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FULL PAPER

MRI of suspected appendicitis during pregnancy: interradiologist agreement, indeterminate interpretation and the meaning of non-visualization of the appendix

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Objective: To determine the degree of interradiologist agreement between the MRI features of appendicitis during pregnancy, the outcomes associated with an indeterminate interpretation and the negative predictive value of non-visualization of the appendix.

Methods: Our study was approved by the institutional review board at the Washington University in St. Louis, Missouri (WUSTL) and was HIPAA (Health Insurance Portability and Accountability Act of 1996)-compliant. The informed consent requirement was waived. Cases of suspected appendicitis during pregnancy evaluated using MRI were retrospectively identified using search queries. Scans were re-reviewed by two radiologists (7 and 9 years experience, respectively) to evaluate the interradiologist agreement of different MRI features of appendicitis during pregnancy (visualization of the appendix, appendiceal diameter, appendiceal wall thickening, periappendiceal fat stranding, fluid-filled appendix and periappendiceal fluid). The radiologists were blinded to patient outcome, patient intervention, laboratory data, demographic data and the original MRI reports. Clinical outcomes were documented by surgical pathology or clinical observation. Interradiologist agreement was analysed using Cohen's κ , while patient demographic and clinical data was analysed using Student's *t*-testing.

Results: 233 females with suspected appendicitis during pregnancy were evaluated using MRI over a 13-year period (mean age, 28.4 years; range, 17–38 years). There were 14 (6%) positive examinations for appendicitis during pregnancy, including 1 patient whose MRI was interpreted as negative, proven by surgical pathology. The presence of periappendiceal soft-tissue stranding and the final overall impression had the most interradiologist agreement ($\kappa = 0.81$ – 1). There were no pregnant patients found to have acute appendicitis who had an indeterminate MR interpretation or when the appendix could not be visualized.

Conclusion: The final impression by the two retrospectively reviewing radiologists of MR examinations performed for suspected appendicitis during pregnancy had near-perfect agreement. In patients where the appendix could not be visualized or in patients that were interpreted as indeterminate, no patients had acute appendicitis.

Advances in knowledge: MR impression for suspected appendicitis in the pregnant patient has high interradiologist agreement, and a non-visualized appendix or lack of inflammatory findings at the time of MR, reliably excludes surgical appendicitis.

INTRODUCTION

Appendicitis is the most common non-obstetric surgical emergency encountered in pregnant patients.^{1,2} Unfortunately, in the pregnant patient, the diagnosis of appendicitis is often clinically difficult owing to normal laboratory and physiological alterations as well as the broad range of symptomology seen during normal pregnancy.^{3–5} In addition, cranial displacement of the appendix by the

gravid uterus can lead to confusing physical examination signs.^{6,7}

Prompt diagnosis of acute appendicitis decreases the morbidity and mortality in both the pregnant patient and the foetus.⁸ Conversely, false-positive diagnoses can also lead to unnecessary surgical interventions, increasing the rate of pre-term birth, labour and foetal loss.^{9,10} Imaging

plays a central role in diagnosis and directing management. Owing to lack of radiation and better visualization of the appendix relative to ultrasound, MRI is being increasingly utilized in the diagnosis of appendicitis during pregnancy, usually following an inconclusive ultrasound examination.

MRI has acceptable negative laparotomy rates and decreases likelihood of perforation when used in the emergent setting in pregnant patients.¹¹ A meta-analysis performed by Long et al¹² reported sensitivities, specificities, positive- and negative-predictive values of MRI for the diagnosis of appendicitis during pregnancy of 91, 98, 86 and 99%, respectively. To our knowledge, the radiology literature has reported approximately 1200 patients with MRI for the evaluation of appendicitis during pregnancy, the largest single study performed by Pedrosa et al with 148 patients (14 positive patients) which found similar sensitivities, specificities, as well as positive and negative-predictive values (100, 93, 61 and 100%, respectively).¹¹⁻¹⁹

While the current literature supports the use of MRI in clinical practice, to our knowledge, there remain gaps in knowledge about the interradiologist agreement of MR features of appendicitis (enlarged appendiceal diameter, signs of periappendiceal inflammation, fluid-filled appendix and increased appendiceal wall thickness), the outcomes associated with indeterminate interpretations (those that are not clearly positive or negative) and the negative-predictive value of non-visualization of the appendix on MRI. The purpose of our study was, therefore, to address these gaps in knowledge through review of the largest single-centre experience to date.

METHODS AND MATERIALS

Retrospective patient inclusion

After approval by the WUStL institutional review board and waiver of consent, a HIPAA-compliant, retrospective query of the radiology information system search tool was performed to discover all MR examinations performed for the evaluation of suspected acute appendicitis in the pregnant patient performed at Barnes Jewish Hospital (St. Louis, MO, USA) from January 2003 to April 2015. MR examinations were discovered with the radiology information system tool using the search terms "MRI", "pelvis", "abdomen", "pregnant", "gravid", "right lower quadrant pain

(RLQ)" and/or "appendicitis". Each subsequent examination was reviewed by two of the authors to document that the examination was performed with the MRI protocol to evaluate acute appendicitis during pregnancy. Patients were excluded if the appendiceal inflammation was deemed secondary to an aetiology of non-appendiceal origin, MRI examinations performed were not using the correct protocol or if imaging was considered non-diagnostic by the reviewing radiologists.

