Acute abdominal pain : considerations on diagnosis and management

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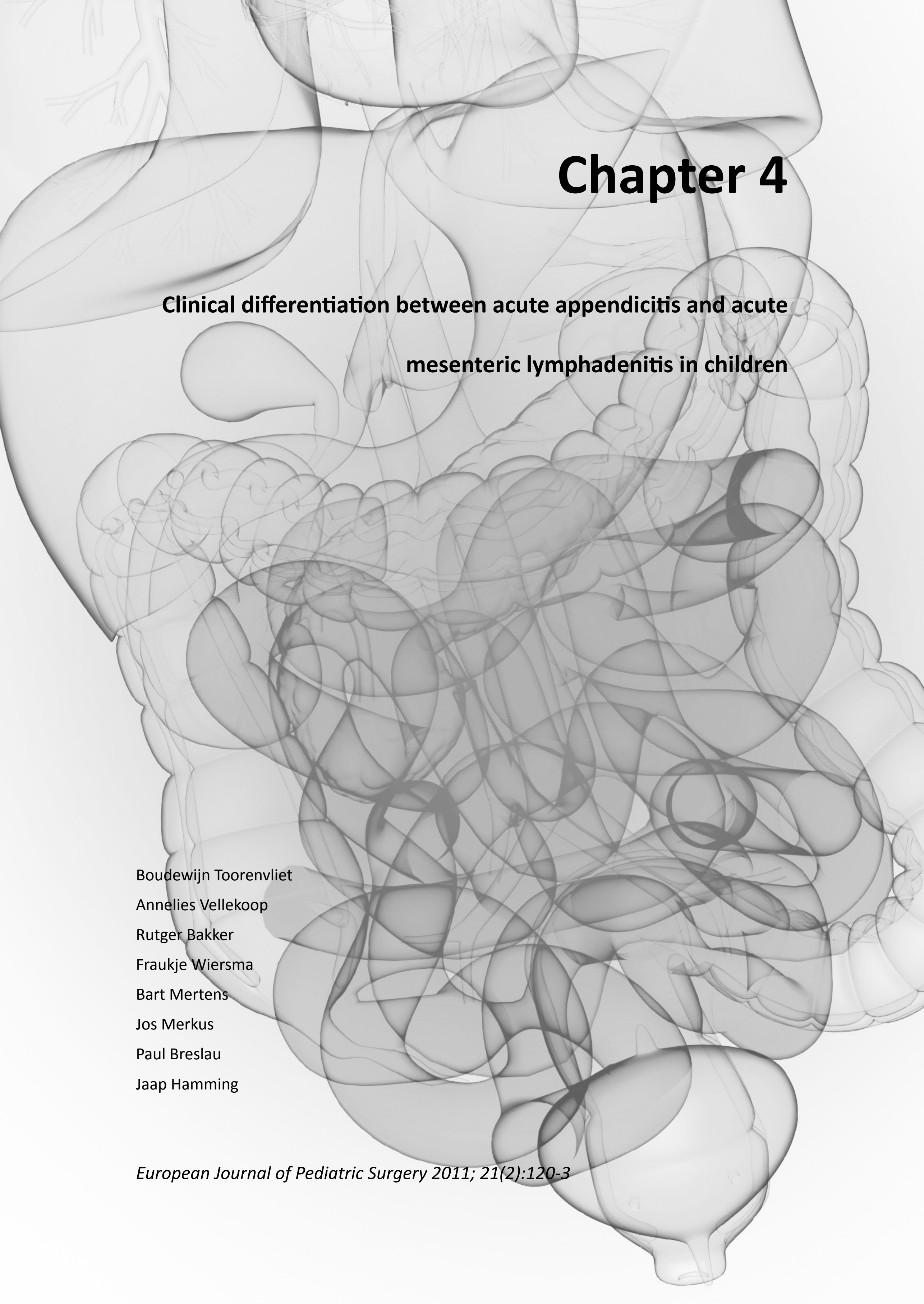

Chapter 4

Clinical differentiation between acute appendicitis and acute mesenteric lymphadenitis in children

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European Journal of Pediatric Surgery 2011; 21(2):120-3

Abstract

Introduction: Acute mesenteric lymphadenitis in children has a clinical presentation very similar to that of acute appendicitis. The aim of this study was to evaluate whether it is possible to clinically differentiate between acute appendicitis and acute mesenteric lymphadenitis in children.

