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Sonographic diagnosis of acute appendicitis in children: a three-year retrospective.

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Abstract

Background

Ultrasound is commonly used as a tool for investigation of acute appendicitis in children. The accuracy of ultrasound in appendicitis depends on the ability to visualise the appendix and the potential contribution from secondary signs.

Study design

The study was a retrospective analysis of children referred for sonographic investigation of possible acute appendicitis at an Australian tertiary paediatric hospital between January 2008 and December 2010.

Methods

Radiology reports, ultrasound images, and electronic medical records were evaluated for eligible patients. The ability to visualise the appendix, and determine secondary sonographic signs was evaluated for diagnostic accuracy.

Results

The study identified 457 eligible children, with the appendix visualised on ultrasound in 40.7% of cases. Using a binary diagnostic model that incorporated equivocal results, sensitivity of ultrasound to diagnose acute appendicitis was 88.1%, specificity 91.4%, and accuracy 90.4%. Ultrasound was found to have a high negative predictive value (96.3%) and the presence of echogenic mesentery had a positive predictive value of 89.4%.

Conclusion

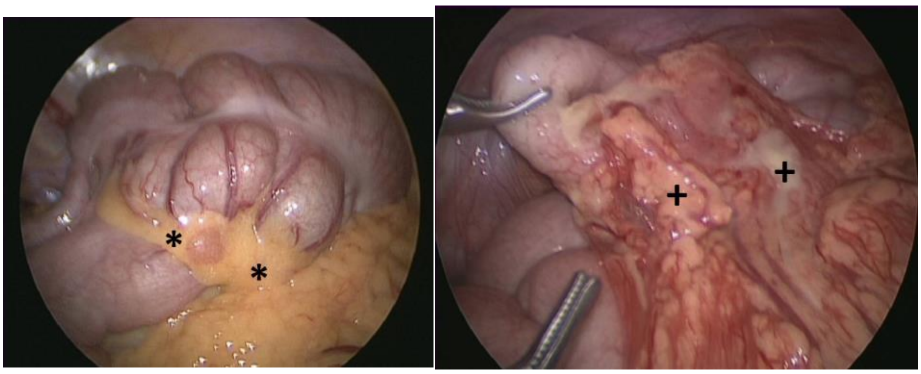
Our results compare favourably with other studies, but indicate the potential for improvement in accuracy and visualisation, with a future study incorporating new methods of categorising ultrasound findings currently being undertaken.

Keywords: appendicitis, ultrasound, pediatrics, ultrasonography, sensitivity and specificity, children

