Predictors of Chronic Abdominal Pain Affecting the Well-Being of Children in Primary Care

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ABSTRACT

PURPOSE Abdominal pain is a frequent symptom among children but is rarely associated with organic disease. Although it may persist for years, no factors have been identified that predict its prognosis. Our aim was to determine whether patient characteristics at initial consultation can predict chronic abdominal pain severe enough to influence the child's well-being at 1 year of follow-up.

METHODS We conducted this prospective cohort study in primary care, including consecutive children aged 4 to 17 years seen for abdominal pain by their family physician. Multivariate logistic regression analysis was used to identify prognostic factors that predicted chronic abdominal pain 1 year later. Discriminative ability of identified predictors was assessed using the area under the receiver operating characteristic curve and explained variance.

RESULTS The risk of having chronic abdominal pain at 1 year of follow-up was 37.1% in the cohort overall. Increasing age, waking up at night with pain, high levels of other somatic complaints, and chronic abdominal pain at baseline independently predicted chronic abdominal pain at 1 year. These predictors had a poor to moderate discriminative ability, however; the area under the receiver operating characteristic curve was only 0.69, and the predictors collectively explained only 14.3% of variance in the development of chronic abdominal pain. The absolute risk ranged from 19.4% among children having none of the predictors to 65.5% among children having 3 or 4 predictors.

CONCLUSIONS Chronic abdominal pain sufficient to affect well-being is common among children initially seen for abdominal pain by family physicians. Although the risk of this outcome increases with number of predictors, these predictors are of limited value in identifying children in whom pain will become chronic, suggesting that other, as yet unidentified factors play an important role.

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INTRODUCTION

Abdominal pain in children accounts for about 5% of childhood consultations in general practice in the Netherlands,[1] which is in agreement with studies performed in Australia and the United States reporting similar numbers of 2% to 4%.[2,3] Most cases are considered medically unexplained and are labeled as functional abdominal pain (FAP).[4] In 10% to 15% of schoolchildren, abdominal pain persists or returns regularly, which increases health care use and has implications for the child's well-being in that they have poorer school attendance, withdraw from social activities, and show impaired physical abilities.[5-7] One in 3 children with chronic FAP continues to experience this pain for at least 5 years, underscoring the burden of disease.[8] In addition, childhood FAP has been linked to functional gastrointestinal (GI) disorders in adulthood, such as irritable bowel syndrome.[9-13]

Despite evidence that childhood FAP may persist for years, few factors have been identified that predict whether it interferes with the child's well-being.[13] Recently, a high level of non-GI symptoms was found to be associated with a greater likelihood of functional GI disorders in young adulthood.[14] This finding suggests that having other somatic symptoms, in addition to abdominal pain, may be a potentially useful clinical marker of increased risk

for poor long-term outcomes in children with FAP. Having a parent with GI symptoms is another factor related to persistence of abdominal pain.[12] Because these factors can easily be incorporated into the medical evaluation, they have potential clinical utility. Ideally, family physicians would be able to identify children at risk for long-term abdominal pain and make more appropriate management decisions at an earlier stage, such as using more stringent follow-up or consulting other (mental) health care workers. The present study therefore aimed to determine which patient characteristics easily incorporated into the initial medical evaluation could predict chronic abdominal pain (CAP) that is severe enough to interfere with a child's well-being 1 year later.

METHODS

Design, Setting, and Patients

This was an observational prospective cohort study with a 1-year follow-up. A total of 53 family physicians were recruited in Rotterdam, a large multicultural city, and its rural surroundings. The included practices comprise a population of about 16,000 children aged 4 to 17 years. During a 2-year period, consecutive children in this age-group consulting with a new symptom of abdominal pain were invited to participate in the study. Abdominal pain was defined as new if the child had not visited the family physician during the past 3 months for the same symptom. We excluded children with a previous diagnosis of inflammatory bowel disease, celiac disease, or lactose intolerance, and children unable to complete questionnaires because of language or cognitive problems. As this was an observational study, no diagnostic work-up tool was used, and the extent of diagnostic work-up to exclude possible organic disease was left to the family physician's discretion. Parental consent was obtained for all participants; child consent was also obtained for children aged 12 years or older. The study protocol was approved by the local ethics committee.

