Diagnostic accuracy of magnetic resonance imaging for acute appendicitis during pregnancy: A systematic review

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ABSTRACT

BACKGROUND: The purpose of this study was to present a systematic review and meta-analysis of the diagnostic accuracy of magnetic resonance imaging (MRI) in the diagnosis of acute appendicitis in pregnant women.

METHODS: A literature search was conducted using the databases of PubMed, Ovid MEDLINE, EMBASE, and the Cochrane Library. The inclusion criteria were the use of MRI, as a diagnostic protocol for acute appendicitis in pregnant women, and the availability of diagnostic parameters, such as sensitivity and specificity. For each selected study, the basic demographic information and measures of diagnostic accuracy, such as sensitivity, specificity, and positive and negative predictive values, were extracted. Forest plots and summary receiver operating characteristic curves (SROC) were also obtained for diagnostic accuracy of MRI for acute appendicitis during pregnancy.

RESULTS: A total of 22 studies and the data of 2392 patients were analyzed. Most studies had high sensitivity, with the exception of a few that had sensitivities of 0.18, 0.5, and 0.6. With respect to specificity, most results were close to 1.0, and the lowest result was 0.92. The SROC curves showed high levels of accuracy, as evidenced by an area under the curve value of 0.9922.

CONCLUSION: MRI showed overall high accuracy for diagnosing acute appendicitis in pregnant women. Therefore, it is a good diagnostic tool as a first-line imaging method for suspected appendicitis in pregnant women.

Keywords: Appendicitis; magnetic resonance imaging; pregnancy; systematic review

INTRODUCTION

In addition to obstetric emergency, acute appendicitis in pregnant women is a common condition requiring surgery. Late diagnosis of appendicitis increases the risk of fetal loss. [1–3] Pregnant women with appendicitis have higher incidences of complications, such as peritonitis, septic shock, bowel obstruction, and post-operative infection compared with non-pregnant women with appendicitis.[4] However, the diagnosis of acute appendicitis in this population may be difficult due to the anatomical or physiologic changes in pregnancy that results in a lack of typical symptoms or physical examination findings that observed in non-pregnant patients with appendicitis.[3,5] The high sensitivity and specificity of computed tomography (CT) resulted in the most frequent use of this diagnostic tool; however, its usage in pregnant women is very limited. The diagnosis of appendicitis with ultrasonography (US) depends on the physician technique, making the applicability of this method poor.[6–9] The only meta-analysis to date on the diagnostic accuracy of magnetic resonance imaging (MRI) for acute appendicitis in pregnant patients consisted of only five cases, and the results of many other studies on this question reported wide ranges in accuracy measures.[10]

Therefore, the purpose of this systematic literature review and meta-analysis study was to evaluate the diagnostic accuracy of MRI for the diagnosis of acute appendicitis in pregnant women.

MATERIALS AND METHODS

Data Sources and Search Strategy

The literature used in this study was extracted from the databases of PubMed, Ovid MEDLINE, EMBASE, and the Cochrane Library, and keyword searches were performed for

the words "appendicitis," "pregnancy," "gestational period," "pregnant," "magnetic resonance," "MR," and "MRI" or combinations of these in titles and abstracts, without limitations on the date and language. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses[10] guidelines, and two researchers conducted each step of the study independently.

Eligibility Criteria and Study Selection

The inclusion criteria were the use of MRI as a diagnostic protocol for acute appendicitis in pregnant women and the availability of diagnostic parameters, such as sensitivity, specificity, and the positive predictive value (PPV) and negative predictive value (NPV). Surgical pathology or clinical follow-up was used as diagnostic reference standards for acute appendicitis. Each piece of literature that was selected as relevant based on the title and abstract content was subjected to full-text screening. The articles to be included in the study were finally examined by two or more investigators, and any disagreements were settled by discussion.

Assessment of Methodological Quality

The study quality and applicability were assessed using the quality assessment of diagnostic accuracy studies (QUADAS-II),[11] which consists of the four domains of patient selection, index test, reference standards, and flow and timing and are designed to assess risk of bias and applicability for each domain by answering 14 questions as "low," "high," and "unclear" (Table 1). Two researchers (SK Oh & SU Cho) as-

sessed each study independently, and any disagreements were settled by discussion.

