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Properties of ultrasound-rapid MRI clinical diagnostic pathway in suspected pediatric appendicitis

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Objective: to determine diagnostic accuracy of an US-MRI clinical diagnostic pathway to detect appendicitis in the emergency department (ED).
Study design: prospective cohort study of 624 previously healthy children 4–17 years old undergoing US for suspected appendicitis and clinical re-assessment. Children with non-diagnostic USs and persistent appendicitis concern/conclusive US-reassessment discrepancies underwent ultra-rapid MRI (US-MRI pathway), interpreted as positive, negative or non-diagnostic. Cases with missed appendicitis, negative appendectomies, and CT utilization were considered clinically diagnostically inaccurate. Primary outcome was the proportion of accurate diagnoses of appendicitis/lack thereof by the pathway.
Results: 150/624 (24%) children had appendicitis;255 USs (40.9%) were non-diagnostic. Of 139 US-MRI pathway children (after 117 non-diagnostic and 22 conclusive USs), 137 [98.6%; 95% CI 0.96–1.00] had clinically accurate outcomes (1 CT, 1 negative appendectomy): sensitivity 18/18 [100%], specificity 119/121 [98.3%], positive predictive value 18/20 [90.5%], negative predictive value 119/119 [100%]. MRI imaging accuracy was 134/139 (96.4%); 3 MRIs were non-diagnostic (no appendicitis).
In the overall algorithm, 616/624 [98.7% (0.97–0.99)] patients had accurate outcomes: 147/150 (98.0%) appendicitis cases had confirmatory surgeries (3 CTs) and 469/474 (98.9%) appendicitis-negative children had no surgery/CT.
Conclusion: this study demonstrated high clinical accuracy of the US-rapid-MRI pathway in suspected pediatric appendicitis after non-diagnostic US.

1. Introduction

Appendicitis represents the most common surgical emergency in children [1]. Its diagnosis remains challenging because no single clinical feature, laboratory test or clinical risk score eliminate the need for imaging [2]. Because screening ultrasound (US) frequently fails to visualize the appendix, the American College of Radiology recommends CT in children who have non-diagnostic USs, with MRI as an option in suitable centers [3]. Because CT uses malignancy-inducing radiation, and requires intravenous contrast [4], pediatric CT use has significantly declined in the United States (U.S.) and has been very low in Canada [5,6].

In contrast, MRI use in children increased from 9 to 21/1000 person-years in the U.S., and from 4 to 16/1000 person-years in Ontario between 2000 and 2016 [7]. The advantages of MRI include high soft-tissue resolution, absence of ionizing radiation, and lack of need for contrast [8,9]. Meta-analyses highlight excellent performance of MRI in suspected pediatric appendicitis [10,11], with ultra-rapid protocols demonstrating comparable characteristics [12]. Rapid MRI may be most useful when performed after a non-diagnostic US. [13]

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The majority of pediatric MRI studies performed in this context are limited by retrospective design, [8,9,14-17] lack of focus on MRI as interval imaging [18] and on children with persistent concern about appendicitis after screening US [19,20]. A recent systematic review further highlights that the summary estimates of MRI performance may be biased due to low standards of follow-up [21]. Additionally, non-emergent MRI use in an acute-care setting may be challenged by limited timely access and the need for patient cooperation [22]. To this effect, there is paucity of information about the value of MRI for assessment of clinically suspected appendicitis within the constraints of limited access to non-emergent MRI in busy tertiary pediatric centers [19]. Therefore, the "real-life" clinical diagnostic performance of the MRI in children with suspected appendicitis is not established.

To address this knowledge gap, the primary objective of this prospective tertiary-care pediatric emergency department (ED) study was to determine the clinical diagnostic accuracy of the screening US-ultra-fast MRI pathway in previously healthy children 4–17 years of age with persistent clinical concern about appendicitis following a non-diagnostic screening US or with a discrepancy between a conclusive screening US and clinical re-examination. We hypothesized that the US-MRI pathway would have a 95% probability of being at least as accurate as the previously evaluated serial US pathway [23] (which was 94% accurate), with a 97% clinical diagnostic accuracy and a 95% confidence interval (CI) 94% to 100%. The secondary objective was to determine the performance of the overall study algorithm in all eligible children, and to compare the diagnostic accuracy of this algorithm to that of the serial US pathway [23]. Similar to this pathway, the serial US pathway used an interim US for non-diagnostic screening USs with persistent clinical concern about appendicitis [23]; CT was only used in exceptional cases in both pathways [23].

2. Methods

Study Design, Setting and Population: This was a prospective cohort study evaluating the clinical diagnostic accuracy of the US-MRI pathway in children with persistent clinical concern about appendicitis after a non-diagnostic screening US or those who had conclusive US results with discrepant clinical re-assessment - for example, negative US with a concerning re-examination and vice-versa (Fig. 1). The study was approved by the research ethics board of our institution and a written consent was obtained from all participants.

