Diagnostic Imaging for Pediatric Appendicitis

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Case Example

An 11-year-old, 45 kg, female presents to a community emergency department with 8 hours of abdominal pain. The emergency physician requests surgical consultation in anticipation of possible transfer and reports that the patient has tenderness to palpation in the right lower quadrant, but is afebrile and has a normal white blood cell count. She would like to know if you would like imaging for this patient and, if so, what?

Introduction

Appendectomy is the most common urgent surgical procedure in children, with approximately 80,000 appendectomies performed annually in the United States [1]. Appendicitis was traditionally diagnosed clinically, based on history and physical exam, and surgeons accepted a 10–20% rate of finding a normal appendix at surgery (negative appendectomy) [2]. With improving technology, abdominal ultrasonography (U/S) gained popularity in the late 1980s [3]. As computed tomography (CT) became more ubiquitous, its use supplanted U/S [4]. Magnetic resonance imaging (MRI) use has increased slowly over the past few years as the harms of CT-associated radiation have been acknowledged and publicized. The increase in accuracy and availability of diagnostic imaging has resulted in a decrease in the negative appendectomy rate, from 20% to 2%, over the past three decades [2, 5]. Today, nearly 100% of pediatric patients undergo some type of imaging to establish a diagnosis of appendicitis; CT accounts for more than 50% of these studies [6]. The choice of

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imaging modality is highly dependent on clinician decision-making, as well as local availability and practices.

The ideal diagnostic imaging modality would expeditiously and accurately diagnose appendicitis without exposing the patient to additional harms and would be cost-effective. Each modality has limitations, risks, and benefits, which should be considered based on the clinical scenario. Adjuncts to imaging, such as radiology report templates, clinical scoring systems, and standardized algorithms for patient evaluation, have enhanced the value of diagnostic studies. Moreover, individual modalities should be thought of in conjunction with other study types as well as contextual and patient-related factors. The following review describes the advantages and limitations of each modality, followed by a discussion of ways to enhance the diagnostic utility of various imaging strategies.

Literature Review

Ultrasonography

Graded compression U/S was first described for the diagnosis of appendicitis in 1986 [3]. The traditional criterion for diagnosis of appendicitis by U/S is an appendiceal maximal outer diameter (MOD) >6 mm. Searle et al. looked at normal appendiceal diameter by age and found that the appendiceal diameter does not increase significantly above age 3 [7]. A retrospective review by Goldin et al. found that using diagnostic criteria of MOD ≥7 mm or wall thickness >1.7 mm had a sensitivity of 99% and specificity of 95% [8]. Among published meta-analyses of the diagnostic accuracy of U/S, sensitivity ranges from 0.88 to 0.91 and specificity from 0.90 to 0.97 (Table 5.1) [9–12]. Figure 5.1 shows the imaging findings of appendicitis by U/S.

While MOD is a central component of U/S diagnosis of appendicitis, one criticism of U/S is the frequency of lack of visualization (full or partial) of the appendix, which occurs 18–75% of the time [19–21]. According to a multicenter prospective observational study by Mittal et al., U/S had a specificity of 97% and a sensitivity of 72.5% for the diagnosis of appendicitis in children ages 3–18 [22]. The primary reason for

Table 5.1 Ranges of sensitivity and specificity for different imaging modalities by source [9–18]

	Ultrasonography (U/S)	Computed tomography (CT)	Magnetic resonance imaging (MRI)
Test characteristics			
Sensitivity:			
Single studies	0.44–1.00	0.76–0.97	0.85–1.00
Meta-analyses	0.88–0.91	0.90–0.95	0.96–0.98
Specificity:			
Single studies	0.86–0.97	0.83–0.99	0.96–0.98
Meta-analyses	0.90–0.97	0.92–0.95	0.96–0.97

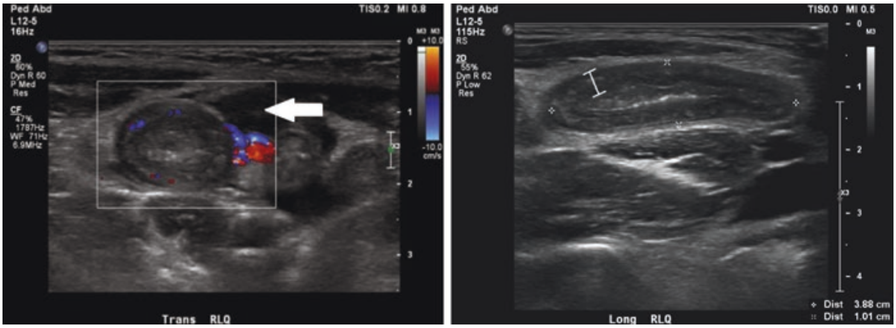

Fig. 5.1 Ultrasound positive for appendicitis. Transverse view (left) demonstrates periappendiceal free fluid (arrow). Longitudinal view (right) highlights appendiceal wall thickening, with a maximal outer diameter of 1.01 cm

the lower sensitivity was the frequency with which the appendix was not visualized. In cases where the appendix was visualized, the sensitivity was 97.9%, and the specificity was 91.7%. However, lack of visualization has a high negative predictive value for appendicitis [23]. The combination of lack of visualization and absence of secondary findings reduces the likelihood of appendicitis to less than 2% [24].

Secondary findings that may support the diagnosis of appendicitis include appendiceal wall thickness ≥3 mm, non-compressibility of the appendix, wall hyperemia on color Doppler, periappendiceal mesenteric fat stranding, presence of an appendicolith, free fluid, a periappendiceal hypoechoic halo indicative of appendiceal wall edema, lymphadenopathy, and abdominal tenderness during U/S examination. Published literature provides contradictory data on the diagnostic value of secondary signs for the diagnosis of appendicitis with U/S. Goldin et al. reported that incorporating secondary findings into diagnostic criteria did not increase the sensitivity or specificity of U/S [8]. Trout et al. found that periappendiceal fat stranding was the only secondary finding that was statistically significant in predicting the presence of appendicitis [25]. In one retrospective review of imaging in negative appendectomies, the most common U/S findings that misled radiologists were noncompressibility (56%) and sonographic tenderness (56%), followed by RLQ lymphadenopathy (50%) [26]. Nevertheless, the presence of secondary findings in the setting of a non-visualized appendix or the absence of secondary findings in the setting of a borderline MOD may increase diagnostic accuracy [20].

The primary limitation of U/S is its operator dependence. Techniques for improved appendix visualization have been reported, including standard supine scanning, followed by left posterior oblique scanning if the appendix is not visualized, and then "second-look" supine scanning [27]. Increased use of U/S, i.e., practice, is also associated with decreased non-visualization of the appendix and improved diagnostic accuracy [19]. Sensitivity is higher at centers with higher U/S utilization, and nondiagnostic U/S studies are more prevalent at community hospitals, where CT is more often employed as the first imaging test [22, 28].

