Role of Emergency Magnetic Resonance Imaging in the Workup of Suspected Appendicitis in Pregnant Women

Michal M. Amitai MD[1]*, Eldad Katorza MD[2]*, Larisa Guranda MD[1], Sara Apter MD[1], Orith Portnoy MD[1], Yael Inbar MD[1], Eli Konen MD[1], Eyal Klang MD[1] and Yael Eshet MD[1]

Departments of [1]Diagnostic Imaging and [2]Obstetrics and Gynecology, Sheba Medical Center, Tel Hashomer, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ABSTRACT: **Background:** Pregnant women with acute abdominal pain pose a diagnostic challenge. Delay in diagnosis may result in significant risk to the fetus. The preferred diagnostic modality is magnetic resonance imaging (MRI), since ultrasonography is often inconclusive and computed tomography (CT) would expose the fetus to ionizing radiation

Objectives: To describe the process in setting up an around-the-clock MRI service for diagnosing appendicitis in pregnant women and to evaluate the contribution of abdominal MR in the diagnosis of acute appendicitis.

Methods: We conducted a retrospective study of consecutive pregnant women presenting with acute abdominal pain over a 6 year period who underwent MRI studies. A workflow that involved a multidisciplinary team was developed. A modified MRI protocol adapted to pregnancy was formulated. Data regarding patients' characteristics, imaging reports and outcome were collected retrospectively.

Results: Forty-nine pregnant women with suspected appendicitis were enrolled. Physical examination was followed by ultrasound: when positive, the patients were referred for MR scan or surgery treatment; when the ultrasound was inconclusive, MR scan was performed. In 88% of women appendicitis was ruled out and surgery was prevented. MRI diagnosed all cases with acute appendicitis and one case was inconclusive. The overall statistical performance of the study shows a negative predictive value of 100% (95%CI 91.9–100%) and positive predictive value of 83.3% (95%CI 35.9–99.6%).

Conclusions: Creation of an around-the-clock imaging service using abdominal MRI with the establishment of a workflow chart using a dedicated MR protocol is feasible. It provides a safe way to rule out appendicitis and to avoid futile surgery in pregnant women.

IMAJ 2016; 18: 600–604

KEY WORDS: abdomen, magnetic resonance imaging (IMR), appendix, ultrasound, pregnancy

For Editorial see page 625

Acute appendicitis has been estimated to occur in approximately 1 in 1400–6600 pregnancies and accounts for up to 25% of non-obstetric surgeries during pregnancy, making it the most common cause of abdominal pain in pregnancy that requires surgery [1-4]. Delay in diagnosis of acute appendicitis in pregnant women may result in significant risk to the fetus, with a fetal mortality of up to 35%–55% reported in patients with perforated appendicitis versus 1.5% for a non-ruptured appendix [5,6]. Furthermore, unnecessary appendectomies were reported to be associated with spontaneous abortions and premature deliveries.

Diagnosis of acute appendicitis during pregnancy is challenging as symptoms of abdominal pain, elevated body temperature, nausea and vomiting, as well as laboratory markers, such as leukocytosis and elevated C-reactive protein (CRP) are present in normal pregnancies [4]. Physical examination can be misleading. CT, the imaging modality of choice in non-pregnant adults [7], is associated with a substantial ionizing radiation dose. Although the risk of anomalies is considered very low at < 5 mGy compared with other risks of pregnancy [8], every attempt to decrease radiation exposure to the fetus without compromising maternal care is warranted.

Abdominal ultrasound examination, considered accessible and safe, is not always unequivocal, especially in advanced pregnancies, due to overlying bowel gas, the gravid uterus and pregnancy-related obesity (reported sensitivity 67–100% and specificity 83–96%) [9]. Israel et al. [10] report particularly poor sensitivity for ultrasound in suspected appendicitis; in their study of 33 patients, 80% sensitivity for magnetic resonance imaging (MRI) versus 20% for ultrasound was found; the appendix could not be identified on ultrasound in 29 patients, including 3 with proven appendicitis.

