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ORIGINAL RESEARCH CONTRIBUTION

Computed Tomography With Intravenous Contrast Alone: The Role of Intra-abdominal Fat on the Ability to Visualize the Normal Appendix in Children

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Abstract

Background: Computed tomography (CT) with enteric contrast is frequently used to evaluate children with suspected appendicitis. The use of CT with intravenous (IV) contrast alone (CT IV) may be sufficient, however, particularly in patients with adequate intra-abdominal fat (IAF).

Objectives: The authors aimed 1) to determine the ability of radiologists to visualize the normal (nondiseased) appendix with CT IV in children and to assess whether IAF adequacy affects this ability and 2) to assess the association between IAF adequacy and patient characteristics.

Methods: This was a retrospective 16-center study using a preexisting database of abdominal CT scans. Children 3 to 18 years who had CT IV scan and measured weights and for whom appendectomy history was known from medical record review were included. The sample was chosen based on age to yield a sample with and without adequate IAF. Radiologists at each center reread their site's CT IV scans to assess appendix visualization and IAF adequacy. IAF was categorized as "adequate" if there was any amount of fat completely surrounding the cecum and "inadequate" if otherwise.

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Results: A total of 280 patients were included, with mean age of 10.6 years (range = 3.1 to 17.9 years). All 280 had no history of prior appendectomy; therefore, each patient had a presumed normal appendix. A total of 102 patients (36.4%) had adequate IAF. The proportion of normal appendices visualized with CT IV was 72.9% (95% confidence interval [CI] = 67.2% to 78.0%); the proportions were 89% (95% CI = 81.5% to 94.5%) and 63% (95% CI = 56.0% to 70.6%) in those with and without adequate IAF (95% CI for difference of proportions = 16% to 36%). Greater weight and older age were strongly associated with IAF adequacy ($p < 0.001$), with weight appearing to be a stronger predictor, particularly in females. Although statistically associated, there was noted overlap in the weights and ages of those with and without adequate IAF.

Conclusions: Protocols using CT with IV contrast alone to visualize the appendix can reasonably include weight, age, or both as considerations for determining when this approach is appropriate. However, although IAF will more frequently be adequate in older, heavier patients, highly accurate prediction of IAF adequacy appears challenging solely based on age and weight.

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The evaluation of children with suspected appendicitis frequently includes diagnostic imaging, most often computed tomography (CT).[1–3] Institutions vary on the specific CT protocols used, particularly on the types of contrast administered (oral, rectal, and/or intravenous [IV]).[4–6] Enteric contrast is believed to improve appendix visualization in children, who may lack the intra-abdominal fat (IAF) of adults that serves as a natural contrast for inflammation in the abdomen. While oral contrast protocols are sensitive and specific, drinking contrast prolongs emergency department (ED) length of stay, and children with abdominal pain often find it difficult to tolerate the oral contrast.[7–9] Additionally, if contrast fails to reach the area of the appendix, the child may be exposed to additional radiation as "delayed" imaging may be obtained. Rectal contrast is an alternative that addresses some of these issues, but its use depends on provider comfort with rectal administration and availability during off-hours and is an added discomfort for the patients.[10–12]

Given the difficulties with enteric contrast, prior studies have examined whether children could undergo abdominal CT imaging without its use.[12,13] In one observational study, abdominal CT with only IV contrast (CT IV) and CT with enteral and IV contrast together had similar sensitivities (93 and 92%, respectively) and specificities (92 and 87%).[12] In a separate study, CT IV sensitivity was 97%, and specificity 93%.[13] Yet, despite this evidence, CT IV has not been widely adopted. Reasons for the reluctance to use CT IV might include the limitations of those prior studies such as single-institution designs, small sample sizes, and reliance on radiologists experienced with the CT IV protocol.[10] To address these prior potential limitations, we conducted a multicenter study with the aim to determine the ability of radiologists to visualize the normal (nondiseased) appendix on CT IV in children and to examine whether this ability depended upon the adequacy of patient IAF (as currently believed). Additionally, we examined whether a patient's degree of IAF was associated with sex, age, and weight, potentially enabling the identification of those children who could forego enteric contrast.

METHODS

Study Design

This was a retrospective study at 16 centers in the Pediatric Emergency Care Applied Research Network (PECARN) using a preexisting database of abdominal CT scans that were obtained for an unrelated study of children who had blunt abdominal trauma.[14] Institutional review board (IRB) approval was obtained at all sites with waiver of written informed consent.

Study Setting and Population

We included patients aged 3 to 18 years old who had CT IV and had recorded weights in their ED medical records for their index visits. We excluded patients whose CT scans identified intra-abdominal injuries. Patients with only small amounts of intra-abdominal free fluid on CT were eligible, as this can be a normal (physiologic) finding and was not believed to confound our study outcomes.

