Diagnostic Accuracy of Point-of-Care Ultrasound for Intussusception: A Multicenter, Noninferiority Study of Paired Diagnostic Tests



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Study objective: To determine the diagnostic accuracy of point-of-care ultrasound (POCUS) performed by experienced clinician sonologists compared to radiology-performed ultrasound (RADUS) for detection of clinically important intussusception, defined as intussusception requiring radiographic or surgical reduction.

Methods: We conducted a multicenter, noninferiority, observational study among a convenience sample of children aged 3 months to 6 years treated in tertiary care emergency departments across North and Central America, Europe, and Australia. The primary outcome was diagnostic accuracy of POCUS and RADUS with respect to clinically important intussusception. Sample size was determined using a 4-percentage-point noninferiority margin for the absolute difference in accuracy. Secondary outcomes included agreement between POCUS and RADUS for identification of secondary sonographic findings.

Results: The analysis included 256 children across 17 sites (35 sonologists). Of the 256 children, 58 (22.7%) had clinically important intussusception. POCUS identified 60 (23.4%) children with clinically important intussusception. The diagnostic accuracy of POCUS was 97.7% (95% confidence interval [CI] 94.9% to 99.0%), compared to 99.3% (95% CI 96.8% to 99.9%) for RADUS. The absolute difference between the accuracy of RADUS and that of POCUS was 1.5 percentage points (95% CI -0.6 to 3.6). Sensitivity for POCUS was 96.6% (95% CI 87.2% to 99.1%), and specificity was 98.0% (95% CI 94.7% to 99.2%). Agreement was high between POCUS and RADUS for identification of trapped free fluid (83.3%, n=40/48) and decreased color Doppler signal (95.7%, n=22/23).

Conclusion: Our findings suggest that the diagnostic accuracy of POCUS performed by experienced clinician sonologists may be noninferior to that of RADUS for detection of clinically important intussusception. Given the limitations of convenience sampling and spectrum bias, a larger randomized controlled trial is warranted. [Ann Emerg Med. 2021;78:606-615.]

Please see page 607 for the Editor's Capsule Summary of this article.

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SEE EDITORIAL, P. 616

INTRODUCTION

Background

Intussusception is the most common cause of bowel obstruction among children less than 6 years of age, occurring in 26 to 90 children per 100,000 live births. Abdominal ultrasonography is the initial diagnostic test of choice prior to radiographic or surgical reduction as definitive treatment for ileocolic intussusception. In contrast, small-bowel (ileoileal) intussusception is often

transient and reduces spontaneously without intervention, particularly in younger children. Although the current standard of care is radiology-performed diagnostic ultrasound (RADUS), typically performed by ultrasound technicians and interpreted by radiologists, recently published point-of-care ultrasound (POCUS) guidelines include identification of intussusception as an application for emergency physicians. 11-13

Importance

Few studies have evaluated the use of POCUS by pediatric emergency physicians for the diagnosis of

Editor's Capsule Summary

What is already known on this topic

Recent guidelines suggesting point-of-care ultrasound for the diagnosis of intussusception are based on limited evidence.

What question this study addressed

Is point-of-care ultrasound performed by an expert emergency sonographer inferior to radiology US for the diagnosis of intussusception requiring reduction?

What this study adds to our knowledge

In this 18-center prospective observation study of children 3 months to 3 years being evaluated for intussusception, the accuracy of point-of-care ultrasound was not inferior to radiology ultrasound. Point-of-care ultrasound had a sensitivity of 96.6% (95% CI 87.2 to 99.1) and specificity of 98.0% (95% CI 94.7 to 99.2) for intussusception requiring reduction.

How this is relevant to clinical practice

Point-of-care ultrasound can stratify the risk of intussusception requiring reduction, especially when access to radiology ultrasound is delayed. Larger studies are needed before point-of-care ultrasound can replace radiology ultrasound.

intussusception. ¹⁴⁻¹⁸ One prospective study included only 13 cases of ileocolic intussusception and reported a POCUS sensitivity of 85% (95% confidence interval [CI] 54% to 97%) and specificity of 97% (95% CI 89% to 99%) compared to RADUS. ¹⁵ A more recent study included only 9 cases of intussusception and reported similar test characteristics. ¹⁷ In contrast, the sensitivity and specificity of RADUS are reported to range from 98% to 100% and 88% to 98%, respectively, with respect to barium/air enema or surgical findings. ^{4,19,20} Recent systematic reviews evaluating the diagnostic accuracy of POCUS for identifying intussusception found no significant difference in accuracy between POCUS and RADUS, but the quality of evidence from included studies was limited by small sample sizes, retrospective designs, and inclusion of abstracts. ²¹⁻²³

Goals of This Investigation

To better understand the diagnostic accuracy of POCUS for identifying intussusception, we conducted a multicenter, prospective, noninferiority study comparing the accuracy of paired POCUS and RADUS diagnostic

tests, utilizing experienced clinician sonologists. Our primary aim was to determine whether the diagnostic accuracy of POCUS performed by ultrasound-trained pediatric emergency physician sonologists was noninferior to that of RADUS for the detection of clinically important intussusception, defined as an intussusception requiring radiographic or surgical reduction. Our secondary aims were to determine the agreement between POCUS and RADUS for identification of secondary sonographic findings and to determine the overall frequency of complications.

MATERIALS AND METHODS

Study Design and Setting

We conducted a multicenter, prospective, noninferiority study of paired diagnostic tests across 17 tertiary care pediatric emergency departments (EDs) in North and Central America, Europe, and Australia from October 2018 to December 2020. Twelve sites were universitybased academic medical centers with affiliated children's hospitals, 4 were large community children's hospitals, and one was a large urban academic center with a dedicated pediatric ED. Radiology ultrasound services were available 24 hours a day, 7 days a week at 12 sites; they were available only during daytime hours with technicians called in at night and offsite radiology reads at 5 sites. This study was conducted in accordance with the Standards for Reporting of Diagnostic Accuracy guidelines.²⁴ The institutional review board or ethics committee at each participating site approved this study.

Selection of Participants

Children aged 3 months to 6 years presenting with clinical suspicion for intussusception and RADUS orders were eligible for inclusion. Children with imaging results from referring facilities for whom the sonologist was aware of results were excluded.

Enrollment occurred consecutively when a study sonologist was available to perform POCUS. Children were screened for enrollment by a member of the study team (study sonologist or trained research assistant) who monitored chief complaints, notes within the medical record, or requests for RADUS. If the POCUS study would cause a delay in care, it was performed immediately after RADUS, with the study sonologist remaining blinded to RADUS results.

Methods of Measurement and Data Collection

Thirty-five sonologists participated in enrollment. Study sonologists were pediatric emergency physicians who had

completed an ultrasound fellowship, held a Registered Diagnostic Medical Sonographer designation, or had previously completed at least 20 abdominal POCUS exams with at least 1 positive intussusception study. All study sonologists were required to watch a standardized training video, which reviewed study procedures and our POCUS scanning protocol, including the technique, image acquisition/storage, measurements, and secondary findings (available online at https://www.youtube.com/watch?v=Kgp2epO9LKg&feature=youtu.be).

Our POCUS protocol required use of a linear, highfrequency (5 to 10 MHz, 6 to 15 MHz) transducer. The manufacturers and models of ultrasound machines varied by site. With the patient in a supine position, the sonologist was instructed to move the transducer superiorly from the right lower quadrant to the hepatic flexure, right to left to the splenic flexure, then inferiorly to the left lower quadrant. Sonologists could also scan the midabdominal region at their discretion. At least 2 still images or video clips were obtained in transverse and longitudinal planes in each quadrant, for a total of 8 images/clips. If fewer than 8 images/clips were obtained, we used what was obtained in analysis. If an intussusception was identified, the sonologist captured at least 1 still image in the short axis plane of the intussusception (with a caliper measurement of the maximal intussusception diameter), 1 still image in the longitudinal plane, and 1 still image with color Doppler over the intussusception. Deidentified images were shared with the principal investigator by secure electronic transfer for quality assurance purposes.

Study sonologists recorded the start and end times of POCUS scanning and a confidence rating of their POCUS interpretation (positive or negative) as follows: not at all, somewhat, moderately, very, or completely. If an intussusception was identified, sonologists classified the intussusception as ileoileal or ileocolic; they also identified the presence or absence of trapped free fluid, color Doppler signal, and echogenic foci within the intussusception.

POCUS studies were considered positive for intussusception if at least one of the following criteria occurred: 1) presence of a target-shaped mass ≥2.0 cm in transverse axis diameter or 2) sonologist's clinical judgment that the intussusception would require intervention (ie, determined to be ileocolic by the study sonologist). We chose 2.0 cm as a cutoff because this value lies approximately 1 to 2 standard deviations above the mean for ileoileal intussusceptions and 1 to 2 standard deviations below the mean for ileocolic intussusceptions. ^{8,25-29} Given that some clinically important intussusceptions could be misclassified based on size alone, our definition of a positive POCUS allowed for sonologist clinical judgment. A

negative POCUS study was defined as the absence of a target sign in all 4 quadrants and sonologist judgment that an intussusception was not present. For RADUS studies, the impression of the attending radiologist was the final determination of a positive or negative study.

Study data were collected and managed using a secure online database (REDCap). 30 Study sonologists recorded demographic information, presenting signs and symptoms, and POCUS results. Further data elements, including physical examination findings, RADUS results, enema or surgical care, and disposition, were abstracted from the medical record. Enrolling physicians or research assistants followed up with guardians by telephone interview 7 to 14 days after the index ED visit. Of primary interest was whether the patient sought care at an outside facility within 7 days of the index visit and whether intussusception was identified. Additional information regarding complications was recorded.

Outcome Measures

The primary outcome was whether POCUS and RADUS correctly detected clinically important intussusception. The reference standard for clinically important intussusception was defined as an intussusception that required radiographic (ie, enema) or surgical reduction during or within 7 days of the incident ED visit.

Secondary outcomes included agreement between POCUS and RADUS for identification of secondary sonographic findings, including maximal diameter measurement and presence of trapped free fluid, decreased color Doppler signal, and echogenic foci. Additional outcomes included the frequency of serious complications, defined as peritonitis, bowel perforation, intestinal obstruction, shock, or death.

Sample Size

Sample size was based on the primary comparison of diagnostic accuracy, defined as the proportion of positive outcomes divided by all (positive and negative) outcomes.³¹ Previous investigations suggested that both the sensitivity and specificity of RADUS for the detection of intussusception were 98%.⁴ Based on consensus among study investigators and further consultation with experts in the field, we considered a diagnostic accuracy of 94% for POCUS to be acceptable, compared to 98% for RADUS. Thus, our noninferiority margin was set at 4% a priori. Noninferiority would be demonstrated if the upper limit of the 95% CI for the absolute difference in RADUS and POCUS diagnostic accuracy did not cross the

noninferiority margin. Based on a 2-sample proportion test, assuming RADUS and POCUS accuracy at both 98%, a one-tailed alpha of 2.5%, noninferiority margin of 4%, and 90% power, 258 POCUS tests and 258 RADUS test were required. Thus, we targeted enrollment of 258 children with paired POCUS and RADUS tests. Even though diagnostic tests were paired, this power analysis also assumes independent POCUS and RADUS samples because there was no information on the correlation of tests within patients. Assuming paired POCUS and RADUS tests are positively correlated, this power calculation is conservative in having, at most, a type I error rate of 2.5%. 32,33 Correlation between patients may require a larger sample size; however, we did not have any information on potential correlation (ie, within sonologist correlations).

Primary Data Analysis

The primary analysis was a comparison of the accuracy of POCUS and RADUS tests to detect clinically important intussusception. We report estimates of the absolute differences and 95% CIs using methodology for paired binary outcomes.³² We used generalized linear mixed models to estimate whether POCUS and RADUS tests were correct with respect to clinical intussusception. A logistic regression was used to estimate accuracy, sensitivity, and specificity of POCUS tests, and it included random effects for sonologists to account for potential variation across providers and fixed effects for whether the patient had clinical intussusception. A linear regression model was used to estimate within-pair differences of indicators of whether RADUS and POCUS tests correctly did or did not identify clinical intussusception. The model included random effects for sonologists and fixed effects for the indicator of clinical intussusception, and robust standard errors were used to account for heteroscedasticity. This model was used to estimate the difference between RADUS and POCUS accuracy (ie, primary comparison), sensitivity, and specificity.

POCUS test characteristics were also examined by sonologist confidence, dichotomized as low (not at all, somewhat, moderately) or high (very, completely). Two post hoc sensitivity analyses were performed: one to evaluate the proportion of correct POCUS interpretations among children with and without recent history of intussusception, given that this history may have influenced the sonologists' diligence in evaluating for intussusception; and another to evaluate the diagnostic accuracy, sensitivity, and specificity of POCUS after excluding site B, given the higher proportion of positive cases from this site.

A Bland-Altman plot was used to compare agreement between POCUS and RADUS measurements when both were available. We also report the proportion of children with agreement of POCUS and RADUS findings of trapped free fluid, decreased color Doppler signal, and echogenic foci. Median values for POCUS scanning duration and time from RADUS order to RADUS results are described, as are frequencies of serious complications.

To determine interrater reliability for POCUS images/clips, 2 investigators (VW and ABS) interpreted a random sample of 52 (20%) POCUS studies. Reviewers were blinded to the initial sonologist interpretation and all clinical information, and measurements and color Doppler were removed prior to review. Binary interpretations of "no and/or ileoileal intussusception" versus "ileocolic intussusception" were evaluated using Cohen's kappa, and the ordered interpretations of "no intussusception," "ileoileal intussusception," and "ileocolic intussusception" were evaluated using weighted kappa. All analysis was performed using SAS Enterprise Guide (version 7.12; SAS Institute, Inc., Cary, NC).

RESULTS

Characteristics of Study Subjects

Overall, 262 children were enrolled, of whom 256 were included in the primary analysis (Figure 1). The median age was 21.1 months (interquartile range [IQR] 8.9 to 40.6), and most children presented with concern for abdominal pain (82.8%) or fussiness (80.5%) (Table 1). At least 8 images/clips were available for 243 children (94.9%), and POCUS occurred prior to RADUS in 248 children (96.9%). There were 35 enrolling sonologists (range 1 to 8 per site), 17 of whom completed an emergency ultrasound fellowship (Table E1, available at http://www.annemergmed.com). The median enrollment duration per site was 18 months (IQR 15 to 23), and the median number of intussusception cases per site enrollment duration was 15 (IQR 12 to 19) (Table E1, available at http://www.annemergmed.com).

Main Results

In total, 58 (22.7%) children had cases of clinically important intussusception, of which 55 (21.5%) were treated with radiographic reduction and 16 (6.3%) required surgical reduction (Table 2). Of those treated surgically, 3 (1.2%) proceeded directly to the operating room without radiographic reduction attempt. POCUS identified 60 (23.4%) cases as positive for clinically important intussusception, of which 4 were false positives and 2 were false negatives (Figure 2). Similar results were seen when

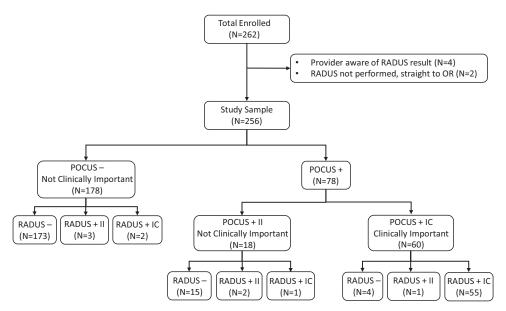


Figure 1. Study flow chart. IC, ileocolic; II, Ileoileal.

comparing RADUS to clinically important intussusception and POCUS to RADUS (Figure 2). Findings associated with false positive and negative POCUS and RADUS examinations are shown in Table E2 (available at http://www.annemergmed.com).

With respect to clinically important intussusception, the diagnostic accuracy of POCUS was 97.7% (95% CI 94.9% to 99.0%), compared to 99.3% (95% CI 96.8% to 99.9%) for RADUS (Table 3). The absolute difference between RADUS and POCUS accuracy was 1.5 percentage points (95% CI - 0.6 to 3.6), with the upper limit of the 95% CI being within the noninferiority margin of 4 percentage points. There was 96.9% agreement between POCUS and RADUS with respect to clinically important intussusception (Cohen's kappa 0.911 [95% CI 0.852 to 0.972]). Among sonologists with high reported confidence, diagnostic accuracy was 98.1% (95% CI 95.2% to 99.3%), compared to 94.4% (95% CI 81.9% to 98.5%) among those with low confidence (difference 3.7%, 95% CI -1.2% to 16.4%) (Table E3, available at http://www. annemergmed.com). In a sensitivity analysis excluding site B, the diagnostic accuracy of POCUS was 97.5% (95% CI 94.2% to 99.0%), sensitivity was 92.9% (95% CI 75.4% to 98.2%), and specificity was 97.9% (95% CI 94.5% to 99.2%).

Although the rates of clinically important intussusception varied by sonologists (Figure 3), this did not manifest in large variation in diagnostic accuracy (Table E4, available at http://www.annemergmed.com), as mixed effects logistic regression suggested low or no variation in accuracy by sonologists (ie, the estimated standard

deviation of sonologist-specific random effects was 0). Site B enrolled a higher proportion of children with intussusception compared to other sites, although this site also had a higher proportion of children transferred to its ED (47% versus 11%; risk difference 37%, 95% CI 21% to 53%; Table E1 [available at http://www.annemergmed.com]) and a higher proportion of children who presented with bloody stools (63% versus 16%; risk difference 47%, 95% CI 30% to 61%), a late finding in intussusception, compared to all other sites. We found no difference in the proportion of children with correct POCUS interpretation when comparing children with a history of intussusception in the previous 14 days (n=12/12, 100.0%) to those without a history (n=237/243, 97.5%; difference 2.5%, 95% CI –5.3% to 21.9%).

Measurements of intussusception for both POCUS and RADUS were available for 26 children. The average difference of RADUS and POCUS measurements (ie, bias) was 0.44 cm (95% CI 0.11 to 0.78), suggesting that RADUS measurements were slightly higher than POCUS measurements (Figure E1, available at http://www. annemergmed.com). There was also an upward linear trend, which was likely driven by 2 outlying RADUS values. Agreement between POCUS and RADUS was 83.3% (95% CI 70.4% to 91.3%; n=40/48) for the presence of trapped free fluid, 95.7% (95% CI 78.1% to 99.9%; n=22/23) for decreased color Doppler signal, and 80.0% (95% CI 44.4% to 97.5%; n=8/10) for the presence of echogenic foci. The median POCUS scanning time was 6 minutes (IQR 4 to 9), and the median time to RADUS results was 65 minutes (40 to 106).

Table 1. Demographic and clinical characteristics.

Characteristic	Total N=256	
Demographics		
Age, months, median (IQR)	21.1 (8.9-40.6)	
Male, n (%)	142 (55.5)	
Race, n (%)		
White	187 (73.1)	
Black	41 (16.0)	
Asian, American Indian, Pacific Islander, Other	23 (9.0)	
Unknown	5 (1.9)	
Ethnicity, n (%)		
Non-Hispanic	172 (67.2)	
Hispanic	79 (30.8)	
Unknown	5 (2.0)	
Presenting Symptoms, n (%)*		
Symptom duration, hours, median (IQR)	24 (8-48)	
Abdominal pain	211 (82.8)	
Fussiness	206 (80.5)	
Colicky abdominal pain	162 (76.8)	
Vomiting	161 (62.9)	
Poor feeding	155 (61.0)	
Legs drawing up	98 (38.4)	
Diarrhea	93 (36.3)	
Fever	68 (26.9)	
Bloody stool	59 (23.1)	
History of intussusception within 14 days, n (%)	12 (4.7)	
History of past abdominal surgeries, n (%)	7 (2.7)	
ED disposition, n (%)		
Home	163 (63.7)	
General floor or observation/short stay	82 (32.0)	
ICU	2 (0.8)	
OR^\dagger	9 (3.5)	

^{*}Vomiting, diarrhea, abdominal pain, legs drawing up, bloody stool (n=255); poor feeding (n=254); fever (n=253); colicky abdominal pain (n=211).

Telephone follow-up data was available for 190 (74.2%) children. Children lost to follow-up were similar in terms of demographics and presence of clinically important intussusception at the index visit (Table E5, available at http://www.annemergmed.com). Fourteen children (7.4%) had an ED return visit within 7 days of discharge. Serious complications occurred in 5 (2.0%) children (Table E6, available at http://www.annemergmed.com). All children with serious complications were correctly identified by POCUS at the index visit.

Interrater reliability was high between 2 study sonologists. For the binary interpretation of POCUS

Table 2. Summary of intussusception diagnosis by POCUS, RADUS, and clinical importance.

Diagnostic		Summary
tool	Characteristic	(N=256)
POCUS	Positive for intussusception	78 (30.5)
	Positive for ileoileal	18 (7.0)
	Positive for ileocolic	60 (23.4)
	Median scan time (IQR), minutes	6 (4-9)
	Mean diameter measure (SD), cm*	2.6 (0.8)
RADUS	Positive for intussusception	64 (25.0)
	Positive for ileoileal	6 (2.3)
	Positive for ileocolic	58 (22.7)
	Median time to results (IQR), minutes	65 (40-106)
	Mean diameter measure (SD), cm*	3.0 (1.0)
Clinical importance	Treated for intussusception	58 (22.7)
	Radiographic reduction	55 (21.5)
	OR reduction	16 (6.3)
	Returned within 7 days with ileocolic intussusception	1 (0.4)

Data are presented as N (%) unless otherwise indicated.

findings, Cohen's kappa was 0.835 (95% CI 0.615 to 1.000), and for the ordered 3-level interpretation, weighted kappa was 0.747 (95% CI 0.518 to 0.976).

LIMITATIONS

Our study is limited by convenience sampling, which is consistent with previous POCUS studies, particularly those conducted in pediatric EDs (where relatively fewer staff members are qualified as clinician sonologists compared to general ED settings). Dedicated POCUS training may overcome this limitation over time. Convenience sampling may have contributed to sampling and spectrum bias. Site

Index tes	t	Reference standard			
		Clinically important		RADUS	
		Yes	No	+	_
POCUS	+	56	4	55	5
	-	2	194	3	193
RADUS	+	57	1		
	-	1	197		

Figure 2. Cross tabulations of POCUS and RADUS results for ileocolic intussusception with respect to reference standards. Clinically important intussusception was defined as intussusception requiring radiographic or surgical reduction.

[†]Total requiring surgical reduction (n=16): status listed as admit to OR, but admitted to general floor thereafter (n=9), status listed as admit to general floor (n=7).

^{*}Available for 74 of 78 children with POCUS study positive and 30 of 64 children with RADUS study positive for intussusception.

Table 3. Test characteristics for POCUS and RADUS diagnosis of intussusception with respect to references standards.

	<u> </u>					
Index test	Reference standard	Measure	Summary (95% CI)			
POCUS	Clinical importance	Accuracy	97.7 (94.9-99.0)			
		Sensitivity	96.6 (87.2-99.1)			
		Specificity	98.0 (94.7-99.2)			
		Positive predictive value	92.3 (78.8-97.5)			
		Negative predictive value	99.1 (96.2-99.8)			
RADUS	Clinical importance	Accuracy	99.3 (96.8-99.9)			
		Sensitivity	98.3 (88.7-99.8)			
		Specificity	99.5 (96.5-99.9)			
		Positive predictive value	98.3 (90.9-99.7)			
		Negative predictive value	99.5 (97.2-99.9)			
POCUS	RADUS	Accuracy	97.0 (94.0-98.6)			
		Sensitivity	94.8 (85.1-98.3)			
		Specificity	97.5 (94.1-99.0)			
		Positive predictive value	89.8 (75.1-96.3)			
		Negative predictive value	98.6 (95.3-99.6)			

B enrolled a much higher proportion of children with intussusception compared to other sites. This may have been driven by the fact that this hospital serves as a national

referral center and had a significantly higher proportion of children transferred to its ED and a higher proportion present with bloody stools compared to other sites, which may have skewed enrollments to include children more likely to have intussusception. Enrollment differences at site B may have also been due to more judicious use of ultrasound and only scanning those with higher pretest probability of intussusception. Conversely, site A had a similar rate of positivity compared to other sites but enrolled 80 (31%) children, suggesting more liberal use of ultrasound at this site. However, our mixed effects logistic regression model suggested low or no variation in diagnostic accuracy across sites, but this may be due to very low variation in the outcome, especially relative to the sample size and number of sites. Another limitation is that sonologists may have completed the POCUS after taking a history and examining the child, which may have influenced how diligently the sonologist evaluated for intussusception. However, this was a practical approach and is similar to how POCUS is used as an adjunct to the physical examination. Additionally, 66 (25.8%) families were unable to be contacted for follow-up, and it is possible they may have revisited a different ED. Lastly, although we enrolled 262 children, our total sample size of 256 was below the target of 258 after we applied exclusion criteria. Thus, our results are slightly underpowered (below 90%).

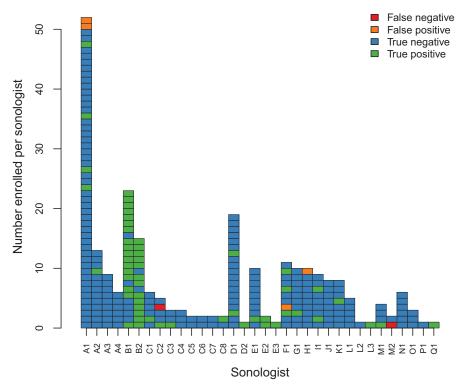


Figure 3. Test characteristics of POCUS for clinically important intussusception by number of children enrolled per site (N=256).

DISCUSSION

In this multicenter, observational study of a convenience sample of children, we showed that the diagnostic accuracy of POCUS for the detection of clinically important intussusception was noninferior to that of RADUS. Interrater reliability for POCUS studies was high, as was agreement between POCUS and RADUS for secondary sonographic findings. Our results suggest that POCUS may have utility as a screening tool for children with suspected intussusception when used by experienced pediatric ED physicians.

Previous retrospective studies have suggested that POCUS has reasonable sensitivity and specificity for detecting intussusception in children. 14,16,18 Chang et al 18 studied 186 children diagnosed with intussusception and reported a sensitivity of 90% among sonologists with focused training versus 79% among sonologists without focused training. This study included novice sonologists with limited training in bowel ultrasonography, which suggests that accurate POCUS diagnosis of intussusception might not require the level of experience of the sonologists that participated in our study. We chose to include only experienced sonologists because this more accurately reflects the current state of POCUS within pediatric EDs, where POCUS users with more training may be more likely to perform POCUS and consult radiology for reduction without RADUS, whereas novice users may be more apt to rely solely on RADUS. In our sample, 2 children with ileocolic intussusception had management decisions based solely on POCUS results. Additional retrospective studies reported POCUS sensitivities ranging from 96% to 100% and specificities from 93% to 94% compared to RADUS. 14,16 While these studies provide preliminary evidence for the use of POCUS as a diagnostic tool for intussusception, they are limited by their retrospective design. This limitation is particularly important, as POCUS studies may be performed but not saved to the medical record.³⁴ Such practice may have led to biased samples that only included children with archived images and those who were more likely to have intussusception.

To date, adoption of POCUS for intussusception has been limited, which is likely attributable to fewer training opportunities in pediatric EDs and the need to involve radiology for positive cases. Two prospective studies have evaluated POCUS use for intussusception in children, reporting a POCUS sensitivity of 85% to 89% and specificity of 97% to 98% compared to RADUS. 15,17 However, these studies included a limited number of children diagnosed with intussusception (n=9 and n=13, respectively). More recently, there have been 3 systematic reviews and meta-analyses focusing on POCUS diagnostic

accuracy for intussusception, which report a pooled sensitivity ranging from 91% to 98% and specificity of 94% to 99%, and one showed no difference in accuracy when comparing POCUS to RADUS using metaregression. However, all 3 systematic reviews were comprised of the 3 available retrospective studies, 1 of the prospective studies, and also various abstracts. Thus, further prospective evaluation is needed.

Our study has several strengths. First, we provide the largest prospective study to date comparing POCUS to RADUS for diagnosing intussusception. Second, our study was conducted across multiple institutions from various geographic regions, which led to inclusion of a diverse study population and may make our results more generalizable. Third, we used a reference standard of clinically important intussusception, which is a pragmatic study outcome. Fourth, we utilized telephone follow-up to track complications. This is important because some physicians may be hesitant to rely solely on POCUS for fear of missing an intussusception and subsequent complication. We show that rates of serious complications are low, which may further allay concerns regarding adoption of POCUS as a screening tool for children with suspected intussusception. Last, we report high agreement between POCUS and RADUS for most secondary sonographic findings. The exception was intussusception measurements by POCUS, which were significantly smaller than those obtained by RADUS. This may have been due to sonologists not measuring the full outer wall thickness and instead measuring the inner fat core.²⁶ Previous investigations showed that the presence of trapped free fluid, decreased color Doppler signal, and intramural echogenic foci on RADUS were associated with failed radiographic reduction. 38-41 Although we did not formally evaluate whether these POCUS findings were predictors of failed radiographic reduction, our findings can be used to inform future research.

Several of our ultrasound findings are worth mentioning. One of the 2 false negative POCUS studies was identified as ileoileal but measured 2.2 cm, and it was ultimately determined to be ileocolic. Hence, POCUS correctly identified an abnormality but misclassified the finding. Of the 4 false positive POCUS studies, one had a RADUS report with thickening of the terminal ileum with an edematous ileocecal valve, and another had a report with enteritis of the terminal ileum. Given these findings, it is possible that an intussusception may have spontaneously reduced prior to RADUS. This is supported by a recent retrospective study of 317 children showing that 11% had spontaneous resolution of

intussusception, most of which reduced between the time of imaging and enema administration. 42

Use of POCUS for evaluation of intussusception has a number of benefits. The presence or absence of intussusception by POCUS may guide the need for transfer from general EDs to children's hospitals specifically for RADUS or pediatric surgical evaluation, thereby preventing unnecessary transfers in children with negative POCUS or expediting transfers among those with positive studies. In our study, 41 children were referred from outside facilities, of whom 19 (38%) had negative intussusception evaluations, presuming there were no other indications for transfer. Further, if POCUS identifies an intussusception, this information may lead to more focused evaluation (ie, less need for abdominal radiograph or laboratory evaluation). Additionally, POCUS may facilitate differentiation of ileoileal and ileocolic intussusception, as suggested by one recent retrospective study of 37 children, of whom 21 had ileoileal intussusception identified by POCUS and only 2 (9.5%) required intervention. POCUS use may also hasten patient throughput in the ED among children with suspected intussusception. After implementation of a protocol recommending POCUS first for suspected intussusception, Kim et al⁴³ showed that ED length of stay decreased by an average of 226 minutes. If a treating provider was to obtain POCUS early in a child's ED visit, reliance on POCUS alone may aid in more rapid diagnosis of intussusception and may facilitate patient throughput in some cases.

In conclusion, we show that the diagnostic accuracy of POCUS, when performed by experienced pediatric ED clinician sonologists, is noninferior to that of RADUS for the detection of clinically important intussusception and that POCUS may be useful as an initial diagnostic test. Future research should evaluate the diagnostic accuracy of POCUS among providers with less POCUS experience in bowel sonography, the utility in general ED settings, and whether POCUS improves ED resource utilization among children with suspected intussusception.

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REFERENCES

- Waseem M, Rosenberg HK. Intussusception. Pediatr Emerg Care. 2008;24:793-800.
- Buettcher M, Baer G, Bonhoeffer J, et al. Three-year surveillance of intussusception in children in Switzerland. Pediatrics. 2007;120:473-480.
- Clark AD, Hasso-Agopsowicz M, Kraus MW, et al. Update on the global epidemiology of intussusception: a systematic review of incidence rates, age distributions and case-fatality ratios among children aged <5 years, before the introduction of rotavirus vaccination. *Int J Epidemiol*. 2019;48:1316-1326.
- Hryhorczuk AL, Strouse PJ. Validation of US as a first-line diagnostic test for assessment of pediatric ileocolic intussusception. *Pediatr Radiol*. 2009;39:1075-1079.
- Daneman A, Navarro O. Intussusception. Part 1: a review of diagnostic approaches. Pediatr Radiol. 2003;33:79-85.
- Daneman A, Navarro O. Intussusception. Part 2: An update on the evolution of management. Pediatr Radiol. 2004;34:97-108 [quiz 187].
- Park BL, Rabiner JE, Tsung JW. Point-of-care ultrasound diagnosis of small bowel-small bowel vs ileocolic intussusception. Am J Emerg Med. 2019;37:1746-1750.
- Wiersma F, Allema JH, Holscher HC. Ileoileal intussusception in children: ultrasonographic differentiation from ileocolic intussusception. *Pediatr Radiol*. 2006;36:1177-1181.
- Doi O, Aoyama K, Hutson JM. Twenty-one cases of small bowel intussusception: the pathophysiology of idiopathic intussusception and the concept of benign small bowel intussusception. *Pediatr Surg Int*. 2004;20:140-143.
- Tiao MM, Wan YL, Ng SH, et al. Sonographic features of small-bowel intussusception in pediatric patients. Acad Emerg Med. 2001;8:368-373.
- American College of Emergency Physicians, Policy Statement.
 Ultrasound guidelines: emergency, point-of-care, and clinical ultrasound guidelines in medicine. 2016. Available at: https://www.acep.org/globalassets/new-pdfs/policy-statements/ultrasound-guidelines—emergency-point-of-care-and-clinical-ultrasound-guidelines-in-medicine.pdf. Accessed June 13, 2021.
- Vieira RL, Hsu D, Nagler J, et al. Pediatric emergency medicine fellow training in ultrasound: consensus educational guidelines. Acad Emerg Med. 2013;20:300-306.
- Marin JR, Lewiss RE; American Academy of Pediatrics Committee on Pediatric Emergency Medicine, et al. Point-of-care ultrasonography by pediatric emergency medicine physicians. *Pediatrics*. 2015;135:e1113-e1122.
- Lam SH, Wise A, Yenter C. Emergency bedside ultrasound for the diagnosis of pediatric intussusception: a retrospective review. World J Emerg Med. 2014;5:255-258.
- Riera A, Hsiao AL, Langhan ML, et al. Diagnosis of intussusception by physician novice sonographers in the emergency department. *Ann Emerg Med*. 2012;60:264-268.
- Trigylidas TE, Hegenbarth MA, Patel L, et al. Pediatric emergency medicine point-of-care ultrasound for the diagnosis of intussusception. J Emerg Med. 2019;57:367-374.
- Arroyo AC, Zerzan J, Vazquez H, et al. Diagnostic accuracy of point-ofcare ultrasound for intussusception performed by pediatric emergency medicine physicians. J Emerg Med. *Published online January*. 2021;19. https://doi.org/10.1016/j.jemermed.2020.11.030.
- Chang YJ, Hsia SH, Chao HC. Emergency medicine physicians performed ultrasound for pediatric intussusceptions. *Biomed J.* 2013;36:175-178.
- Bhisitkul DM, Listernick R, Shkolnik A, et al. Clinical application of ultrasonography in the diagnosis of intussusception. *J Pediatr*. 1992;121:182-186.
- Verschelden P, Filiatrault D, Garel L, et al. Intussusception in children: reliability of US in diagnosis—a prospective study. *Radiology*. 1992;184:741-744.
- 21. Tsou PY, Wang YH, Ma YK, et al. Accuracy of point-of-care ultrasound and radiology-performed ultrasound for intussusception: A systematic review and meta-analysis. *Am J Emerg Med*. 2019;37:1760-1769.

- Hom J, Kaplan C, Fowler S, et al. Evidence-based diagnostic test accuracy of history, physical examination, and imaging for intussusception: a systematic review and meta-analysis. *Pediatr Emerg Care*. Published online September 15, 2020. https://doi.org/ 10.1097/PEC.00000000000002224.
- Lin-Martore M, Kornblith AE, Kohn MA, et al. Diagnostic accuracy of point-of-care ultrasound for intussusception in children presenting to the emergency department: a systematic review and meta-analysis. West J Emerg Med. 2020;21:1008-1016.
- Bossuyt PM, Reitsma JB, Bruns DE, et al. Toward complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Acad Radiol. 2003;10:664-669.
- 25. Kim JH. US features of transient small bowel intussusception in pediatric patients. *Korean J Radiol*. 2004;5:178-184.
- Lioubashevsky N, Hiller N, Rozovsky K, et al. Ileocolic versus smallbowel intussusception in children: can US enable reliable differentiation? *Radiology*. 2013;269:266-271.
- Park NH, Park SI, Park CS, et al. Ultrasonographic findings of small bowel intussusception, focusing on differentiation from ileocolic intussusception. Br J Radiol. 2007;80:798-802.
- Ayaz UY, Dilli A, Ayaz S, et al. Ultrasonographic findings of intussusception in pediatric cases. Med Ultrason. 2011;13:272-276.
- **29.** Ko SF, Lee TY, Ng SH, et al. Small bowel intussusception in symptomatic pediatric patients: experiences with 19 surgically proven cases. *World J Surg.* 2002;26:438-443.
- Harris PA, Taylor R, Thielke R, et al. Research Electronic Data Capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009:42:377-381.
- **31.** Ahn S, Park SH, Lee KH. How to demonstrate similarity by using noninferiority and equivalence statistical testing in radiology research. *Radiology*. 2013;267:328-338.
- 32. Liu JP, Hsueh HM, Hsieh E, et al. Tests for equivalence or non-inferiority for paired binary data. Stat Med. 2002;21:231-245.
- **33.** Connor RJ. Sample size for testing differences in proportions for the paired-sample design. *Biometrics*. 1987;43:207-211.
- 34. Hall MK, Hall J, Gross CP, et al. Use of point-of-care ultrasound in the emergency department: insights from the 2012 Medicare national payment data set. J Ultrasound Med. 2016;35:2467-2474.
- 35. Muniz A. Ultrasound diagnosis of intussusception by emergency physicians. *Acad Emerg Med*. 2010;17:S42.
- Trigylidas TE, Kelly JC, Hegenbarth MA, et al. 395 Pediatric emergency medicine-performed point-of-care ultrasound (POCUS) for the diagnosis of intussusception. *Ann Emerg Med*. 2017;70:S155.
- Zerzan J, Arroyo A, Dickman E, et al. Diagnosing intussusception by bedside ultrasonography in the pediatric emergency department. Acad Emerg Med. 2012;19:S151.
- **38.** He N, Zhang S, Ye X, et al. Risk factors associated with failed sonographically guided saline hydrostatic intussusception reduction in children. *J Ultrasound Med.* 2014;33:1669-1675.
- Khorana J, Singhavejsakul J, Ukarapol N, et al. Prognostic indicators for failed nonsurgical reduction of intussusception. Ther Clin Risk Manag. 2016;12:1231-1237.
- Ntoulia A, Tharakan SJ, Reid JR, et al. Failed intussusception reduction in children: correlation between radiologic, surgical, and pathologic findings. AJR Am J Roentgenol. 2016;207:424-433.
- 41. Stranzinger E, Dipietro MA, Yarram S, et al. Intramural and subserosal echogenic foci on US in large-bowel intussusceptions: prognostic indicator for reducibility? *Pediatr Radiol*. 2009;39:42-46.
- Roben ECZ, Horowitz R. Rate of spontaneous resolution of ideopathic ileocolic intussusception. Academic Journal of Pediatrics & Neonatology. 2018;7:0018-0023.
- 43. Kim JH, Lee JY, Kwon JH, et al. Point-of-care ultrasound could streamline the emergency department workflow of clinically nonspecific intussusception. *Pediatr Emerg Care*. 2020;36:e90-e95.