Abdominal MRI, employing non-ionizing radiation, has no identifiable adverse effect on the pregnancies or neonatal outcomes [11]. In a previous study [12], the sensitivity, specificity, and positive and negative predictive values (PPV, NPV) of MRI in patients with suspected appendicitis were 91%, 98%, 86% and 99% respectively. MRI is associated with a lower rate of negative laparotomies [13]. The ability to detect other abdominal pathologies causing acute abdominal pain has also been described [14]. However, the availability of MRI is relatively

*The first two authors contributed equally to this study

low and its cost is high. Our institution has decided to gradually make MRI more available to pregnant women presenting with acute abdominal pain to the emergency department.

The aims of this study were to establish a workflow chart using abdominal MRI as an emergency diagnostic tool, and to evaluate the contribution of MRI additional to ultrasound scan in this unique clinical condition. To the best of our knowledge, the existing literature does not refer to the steps needed to establish such a round-the-clock emergency-based MRI imaging service.

PATIENTS AND METHODS

In May 2007 we initiated a service of MR imaging for pregnant women presenting with abdominal pain to the emergency department (ED) of our tertiary medical center. During this process of setting up this service and until March 2013, MRI was performed in 49 consecutive pregnant women to exclude appendicitis. We retrospectively analyzed the data of their medical charts and imaging reports. No lower limit of gestational age was set (gestational age range was 6–37 weeks, mean 25, standard deviation 8).

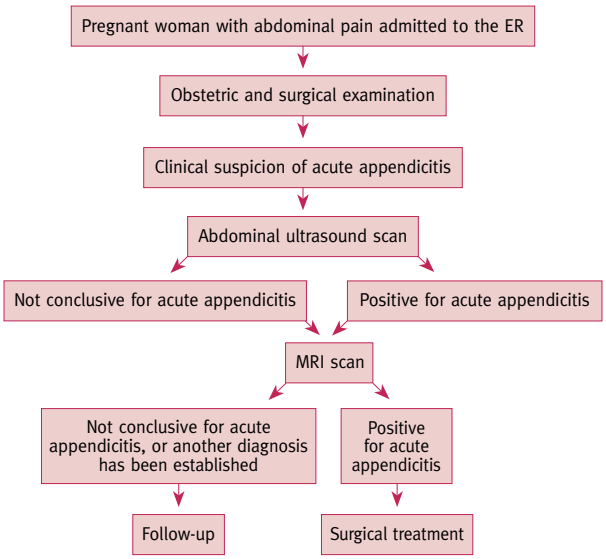
During this period, a workflow that involved surgeons, gynecologists, radiologists and MRI technicians was dynamically created as follows: When a pregnant woman with abdominal pain was admitted to the emergency department she was examined by a gynecologist or a surgeon. If appendicitis was suspected, the woman was referred for ultrasound examination. If the ultrasound did not trace a tubular structure consistent with acute appendicitis, the surgeon coordinated a MRI study with the on-call staff radiologist in order to avoid a futile operation. If the ultrasound examination was suspicious for acute appendicitis the patient was referred for MRI to confirm the diagnosis. At the beginning of the study, a few patients with positive abdominal ultrasound scan and high clinical suspicion for acute appendicitis, for which MR scan was not available immediately, were referred directly to surgery. This pathway was later eliminated from the diagnostic algorithm.

When the MRI scan was positive for acute appendicitis the patient was referred for surgical treatment. Women with inconclusive MRI were observed. A summary of this workflow is presented in Figure 1. The surgeons/gynecologists informed the pregnant woman about the advantages and risks of MRI and obtained a written informed consent.

In the early stages of the study, scans were performed only during working hours and interpreted by experienced abdominal MRI radiologists. Starting in mid-2011, scans were also done round the clock, with initial interpretation by the on-call senior staff radiologist.