Data Synthesis and Analysis

For each selected study, basic demographic information and data on diagnostic sensitivity, specificity, PPV, and NPV were extracted, and 95% confidence intervals (CIs) of sensitivity and specificity were calculated. Meta-Disc[12] and Review Manager (version 5.3) were used for data input and analysis. The homogeneity and heterogeneity of the studies were analyzed using fixed effects (Mantel-Haenszel) and random-effects models (DerSimonian and Laird). The forest plots and summary receiver operating characteristic (SROC) curves were also constructed to evaluate the diagnostic accuracy of MRI for acute appendicitis during pregnancy.

RESULTS

Search Results

The initial search in PubMed, MEDLINE, EMBASE, and Cochrane Library resulted in 289 studies. After removing duplicates, the titles and abstracts of each of the remaining 167 studies were reviewed for relevance, and 124 of these studies were excluded from the study. Full articles were reviewed, and those that did not provide diagnostic parameters (sensitivity, specificity, PPV, and NPV) or classified as review articles, case reports, letters, comments, and duplicated samples were excluded from the study. Finally, 22 studies met the purpose and inclusion criteria of this study (Fig. 1).

| Table 1. The QUADAS-2 tool for the quality assessment of diagnostic accuracy studies			
Item	**Yes**	**No**	**Unclear**
1. Was the spectrum of patients representative of the patients who will receive the test in practice?			
2. Were selection criteria clearly described?			
3. Is the reference standard likely to correctly classify the target condition?			
4. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?			
5. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?			
6. Did patients receive the same reference standard regardless of the index test result?			
7. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?			
8. Was the execution of the index test described in sufficient detail to permit replication of the test?			
9. Was the execution of the reference standard described in sufficient detail to permit its replication?			
10. Were the index test results interpreted without knowledge of the results of the reference standard?			
11. Were the reference standard results interpreted without knowledge of the results of the index test?			
12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?			
13. Were uninterpretable/ intermediate test results reported?			
14. Were withdrawals from the study explained?			
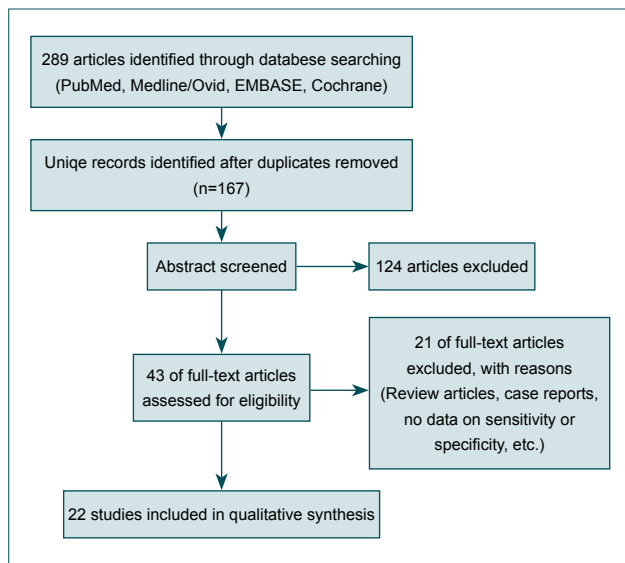
Figure 1. Flow diagram of study selection process.

Study Characteristics and Quality Assessment

The total number of patients enrolled, mean age, authors, journal name, year of publication, study design, MRI scanner type, and primary data outcome including true positives, false positives, true negatives, and false negatives extracted from all included studies are shown in Table 2.[13–34]

The mean score calculated using the QUADAS-II was 10.3 points (range: 6–13). Figure 2 shows the risk of bias summary of the included studies. The high-, moderate-, and low-risk proportion of bias was shown in each of the seven domains of QUADAS-II. The overall risk of bias and applicability concerns were rather low.

