# Utility of Hepatic Transaminases in Children With Concern for Abuse

**WHAT'S KNOWN ON THIS SUBJECT:** Routine screening of potentially abused children with hepatic transaminases has been recommended, using a threshold of 80 IU/L to determine the need for further testing, but practice is variable, and this threshold has not been validated.

**WHAT THIS STUDY ADDS:** This study identified abdominal injury in a significant fraction of potentially abused children with transaminases >80 IU/L.


## abstract

**OBJECTIVE:** Routine testing of hepatic transaminases, amylase, and lipase has been recommended for all children evaluated for physical abuse, but rates of screening are widely variable, even among abuse specialists, and data for amylase and lipase testing are lacking. A previous study of screening in centers that endorsed routine transaminase screening suggested that using a transaminase threshold of 80 IU/L could improve injury detection. Our objectives were to prospectively validate the test characteristics of the 80-IU/L threshold and to determine the utility of amylase and lipase to detect occult abdominal injury.

**METHODS:** This was a retrospective secondary analysis of the Examining Siblings To Recognize Abuse research network, a multicenter study in children younger than 10 years old who underwent subspecialty evaluation for physical abuse. We determined rates of identified abdominal injuries and results of transaminase, amylase, and lipase testing. Screening studies were compared by using basic test characteristics (sensitivity, specificity) and the area under the receiver operating characteristic curve.

**RESULTS:** Abdominal injuries were identified in 82 of 2890 subjects (2.8%; 95% confidence interval: 2.3%–3.5%). Hepatic transaminases were obtained in 1538 (53%) subjects. Hepatic transaminases had an area under the receiver operating characteristic curve of 0.87. A threshold of 80 IU/L yielded sensitivity of 83.8% and specificity of 83.1%. The areas under the curve for amylase and lipase were 0.67 and 0.72, respectively.

**CONCLUSIONS:** Children evaluated for physical abuse with transaminase levels >80 IU/L should undergo definitive testing for abdominal injury. *Pediatrics* 2013;131:268–275



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**KEY WORDS**

child abuse, abdominal injury, sensitivity, specificity, hepatic transaminases


**ABBREVIATIONS**

ALT—alanine aminotransferase
AST—aspartate aminotransferase
AUC—area under the curve
CI—confidence interval
CT—computed tomography
ExSTRA—Examining Siblings To Recognize Abuse
OR—odds ratio
ROC—receiver operating characteristic

Dr Lindberg conceptualized and designed the study, coordinated and supervised data collection, performed the analyses, drafted the initial manuscript, and approved the final manuscript as submitted; Drs Shapiro, Steiner, and Berger coordinated and supervised data collection, reviewed and revised the manuscript, and approved the final manuscript as submitted; and Dr Blood provided additional statistical analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted.


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Physical abuse is a significant source of morbidity and mortality in children,[1,2] and intraabdominal injuries are second only to head injuries as a cause of death.[3] In children with concern for physical abuse and an offered history of minor trauma, identifying an intraabdominal injury can increase the perceived likelihood of abuse because intraabdominal injuries are unlikely to result from minor trauma.[4–9] Therefore, diagnosing an abusive intraabdominal injury can help to protect a child from future abuse, even if the injury itself would be self-limited. Whereas classic signs and symptoms of intraabdominal injury, such as abdominal tenderness, bruising, or distention, can increase concerns for abdominal injury, none of these findings is sufficiently sensitive.[10–13]

For these reasons, expert statements have long recommended routine transaminase testing, with or without amylase and lipase testing, in children with concern for physical abuse.[14–16] Nevertheless, past studies of transaminase screening have shown that practice is highly variable, with screening rates as low as 21%.[13,17] To our knowledge, there are no published data to support the use of amylase and lipase testing in potentially abused children.

In 2009, we published an observational, multicenter study of screening in centers that endorsed transaminase screening as their standard of care for children with concern for physical abuse.[13] Whereas intraabdominal injuries were recognized in only 3.2% of the population as a whole, they were identified in 15.8% of those with an initial aspartate aminotransferase (AST) or alanine aminotransferase (ALT) value >80 IU/L. However, even in centers where screening was considered to be standard of care, it was omitted in nearly a quarter of eligible patients, and definitive testing was obtained in only 53% of subjects with elevated transaminases. These results also did not determine whether routine screening identified injuries that would have been missed if testing had been performed at the discretion of the abuse expert, or whether routine testing reduced testing variability according to race or ethnicity.

The main objective of this study was to validate the test characteristics of an 80-IU/L threshold for transaminases to detect occult intraabdominal injury in children evaluated for physical abuse. Our secondary objectives were to determine rates of abdominal screening after the publication of our previous study and to determine test characteristics of amylase and lipase in children without transaminase elevation.

## METHODS

This study was a retrospective secondary analysis of data from the Examining Siblings To Recognize Abuse (ExSTRA) research network, a multicenter, observational, cross-sectional network of 20 child abuse teams that endorsed a common screening protocol for the siblings and household contacts of children younger than 10 years old evaluated for potential physical abuse.[18] All participating centers and the data coordinating center obtained approval from their local Institutional Review Board to conduct the main study with a waiver of informed consent. This secondary analysis of data that had been collected for another purpose, and that had been purged of all patient identifiers, was determined by each Institutional Review Board to be exempt from review as human subjects research.

### Patients and Centers

Between January 15, 2010, and April 30, 2011, 2890 index children were enrolled in the ExSTRA research network and form the cohort for this analysis. Subjects were enrolled if they were <10 years (120 months) old and had undergone subspecialty evaluation for concerns of physical abuse. To prevent inclusion bias, each center established an independent method to determine the number of eligible subjects and enrolled >90% of eligible subjects on the basis of monthly censuses. Data from siblings and other contacts of enrolled index children were abstracted for the primary analysis but were not used for this secondary analysis. Each participating center had ≥1 dedicated child abuse physician. Of 20 participating centers, 8 had previously endorsed routine screening as participants in our previous study. For this study, no protocol for abdominal injury screening was endorsed and no interventions were undertaken to increase screening.

Child abuse physicians recorded results of hepatic transaminases and any further testing to diagnose intraabdominal injury. A subject was considered to have undergone definitive testing for intraabdominal injury if he or she had an abdominal computed tomography (CT), MRI, surgical exploration, or autopsy. Intraabdominal injury was defined as radiographic or pathologic evidence of injury to the liver, spleen, pancreas, bowel, mesentery, kidney, adrenal, bladder, or abdominal vasculature. Bony injuries (of the spine, ribs, or pelvis) or isolated elevation of laboratory studies (as when elevated lipase was considered to diagnose traumatic pancreatitis) were not considered intraabdominal injuries. The ultimate perceived likelihood for abuse was coded for each subject by the consulting child abuse physician by using a previously published 7-point scale in which 7 represents definite inflicted injury.[19]

### Statistical Analysis

Categorical variables were compared between those tested and not tested by using $\chi^2$ tests, and continuous variables were compared by using the Mann-Whitney *U* test. Odds ratios (ORs) of testing and definitive imaging were calculated for dichotomous variables. Sensitivity, specificity, and likelihood ratios for detecting abdominal injuries were calculated for transaminase levels by using the highest value (AST or ALT) of the first transaminases obtained, and for amylase and lipase. Receiver operating characteristic (ROC) analysis was undertaken for transaminases, amylase, and lipase tests. Analyses were undertaken by using PASW Statistics 18 (IBM SPSS Statistics, IBM Corporation, Armonk, NY).

## RESULTS

Of 2890 subjects enrolled, 82 (2.8%; 95% confidence interval [CI]: 2.3%–3.5%) had ≥1 intraabdominal injury identified by any modality (abdominal CT, surgical exploration, or autopsy; Fig 1). Characteristics of the subjects with intraabdominal injuries identified are shown in Table 1. The perceived likelihood of abuse among children with intraabdominal injuries identified was high, with only 3 subjects (3.7%) having a level of concern that was ≤3 on the 7-point scale of abuse likelihood.[19] Mortality was higher among subjects with intraabdominal injuries identified than in the overall ExSTRA cohort (9 of 82, 11.0%; 95% CI: 5.1%–19.8% for subjects with intraabdominal injuries; 73 of 2890, 2.5%; 95% CI: 2.0%–3.1% overall). Subjects with intraabdominal injuries identified were older than other subjects (median age of 20.5 months for those with intraabdominal injuries, 11.0 months for all others; $P = .025$).

The types of intraabdominal injuries identified are shown in Table 2. Among the 82 children with intraabdominal injuries identified, the combination of abdominal bruising, tenderness or distention, or abnormal bowel sounds identified 47 children, for a sensitivity of 57.3%.

### Hepatic Transaminases

A total of 1538 (53.2%) subjects underwent transaminase testing. Subjects who underwent transaminase screening were younger and less likely to be male. They had more nonabdominal injuries identified, were more likely to die or require ICU admission, and had a higher perceived likelihood of abuse at the completion of their evaluation (Table 3). Subjects who were of nonwhite race or Hispanic ethnicity were tested more frequently than white, non-Hispanic subjects (55.2% vs 51.2%; OR: 1.17; 95% CI: 1.01–1.37).

Among 1538 children with transaminases obtained, 298 (19.4%) underwent

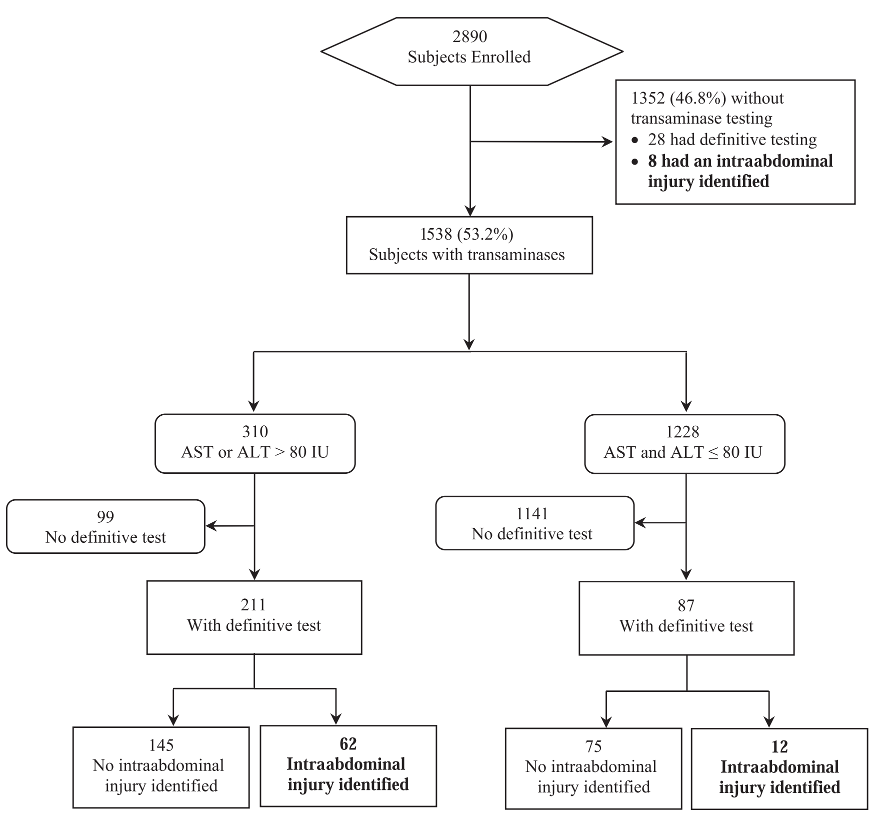


**FIGURE 1**
Patient flow.

**TABLE 1** Characteristics of Subjects With Intraabdominal Injuries Identified (*n* = 82)

| | |
|---|---|
| Age in months, median (IQR) | 20.5 (5–34) |
| Male, *n* (%) | 48 (58.5) |
| Race/ethnicity, *n* (%) | |
| White/non-Hispanic | 31 (37.8) |
| Nonwhite or Hispanic | 49 (59.8) |
| Unknown/not reported | 2 (2.4) |
| Identified injuries, *n* (%)[a] | |
| Fractures | 45 (54.9) |
| Traumatic brain injury | 31 (37.8) |
| Cutaneous injury | 60 (73.2) |
| None of the above | 9 (11.0) |
| ICU admission, *n* (%) | 43 (52.4) |
| Death, *n* (%) | 9 (11.0) |
| Ultimate level of concern for abuse, *n* (%) | |
| 1 (definitely not) | 1 (1.2) |
| 2 (no concern) | 2 (2.4) |
| 3 (mild concern) | 0 (0.0) |
| 4 (intermediate concern) | 1 (1.2) |
| 5 (very concerning) | 6 (7.3) |
| 6 (substantial evidence) | 11 (13.4) |
| 7 (definitely inflicted) | 61 (74.4) |

IQR, interquartile range; TBI, .

[a] