Predictors of Intussusception in Young Children

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Objective: To identify predictors of intussusception in young children.

Design: A retrospective cross-sectional study.

Setting and Patients: A consecutive sample of children younger than 5 years on whom contrast enemas were performed because of suspected intussusception seen at an urban children's hospital from 1990 to 1995.

Methods: We evaluated historical, clinical, and radiographic variables. Variables documented in 75% or more of the medical records and associated with intussusception (P < .20) in the univariate analysis were evaluated in a multiple logistic regression analysis. Variables retaining significance (P < .05) in the multivariate analysis were considered independent predictors of intussusception. We used bootstrap resampling techniques to validate the multivariate model.

Results: Sixty-eight (59%) of the 115 patients had intussusception. Univariate predictors of intussusception included male sex, age younger than 2 years, history of emesis, rectal bleeding, lethargy, abdominal mass, and a highly suggestive abdominal radiograph. In the multivariate analysis, we identified only 4 independent predictors (adjusted odds ratio; 95% confidence interval): a highly suggestive abdominal radiograph (18.3; 4.0-83.1), rectal bleeding (17.3; 2.9-104.0), male sex (6.2; 1.2-32.3), and a history of emesis (13.4; 1.4-126.0). We identified 3 of these 4 variables (all but emesis) as independent predictors in more than 50% of 1000 bootstrap data samples.

Conclusions: Rectal bleeding, a highly suggestive abdominal radiograph, and male sex are variables independently associated with intussusception in a cohort of children suspected of having this diagnosis. Knowledge of these variables may assist in clinical decision making regarding diagnostic and therapeutic interventions.


Editor's Note: Watch out for fecal blood on the bootstraps. Catherine D. DeAngelis, MD

INTUSSUSCEPTION is the most common cause of intestinal obstruction in infants and young children. Intussusception occurs when one segment of bowel telescopes into another, leading to venous compression and bowel wall edema. If not diagnosed and treated early, the disease process may progress to arterial obstruction, bowel necrosis, perforation, and, rarely, death. Patients with intussusception frequently present with abdominal pain and vomiting, and may be difficult to distinguish from patients with more benign gastrointestinal conditions. A number of epidemiological and clinical factors associated with intussusception have been cited in the literature and include age younger than 12 months, male sex, vomiting, abdominal pain, abdominal mass, rectal bleeding, and lethargy. The 4 symptoms and signs classically described in patients with intussusception (vomiting, abdominal pain, abdominal mass, and bloody stool), however, are present together in fewer than one half of patients with the disease.

The diagnosis of intussusception is made by air or liquid contrast enema or by ultrasound examination. Contrast enema is considered the criterion standard for diagnosis; however, this procedure is more time-consuming and invasive than diagnostic ultrasound, and requires the use of ionizing radiation. The identification of reliable predictors of intussusception may help in clinical decision making regarding the use of diagnostic ultrasound and air or liquid contrast enema in the evaluation of possible intussusception.

Most previous studies have not assessed variables predictive of intussusception using multivariate statistical methods. Therefore, those studies are limited by the lack of adjustment for other important factors.
PATIENTS AND METHODS

We performed a retrospective cross-sectional study of a consecutive sample of children aged 1 month to 5 years on whom contrast enemas were performed to evaluate the possibility of intussusception. These contrast enemas were performed in the radiology department of a large urban children’s hospital between January 1990 and June 1995. The study was approved by the institutional review board of the participating hospital.

INCLUSION CRITERIA

All children aged 1 month to 5 years who had contrast enemas performed specifically to confirm or exclude the diagnosis of intussusception were eligible for the study. To avoid information bias, however, only patients who had histories and physical examinations documented in the medical record prior to the contrast enema were considered eligible for study (ie, in some cases, the documentation of the physical examination was timed after the performance of the contrast enema or was missing from the medical record entirely). In cases of multiple physical examinations prior to the contrast enema, data from the physical examination documented closest in time prior to the enema were used in the analysis. These examinations may have been performed in a hospital emergency department, an outpatient clinic, or hospital ward, but were included as long as the other criteria were met. Physical examinations performed by physicians-in-training (ie, residents) were not analyzed.

EXCLUSION CRITERIA

Patients were excluded from the study if the diagnosis of intussusception was known (from ultrasound or contrast enema examination) prior to the history and physical examination documented in the medical record.