Comparison of Diagnostic Accuracy

The forest plots comparing the sensitivity, specificity, and CIs of each study are shown in Figure 3. However, due to the high heterogeneity (I2 >40%), pooled sensitivity and specificity were not suggested. Most included studies had high sensitivity, with the exception of a few that had sensitivities of 0.18, 0.5, and 0.6. Regarding specificity, most results were close to 1.0, and the lowest value was at 0.92 (Table 2). The SROC curves showed high levels of accuracy evidenced by an area under the curve of 0.9922 (standard error: 0.0034) and a Q-value of 0.9642 (standard error: 0.0093) (Fig. 4).
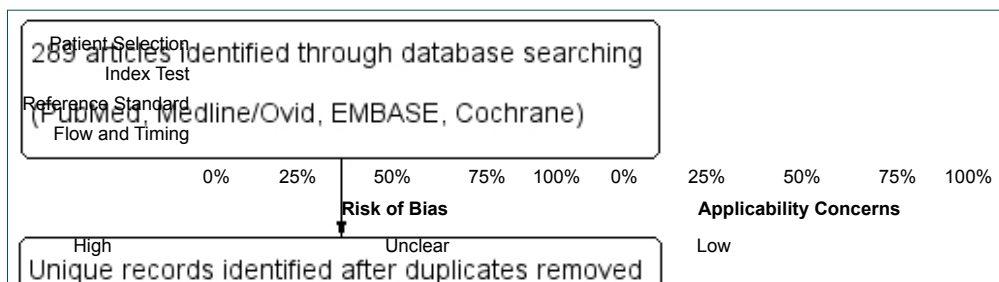

Figure 2. Summary Results of Quality Assessment using the QUADAS-2 instrument. Risk of bias graph about each risk of bias item is presented as percentages (green: low risk of bias, red: high risk of bias, yellow: unclear risk of bias).
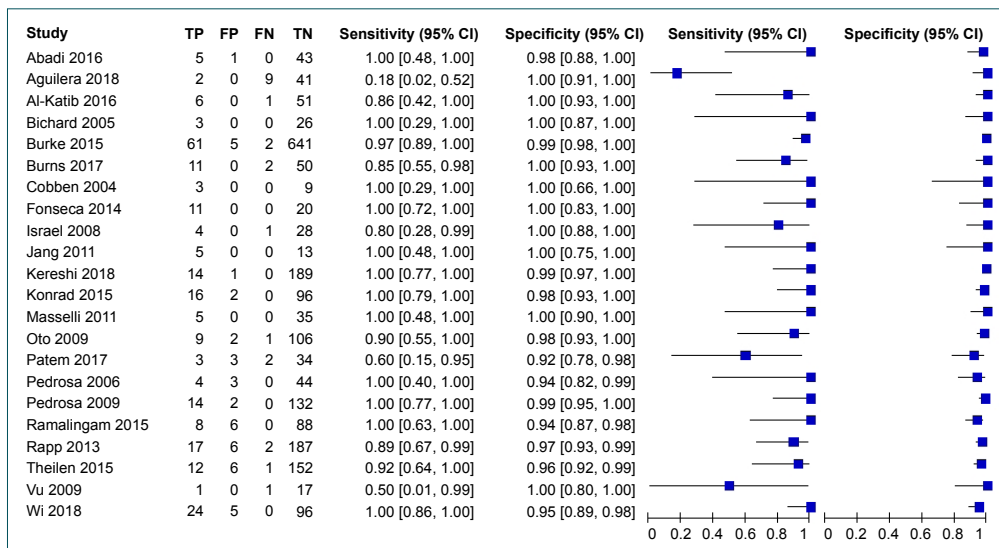
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Abadi 2016	5	1	0	43	1.00 [0.48, 1.00]	0.98 [0.88, 1.00]
Aguilera 2018	2	0	9	41	0.18 [0.02, 0.52]	1.00 [0.91, 1.00]
Al-Katib 2016	6	0	1	51	0.86 [0.42, 1.00]	1.00 [0.93, 1.00]
Bichard 2005	3	0	0	26	1.00 [0.29, 1.00]	1.00 [0.87, 1.00]
Burke 2015	61	5	2	641	0.97 [0.89, 1.00]	0.99 [0.98, 1.00]
Burns 2017	11	0	2	50	0.85 [0.55, 0.98]	1.00 [0.93, 1.00]
Cobben 2004	3	0	0	9	1.00 [0.29, 1.00]	1.00 [0.66, 1.00]
Fonseca 2014	11	0	0	20	1.00 [0.72, 1.00]	1.00 [0.83, 1.00]
Israel 2008	4	0	1	28	0.80 [0.28, 0.99]	1.00 [0.88, 1.00]
Jang 2011	5	0	0	13	1.00 [0.48, 1.00]	1.00 [0.75, 1.00]
Kereshi 2018	14	1	0	189	1.00 [0.77, 1.00]	0.99 [0.97, 1.00]
Konrad 2015	16	2	0	96	1.00 [0.79, 1.00]	0.98 [0.93, 1.00]
Masselli 2011	5	0	0	35	1.00 [0.48, 1.00]	1.00 [0.90, 1.00]
Oto 2009	9	2	1	106	0.90 [0.55, 1.00]	0.98 [0.93, 1.00]
Patem 2017	3	3	2	34	0.60 [0.15, 0.95]	0.92 [0.78, 0.98]
Pedrosa 2006	4	3	0	44	1.00 [0.40, 1.00]	0.94 [0.82, 0.99]
Pedrosa 2009	14	2	0	132	1.00 [0.77, 1.00]	0.99 [0.95, 1.00]
Ramalingam 2015	8	6	0	88	1.00 [0.63, 1.00]	0.94 [0.87, 0.98]
Rapp 2013	17	6	2	187	0.89 [0.67, 0.99]	0.97 [0.93, 0.99]
Theilen 2015	12	6	1	152	0.92 [0.64, 1.00]	0.96 [0.92, 0.99]
Vu 2009	1	0	1	17	0.50 [0.01, 0.99]	1.00 [0.80, 1.00]
Wi 2018	24	5	0	96	1.00 [0.86, 1.00]	0.95 [0.89, 0.98]