To check for possible selection bias, we compared important characteristics of eligible included children and eligible nonincluded children. Relative to eligible nonincluded children, the included children were younger (mean age = 8.5 and 9.2 years, respectively), less frequently received a diagnosis of gastroenteritis, and more frequently received a diagnosis of generalized abdominal pain; no difference in sex was found. The design of the study and representativeness of included children are described in detail elsewhere.[15]

Outcome Definition

The primary outcome measure was CAP that interfered with the child's well-being at 1 year of follow-up. This outcome was defined as the presence of abdominal pain at least once each month in the past 3 months, severe enough for the child to stay home from school, to stop or avoid play, to take medication for the pain, or to rate the pain as moderate to severe.[16]

Potential Predictors

For potential positive predictors of CAP, we chose to investigate factors that could easily be incorporated into the initial medical evaluation. First, we selected candidate predictors on the basis of the results of a systematic review of predictors of childhood CAP in specialist care[13]—age, sex, and a family history of GI symptoms—and we investigated dyspepsia due to abdominal pain as it is thought to be positively associated with CAP. We also investigated levels of other somatic symptoms in children, in addition to the abdominal pain, because of their reported association with poor long-term outcome,[12] and body mass index because of a possible association between overweight and recurrent abdominal pain.[17] We investigated waking up at night because of abdominal pain as a possible positive predictor. Historically, this factor has been considered a red flag symptom, but more recent data suggest an association with FAP.[18,19]

In addition to assessing positive predictors after 1 year, we also investigated several red flag symptoms: vomiting, fever, blood on stools, and dysuria. We hypothesized that these symptoms are related to organic diseases that are mostly self-limiting or worsen in the long term, thus being recognized and treated as such. We therefore label these red flag symptoms as negative predictors, that is, we expected them to predict the absence of CAP. Furthermore, we added epigastric pain as a red flag symptom as a systematic review found a significant association between such pain and *Helicobacter pylori* infection in children.[20]

Measurements

Data on age, sex, red flag symptoms, and family history were obtained using self-administered standardized questionnaires (completed by children if they were aged 9 years or older, by parents, or by both). Children were considered to have a positive family history of GI symptoms when at least 1 parent reported a history of irritable bowel syndrome or *H pylori* gastritis, or if 1 parent, or a first- or second-degree relative, had a history of inflammatory bowel disease or CAP. Dyspepsia was defined as belching, bloating, regurgitation, or a combination thereof. Data on the child's defecation were obtained using a standardized bowel questionnaire. The child's body mass index was categorized as normal or overweight using child-adjusted cutoff points.[21] Pain intensity was determined on an 11-point numerical rating scale in children aged 8 to 17 years and on a 6-point pain faces scale for children

younger than 8 years.[22] Moderate to severe pain was defined as a score of 3 or higher on the numerical rating scale and 4 or higher on the pain faces scale. CAP at baseline was assessed and defined as described above. For assessment of other somatic symptoms, we used the somatic syndrome scale of the Child Behavior Checklist,[23,24] which identifies children with medically unexplained (somatic) symptoms at a level comparable to that in referred children with somatization problems (Table 1). These children were defined as having high levels of other somatic symptoms.

Statistical Analyses

Continuous variables are expressed as mean (SD) values. Binary and categorical variables are presented as counts and percentages of the number of patients responding per item. Differences between children included in the analyses and those lost to follow-up were analyzed using independent sample t tests (age) and χ^2 tests (sex and presence of CAP). Multiple imputation (n = 10 data sets) of missing values was undertaken using an imputation model containing all predictor variables and the outcome measure.

Univariate logistic regression analyses were used to study the association between potential predictors and the primary outcome. For the multivariate prediction model, we performed a backward elimination approach with all the preselected candidate variables; at each step, the least significant variable was removed stepwise from this model. The final model contains only those variables that explained the outcome in our population at a significance level of $P < .157$, according to the Akaike information criterion.[24] We determined odds ratios (ORs) for each variable, as well as the area under the receiver operating characteristic curve (ROC) for the model with 95% CIs. The performance of the final prediction model was tested for explained variance (the Nagelkerke R^2), which shows the percentage of variance between patients in the outcome that is explained by the predictors. Finally, we examined the odds of CAP by the number of identified predictors that children were exposed to, dichotomizing age as younger than 10 years, or 10 years or older. All analyses were conducted with SPSS for Windows, release 20.0 (SPSS, Inc).