Imaging protocol and imaging interpretation

All imaging was performed in the supine position using a 1.5-T MRI (Siemens, Erlangen, Germany) with a phased-array surface coil. No oral or i.v. contrast was administered. Images were obtained from the level of the liver hilum through the pubic symphysis. The parameters for MRI sequences are provided (Table 1). The entire MRI protocol takes approximately 30 min to complete. In addition to the sequences performed listed in Table 1, sagittal steady-state free precession images were also performed from 2003 to 2008.

Initial interpretations at the time of the original examination were provided by one of the staff abdominal imaging radiologists or MRI fellows on any given day, four of whom are authors. Retrospectively, each initial interpretation was read by two of the authors. Interpretations that mentioned "findings concerning for acute appendicitis", "compatible with acute appendicitis" or simply stated "acute appendicitis" were classified as positive for acute appendicitis. Reports that mentioned "indeterminate for acute appendicitis", "may represent early appendicitis, but correlation..." or "appendicitis cannot be excluded" were classified as indeterminate for acute appendicitis. Reports that mentioned "the appendix is not visualized, but there are no signs of appendicitis", "no evidence of appendicitis" or "normal appendix" were classified as "negative for acute appendicitis". This served as the clinical interpretation for purposes of analysis.

All MR examinations were then independently rereviewed by two, subspecialty-trained radiologists with 9 and 7 years of experience. One of the radiologists was involved in the training (residency and fellowship) of the other radiologist. The reviewers were blinded to patient outcome, patient name, patient intervention, laboratory data, demographic data, original MRI reports,

Table 1. Evaluation of suspected appendicitis during pregnancy MRI protocol

MRI (Siemens, Erlagen, Germany)
Coil: phased-array
Coverage: diaphragm to iliac crest
Coronal/transaxial/sagittal single-shot TSE T ₂ weighted imaging: TR 1000 ms; TE 83-95 ms; ST 5 mm; matrix 320 × 320 (coronal), 260 × 320 (transaxial), 320 × 260 (sagittal)
Transaxial single-shot TSE T ₂ weighted imaging with FS: TR 1000 ms; TE 95 ms; ST 5 mm; matrix 260 × 320; FS technique: spectral attenuated inversion recovery
Coronal/transaxial TrueFISP imaging with FS: TR 4 ms; TE 2 ms; ST 6 mm; matrix 512 × 512 (coronal), 512 × 512 (transaxial); FS technique: spectral attenuated inversion recovery
Transaxial fast low-angle T ₁ weighted imaging with FS: TR 181 ms; TE 2.39 ms; matrix 250 × 320; FS technique: spectral attenuated inversion recovery

FS, fat saturation; TE, echo time; TR, repetition time; TSE, turbo spin echo.

follow-up imaging and initial sonography (if performed). Variables assessed for each patient were binary (yes or no) and included: visualization of the appendix, appendiceal diameter (≥ 8 mm), appendiceal wall thickening (≥ 2 mm), periappendiceal fat stranding, fluid-filled appendix and periappendiceal/RLQ fluid. In addition, each reviewer was then asked to give their final impression—"positive for acute appendicitis", "indeterminate for acute appendicitis" or "negative for acute appendicitis". The final impression was based on a subjective assessment based on a combination of all MRI features, reflecting clinical practice. This constituted the examination interpretation or index test for statistical analysis.

Patient demographics and outcomes

Demographic information, laboratory data, BMI, maternal age and gestational age at the initial time of presentation were collected by two of the authors from the patient's chart. Patient outcomes were classified as surgical, non-surgical observation or discharged.

Reference standard

Surgical pathology was used as reference standard for the presence or absence of acute appendicitis for patients who underwent surgery. When no surgical procedures were performed, clinical observation without progression to surgery and/or discharge was used as reference standards for the absence of acute appendicitis. Patients that were interpreted as indeterminate were categorized as false positives for the purpose of the statistical analysis.

Statistical analysis

The patient demographic and clinical data were assessed by comparing the SDs between patients that proved to have appendicitis during pregnancy and those that did not. We also compared the mean gestational age to whether or not the appendix could be visualized for each radiologist. These values were compared using Student's *t* testing. $p < 0.05$ was considered to indicate a significant difference.

An analysis of the mean gestational age in relation to the final MRI impression for each radiologist was also performed using analysis of variance. $p < 0.05$ was considered to indicate a significant difference.

Interradiologist agreement of binary MRI features of appendicitis and final MRI impression was calculated using Cohen's κ .

For the final MRI impression, a weighted Cohen's κ was used to provide a penalty for major disagreement vs minor disagreement. This was used to reflect the implications of disagreements between radiologists for negative, indeterminate and positive for appendicitis interpretations. The κ -value for the final impression was calculated as a quadratic, weighted κ -value with heavier weighting for disagreements when an indeterminate interpretation was involved, and even heavier weighting when there were disagreements on positive interpretations. κ -values < 0 were considered as no, 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial and 0.81–1 as almost perfect agreement. All statistical analyses were performed using SPSS, v. 24, software (IBM, North Castle, NY).

