Received:
28 January 2019

Revised:
09 May 2019

Accepted:
13 May 2019

<https://doi.org/10.1259/bjr.20190102>

Cite this article as:

Rawolle T, Reismann M, Minderjahn M, Bassir C, Hauptmann K, Rothe K, et al. Sonographic differentiation of complicated from uncomplicated appendicitis. *Br J Radiol* 2019; **92**: 20190102.

FULL PAPER

Sonographic differentiation of complicated from uncomplicated appendicitis

¹TANJA RAWOLLE, ¹MARC REISMANN, MD, PhD, ¹MAXIMILIANE I MINDERJAHN, ²CHRISTIAN BASSIR, MD, ³KATHRIN HAUPTMANN, ¹KARIN ROTHE, MD, PhD and ¹JOSEPHINE REISMANN, MD

¹Department of Pediatric Surgery, Charité – Universitätsmedizin Berlin, Augustenburger Platz, Berlin, Germany

²Department of Pediatric Radiology, Charité – Universitätsmedizin Berlin, Augustenburger Platz, Berlin, Germany

³Department of Pathology, Charité – Universitätsmedizin Berlin, Augustenburger Platz, Berlin, Germany

Address correspondence to: Dr Josephine Reismann

E-mail: j.reismann@gmx.de; Josephine.reismann@charite.de

Objective: This study aims to differentiate acute uncomplicated and complicated appendicitis, by investigating the correlation between sonographic findings and histological results in different types of paediatric appendicitis.

Methods: This is a retrospective study of 1017 paediatric patients (age < 18 years) who underwent ultrasound by paediatric radiologists before appendectomy at our institution between 2006 and 2016. Histologically, uncomplicated appendicitis was primarily associated with transmural infiltration of neutrophil granulocytes, while complicated appendicitis was characterised by transmural myonecrosis. Logistic regression analyses were used to investigate the association between sonographic and histological findings.

Results: Out of 566 (56%) male and 451 (44%) female patients with a mean age of 10.7 years, uncomplicated appendicitis was histologically diagnosed in 446 (44%) children and complicated appendicitis was diagnosed in 348 (34%) cases. The following ultrasound findings were significantly associated with complicated appendicitis in multivariate regression: an increased appendiceal diameter (OR = 1.3, $p < .001$), periappendiceal fat inflammation (OR = 1.5, $p = 0.02$), the presence of an

appendicolith (OR = 1.7, $p = 0.01$) and a suspected perforation (OR = 6.0, $p < .001$) by the pediatric radiologist. For complicated appendicitis, an appendiceal diameter of more than 6 mm had the highest sensitivity (98%), while a sonographically suspected perforation showed the highest specificity (94%).

Conclusion: Abdominal sonography by paediatric radiologists can differentiate between uncomplicated and complicated appendicitis in paediatric patients by using an increased appendiceal diameter, periappendiceal fat inflammation, the presence of an appendicolith and a suspected perforation as discriminatory markers.

Advances in knowledge: This paper demonstrates expanded information on ultrasound, which is not only an essential tool for diagnosing appendicitis, but also a key method for distinguishing between different forms of appendicitis when performed by paediatric radiologists. Compared with previous studies, the crucial distinction features in our analysis are 1) the definition of gangrene and not primarily perforation as an acute complicated appendicitis enabling early decision-making by sonography and 2) a large number of patients in a particularly affected age group.

INTRODUCTION

The distinction between different forms of acute appendicitis (AA)^a through the use of abdominal ultrasound by (paediatric) radiologists will become more important in the near future due to the fact that epidemiological and immunological studies strongly support the view that histologically phlegmonous appendicitis (corresponding to clinical acute uncomplicated appendicitis; AUA^b) and histologically gangrenous appendicitis possibly leading to perforation (corresponding to clinical acute complicated appendicitis; ACA^c) seem to be independent entities.^{1–5}

The differentiation is relevant for various reasons. Early detection of complicated appendicitis including gangrene with or without perforation is crucial for timely application of special antibiotic regimens and for estimation of the optimal time point for surgery.⁶ Furthermore, this kind of differentiation might even offer the possibility of different treatment options. Nowadays, acute appendicitis is the most common diagnosis of paediatric patients who undergo surgical treatment and patients still experience a remarkably high rate of postoperative complications, despite the fact that most of the procedures are performed

laparoscopically.^{7–9} However, recent and upcoming paediatric studies have confirmed or the aim to support that nonoperative management with antibiotics is a feasible and safe option for patients with acute uncomplicated phlegmonous appendicitis while appendectomy remains the appropriate treatment for acute complicated appendicitis defined by gangrene or perforation.^{10–15} Of note, conservative treatment leads to symptom relief just after one day and thus is not inferior to appendectomy concerning this matter.¹⁶ Therefore, the use of ultrasound for the pre-operative differentiation between gangrenous/perforated appendicitis and uncomplicated appendicitis is important, especially in regard of defining treatment groups.