Additionally, U/S is commonly thought to perform worse than other imaging modalities in overweight or obese patients [29–31]. Increased abdominal wall thickness and retrocecal location are associated with decreased rates of visualization in adult studies [32]. However, U/S has been shown to maintain its diagnostic utility in children regardless of patient body habitus [33]. Techniques to improve visualization in patients with a large body habitus include posterior manual compression and use of lower-frequency transducers [34].

Utilizing a standardized radiology report template that incorporates secondary signs has been shown to improve U/S diagnostic clarity. Nielsen et al. formulated a template that defined an abnormal appendix as one with a MOD ≥7 mm and a maximal wall thickness ≥1.7 mm [35]. Secondary signs included hyperechogenic periappendiceal fat, fluid collection consistent with abscess, and local dilation and hypoperistalsis of bowel. For their final impression, radiologists were required to choose between four categories: (1) normal appendix, (2) appendix not visualized or partially visualized without secondary signs of appendicitis, (3) appendix not visualized or partially visualized with secondary signs of appendicitis, and (4) acute appendicitis. Categories 3 and 4 were considered positive for appendicitis. This template nearly eliminated nondiagnostic exams and improved diagnostic accuracy. Sensitivity improved from 67% to 92%. In other studies, the use of U/S templates has reduced use of CT, improved diagnostic accuracy, and reduced costs [36–38].

Rapidity of the test and repeatability are additional benefits of U/S. Increased sensitivity with increased duration of abdominal pain and repeated scans has been reported [39, 40]. U/S alone and in conjunction with algorithms that include U/S first have demonstrated lower costs and decreased use of CT [41–45]. The trend toward increased U/S use has not produced a concomitant increase in negative appendectomies, time to surgery, perforations, or missed appendicitis [4, 46–48].

Computed Tomography

CT findings of appendicitis are similar to those seen on U/S: appendiceal MOD >6 mm, increased wall thickness (target sign), wall hyperemia, periappendiceal mesenteric fat stranding, presence of an appendicolith, free fluid, and abscess [49]. Figure 5.2 demonstrates imaging by CT of confirmed appendicitis. Non-visualization of the appendix is possible on CT and argues against appendicitis with a very high (99%) negative predictive value [50]. The advantages of CT are its high sensitivity and specificity, operator independence, relatively quick acquisition time, widespread availability, and ability to identify alternate diagnoses.

CT has strong test characteristics in all populations, somewhat better than U/S, with a sensitivity of 0.90–0.95 and specificity of 0.92–0.95 (Table 5.1) [9, 13, 14]. Sensitivity and specificity improve slightly with intravenous contrast, but enteric contrast is generally unnecessary [51]. In children, however, several systematic reviews have shown that the sensitivity and specificity of CT are similar to U/S [9, 15]. CT's lower performance in children is due to relative lack of body fat, which makes distinguishing the appendix from surrounding structures more difficult [10, 52, 53]. In

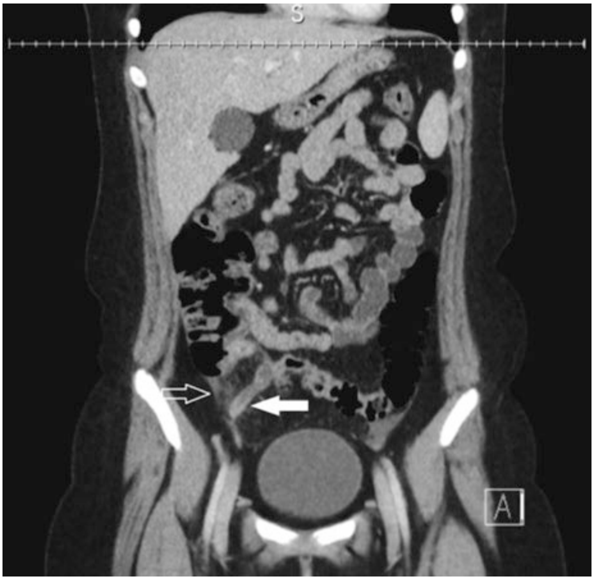

Fig. 5.2 CT scan demonstrates dilated appendix (solid arrow) with periappendiceal mesenteric fat stranding (hollow arrow)

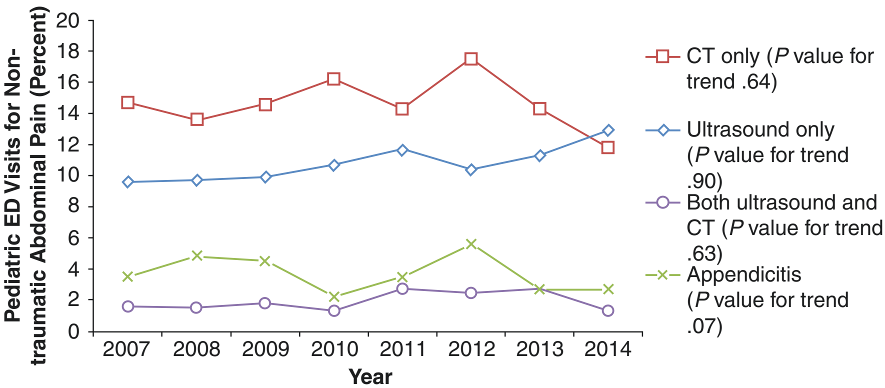

Fig. 5.3 Imaging trends in the United States for pediatric abdominal pain patients presenting to the emergency department [55]

contrast to U/S, CT's high sensitivity and specificity remain consistent across institutions. In their meta-analysis of 9, 356 pediatric patients, Doria et al. reported little variation between hospitals of institution-specific sensitivity and specificity [10].

CT is now ubiquitous in the United States, with more than 34 scanners per million population as of 2007 [54]. Fourteen percent of children presenting to the emergency department with non-traumatic abdominal pain undergo CT (Fig. 5.3) [55]. Being faster than MRI, CT is useful for obtaining high-quality imaging in younger children, who may not be able to remain still a prolonged time period. However, CT completion may take significantly longer than U/S from time of order to performance [56]. CT also identifies extra-appendiceal findings suggestive of other diagnoses more often than U/S [57, 58]. Because of these properties, CT may reduce the rate of negative appendectomies in children younger than 5 and girls older than 10 years of age [59].