RESULTS

During our study period from January 2003 to April 2015, a total of 240 pregnant patients were evaluated for acute appendicitis using the MRI protocol for the evaluation of suspected appendicitis during pregnancy. Seven of these patients were excluded for RLQ inflammation secondary to a non-appendiceal origin such as Crohn disease. There were a total of 14 positive patients proven by our reference standard, providing an overall incidence in our population of 6%. One-fourteenth of these patients' MRI examinations was initially interpreted as negative for appendicitis on the original MRI report and by both reviewing radiologists.

There was no significant difference in maternal age, gestational age and BMI between patients with appendicitis and those without ($p > 0.05$), as seen in Table 2. The mean patient age was 28.4 years, ranging from 17 to 38 years old. The degree of leukocytosis was greater in pregnant patients with appendicitis (16.1 ± 3.7) vs the patients without appendicitis (11.3 ± 4.0) ($p = 0.005$).

Of the 233 patients that comprised the study population, the initial MRI interpretations categorized 19 (8.5%) as positive for appendicitis, 15 (6.5%) as indeterminate and 199 (85%) as negative for appendicitis. Figure 1 demonstrates the outcomes of patients undergoing MRI relative to the initial clinical interpretations.

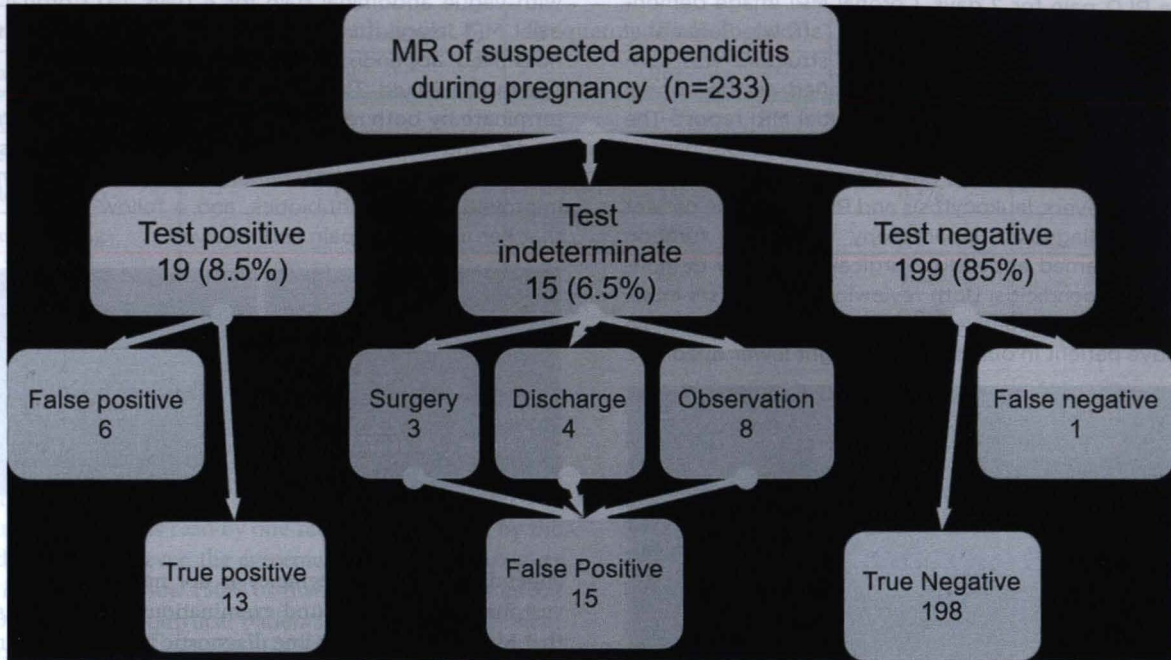
Upon retrospective review, Radiologist 1 interpreted 15, 9 and 208 patients as positive, indeterminate and negative for acute appendicitis, respectively. Radiologist 2 interpreted 14, 7 and 211 patients as positive, indeterminate and negative for acute appendicitis. The sensitivity, specificity, positive predictive value, and

Table 2. Patient demographic and laboratory results

	All patients (N = 233)	Patients with appendicitis during pregnancy (N = 13)	Patients without appendicitis during pregnancy (N = 220)	p-value
Maternal age	28.4 \pm 6.3	29 \pm 5.3	28 \pm 6.5	0.42
Gestational age (weeks)	15.1 \pm 7.1	15.8 \pm 6.6	15.1 \pm 7.2	0.756
BMI	29.6 \pm 8.2	32.7 \pm 8.27	29.5 \pm 8.25	0.397
White blood cell count (thousands)	11.3 \pm 4.01	16.1 \pm 3.7	11.1 \pm 3.9	0.005

BMI, body mass index.

Figure 1. Summary of initial MRI interpretations and subsequent management.



negative predictive value for Radiologist 1 were 92.9, 95, 54.2 and 99.5%, respectively. For Radiologist 2, the sensitivity, specificity, positive predictive value, and negative predictive value were 92.9, 96.3, 61.9 and 99.5%, respectively. Figure 2 demonstrates the single false-negative scan—the patient was interpreted as negative by both radiologists. Figures 3 and 4 demonstrate patient examples that were interpreted as positive for acute appendicitis and indeterminate for acute appendicitis, respectively, on re-review.