Different studies tried to preoperatively distinguish AUA and ACA by means of imaging methods as MRI or CT. Even if these methods achieved high specificity values between 85 and 99% for detecting perforated appendicitis, they were associated with either radiation exposure or injection of a contrast medium.^{17,18} However, ultrasound is considered to be the most appropriate imaging method to diagnose paediatric AA with a specificity greater than 98%.¹⁹ Moreover, ultrasound was recently shown to be a reliable imaging method to differentiate between perforated and non-perforated appendicitis by means of highly specific findings like the loss of the echogenic submucosal layer and complex periappendiceal fluid.^{20–22} Blumfield et al presented a score combining laboratory values, clinical presentations and ultrasound findings that yielded specificity for ACA of up to 99%.²³ However, these authors concentrated on the differentiation of perforated and non-perforated appendicitis, while current evidence suggests that complicated appendicitis is already given earlier in the pathophysiological process by the presence of transmural myonecrosis.⁶ The present study aims to investigate ultrasound as a discriminatory tool to differentiate between acute uncomplicated appendicitis and acute complicated appendicitis. The outstanding importance of this paper is demonstrated by the extended number of exclusively paediatric and adolescent patients.

^a acute appendicitis

^b acute uncomplicated appendicitis

^c acute complicated appendicitis

METHODS

This is a single-center retrospective study of all patients aged 0–17 years who underwent ultrasound for suspected acute appendicitis at the department of paediatric surgery of Charité Universitätsmedizin Berlin, Germany between December 2006 and September 2016. Our institutional review board and the ethical committee approved this study.

Study population

Eligible participants were identified by searching our hospital information system for all paediatric patients who underwent appendectomy. Medical charts of all patients who received ultrasound examinations before appendectomy were reviewed for gender, age, date of admission, date of operation, histopathology

and ultrasound findings. Exclusion criteria consisted of missing histopathology, missing data, secondary or elective appendectomy, oxyuriasis and carcinoid (Figure 1).

Ultrasound examination

All ultrasound examinations were performed or directly supervised by experienced consultant paediatric radiologists, who were all members of the board, in case of suspected appendicitis. Radiologists had access to the medical charts and anamnesis of patients. The abdominal sonography was performed with a convex or linear transducer (1 and 12 MHz) adapted to the patient's body constitution. The radiologists' reports were analysed for ultrasonographic features standardly examined and according to previous studies, including the following: the appendiceal wall diameter, periappendiceal fat inflammation, free abdominal fluid, abscess, conglomerate, appendicolith and lymphadenitis.^{20–24} Therefore, the appendiceal diameter was measured from outer wall to outer wall. Appendiceal wall oedema was defined as an obliteration of the layers. Periappendiceal fat inflammation was diagnosed when an increased echogenicity of the periappendiceal tissue was observed. Free abdominal fluid was defined as both simple and complex localised fluid, whether in direct proximity of the appendix or not, whereas an abscess was diagnosed when a walled-off accumulation of periappendiceal fluid was identified. Conglomerate was defined as an appendix grouped together with or indistinguishable from other intestinal structures. An appendicolith was diagnosed when an intraluminal hyperechogenic focus with an acoustic shadow was identified. Lymphadenitis was defined as sonographically detectable lymph nodes. In some cases the radiologist documented a suspected perforation due to the overall composition of pathological changes. During the review process, vague ultrasound reports were discussed with the most experienced radiologist to classify the ultrasound findings according to our categories.

Histopathological classification

Histopathological analyses were retrospectively reviewed to classify appendicitis. The following three groups of appendicitis were differentiated: phlegmonous, gangrenous and perforated appendicitis. Phlegmonous appendicitis was defined by transmural neutrophilic infiltration of the appendix without gangrene or perforation. Gangrenous appendicitis was characterised by ischemic areas with transmural myonecrosis, while perforation was defined by the presence of a transmural defect.²⁵ In clinical settings the histological finding of phlegmonous appendicitis directly corresponds with uncomplicated courses (AUA), whereas gangrenous appendicitis and perforation are categorised as acute complicated appendicitis (ACA), as stated in the literature.^{6,25}

Correlations between ultrasound findings and histopathological results are visualised in Figure 2.