Despite strong test characteristics, ease, and efficiency of performance, the ionizing radiation produced by CT raises concern. Focused exams and low-dose techniques, which have demonstrated equivalence to traditional techniques, have reduced radiation exposure but cannot eliminate it [60]. Children are particularly vulnerable to the effects of radiation, as their developing tissues are more sensitive and they have a longer remaining life span during which oncogenic effects may manifest [61]. Age at time of exposure impacts the risk of malignancy, with age inversely related to risk [62]. With growing recognition of the harms of healthcare-associated pediatric radiation exposure, limiting the utilization of CT is strongly recommended by national bodies such as the American College of Radiologists, the National Cancer Institute, the American Academy of Pediatrics, the American Pediatric Surgical Association, the Image Gently Alliance, and the Joint Commission [61, 63–66].

In the United States, individuals are exposed to approximately 3 mSv of background radiation per year. For reference, 1 mSv is equivalent to 1 mGy if the radiation type is gamma rays. An abdominal CT scan delivering 10 mSv is expected to cause cancer in the lifetime of 1 in 1000 male patients who are 10 years old at the time of imaging [67]. An estimated 4–9 million CT scans are performed annually on US children, 11% of which are obtained to evaluate for appendicitis [68, 69]. One year's worth of pediatric CTs is projected to cause 4870 cancers, but the true risk is unknown [70].

CT use in pediatric patients is associated with community, non-children's hospitals (NCH), older children, females, and patients with higher body mass index [71, 72]. Multiple studies have demonstrated that NCHs are more likely than children's hospitals (CH) to utilize CT to diagnose pediatric appendicitis [71–73]. The majority of pediatric patients with suspected appendicitis undergo CT, likely because 66–82% of these patients initially present to community and NCHs [74, 75]. Anderson et al. have also showed that the size-specific dose estimate and effective dose of radiation are significantly higher and have greater variance at NCHs that are not involved in a dose reduction program (Fig. 5.4) [76, 77].

CHs have led the effort to reduce CT utilization in children. As MRI has become increasingly available, it has begun to replace CT as a secondary modality after inconclusive U/S and is less commonly used as the primary study [72]. In addition to the radiation risk, CT use is not associated with better patient outcomes [78]. Other disadvantages of CT compared to U/S include cost and potential for allergic reaction or kidney injury from iodinated contrast agents. With radiation dose being cumulative, repeat CTs are not recommended.

Magnetic Resonance Imaging

The diagnostic features of appendicitis on MRI are similar to those previously mentioned. A study by Leeuwenburgh et al. described nine MRI features predictive of appendicitis: appendix diameter >7 mm, appendicolith, periappendiceal fat

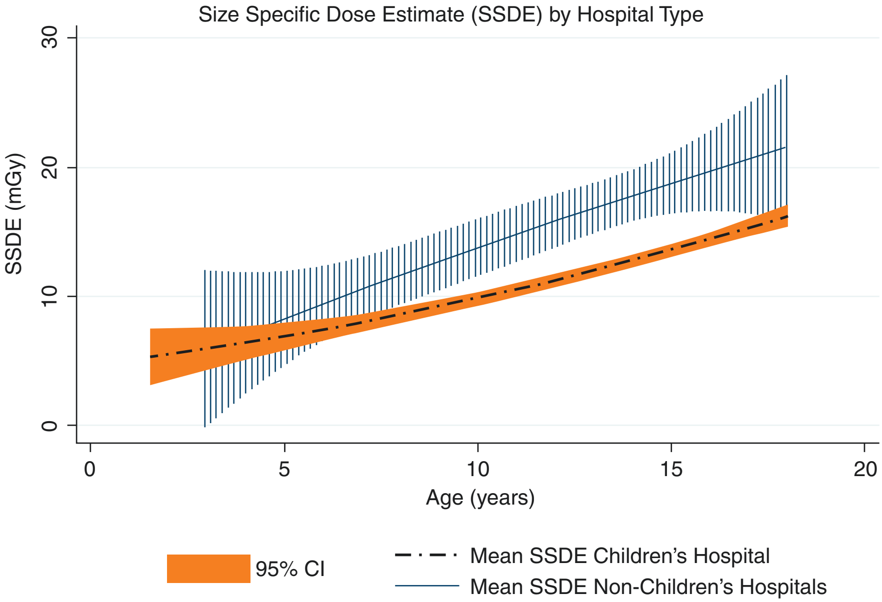

Fig. 5.4 Size-specific dose estimate by patient age at children's hospitals compared to non-children's hospitals [76]

infiltration, periappendiceal fluid, absence of gas in the appendix, appendiceal wall destruction, restricted diffusion of the appendiceal wall, and lumen or focal fluid collections [79]. Systematic reviews and meta-analyses have reported sensitivity from 0.96 to 0.99 and specificity ranging from 0.96 to 0.97 (Table 5.1) [9, 16–18]. In addition to strong test characteristics, MRI is also operator independent, provides alternative diagnoses as frequently as CT, and does not expose patients to ionizing radiation [80]. Figure 5.5 shows an MRI demonstrating appendicitis.

MRI does have several limitations, especially in the pediatric population. MRI may take longer to perform than either U/S or CT. The youngest children, those who cannot cooperate, or those with claustrophobia may require sedation to complete the exam. MRI is not as widely available as the other modalities and is more expensive as a stand-alone test than its comparators.

Traditional MRIs, with or without contrast, take longer to perform than U/S or CT. However, at centers where it is available, "fast" MRI has mitigated this problem. 3-T MRI produces a magnetic field twice as powerful as the more common 1.5T MRI, which typically decreases scanning time by half while retaining strong test characteristics [81]. In combination with 3-T MRI machines, parallel processing and newer body coils aid in reducing scan time, making it possible to scan children with free breathing, no IV contrast, and no sedation [82]. The benefit of gadolinium enhanced images has not been conclusively established [17, 83, 84].

Fig. 5.5 MRI demonstrates dilated appendix with periappendiceal enhancement consistent with inflammation

MRI is not as widely available as CT or U/S [54]. Hospital characteristics such as higher total expenditures and network affiliation are associated with its availability [85]. Even where available, MRI use has increased very slowly, comprising only 1–2% of all imaging for suspected appendicitis [47]. Otero et al., in a large retrospective study of trends and costs over time, found that while imaging costs of all studies increased slightly, it was at a much lower rate than overall hospital costs [47]. However, MRI only accounted for approximately 1% of imaging in that review. Heverhagen et al. reported that MRI is cost-effective as an isolated imaging modality because it decreases the rate of negative laparotomy, but their study did not compare MRI to U/S or CT [86]. Anderson et al. demonstrated a small, yet significant, increase in radiology costs with a large increase in MRI use (from 1% to 25%) in a single institution [46].