The mean gestation ages for patients interpreted as negative, positive and indeterminate for appendicitis during pregnancy for Radiologist 1 were 16.1, 16.6 and 13.5 weeks ($p = 0.44$). For Radiologist 2, the mean gestational ages were 16, 16.7 and 14.2 weeks for negative, positive and indeterminate interpretations ($p = 0.61$), respectively. For Radiologist 1, the mean gestational ages were 15.2 weeks for those where the appendix could be visualized, and 24.9 weeks for those patients where the appendix could not be visualized ($p = 0.41$). The mean gestational ages for patients in which the appendix could and could not be visualized by Radiologist 2 were 15.1 and 21.1 ($p = 0.002$), respectively.

Table 3 shows the interradiologist agreement for different features on MRI, and Table 4 demonstrates the agreement data for each MRI feature. The agreement for visualization of the appendix ($\kappa = 0.274 \pm 0.154-0.394$), presence of fluid-filled appendix ($\kappa = 0.376 \pm 0.194-0.558$) and the presence of periappendiceal/RLQ fluid ($\kappa = 0.229 \pm 0.122-0.396$) was fair. The presence of a dilated appendix ($\kappa = 0.680 \pm 0.486-0.874$) and appendiceal wall thickening ($\kappa = 0.712 \pm 0.533-0.890$) had substantial agreement. Agreement was near perfect on the presence of periappendiceal soft-tissue stranding ($\kappa = 0.861 \pm 0.728-0.994$).

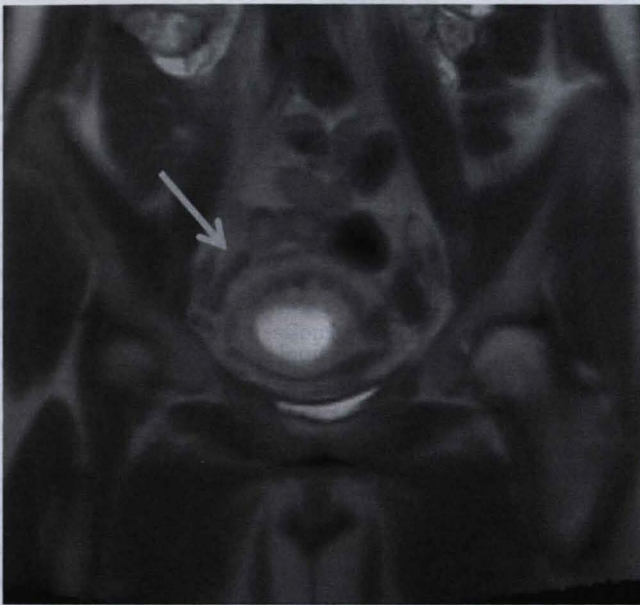
Both radiologists agreed on the final impression in 223 patients (13 positive for acute appendicitis, 3 indeterminate for acute appendicitis and 207 negative for acute appendicitis). There were no patients in which one radiologist interpreted the scan as positive for appendicitis which the other radiologist interpreted as negative for appendicitis. There were 10 patients in which one radiologist interpreted an MR examination as indeterminate and the other radiologist interpreted the scan as negative for appendicitis, but there was a single patient where one radiologist interpreted the scan as positive for appendicitis, which the other radiologist interpreted as indeterminate. Agreement of the final interpretation between radiologists was near perfect ($\kappa = 0.917 \pm 0.858-0.975$).

Of the 14 patients interpreted as indeterminate by either radiologist or on the original MRI interpretation (15 patients), all were negative for acute appendicitis. In 73 patients, the appendix could not be visualized by either radiologist—all were negative for acute appendicitis. The negative-predictive value of non-visualization of the appendix was 100% for both radiologists. None of these patients had signs of RLQ inflammation as evidenced by periappendiceal soft-tissue stranding on MRI.

DISCUSSION

Ultrasound is the initial imaging examination of choice for the evaluation of RLQ pain, as recommended by the American College of Radiology Appropriateness Criteria.²⁰ However, prior studies have demonstrated that the appendix could not be visualized using ultrasound in a large proportion of pregnant patients, with some patient series approaching a non-visualization rate of 97%.^{21,22} Indeed, the American College of Radiology recommends MRI as the second imaging examination of choice in inconclusive cases, which comprise the majority of ultrasound

Figure 2. A 22-year-old female, 6 weeks gestation, presented with acute RLQ pain for 2 days. Coronal MRI image demonstrates a tubular structure in the RLQ (arrow). Sequential images (not included) showed that this structure was continuous with the cecum. This was identified as the normal appendix by both radiologists and the initial MRI report. The appendix measured 5 mm in diameter. She was discharged after her symptoms improved, but re-presented 2 days later with worsening fevers, leukocytosis and RLQ pain. The patient was taken for diagnostic laparoscopy where the surgeon identified an inflamed appendix. Surgical pathology demonstrated acute appendicitis. Both reviewing radiologists interpreted this patient as negative, and this patient was the single false negative patient in our study. RLQ, right lower quadrant.



examinations for the evaluation of suspected appendicitis in the pregnant patient.²⁰ Other studies have found that a sequential multimodality imaging approach in the evaluation of suspected

Figure 3. A 27-year-old female, 33 weeks gestation, presented with diffuse abdominal pain and fever for 1 day. (a) Coronal and (b) axial MRI images demonstrate a dilated, thick-walled, appendix (arrow) that measured 10 mm in diameter with surrounding periappendiceal fat stranding. This was interpreted as acute appendicitis on the initial MRI report and by both reviewing radiologists. The patient underwent an appendectomy, which demonstrated acute appendicitis on surgical pathology; subsequently, the patient underwent premature labour, and except for pre-term delivery, the newborn had an uncomplicated course.