Seven of 12 radiologists who were not dedicated abdominal imaging specialists learned to detect the appendix and make a diagnosis of acute appendicitis by participating in an interactive oriented teaching session, reviewing cases of appendicitis and normal appendix in pregnant women. Nevertheless, during the entire study period, dedicated abdominal imaging specialists were available for consultation after working hours in case of doubt.

Figure 1. Suggested algorithm for diagnostic evaluation of suspected appendicitis in pregnancy



Technologists were trained in a separate dedicated teaching session to conduct the modified protocol and to detect appendicular inflammation. They were required to perform the study as soon as possible, and within 12 hours. The staff on-call radiologist provided a preliminary report, which was revised by a dedicated abdominal radiologist the following morning. Clinical decisions were based on the preliminary report.

All scans were performed using a 1.5T whole-body MR scanner (GE Excite, General Electric, Milwaukee, WI, USA) equipped with high performance gradients, using manufacturer-supplied 8-channel cardiac coils.

A modified MRI protocol adapted to pregnancy was formulated. The imaging protocol included the following non-contrast scans: T2 SSFSE coronal, SSFP coronal, SSFP axial, T2 SSFSE sagittal, T2 FS axial, T2 axial, T1 SPGR axial, and T1 SPGR coronal. The field of view extended from the diaphragm cranially to the symphysis pubis caudally. These sequences were chosen in order to include all three orthogonal planes for better spatial resolution due to the fact that the appendix in pregnancy is displaced. SSFP was added for better differentiation between bowel content and adjacent structures, which facilitates the detection of the illeo-cecal valve and eventually the normal or inflamed appendix [Figure 2]. A potential pitfall in the diagnosis of a dilated appendix was the presence of a dilated ovarian vein [Figure 3], a common finding in pregnancy, which is adjacent to the appendix in a pregnant woman. Therefore, a magnetic resonance venography (MRV) (time-of-flight acquisition) sequence was added after

Figure 2. MRI features of normal and pathological appendix during pregnancy. **[A]** T2-weighted coronal MRI image demonstrating normal appendix. The appendix is presented as a blind-ended, tubular structure protruding from the cecum (arrow). **[B]** Acute appendicitis: the appendix is fluid full and dilated. Peri-appendicular fat stranding (arrow head). **[C]** Appendicolith in the tip of the lumen (arrow). In addition to the appendicolith there is a small amount of fluid in the paracolic gutter implying that this is not an innocent appendicolith. **[D]** Inflammatory mass in the right lower quadrant consistent with thickened wall appendix surrounded by fat stranding (arrow head) and thickening of the adjacent peritoneum