DATA COLLECTION

Each chart was reviewed in a systematic fashion by a single investigator (T.O.’D.) masked to the results of the contrast enema at the time of chart review. Demographic, historical, and clinical data were collected from each eligible patient’s medical record and transcribed onto a structured data sheet prior to investigator review of the contrast enema results. For the purposes of this study, the plain abdominal radiographs were interpreted by a single pediatric radiologist (L.P.) who was unaware of the contrast enema findings. The radiographs were categorized as follows: (1) not suggestive of intussusception (normal bowel gas pattern and no signs of mass or obstruction), (2) moderately suggestive of intussusception (abnormal but non-specific bowel gas pattern and no obvious mass or obstruction), and (3) highly suggestive of intussusception (soft tissue mass, evidence of bowel obstruction or a visible intussusceptum).24-26 In each case, contrast enema was performed using water-soluble contrast material (Gastrografin) by an attending pediatric radiologist. Patients were considered to have intussusception if the radiologist performing the contrast enema documented intussusception in the written report.

STATISTICAL ANALYSIS

All statistical tests were performed using Stata 5.0 statistical software.27 Univariate Analysis

To minimize the chance of spurious statistical associations with intussusception, variables were chosen for univariate analysis if they met either of the following criteria: (1) the variable had been demonstrated in a previous study to be associated with intussusception, or (2) there was biologic plausibility to the association of a given variable with intussusception. Categorical variables were compared between patient groups using the χ2 test. Continuous variables were analyzed using the t test. All statistical tests were conducted based on 2-tailed alternatives and P≤.05 was considered significant.

Multivariate Analysis

Variables were considered for evaluation in a backward elimination logistic regression analysis if they met both of the following criteria: (1) the variable of interest was recorded in 75% or more of the medical records and (2) the variable was associated with intussusception in the univariate analysis with P≤.20. The choice of this α level for entry allows for consideration of variables that show a trend toward significance in the univariate analysis, and may achieve significance in the presence of other variables.28 Variables that retained an association with intussusception with a P≤.05 in the multivariate analysis were considered to be independent predictors of intussusception. We calculated the area under the receiver operating characteristic (ROC) curve for the model. The area under an ROC curve is a representation of the predictive accuracy of a model. An area under the ROC curve of 0.5 represents a model with chance predictive ability and an area under the ROC curve of 1 represents a perfectly sensitive and specific model. We also calculated the model pseudo R2 (the proportion of variation explained by the model) and the Hosmer-Lemeshow goodness-of-fit statistic for the final model identified in the multivariate analysis.29

Bootstrap Validation

To validate the multivariate model, we created 1000 bootstrap samples, using computer-generated random sampling. Bootstrapping refers to a process by which new databases (‘samples’) of the same size as the original database are created by random sampling of the original database with replacement.29,30 In a given bootstrap sample, a data point from the original database may by chance be selected once, more than once, or not at all. This method can be used to validate multivariate models (ie, assess the stability of a model), as well as to estimate confidence intervals (CIs) and SEs.29,30 To assess the stability of our model, we repeated the multivariate analysis on 1000 random bootstrap samples of our data to identify the frequency with which each candidate variable, alone and in combination, would be selected into the prediction model.

Clinical Prediction

For the purposes of developing a stable prediction model, we chose a priori to construct a clinical prediction algorithm using only variables that were selected as independent predictors in more than 50% of the multivariate analyses using the 1000 bootstrap data samples.31
predictive and confounding variables. The objective of this study was to identify and validate independent predictors of intussusception in young children using multivariate statistical techniques.

RESULTS

During the 5½-year study period, 143 patients aged 1 month to 5 years had contrast enemas performed to evaluate the possibility of intussusception. Twenty-eight of these patients were ineligible for study because their histories and physical examination results were documented after the contrast studies were performed. Thus, 115 patients met inclusion criteria for the study, of whom 68 (59%) had intussusception confirmed by contrast enema study.

UNIVARIATE ANALYSIS

Sixteen variables met the criteria for univariate analysis (Table 1). Of the 10 variables associated with intussusception with \( P \geq .20 \) in the univariate analysis, 8 were documented in 75% or more of the patient records and therefore met entry criteria for the multivariate analysis. For the purposes of evaluation in the multivariate analysis, a history of rectal bleeding and physical examination evidence of rectal bleeding (gross or occult) were collapsed into one variable to avoid collinearity. This left 7 variables as candidate predictors for the multivariate analysis.