The utility of MRI as the first imaging test for appendicitis has not been established; nevertheless, it is a reliable alternative to CT when U/S is inconclusive. The slow transition from CT to MRI as the secondary imaging modality has not shown a change in outcomes. Several studies have reported no difference in time to antibiotic administration, time to surgery, negative appendectomy, perforation rate, or length of stay [46, 82, 87]. Future studies are necessary to evaluate the repercussions of this change in imaging strategy.

Discussion

Imaging for suspicion of pediatric appendicitis has become a common practice in the United States. As a result, tolerance for negative appendectomies and missed diagnoses has significantly decreased. Based on the available literature and current guidelines, U/S should be the first-line imaging modality in children with suspected appendicitis [88, 89]. MRI, where available, should be considered as a second-line exam in lieu of CT. CT may be beneficial when MRI cannot be performed, in older or obese children and in exigent circumstances. Imaging for suspected appendicitis is cost-effective for the reduction of negative appendectomies and decreased length of stay [90].

Imaging is rarely performed in isolation of history and physical and laboratory tests. The incorporation of commonly performed blood tests, such as a complete blood count, has demonstrated improved predictive value when used in conjunction with U/S [91]. The Alvarado Score, the Pediatric Appendicitis Score (PAS), the Appendicitis Inflammatory Response (AIR) Score, and similar tools have been used with great success to triage patients for imaging, to choose the imaging modality, or to support imaging results [43, 92–96]. Saucier et al. used the PAS to selectively image pediatric patients with U/S first, while Bachur et al. integrated the PAS with U/S results to determine next steps [43, 97]. Blitman et al. found a negative predictive value of 99.6% in patients with a low Alvarado Score and inconclusive U/S [92].

There is strong evidence that clinical guidelines or pathways for the diagnosis of appendicitis are efficient and cost-effective; they also reduce radiation exposure even if CT is included in the algorithm [40, 43, 46, 82, 98, 99, 100]. Published pathways are varied but generally include an U/S first protocol [101]. The LeBonheur pathway, as described by Saucier et al., had a diagnostic accuracy of 94% and was shown to be the 2nd most cost-effective strategy compared to U/S of all patients, clinical judgment alone, CT of all patients, overnight observation with surgical evaluation, and no imaging [102]. U/S of all patients was the most cost-effective; however, stratification by PAS had improved diagnostic accuracy with only a moderate increase in cost. U/S as the initial imaging modality with CT or MRI reserved for inconclusive U/S results increases overall diagnostic accuracy and decreases cost without sacrificing time to antibiotics or surgery [103, 104].

Continuing Controversies and Areas for Study

The evidence supports the use of U/S as the first diagnostic imaging test in children with suspected appendicitis. The utility of MRI first or MRI second has not been conclusively established, and more studies are needed to evaluate MRI alone or as part of an algorithm. Moreover, the role of CT, in light of radiation concerns, has not been fully determined. Several authors have suggested that MRI should replace CT as the secondary imaging modality after inconclusive U/S, but this practice has not been widely implemented, and the repercussions of such a shift have not been fully investigated. The Cochrane Collaboration is in the process of conducting a systematic review and meta-analysis of U/S and MRI for the diagnosis of acute appendicitis [105, 106]. They are also conducting a systematic review for evidence of the benefit of CT for acute appendicitis in adults.

Case Example Discussion

The case mentioned in the beginning of this chapter highlights the conundrums of imaging for suspected appendicitis in children. In this female patient with right lower quadrant pain, multiple diagnoses must be considered, including appendicitis, gynecologic pathologies such as ovarian torsion, or mesenteric adenitis. An ultrasound should be ordered for this patient. If the ultrasound is inconclusive, the emergency physician ought to consider the characteristics of their facility, transfer logistics, and patient/family preferences prior to ordering additional or repeat imaging.

In this case you recommended an U/S, which was obtained first. It demonstrated free pelvic fluid but was nondiagnostic. After you discussed the U/S results, the emergency physician ordered an MRI of the abdomen and pelvis on your recommendation, which showed a dilated appendix with periappendiceal inflammation and a normal right ovary. The patient was started on antibiotics, and an appendectomy was successfully performed several hours later.

Conclusion

Imaging for suspected pediatric appendicitis is an invaluable diagnostic tool, but modality selection can be controversial. First-line U/S is the evidence-based recommendation of the authors and the American College of Radiology [88]. Additional imaging is at the discretion of the provider, and multiple factors should be considered including availability of secondary modalities, exam and laboratory findings, surgeon assessment, patient characteristics, and patient/family preference.

Clinical Pearls

- Imaging is a valuable tool that has significantly improved our ability to correctly diagnose appendicitis and lower our negative appendectomy rate.
- U/S is a useful and safe first-line mode of imaging, but is operator dependent.
- MRI may provide a nonionizing radiation imaging option with a similar accuracy to CT scan.

References

1. Agency for Healthcare Research and Quality. HCUPnet: a tool for identifying, tracking, and analyzing national hospital statistics [Internet]. 2011. Available from: http://hcupnet.ahrq.gov/
2. Kaiser S, Mesas-Burgos C, Söderman E, Frenckner B. Appendicitis in children – impact of US and CT on the negative appendectomy rate. Eur J Pediatr Surg [Internet]. 2004;14(4):260–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15343467