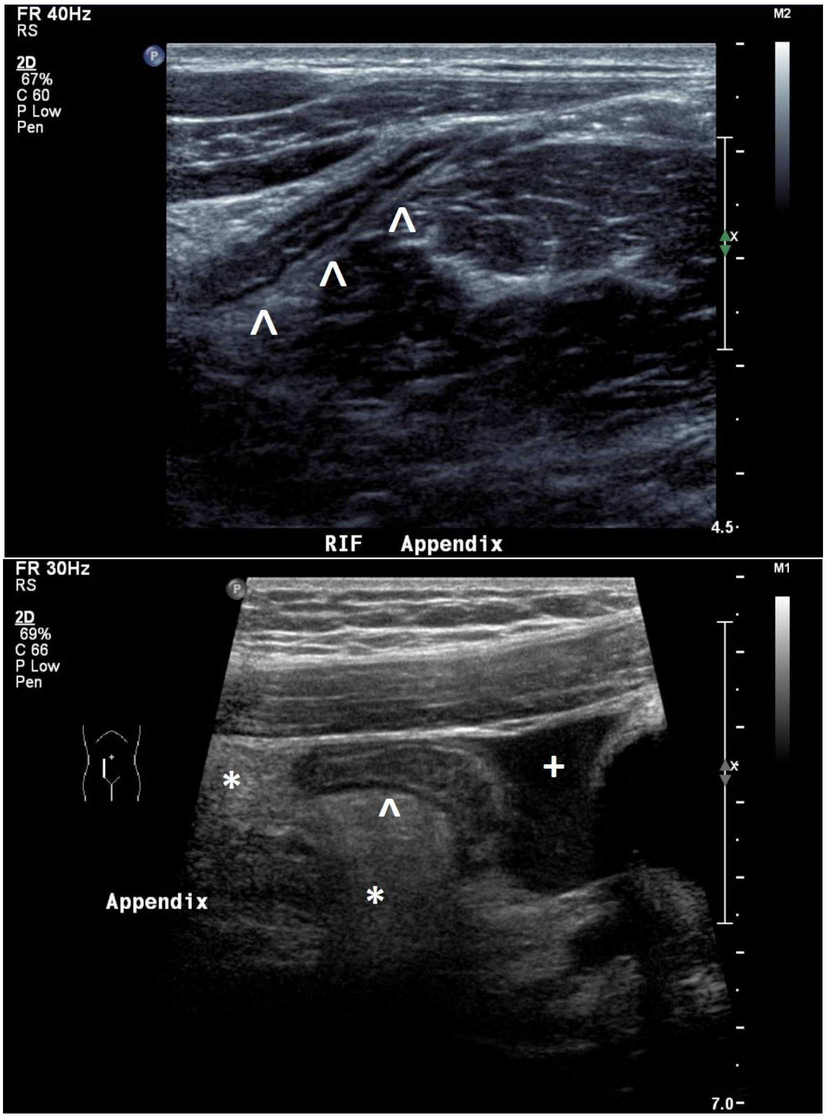
Introduction

Acute appendicitis is the most common surgical emergency in Australia, accounting for almost 10% of emergent surgeries[1]. Ultrasound is an important first-line imaging tool in children with suspected appendicitis due to the lack of potentially harmful ionizing radiation compared with that generated by computed tomography (CT)[2]. Whilst magnetic resonance imaging (MRI) has been demonstrated to be a potential first-line modality in children with appendicitis[3], it is not yet widely available in Australia. The sensitivity and specificity of paediatric appendiceal sonography diagnosing appendicitis are reported to be approximately 90%[4]. These figures can be misleading, with varied interpretation of equivocal ultrasound results. Equivocal results are particularly common when the appendix is not identified[5]. Visualisation of the appendix has been documented in as few as 29% of ultrasound examinations[6], and as many as 99%[7]. These cases with insufficient sonographic evidence to warrant appendectomy are often deemed to be negative and are sometimes excluded from statistical analysis altogether.

In cases where the appendix is not seen and a radiological diagnosis remains equivocal, secondary sonographic signs of appendicitis may support a positive finding or, in their absence, a negative result[8]. These secondary sonographic signs may include: the presence of free fluid; inflammation of the peri-appendiceal mesentery (Figure 1a and 1b) that demonstrates a more echogenic appearance in comparison to the contralateral iliac fossa (Figures 2a and 2b); the presence of an appendicolith, dilated bowel loops, and echogenic debris in the urinary bladder. This audit aims to determine the accuracy of appendiceal sonography diagnosing appendicitis in children at an Australian tertiary children's hospital; in order to compare with published standards and identify potential areas of improvement for a future prospective study.



1. Normal (a) peri-appendiceal mesentery (*), compared to (b) inflamed mesentery (+) at surgery



2. Appendices (^) with no mesenteric inflammation (a) on ultrasound, compared to (b) echogenic mesentery (*) and free fluid (+), both secondary signs of acute appendicitis.

Methods

Study Design

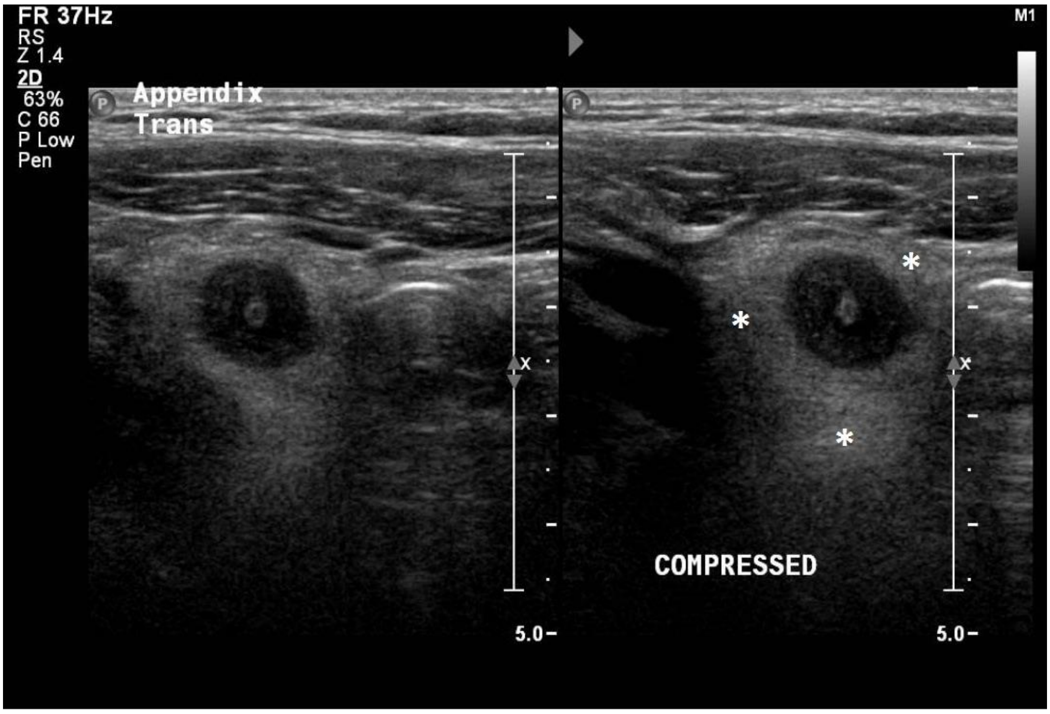
The study was a retrospective review of children who presented to a tertiary Australian children's hospital between January 2008 and December 2010 and underwent an ultrasound study for suspected appendicitis. Ethics approval was granted by the hospital Human Research and Ethics Committee.