Study Protocol

Research coordinators at each site reviewed local medical records to verify that the weight in the PECARN blunt abdominal trauma database was accurate and was measured (rather than estimated). We determined if patients had undergone appendectomies prior to the date of their CT. While both patients with and without appendectomies were eligible for our study, patients whose surgical histories were unavailable for verification were excluded. We determined appendectomy history by review of: 1) ED charts from the day of the CT, 2) electronic pathology and operative reports, and 3) hospital records for up to two prior visits preceding the date of the CT, specifically examining surgical history. Surgical history was considered available if discrete documentation was found in the medical record. Finally, we excluded patients who, upon CT screen by the radiologist, were noted to have oral contrast used or if there were abnormalities on CT (e.g., prior surgery) that could prevent the appendix from being visualized.

CT Interpretation. Radiologists at each participating site were provided a list from the PECARN data center of their site's CT IV scans to review. They were blinded to

patient weight and surgical history and were instructed not to refer to previous CT reports (which might comment on the appendix). Radiologists reviewed each CT and completed a standardized data collection form that included CT imaging parameters, their characterization of the patient's IAF, and their ability to visualize the normal appendix (yes or no). The same radiologist at each site judged these findings for each patient at that site. Based on the prior work of Basak et al.,[15] a patient's IAF was defined for this study as either "adequate" or "inadequate," dependent on the presence and distribution of cecum fat. To reduce the risk of bias from the same radiologist assessing for both appendix presence and IAF adequacy, the wording for the question regarding IAF was asked as "Is there any degree of fat completely surrounding the cecum?" rather than asked specifically as IAF adequacy. IAF was categorized as "adequate" if the radiologist visualized any amount of fat completely surrounding the cecum or as "inadequate" if the fat did not completely surround the cecum. At six sites, two radiologists reviewed a subset of CT scans to assess the degree of interobserver reliability for appendix visualization and IAF characterization.

Sample Size

We based our sample size (n = 280) on the ability to detect a 10% difference in the proportion for whom the radiologist visualized the appendix between patients with and without adequate IAF ($\alpha = 0.05$, $B = 0.2$; two-tailed test). We assumed that the proportion of patients whose appendix would be visualized on CT IV with adequate IAF would be 95%. To assure a final study population with a potentially even distribution of children in both the IAF adequate and the IAF inadequate groups, we used age as a surrogate for IAF based on the work of Grayson et al.,[16] who illustrated that children older than 10 years had more IAF on CT scan than did younger children. Therefore, the data center randomly sampled 140 patients younger, and 140 patients at least 10 years of age, from the PECARN database.

Data Analysis

We calculated 95% confidence intervals (CIs) for the proportions of patients whose appendices were visualized on CT IV in order to describe the radiologist's ability to visualize the normal appendix for those with and without adequate IAF. To assess interrater reliability between radiologists for the ability to detect the appendix and for IAF adequacy, we used the unweighted kappa statistic. We used logistic regression to determine the association between IAF adequacy and the ability to visualize the normal appendix and to assess the association between IAF adequacy and sex, age, and weight. Due to the clustered nature of our data, initially a random intercepts model was considered. However, the results of this model did not differ substantially from the logistic regression. Therefore, we have chosen to present the results of the logistic regression for ease of interpretation.

RESULTS

We screened 468 patients with CT IV previously enrolled in the PECARN abdominal trauma study.[14] Of these, 124 were excluded for the following reasons: patient weight estimated (n = 62), surgical history unavailable (n = 23), no recorded weight (n = 21), CT performed with oral contrast (n = 9), lack of one site IRB approval (n = 4), and no radiologist screen completed (n = 5). An additional 27 patients were excluded after radiologist screening. The PECARN data center then randomly selected from the 317 remaining patients (153 younger than 10 years and 164 older) to achieve the desired 280 patient sample for attending or fellow radiologist (n = 26) review. All CTs used in this study were conducted with standard collimation cuts (range = 2.5 to 5.0 mm/slice).

The mean patient age was 10.6 years (range = 3.1 to 17.9 years). As per study design, 50% were younger than 10 years. A majority of patients (171 of 280, 61%) were male. All 280 patients analyzed had no history of prior appendectomy, and thus every study CT scan should have had a normal appendix present.

Radiologists visualized the normal appendix in 204/280 patients (72.9%; 95% CI = 67.2% to 78.0%) and noted 102 of 280 patients (36.4%) to have adequate IAF. Radiologists visualized the appendix in 91 of 102 patients (89.2%) with adequate IAF and 113 of 178 patients (63.4%) with inadequate IAF (95% CI for difference of proportions = 16% to 36%).