The study took place from December 2016 through December 2021 at a Canadian tertiary-care pediatric ED with approximately 80,000 annual pediatric ED visits. We assessed a convenience sample of previously healthy children 4 to 17 years old in whom the ED staff/fellow suspected acute appendicitis and ordered a screening US. Because of overnight unavailability of the research team and of MRI for non-emergent purposes, the study proceeded 7 days a week from 7 AM to 11 PM. We excluded children with chronic co-morbidities, those with previous abdominal surgery except for pyloric stenosis, children with neuro-developmental or behavioral problems, unstable cardio-respiratory status, contraindications to MRI imaging (pacemakers, metallic foreign bodies in the eye, aneurysm clips or claustrophobia) and families with inadequate command of the English language.

2.1. Study protocol

Prior to the study, all ED and diagnostic staff physicians/fellows were trained in the study operations and imaging cutoffs to be used in the study. Following eligibility screening and informed consent, trained research assistants documented relevant demographic, clinical, and imaging information. Screening USs were performed by experienced registered sonographers in consultation with staff pediatric radiologists

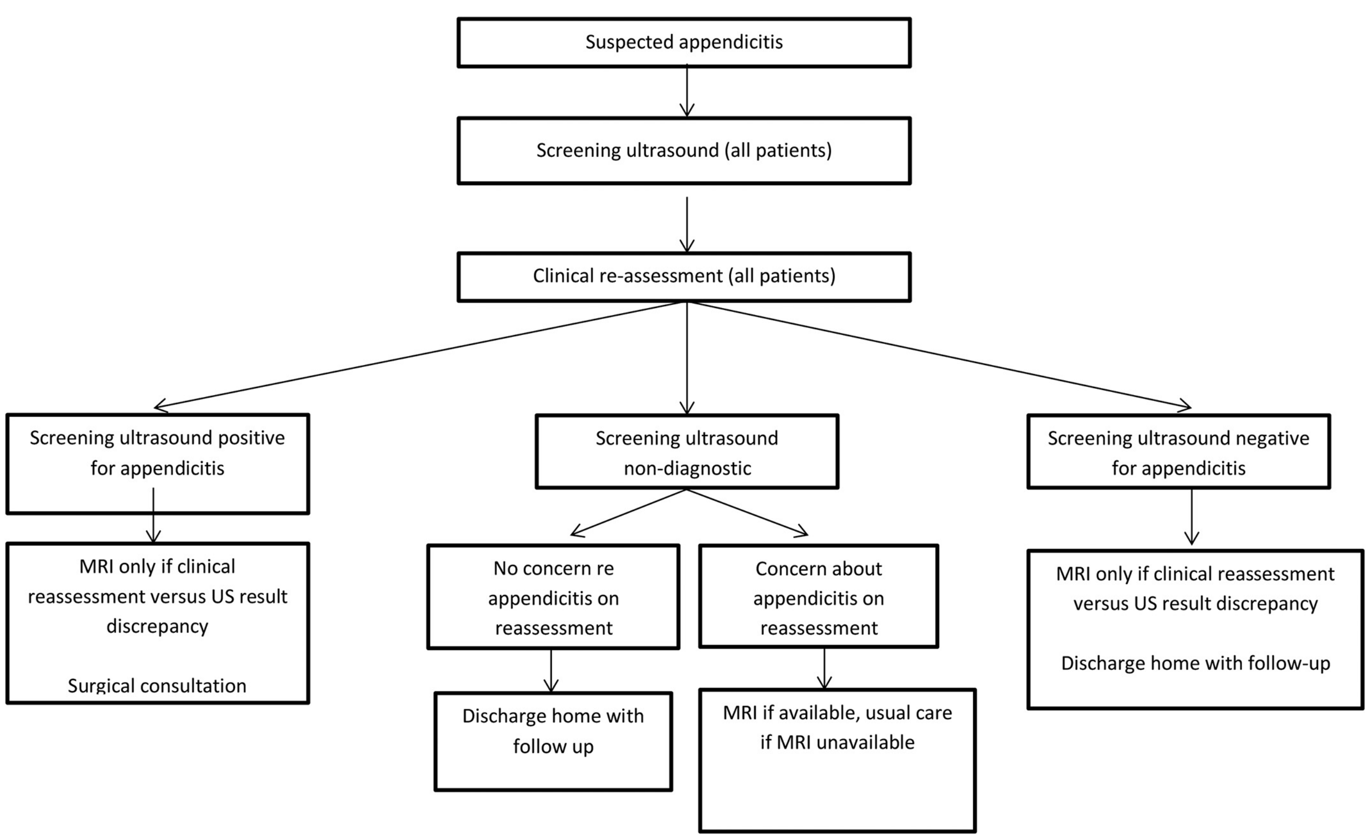

Fig. 1. Ultrasound - MRI Clinical Diagnostic Algorithm.

during the day and by trained diagnostic imaging fellows during weeknights and weekends. Ultrasounds were done using curvilinear (3.5–7-MHz) and high-resolution linear (7- to 14-MHz) array transducers (Aplio TM 500, Toshiba Medical Systems Inc.; LOGIQ, General Electric Healthcare.iU22, Philips Healthcare) to obtain gray-scale and color Doppler scans of the abdomen, with the graded-compression technique and interpreted by staff pediatric radiologists during the day and by staff-supervised trained diagnostic imaging fellows during evenings and weekends, and the results were immediately communicated to the ED staff. The readers knew that appendicitis was the putative diagnosis but were unaware of the clinical details. They classified the US as positive, negative or non-diagnostic for appendicitis, as per the criteria below [24-26].