MULTIVARIATE ANALYSIS

The data from 72 (41 with intussusception) of the 115 patients who had all 7 of the univariate correlates of intussusception recorded were entered into the multiple logistic regression analysis (Table 2). The prevalence of intussusception in the 43 patients excluded from this multivariate analysis because of missing data was similar to that of patients included in the multivariate analysis (27/43 [63%] vs 41/72 [57%]; odds ratio, 1.3; 95% CI, 0.6-2.7; \( P = .54 \)). Four independent predictors of intussusception were identified in the multivariate analysis (\( P \leq .05 \)): a highly suggestive abdominal radiograph, rectal bleeding, male sex, and a history of emesis. The area under the ROC curve for this model was 0.90 and the pseudo \( R^2 \) was 0.46. The Hosmer-Lemeshow goodness-of-fit statistic (\( P = .89 \)) indicated a well-fit model.

Table 1. Univariate Analysis*

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Intussusception, No. (%) of Patients</th>
<th>P</th>
<th>OR (95% CI)</th>
<th>% of Charts Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Historical variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;2 y</td>
<td>65/68 (96) 32/47 (68)</td>
<td>&lt;.001</td>
<td>10.2 (2.9-35.0)</td>
<td>100</td>
</tr>
<tr>
<td>Male sex</td>
<td>47/68 (69) 27/47 (57)</td>
<td>.20</td>
<td>1.7 (0.9-3.6)</td>
<td>100</td>
</tr>
<tr>
<td>History of intussusception</td>
<td>2/57 (4) 2/42 (5)</td>
<td>.75</td>
<td>0.7 (0.1-4.3)</td>
<td>86</td>
</tr>
<tr>
<td>Emesis</td>
<td>63/66 (95) 33/45 (73)</td>
<td>.001</td>
<td>7.6 (2.1-27.0)</td>
<td>97</td>
</tr>
<tr>
<td>Bilious emesis</td>
<td>26/46 (57) 12/31 (39)</td>
<td>.13</td>
<td>2.1 (0.8-5.2)</td>
<td>67</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>25/32 (78) 24/29 (83)</td>
<td>.65</td>
<td>0.7 (0.2-2.6)</td>
<td>53</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>40/57 (70) 11/42 (26)</td>
<td>&lt;.001</td>
<td>6.6 (2.7-16.0)</td>
<td>86</td>
</tr>
<tr>
<td>Lethargy</td>
<td>30/36 (83) 10/20 (50)</td>
<td>.008</td>
<td>5.0 (1.5-17.0)</td>
<td>49</td>
</tr>
<tr>
<td>Poor feeding</td>
<td>32/40 (80) 22/30 (73)</td>
<td>.51</td>
<td>1.5 (0.5-4.3)</td>
<td>61</td>
</tr>
<tr>
<td>Clinical variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature ( &gt;38.0^\circ C )</td>
<td>13/66 (20) 11/47 (23)</td>
<td>.64</td>
<td>0.8 (0.3-2.0)</td>
<td>98</td>
</tr>
<tr>
<td>Listless/lethargic appearance</td>
<td>31/63 (49) 8/43 (19)</td>
<td>.001</td>
<td>4.2 (1.7-10.0)</td>
<td>92</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>15/44 (34) 11/39 (28)</td>
<td>.56</td>
<td>1.3 (0.5-3.3)</td>
<td>72</td>
</tr>
<tr>
<td>Abdominal pain on palpation</td>
<td>22/55 (40) 14/40 (35)</td>
<td>.62</td>
<td>1.2 (0.5-2.9)</td>
<td>82</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>25/63 (40) 6/41 (15)</td>
<td>.006</td>
<td>3.8 (1.4-10.0)</td>
<td>90</td>
</tr>
<tr>
<td>Fecal blood</td>
<td>40/48 (83) 15/38 (39)</td>
<td>&lt;.001</td>
<td>7.7 (2.9-21.0)</td>
<td>75</td>
</tr>
<tr>
<td>Highly suggestive abdominal radiograph</td>
<td>51/59 (86) 13/44 (30)</td>
<td>&lt;.001</td>
<td>15.0 (5.7-40.0)</td>
<td>89</td>
</tr>
</tbody>
</table>

* OR indicates odds ratio; CI, confidence interval.