Participants

Children were identified for the study using a string search of reports for the keyword 'appendicitis' in the defined dates within the Karisma radiology information system (RIS) (Kestral, Melbourne, Australia). Children were excluded if they had already undergone an appendectomy, or had some other concomitant pathological process. Consecutive studies were included regardless of operator, or being performed in-hours or on-call.

Test methods

Appendiceal ultrasound studies were performed with the patient supine, using the graded compression technique[9]. A linear transducer (L12-5 MHz, Philips Healthcare, Bothell, WA, USA) was used in transverse and longitudinal planes to apply graded compression to the right lower quadrant to displace the caecal contents with sufficient pressure to visualise the psoas muscle posteriorly. For larger children, a lower frequency transducer (L9-3, C8-5) was utilised to obtain greater penetration depth. When identified, the appendix was examined from base to tip, compressed (Figure 3), the calibre measured, and interrogated with colour Doppler. The peri-appendiceal region was examined for the presence of secondary signs of appendicitis: free fluid (greater than a trace or physiological amount), echogenic mesentery, mesenteric lymph nodes, or evidence of abscess/perforation. A Philips iU22 ultrasound platform was used for all studies (Philips Healthcare, Bothell, WA, USA). Images were recorded and sent to PACS (Carestream, Rochester, NY, USA). Sonography was performed by: general sonographers with paediatric experience; radiology registrars on a paediatric rotation; consultant paediatric radiologists; or a combination of these staff.



3. Non-compressible appendix in transverse plane, surrounded by echogenic mesentery (asterisks)

Ultrasound was considered positive for appendicitis when the appendix was identified completely and measured greater than 6mm in maximum outer diameter. Other criteria that supported this finding were non-compressibility, and increased vascularity of the appendiceal wall with Doppler imaging[10]. Ultrasound reports were authorised by a consultant paediatric radiologist. The positive reference standard for this review was a histological assessment of the appendix post-appendectomy stating the presence of acute appendicitis. If surgery was performed without appendectomy, the operation report was used. Patients who did not undergo surgery and were discharged without re-presenting within 30 days were considered to be negative.