All study patients had a comprehensive screening abdominal US, to rule out other pathologies. If the ED physician suspected or if the radiologist detected an ovarian problem, a color Doppler of the ovaries was also performed in all menstruating females. Following the screening US, all study children underwent a clinical re-examination by the ED staff physician. Children with negative screening USs and a reassuring clinical re-examination were discharged home, those with positive USs were evaluated by the pediatric surgeons and underwent appendectomy where appropriate. Children with non-diagnostic USs (i.e. those in whom the screening US did not confirm or rule-out appendicitis) and persistent clinical concern about appendicitis and those in whom there was a disagreement between a conclusive US result and clinical reassessment underwent MRI. Children enrolled during the study hours when the MRI was not available underwent interval US, CT or no interval imaging, according to the clinical decision of the treating ED staff physician/pediatric surgeon. These children were counted in the overall study algorithm.

The ultra-rapid, non-sedated and non-contrasted MRI imaging acquisition was preferentially performed on a 3.0 Tesla MRI scanner (Siemens, Erlangen, Germany, MAGNETOM TrioTim Syngo b17) by registered diagnostic imaging technologists. We used an MRI protocol that included non-fat suppressed coronal and axial T2 HASTE, fat suppressed axial T2 HASTE, axial SPAIR and diffusion-weighted (b-values of 0. 50, 100, 400, 800 s/mm2) MRI sequences. MRI interpretation was done by pediatric radiology staff during weekdays, and by trained diagnostic imaging fellows during evenings, nights and weekends, with staff consultation as appropriate. These MRI interpretations were communicated to the ED staff and incorporated into clinical care.

Children with a positive MRI/other interval imaging received a consultation with a pediatric surgeon who decided on further management. Those with negative MRI were discharged home or treated for alternate diagnoses. Children with non-diagnostic MRIs underwent an assessment by a pediatric surgeon. One month later, the study research assistants contacted all patients without surgery to confirm that appendicitis was not diagnosed at this or another institution and reviewed the electronic patient charts for histological findings and for alternate diagnoses.

2.2. Definitions

The final diagnosis of appendicitis was based on the histological evidence of appendicitis at surgery, as interpreted by a staff pediatric pathologist, blinded to the imaging results. No appendicitis meant the pathologist found no evidence of appendicitis, or there was no appendicitis in the children who did not undergo an operation within 1 month of the index visit. Perforated appendicitis was diagnosed on US or MRI by the presence of a peri-appendiceal abscess/phlegmon and confirmed in the operative report.

An US was considered positive in the presence of a noncompressible appendix with a diameter of ≥7 mm and other supportive criteria such as hyperechoic peri-appendiceal fat, loss of echogenic submucosal layer, fluid around the appendix and hyperemia in the appendix on color Doppler, or if there was a peri-appendiceal collection/abscess in the absence of a visualized appendix [24-26]. It was considered negative if a sufficient length of a normal appendix could be visualized. Sufficient length refers to the scenario where the staff radiologist judged that enough of a normal-appearing appendix was visualized to assign a normal diameter measurement. If the appendix was not adequately visualized or had a diameter <7 mm with peri-appendiceal inflammatory signs, had a diameter between 7.0 mm and <10 mm with normal appearance and no inflammatory signs or was for any reason not visualized at all in the absence of peri-appendiceal collections, the result was considered non-diagnostic [27].

The MRI examinations were considered positive if the appendix diameter was >10 mm [27] in the presence of peri-appendiceal inflammation such as peri-appendiceal fluid or fat stranding or if the appendiceal wall thickness was ≥2.5 mm [15,28]. MRI was negative if the normal-appearing appendix was <10 mm [27,29] or was not seen in the absence of peri-appendiceal inflammation. It was considered non-diagnostic if the appendix was not seen but the above secondary signs were present or if the appendix appeared normal but its diameter exceeded 10 mm [27,29].

2.2.1. Pathway definition and accuracy

The US-MRI pathway included the children who underwent interval MRI. In contrast, the overall US-MRI management algorithm included all study children, irrespective of the screening US result or MRI performance. We considered patients to have a clinically diagnostically accurate result if they did not have a CT and underwent surgery at the index hospital visit (irrespective of the imaging result) and had confirmed appendicitis managed with appendectomy or antibiotics with image-guided abscess drainage as needed, or if they were discharged home without surgery and did not have appendicitis diagnosed at any institution at the 1-month telephone follow-up. We considered all other outcomes as diagnostically inaccurate, including children with no evidence of appendicitis at surgery and those who returned with missed appendicitis.

2.2.2. Ultrasound and MRI accuracy

These were determined by agreement between the final diagnosis of appendicitis and imaging interpretation. A non-diagnostic image in a child with appendicitis was considered a false-negative result; a non-diagnostic image in a child without appendicitis was deemed a false-positive result.