3. Puylaert JB. Acute appendicitis: US evaluation using graded compression. Radiology. 1986;158(2):355–60.
4. Bachur RG, Levy JA, Callahan MJ, Rangel SJ, Monuteaux MC. Effect of reduction in the use of computed tomography on clinical outcomes of appendicitis. JAMA Pediatr [Internet]. 2015;02115(8):1–6. Available from: http://archpedi.jamanetwork.com/article.aspx?doi=10.1001/jamapediatrics.2015.0479%5Cn; http://www.ncbi.nlm.nih.gov/pubmed/26098076%5Cn; http://archpedi.jamanetwork.com/data/Journals/PEDS/0/poi150021.pdf
5. Raja AS, Wright C, Sodickson AD, Zane RD, Schiff GD, Hanson R, et al. Negative appendectomy rate in the era of CT: an 18-year perspective. Radiology [Internet]. 2010;256(2):460–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20529988
6. Kotagal M, Richards M, Flum D, Acierno S, Weinsheimer R, Goldin A. Use and accuracy of diagnostic imaging in the evaluation of pediatric appendicitis. J Pediatr Surg [Internet]. 2015;50(4):642–6. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L603516778%5Cn, https://doi.org/10.1016/j.jpedsurg.2014.09.080%5Cn, http://elvis.ubvu.vu.nl:9003/vulink?sid=EMBASE&issn=15315037&id=doi:10.1016/j.jpedsurg.2014.09.080&atitle=Use+and+ac
7. Searle AR, Ismail KA, Macgregor D, Hutson JM. Changes in the length and diameter of the normal appendix throughout childhood. J Pediatr Surg [Internet] 2013;48(7):1535–1539. Available from: https://doi.org/10.1016/j.jpedsurg.2013.02.035
8. Goldin AB, Khanna P, Thapa M, McBroom JA, Garrison MM, Parisi MT. Revised ultrasound criteria for appendicitis in children improve diagnostic accuracy. Pediatr Radiol. 2011;41(8):993–9.
9. Zhang H, Liao M, Chen J, Zhu D, Byanju S. Ultrasound, computed tomography or magnetic resonance imaging – which is preferred for acute appendicitis in children? A meta-analysis. Pediatr Radiol [Internet]. 2017;47(2):186–96. Available from: https://doi.org/10.1007/s00247-016-3727-3
10. 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;241(1):83–94.
11. Lowe LH, Penney MW, Stein SM, Heller RM, Neblett WW, Shyr Y, et al. Unenhanced limited CT of the abdomen in the diagnosis of appendicitis in children: comparison with sonography. Am J Roentgenol. 2001;176(1):31–5.
12. Matthew Fields J, Davis J, Alsup C, Bates A, Au A, Adhikari S, et al. Accuracy of point-of-care ultrasonography for diagnosing acute appendicitis: a systematic review and meta-analysis. Acad Emerg Med. 2017;24(9):1124–36.
13. Sivit CJ, Applegate KE, Stallion A, Dudgeon DL, Salvator A, Schluchter M, et al. Imaging evaluation of suspected appendicitis in a pediatric population. Am J Roentgenol [Internet]. 2000;175(4):977–80. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11000147
14. Xiong B, Zhong B, Li Z, Zhou F, Hu R, Feng Z, et al. Diagnostic accuracy of noncontrast CT in detecting acute appendicitis: a meta-analysis of prospective studies. Am Surg. 2015;81(6):626–9.
15. Dahabrehm I, Adam G, Halladay C, Steele D, Daiello L, Weiland L, et al. Diagnosis of right lower quadrant pain and suspected acute appendicitis. Agency Healthc Res Qual [Internet]. 2015;(157). Available from: https://www.effectivehealthcare.ahrq.gov/ehc/products/528/2158/appendicitis-report-151214.pdf
16. Repplinger MD, Levy JF, Peethumnongsin E, Gussick ME, Svenson JE, Golden SK, et al. Systematic review and meta-analysis of the accuracy of MRI to diagnose appendicitis in the general population. J Magn Reson Imaging. 2016;43(6):1346–54.
17. Moore MM, Kulaylat AN, Hollenbeak CS, Engbrecht BW, Dillman JR, Methratta ST. Magnetic resonance imaging in pediatric appendicitis: a systematic review. Pediatr Radiol [Internet]. 2016;46(6):928–39. Available from: https://doi.org/10.1007/s00247-016-3557-3
18. Duke E, Kalb B, Arif-Tiwari H, Daye ZJ, Gilbertson-Dahdal D, Keim SM, et al. A systematic review and meta-analysis of diagnostic performance of MRI for evaluation of acute appendicitis. Am J Roentgenol. 2016;206(3):508–17.

19. 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 [Internet]. 2012;42(7):813–23. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22947273%5Cn; http://www.ncbi.nlm.nih.gov/pubmed/22402833
20. Wiersma F, Toorenvliet BR, Bloem JL, Allema JH, Holscher HC. US examination of the appendix in children with suspected appendicitis: the additional value of secondary signs. Eur Radiol. 2009;19(2):455–61.
21. Junewick J, Dombrowski K, Woolpert L, Vandop S, Schreiner M, Sutton P, et al. Rate of and factors affecting sonographic visualization of the appendix in asymptomatic children. Emerg Radiol. 2013;20(2):135–8.
22. Mittal MK, Dayan PS, Macias CG, Bachur RG, Bennett J, Dudley NC, et al. Performance of ultrasound in the diagnosis of appendicitis in children in a multicenter cohort. Acad Emerg Med. 2013;20(7):697–702.
23. Cohen B, Bowling J, Midulla P, Shlasko E, Lester N, Rosenberg H, et al. The non-diagnostic ultrasound in appendicitis: is a non-visualized appendix the same as a negative study? J Pediatr Surg [Internet]. 2015;50(6):923–7. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0022346815001839
24. Nah SA, Ong SS, Lim WX, Amuddhu SK, Tang PH, Low Y. Clinical relevance of the nonvisualized appendix on ultrasonography of the abdomen in children. J Pediatr [Internet]. 2017;182:164–169.e1. Available from: https://doi.org/10.1016/j.jpeds.2016.11.062
25. Trout AT, Sanchez R, Ladino-torres MF. Reevaluating the sonographic criteria for acute appendicitis in children : Acad Radiol [Internet] 2012;19(11):1382–94. Available from: https://doi.org/10.1016/j.acra.2012.06.014
26. Kim SH, Choi YH, Kim WS, Cheon JE, Kim IO. Acute appendicitis in children: ultrasound and CT findings in negative appendectomy cases. Pediatr Radiol. 2014;44(10):1243–51.
27. Chang ST, Jeffrey RB, Olcott EW. Three-step sequential positioning algorithm during sonographic evaluation for appendicitis increases appendiceal visualization rate and reduces CT use. AJR Am J Roentgenol. 2014;203(5):1006–12.
28. Alter SM, Walsh B, Lenehan PJ, Shih RD. Ultrasound for diagnosis of appendicitis in a community hospital emergency department has a high rate of nondiagnostic studies. J Emerg Med [Internet]. 2017;52(6):833–8. Available from: https://doi.org/10.1016/j.jemermed.2017.01.003
29. Sivit CJ, Applegate KE, Berlin SC, Myers MT, Stallion A, Dudgeon DL, et al. Evaluation of suspected appendicitis in children and young adults: helical CT. Radiology. 2000;216(2):430–3.
30. Hörmann M, Scharitzer M, Stadler A, Pokieser P, Puig S, Helbich T. Ultrasound of the appendix in children: is the child too obese? Eur Radiol [Internet]. 2003;13(6):1428–31. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12764662
31. Puig S, Staudenherz A, Felder-Puig R, Paya K. Imaging of appendicitis in children and adolescents: useful or useless? A comparison of imaging techniques and a critical review of the current literature. Semin Roentgenol. 2008;43:22–8.
32. Butler M, Servaes S, Srinivasan A, Edgar JC, Del Pozo G, Darge K. US depiction of the appendix: role of abdominal wall thickness and appendiceal location. Emerg Radiol. 2011;18(6):525–31.
33. Yiğiter M, Kantarci M, Yalçin O, Yalçin A, Salman AB. Does obesity limit the sonographic diagnosis of appendicitis in children? J Clin Ultrasound. 2011;39(4):187–90.
34. Gongidi P, Bellah RD. Ultrasound of the pediatric appendix. Pediatr Radiol. 2017;47(9):1091–100.
35. Nielsen JW, Boomer L, Kurtovic K, Lee E, Kupzyk K, Mallory R, et al. Reducing computed tomography scans for appendicitis by introduction of a standardized and validated ultrasonography report template. J Pediatr Surg [Internet]. 2015;50(1):144–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25598112
36. Nordin AB, Sales S, Nielsen JW, Adler B, Bates DG, Kenney B. Standardized ultrasound templates for diagnosing appendicitis reduce annual imaging costs. J Surg Res [Internet]. 2018;221(614):77–83. Available from: https://doi.org/10.1016/j.jss.2017.07.002