Statistical analysis

Categorical variables are reported as frequencies and percentages, whereas continuous variables are given as mean $\pm$ standard deviation (SD) values. Age is given as mean and range. Univariate logistic regression analysis was performed on each

Figure 1. Patient flow diagram.

sonographic finding regarding the histopathological diagnosis of acute complicated appendicitis. To determine a proper model for the multivariate regression analysis a backward variable elimination algorithm was performed based on the $-2 \times \text{Log-Likelihood}$ criterion where variables with $p \geq 0.1$ were eliminated. For this reason, only the following five variables were included in the multivariate regression: the appendiceal wall diameter, periappendiceal fat inflammation, conglomerate, the presence of an appendicolith and a suspected perforation. Results are presented as Odds Ratios (OR) with a confidence interval of 95%. Sensitivity, specificity, positive and negative predictive value for each sonographic finding were calculated. Data was statistically analysed with SPSS (IBM) version 25. Significant differences were defined by a corrected error probability of $p \leq 0.05$.

Since the study is retrospective and observational, we did not perform a sample size calculation (power analysis) before the commencement of the study. However, with a sample size of $n =$

794 patients ($n = 446$ with AUA; $n = 348$ with ACA) the study has sufficient statistical power to detect small effect sizes. Assuming that for a binary variable X the probability $P(\text{complicated} | X = 0) = 0.438$ (relative frequency of cases with complicated appendicitis) the Wald test (logistic regression) has a power of more than 80% to detect an odds ratio $OR = (P(\text{complicated} | X = 1) / P(\text{not complicated} | X = 1)) / (P(\text{complicated} | X = 0) / P(\text{not complicated} | X = 0))$ of $OR = 1.492$. The test is two-sided and the level of significance is $\alpha = 0.05$. The power analysis was carried out using the software PASS 16.

RESULTS

Patient sample

1017 out of 1102 patients who received ultrasound due to suspected acute appendicitis (AA) and who underwent appendicectomy, met the inclusion criteria (566 (56%) male and 451 (44%) female patients). Patients were excluded from further

Figure 2. Negative: a: normal sonography of appendix; b: normal histopathological conditions with normal wall structure and no signs of inflammation. Phlegmonous (= acute uncomplicated appendicitis): c: appendix with marked echogenic reaction; d: diffuse granulocytic infiltration of the wall into the subserous fatty tissue and the mesenterium. Gangrenous (= acute complicated appendicitis): e: wall oedema, beginning fragmentation of the wall structure; f: microabscesses in the wall and circumscribed almost complete wall necrosis. Severe fibrinous-purulent serositis. Fibrinous-purulent inflammation of adjacent fatty tissue.

analysis due to secondary appendicectomies ($n = 34$), missing histopathology ($n = 21$), missing data ($n = 12$), elective appendectomy ($n = 8$), oxyuriasis ($n = 4$) and carcinoids ($n = 6$) (Figure 1). Histopathologically 794 (78%) cases provided a diagnosis of acute appendicitis including 446 (56%) patients with AUA and 348 (44%) children with ACA. The negative appendectomy rate was 22% ($n = 223$).

The patients mean age was 10.7 (0–17) years. In comparison, patients suffering from AA (AUA and ACA) were significantly younger than patients, who turned out to be negative (10.2 (0–17) vs 12.3 (1–17), $p < .001$). It was more common for male patients to be diagnosed with histopathological proven AA than female patients ($n = 477$, 60% vs $n = 317$, 40%, $p < .001$), while gender composition in patients with negative histology was reversed (male: $n = 88$, 39% vs female: $n = 135$, 61%, $p < .001$).

The appendix was sonographically detectable in 862 (85%) patients, whereby radiologists were significantly less successful in locating the appendix in patients with negative histology as with AA ($n = 54$, 24% vs $n = 101$, 13%; $p < .001$). There were also significant differences between both groups (AA vs negative histology) regarding mean appendiceal diameter values (9.8 ± 2.5 mm vs 7.2 ± 1.6 mm, $p < .001$). The sonographers expected a phlegmon in 180 (18%) patients, which was 48% consistent with the histopathological diagnosis. In 145 (14%) cases, radiologists suspected a perforation matching 67% ($n = 97$) with the histopathological result. In 692 (68%) sonographic reports the radiologists did not differentiate between AUA and ACA (Table 1).

Acute complicated appendicitis

Patients with ACA ($n = 348$) included 270 (78%) cases with histopathologically diagnosed perforation and 78 (22%) cases in which a gangrenous appendix was identified. Mean age of ACA was 9.4 years (0–17) and was thus significantly younger than the mean age of patients with AUA (10.9 (1–17), $p < .001$). The gender composition was comparable in both groups (ACA vs AUA). The mean appendiceal diameter of patients with ACA was significantly increased compared to that of patients with AUA (10.5 ± 2.6 mm vs 9.3 ± 2.2 mm, $p < .001$) (Table 1).