2.2.3. Outcome measures

We classified the patients according to 1) presence or absence of appendicitis, and 2) diagnostically accurate versus inaccurate clinical outcome by the US-MRI pathway and by the overall algorithm. The primary outcome was the proportion of children with an accurate clinical diagnosis of appendicitis/lack thereof by the US-MRI pathway, defined as the clinically accurate cases divided by the total number of cases on the pathway. Secondary outcomes included a) the proportion of children on the overall algorithm who had a diagnostically accurate result, b) sensitivity, specificity, positive and negative predictive value and positive and negative likelihood ratio of the US-MRI pathway and of the overall algorithm, and c) diagnostically accurate interval imaging by MRI.

2.2.4. Data analysis

The sample size calculation was based on the 95% confidence interval (CI) around the proportion of children with a clinically diagnostically accurate US-MRI pathway result. A sample size of 136 patients with MRI produces a 95% CI 94% -100% around a proportion of diagnostically accurate pathway cases of 97%. This lower-bound 95% CI of 94% is equal to the previously established benchmark proportion of diagnostically accurate cases by a previously evaluated serial US diagnostic pathway [23].

The primary analysis consisted of the determination of the 95% CI around the proportion of diagnostically accurate cases on the US-MRI pathway. As secondary analyses, the relevant 95% CIs around the sensitivity, specificity, positive and negative predictive values of the MRI-US pathway and the overall management algorithm were also calculated. The differences in the proportions of the categorical variables in the participants with and without appendicitis were compared using the chi-square test. Student's t-test was used to assess the differences between normally distributed continuous variables. The chi-square test was used to assess the difference in the clinical accuracy between the overall algorithm and the serial US pathway [23]. A two-tailed p-value of <0.05 was used to denote statistical significance.

3. Results

3.1. Study population

Of the 2775 children with US for suspected appendicitis during the study period, 1375 presented when the research assistants were off duty and 1400 were screened. Of these, 776 were excluded for exclusion criteria, lack of research staff and refusal to participate (Fig. 2) and 624 children were enrolled. The non-approached population had a comparable rate of appendicitis to the enrolled cohort: 371/1375 (27.0%) vs. 150/624 (24.0%).

Of the 624 study patients, 150 (24.0%) had appendicitis confirmed by surgery and histopathology, and 32/150 (21.3%) had pathology-proven perforated appendicitis: 145 (96.7%) children underwent primary appendectomy with or without surgical drainage and 5 (3.3%) underwent interval appendectomy. Of the 474 children without appendicitis, 95 (20.0%) had alternate diagnoses mimicking appendicitis. The clinical and demographic characteristics of the participating children are summarized in Table 1. The follow-up rate of the non-operated children at 1 month was 100%.