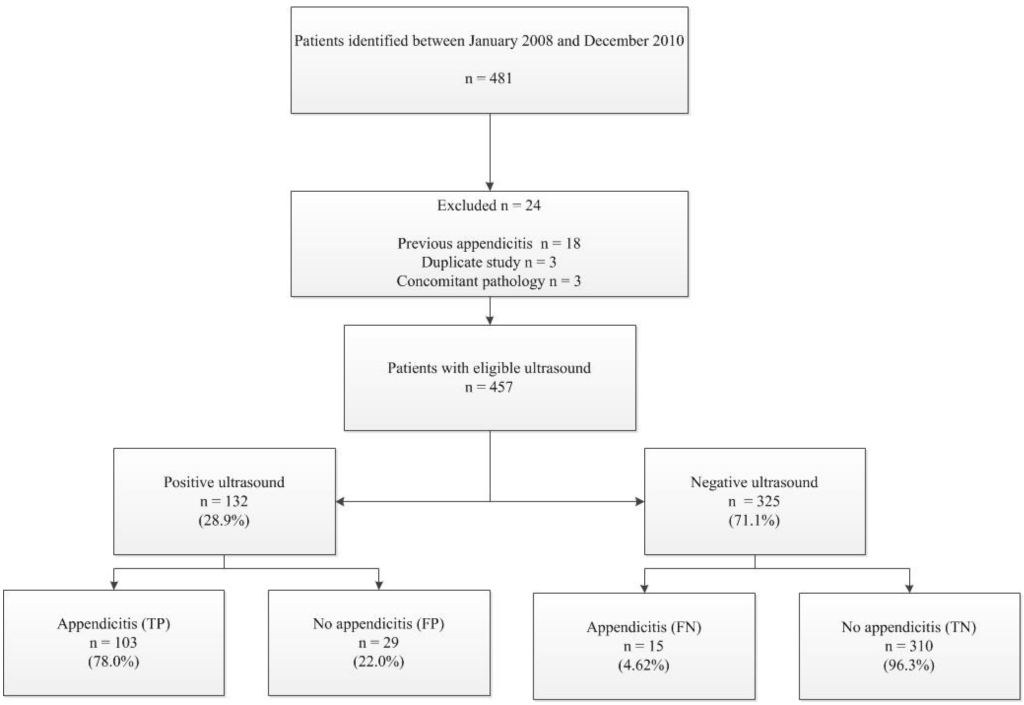
Data was collected by a sonographer from eligible electronic medical records, radiology reports, and ultrasound images on PACS. Source data verification of ultrasound images was performed using a 10% random audit of eligible studies. This was conducted by a consultant paediatric radiologist blinded to the original data collected in order to identify any statistically significant difference in the evaluation of potentially subjective variables between the primary data collector and another author blinded to the initial data coding. An example of variables thought to have an inherent degree of subjectivity, that may not have been clearly articulated in the radiology report were: whether the mesentery was echogenic; was there hyperaemia in the appendiceal wall; and the rounding of appendiceal diameter to the nearest millimeter.

Statistical Analysis
Statistical analysis was performed using IBM SPSS Statistics (version 22, Armonk, NY, USA). Missing data was frequently encountered for some criteria due to the retrospective nature of the study and was coded accordingly. Descriptive statistics, sensitivity, specificity, accuracy, and diagnostic yield for categorical data were calculated. Two approaches were taken regarding analysis of equivocal outcomes. The first incorporated the equivocal studies into the overall statistics to give a binary, positive or negative result, and the second excluded studies when the appendix was not seen on ultrasound as these are usually considered equivocal[5]. Likelihood ratios were calculated for the overall method. A receiver operating characteristic (ROC) curve was used to analyse appendix diameter, ANOVA to compare appendix visualisation rates between years of the study, and the Mann-Whitney U Test was used to determine statistical significance between the diameter in children with and without appendicitis. Independent samples t-tests were used to assess age of patient and the visibility of their appendix. A sample of 500 children was

intended based on a literature review of similar studies[4,11–13]. Statistical significance was considered to be $p < 0.05$. The inter-rater agreement after source data verification between the blinded radiologist and original data collection was good for both categorical variables (Cohen's $\kappa = 0.898$, 95% CI, 0.849 to 0.947) and for appendix diameter as a continuous variable (Pearson's $r = 0.966$, $n = 22$, $p < 0.001$).

Results

There were 481 potential ultrasound reports that included the term 'appendicitis' identified within the three-year study period. Of these, 29 were excluded as follows: previous appendectomy (n = 18), duplicate study (n = 3), or concomitant pathology present before the examination (renal, omental infarct, and pancreatitis; n = 3) (Figure 4). Of the remaining 457 eligible studies, 251 were female (54.9%) and 206 male (45.1%). Patient ages ranged from 1 month to 17 years 10 months, with a mean age of 9 years 11 months (SD = 3 years 11 months). The appendix was identified in 186 ultrasound examinations (40.7%).