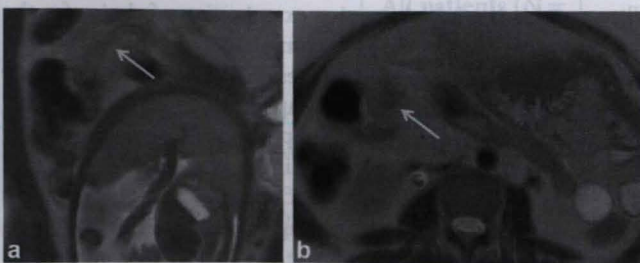
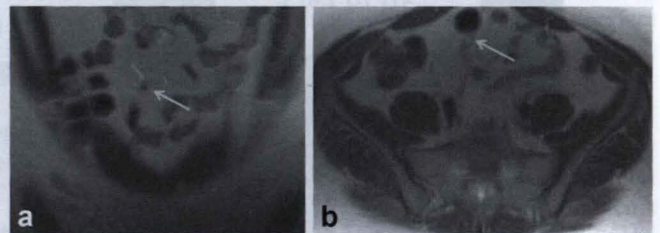


Figure 4. A 32 year-old female, 8 weeks gestation, presented with vague abdominal pain for 4 days. (a) Coronal and (b) axial MRI images demonstrate a minimally dilated (8 mm), fluid-filled appendix (arrow) with a small amount of periappendiceal fluid. This examination was interpreted as indeterminate by both reviewing radiologists and the original MRI report, and was categorized as a false-positive. This patient was admitted for short inpatient observation. Her symptoms improved without antibiotics, and a follow-up note showed that her abdominal pain had resolved.



appendicitis during pregnancy is not necessary given that the vast majority of ultrasound examinations are inconclusive, and that MRI should be first-line diagnostic imaging examination of choice.^{18,23,24} The time spent performing an ultrasound examination, which is likely to be inconclusive, may delay accurate diagnosis and endanger foetal and maternal well-being; delay of diagnosis upwards of 24 h increases maternal morbidity and mortality, as well as the rate of appendiceal perforation by upwards of 66%.⁸ Alternatively, surgically exploring a pregnant patient increases the risk of pre-term delivery. MRI has been shown to decrease the negative laparotomy rate without significant changes to perforation rate.²⁵

Unlike on other cross-sectional modalities, non-visualization of appendicitis on ultrasound does not serve as a predictor of the absence of appendicitis, and further imaging is often warranted.^{6,12} MRI has been shown to be an excellent diagnostic tool in patients in whom an ultrasound examination cannot visualize the appendix, as it can be used to accurately diagnose abdominal pain from non-appendiceal origin. Likewise, no demonstrable risks or complications have been linked to the use of MRI during pregnancy.²⁶⁻²⁸ Its validity for the diagnosis of appendicitis during pregnancy, and its utility for decreasing negative laparotomy and perforation rates has been previously reported.^{11,29} For these reasons, the clinical practice at our institution is to proceed directly to MRI, foregoing ultrasound, when a pregnant patient presents with suspected appendicitis. As MRI becomes more widely used for this indication, it becomes important to validate the MRI signs of appendicitis during pregnancy.

Accordingly, we evaluated which MRI signs of appendicitis during pregnancy are most reliable between radiologists. We found that periappendiceal soft-tissue stranding, appendiceal wall thickening and increased appendiceal diameter had the highest interradiologist agreement. The objective nature of appendiceal diameter and wall thickening may account for the higher agreement. In addition, the superior soft-tissue contrast of MRI lends itself to evaluating for the presence of

Table 3. Interradiologist agreement for the MRI features of suspected appendicitis during pregnancy

MRI features	Frequency (Radiologist 1)	Frequency (Radiologist 2)	κ	95% CI
Visualization	214	163	0.274	0.154–0.394
Diameter \geq 8 mm	19	12	0.680	0.486–0.874
Wall thickening present	16	19	0.712	0.533–0.890
Fluid-filled appendix	12	33	0.376	0.194–0.558
Soft-tissue stranding	16	16	0.861	0.728–0.994
Periappendiceal fluid	48	66	0.229	0.122–0.396
Final impression			0.917	0.858–0.975

periappendiceal soft-tissue stranding. These signs (soft-tissue stranding, wall thickening and/or diameter) were equivocally present in 26 negative patients as identified by at least one radiologist, with the combination of the three findings interpreted as present in one patient as read by one radiologist, but not by the other radiologist. However, the agreement between radiologists in these instances was low (50% of the features were disagreed upon). Despite these equivocal patients, the overall agreement was high. As such, these three features may be the most useful in the MRI diagnosis of appendicitis during pregnancy.