Figure 3. Forest plots for sensitivity and specificity of all included studies. Each study is identified by name of first author and year of publication. Horizontal lines represents 95% confidence intervals.

Table 2. Characteristics of the included studies

Year	Author	Journal	Sample size	Mean age (years)	Study design	Scanner type	TP	FP	FN	TN	Sensitivity	Specificity	PPV (%)	NPV (%)
2018	Kereshi et al.[13]	Abdom Radiol	204	29	Retrospective	1.5T	14	1	0	189	1.00	0.99	93.3	100
2018	Aguilera et al.[14]	Am Surg	52	25	Retrospective	1.5T	2	0	9	41	0.18	1.00	100	82.0
2018	Wi et al.[15]	Abdom Radiol	125	32	Retrospective	1.5T	24	5	0	96	1.00	0.95	82.8	100
2017	Burns et al.[16]	Can Assoc Radiol J	63	31	Retrospective	1.5T	11	0	2	50	0.85	1.00	100	96.1
2017	Patel et al.[17]	Abdom Radiol	34	25.5	Retrospective	1.5T	3	3	2	34	0.60	0.92	50.0	94.4
2016	Abadi et al.[18]	Isr Med Assoc J	49	NA	Retrospective	1.5T	5	1	0	43	1.00	0.98	83.3	100
2016	Al-Katib et al.[19]	Abdom Radiol	58	28	Retrospective	1.5T	6	0	1	51	0.86	1.00	100	98.1
2015	Konrad et al.[20]	Abdom Imaging	114	NA	Retrospective	1.5T	16	2	0	96	1.00	0.98	88.9	100
2015	Theilen et al.[21]	Am J Obstet Gynecol	171	NA	Retrospective	1.5T	12	6	1	152	0.92	0.96	66.7	99.3
2015	Burke et al.[22]	Am J Obstet Gynecol	709	27.5	Retrospective	1.5T	61	5	2	641	0.97	0.99	92.4	99.7
2015	Ramalingam et al.[23]	Emerg Radiol	102	26.2	Retrospective	1.5T	8	6	0	88	1.00	0.94	57.1	100
2014	Fonseca et al.[24]	JAMA Surgery	31	NA	Retrospective	1.5T	11	0	0	20	1.00	1.00	100	100
2013	Rapp et al.[25]	Radiology	212	26	Retrospective	1.5T	17	6	2	187	0.89	0.97	73.9	98.9
2011	Jang et al.[26]	Acta Radiologica	18	31.7	Retrospective	1.5T	5	0	0	13	1.00	1.00	100	100
2011	Masselli et al.[27]	Abdom Imaging	40	28	Prospective	1.5	5	0	0	35	1.00	1.00	100	100
2009	Vu et al.[28]	J Surg Res	19	31	Retrospective	1.5T	1	0	1	17	0.50	1.00	100	94.4
2009	Pedrosa et al.[29]	Radiology	148	29	Retrospective	1.5T	14	2	0	132	1.00	0.99	87.5	100
2009	Oto et al.[30]	Abdom Imaging	118	24.7	Retrospective	1.5T	9	2	1	106	0.90	0.98	81.8	99.1
2008	Israel et al.[31]	J Magn Reson Imaging	33	25.6	Retrospective	1.5T	4	0	0	28	0.80	1.00	100	96.5
2006	Pedrosa et al.[32]	Radiology	51	28.3	Retrospective	1.5T	4	3	0	44	1.00	0.94	57.1	100
2005	Birchard et al.[33]	Am J Roentgenol	29	25	Prospective	1.5T	3	0	0	26	1.00	1.00	100	100
2004	Cobben et al.[34]	Am J Roentgenol	12	28	Prospective	1.5T	3	0	0	9	1.00	1.00	100	100