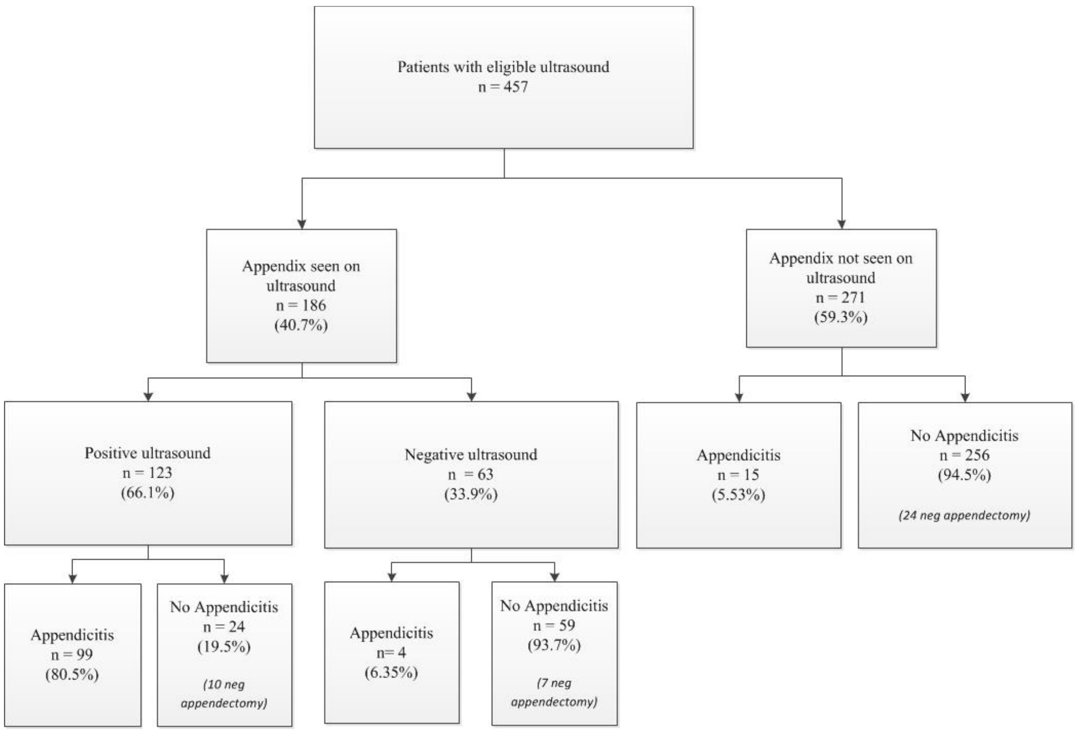
4. Flowchart of patient selection process and subsequent outcomes

Of the 457 eligible studies, 132 (28.9%) were positive on ultrasound and 325 (71.1%) negative (Table 1). A negative result included studies where the appendix was visualized but not considered pathological and also when it was not visualised. Of the cases that were considered positive on ultrasound, 29 (21.9%) were found to be negative at surgery, with five cases of lymphoid hyperplasia prominent amongst these. Fifteen cases (4.61%) negative on ultrasound were subsequently found to have histologically confirmed appendicitis at surgery as clinical symptoms were thought to warrant laparoscopy. Three of the false negative studies demonstrated the appendix, with appendiceal diameters on ultrasound of: 8mm and the presence of prominent lymph nodes; 5mm with lymph nodes and free fluid; and 4 mm with a carcinoid tumour at histology. Of the false negative studies not seen on ultrasound (n = 15), 11 had one or more secondary signs of appendicitis, one was a pelvic appendix, and another showed only evidence of early appendicitis at histology. There were 41 incidences of a normal appendix being removed, a negative appendectomy rate (NAR) of 8.97%.

Table 1. Cross-tabulation of ultrasound diagnosis (index test) vs reference test

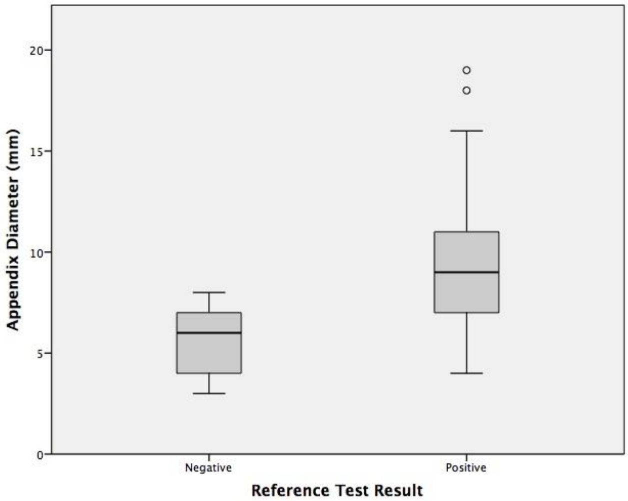
	Reference Positive	Reference Negative
Ultrasound Positive	103	29
Ultrasound Negative	15	310

(A positive reference test was histologically confirmed acute appendicitis. The reference test was considered negative if: a normal appendix at histology; a normal appendix in theatre according to operation report but not removed; or the patient was discharged and did not re-present within 30 days)