Table 2. Independent Predictors of Intussusception Identified in the Multivariate Analysis

<table>
<thead>
<tr>
<th>Independent Predictor</th>
<th>Adjusted OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly suggestive abdominal radiograph</td>
<td>18.3 (4.0-83.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>17.3 (2.9-104.0)</td>
<td>.002</td>
</tr>
<tr>
<td>History of emesis</td>
<td>13.4 (1.4-126.0)</td>
<td>.02</td>
</tr>
<tr>
<td>Male sex</td>
<td>6.2 (1.2-32.3)</td>
<td>.03</td>
</tr>
</tbody>
</table>

* OR indicates odds ratio; CI, confidence interval.

BOOTSTRAP VALIDATION

In 1000 randomly selected bootstrap samples, 3 of the independent predictors were selected more than 50% of the time: a highly suggestive abdominal radiograph (93%), rectal bleeding (69%), and male sex (54%). The frequency of selection of the other variables were history of emesis, 44%; abdominal mass, 9%; age, 8%; and listless or lethargic appearance, 8%. Figure 1 demonstrates the frequency with which the 3 independent predictors (highly suggestive abdominal radiograph, rectal bleeding, and male sex), alone and in combination, were selected in the 1000 bootstrap samples. This is a more strict criterion for model agreement than identifying the frequency with which each individual predictor is selected. In 84% of the bootstrap samples, at least 2 of these
3 independent predictors were selected together in the multivariate model.

**CLINICAL PREDICTION**

Of the independent predictors of intussusception that were selected in more than 50% of bootstrap samples, a highly suggestive abdominal radiograph and rectal bleeding were the most important (Table 3). Fifty-one (80%) of 64 (95% CI, 68%-89%) patients with highly suggestive abdominal radiographs had intussusception. Six (38%) of 16 (95% CI, 15%-65%) patients with moderately suggestive abdominal radiographs had intussusception. Six (38%) of 23 (95% CI, 1%-28%) patients with nonsuggestive abdominal radiographs, however, also had intussusception. Of the 71 patients with either a history or physical examination evidence of rectal bleeding, 52 (73%; 95% CI, 61%-83%) had intussusception. A negative stool heme test, however, did not exclude the diagnosis as 8 (26%) of 31 patients documented to be negative for fecal blood on examination (95% CI, 12%-45%) also had intussusception. Male sex was the least useful of these 3 independent predictors. Of patients with intussusception, 69% were male compared with 57% of patients without intussusception.

Combinations of independent predictors allowed for more accurate assessment of risk of intussusception (Figure 2). Of the 17 patients without either rectal bleeding or highly suggestive abdominal radiographs, none had intussusception (95% CI, 0%-16%). Conversely, of the 43 patients with both rectal bleeding and highly suggestive abdominal radiographs, 38 (84%; 95% CI, 71%-94%) had intussusception.

Twenty-four (21%) of the 115 patients were missing data on abdominal radiographs (n = 9), fecal blood status (n = 12), or both (n = 3). Eight of the 9 patients who were missing abdominal radiographs alone had intussusception, and 7 of these 8 patients had fecal blood. Eight of the 12 patients missing information about fecal blood alone had intussusception, of whom 7 had highly suggestive abdominal radiographs. One (male) of the 3 patients who were missing data on both predictors had intussusception.

In this study, several variables were found to be associated with intussusception in the univariate analysis. The major contribution of this study, however, is the identification and validation of independent predictors of intussusception by multivariate analysis. Of the univariate predictors, only rectal bleeding, a highly suggestive abdominal radiograph, and male sex retained significance in the multivariate analysis and were selected as independent predictors in more than 50% of 1000 bootstrap data samples. We therefore developed a clinical prediction rule based on these 3 independent predictors of intussusception.

We did not find significant differences between patients with and without intussusception with regard to history of abdominal pain or abdominal pain on palpation. A history of intermittent drawing up of the legs1,5 was recorded infrequently and thus could not be analyzed fully. A history of lethargy, commonly reported in patients with intussusception,12-13 was associated with intussusception in our univariate analysis. Because information regarding this variable was recorded in only 49% of the medical records, it did not meet entry criteria for the multivariate analysis. The presence or absence of lethargy on examination, however, was documented in the majority of patient records. This variable was significant in the univariate analysis, but was not found to be independently predictive of intussusception in the multivariate analysis.

In our study, as in previous studies, rectal bleeding (gross or occult) was identified as an important predictor of intussusception.8,11-13 Intussusception also occurred, however, in 24% of patients without a history or examination evidence of rectal bleeding. We also found male sex to be an independent predictor of intussusception. The male-female ratio of patients with intussusception in our study (2.2:1) is similar to that in several other series.8,11,12 This predominance persisted after adjusting for a highly suggestive abdominal radiograph and the presence of rectal bleeding. Although male patients with signs and symptoms of intussusception should be considered somewhat more likely to have the disease, this variable was the least important of the predictors in our model.