To identify associations between sonographic findings and ACA, univariate and multivariate logistic regression analyses were performed. In univariate logistic regression, the following sonographic findings were significantly associated with ACA: an increased appendiceal diameter (OR = 1.3, $p < .001$), periappendiceal fat inflammation (OR = 2.3, $p < .001$), free abdominal fluid (OR = 1.4, $p = 0.02$), abscess (OR = 14.0, $p < .001$), conglomerate (OR = 17.7, $p < .001$), appendicolith (OR = 2.3, $p < .001$) and the suspicion of a perforation expressed by the radiologist (OR = 8.8, $p < .001$) (Table 2).

Table 1. Distribution of age, sex and sonographic findings

Characteristic	Total ($n = 1017$)	AA ($n = 794$)	AUA ($n = 446$)	ACA ($n = 348$)	Negative ($n = 223$)
Age (years)	10.7 (0–17)	10.2 (0–17)	10.9 (1–17)	9.4 (0–17)	12.3 (1–17)
Sex					
Male	566 (56%)	478 (60%)	263 (59%)	215 (62%)	88 (40%)
Female	451 (44%)	316 (40%)	183 (41%)	133 (38%)	135 (60%)
Appendiceal wall diameter (mm)	9.3 ± 2.5	9.8 ± 2.5	9.3 ± 2.2	10.5 ± 2.6	7.2 ± 1.6
Appendiceal wall oedema	74 (7%)	68 (9%)	42 (9%)	26 (7%)	6 (3%)
Periappendiceal fat inflammation	452 (44%)	426 (54%)	225 (51%)	201 (58%)	26 (12%)
Free abdominal fluid	419 (41%)	348 (44%)	187 (42%)	161 (46%)	71 (32%)
Abscess	16 (2%)	16 (2%)	2 (<1%)	14 (4%)	0
Conglomerate	10 (1%)	10 (1%)	1 (<1%)	9 (3%)	0
Appendicolith	135 (13%)	124 (16%)	54 (12%)	70 (20%)	11 (5%)
Lymphadenitis	165 (16%)	132 (17%)	79 (18%)	53 (15%)	33 (15%)

AA: acute appendicitis, AUA: acute uncomplicated appendicitis, ACA: acute complicated appendicitis.

Table 2. Sonographic findings and associations with acute complicated appendicitis ($n = 348$) in 1017 patients with suspected acute appendicitis

Sonographic finding	Univariate Logistic Regression		Multivariate Logistic Regression ^a	
	<i>P</i> -value	OR (95% CI)	<i>P</i> -value	OR (95% CI)
Appendiceal wall diameter a	<.001	1.34 (1.26–1.43)	<.001	1.27 (1.18–1.36)
Appendiceal wall oedema	0.86	1.05 (0.64–1.71)		
Periappendiceal fat inflammation	<.001	2.28 (1.75–2.97)	0.02	1.51 (1.08–2.11)
Free abdominal fluid	0.02	1.37 (1.06–1.78)		
Abscess	<.001	13.98 (3.16–61.86)		
Conglomerate	<.001	17.74 (2.24–140.56)	0.11	6.66 (0.66–67.51)
Appendicolith	<.001	2.34 (1.62–3.38)	0.01	1.73 (1.12–2.67)
Lymphadenitis	0.54	0.89 (0.63–1.28)		
Expected perforation	<.001	8.75 (5.79–13.21)	<.001	6.03 (3.78–9.62)

P values are specified to two significant digits unless <.001. OR: odds ratio.

^a $n = 862$ patients with sonographically detectable appendixes.

In multivariate analysis, statistically significant positive associations with ACA were only found for an increased appendiceal diameter (OR = 1.3, $p < .001$), periappendiceal fat inflammation (OR = 1.5, $p = 0.02$), the presence of an appendicolith (OR = 1.7, $p = 0.01$) and a suspected perforation by the paediatric radiologist (OR = 6.0, $p < .001$) among the sonographic findings examined (Table 2).

The highest sensitivity (98%) of all investigated parameters that were significantly associated with ACA had an appendiceal diameter of more than 6 mm, whereas specificity (11%) is very low for this characteristic. Higher specificity values are observed with increasing appendiceal diameters (>6 mm) at the expense of sensitivity values. The most specific (94%) sonographic finding

of ACA is an expected perforation by the paediatric radiologist (Table 3). The concordance rate of a suspected perforation by the paediatric radiologist and histopathology was 67% ($n = 97$). However, the remaining 33% ($n = 48$) had the following histopathological results: 20% ($n = 29$) phlegmonous appendicitis, 10% ($n = 14$) gangrenous appendicitis and 3% ($n = 5$) negative histopathology.