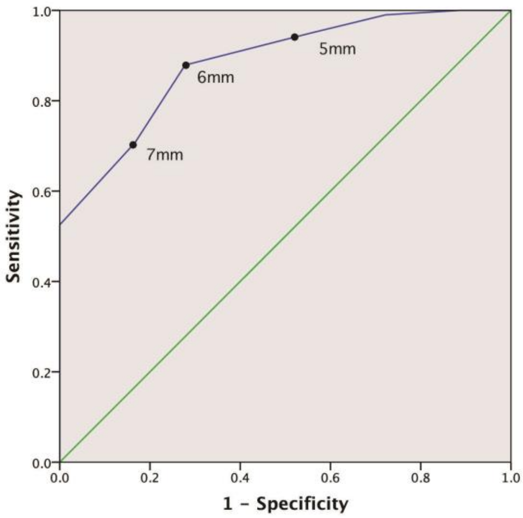


5. Flowchart of patient outcomes, excluding cases where the appendix was not seen on ultrasound

When all eligible ultrasound reports were included, the sensitivity was 88.1% and specificity 91.4%, with an accuracy of 90.4%. Positive predictive value (PPV) of ultrasound was 78.0% and negative predictive value (NPV) 96.3%, whilst the likelihood ratios were LR+ = 10.2 and LR- = 0.13. When only the 186 studies that visualized the appendix with ultrasound were included, 123 (66.1%) were positive for appendicitis and 63 negative (33.9%), with a sensitivity of 96.1% and specificity of 71.1%, PPV = 80.0%, and NPV = 93.7% (Figure 5). A significant difference was demonstrated between the appendiceal diameter of children with and without appendicitis using a 6mm cut off U = 207.5, z = -4.99, $p < 0.01$ (Figure 6). The area under the curve after ROC curve analysis of appendix diameter and the reference test was 0.88 (95% CI 0.80 to 0.95, $p < 0.01$), with a cutoff diameter of > 6mm having a sensitivity of 87.9% and specificity of 70.6% (Figure 7).



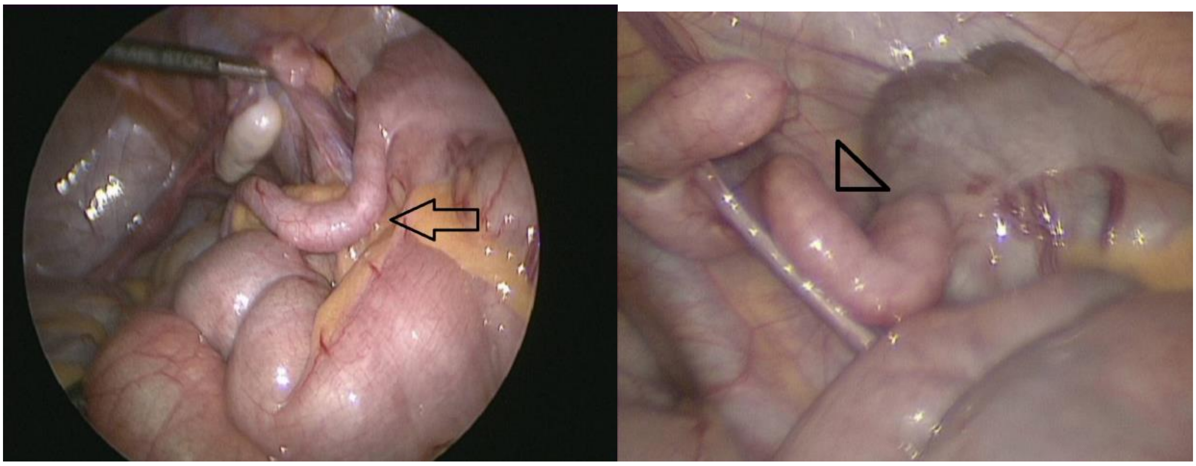
6. Box and Whisker plot of appendiceal diameters of patients with a positive and negative reference test result.



7. ROC curve – Confirmed appendicitis and appendix diameter (AUC = 0.88, 95% CI 0.80 - 0.95)

Discussion

The high NPV (96.3%) of the overall study demonstrates that ultrasound is a useful test to rule out the presence of appendicitis, even with a relatively low diagnostic yield, identifying the appendix 40.7% of the time. Similarly, the likelihood ratios (LR+ = 10.2 and LR- = 0.13) calculated from the study are sufficient to potentially influence a clinician's decision-making pathway and pre-test probability. This is reflected in the NAR of 8.97%, with 41 negative appendectomies performed. Nine of these cases were found to have lymphoid hyperplasia, causing a dilatation of the appendiceal lumen and an increase in appendiceal diameter (Figure 8a and 8b), five of which were seen on ultrasound and considered positive as their diameters ranged between 6 – 8mm (Figure 9). Despite this the ROC curve analysis of diameter revealed that 6mm was the most accurate dichotomous cutoff in our sample. A recent publication has proposed applying three diagnostic categories to appendiceal diameter[14], considering those appendices between 6 - 8mm to be equivocal for appendicitis and those that measure greater than or less than this range, positive and negative for appendicitis respectively. This is in agreement with a number of our inaccurate diagnoses.



