Enema ± surgery
Wright et al.	Inpatient	Radiologist	Unclear	Children referred for abdominal sonography with any degree of intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Air enema for US positive cases; follow-up for US negative cases
Sarihan et al.	Unclear	Radiologist	Sonochrome (GE), and RT-X 200 (GE)	Clinically suspected intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Barium enema ± surgery
Lim et al.	ED	Radiologist	UM-9 HDI (ATL)	Clinically suspected intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Air enema or surgery for US positive or highly suspected cases; follow-up for US negative cases
Shanbhogue et al.	Unclear	Radiologist	Octoson (Ousonic) and Aloka	Clinically suspected intussusception with plain abdominal radiographs	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Barium enema for US positive or highly suspected cases; follow-up for US negative cases
Verschelden et al.	Unclear	Radiologist	Unclear	Clinically suspected intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Barium or air enema
Bhisitkul et al.	ED	Unclear	Acuson 128 (Acuson)	Clinically suspected intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Barium enema
Henderson et al.	ED	Unclear	Unclear	Clinically suspected intussusception with 2-view plain abdominal radiographs and abdominal US obtained	Unclear	Enema (air or barium) or surgery for US positive or highly suspected cases; follow-up for US negative cases
Riera et al.	ED	Unexperienced EM physician	Sonsite MicroMaxx (SonoSite)	Clinically suspected intussusception	Doughnut/target sign (cross-section view)	Ultrasonography done by radiologists
Lin et al.	ED	Experienced EM physician	TITAN (Sonosite)	Children (<18 y/o) with acute abdominal pain and abdominal US obtained	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Clinical diagnosis based on patients' presentation, imaging results and pathology findings
Usang et al.	Inpatient	Radiologist	Unclear	Admitted due to clinically suspected intussusception and have abdominal US obtained	Unclear	Barium enema ± surgery
Lam et al.	ED	Unexperienced EM physician	Sonsite M-Turbo (Sonosite)	Children (<18 y/o) suspected with intussusception with abdominal US and a following diagnostic imaging study obtained	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Diagnostic imaging (e.g. barium/air enema, CT, US)
Chang et al.	ED	EM physician	Unclear	Clinically suspected intussusception	Unclear	Air enema
Lim et al.	ED	Radiologist	HDI 3000 or 5000 (Philips)	Clinically suspected intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Air enema for US positive cases; follow-up for US negative cases
van Houwelingen et al.	Inpatient	Unclear	Unclear	Cancer children s/p laparotomy for tumor resection with post-operative intussusception and abdominal US obtained.	Doughnut/target sign (cross-section view), pseudokidney/sandwich sign (longitudinal view), and small-bowel obstruction (multiple loops of dilated fluid- and debris-filled small bowel)	Surgery
Hryhorczuk et al.	mixed	Scan by sonography technicians interpreted radiologist	Unclear	Clinically suspected intussusception	Unclear	Enema (air or barium) or surgery for US positive or highly suspected cases; follow-up for US negative cases

Table 2 (continued)

Authors	US setting	Performers	US brand	Inclusion criteria	Sonographic diagnostic criteria (index test)	Gold standard (reference test)
Justice et al.	ED	Radiologist	Vingmed	Children (<2 y/o) suspected with intussusception	Unclear	Air enema ± surgery
Smoljanić et al.	Unclear	Unclear	Unclear	Clinically suspected intussusception	Unclear	Barium enema ± surgery
Barzilai et al.	Unclear	Unclear	Unclear	Clinically suspected intussusception	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Enema or surgery for US positive or highly suspected cases; follow-up for US negative cases
Arnaud et al.	Unclear	Unclear	Unclear	Clinically suspected intussusception	Doughnut/target sign (cross-section view)	Enema ± surgery
Pracros et al.	Unclear	Radiologist	Unclear	Clinically suspected intussusception	Doughnut/target sign (cross-section view), pseudokidney/sandwich sign (longitudinal view), and continuity between the intussusceptum and the intestinal lumen	Barium enema ± surgery
Zerzan et al.*	ED	Unexperienced EM physician	Unclear	Clinically suspected intussusception	Unclear	POCUS interpreted by radiologists
Trigylidas et al.*	ED	Experienced EM physician	Unclear	Clinically suspected intussusception	unclear	POCUS interpreted by radiologists
Jones et al.*	Unclear	Radiologist	Unclear	Clinically suspected intussusception	Unclear	Air enema and discharge summary
Muniz et al.*	ED	EM physician	SonoSite	Clinically suspected intussusception	Unclear	POCUS interpreted by radiologists
Wood et al.	Unclear	Radiologist	Acuson	Children with clinically suspected intussusception presented during day time	Doughnut/target sign (cross-section view), and pseudokidney/sandwich sign (longitudinal view)	Barium enema