Methods: A prospective cohort analysis was performed for all children (<17 years) presenting to the emergency department of our institution with acute abdominal pain between June 2005 and July 2006. The relevant clinical parameters, clinical and radiological diagnoses and all management decisions were scored prospectively. Ultrasound was the primary imaging modality for the majority of patients. All patients were re-evaluated until a final diagnosis was attained. The Alvarado score was calculated retrospectively, and a logistic regression model was used to analyze the diagnostic potential of the clinical parameters.

Results: Two hundred and eighty-nine patients were eligible for analysis. Thirty-eight patients had acute mesenteric lymphadenitis, and 69 patients had acute appendicitis as a final diagnosis. The positive predictive values of the clinical diagnosis, the Alvarado score and the logistic regression model were 0.62, 0.81 and 0.79 respectively. Ultrasound had a positive predictive value of 96% for acute appendicitis.

Conclusion: It is not possible to accurately distinguish acute mesenteric lymphadenitis from acute appendicitis in children using clinical evaluation alone. Ultrasound should be performed in equivocal cases.

Introduction

Acute appendicitis is the most common surgical emergency in children, but its accurate clinical diagnosis continues to challenge physicians. The clinical presentation of acute mesenteric lymphadenitis is often difficult to differentiate from that of acute appendicitis[1,2], and acute mesenteric lymphadenitis has been a common finding during negative surgical explorations for suspected appendicitis[3]. As acute mesenteric lymphadenitis is a self-limiting disease, and because negative explorations for suspected appendicitis should be kept to a minimum, it is important to make an accurate diagnosis before taking management decisions. Some authors encourage the use of clinical scores to help diagnose acute appendicitis[4,5], some promote the use of additional radiological imaging[6], whilst others suggest using both[7].

This study attempted to investigate whether it is possible to clinically distinguish acute appendicitis from acute mesenteric lymphadenitis in children. Our hypothesis was that this is not possible and that additional imaging is necessary for an accurate diagnosis.

Methods

This study was performed in a middle-sized urban teaching hospital with a 24 hour emergency service. All consecutive patients under 17 years old with acute abdominal pain evaluated at the emergency department between June 2005 and July 2006 were included in the study. A surgical resident always made the primary assessment, and a consultant surgeon evaluated the patient if necessary. All patients were assessed using a structured diagnostic and management strategy algorithm. First, a “clinical diagnosis” was made based on the patient’s history, physical examination, and biochemical blood and urine analysis. All clinical parameters were registered on a study form. It is not common practice to use clinical scores for appendicitis at our hospital, and residents were not asked to do so for this study. Nonetheless, all parameters necessary to calculate the Alvarado score[4] were scored prospectively on the study form. After conferring with the consulting surgeon, a decision was made whether or not to perform additional radiological imaging. Suspected appendicitis was always considered an indication for additional imaging, and ultrasound is the primary examination used in our hospital for the evaluation of acute abdominal pain in children. All ultrasound examinations were performed by 1 of 5 certified radiologists with similar levels of experience. The abdomen was examined using an ATL HDI 5000 ultrasound system (ATL HDI 5000; Philips Medical Systems, Bothell, WA, USA). All abdominal organs were examined with special attention paid to the appendix, using the graded compression technique[8]. Mesenteric lymphadenitis was diagnosed by ultrasound if three or more enlarged (short axis, 8 mm or more), hypervascular mesenteric lymph nodes were depicted[9]. All patients that were not admitted to the surgical ward following surgical consultation at the emergency department were given appointments for re-evaluation at the out-patient clinic within 24 hours. There, the diagnosis and management strategies were reassessed by the consultant surgeon or a surgical resident under the supervision of a consultant surgeon. Additional radiological examinations were made if deemed necessary. Patients were discharged from outpatient follow-up only when a final diagnosis had been made and the treatment successfully initiated or completed, or if the patient no longer had abdominal complaints. The final diagnosis was based on intraoperative findings and/or pathological examination of the resected organ. If patients were not operated, the final diagnosis was made by the clinical and/or radiological diagnosis in combination with the clinical response to medical therapy at standard re-evaluation and follow-up as described above.