DISCUSSION

The differentiation between AUA and ACA aroused new interest due to recent studies indicating that an antibiotic-only treatment for children with AUA is safe.^{10,13} Therefore, imaging modalities seem to be a suitable method to accomplish a reliable distinction between AUA and ACA. Moreover,

Table 3. Sensitivity and specificity values of sonographic findings for acute complicated appendicitis

Sonographic finding	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Appendiceal wall diameter				
>5 mm	99.4 (97.4,99.9)	2.1 (1.2,3.5)	34.6 (34.3,34.9)	87.5 (61.5,96.8)
>6 mm	98.0 (95.9,99.2)	11.4 (9.1,14.0)	36.5 (25.8,37.2)	91.6 (83.5,95.9)
>7 mm	94.5 (91.6,96.7)	25.7 (22.4,29.2)	39.8 (38.6,41.1)	90.1 (85.2,93.5)
>8 mm	81.9 (77.4,85.8)	43.9 (40.1,47.8)	43.2 (41.2,45.2)	82.4 (78.6,85.6)
>9 mm	68.1 (62.9,73.0)	58.1 (54.3,61.9)	45.8 (43.0,48.7)	77.8 (74.8,80.5)
Appendiceal wall oedema	7.5 (4.9,10.8)	92.8 (90.6,94.7)	35.1 (25.5,46.2)	65.9 (65.0,66.7)
Periappendiceal fat inflammation	57.8 (52.4,63.0)	62.5 (58.5,66.1)	44.5 (41.2,47.8)	74.0 (71.3,76.5)
Free abdominal fluid	46.3 (40.9,51.7)	61.4 (57.6,65.1)	38.4 (35.0,42.0)	68.7 (66.2,71.1)
Abscess	4.0 (2.2,6.7)	99.7 (98.9,100)	87.5 (61.5,96.8)	66.6 (66.1,67.1)
Conglomerate	2.6 (1.2,4.9)	99.9 (99.2,100)	90.0 (53.4,98.6)	66.3 (66.0,66.7)
Appendicolith	20.1 (16.0,24.7)	90.3 (87.8,92.4)	51.9 (44.1,59.5)	68.5 (67.2,69.7)
Lymphadenitis	15.2 (11.6,19.4)	83.3 (80.2,86.0)	32.1 (26.0,39.0)	65.3 (64.1,66.6)
Expected perforation	31.9 (27.0,37.1)	94.9 (93.9,96.5)	76.6 (69.5,82.4)	72.8 (71.3,74.3)

NPV, negative predictive value; PPV, positive predictive value.

Data in parentheses are the 95% confidence interval.

ultrasound as a radiation-free tool is the imaging method of choice for evaluating paediatric patients with suspected AA and was even shown to be useful to improve diagnostic accuracy of advanced imaging methods like CT.²⁶ Accordingly, this study has a focus on the ultrasonographic findings in different forms of appendicitis in a great cohort of paediatric patients. Advantageously, this study only took into account ultrasound reports performed by highly trained paediatric radiologists to support the diagnostic process. Whereas most hospitals rely on ultrasound by emergency physicians with different levels of experience, which could lead to inconclusive results as well as limited sensitivity and specificity.²⁷ Thus, we hoped to identify sonographic findings that could broaden the approach and aid differentiation between uncomplicated and complicated appendicitis, including gangrenous and perforated appendicitis.

Firstly, we were able to confirm that in multivariate analysis, an increased appendiceal diameter and the presence of an appendicolith are significantly associated with acute complicated appendicitis. Furthermore, in comparison to studies with much smaller patient numbers, we were able to add the fact that periappendiceal fat inflammation was significantly associated with an acute complicated appendicitis.^{20,21} On top of that, we could gain evidence that the preoperatively suspected histological categorisation (perforation) of appendicitis determined by a paediatric radiologist using ultrasound is a highly specific diagnostical component.

Moreover, our study confirmed that an appendiceal diameter greater than 6 mm achieved the highest sensitivity for ACA (98%). On the other hand, specificity was quite insufficient (11%). In addition, appendiceal diameter values of patients with negative appendicectomy ranged from 2 to 13 mm, which indicates that relying on an appendiceal diameter greater than 6 mm could lead to appendicectomy not only in patients with uncomplicated appendicitis, but also in children without appendicitis. Moreover, Park *et al* observed that faecal impaction of the appendix leads to misdiagnosis of acute appendicitis by increasing the appendiceal diameter without any inflammation as well.²⁸ This points out that a critical value of the appendiceal diameter for appendicitis is not feasible, although a 6 mm diameter is frequently defined as the diagnostic cutoff for appendicitis.¹⁹ However, specificity can be improved by increasing appendiceal diameter values to the detriment of sensitivity values.