37. Fallon SC, Orth RC, Guillerman RP, Munden MM, Zhang W, Elder SC, et al. Development and validation of an ultrasound scoring system for children with suspected acute appendicitis. Pediatr Radiol [Internet]. 2015. Available from: http://link.springer.com/10.1007/s00247-015-3443-4
38. Larson DB, Trout AT, Fierke SR, Towbin AJ. Improvement in diagnostic accuracy of ultrasound of the pediatric appendix through the use of equivocal interpretive categories. AJR Am J Roentgenol [Internet]. 2015;204(4):849–56. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25794076
39. Bachur RG, Dayan PS, Bajaj L, MacIas CG, Mittal MK, Stevenson MD, et al. The effect of abdominal pain duration on the accuracy of diagnostic imaging for pediatric appendicitis. Ann Emerg Med [Internet]. 2012;60(5):582–590.e3. Available from: https://doi.org/10.1016/j.annemergmed.2012.05.034
40. Schuh S, Chan K, Langer JC, Kulik D, Preto-Zamperlini M, Aswad NA, et al. Properties of serial ultrasound clinical diagnostic pathway in suspected appendicitis and related computed tomography use. Acad Emerg Med. 2015;22:1–9.
41. Ramarajan N, Krishnamoorthi R, Barth R, Ghanouni P, Mueller C, Dannenburg B, et al. An interdisciplinary initiative to reduce radiation exposure: evaluation of appendicitis in a pediatric emergency department with clinical assessment supported by a staged ultrasound and computed tomography pathway. Acad Emerg Med. 2009;16(11):1258–65.
42. Krishnamoorthi R, Ramarajan N, Wang NE, Newman B, Rubesova E, Mueller CM, et al. Effectiveness of a staged US and CT protocol for the diagnosis of pediatric appendicitis: reducing radiation exposure in the age of ALARA. Radiology [Internet]. 2011;259(1):231–9. Available from: http://pubs.rsna.org/doi/10.1148/radiol.10100984
43. Saucier A, Huang EY, Emeremni CA, Pershad J. Prospective evaluation of a clinical pathway for suspected appendicitis. Pediatrics [Internet]. 2014;133(1):e88–95. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24379237
44. Luo C-C, Chien W-K, Huang C-S, Lo H-C, Wu S-M, Huang H-C, et al. Trends in diagnostic approaches for pediatric appendicitis: nationwide population-based study. BMC Pediatr [Internet]. 2017;17(1):188. Available from: http://bmcpediatr.biomedcentral.com/articles/10.1186/s12887-017-0940-7
45. Kharbanda AB, Dudley NC, Bajaj L, Stevenson MD, Macias CG, Mittal MK, et al. Validation and refinement of a prediction rule to identify children at low risk for acute appendicitis. Arch Pediatr Adolesc Med [Internet]. 2012;166(8):738–44. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3790639&tool=pmcentrez&rendertype=abstract
46. Anderson K, Bartz-Kurycki M, Austin M, Kawaguchi A, John S, Kao L, et al. Approaching zero: implications of a computed tomography reduction program for pediatric appendicitis evaluation. J Pediatr Surg. 2017;52:1909–15.
47. Otero HJ, Crowder L. Imaging utilization for the diagnosis of appendicitis in stand-alone children's hospitals in the United States: trends and costs. J Am Coll Radiol [Internet]. 2017;1(6). Available from: https://doi.org/10.1016/j.jacr.2016.12.013
48. Lee J, Ko Y, Ahn S, Park JH, Kim HJ, Hwang SS, et al. Comparison of US and CT on the effect on negative appendectomy and appendiceal perforation in adolescents and adults: a post-hoc analysis using propensity-score methods. J Clin Ultrasound. 2016;44(7):401–10.
49. Choi D, Park H, Lee YR, Kook SH, Kim SK, Kwag HJ, et al. The most useful findings for diagnosing acute appendicitis on contrast-enhanced helical CT. Acta Radiol. 2003;44(6):574–82.
50. Garcia K, Hernanz-schulman M, Bennett DL, Morrow SE, Kan JH. Suspected appendicitis in children: diagnostic importance of normal abdominopelvic CT findings with nonvisualized appendix. Radiology. 2009;250(2):531–7.
51. Rentea RM, Peter SDS, Snyder CL. Pediatric appendicitis: state of the art review. Pediatr Surg Int. 2017;33(3):269–83.
52. Acheson J, Banerjee J. Management of suspected appendicitis in children. Arch Dis Child Educ Pract [Internet]. 2010;95(1):9–13. Available from: http://ep.bmj.com/cgi/doi/10.1136/adc.2009.168468
53. Friedland JA, Siegel MJ. CT appearance of acute appendicitis in childhood. Am J Roentgenol. 1997;168(2):439–42.