RESULTS

Study Sample

A total of 348 children were recruited, of whom 305 (87.6%) participated. After 1 year, 22 children (7.2%) were lost to follow-up. One child was admitted to a hospital; the remaining 21 children were lost because they, their parents, or both were not interested in further participation (8 because of lack of time, 7 for unknown reasons, and 6 because they were free of abdominal pain). These children did not differ from the included children with respect to age, sex, and presence of CAP at baseline (data not shown).

Analyses were based on 283 children, of whom 177 (62.5%) were girls; their mean age was 8.3 (SD 2.9) years. In total, 105 children (37.1%) fulfilled the criteria for CAP at 1 year of follow-up. Univariate associations between patient characteristics and this outcome are shown in Table 2.

Predictors of Pain

In multivariate analysis, increasing age, waking up at night because of abdominal pain, high levels of other somatic symptoms, and CAP at baseline independently predicted the presence of CAP 1 year later (Table 3). The area under the ROC for the original data set was 0.69 (95% CI, 0.63-0.76), and this model explained 14.3% of the variance in the outcome measure. After multiple imputation, the area under the ROC ranged from 0.66 to 0.69, and the explained variance ranged from 9.8% to 13.6%.

The number of positive predictors influenced the absolute risk of having CAP at 1 year. The risk ranged from 19.4% among children having none of the predictors to 65.5% among children having 3 or 4 predictors (Table 4).

Epigastric pain was the only negative candidate predictor that was associated with CAP at 1 year at our predefined .157 significance level ($P = .08$). Adding epigastric pain to the multivariate model of positive predictors did not alter the area under the ROC, however.

Table 1. Overview of Questions on the Somatic Complaints Syndrome Scale of the Child Behavior Checklist

Questions for Children Aged 4-5 Years	Questions for Children Aged 6-16 Years
Do you/does your child experience:	**Do you/does your child experience:**
Pain in general (without medical explanation; not abdominal pain or headaches)?	Pain in general (without medical explanation; not abdominal pain or headaches)?
Headaches?	Headaches?
Nausea, feels sick?	Nausea, feels sick?
Constipation?	Constipation?
Vomiting, throwing up?	Vomiting, throwing up?
Can't stand having things out of place?	Problems with eyes (not if corrected by glasses)?
Diarrhea or loose bowels (when not sick)?	Rashes or other skin problems?
Doesn't eat well?	Nightmares?
Painful bowel movements?	Feels dizzy or lightheaded?
Too concerned with neatness or cleanliness?	Overtired without good reason?

Table 2. Univariate Association of Candidate Predictors With Chronic Abdominal Pain

Predictor	CAP (n = 105)	No CAP (n = 178)	Original OR (95% CI)[a]	Pooled OR (95% CI)[b]	P Value[c]
Candidate positive predictors					
Age, mean (SD), y	8.8 (3.2)	8.0 (2.7)	1.10 (1.02-1.20)	1.09 (1.00-1.18)	.05
Sex, female, No. (%)	73 (69.5)	104 (58.4)	1.62 (0.97-2.71)	1.47 (0.89-2.44)	.14
Dyspepsia, No. (%)	53 (50.5)	74 (44.0)	1.30 (0.79-2.11)	1.27 (0.78-2.06)	.33
Waking up at night because of pain, No. (%)	53 (50.5)	56 (31.5)	2.22 (1.35-3.65)	2.08 (1.29-3.36)	.003
Overweight, No. (%)[d]	15 (14.3)	13 (7.3)	2.12 (0.96-4.64)	1.81 (0.82-4.00)	.14
High level of other somatic symptoms, No. (%)	28 (26.7)	20 (11.2)	2.87 (1.52-5.42)	2.58 (1.38-4.82)	.003
CAP at baseline, No. (%)	58 (55.2)	73 (41.0)	1.78 (1.09-2.89)	1.63 (1.01-2.62)	.04
Parent with functional GI complaints, No. (%)	37 (35.6)	49 (28.0)	1.42 (0.85-2.39)	1.60 (0.88-2.90)	.13
Candidate negative predictors					
Vomiting, No. (%)	16 (15.2)	30 (16.9)	0.89 (0.46-1.72)	0.91 (0.47-1.75)	.77
Fever, No. (%)	20 (19.0)	28 (15.7)	1.26 (0.67-2.37)	1.23 (0.65-2.31)	.52
Dysuria, No. (%)	8 (7.6)	9 (5.1)	1.55 (0.58-4.15)	1.36 (0.31-3.62)	.53
Blood on stools, No. (%)	3 (2.9)	4 (2.3)	1.27 (0.28-5.80)	1.15 (0.25-5.29)	.86
Epigastric pain, No. (%)	5 (4.9)	20 (12.6)	0.36 (0.13-0.99)	0.45 (0.18-1.10)	.08