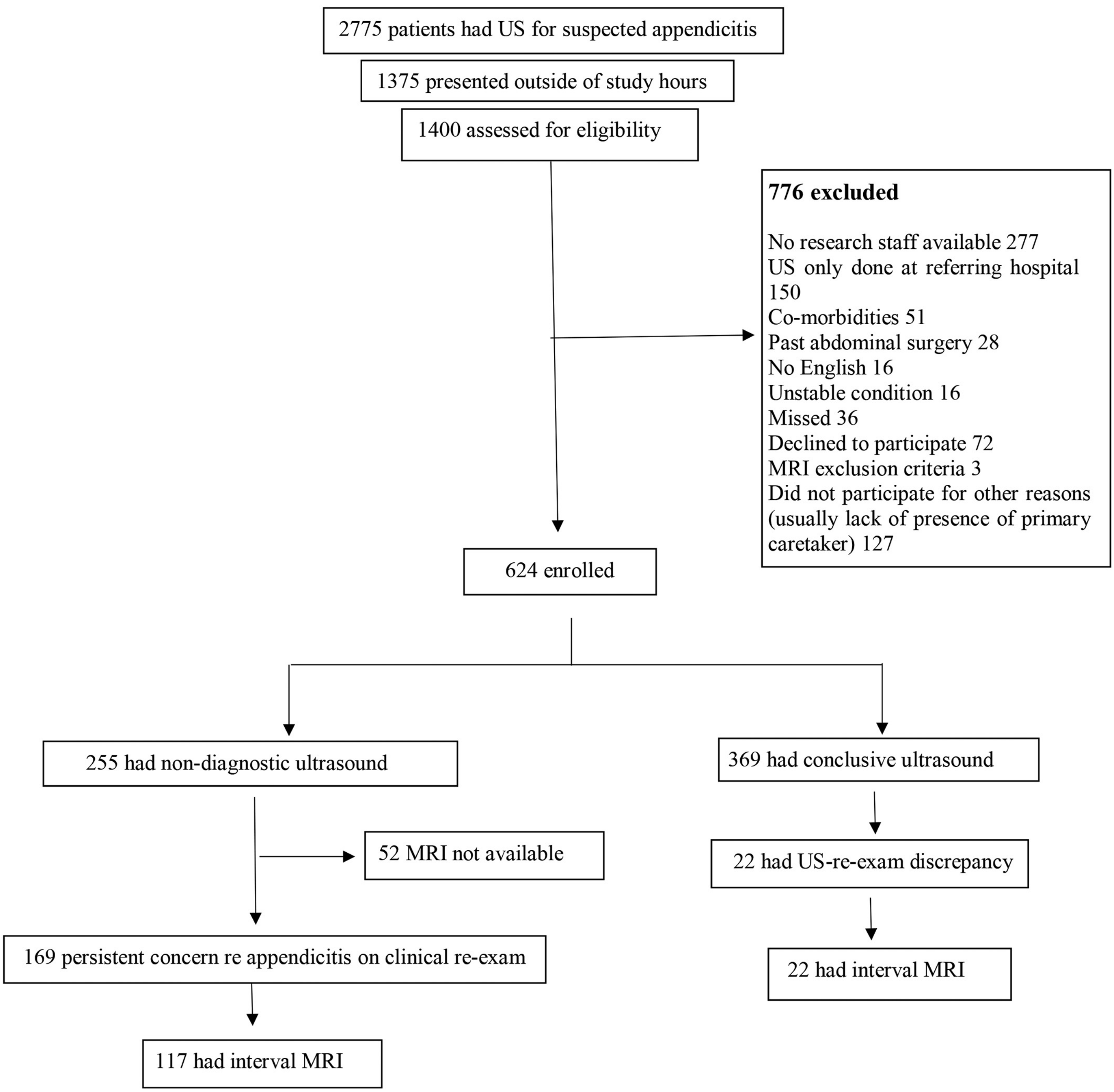

Fig. 2. Enrollment in the study.

3.2. Conclusive screening ultrasound

The imaging accuracy of the screening US was 351/624 (56.3%, 95% CI 0.52–0.60) [Table 2]. The screening US had sensitivity79.3% (0.72–0.85), specificity 48.9% (0.45–0.54), positive predictive value 88.8% (0.82–0.93) and negative predictive value 98.7% (0.96–0.99). Of the 134 children with positive US results, 18 (13.4%) also underwent MRI because of the discrepancy between US results and clinical re-assessment: 7 (38.9%) MRIs confirmed appendicitis and 11 (61.1%) MRIs ruled appendicitis out in the 15 false positive US interpretations (73.3%). Because of concerning clinical re-assessment, 4/235 (1.7%) children with negative US interpretations also underwent MRI interrogation; all were negative for appendicitis. All 3 children with false negative screening US readings had their appendicitis diagnosis established after a clinical re-assessment in the ED and pathologically thereafter.

Based on these results and surgical consultations, 123 patients with conclusive screening US examinations were treated for appendicitis: 96 (78.0%) underwent simple appendectomy with positive pathology, 26 (21.2%) were managed with abscess drainage, antibiotics and appendectomy (4 interval appendectomies), and 1 (0.8%) child with false positive US, negative MRI and concerning symptoms underwent appendectomy but had no evidence of appendicitis at pathology (false positive clinical result). None of the 246 children without treatment for appendicitis had appendicitis. Therefore, 368/369 children (99.7%) with conclusive US results had a clinically accurate result.

3.3. Imaging accuracy of MRI

A total of 255/624 (40.9%) children had a non-diagnostic screening US result; 28/255 (11.0%) had appendicitis. In the 117 patients with non-diagnostic screening USs and MRI, MRI accurately identified appendicitis in 100% cases, ruled out appendicitis in 96.2% negative cases and 2.6% MRIs were non-diagnostic (Table 2) due to normal-sized appendix with peri-appendiceal inflammatory fluid in two children and fat stranding in another child. A total of 86/117 children (73.5%) had a non-visualized appendix with no right lower quadrant inflammatory signs on the screening US; 7 of these 86 patients (8.1%) had appendicitis accurately identified by MRI, MRI ruled appendicitis out in 77/79 children without appendicitis and 2 MRIs in this group were non-diagnostic.

The imaging accuracy of MRI after non-diagnostic USs was 96.6% (95% CI 0.92–0.99), with sensitivity 100% (0.76–1.00), specificity 96.2% (0.91–0.99), positive predictive value 92.3% (0.64–1.00) and negative predictive value 100% (0.97–1.00)-Table 2.

A total of 139 children underwent MRI: 117 (84.2%) after non-diagnostic US and 22 (15.8%) after conclusive US (US-MRI pathway). The imaging accuracy of MRI in the US-MRI pathway was 96.4% (0.93–0.99), with sensitivity 100% (0.82–1.00), specificity 95.9% (0.92–0.99), positive predictive value 90.0% (0.70–0.97) and negative predictive value 100% (0.97–1.00), Table 2. None of the children with negative or non-diagnostic MRIs had appendicitis.

Table 1
Characteristics of patients with and without appendicitis.

	Appendicitis $N = 150$	No Appendicitis $N = 474$	Difference (95% CI) *P* value for difference
Age in years (mean ± SD)	10.03 ± 3.19	10.03 ± 3.63	0.00(−0.65 to 0.65) 1.00
Sex (% male)	88 (58.7)	222 (46.8)	OR 1.61(1.11 to 2.34) 0.012
Duration of abdominal pain in hours (mean ± SD)	33.35 ± 24.96	44.60 ± 41.15	11.25 (4.28 to 18.22) 0.002
PAS score (mean ± SD)	6.1 ± 2.0	4.3 ± 1.6	−1.80 (−2.12 to −1.48) <0.0001

SD = standard deviation.
CI = confidence interval.
PAS = pediatric appendicitis score.
OR = odds ratio.