54. OECD. Number of magnetic resonance imaging (MRI) units and computed tomography (CT) scanners. Health (Irvine Calif) [Internet]. 2010;120:363–4. Available from: http://www.cdc.gov/nchs/data/hus/2010/120.pdf
55. Niles LM, Goyal MK, Badolato GM, Chamberlain JM, Cohen JS. US emergency department trends in imaging for pediatric nontraumatic abdominal pain. Pediatrics [Internet]. 2017;140(4):e20170615. Available from: http://pediatrics.aappublications.org/lookup/doi/10.1542/peds.2017-0615%0A, http://www.ncbi.nlm.nih.gov/pubmed/28916590
56. Reich B, Zalut T, Weiner SG. An international evaluation of ultrasound vs. computed tomography in the diagnosis of appendicitis. Int J Emerg Med. 2011;4(1):1–7.
57. Halverson M, Delgado J, Mahboubi S. Extra-appendiceal findings in pediatric abdominal CT for suspected appendicitis. Pediatr Radiol. 2014;44(7):816–20.
58. Hernanz-Schulman M. CT and US in the diagnosis of appendicitis: an argument for CT. Radiology. 2010;255(1):3–7.
59. Bachur RG, Hennelly K, Callahan MJ, Chen C, Monuteaux MC. Diagnostic imaging and negative appendectomy rates in children: effects of age and gender. Pediatrics [Internet]. 2012;129(5):877–84. Available from: http://pediatrics.aappublications.org/cgi/doi/10.1542/peds.2011-3375
60. Kim K, Kim YH, Kim SY, Kim S, Lee YJ, Kim KP, et al. Low-dose abdominal CT for evaluating suspected appendicitis. N Engl J Med [Internet]. 2012;366(17):1596–605. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMoa1110734
61. Brody AS, Frush DP, Huda W, Brent RL. Radiation risk to children from computed tomography. Pediatrics. 2007;120(3):677–82.
62. Goske M, Applegate K, Frush D, Schulman MH, Morrison G. CT scans in childhood and risk of leukaemia and brain tumours. Lancet [Internet]. 2012;380(9855):1737–8. Available from: https://doi.org/10.1016/S0140-6736(12)61980-1
63. Cohen MD. ALARA, image gently and CT-induced cancer. Pediatr Radiol [Internet]. 2015:465–70. Available from: http://link.springer.com/10.1007/s00247-014-3198-3
64. Nosek AE, Hartin CW, Bass KD, Glick PL, Caty MG, Dayton MT, et al. Are facilities following best practices of pediatric abdominal CT scans? J Surg Res [Internet]. 2013;181(1):11–5. Available from: https://doi.org/10.1016/j.jss.2012.05.036
65. National Cancer Institute. Radiation risks and pediatric computed tomography – National Cancer Institute [Internet]. Society of pediatric radiology. 2012. Available from: http://www.cancer.gov/cancertopics/causes-prevention/risk/radiation/pediatric-ct-scans
66. American Academy of Pediatrics. AAP – No CT scans to evaluate abdominal pain Choosing Wisely [Internet]. Choosing Wisely. 2013. Available from: http://www.choosingwisely.org/clinician-lists/american-academy-pediatrics-ct-scans-to-evaluate-abdominal-pain/
67. National Research Council. 2006. Health risks from exposure to low levels of ionizing radiation: BEIR VII Phase 2. Washington, DC: The National Academies Press. https://doi.org/10.17226/11340.
68. Brenner DJ, Elliston CD, Hall EJ, Berdon WE. Estimated risks of radiation-induced fatal cancer from pediatric CT. AJR. 2001;176(2):289–96.
69. Brenner DJ, Hall EJ. Computed tomography – an increasing source of radiation exposure. N Engl J Med. 2007;357(22):2277–84.
70. Miglioretti DL, Johnson E, Williams A, Greenlee RT, Weinmann S, Solberg LI, et al. The use of computed tomography in pediatrics and the associated radiation exposure and estimated cancer risk. JAMA Pediatr [Internet]. 2013;167(8):700–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23754213
71. Glass CC, Saito JM, Sidhwa F, Cameron DB, Feng C, Karki M, et al. Diagnostic imaging practices for children with suspected appendicitis evaluated at de fi nitive care hospitals and their associated referral centers. J Pediatr Surg [Internet]. 2016;51(6):912–6. Available from: https://doi.org/10.1016/j.jpedsurg.2016.02.055
72. Anderson K, Bartz-Kurycki M, Austin M, Kawaguchi A, Kao LS, Lally KP, et al. Hospital type predicts computed tomography use for pediatric appendicitis. J Pediatr Surg. 2018;54(4):723–7.

73. Tinsley Anderson K, Putnam LR, Caldwell KM, Diffley MB, Hildebrandt AA, Covey SE, et al. Imaging gently? Higher rates of computed tomography imaging for pediatric appendicitis in non–children's hospitals. Surgery [Internet]. 2016;161(5):1326–33. Available from: https://doi.org/10.1016/j.surg.2016.09.042
74. Tian Y, Heiss KF, Wulkan ML, Raval MV. Assessment of variation in care and outcomes for pediatric appendicitis at children's and non-children's hospitals. J Pediatr Surg [Internet]. 2015;50(11):1885–92. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0022346815003905
75. Rice-Townsend S, Barnes JN, Hall M, Baxter JL, Rangel SJ. Variation in practice and resource utilization associated with the diagnosis and management of appendicitis at freestanding children's hospitals: implications for value-based comparative analysis. Ann Surg. 2014;6(259):1228–34. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24096770
76. Anderson KT, Greenfield S, Putnam LR, Hamilton E, Kawaguchi A, Austin MT, et al. Don't forget the dose: improving computed tomography dosing for pediatric appendicitis. J Pediatr Surg. 2016;51:1944–8.
77. Kim ME, Orth RC, Fallon SC, Lopez ME, Brandt ML, Zhang W, et al. Performance of CT examinations in children with suspected acute appendicitis in the community setting: a need for more education. Am J Roentgenol [Internet]. 2015;204(4):857–60. Available from: http://www.ajronline.org/doi/10.2214/AJR.14.12750
78. Miano D, Silvis R, Popp J, Culbertson M, Campbell B, Smith S. Abdominal CT does not improve outcome for children with suspected acute appendicitis. West J Emerg Med. 2015;16(7):974–82.
79. Leeuwenburgh MMN, Jensch S, Gratama JWC, Spilt A, Wiarda BM, Van Es HW, et al. MRI features associated with acute appendicitis. Eur Radiol. 2014;24(1):214–22.
80. Dillman JR, Gadepalli S, Sroufe NS, Davenport MS, Smith EA, Chong ST, et al. Equivocal pediatric appendicitis: unenhanced MR imaging protocol for nonsedated children – a clinical effectiveness study. Radiology [Internet]. 2016;279(1):216–25. Available from: http://pubs.rsna.org/doi/10.1148/radiol.2015150941
81. Johnson AK, Filippi CG, Andrews T, Higgins T, Tam J, Keating D, et al. Ultrafast 3-T MRI in the evaluation of children with acute lower abdominal pain for the detection of appendicitis. Am J Roentgenol. 2012;198(6):1424–30.
82. Kulaylat AN, Moore MM, Engbrecht BW, Brian JM, Khaku A, Hollenbeak CS, et al. An implemented MRI program to eliminate radiation from the evaluation of pediatric appendicitis. J Pediatr Surg. 2015;50(8):1359–63.
83. Orth RC, Guillerman RP, Zhang W, Masand P, Iii GSB. Prospective comparison of MR imaging and US for the diagnosis of pediatric appendicitis. Radiology. 2014;272(1):233–40. Available from: http://pubs.rsna.org/doi/full/10.1148/radiol.14132206
84. Rosines LA, Chow DS, Lampl BS, Chen S, Gordon S, Mui LW, et al. Value of gadolinium-enhanced MRI in detection of acute appendicitis in children and adolescents. Am J Roentgenol [Internet]. 2014;203(5):W543–8. Available from: http://www.ajronline.org/doi/abs/10.2214/AJR.13.12093
85. Khaliq AA, Deyo D, Duszak R. The impact of hospital characteristics on the availability of radiology services at critical access hospitals. J Am Coll Radiol [Internet]. 2015;12(12):1351–6. Available from: https://doi.org/10.1016/j.jacr.2015.09.008
86. Heverhagen JT, Pfestroff K, Heverhagen AE, Klose KJ, Kessler K, Sitter H. Diagnostic accuracy of magnetic resonance imaging: a prospective evaluation of patients with suspected appendicitis (Diamond). J Magn Reson Imaging. 2012;35(3):617–23.
87. Aspelund G, Fingeret A, Gross E, Kessler D, Keung C, Thirumoorthi A, et al. Ultrasonography/MRI versus CT for diagnosing appendicitis. Pediatrics [Internet]. 2014;133(4):586–93. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24590746
88. Zelop CM, Javitt MC, Glanc P, Dubinsky T, Harisinghani MG, Harris RD, et al. ACR Appropriateness Criteria® growth disturbances – risk of intrauterine growth restriction. Ultrasound Q. 2013;29(3):147–51.