8. Normal appendix (arrow) (a) and swollen (b) appendix with lymphoid hyperplasia (arrowhead) at surgery

As this was a retrospective study the original binary diagnosis model was used, where equivocal diagnoses (such as those where the appendix is not seen) were integrated into a positive or negative finding. This reflected the potential limitation of ultrasound to confirm or exclude appendicitis, as the appendix is not always identified sonographically. Our visualisation rate was 40.7% which is comparable with studies by Trout *et al* (24.4%)[16], Estey *et al* (37.7%)[17], and Chang *et al* (35.1 – 58.5%)[18], yet significantly lower than other studies that have identified up to an exceptionally high 99% of appendices[7]. This may indicate important differences that provide potential for improvement or a more systematic approach to visualising the appendix. Sensitivity (88.1%) and specificity (91.4%) in this study were similar to other centres[19], but less accurate than recently published findings that integrate secondary sonographic signs into their radiological diagnoses to manage equivocal cases[12,13]. To better compare with these studies, we excluded cases with a non-visualised appendix, yielding a higher sensitivity (96.1%).

9. Lymphoid hyperplasia on ultrasound, note the lack of secondary signs despite the increased diameter.

Of the secondary sonographic signs identified in the eligible studies, the presence of echogenic peri-appendiceal mesentery was the most useful with a sensitivity of 79.5%, specificity of 73.1%, PPV of 89.4%, and an NPV of 55.5%. This is supported by other studies that suggest that echogenic mesentery is a positive predictor of appendicitis[10,12,15]. Most of the cases of appendicitis not visualised on ultrasound had one or more secondary sonographic signs (73.3%).

The incidence of appendicitis in the study was 25.8%. This may underestimate the true incidence, as it was practice for some cases with a strong clinical suspicion of appendicitis to proceed directly to surgery without imaging. Patient age was not a factor with regard to identifying the appendix on ultrasound ($F = 2.99$, $p = 0.07$). Patient size was not able to be measured with this data set and was not assessed. Whilst visualisation of the appendix improved over each year of the study, there was no significant difference between years $F(1, 455) = 2.08$, $p = 0.15$ (Table 2). This was a similar phenomenon to that identified by Trout *et al*[16] and Binkovitz *et al*[20].

Table 2. Appendix visualisation on ultrasound by scan year

Year of Scan	Total Scans	Appendix Seen	% Appendix Seen
2008	144	54	38%
2009	152	63	41%
2010	151	69	46%

Limitations

One of the limitations of this study was missing data, particularly for those variables that necessitated visualising the appendix, such as diameter and compressibility. In order to gather consecutive studies and limit selection bias, all eligible studies were included and there was no control over the experience of the staff performing the ultrasound studies. The decision to consider patients who did not re-present to our facility as negative is also a potential limitation, as there is a possibility patients may have re-presented at another facility. Staff performing the examination were not blinded to the referring clinician's suspected diagnosis, or clinical testing prior to the study. Similarly, surgeons were not blinded to the ultrasound findings, nor the pathologists to the operation report and ultrasound findings. These scenarios may have provided potential sources of bias in the study.

Conclusion

While the results of this study are comparable with a number of previously published standards, it demonstrates scope for improvement of appendix visualisation and thereby decreasing the proportion of equivocal findings. Though appendiceal diameter has traditionally been used as the primary sonographic indicator of appendicitis, we found a cut-off of 6mm was shown to lead to a number of false positive results, contributing to negative appendectomies. Incorporating secondary sonographic features of appendicitis provides a more meaningful finding. In particular, echogenic mesentery has potential value as an independent predictor of appendicitis, even in the absence of a visualised appendix. This study provides an opportunity to validate our accuracy and further explore the utility of secondary signs in an Australian paediatric cohort with a prospective study currently underway.

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Conflict of Interest
The authors declare no conflict of interest in relation to this manuscript.

References
1. Australian Institute of Health and Welfare. Admitted patient care 2013-14: Australian Hospital Statistics. Health services series no. 60 Cat no. HSE 156. Canberra; 2015.
2. Thirumoorthi AS, Fefferman NR, Ginsburg HB, Kuenzler KA, Tomita SS. Managing radiation exposure in children--reexamining the role of ultrasound in the diagnosis of appendicitis. *J Pediatr Surg*. 2012 Dec;47(12):2268–72.
3. Moore MM, Gustas CN, Choudhary AK, Methratta ST, Hulse MA, Geeting G, et al. MRI for clinically suspected pediatric appendicitis: an implemented program. *Pediatr Radiol*. 2012 Sep;42(9):1056–63.
4. Doria AS, Moineddin R, Kellenberger CJ, Epelman M, Beyene J, Schuh S, et al. US or CT for Diagnosis of Appendicitis in Children and Adults? A Meta-Analysis. *Radiology*. 2006 Apr 2;241(1):83–94.
5. Fedko M, Bellamkonda VR, Bellolio MF, Hess EP, Lohse CM, Laack TA, et al. Ultrasound evaluation of appendicitis: importance of the 3 × 2 table for outcome reporting. *Am J Emerg Med*. Elsevier Inc.; 2014 Apr;32(4):346–8.
6. Scrimgeour DSG, Driver CP, Stoner RS, King SK, Beasley SW. When does ultrasonography influence management in suspected appendicitis? *ANZ J Surg.* 2014 May;84(5):331–4.
7. Lee JH, Jeong YK, Park KB, Park JK, Jeong AK, Hwang JC. Operator-dependent techniques for graded compression sonography to detect the appendix and diagnose acute appendicitis. *Am J Roentgenol*. 2005 Jan;184(1):91–7.
8. Reddan T, Corness J, Mengersen K, Harden F. Ultrasound of paediatric appendicitis and its secondary sonographic signs: providing a more meaningful finding. *J Med Radiat Sci*. 2016 Mar;63(1):59–66.
9. Puylaert JB. Acute appendicitis: US evaluation using graded compression. *Radiology*. 1986 Apr 5;158(2):355–60.
10. Kessler N, Cyteval C, Gallix B, Lesnik A, Blayac P-M, Pujol J, et al.

Appendicitis: Evaluation of Sensitivity, Specificity, and Predictive Values of US, Doppler US, and Laboratory Findings. *Radiology*. 2004 Apr 5;230(2):472–8.

11. Schuh S, Man C, Cheng A, Murphy A, Mohanta A, Moineddin R, et al. Predictors of Non-Diagnostic Ultrasound Scanning in Children with Suspected Appendicitis. *J Pediatr*. 2011 Apr 2;158(1):112–8.
12. Wiersma F, Toorenvliet BRB, Bloem JJL, Allema JH, Holscher HC. US examination of the appendix in children with suspected appendicitis: the additional value of secondary signs. *Eur Radiol*. 2009 Apr 4;19(2):455–61.
13. van Atta AJ, Baskin HJ, Maves CK, Rollins MD, Bolte RG, Mundorff MB, et al. Implementing an ultrasound-based protocol for diagnosing appendicitis while maintaining diagnostic accuracy. *Pediatr Radiol*. 2015 Apr;45(5):678-85
14. Trout AT, Towbin AJ, Fierke SR, Zhang B, Larson DB. Appendiceal diameter as a predictor of appendicitis in children: improved diagnosis with three diagnostic categories derived from a logistic predictive model. *Eur Radiol*. 2015 Aug;25(8):2231–8.
15. Lee MW, Kim YJ, Jeon HJ, Park SW, Jung S Il, Yi JG. Sonography of Acute Right Lower Quadrant Pain: Importance of Increased Intraabdominal Fat Echo. *Am J Roentgenol*. 2009 Jan;192(1):174–9.
16. Trout AT, Sanchez R, Ladino-Torres MF, Pai DR, Strouse PJ. A critical evaluation of US for the diagnosis of pediatric acute appendicitis in a real-life setting: how can we improve the diagnostic value of sonography? *Pediatr Radiol*. 2012 Apr 2;42(7):813–23.
17. Estey A, Poonai N, Lim R. Appendix not seen: the predictive value of secondary inflammatory sonographic signs. *Pediatr Emerg Care*. 2013 Apr;29(4):435–9.
18. Chang ST, Jeffrey RB, Olcott EW. Three-step sequential positioning algorithm during sonographic evaluation for appendicitis increases appendiceal visualization rate and reduces CT use. *Am J Roentgenol*. 2014 Nov;203(5):1006–12.
19. Jaremko JL, Crockett A, Rucker D, Magnus KG, Jacob L, Kenneth G, et al. Incidence and Significance of Inconclusive Results in Ultrasound for Appendicitis in Children and Teenagers. *Can Assoc Radiol J*. 2011 Apr 2;62(3):197–202.
20. Binkovitz LA, Unsdorfer KML, Thapa P, Kolbe AB, Hull NC, Zingula SN, et al. Pediatric appendiceal ultrasound: accuracy, determinacy and clinical outcomes. *Pediatr Radiol*. 2015 Dec 18;45(13):1934–44.