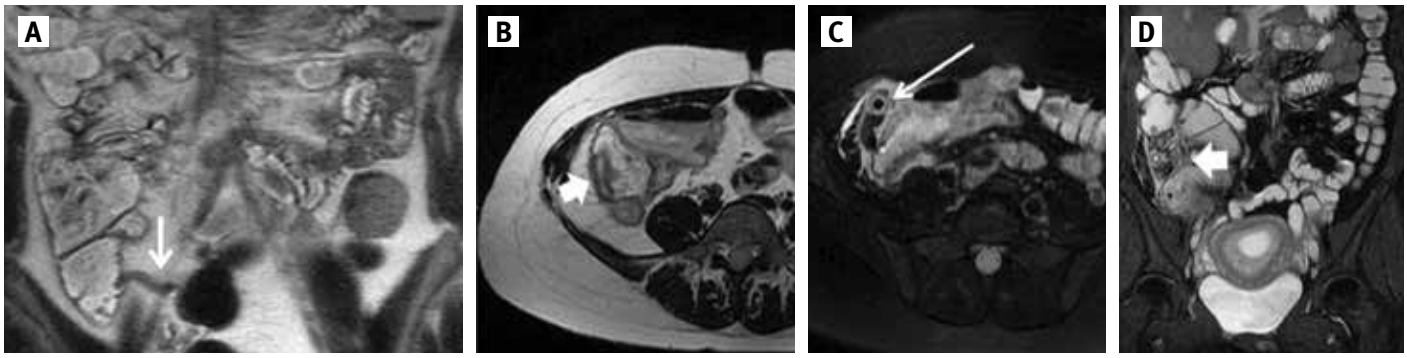
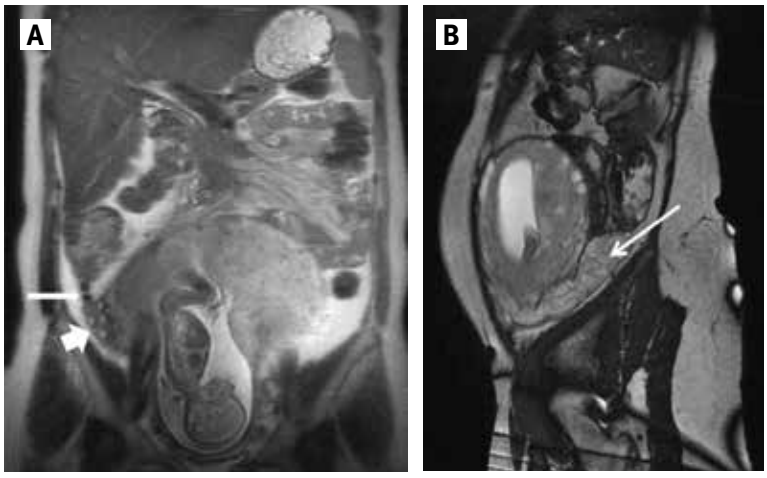


Figure 3. T2 coronal and sagittal steady-state free precession (b-SSFP) pulse sequence. **[A]** Normal appendix (arrow) adjacent to right ovary (arrowhead); this close proximity caused difficulty differentiating between them. **[B]** Ovarian veins plexus (arrow) adjacent to the cecum and appendix are potential pitfalls



24 studies for better differentiation between dilated ovarian veins and the appendix. However, it did not prove beneficial in any of the 25 remaining scans.

Oral injestion of 1.5 liters of mannitol 5% became part of the modified protocol 1 hour before the MRI, as we realized that it facilitated the detection of the cecum, the illeo-cecal valve and the appendix.

Study duration ranged between 20 and 30 minutes. No glucagon or gadolinium was administered. A physician's attendance during the study acquisition was not required. Technicians and on-call radiologists were trained to detect the illeo-cecal valve, the appendix, and appendicular inflammatory signs. The appendix was localized by first recognizing the illeo-cecal valve, and then identifying a blind-ended tubular structure adjacent or protruding from it [Figure 2A]. The tubular structure was inspected on three orthogonal views. Positive MRI findings for appendicitis included: total diameter exceeding 7 mm, appendicular wall thickness > 2 mm, high mural T2 signal secondary to mural edema, and peri-appendicular fat stranding [Figure 2B-D]. The imaging diagnoses were compared with operative findings as the primary reference standard or with clinical follow-up as the secondary reference standard.

After obtaining approval of the institutional ethics review board, relevant demographic, imaging and clinical data of the study patients were retrieved and reviewed from their files and electronic records. Informed consent for data collection was waived.

Patients' white blood cell count (WBC), fever, MRI results, surgical records and post-MRI follow-up were recorded. Fever was defined as body temperature > 38°C, and elevated WBC as > 11,000. Initial MRI reports were correlated with the next day's final report performed by a dedicated abdominal imaging specialist and with surgical and gynecological follow-up outcomes.

Statistical analysis was performed with SigmaStat 1.0 software (Jandel Engineering Ltd, Linslade, Bedfordshire, UK). Continuous variables were compared using the *t*-test while categorical data were compared using Fisher's exact tests where appropriate. A P value < 0.05 was considered significant.