89. Rosen MP, Ding A, Blake MA, Baker ME, Cash BD, Fidler JL, et al. ACR appropriateness Criteria® right lower quadrant painsuspected appendicitis. J Am Coll Radiol [Internet]. 2011;8(11):749–55. Available from: https://doi.org/10.1016/j.jacr.2011.07.010
90. Lahaye MJ, Lambregts DMJ, Mutsaers E, Essers BAB, Breukink S, Cappendijk VC, et al. Mandatory imaging cuts costs and reduces the rate of unnecessary surgeries in the diagnostic work-up of patients suspected of having appendicitis. Eur Radiol [Internet]. 2015;25(5):1464–70. Available from: http://link.springer.com/10.1007/s00330-014-3531-0
91. Anandalwar SP, Callahan MJ, Bachur RG, Feng C, Sidhwa F, Karki M, et al. Use of white blood cell count and polymorphonuclear leukocyte differential to improve the predictive value of ultrasound for suspected appendicitis in children. J Am Coll Surg [Internet]. 2015;220(6):1010–7. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1072751515000940
92. Blitman NM, Anwar M, Brady KB, Taragin BH, Freeman K. Value of focused appendicitis ultrasound and alvarado score in predicting appendicitis in children: can we reduce the use of CT? Am J Roentgenol [Internet]. 2015;204(6):W707–12. Available from: http://www.ajronline.org/doi/10.2214/AJR.14.13212
93. Ohle R, O'Reilly F, O'Brien KK, Fahey T, Dimitrov BD. The Alvarado score for predicting acute appendicitis: a systematic review. BMC Med [Internet]. 2011;9(1):139. Available from: http://bmcmedicine.biomedcentral.com/articles/10.1186/1741-7015-9-139
94. Schneider C, Kharbanda A, Bachur R. Evaluating appendicitis scoring systems using a prospective pediatric cohort. Ann Emerg Med. 2007;49(6):778–84.
95. Samuel M. Pediatric appendicitis score. J Pediatr Surg. 2002;37(6):877–81.
96. Toprak H, Kilincaslan H, Ahmad IC, Yildiz S, Bilgin M, Sharifov R, et al. Integration of ultrasound findings with Alvarado score in children with suspected appendicitis. Pediatr Int. 2014;56(1):95–9.
97. Bachur RG, Callahan MJ, Monuteaux MC, Rangel SJ. Integration of ultrasound findings and a clinical score in the diagnostic evaluation of pediatric appendicitis. J Pediatr. 2015;166(5):1134–9.
98. Wagenaar AE, Tashiro J, Wang B, Curbelo M, Mendelson KL, Perez EA, et al. Protocol for suspected pediatric appendicitis limits computed tomography utilization. J Surg Res [Internet]. 2015;199(1):153–8. Available from: https://doi.org/10.1016/j.jss.2015.04.028
99. Woolf S, Schünemann HJ, Eccles MP, Grimshaw JM, Shekelle P. Developing clinical practice guidelines: types of evidence and outcomes; values and economics, synthesis, grading, and presentation and deriving recommendations. Implement Sci [Internet]. 2012;7(1):61. Available from: http://implementationscience.biomedcentral.com/articles/10.1186/1748-5908-7-61
100. Glass CC, Rangel SJ. Overview and diagnosis of acute appendicitis in children. Semin Pediatr Surg [Internet]. 2016;25(4):198–203. Available from: https://doi.org/10.1053/j.sempedsurg.2016.05.001
101. Russell WS, Schuh AM, Hill JG, Hebra A, Cina RA, Smith CD, et al. Clinical practice guidelines for pediatric appendicitis evaluation can decrease computed tomography utilization while maintaining diagnostic accuracy. Pediatr Emerg Care [Internet]. 2013;29(5):568–73. Available from: http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=23611916&retmode=ref&cmd=prlinks
102. Taylor GA, Anderson KT, Greenfield S, Putnam LR, Hamilton E, Kawaguchi A, et al. Cost-effectiveness of diagnostic approaches to suspected appendicitis in children. J Pediatr Surg [Internet]. 2015;220(4):153–8. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1072751514019115
103. Rosendahl K, Aukland SM, Fosse K. Imaging strategies in children with suspected appendicitis. Eur Radiol Suppl [Internet]. 2004;14(4):L138–45. Available from: http://link.springer.com/10.1007/s00330-003-2077-3

104. Imler D, Keller C, Sivasankar S, Wang NE, Vasanawala S, Bruzoni M, et al. MRI vs. Ultrasound as the initial imaging modality for pediatric and young adult patients with suspected appendicitis. Acad Emerg Med. 2017; Epub ahead (accepted author manuscript). https://doi.org/10.1111/acem.13180
105. Wild J, Abdul N, Ritchie J, Bo R, Freels S, Nelson R. Ultrasonography for diagnosis of acute appendicitis (Protocol). Cochrane Database Syst Rev 2013;(2).
106. D'Souza, et al. Cochrane Database of Systematic Reviews Magnetic resonance imaging (MRI) for diagnosis of acute appendicitis (Protocol) Magnetic resonance imaging (MRI) for diagnosis of acute appendicitis (Protocol). Cochrane Database Syst Rev Art [Internet]. 2016;(1). Available from: www.cochranelibrary.com