CAP = chronic abdominal pain; GI = gastrointestinal; OR = odds ratio.

[a] Original data set ORs.

[b] Pooled ORs after multiple imputation.

[c] P values of imputed data.

[d] According to body mass index using child-adjusted cutoff points.[21]

DISCUSSION

In the present study, 37.1% of children had CAP 1 year after initial consultation for abdominal pain. We identified several positive predictors of CAP: increasing age, waking up at night due to abdominal pain, high levels of other somatic symptoms, and CAP at baseline. Epigastric pain was the only negative predictor identified.

To our knowledge, this is the first prospective cohort study in primary care to investigate potential predictors of poor outcome in children seen for abdominal pain. Furthermore, this is the first study to incorporate the impact on the child's well-being into the outcome measure. Ideally, family physicians would be able to identify children who continue to experi-

ence difficulties in daily functioning due to abdominal pain as this would allow them to make more appropriate management decisions at an earlier stage.

Our finding that 37.1% of children have CAP 1 year after initial consultation is in line with a systematic review that reported persistence of abdominal pain in 29.1% of children after a median follow-up of 5 years.[7] Both our study and this review identified CAP at baseline to be a predictor for the persistence of abdominal pain, while another study among school-aged children in an open population identified a history of pain as a predictor for chronic benign pain in general.[26]

We found that older children were more likely to have CAP. In contrast, the aforementioned review reported conflicting evidence for an association between age and the persistence of chronic FAP.[13] A more recent study of Helgeland et al,[27] however, supports our finding. This latter study included children aged 8 to 15 years with recurrent abdominal pain referred to a general outpatient pediatric clinic; the authors reported a significant association between older age and higher levels of abdominal pain at 6 to 9 months of follow-up. A possible explanation is that parents with younger children may visit the family physician shortly after symptom onset, whereas they may be inclined to wait out the clinical course in older children; therefore, only a subset of older children with a longer duration of abdominal pain, with concurrent worse prognosis, might visit their family physician. Another explanation may be that reaching puberty is associated

Table 3. Multivariate Association of Candidate Predictors With Chronic Abdominal Pain

Predictor	OR (95% CI)[a]	P Value[b]
Positive predictors		
Age	1.08 (0.99-1.17)	.09
Waking up at night because of pain	2.28 (1.38-3.77)	.001
High levels of other somatic symptoms	2.18 (1.14-4.19)	.02
CAP at baseline	1.77 (1.07-2.95)	.03
Negative predictors		
Epigastric pain	0.45 (0.18-1.10)	.08

CAP = chronic abdominal pain; OR = odds ratio.

[a] Pooled ORs after multiple imputation.

[b] P value of imputed data. Values were statistically significant if less than .157.

Table 4. Risk of Chronic Abdominal Pain by Number of Positive Predictors

Number of Predictors[a]	Odds Ratio[b] (95% CI)	Absolute Risk,[c] %
0	Reference	19.4
1	2.25 (0.92-5.48)	34.9
2	3.91 (1.52-10.08)	48.2
3 or 4	8.00 (2.90-22.09)	65.5

[a] Out of age ≥10 years, waking up at night because of pain, high levels of other somatic symptoms, and chronic abdominal pain at baseline.

[b] Pooled ORs after multiple imputation.

[c] After multiple imputation.

with many psychological and physiologic changes that may cause abdominal pain to interfere with well-being.