RESULTS

Between 2007 and 2013, 49 women (age 19–42 years, gestational age 6–37 weeks) were referred for MRI to rule out appendicitis. Three (6%) had twin pregnancies. All women presented with abdominal pain, 23 (47%) had elevated WBC and only 2 (4%) had fever. The time between ultrasound and MR scan was 2.5 to 13 hours (average 5.25 hours). Of the 49 women who underwent MRI, only 5 (10%) had a preliminary report diagnosing appendicitis, which was later confirmed surgically. In this subgroup of true appendicitis there was no statistical significance regarding

maternal age, gestational week, presenting symptoms, fever, WBC count, or time between ultrasound and MR scan.

STAFF PERFORMANCE

Of 12 radiologists participating, only 5 were dedicated abdominal imaging specialists. Although in 31% of cases the on-call radiologist was not an abdominal imaging specialist, in only one case was a discordance found between the initial interpretation of the on-call radiologist and the final report of the abdominal specialist (2%) the following day. The initial interpretation was of appendicitis, which was confirmed surgically; however, on reviewing the images, the suspected inflamed tubular structure did not match the appendix according to the most experienced abdominal imager who could not detect the inflamed appendix.

MRI YIELD

In four of five women, appendicitis was found on MRI but not on ultrasound. In 44 women (100%) the study was negative for appendicitis, preventing a futile surgery. One woman (2%) who had an inconclusive MRI report and improved clinically without surgery was considered false positive for statistical analysis. One patient underwent surgery, although the MRI was negative for appendicitis: no appendicitis was found on surgery. In 11 women (22%) the appendix was not identified on MRI and no other signs of inflammation were seen; these studies were interpreted as negative. A follow-up of those women indicated that all symptoms resolved spontaneously.

The overall statistical performance of the study shows a NPV of 100%: 95% confidence interval (95%CI) 91.9–100% and PPV 83.3% (95%CI 35.9–99.6%). In five women appendicitis was suspected on ultrasound: in one of them appendicitis was confirmed on MRI and surgery; in three, appendicitis was ruled out on both MRI and follow-up; and in one, MRI was equivocal and the patient improved clinically under observation. A definitively unnecessary operation was prevented in 4 of 49 women (8%). In the other 39 women, in whom MRI ruled out appendicitis and were not operated, follow-up confirmed the diagnosis. In 6 women (12%) other pathological findings were seen that were possibly responsible for the symptoms: terminal ileum wall thickening (2 women), omental infarct, pyelonephritis, free fluid close to the right kidney, and high signal in the right ovary. The most common incidental finding was hydronephrosis and hydroureter, mainly on the right, found in 12 women.

DISCUSSION

The use of MRI for diagnosis in the emergency department has increased rapidly in the last decade. Pines et al. [15] reported an 85% increase in MRI imaging in the ED in the United States between 2005 and 2009. However, in most medical centers, MRI is unavailable as a round-the-clock service in the ED. Rapp et al. [13] compared two periods – the first when only ultrasound was used, and the second after MRI was introduced – and found that negative laparotomy rates decreased from 55% to 29%. This report correlates with our impression, since in 4 women (8%) in our study appendicitis was suspected on ultrasound and a negative laparotomy was avoided due to the MRI results.

Recent large studies that investigated the utility of MRI for suspected appendicitis in pregnant women found a high diagnostic rate with significant sensitivity and specificity. These studies recommend MRI as the imaging modality of choice for this unique population [16,17].