All hospital records were reviewed by 2 surgical residents (BT and RB), who double checked the available information and verified the final diagnoses for all patients in the database. Patients were excluded from analysis if they did not show up for the re-evaluation appointment or if the study form was missing or incomplete. For all these patients, the hospital records were searched and patients were contacted for additional information. If the patients could not be successfully contacted, their general practioner was consulted for the patient’s medical records.

Statistical analysis was performed using SPSS 16.0. Student’s t-test was used for continuous variables and Fischer’s exact test for binomial variables. A 2 tailed p-value smaller than 0.05 was considered significant. To assess the predictive diagnostic potential of clinical parameters, a logistic regression model with ridge shrinkage penalization was applied[10]. Double cross-validatory joint estimation and calibration was used to obtain unbiased estimates of predictive performance[11]. All patients with acute mesenteric lymphadenitis as a final diagnosis were contacted by phone three years after the end of the study period for follow-up.

Results

During the study period, 345 patients under the age of 17 were eligible for inclusion. Thirteen patients (3.8%) were excluded from analysis when they did not show up for re-evaluation and another 43 patients (12.5%) were excluded as their study forms were incomplete or missing. For 6 of these patients no follow-up details were acquired (1.7%). Of the 50 patients excluded from analysis for whom follow-up was successful, five had acute appendicitis and were treated at our own hospital. They were excluded because their study forms were missing or incomplete. Two hundred and eighty-nine patients were eligible for analysis.

Two hundred and sixteen patients (74.7%) were evaluated at the emergency department at the request of a general practitioner (183) or a consultant from another specialty (33). One hundred and seventy of these referrals (78.7%) were due to suspected appendicitis.

Two hundred of the 289 patients (69.2%) underwent additional radiological imaging. Ultrasound was performed 142 times at primary evaluation and 69 times at re-evaluation. Eleven patients had additional imaging on both days. Eight children (4.0%) underwent complementary computed tomography (CT) after an inconclusive ultrasound.

Appendicitis

Acute appendicitis was the clinical diagnosis for 98 patients of whom 93 underwent additional radiological imaging (94.9%). Sixty-one of these patients (62.2%) ultimately had acute appendicitis as a final diagnosis (figure 1). Fifty-eight patients were operated for acute appendicitis on the day of primary evaluation and 11 patients were operated for appendicitis at re-evaluation. The perforation rate was 34.5% and 27.3% respectively. A total of 71 patients were operated for suspected appendicitis, two of whom ultimately had a non-inflamed appendix (2.8%). Therefore 69 patients had acute appendicitis as a final diagnosis.

Acute mesenteric lymphadenitis

Nineteen patients were suspected to have acute mesenteric lymphadenitis after clinical evaluation. All of these patients had additional radiological imaging (ultrasound only), but only 8 (42.1%) had acute mesenteric lymphadenitis as a final diagnosis. Thirty-eight patients had mesenteric lymphadenitis as a final diagnosis, all of whom underwent additional imaging (37 patients had an ultrasound, 1 patient had a complementary CT after an inconclusive ultrasound). Nineteen patients, who were suspected to have acute appendicitis after clinical evaluation, had mesenteric lymphadenitis as a final diagnosis (figure 1). Twenty-seven patients were diagnosed as having mesenteric lymphadenitis at primary evaluation, and 11 were diagnosed at re-evaluation. Six of the 38 patients were admitted to the hospital, the others were re-evaluated at the out-patient clinic. Follow-up after three years was successful for 35 of the 38 patients (92.1%) with mesenteric lymphadenitis as a final diagnosis. Thirty-two of these 35 patients (91.4%) had no more episodes of abdominal pain after their evaluation for acute abdominal pain during the study period. Three patients had episodes of recurrent abdominal pain but did not seek medical help.