Most interestingly, in this study periappendiceal fat inflammation was significantly associated with ACA, whereas previous studies could only suggest a positive association with perforation without significance.^{20,21} This might be primarily attributable to the substantially greater study population investigated in this research. Besides, the inclusion of gangrenous appendicitis as complicated appendicitis versus only perforation could have an effect. This would be compatible with the results of Xu *et al*, who suggested associations between periappendiceal fat inflammation and ACA including gangrene - but without statistical significance in a small study group.²⁴

The presence of an appendicolith was a highly specific (90%) sonographic finding for ACA. The importance of detecting appendicoliths as a sign of ACA was also promoted by Mahida *et al* who reported a failure rate of 60% for conservative treatment of children with an appendicolith.²⁹ Moreover, Gonzalez *et al* already suggested that ultrasound is a reliable test to identify complicated appendicitis and patients with appendicoliths (sensitivity: 58%; specificity: 78%) to exclude them from nonoperative treatment.³⁰ Interestingly, our study's data showed that children with appendicoliths were significantly younger than those without appendicoliths (9.6 (1–17) vs 10.8 (0–17) years, $p < .001$), which was consistent with age groups comparing ACA and AUA (9.4 (0–17) vs 10.9 (1–17) years, $p < .001$). This fact validated the presence of an appendicolith to be a key criterion for differentiating complicated from uncomplicated appendicitis.

Besides, our study investigated the predictive value of the radiologist's tentative diagnosis of perforation for the first time to show whether it is feasible to rely on the assessment of highly trained paediatric radiologists. We were able to demonstrate that a suspected perforation was significantly associated with ACA with a sensitivity of 32% and specificity of 94%. The concordance rate of a suspected perforation by the paediatric radiologist and histopathology was 67%. However, the remaining patients had a phlegmonous appendicitis ($n = 29$), a gangrenous appendicitis ($n = 14$), or negative histopathology ($n = 5$). Because only 32% of ultrasound reports contained a tentative diagnosis of the radiologist, the true significance of this finding is unclear and needs to be verified in prospective studies.

Loss of the echogenic submucosal layer was a reproducible sonographic finding associated with perforation in previous studies.^{21,24} Xu *et al* even demonstrated that this characteristic is not only a sign of perforation, but also an indication of ACA including appendiceal gangrenes.²⁴ By evaluating the appendiceal wall oedema, we could not support these results.

An interesting finding in our study was the mean negative appendicectomy rate of 21.8%. This was due to the overestimation of clinical signs of appendicitis in the first years of the retrospective study period (maximum 28.5% in 2009). The negative appendicectomy rate was able to be substantially reduced down to 11.1% in the year 2015 through the use of primarily ultrasound-based decision making. This finding emphasizes the value of ultrasound investigation within the diagnostic process and decision making in appendicitis as a central imaging tool.

Our study has some limitations: First of all, this study was limited by its retrospective design so that ultrasound findings might not have been reported in full detail. Secondly, the investigated parameters were not standardised. Moreover, our retrospective analysis was limited due to the fact that the radiologists looked for signs of acute appendicitis without the need to specify different entities. Due to these limitations of our study, we plan a prospective study with a standardised investigation sheet. Hereby, we plan to simultaneously offer the possibility to investigate if there were other factors the radiologists considered to differentiate between the types of appendicitis, which led to

the high specificity of their prognosis. We hope to be able to add more information on ultrasound findings, for instance appendiceal intraluminal fluid in ultrasound examinations as this feature was considered important for differentiating between AUA and ACA.¹⁵

CONCLUSION

In conclusion, our results show that ultrasound is not only helpful for differentiating between unperforated and perforated appendicitis, but also plays an important role in predicting complicated appendicitis including gangrenes and perforation. Not only are factors such as an increased appendiceal diameter, periappendiceal fat inflammation and the presence of an appendicolith significantly associated with ACA, but so is a

sonographically suspected perforation conducted by a paediatric radiologist. Therefore, all of the afore mentioned can act as major guiding characteristics for a physician when planning adequate treatment.

ACKNOWLEDGMENT

The authors want to thank Konrad Neumann, Department of Biometry and Clinical Epidemiology, Charité – Universitätsmedizin Berlin (Germany) for his support with statistics.

FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

REFERENCES

- Rubér M, Andersson M, Petersson BF, Olaison G, Andersson RE, Ekerfelt C. Systemic Th17-like cytokine pattern in gangrenous appendicitis but not in phlegmonous appendicitis. *Surgery* 2010; **147**: 366–72. doi: <https://doi.org/10.1016/j.surg.2009.09.039>
- Reismann J, Schädlich D, Minderjahn MI, Rothe K, Reismann M. Eosinophilia in pediatric uncomplicated appendicitis is a time stable pattern. *Pediatr Surg Int* 2019; **35**: 335–340Epub ahead of print. doi: <https://doi.org/10.1007/s00383-018-4423-1>
- Minderjahn MI, Schädlich D, Radtke J, Rothe K, Reismann M. Phlegmonous appendicitis in children is characterized by eosinophilia in white blood cell counts. *World J Pediatr* 2018; **14**: 504–9. doi: <https://doi.org/10.1007/s12519-018-0173-3>
- Rubér M, Berg A, Ekerfelt C, Olaison G, Andersson RE. Different cytokine profiles in patients with a history of gangrenous or phlegmonous appendicitis. *Clin Exp Immunol* 2006; **143**: 117–24. doi: <https://doi.org/10.1111/j.1365-2249.2005.02957.x>
- Andersson R, Hugander A, Thulin A, Nyström PO, Olaison G. Indications for operation in suspected appendicitis and incidence of perforation. *BMJ* 1994; **308**: 107–10. doi: <https://doi.org/10.1136/bmj.308.6921.107>
- Imaoka Y, Itamoto T, Takakura Y, Suzuki T, Ikeda S, Urushihara T. Validity of predictive factors of acute complicated appendicitis. *World J Emerg Surg* 2016; **11**: 1–5. doi: <https://doi.org/10.1186/s13017-016-0107-0>
- Rentea RM, Peter SDS, Snyder CL. Pediatric appendicitis: state of the art review. *Pediatr Surg Int* 2017; **33**: 269–83. doi: <https://doi.org/10.1007/s00383-016-3990-2>
- Rentea RM, St Peter SD. Contemporary management of appendicitis in children. *Adv Pediatr* 2017; **64**: 225–51. doi: <https://doi.org/10.1016/j.yapd.2017.03.008>
- Linnaus ME, Ostlie DJ. Complications in common General pediatric surgery procedures. *Semin Pediatr Surg* 2016; **25**: 404–11. doi: <https://doi.org/10.1053/j.sempedsurg.2016.10.002>
- Svensson JF, Patkova B, Almström M, Naji H, Hall NJ, Eaton S, et al. Nonoperative treatment with antibiotics versus surgery for acute nonperforated appendicitis in children: a pilot randomized controlled trial. *Ann Surg* 2015; **261**: 67–71. doi: <https://doi.org/10.1097/SLA.0000000000000835>
- López JJ, Deans KJ, Minneci PC. Nonoperative management of appendicitis in children. *Curr Opin Pediatr* 2017; **29**: 358–62. doi: <https://doi.org/10.1097/MOP.0000000000000487>
- Steiner Z, Buklan G, Gutermacher M, Litmanovitz I, Landa T, Arnon S. Conservative antibiotic treatment for acute uncomplicated appendicitis is feasible. *Pediatr Surg Int* 2018; **34**: 283–8. doi: <https://doi.org/10.1007/s00383-018-4226-4>
- Hartwich J, Luks FI, Watson-Smith D, Kurkchubasche AG, Muratore CS, Wills HE, et al. Nonoperative treatment of acute appendicitis in children: a feasibility study. *J Pediatr Surg* 2016; **51**: 111–6. doi: <https://doi.org/10.1016/j.jpedsurg.2015.10.024>
- Hall NJ, Eaton S, Abbo O, Arnaud AP, Beaudin M, Brindle MZani A, Davies D, Skarsgard E, et al. Appendectomy versus non-operative treatment for acute uncomplicated appendicitis in children: study protocol for a multicentre, open-label, non-inferiority, randomised controlled trial. *BMJ Paediatr Open* 2017; **118** 05 2017. doi: <https://doi.org/10.1136/bmjpo-2017-000028>
- Steiner Z, Buklan G, Stackiewicz R, Gutermacher M, Litmanovitz I, Golani G, et al. Conservative treatment in uncomplicated acute appendicitis: reassessment of practice safety. *Eur J Pediatr* 2017; **176**: 521–7. doi: <https://doi.org/10.1007/s00431-017-2867-2>
- Knaapen M, van der Lee JH, Heij HA, van Heurn ELW, Bakx R, Gorter RR. Clinical recovery in children with uncomplicated appendicitis undergoing non-operative treatment: secondary analysis of a prospective cohort study. *Eur J Pediatr* 2019; **178**: 235–42. doi: <https://doi.org/10.1007/s00431-018-3277-9>
- Kim MS, Park HW, Park JY, Park H-J, Lee S-Y, Hong HP, et al. Differentiation of early perforated from nonperforated appendicitis: MDCT findings, MDCT diagnostic performance, and clinical outcome. *Abdom Imaging* 2014; **39**: 459–66. doi: <https://doi.org/10.1007/s00261-014-0117-x>
- Rosenbaum DG, Askin G, Beneck DM, Kovanlikaya A. Differentiating perforated from non-perforated appendicitis on contrast-enhanced magnetic resonance imaging. *Pediatr Radiol* 2017; **47**: 1483–90. doi: <https://doi.org/10.1007/s00247-017-3900-3>
- Gongidi P, Bellah RD. Ultrasound of the pediatric appendix. *Pediatr Radiol* 2017; **47**: 1091–100. doi: <https://doi.org/10.1007/s00247-017-3928-4>
- Carpenter JL, Orth RC, Zhang W, Lopez ME, Mangona KL, Guillerman RP. Diagnostic performance of US for differentiating perforated from Nonperforated pediatric appendicitis: a prospective cohort study. *Radiology* 2017;