Table 2
Imaging Performance of Screening Ultrasound and Interval MRI.

Screening US	Appendicitis	No Appendicitis	Total
Positive	119	15	134
Non-Diagnostic	28	227	255
Negative	3	232	235
Total	150	474	624
Interval MRI post Non-Diagnostic US	**Appendicitis**	**No Appendicitis**	**Total**
Positive	12	1	13
Non-Diagnostic	0	3	3
Negative	0	101	101
Total	12	105	117
Interval MRI in US-MRI Pathway	**Appendicitis**	**No Appendicitis**	**Total**
Positive	18	2	20
Non-Diagnostic	0	3	3
Negative	0	116	116
Total	18	121	139

US: ultrasound.
MRI: Magnetic Resonance Imaging.

3.4. Clinical accuracy of the US-MRI pathway

After clinical re-assessment, concern about appendicitis abated in 86/255 (33.7%) patients with non-diagnostic screening USs and persisted in 169 (66.3%) (Fig. 2). In this latter group, 117/169 (69.2%) children underwent interval MRI. The reasons for lack of an MRI examination were non-feasibility of study coverage in 49 (94.2%) patients, and behavioral issues in 3 (5.8%). The median time to MRI was 4.5 h. All patients tolerated the procedure well.

A total of 116/117 (99.1%) children who underwent an MRI examination after a non-diagnostic US had an accurate clinical outcome without a CT: 10 (8.5%) had pathology-confirmed appendicitis at surgery, 2 (1.7%) had perforated appendicitis managed with surgical drainage and antibiotics, 104 (88.9%) were discharged home without surgery and had no appendicitis at follow-up, and 1 (0.9%) child with a non-diagnostic MRI had a CT prior to discharge to confirm lack of appendicitis (Fig.3). The clinical accuracy of the US/MRI pathway after a non-diagnostic US was 116/117 or 99.1% (95% CI 0.95–1.00).

Of the 139 study children on the US-MRI pathway, 137 (98.6%, 0.96–1.00) had a clinically accurate outcome (inaccurate results: one CT and one negative appendectomy), with sensitivity 100% (0.82–1.00), specificity 98.3% (0.94–0.99), positive predictive value 90.5% (0.78–1.00) and negative predictive value 100% (0.97–1.00), positive likelihood ratio 60.5 (15.3–239.2) and negative likelihood ratio of zero.

3.5. Clinical accuracy of the overall US-MRI algorithm

In the overall algorithm, 616/624 (98.7%) patients had a clinically accurate outcome without a CT scan: 147/150 (98.0%) children with appendicitis had pathology-confirmed appendicitis (3 had a CT) and 469/474 (98.9%) children without appendicitis were discharged home without surgery (1 child with a positive screening US had appendectomy without evidence of appendicitis and 4 had a CT). No study patient was diagnosed with appendicitis after discharge home from the index ED visit.

The clinical accuracy of the overall algorithm was 98.7% (0.97–0.99, $N = 616/624$), with sensitivity 98.0% (0.94–0.99, $N = 147/150$),