Surprisingly, there was minimal interradiologist agreement for the actual visualization of the appendix and periappendiceal

Table 4. Agreements for each MRI feature of suspected appendicitis during pregnancy

		Reader 1		
Reader 2	Visualization of the appendix			
	No	Yes	Total	
No	16	54	70	
Yes	3	160	163	
		Appendiceal diameter \geq 8 mm		
No	140	8	148	
Yes	1	11	12 (160)	
		Appendiceal wall thickening		
No	138	3	141	
Yes	6	13	19 (160)	
		Fluid-filled appendix		
No	125	2	127	
Yes	23	10	33 (160)	
		Periappendiceal/RLQ soft-tissue stranding		
No	145	2	147	
Yes	2	14	16 (167)	
		Periappendiceal/RLQ free fluid		
No	140	23	163	
Yes	41	25	66 (229)	

RLQ, right lower quadrant.

fluid. This likely stems from differing thresholds for calling a tubular structure the normal appendix. The degree of certainty needed to differentiate the appendix from other tubular structures in the RLQ (and in particular, the ovarian vein) may have been a source of disagreement between the radiologists. Prior literature has demonstrated the changing position of the appendix with progression of pregnancy.^{21,30,31} Normal physiological changes from an enlarging uterus cause dilated ovarian veins and increasing mass effect on surrounding structures which can make confident identification of the appendix difficult. The difficulty in visualizing an appendix with increasing gestational age is underlined by a study by Lehnert et al²² which failed to identify the appendix by ultrasound in 97% of pregnant patients, all of whom were in the second or third trimester.

It is difficult to determine if gestational age plays a significant role in the visualization of the appendix with MRI as it does on ultrasound; prior studies have demonstrated that gestational age does not affect visualization of the appendix on MRI.²⁴ Our study demonstrated that the number of patients in which the appendix could be identified by each radiologist was inversely related to the gestational age of the patient, but was only statistically significant for Radiologist 2. Although Radiologist 1 also had a difference between mean gestational age (15.2 vs 24.9 weeks) for the visualization of the appendix, the difference between the means was not statistically significant (p value = 0.41). However, we found there was no correlation between the gestational age and the final MRI impression for either radiologist.

Similarly, differing thresholds also existed for the amount of T2 hyperintensity necessary to indicate that the appendix was fluid-filled. There was also weak agreement of RLQ/periappendiceal fluid. In retrospect, almost all of these pregnant patients had some quantity of free fluid in the pelvis, and subsequently the radiologists were unsure when to indicate the presence of RLQ/periappendiceal fluid secondary to a potential appendiceal source or related to physiological changes of pregnancy. When taking all findings into account, however, the agreement on the final impression was near perfect, with a weighted κ -score of 0.917, confirming that MRI overall is a reliable test for the diagnosis or exclusion of appendicitis during pregnancy. These results perhaps underline the strength of MRI in evaluating for soft-tissue inflammation and that the absence of obvious signs

of RLQ inflammation effectively excludes acute appendicitis, regardless of the ability to visualize the appendix.

Our single patient with a false-negative MR interpretation as per the original MRI report was also interpreted as negative for appendicitis by both radiologists on retrospective review. The patient was discharged, but returned 2 days later and was taken for diagnostic laparoscopy. In retrospect, even with the knowledge of the surgical pathology, both radiologists were able to identify a normal-appearing appendix without signs of RLQ inflammation. The patient may have developed acute appendicitis between presentations, or this may be a patient of acute, early appendicitis below the resolution of MRI.

We found that there were no patients with appendicitis during pregnancy when either radiologist or the initial MRI report interpreted the examination as indeterminate for acute appendicitis. Although some of these patients may have had mild or abortive appendicitis, all agreed to conservative management. These findings suggest the utility of MRI to triage patients to conservative vs surgical management.

We also found that there were no patients with appendicitis when either radiologist failed to identify the appendix (73 patients), which explains why we found no correlation between gestation age and the final MRI impression. Notably, none of these patients demonstrated MRI signs of RLQ inflammation. This is congruent with prior CT literature, which also supports the absence of acute appendicitis in patients where the appendix or RLQ inflammation is not visualized.^{32,33}

Our study had several limitations, including its retrospective observational nature which inherently may introduce bias. Although our study is currently the largest single-centre study, to our knowledge, evaluating 233 patients with suspected appendicitis during pregnancy, the incidence of the disease in our study population was low (6%) and reflects its relative rarity. Owing to the relatively low incidence of acute appendicitis in our study population, there may be overestimation of the negative-

predictive value of appendix non-visualization. Although the incidence of appendicitis during pregnancy in our study was low (6%), it reflects the relative rarity of this entity during pregnancy. There may, therefore, be overestimation of those incidences previously reported, as our study demonstrates an incidence more similar to that reported by the largest multi-centre study which found an incidence closer to 9%.¹⁹ A recent, separate study at a single centre by Ramalingam et al demonstrated an incidence closer to 6%. The low incidence of positive disease prohibits the determination of the positive- and negative-predictive values for most individual MRI features. In addition, there was no formal training session involved for documenting if a particular MRI sign was present, which may have underestimated the interradiologist agreement of the more subjective findings, including RLQ/periappendiceal fluid and a fluid-filled appendix. We also recognize that patients interpreted as negative or indeterminate for appendicitis could have been lost to follow up, presented to an outside facility for surgical intervention or could have had acute appendicitis that resolved after antibiotic administration, could have represented self-limited appendicitis or represented early appendicitis below the resolution of MR imaging. Finally, as one of the radiologists was involved in the training of the other, the high level of interradiologist agreement may be higher than would be expected from two radiologists trained independently of each other.