Our finding that female sex is not a predictor of poor prognosis agrees with the existing strong evidence from the review of Gieteling et al.[13] We could not support the reported finding of this review that having a parent with functional GI symptoms predicts a poor outcome of abdominal pain.

The association of the coexistence of multiple somatic complaints and childhood FAP is generally accepted.[4] One study found that high levels of non-GI symptoms were associated with a greater likelihood of functional GI disorders in young adulthood.[14] In agreement, we found a significant association between high levels of other somatic symptoms at baseline and CAP 1 year later, suggesting that such symptoms in children consulting for abdominal pain may help identify those at higher risk for poor prognosis.

Waking up at night because of abdominal pain predicted CAP. Although this symptom is a red flag symptom according to the pediatric Rome criteria III (PRC-III), none of the affected children had a severe organic illness. It is more likely to be an indicator of a sleeping disorder. The association between sleep disturbances and FAP has been reported: a primary care study from Australia found that children with abdominal pain had 4 times the risk of sleep disturbances.[18] Also, FAP is reportedly associated with increased difficulty initiating and maintaining sleep, symptoms that were defined as behavioral sleep-disorder symptoms, which are common in children with medical and psychiatric disorders.[19]

To our knowledge, we are the first to find a negative association between epigastric pain and CAP. A possible explanation is that epigastric pain is caused by, for example, gastritis or gastroenteritis, conditions that are mostly self-limiting. The hypothesis that epigastric pain is potentially caused by organic pathology is not new, however; a systematic review reported a possible association between epigastric pain in children and *H pylori* infection, and the Maastricht III consensus recommends testing of

children with "upper gastrointestinal symptoms" for this bacterium.[28] Another explanation may be that physicians tend to test more extensively in children with epigastric pain, which consequently results in a higher percentage being identified as having organic disease.

Limitations

This study had noteworthy limitations. First, we focused on potential predictors that could be incorporated in the medical evaluation during the first consultation for abdominal pain. Because long-term abdominal pain without organic cause is a complex interaction of biologic, psychological, and social factors, however, we may have missed some features of this symptom complex, such as essential psychosocial factors. This lack of capture of potentially relevant factors might account for the low explained variance of our model and only moderate ability to predict CAP.

Second, the follow-up period of 1 year was relatively short given that in about 29% of children with chronic FAP, the pain persists for approximately 5 years.[8] An earlier study, however, identified 3 trajectories of childhood abdominal pain; a high-risk group did not improve at all over 5 years, whereas the low- and short-term risk groups showed improvement after only 2 months and maintained this improvement after 5 years.[29] Our follow-up of 1 year is therefore probably justified and is representative for a poor prognosis.

Implications

We identified 4 independent predictors of the presence of CAP after 1 year. The cohort as a whole had a 37.1% probability of having CAP after 1 year; however, the probability ranged from 19.4% in children with none of these predictors to 65.5% among those having 3 or 4. Adequate follow-up of these children therefore seems warranted.

Nevertheless, these predictors explain only 14.3% of the variance in the outcome measure, implying that on the basis of simple medical evaluation alone, the family physician is unable to accurately predict the prognosis of a child consulting with abdominal pain. Apparently, other yet to be identified psychosocial, environmental, or family stressors play a role. This complex multifactorial etiology implies that identifying potential prognostic factors in children with a poor prognosis might require a thorough and potentially more time-consuming evaluation of these factors. It also raises the question as to whether children who have persistent pain after adequate follow-up by their family physician should be managed by the family physician alone, or whether one should opt for a primary care multidisciplinary team including health care workers trained in evaluating psychosocial, environmental, and family stressors.

As long as there is no evidence-based (psychosocial) treatment, however, we believe that a stringent, proactive follow-up of the child with medically unexplained abdominal pain by the family physician is warranted. During follow-up, worsening of the pain or appearance of additional symptoms may alert the family physician to an organic cause or psychosocial problems that become evident after several visits. In such cases, the family physician might request additional diagnostic testing, refer to a secondary care (mental health care) specialist, or treat the child where appropriate.

Given the high level of CAP sufficient to affect well-being among children seen by family physicians, future research is warranted. This research should focus on identifying other risk factors involved in the development and persistence of CAP in primary care.

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