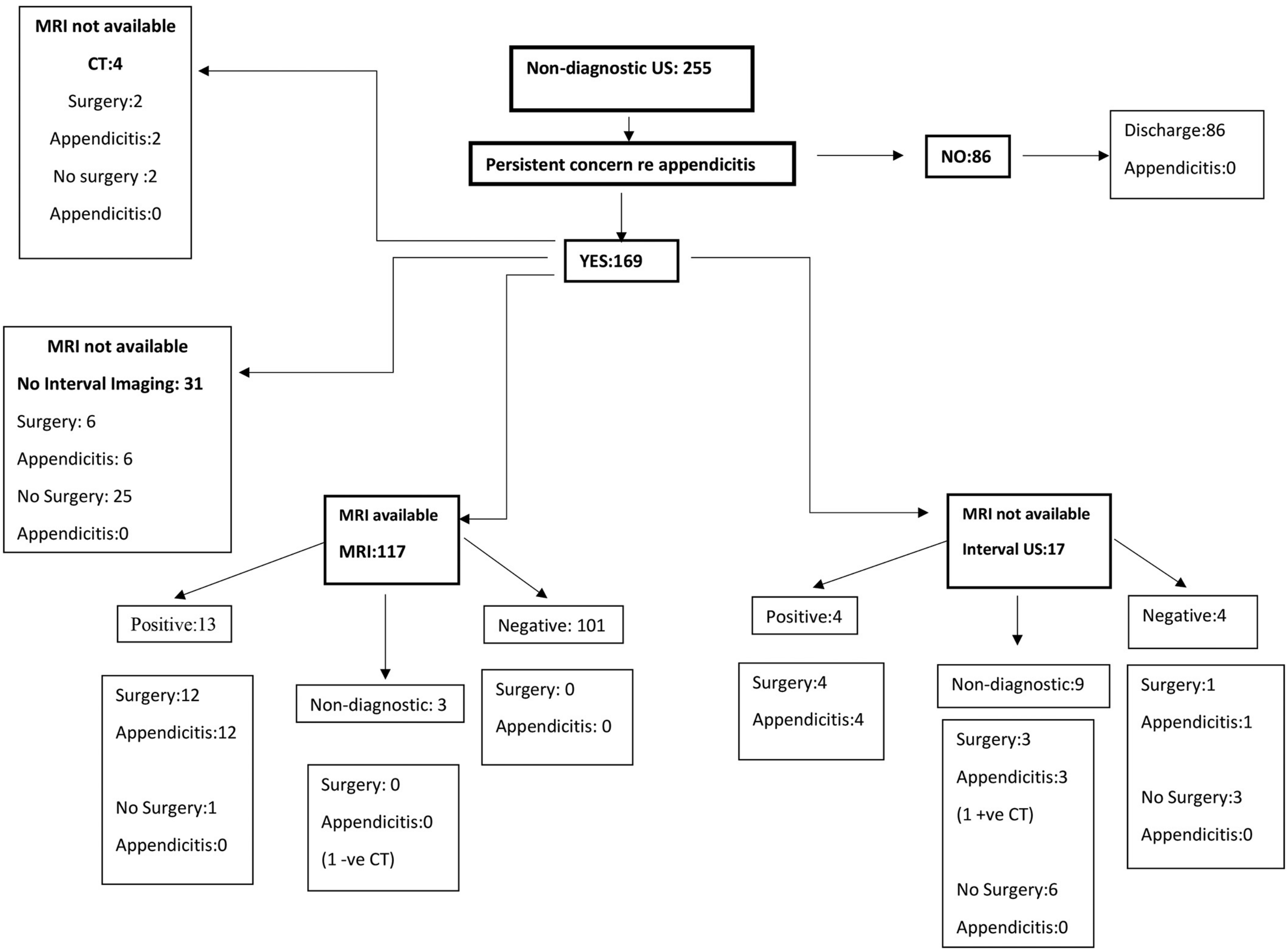

Fig. 3. Management of Children with Non-Diagnostic Screening Ultrasounds.

specificity 98.9%, 0.98–1.00, $N = 469/474$, positive predictive value 96.7% (0.92–0.99, $N = 147/152$) and negative predictive value 99.4% (0.98–1.00, $N = 469/472$); positive likelihood ratio 92.9 (38.8–222.2), negative likelihood ratio 0.02 (0.01–0.06). The negative appendectomy rate in the overall US-MRI algorithm was 1/151 appendicitis-treatment procedures (0.66%).

The clinical accuracy of the overall US-MRI algorithm was significantly higher than that of the previously examined serial US pathway: 98.7%, $N = 616/624$ versus 93.2%, $N = 274/294$, respectively; 95% CI for the difference 0.02–0.08, $p < 0.0001$).

3.6. CT examinations

The 7 CT examinations involved 4 (57.1%) children with non-diagnostic screening USs (2 had perforated appendicitis on CT, 1 had inflammatory bowel disease and 1 had a normal appendix), 2 (28.6%) children with non-diagnostic interval USs (1 had a fluid collection and perforated appendicitis on CT and the other had a normal appendix) and 1 (14.3%) patient with a non-visualized appendix and ileitis on MRI who had a normal appendix and ileitis on CT.

3.7. Alternate diagnoses

A total of 51/121 (42.1%) children without appendicitis who underwent MRI after non-diagnostic screening US had alternate diagnoses: terminal ileitis/colitis in 16, ovarian cyst in 13, mesenteric adenitis in 11, omental infarct in 5, pneumonia in 2, ovarian torsion, pubic osteomyelitis, cholecystitis, polycystic ovary in 1 patient each.

4. Discussion

In this study which took place in the context of limited “real world” MRI availability in the ED setting, we have established a very high clinical accuracy of the US-rapid MRI pathway in children with persistent concern about appendicitis after a non-diagnostic screening US. The clinical accuracy of the overall study algorithm was significantly higher than that previously found in a serial US pathway [23].

Several previous studies have prospectively examined MRI performance in suspected pediatric appendicitis. The two earliest works evaluated MRI as the sole imaging method in unselected patients. [30,31] Orth and colleagues later concluded that non-enhanced MRI demonstrates high diagnostic accuracy, similar to that of US [18]. However, MRI and US examinations were performed in varying order, MRI was not used as interval imaging, and MRI interpretations were not used in the clinical decision-making. Thieme et al. compared diagnostic accuracy of three imaging pathways using US only, conditional MRI after negative or non-diagnostic US and MRI only [20]. The authors found that the MRI-containing strategies had higher sensitivities than US but did not focus on conditional MRI after a non-diagnostic US result. Most recently, our Canadian colleagues demonstrated that MRI improves diagnostic certainty in suspected pediatric appendicitis [19]. Almost a half of the children undergoing MRI did not have a preceding

US, the sequence of imaging varied and the number of children with MRI after non-diagnostic USs was modest. In contrast, our US-MRI pathway focused on patients with persistent concern about appendicitis after non-diagnostic screening USs and those with controversies between conclusive US interpretation and clinical re-examination and established the clinical benefit of MRI in these children. Which children are ultimately selected for MRI depends on local resources and individual physician risk tolerance. While previous studies have identified the children with a non-visualized appendix and no secondary inflammatory signs at a low risk of appendicitis [32], other authors report the appendicitis rate in this sub-group up to 8.6% [17]. Because of the serious consequences of missed appendicitis, many clinicians may consider MRI in this relatively low-risk group, provided it is available.

Previously reported rate of non-diagnostic MRI examinations in suspected pediatric appendicitis varies between zero and 22% [12,17-20,33,34]. One reason for this disparity may be the use of variable definitions of non-diagnostic MRI examinations, frequently limited to non-visualization of the appendix [8,19,33,34] or lack of a related definition [12,18]. Evidence suggests that non-visualization of the appendix in the absence of secondary inflammatory signs on MRI carries a 100% negative predictive value and should be considered a negative study [33]. While two studies have investigated MRI thresholds for pediatric appendicitis [15,28], a normal appendix grows during childhood and the diameters in otherwise normal appendices extend up to 10 mm [27]. Using this information, we have demonstrated that the rate of non-diagnostic interval MRIs is low.

The negative appendectomy rate in this study was at the lower end of the 0–10% rate previously reported in pediatric studies of MRI after a non-diagnostic US [8,15,18,20], and also lower than that found in a previously evaluated serial US pathway [23] and in the U.S.-wide appendicitis studies by Bachur and other experts [5,8,35] Protocolized re-assessment after screening US and high MRI identification of alternate diagnoses may have contributed to this successful outcome. [8-10,17,36]

While 7.9% of children who had an MRI examination in the study by Komanchuk and colleagues had a CT [19], most previous studies of MRI in pediatric appendicitis do not discuss concomitant CT use. In contrast, in our study MRI performance was accompanied by a negligible CT use, likely due to a high rate of conclusive MRI results, facilitated by excellent soft tissue resolution of MRI [9]. Note should be made, however, that both this study and that by Komanchuk's team were conducted in Canada, and the effect of concomitant utilization of CT on the diagnostic performance of the specific pathway may vary in other countries according to local guidelines for utilization of second-line imaging techniques for the diagnosis of appendicitis. A recent meta-analysis of studies conducted in different countries showed that CT and MRI, when independently performed after an equivocal screening US, have comparable high accuracy in diagnosing appendicitis in children and adults [37]. An advantage of MRI over CT as a second-line imaging modality for appendicitis includes the lack of ionizing radiation which is particularly relevant in pediatric patients.

Despite the aforementioned advantages, integration of MRI into care of suspected pediatric appendicitis remains low, with only 1.4% U.S. children undergoing appendectomy after MRI [38]. One reason for this practice may be limited timely access to MRI as this modality may often be prioritized to emergent cases such as stroke. MRI-related costs represent another obstacle. Interestingly, investigators in the Netherlands found that MRI use for suspected appendicitis in children could lead to significant net savings [36]. Future multi-center studies are necessary to evaluate the economic impact of MRI in suspected appendicitis, incorporating associated reduction in negative appendectomies, rapid scanning time used in the ultra-fast protocols and potential reduced length of hospital stay.

Our study has limitations. This was a single tertiary care center study, with a modest number of patients, and potentially limited generalizability to some other pediatric EDs and to community hospitals. Future multi-center studies validating the US-MRI pathway in academic and community settings would be beneficial. While there is a reason to believe that children with suspected appendicitis presenting during the night are comparable to their daytime-arriving counterparts, generalizability of our results to that sub-population may also be limited. Not all children with concern about appendicitis after a non-diagnostic US had MRI. However, our results confirm excellent outcomes associated with the use of the US-MRI pathway in the context of limited access to MRI imaging.

4.1. Conclusion

In the context of limited MRI availability in the ED, this study demonstrated feasibility and a high clinical accuracy of the US-MRI pathway in suspected pediatric appendicitis. This strategy is useful in children with non-diagnostic screening USs and persistent concern about appendicitis and those with discrepancies between conclusive USs and clinical re-assessment. The clinical accuracy of the overall study algorithm was significantly higher than that previously found in a serial US pathway.

CRediT authorship contribution statement

Suzanne Schuh: Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Conceptualization. **Carina Man:** Writing – review & editing, Software, Project administration, Methodology, Data curation. **Eman Marie:** Writing – review & editing, Methodology, Investigation. **Ghufran Hassan A. Alhashmi:** Writing – review & editing, Methodology, Investigation. **Dan Halevy:** Writing – review & editing, Methodology, Investigation. **Paul W. Wales:** Writing – review & editing, Conceptualization, Funding acquisition. **Dana Singer-Harel:** Writing – review & editing, Methodology, Data curation. **Aya Finkelstein:** Writing – review & editing, Methodology, Data curation. **Judith Sweeney:** Writing – review & editing, Methodology, Data curation. **Andrea S. Doria:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Short Running Title: Ultrasound-MRI Pathway in Suspected Pediatric Appendicitis.

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