Abbreviation: ED = emergency department; EM = emergency medicine; US = ultrasonography.

* These studies contained abstract only.

4. Discussion

To our knowledge, this is the first meta-analysis that summarizes the diagnostic accuracy of ultrasound for intussusception in children and compares the diagnostic accuracy between POCUS and RADUS. Our findings revealed that ultrasound has excellent sensitivity and specificity in detecting intussusception. Additionally, the meta-regression showed that the diagnostic accuracy of POCUS for intussusception is not significantly different from that of RADUS. Taken together, our findings not only validated the excellent diagnostic accuracy of ultrasound for diagnosing intussusception, but also supported the use of POCUS performed by clinicians at the bedside to diagnose intussusception.

Enema is considered the gold standard for diagnosing and treating intussusception. However, the need for experienced pediatric radiologists and the radiation exposure prevent the universal use of enema as a screening tool for intussusception. Ultrasound provides an effective alternative. Current work summarizes the high diagnostic accuracy of ultrasound for intussusception in general, or respectively as POCUS and RADUS, compatible with prior radiology literature [6,7]. These findings support the increasingly popularity of using bedside ultrasound to assess intussusception and other pediatric abdominal emergencies [48]. However, attention must be drawn to a few studies included in this review where ultrasound demonstrated relatively low diagnostic accuracy for intussusception. Usang et al. showed ultrasonography for intussusception has a sensitivity of 87% and specificity of 50% which differed greatly from radiologic literature [38]. Potential explanations are their unspecified diagnostic criteria for intussusception and the mixed

training level of sonographers. More than 50% of cases were outsourced by sonographers with unknown training in ultrasound in private ultrasound companies. Since ultrasound is highly operator-dependent, the lack of experience would result in misclassification bias, explaining the low sensitivity and specificity in this particular study. Another study by van Houwelingen et al. exclusively enrolled cancer patients post-operatively where patients' symptoms might present atypically. The selective population may partially explain the below average accuracy of ultrasound [31]. A retrospective study conducted by Chang et al. similarly demonstrated a low sensitivity of ultrasonography for intussusception [45]. This study lacked specific patient selection criteria for intussusception and had a high prevalence of intussusception (80%), which suggests a selective population as well. These factors may partially explain the low sensitivity. Taken together, it suggests that the diagnostic accuracy of ultrasonography greatly depends on the operator's experience, settings, and patient populations.

This meta-analysis shows that there is excellent diagnostic accuracy of POCUS for intussusception which does not differ from that of RADUS. Because of the relatively low prevalence of intussusception, and the inadequate numbers of studies investigating the competency of emergency medicine physicians performing POCUS for intussusception, this study helps to summarize the best evidence thus far. Compared with enema, using ultrasound to detect intussusception comes with several advantages, including the ability to diagnose small bowel obstruction and to evaluate alternative causes of a patient's symptoms (e.g. hydronephrosis, appendicitis) [6,49]. Another important merit of POCUS versus RADUS is the reduced time to diagnosis and treatment.

Table 3
Summary of subgroup analysis of the included studies by different study characteristics

Variables	n	Sensitivity (95% CI)	Specificity (95% CI)	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUROC (95% CI)	I^2 (95% CI)
Outcome								
Intussusception	30	0.98 (0.96–0.98)	0.98 (0.95–0.99)	43.8 (18.0–106.7)	0.03 (0.02–0.04)	1732 (530–5663)	0.99 (0.98–1.00)	92 (86–99)
Performers								
POCUS	7	0.94 (0.88–0.97)	0.98 (0.62–1.00)	45.0 (1.7–1209.0)	0.06 (0.03–0.13)	724 (17–30,076)	0.96 (0.94–0.97)	95 (90–99)
RADUS	16	0.98 (0.96–0.99)	0.97 (0.94–0.99)	41.4 (16.8–102.1)	0.02 (0.01–0.05)	2095 (461–9523)	1.00 (0.98–1.00)	0 (0–100)

Abbreviation: n = numbers of studies; PLR = positive likelihood ratio; NLR = negative likelihood ratio; DOR = diagnostic odds ratio; AUROC = area under receiver operating characteristic curve; CI = confidence interval; POCUS: point-of-care ultrasound; RADUS: radiology-performed ultrasonography.
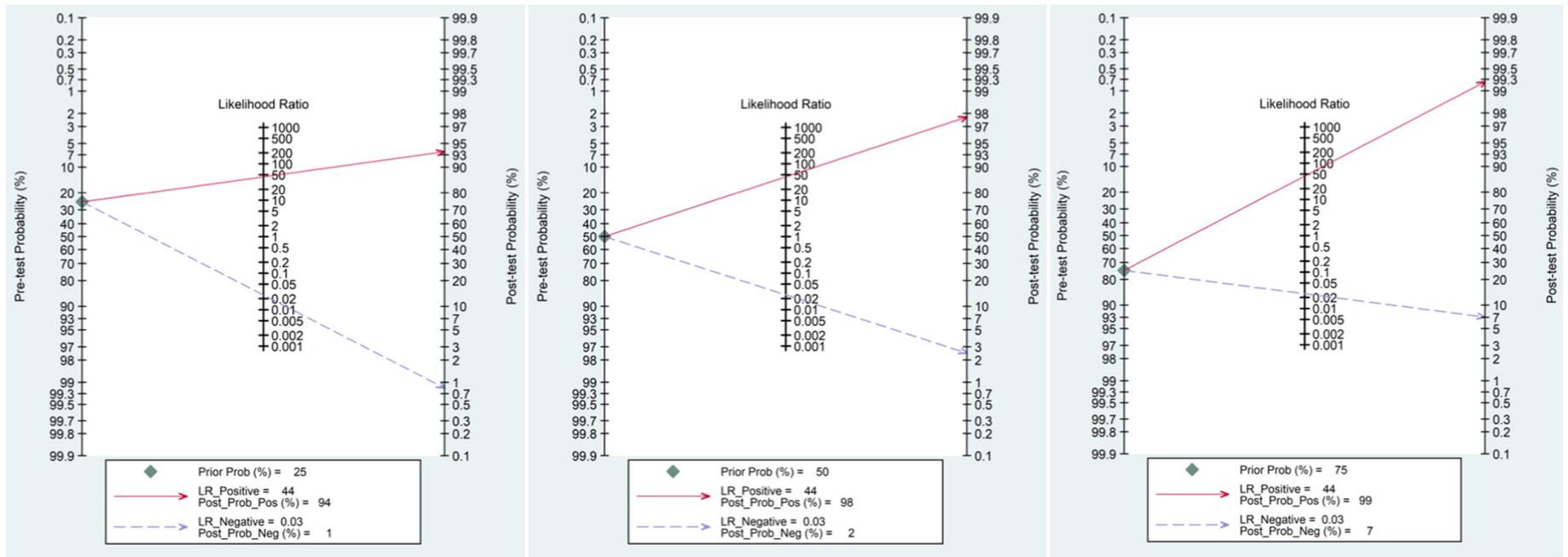
Fig. 4. Fagan's analysis graph for calculating post-test probabilities corresponding to different pre-test probabilities for intussusception.

Earlier diagnosis leads to earlier treatment and subsequently less morbidity. Chang et al. demonstrated that children with intussusception who were diagnosed by the PEM physicians who received POCUS training had significantly shorter time to reduction [45]. This is compatible with a recent study that demonstrates the use of POCUS in ED is associated with shorter length of stay in ED, door-to-reduction time, and ED observation time [43]. Despite these favorable characteristics of POCUS, it is worth noting that RADUS trends toward sensitivity, specificity, diagnostic odds ratio (DOR) and AUROC as compared to POCUS, although the difference is not statistically significant. It is also noted that the confidence interval of the diagnostic accuracies of POCUS group are wider than that of the RADUS counterpart. First, it could result from the relatively small sample size from the POCUS group with only 7 studies. Second, the lack of confidence of novice physicians in performing a new skill, POCUS, might also play a role. Furthermore, it is reasonable that this trend exists as Emergency Medicine physicians receive less training in ultrasonography as compared to radiologists. Among the included studies, the amount of POCUS training that EM physicians received ranged from an hour of didactics to a month of hands-on sonography training [4,12,45]. However, based on the history of sonography development and prior studies, ultrasonography is a skill that could be cultivated with structured training [7,9], and it is expected that the EM physicians will become more experienced in ultrasound in the future.

This study has several limitations. First, a major limitation of this study is the selective use of definitive diagnostic tests (e.g. enema, surgery) among the patients highly suspected of intussusception. This could lead to misclassification bias for underdiagnosing intussusception among the patients who were clinically observed. However, this is a reasonable clinical practice as it limits the use of a study that is both invasive and associated with radiation for children with lower pre-test probability for intussusception. There was also notable selection bias in the retrospective studies where only patients presenting with atypical symptoms who required ultrasonography for confirmation were enrolled. This could partially explain the comparatively lower diagnostic accuracy in the retrospective studies as compared to the prospective studies. Thus, the actual diagnostic accuracy of ultrasound for intussusception should be underestimated. Third, as aforementioned, ultrasound is operator dependent. The diagnostic accuracy of POCUS in the included studies may not be generalizable to all settings. Another limitation includes the variability in interpreting the diagnostic criteria for intussusception, such as target signs, adopted among included studies. For instance, some studies considered the presence of either the target or doughnut signs on cross-sectional view, or the pseudokidney or sandwich signs on longitudinal view as positive for intussusception, while others only used doughnut or target signs alone to diagnose intussusception. Furthermore, the cutoff for the diameter of target signs to determine intussusception was not specified among the included studies, which could contribute to differences in sensitivity and specificity between studies. Lastly, none of the included studies were randomized controlled trials which controls for measurable and unmeasurable confounders. Our conclusion that the diagnostic accuracy of POCUS does not differ from that of RADUS could be confounded by unmeasured factors. Future high-quality randomized controlled trials are needed.

Current evidence suggests ultrasound can reliably diagnose intussusception. Our findings support the excellent diagnostic accuracy of ultrasound for intussusception and further suggest that the diagnostic accuracy of POCUS does not differ from that of RADUS.

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Declaration of Competing Interest

The authors have no conflicts of interest relevant to this article to disclose.

Author contribution

Dr. Tsou, and Dr. Wang conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Ma, Dr. Gillon, Dr. Deanehan, Dr. Chou, Dr. Huang, Dr. Lin and Miss Hsu designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript.

Dr. Lee conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

References

[1] Buettcher M, Baer G, Bonhoeffer J, Schaad UB, Heininger U. Three-year surveillance of intussusception in children in Switzerland. Pediatrics 2007;120(3):473–80.
[2] West KW, Stephens B, Vane DW, Grosfeld JL. Intussusception: current management in infants and children. Surgery 1987;102(4):704–10.
[3] Yamamoto LG, Morita SY, Boychuk RB, et al. Stool appearance in intussusception: assessing the value of the term "currant jelly". Am J Emerg Med 1997;15(3):293–8.
[4] Lam SH, Wise A, Yenter C. Emergency bedside ultrasound for the diagnosis of pediatric intussusception: a retrospective review. World J Emerg Med 2014;5(4):255–8.
[5] Ogundoyin OO, Olulana DI, Lawal TA. Childhood intussusception: impact of delay in presentation in a developing country. Afr J Paediatr Surg 2016;13(4):166–9.
[6] Hryhorczuk AL, Strouse PJ. Validation of US as a first-line diagnostic test for assessment of pediatric ileocolic intussusception. Pediatr Radiol 2009;39(10):1075–9.
[7] Verschelden P, Filiatrault D, Garel L, et al. Intussusception in children: reliability of US in diagnosis—a prospective study. Radiology 1992;184(3):741–4.
[8] Ko HS, Schenk JP, Troger J, Rohrschneider WK. Current radiological management of intussusception in children. Eur Radiol 2007;17(9):2411–21.
[9] Eshed I, Gorenstein A, Serour F, Witzling M. Intussusception in children: can we rely on screening sonography performed by junior residents? Pediatr Radiol 2004;34(2):134–7.
[10] American College of Emergency P. Emergency ultrasound guidelines. Ann Emerg Med 2009;53(4):550–70.
[11] Kairam N, Kaiafis C, Shih R. Diagnosis of pediatric intussusception by an emergency physician-performed bedside ultrasound: a case report. Pediatr Emerg Care 2009;25(3):177–80.
[12] Riera A, Hsiao AL, Langhan ML, Goodman TR, Chen L. Diagnosis of intussusception by physician novice sonographers in the emergency department. Ann Emerg Med 2012;60(3):264–8.
[13] Leeflang MM, Deeks JJ, Gatsonis C, Bossuyt PM, Cochrane Diagnostic Test Accuracy Working Group. Systematic reviews of diagnostic test accuracy. Ann Intern Med 2008;149(12):889–97.
[14] McInnes MDF, Moher D, Thombs BD, et al. Preferred reporting items for a systematic review and meta-analysis of diagnostic test accuracy studies: the PRISMA-DTA statement. JAMA 2018;319(4):388–96.

[15] Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155(8):529–36.

[16] Arends LR, Hamza TH, van Houwelingen JC, Heijenbrok-Kal MH, Hunink MG, Stijnen T. Bivariate random effects meta-analysis of ROC curves. Med Decis Making 2008;28 (5):621–38.

[17] Harbord RM, Whiting P, Sterne JA, et al. An empirical comparison of methods for meta-analysis of diagnostic accuracy showed hierarchical models are necessary. J Clin Epidemiol 2008;61(11):1095–103.

[18] Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327(7414):557–60.

[19] van Enst WA, Ochodo E, Scholten RJ, Hooft L, Leeflang MM. Investigation of publication bias in meta-analyses of diagnostic test accuracy: a meta-epidemiological study. BMC Med Res Methodol 2014;14:70.

[20] Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000;56(2):455–63.

[21] Galbraith RF. Graphical display of estimates having differing standard errors. Technometrics 1988;30(3):271–81.

[22] Zerzan J, Arroyo A, Dickman E, Vazquez H. Diagnosing intussusception by bedside ultrasonography in the pediatric emergency department. Society for Academic Emergency Medicine annual meeting abstracts; 2012. p. s83–4.

[23] Trigylidas TE, Kelly JC, Hegenbarth MA, Kennedy C, Patel L, O'Rourke K. 395 pediatric emergency medicine-performed Point-of-Care Ultrasound (POCUS) for the diagnosis of intussusception. Ann Emerg Med 2017;70(4):S155.

[24] Muniz A. Ultrasound diagnosis of intussusception by emergency physicians. Society for Academic Emergency Medicine annual meeting abstracts; 2010. p. s42.

[25] John SD. The value of ultrasound in children with suspected intussusception. Emerg Radiol 1998;5(5):297–305.

[26] Ja Lim K, Lee K, Yoon DY, et al. The role of US in finding intussusception and alternative diagnosis: a report of 100 pediatric cases. Acta Radiol 2015;56(2):228–33.

[27] Henrikson S, Blane CE, Koujok K, Strouse PJ, DiPietro MA, Goodsitt MM. The effect of screening sonography on the positive rate of enemas for intussusception. Pediatr Radiol 2003;33(3):190–3.

[28] Henderson AA, Anupindi SA, Servaes S, et al. Comparison of 2-view abdominal radiographs with ultrasound in children with suspected intussusception. Pediatr Emerg Care 2013;29(2):145–50.

[29] Harrington L, Connolly B, Hu X, Wesson DE, Babyn P, Schuh S. Ultrasonographic and clinical predictors of intussusception. J Pediatr 1998;132(5):836–9.

[30] Bhisitkul DM, Listernick R, Shkolnik A, et al. Clinical application of ultrasonography in the diagnosis of intussusception. J Pediatr 1992;121(2):182–6.

[31] van Houwelingen LT, Seims AD, Ortega-Laureano L, et al. Use of ultrasound in diagnosing postoperative small-bowel intussusception in pediatric surgical oncology patients: a single-center retrospective review. Pediatr Radiol 2018;48(2):204–9.

[32] Stanley A, Logan H, Bate TW, Nicholson AJ. Ultrasound in the diagnosis and exclusion of intussusception. Ir Med J 1997;90(2):64–5.

[33] Smoljanitsh Z, Zhivitsh G, Krstitsh Z, Milanovitsh D, Vukanitsh D, Lukach R. Intestinal intussusception in children. Ultrasonic diagnosis. Srp Arh Celok Lek 2000;128(7–8):259–61.

[34] Shanbhogue RLK, Hussain SM, Meradji M, Robben SGF, Vernooij JEM, Molenaar JC. Ultrasonography is accurate enough for the diagnosis of intussusception. J Pediatr Surg 1994;29(2):324–8.

[35] Pracros JP, Tran-Minh VA, Morin DFCH, Deffrenne-Pracros P, Louis D, Basset T. Acute intestinal intussusception: ultrasonic diagnosis and air insufflation. Pédiatrie (Marseille) 1990;45(2):109–13.

[36] Jones T, Das I, Au-Yong K, Johnson K. An evaluation of the diagnostic accuracy of ultrasound in the diagnosis of intussusception. J Pediatr Surg 1994;29(2):324–8.

[37] Arnaud O, Weil D, Boscq M, Michel L, Robert M. Value of ultrasonics in the diagnosis of acute intestinal invagination in infants and children. Apropos of a series of 60 cases. Arch Fr Pediatr 1996;43(6):407–8.

[38] Usang U, Inah G, Inyang A, Ekabua A. Intussusception in children: comparison between ultrasound diagnosis and operation findings in a tropical developing country. Afr J Paediatr Surg 2013;10(2):87–90.

[39] Wright JE, Slater S. Suspected intussusception: is ultrasound a reliable diagnostic aid? Aust N Z J Surg 1996;66(10):686–7.

[40] Wood SK, Kim JS, Suh SJ, Paik TW, Choi SO. Childhood intussusception: US-guided hydrostatic reduction. Radiology 1992;182(1):77–80.

[41] Sarihan H, Dinc H, Abes M, Cay A, Serce K. The role of sonography in diagnosis of intussusception. Pediatrik Cerrahi Dergisi 1996;10(1–2):32–5.

[42] Lin WC, Lin CH. Re-appraising the role of sonography in pediatric acute abdominal pain. Iran J Pediatr 2013;23(2):177–82.

[43] Kim JH, Lee JY, Kwon JH, Cho HR, Lee JS, Ryu JM. Point-of-care ultrasound could streamline the emergency department workflow of clinically nonspecific intussusception. Pediatr Emerg Care 2017. https://doi.org/10.1097/PEC.0000000000001283.

[44] Justice FA, de Campo M, Liem NT, Son TN, Ninh TP, Bines JE. Accuracy of ultrasonography for the diagnosis of intussusception in infants in Vietnam. Pediatr Radiol 2007;37(2):195–9.

[45] Chang YJ, Hsia SH, Chao HC. Emergency medicine physicians performed ultrasound for pediatric intussusceptions. Biom J 2013;36(4):175–8.

[46] Barzilai M. Ultrasound in suspected intussusception. Harefuah 1994;127(1–2):5–8, 64.

[47] Lim HK, Bae SH, Lee KH, Seo GS, Yoon GS. Assessment of reducibility of ileocolic intussusception in children: usefulness of color Doppler sonography. Radiology 1994;191(3):781–5.

[48] Marin JR, Abo AM, Arroyo AC, et al. Pediatric emergency medicine point-of-care ultrasound: summary of the evidence. Crit Ultrasound J 2016;8(1):16.

[49] Ko SF, Tiao MM, Hsieh CS, et al. Pediatric small bowel intussusception disease: feasibility of screening for surgery with early computed tomographic evaluation. Surgery 2010;147(4):521–8.