CONCLUSION

We found that the MRI features of periappendiceal stranding, appendiceal diameter and appendiceal wall thickening had the highest degrees of interradiologist agreement and regardless of the singular MRI findings, the final impression had near-perfect agreement between radiologists, in pregnant patients with suspected appendicitis. Moreover, patients whom are indeterminate for appendicitis during pregnancy based on MR interpretations were virtually never found to have appendicitis. Finally, in those patients where the appendix could not be visualized on MR, and in the absence of signs of RLQ inflammation, the negative-predictive value in our study was 100%.

REFERENCES

- Andersen B, Nielsen TF. Appendicitis in pregnancy: diagnosis, management and complications. *Acta Obstet Gynecol Scand* 1999; **78**: 758–62. doi: <https://doi.org/10.1080/j.1600-0412.1999.780903.x>
- Horowitz MD, Gomez GA, Santiesteban R, Burkett G. Acute appendicitis during pregnancy. Diagnosis and management. *Arch Surg* 1985; **120**: 1362–7.
- Sharp HT. The acute abdomen during pregnancy. *Clin Obstet Gynecol* 2002; **45**: 405–13. doi: <https://doi.org/10.1097/00003081-200206000-00011>
- Cappell MS, Friedel D. Abdominal pain during pregnancy. *Gastroenterol Clin North Am* 2003; **32**: 1–58. doi: [https://doi.org/10.1016/S0889-8553\(02\)00064-X](https://doi.org/10.1016/S0889-8553(02)00064-X)
- Mayer IE, Hussain H. Abdominal pain during pregnancy. *Gastroenterol Clin North Am* 1998; **27**: 1–36. doi: [https://doi.org/10.1016/S0889-8553\(05\)70346-0](https://doi.org/10.1016/S0889-8553(05)70346-0)
- Mourad J, Elliott JP, Erickson L, Lisboa L. Appendicitis in pregnancy: new information that contradicts long-held clinical beliefs. *Am J Obstet Gynecol* 2000; **182**: 1027–9. doi: <https://doi.org/10.1067/mob.2000.105396>
- Oto A, Ernst RD, Ghulmiyyah LM, Nishino TK, Hughes D, Chaljub G, et al. MR imaging in the triage of pregnant patients with acute abdominal and pelvic pain. *Abdom Imaging* 2009; **34**: 243–50. doi: <https://doi.org/10.1007/s00261-008-9381-y>
- Tamir IL, Bongard FS, Klein SR. Acute appendicitis in the pregnant patient. *Am J Surg* 1990; **160**: 571–6. doi: [https://doi.org/10.1016/S0002-9610\(05\)80748-2](https://doi.org/10.1016/S0002-9610(05)80748-2)
- McGory ML, Zingmond DS, Tillou A, Hiatt JR, Ko CY, Cryer HM. Negative appendectomy in pregnant women is associated with a substantial risk of fetal loss. *J Am Coll Surg* 2007; **205**: 534–40. doi: <https://doi.org/10.1016/j.jamcollsurg.2007.05.025>