In our study, in four of five women in whom appendicitis was found on MRI, it was not detected on ultrasound, thus 8% of the appendicitis cases (4/49) might have been missed (false negative rate). Moreover, in five women, appendicitis was suspected on ultrasound but only in one of them was it confirmed on MRI and surgery. These results highlight the need for MR scan even when ultrasound is positive. Although a few patients were referred directly to surgery when ultrasound was positive and MR scan was not available immediately, our suggested workflow recommends performing MR scan in all cases prior to an invasive procedure. Kastenberg et al. [18] examined the cost-effectiveness of preoperative imaging for appendicitis after indeterminate ultrasonography in the second or third trimester of pregnancy. They concluded: "Depending on imaging costs and resource availability, both CT and MRI are potentially cost-effective. The risk of radiation-associated childhood cancer from CT has little effect on population-level outcomes or cost-effectiveness but is a concern for individual patients." Another publication states that every attempt to decrease radiation exposure to the fetus without compromising maternal care is warranted [8]. From the cumulative data regarding the imaging mode of choice for acute appendicitis during pregnancy, mainly during the first trimester, MRI seems to be superior to other imaging modalities [19].

We gradually established a service of 24 hour availability to diagnose acute appendicitis in the population of pregnant women to reduce maternal and fetal morbidity. Establishing the service involved the following: creating a workflow process, choosing the appropriate MR protocol, educating the radiology staff (technicians and physicians), and strengthening professional cooperation between physicians from various disciplines. The high PPV and NPV in our series prove the feasibility of our service although more than half the radiologists (7/12) making an initial diagnosis were not dedicated abdominal imaging specialists. Those results are in concordance with Leeuwenburgh et al. [20] who recently published an inter-observer comparison of dedicated and non-dedicated radiologists reading MRI for suspected appendicitis. MR experts and MR non-experts agreed on appendicitis in 89% of cases (as compared to 98% in our study). The NPV in our study was high for 44 patients, implying that when the MRI is negative for pregnant patients with clinical suspicion of appendicitis, surgery can be avoided.

MR has been used to evaluate obstetric disease for over 20 years without any documented harmful effects, based on numerous clinical and laboratory studies [21]. Some concerns linger regarding the heating effects of radiofrequency pulses and of the effects of acoustic noise on the fetus [22]. MRI can be used in pregnant women if considered necessary by the referring physician and attending radiologist, regardless of gestational age, if clinically indicated [23]. In our study, we attempted to not include a patient in the first trimester of pregnancy (< 13 weeks). Nonetheless, we imaged 4 of 49 first-trimester patients due to a high clinical suspicion and non-conclusive ultrasound. Although the use of MR scan during early pregnancy is well established in the literature [7, 17], written informed maternal consent is recommended to document maternal understanding of the risk-benefit ratio and alternative diagnostic options, if any.

In our study we did not inject contrast material to avoid possible gadolinium side effects. The women in our study received oral contrast preparation containing 1.5 L Manitol 5% 1 hour before the MRI study. Those oral preparations act as a biphasic (low signal intensity on T1 sequences and high signal intensity on T2 sequences). Dewhurst and co-authors [24] reported "using negative contrast agent (i.e., dark signal) on both T1- and T2-weighted imaging sequences without causing considerable susceptibility artifact." Several authors have proposed a non-oral contrast technique with good results (i.e., similar sensitivity and specificity as for oral contrast), although these focused primarily on the diagnostic accuracy of MRI. The oral contrast may be an invaluable component of the examination however, as it increases confidence in visualizing the normal appendix and possibly affecting morbidity by avoiding unnecessary laparotomies [13,25]. Reports estimating the impact of MRI on surgical outcomes using an MRI protocol without oral contrast are lacking [14].

Some limitations of the study can be noted. Firstly, this was a retrospective study and not all the patients were evaluated in the final protocol that we created. Secondly, we focused on acute appendicitis, and other pathologies that could be the cause of pain in these patients were only briefly mentioned. Thirdly, the series was small compared to previous studies. Finally, this was a single-center experience and application of our suggested workup is recommended for other medical centers as well.

Our study focused on the importance of a round-the-clock MRI service, choosing the appropriate MR protocol, education for radiologists and technologists, and strengthening professional cooperation among different services. Identification of the appendix, whether healthy or inflamed, is crucial in the clinical management of pregnant patients with suspected acute appendicitis. Our study showed the major contribution and the superiority of abdominal MR scan in this unique clinical condition. We confirmed that when the MRI is negative for appendicitis, unnecessary surgery can be avoided.

Correspondence
Dr. M.M. Amitai
Dept. of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer 52621, Israel
Fax: (972-3) 535-7315, **email:** michal.amitai@sheba.health.gov.il

References

1. 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.
2. Mazze RI, Kallen B. Appendectomy during pregnancy: a Swedish registry study of 778 cases. *Obstet Gynecol* 1991; 77: 835-40.
3. Gilo NB, Amini D, Landy HJ. Appendicitis and cholecystitis in pregnancy. *Clin Obstet Gynecol* 2009; 52: 586-96.
4. Andersen B, Nielsen TF. Appendicitis in pregnancy: diagnosis, management and complications. *Acta Obstet Gynecol Scand* 1999; 78: 758-62.
5. 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.
6. Tracey M, Fletcher HS. Appendicitis in pregnancy. *Am Surg* 2000; 66: 555-9; discussion 559-60.
7. Zoarets I, Poluksht N, Halevy A. Does selective use of computed tomography scan reduce the rate of "white" (negative) appendectomy? *IMAJ* 2014, 16: 335-7.
8. Brent RL, Mettler FA. Pregnancy policy. *AJR* 2004; 182: 819-22; author reply 822.
9. Williams R, Shaw J. Ultrasound scanning in the diagnosis of acute appendicitis in pregnancy. *Emerg Med J* 2007; 24: 359-60.
10. 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.
11. Kanal E, Borgstede JP, Barkovich AJ, et al. American College of Radiology White Paper on MR Safety: 2004 update and revisions. *AJR* 2004; 182: 1111-14.
12. Long SS, Long C, Lai H, Macura KJ. Imaging strategies for right lower quadrant pain in pregnancy. *AJR* 2011; 196: 4-12.
13. 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.
14. Beddy P, Keogan MT, Sala E, Griffin N. Magnetic resonance imaging for the evaluation of acute abdominal pain in pregnancy. *Semin Ultrasound CT MR* 2010; 31: 433-41.
15. Pines JM, Mullins PM, Cooper JK, Feng LB, Roth KE. National trends in emergency department use, care patterns, and quality of care of older adults in the United States. *J Am Geriatr Soc* 2013; 61: 12-17.
16. Burke LM, Bashir MR, Miller FH, et al. Magnetic resonance imaging of acute appendicitis in pregnancy: a 5-year multiinstitutional study. *Am J Obstet Gynecol* 2015; 213: 693 e691-6.
17. Theilen LH, Mellnick VM, Longman RE, et al. Utility of magnetic resonance imaging for suspected appendicitis in pregnant women . *Am J Obstet Gynecol* 2014; 212: 345 e341-6.
18. Kastenberg ZJ, Hurley MP, Luan A, et al. Cost-effectiveness of preoperative imaging for appendicitis after indeterminate ultrasonography in the second or third trimester of pregnancy. *Obstet Gynecol* 2013; 122: 821-9.
19. 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.
20. Leeuwenburgh MM, Wiarda BM, Jensch S, et al. Accuracy and interobserver agreement between MR-non-expert radiologists and MR-experts in reading MRI for suspected appendicitis. *Eur J Radiol* 2014; 83: 103-10.
21. Shellock FG, Crues JV. MR procedures: biologic effects, safety, and patient care. *Radiology* 2004; 232: 635-52.
22. 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.
23. Kanal E, Borgstede JP, Barkovich AJ, et al. American College of Radiology White Paper on MR Safety. *AJR* 2002; 178: 1335-47.
24. Dewhurst C, Beddy P, Pedrosa I. MRI evaluation of acute appendicitis in pregnancy. *J Magn Reson Imaging* 2013; 37: 566-75.
25. Pedrosa I, Lafornara 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.