To assess the reliability of appendix visualization and IAF characterization, two radiologists reviewed a subset of 20% of the CT scans (n = 56). Raw agreement for the presence of the appendix (yes or no) was 69.6%, with an unweighted kappa of 0.33 (95% CI = 0.07 to 0.59). However, raw agreement was 90% when both reviewers agreed on the patient having adequate IAF. The raw agreement between radiologists for describing a patient's degree of IAF was 87.5% (49 of 56), with an unweighted kappa of 0.59 (95% CI = 0.32 to 0.86).

On bivariate analyses, IAF adequacy was associated with older age, greater weight, and female sex (Table 1). While these findings were statistically significant, there was overlap in both age and weight between those with adequate and inadequate IAF. For example, the youngest patient with adequate IAF was 3.2 years old, while there were children with inadequate IAF as old as 17.9 years.

As age and weight were highly correlated (r = 0.83), we developed separate logistic regression models based on these characteristics (Table 2), noting independent relationships between IAF adequacy and age and weight. In Figures 1 and 2, we further explored the potential interactions between sex and age and between sex and weight noted in the logistic models. In each figure, we note that age and weight appear more strongly associated with IAF adequacy for females. Overall, weight appears to be a stronger predictor than age for IAF adequacy for both sexes.

DISCUSSION

In this present study, we note that radiologists across multiple institutions more accurately visualized the normal appendix in the presence of adequate IAF, with moderate interrater agreement of IAF adequacy. Furthermore, we found that IAF adequacy was strongly

Table 1
Bivariate Association Between Patient Characteristics and IAF Adequacy on CT

Characteristic	IAF Adequate (n = 102)	IAF Not Adequate (n = 178)	p value
Age (yr), mean ± SD	11.6 ± 3.87	10.0 ± 4.19	0.002
Weight (kg), mean ± sd (range)	50.9 ± 22.0 (16–121.7)	38.0 ± 19.8 (12.3–127)	<0.001
Sex			0.035
Male (n/N, %)	54/171 (31.6)	117/171 (68.4)	
Female (n/N, %)	48/109 (44.0)	61/109 (55.9)	

IAF = intra-abdominal fat.

Table 2
Logistic Regression Models to Assess Relationship Between Age and Weight and IAF Adequacy

Models	Parameter	Beta	p-value
Model to assess age, AUC = 0.642	Age	0.160	0.001
	Sex	0.706	0.350
	Age × sex	−0.113	0.081
Model to assess weight, AUC = 0.704	Weight	0.048	<0.001
	Sex	0.482	0.477
	Weight × sex	−0.026	0.070

AUC = area under the receiver operating characteristic curve; IAF = intra-abdominal fat.

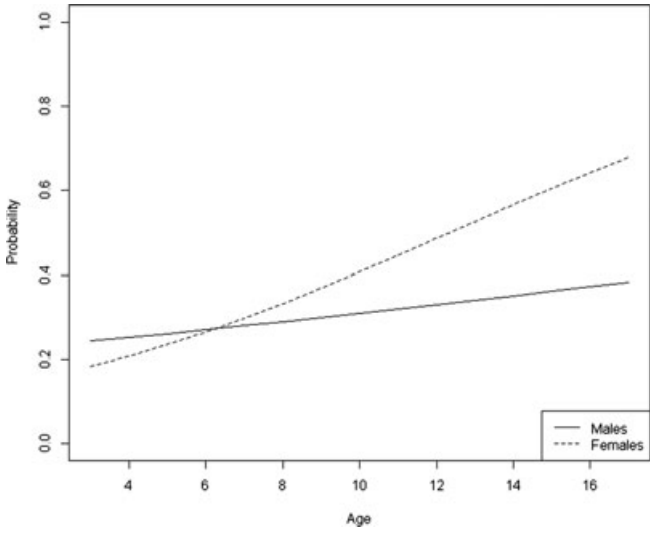

Figure 1. Probability of adequate IAF based on sex and age. IAF = intra-abdominal fat.

associated with patient age and weight, with this association more pronounced in females. However, although clinicians may expect adequate IAF in older, heavier children, the overlap between the clinical characteristics (weight and age) of children with and without adequate IAF precludes providing a specific prediction scheme based on these readily available factors.