TP: True positive; FP: False positive; TN: True negative; FN: False negative; NA: Not available; PPV: Positive predictive value; NPV: Negative predictive value.
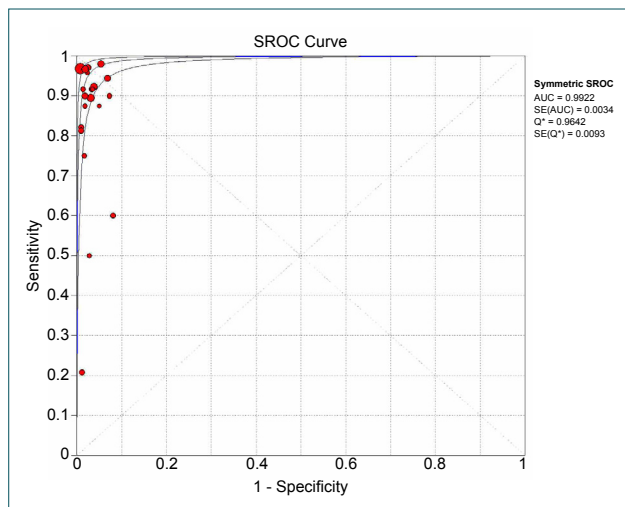
Figure 4. Summary receiver operating characteristics curve of sensitivity and specificity of magnetic resonance imaging for diagnosis of acute appendicitis in pregnant women.

DISCUSSION

Although a high diagnostic sensitivity and specificity of 91–98.5% and 90–98%, respectively, were reported for CT, which is the most commonly used diagnostic tool in cases of acute appendicitis, the radiation exposure and iodinated contrast of CT make its application in pregnant women difficult.[7,8] Therefore, US could be an alternative tool for this purpose; however, it has lower diagnostic accuracy compared with CT. Many studies reported the sensitivity and specificity of ultrasound in diagnosing acute appendicitis to be at 78–88% and 81–94%, respectively.[7,35,36] In addition, the application of US in pregnant patients was shown to lead to an increase in the rate of unnecessary appendectomies compared to the application of US plus CT.[9] These results indicated that a diagnostic tool other than ultrasound could be more suitable in patients with acute appendicitis showing equivocal signs. Especially in pregnant patients, MRI is a good candidate as a first-line imaging tool due to the anatomical changes and radiation exposure of the patients. Chen et al.,[37] who also studied the safety profile of diagnosis with MRI during pregnancy, reported no negative effects on the developing conceptus.

A previous meta-analysis on the diagnostic accuracy of MRI for acute appendicitis in pregnant patients reported that the sensitivity, specificity, PPV, and NPV of MRI were 95.0%, 99.9%, 90.4%, and 99.5%, respectively.[10] However, this study reviewed only five cases with just 229 patients, and the quality assessment, methods for data abstraction, and forest plots were not reported. The meta-analysis on the diagnostic accuracy of MRI for the evaluation of acute appendicitis in pregnant women conducted by Duke et al.[38] included subgroup analysis of patients and reported a pooled sensitivity and specificity of 0.94 (0.87–0.98) and 0.97 (0.96–0.98), respectively.