10. Kort B, Katz VL, Watson WJ. The effect of nonobstetric operation during pregnancy. *Surg Gynecol Obstet* 1993; **177**: 371–6.
11. Pedrosa I, Lafornera M, Pandharipande PV, Goldsmith JD, Rofsky NM. Pregnant patients suspected of having acute appendicitis: effect of MR imaging on negative laparotomy rate and appendiceal perforation rate. *Radiology* 2009; **250**: 749–57. doi: <https://doi.org/10.1148/radiol.2503081078>
12. Long SS, Long C, Lai H, Macura KJ. Imaging strategies for right lower quadrant pain in pregnancy. *Am J Roentgenol* 2011; **196**: 4–12. doi: <https://doi.org/10.2214/AJR.10.4323>
13. Vu L, Ambrose D, Vos P, Tiwari P, Rosengarten M, Wiseman S. Evaluation of MRI for the diagnosis of appendicitis during pregnancy when ultrasound is inconclusive. *J Surg Res* 2009; **156**: 145–9. doi: <https://doi.org/10.1016/j.jss.2009.03.044>
14. Birchard KR, Brown MA, Hyslop WB, Firat Z, Semelka RC. MRI of acute abdominal and pelvic pain in pregnant patients. *Am J Roentgenol* 2005; **184**: 452–8. doi: <https://doi.org/10.2214/ajr.184.2.01840452>
15. Oto A, Ernst RD, Shah R, Koroglu M, Chaljub G, Gei AF, et al. Right-lower-quadrant pain and suspected appendicitis in pregnant women: evaluation with MR imaging—initial experience. *Radiology* 2005; **234**: 445–51. doi: <https://doi.org/10.1148/radiol.2341032002>
16. Cobben LP, Groot I, Haans L, Blickman JG, Puylaert J. MRI for clinically suspected appendicitis during pregnancy. *AJR Am J Roentgenol* 2004; **183**: 671–5. doi: <https://doi.org/10.2214/ajr.183.3.1830671>
17. Israel GM, Malguria N, McCarthy S, Copel J, Weinreb J. MRI vs. ultrasound for suspected appendicitis during pregnancy. *J Magn Reson Imaging* 2008; **28**: 428–33. doi: <https://doi.org/10.1002/jmri.21456>
18. Ramalingam V, LeBedis C, Kelly JR, Uyeda J, Soto JA, Anderson SW. Evaluation of a sequential multi-modality imaging algorithm for the diagnosis of acute appendicitis in the pregnant female. *Emerg Radiol* 2015; **22**: 125–32. doi: <https://doi.org/10.1007/s10140-014-1260-y>
19. Burke LM, Bashir MR, Miller FH, Siegelman ES, Brown M, Alobaidy M, et al. Magnetic resonance imaging of acute appendicitis in pregnancy: a 5-year multiinstitutional study. *Am J Obstet Gynecol* 2015; **213**: 693.e1–693.e6. doi: <https://doi.org/10.1016/j.ajog.2015.07.026>
20. Smith MP, Katz DS, Lalani T, Carucci LR, Cash BD, Kim DH, et al. ACR Appropriateness Criteria® right lower quadrant pain—suspected appendicitis. *Ultrasound Q* 2015; **31**: 85–91. doi: <https://doi.org/10.1097/RUQ.0000000000000118>
21. Pedrosa I, Levine D, Eyvazzadeh AD, Siewert B, Ngo L, Rofsky NM. MR imaging evaluation of acute appendicitis in pregnancy. *Radiology* 2006; **238**: 891–9. doi: <https://doi.org/10.1148/radiol.2383050146>
22. Lehnert BE, Gross JA, Linnau KF, Moshiri M. Utility of ultrasound for evaluating the appendix during the second and third trimester of pregnancy. *Emerg Radiol* 2012; **19**: 293–9. doi: <https://doi.org/10.1007/s10140-012-1029-0>
23. Theilen LH, Mellnick VM, Shanks AL, Tuuli MG, Odibo AO, Macones GA, et al. Acute appendicitis in pregnancy: predictive clinical factors and pregnancy outcomes. *Am J Perinatol* 2017; **34**: 523–8. doi: <https://doi.org/10.1055/s-0036-1593764>
24. Konrad J, Grand D, Lourenco A. MRI: first-line imaging modality for pregnant patients with suspected appendicitis. *Abdom Imaging* 2015; **40**: 3359–64. doi: <https://doi.org/10.1007/s00261-015-0540-7>
25. Rapp EJ, Naim F, Kadivar K, Davarpanah A, Cornfeld D. Integrating MR imaging into the clinical workup of pregnant patients suspected of having appendicitis is associated with a lower negative laparotomy rate: single-institution study. *Radiology* 2013; **267**: 137–44. doi: <https://doi.org/10.1148/radiol.12121027>
26. Kanal E, Barkovich AJ, Bell C, Borgstede JP, Bradley WG, Froelich JW, et al. ACR guidance document for safe MR practices: 2007. *Am J Roentgenol* 2007; **188**: 1447–74. doi: <https://doi.org/10.2214/AJR.06.1616>
27. De Wilde JP, Rivers AW, Price DL. A review of the current use of magnetic resonance imaging in pregnancy and safety implications for the fetus. *Prog Biophys Mol Biol* 2005; **87**: 335–53. doi: <https://doi.org/10.1016/j.pbiomolbio.2004.08.010>
28. Levine D, Zuo C, Faro CB, Chen Q. Potential heating effect in the gravid uterus during MR HASTE imaging. *J Magn Reson Imaging* 2001; **13**: 856–61. doi: <https://doi.org/10.1002/jmri.1122>
29. Bailey LE, Finley RK, Miller SF, Jones LM. Acute appendicitis during pregnancy. *Am Surg* 1986; **52**: 218–21.
30. Oto A, Srinivasan PN, Ernst RD, Koroglu M, Cesani F, Nishino T, et al. Revisiting MRI for appendix location during pregnancy. *AJR Am J Roentgenol* 2006; **186**: 883–7. doi: <https://doi.org/10.2214/AJR.05.0270>
31. Pedrosa I, Zeikus EA, Levine D, Rofsky NM. MR imaging of acute right lower quadrant pain in pregnant and nonpregnant patients. *Radiographics* 2007; **27**: 721–5343. doi: <https://doi.org/10.1148/rg.273065116>
32. Nikolaidis P, Hwang CM, Miller FH, Papanicolaou N. The nonvisualized appendix: incidence of acute appendicitis when secondary inflammatory changes are absent. *AJR Am J Roentgenol* 2004; **183**: 889–92. doi: <https://doi.org/10.2214/ajr.183.4.1830889>
33. Ganguli S, Raptopoulos V, Komlos F, Siewert B, Kruskal JB. Right lower quadrant pain: value of the nonvisualized appendix in patients at multidetector CT. *Radiology* 2006; **241**: 175–80. doi: <https://doi.org/10.1148/radiol.2411050191>

Grade	Complete osseous fusion	Grade B	Undetermined fusion
Grade A	Complete osseous fusion	Grade B	Undetermined fusion
Grade B	Complete osseous fusion	Grade B	Undetermined fusion
Grade C	Complete osseous fusion	Grade B	Undetermined fusion
Grade D	Complete osseous fusion	Grade B	Undetermined fusion
Grade E	Complete osseous fusion	Grade B	Undetermined fusion