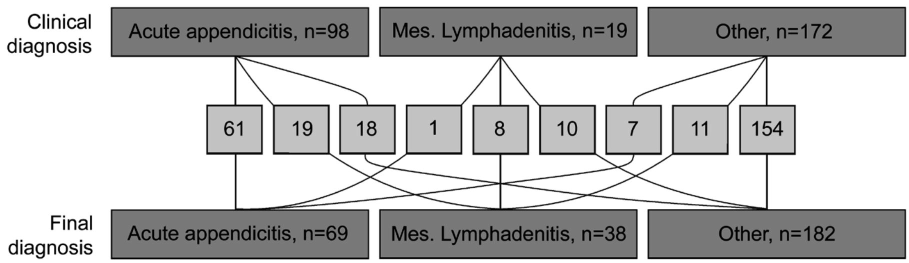

Figure 1. Diagnostic changes between the clinical diagnosis at initial evaluation and the final diagnosis.

Clinical parameters

Patients with mesenteric lymphadenitis were younger, less nauseous, vomited less and reported the migration of pain to the right lower quadrant less often than patients with acute appendicitis. Patients with acute appendicitis had significantly more rebound tenderness and abdominal guarding. The leucocytes counts, the percentage of neutrophilic granulocytes and the serum C-reactive protein levels were higher in patients with acute appendicitis (table 1).

The diagnostic accuracy of the clinical diagnoses, the radiological diagnoses, the Alvarado score and the predictive model using logistic regression are listed in table 2. The Alvarado score could be calculated in retrospect using the clinical parameters obtained during the primary evaluation. We used a cutoff value for appendectomy of 7 or more points out of a total of 10.

Table 1. Clinical parameters.

	LM	AA	p
No. of patients	38	69	
Age (years)	7.9 (SD 3.5)	10.3 (SD 3.7)	0.001*
Male	28 (73.7)	48 (69.6)	0.824
Duration of complaints (days)	2.2 (SD 1.7)	2.1 (SD 1.9)	0.840
Nausea	25 (65.8)	62 (89.9)	0.004*
Vomiting	18 (47.4)	52 (75.4)	0.005*
Anorexia	21 (55.3)	50 (72.5)	0.089
Migration of pain to RLQ	5 (13.2)	28 (40.6)	0.004*
Dysuria	1 (2.6)	6 (8.7)	0.417
Heart rate	93.1 (SD 13.9)	94.7 (SD 18.2)	0.644
Temperature (°C)	37.3 (SD 1.0)	37.5 (SD 0.9)	0.479
RLQ Tenderness	30 (78.9)	62 (89.9)	0.149
Rebound tenderness	8 (21.1)	38 (55.1)	0.001*
Abdominal guarding	2 (5.3)	20 (29.0)	0.005*
Leucocytes ($x10^9$/l)	10.7 (SD 5.1)	14.7 (SD 5.5)	0.000*
Neutrophilic granulocytes (%)	65.4 (SD 21.7)	75.3 (SD 18.4)	0.013*
C-reactive protein	17.8 (SD 19.1)	56.2 (SD 56.8)	0.000*
Erythrocyte sedimentation rate	15.1 (SD 14.9)	18.6 (SD 15.0)	0.246

The number in parentheses are standard deviations (SD) for the given mean values, or percentages for the number of patients tallied.
*, p<0.05; RLQ, right lower quadrant.

Table 2. Diagnostic accuracy.

	TP	FP	FN	TN	Total	Sens	Spec	PPV	NPV	LR+	LR-
All Children (n=289)											
Clinical diagnosis AA	61	37	8	183	289	0.88	0.83	0.62	0.96	5	0.14
Clinical diagnosis ML	8	11	30	240	289	0.21	0.96	0.42	0.89	5	0.83
*Additional radiological examinations (n=211) **											
Additional radiological imaging	64	3	6	138	211	0.91	0.98	0.96	0.96	43	0.09
Children with acute appendicitis or acute mesenteric lymphadenitis as a final diagnosis (n=107)											
Alvarado score (cutoff ≥ 7 / 10)	48	11	21	27	107	0.70	0.71	0.81	0.56	2	0.43
Predictive model	55	15	14	23	107	0.80	0.61	0.79	0.62	2	0.34

AA, Acute Appendicitis; ML, Mesenteric Lymphadenitis; TP, true positive; FP, false positive; FN, false negative; TN, true negative; Sens, sensitivity; Spec, specificity; PPV, positive predictive value; NPV, negative predictive value; +LR, positive likelihood ratio; LR-, negative likelihood ratio;.
*, 96% Ultrasound only, 4% Ultrasound and complementary CT.