Most of the included this studies had high sensitivity, with the exception of some that had sensitivities of 0.18, 0.5, and 0.6. Regarding specificity, most results were close to 1.0, and the lowest value was at 0.92. Aguilera et al.,[14] one of the included studies, reported a very low sensitivity of 18% and a specificity of 100% and speculated that the low sensitivity was attributable to the hardware and its interpretation. They also explained that the inconclusive and false-negative MRI findings could be attributed to the lack of abdominal MRI fellowship training for the radiologists. The relatively low sensitivity (50%) and the specificity of 100% reported by Vu et al.[28] could be explained by the presence of only two patients detected with appendicitis in their study.

Although this systematic review consisted of 22 studies and included a relatively large sample of patients (2392), all studies, apart from three, were of retrospective design. In addition, there was high heterogeneity between the studies, and the pooled sensitivity and specificity could not be reported. Further, 1.5 T MRI was used in all of the included studies, meaning that the results could not be generalized to other cases using 3.0 T MRI. In addition, the included studies had differences in MRI sequences and use of contrast. Moreover, the MRI sequence data were not available in some studies. The number of radiologists participating in the readings and their experience levels also varied among the studies.

Conclusion

To the best of our knowledge, this systematic review included the largest number of patients and studies on the diagnostic accuracy of MRI in pregnant women with acute appendicitis. MRI showed overall high accuracy for diagnosis of acute appendicitis, and it could be considered a good diagnostic tool, as a first-line imaging method for suspected appendicitis in pregnant women. Moreover, it should be considered when US yields inconclusive findings, to avoid unnecessary appendectomy. Prospective studies including larger number of patients, contrast-enhanced images, and single imaging reference standards are recommended to more accurately determine the diagnostic accuracy of MRI for appendicitis in pregnant women.

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Gebelikte akut apandisit için manyetik rezonans görüntülemenin tanısal doğruluğu: Sistematik bir inceleme

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AMAÇ: Bu çalışmanın amacı, hamile kadınlarda akut apandisit tanısında manyetik rezonans görüntülemenin (MRG) tanısal doğruluğunun sistematik bir derlemesini ve meta-analizini sunmaktır.

GEREÇ VE YÖNTEM: PubMed, Ovid MEDLINE, EMBASE ve Cochrane Library veritabanları kullanılarak bir literatür taraması gerçekleştirildi. Çalışmaya alınma kriterleri, hamile kadınlarda akut apandisit için bir tanı protokolü olarak MRI kullanımı ve duyarlılık ve özgüllük gibi tanısal parametrelerin varlığı idi. Seçilen her çalışmadan, duyarlılık, özgüllük ve pozitif ve negatif prediktif değerler gibi tanısal doğruluk ölçüleri ve temel demografik bilgiler çıkarıldı. Hamilelik sırasında akut apandisitte MRG'nin tanısal doğruluğu için Forest grafikleri ve özet alıcı çalışma karakteristik eğrileri (SROC) de elde edildi.

BULGULAR: Toplam 22 çalışma ve 2.392 hastanın verileri analiz edildi. 0.18, 0.5 ve 0.6 duyarlılığa sahip birkaç çalışma dışında, çoğu çalışma yüksek duyarlılığa sahipti. Özgüllük açısından, çoğu sonuç 1.0'a yakındı ve en düşük sonuç 0.92 idi. SROC eğrileri, bir eğri altındaki alanın değeri olan 0.9922 tarafından kanıtlandığı üzere, yüksek düzeyde doğruluk göstermiştir.

TARTIŞMA: Manyetik rezonans görüntüleme, hamile kadınlarda akut apandisit tanısı için genel olarak yüksek doğruluk göstermiştir. Bu nedenle hamile kadınlarda apandisit şüphesi için birinci basamak görüntüleme yöntemi olarak iyi bir tanı aracıdır.

Anahtar sözcükler: Apandisit; hamilelik; manyetik rezonans görüntüleme; sistematik inceleme.