- 282: 835–41. doi: <https://doi.org/10.1148/radiol.2016160175>
21. Blumfield E, Nayak G, Srinivasan R, Muranaka MT, Blitman NM, Blumfield A, et al. Ultrasound for differentiation between perforated and nonperforated appendicitis in pediatric patients. *AJR Am J Roentgenol* 2013; **200**: 957–62. doi: <https://doi.org/10.2214/AJR.12.9801>
22. Tulin-Silver S, Babb J, Pinkney L, Strubel N, Lala S, Milla SS, et al. The challenging ultrasound diagnosis of perforated appendicitis in children: constellations of sonographic findings improve specificity. *Pediatr Radiol* 2015; **45**: 820–30. doi: <https://doi.org/10.1007/s00247-014-3232-5>
23. Blumfield E, Yang D, Grossman J. Scoring system for differentiating perforated and non-perforated pediatric appendicitis. *Emerg Radiol* 2017; **24**: 547–54. doi: <https://doi.org/10.1007/s10140-017-1535-1>
24. Xu Y, Jeffrey RB, Chang ST, DiMaio MA, Olcott EW. Sonographic differentiation of complicated from uncomplicated appendicitis: implications for Antibiotics-First therapy. *J Ultrasound Med* 2017; **36**: 269–77. doi: <https://doi.org/10.7863/ultra.16.03109>
25. Fallon SC, Kim ME, Hallmark CA, Carpenter JL, Eldin KW, Lopez ME, et al. Correlating surgical and pathological diagnoses in pediatric appendicitis. *J Pediatr Surg* 2015; **50**: 638–41. doi: <https://doi.org/10.1016/j.jpedsurg.2014.11.001>
26. Kim MS, Kwon H-J, Kang KA, Do I-G, Park H-J, Kim EY, et al. Diagnostic performance and useful findings of ultrasound re-evaluation for patients with equivocal CT features of acute appendicitis. *Br J Radiol* 2018; **91**: 20170529. doi: <https://doi.org/10.1259/bjr.20170529>
27. Nicole M, Desjardins MP, Gravel J. Bedside sonography performed by emergency physicians to detect appendicitis in children. *Acad Emerg Med* 2018; **25**: 1035–41. doi: <https://doi.org/10.1111/acem.13445>
28. Park NH, Park CS, Lee EJ, Kim MS, Ryu JA, Bae JM, et al. Ultrasonographic findings identifying the faecal-impacted appendix: differential findings with acute appendicitis. *Br J Radiol* 2007; **80**: 872–7. doi: <https://doi.org/10.1259/bjr/80553348>
29. Mahida JB, Lodwick DL, Nacion KM, Sulkowski JP, Leonhart KL, Cooper JN, et al. High failure rate of nonoperative management of acute appendicitis with an appendicolith in children. *Journal of Pediatric Surgery* 2016; **51**: 908–11. doi: <https://doi.org/10.1016/j.jpedsurg.2016.02.056>
30. Gonzalez DO, Lawrence AE, Cooper JN, Sola R, Garvey E, Weber BC, et al. Can ultrasound reliably identify complicated appendicitis in children? *J Surg Res* 2018; **229**: 76–81. doi: <https://doi.org/10.1016/j.jss.2018.03.012>