The utility of plain radiographs in diagnosing intussusception has been the subject of controversy, with regard to their sensitivity and specificity2,24-26,36-41 as well as to interobserver reliability.25,26,38,40 In the present study, a highly suggestive abdominal radiograph was found to be an important independent predictor. Intussusception, however, also occurred in 21% of patients without highly suggestive radiographs, similar to what has been reported previously.2,12 Therefore, although a highly suggestive abdominal radiograph is useful in identifying patients at high risk for intussusception, a negative or only moderately suggestive radiograph does not exclude the diagnosis. In addition, the interpretation of an abdominal radiograph may vary depending on the experience of the physician reviewing the radiograph, the level of comfort with pediatric radiology, and the quality and technique of the radiograph.2,24,26,36,39,40

In a recent prospective study of clinical predictors of intussusception, the authors identified right upper
quadrant abdominal mass, rectal bleeding and the triad of intermittent abdominal pain, vomiting, and right upper quadrant abdominal mass as significantly predictive of intussusception.13 Negative predictors were also identified, but none with sufficient accuracy to obviate evaluation with ultrasound or air or contrast enema. Plain abdominal radiography was not evaluated in that study, and the predictive model was not validated.13 We chose to include abdominal radiography in our study because of its wide availability and frequent use, both in community and academic hospital settings.

Our study differs from most previous studies investigating risk factors for intussusception in that we used multivariate statistical methods and validated our model using bootstrap sampling techniques. Using these methods, we identified 3 stable independent predictors from the many variables found to be associated with intussusception in the univariate analysis. These 3 variables were each selected in more than 50% of 1000 bootstrap data samples. The presence or absence of these independent predictors is easily evaluated in most clinical settings using bedside stool heme testing and plain abdominal radiography.

While the 3 predictors in our model considered alone provide useful information, the predictors in combination allowed for better assessment of risk of intussusception. This study suggests that patients initially suspected of having intussusception, but who have neither evidence of rectal bleeding nor highly suggestive radiographs have a low probability of having this diagnosis. The upper end of the 95% CI for this negative predictive value, however, includes a clinically important false-negative rate (16%). Therefore, the absence of these high-risk predictors does not exclude the possibility of intussusception. In these lower-risk patients, although air or liquid contrast enema may not be immediately indicated, diagnostic ultrasound to exclude the possibility of intussusception should be considered.13,16-21,41 The presence of either rectal blood or a highly suggestive abdominal radiograph in a patient suspected of having intussusception, however, should prompt the clinician to proceed directly to air or liquid contrast enema.

There are several limitations to this study. First, as this study was retrospective, it was limited by incomplete reporting of study variables in the medical records. Missing data prevented many patients eligible for the study from being included in the regression analysis and may have limited the power to detect clinically important associations. In addition, the patient histories and physical examinations used in the analysis of the data were performed by physicians with different specialty training and clinical experience, and included general pediatricians, general emergency physicians, and pediatric emergency physicians. This variety of specialty training, however, likely reflects the true spectrum of practitioners evaluating children at risk for intussusception. Therefore, this enhances the generalizability of the results of this study. Finally, suspicion of intussusception was evident in that all patients in this study had contrast enemas performed (ultrasound for the diagnosis of intussusception was not routinely performed at the study institution during the study period). Because our model was developed on this cohort of patients for whom the possibility of disease was sufficient to warrant imaging for suspected intussusception, the results can only be applied to patients considered to be at similar risk of intussusception rather than to all patients presenting with a particular symptom such as vomiting or rectal bleeding. Clinical and ethical considerations, however, would preclude the study of patients not truly suspected of having intussusception. A prospective study with structured data collection of a larger number of patients at risk of intussusception in different clinical settings could serve to further validate our results.

In conclusion, a highly suggestive abdominal radiograph, rectal bleeding, and male sex are independent predictors of intussusception in a population of children who are suspected of having this diagnosis. A highly suggestive abdominal radiograph and rectal bleeding are the strongest of the 3 predictors. The presence of either or both of these predictors in children in whom intussus-
Intussusception is being considered should prompt the clinician to expedite air or liquid contrast enema. The absence of these predictors is associated with a low probability of disease.

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