Discussion

Our analysis showed that there are many clinical parameters which differ significantly between children with acute mesenteric lymphadenitis and acute appendicitis. Even so, these differences did not result in a clinical differentiation accurate enough to determine the proper management. In our study group of 289 children, the positive predictive value for acute appendicitis and mesenteric lymphadenitis was 0.62 and 0.42 respectively. Using the prospectively scored data to determine the Alvarado score for patients with acute appendicitis or mesenteric lymphadenitis as a final diagnosis, we calculated a positive predictive value of 0.81 for acute appendicitis. This would not have been accurate enough to determine an appropriate management strategy for these patients. Even with the logistic regression model to estimate the potential diagnostic performance of these variables, the positive predictive value was 0.79. Again, this would not be sufficient to manage patients correctly as it would lead to an unacceptable amount of negative explorations.

Making an accurate clinical diagnosis for patients with acute appendicitis remains challenging and a perfect test has yet to be found. Mesenteric lymphadenitis is an important clinical mimic of appendicitis in children[1,2,12], and has been reported as the most common finding during negative surgical explorations for suspected appendicitis[3]. Acute mesenteric lymphadenitis is a self-limiting disease caused by pathogens such as Yersinia Enterocolitica, Campylobacter jejuni, Salmonella enteritidis and Yersinia pseudotuberculosis[13,14]. It is characterized by fever, abdominal pain, nausea and sometimes diarrhea or constipation. In some cases it is associated with an upper respiratory infection[15]. Mesenteric lymphadenitis can be diagnosed quite accurately by ultrasound or CT, and is a common finding when patients are sent for radiological imaging if there is a clinical suspicion that they have acute appendicitis. Some patients can thus be spared a negative exploration. This is important as negative explorations for suspected appendicitis carry a realistic risk of morbidity and increase hospital costs[16]. When additional imaging is required to determine the cause of acute abdominal pain in children with suspected appendicitis, CT has a better accuracy than ultrasound[17]. There is evidence however that the ionizing radiation that children are exposed to when undergoing an abdominal CT increases the lifetime mortality risk from cancer[18]. Pediatric abdominal CT scans should therefore be avoided whenever possible, and we agree with those who propagate the use of abdominal ultrasound as the primary examination of choice in such cases[6,19].

Clinical scores are also frequently used for the diagnosis of acute appendicitis. The Alvarado score and the pediatric appendicitis score described by Samuel were found to increase diagnostic accuracy and thus help the clinician to determine the appropriate management[4,5]. However, when these scores were validated prospectively by others, the accuracies reported by the original authors could not be reproduced[7,20,21]. Schneider et al. concluded that both scores provided useful information for the diagnosis of acute appendicitis, but that neither method was sufficient to determine the need for surgery[20]. The other authors proposed the use of two cutoff scores; a low score for ruling out appendicitis and a higher score for predicting appendicitis[7,21]. They suggested that all patients with intermediate scores should undergo additional radiological examinations to make an accurate diagnosis and determine appropriate management. We found no literature on the performance of clinical scores in differentiating acute appendicitis from conditions mimicking appendicitis such as acute mesenteric lymphadenitis.

During the design of this study, several measures were taken to ensure that an accurate assessment could be made of the diagnostic performance of clinical evaluation and additional imaging. A limitation of this study however, is that we did not score hopping, coughing or percussion pain and thus Samuel's pediatric appendicitis score (PAS) could not be calculated. Having said this, we would not expect a major difference in our results if we had done so, as the performance of the Alvarado score did not differ significantly from the PAS in a prospective analysis of 588 children with suspected appendicitis[20]. Another limitation is that the presence of upper respiratory infections was not scored, and could therefore not be used as a variable in our logistic regression model.

Conclusion

This study showed that it is not possible to accurately distinguish acute mesenteric lymphadenitis from acute appendicitis in children using only clinical evaluation. Even the Alvarado score and our logistic regression model could not differentiate between the two entities with enough diagnostic accuracy to determine the appropriate management. These results support our hypothesis that additional radiological imaging should be performed in children with suspected appendicitis. This allows those patients with acute mesenteric lymphadenitis to be identified that do not require surgery. In our institution, ultrasound was the primary investigation of choice for these cases, and a complementary CT was hardly ever necessary.

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