Our results build on mainly single-center studies that noted that IAF adequacy was related to the accuracy of abdominal CT interpretation.[15–17] Radiologists have cited children's lack of IAF as leading to more indeterminate or incorrect interpretations.[12,16,18–20] In one

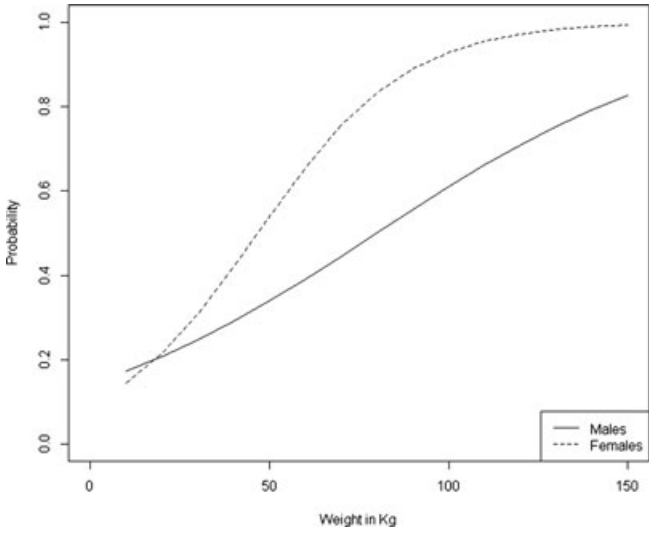

Figure 2. Probability of adequate IAF based on sex and weight. IAF = intra-abdominal fat.

study, the appendix was seen in 68.8% of patients with moderate or marked IAF versus 36.1% with minimal IAF.[16] The IAF highlights inflammation (seen as the classic "fat stranding" on CT) and helps radiologists to rule out appendicitis even in cases when the appendix itself is not visualized.[21–23]

Our finding that 89% of patients with adequate IAF had their appendices visualized on CT IV is similar to the results of prior studies of children being assessed for appendicitis with CT IV. Because we studied visualization of the nondiseased (normal) appendix, the proportion we found in our study can be compared to the specificity of CT IV in studies of children evaluated for appendicitis, which in two prior studies was noted to be 92 and 93%.[12,13] The overall proportion of normal appendices visualized that we noted (72.9%) was substantially lower than the specificity in these studies and may reflect the sampling strategy we used, which resulted in a younger population who were more likely to have inadequate IAF.

Our study helps address the practical problem faced by clinicians regarding whether particular children may forego receiving enteric contrast when attempting to visualize the appendix. Similar to prior studies, we noted a trend toward increasing IAF with increasing age.[16] Our study builds on prior data by identifying weight as a potentially better predictor of IAF

adequacy than age. It must be understood, however, that the data leave unclear the specific weight threshold(s) at which IAF adequacy is assured, as there were heavier children judged to have inadequate IAF. More evaluation of patients across the span of weights and for each sex will be required to potentially determine, for example, the threshold at which a clinically acceptable proportion (e.g., 90%) of children will have adequate IAF.

LIMITATIONS

Our study had the limitation of using CT scans obtained for trauma evaluation rather than patients being evaluated for possible appendicitis. Further research is needed, therefore, to examine the generalizability of our findings, particularly the ability to visualize the normal appendix with CT with IV contrast only, to children of all ages with suspected appendicitis. Another important limitation is the lack of availability of height to use body mass index (BMI) rather than weight to evaluate for an association with IAF adequacy. Although height (and BMI) appears not to be routinely assessed in EDs, use of BMI may be a more robust predictor of IAF adequacy. Additionally, the radiologists did not evaluate any CT scans in patients who had prior appendectomies. We attempted to minimize the potential bias this might cause in CT interpretation (e.g., bias toward stating that the normal appendix was visualized) by blinding radiologists to surgical history. Although our population was younger than in prior studies of those with possible appendicitis, this sampling strategy allowed for a broad distribution of patient ages and weights for which we could assess IAF adequacy. Finally, although multiple radiologists participated in the study, the majority were at large academic centers with substantial pediatric radiology expertise, making the results less generalizable to other settings.

CONCLUSIONS

Our data demonstrate a strong relationship between intra-abdominal fat and patient weight and age. Protocols using computed tomography with intravenous contrast alone to visualize the appendix can reasonably include weight and/or age as considerations for determining when this approach is appropriate. However, although intra-abdominal fat will more frequently be adequate in older, heavier patients, highly accurate prediction of intra-abdominal fat adequacy appears challenging solely based on age and weight. Further study is warranted to assess the generalizability of our results to children with suspected appendicitis.

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APPENDIX A

We acknowledge the efforts of the following individuals participating in PECARN at the time this study was initiated:

PECARN Steering Committee: N. Kuppermann, Chair; E. Alpern, D. Borgialli, J. Callahan, J. Chamberlain, P. Dayan, J. M. Dean, M. Gerardi, M. Gorelick, J. Hoyle, E. Jacobs, D. Jaffe, R. Lichenstein, K. Lillis, P. Mahajan, R. Maio, F. Moler, D. Monroe, R. Ruddy, R. Stanley, M. Tunik, A. Walker.

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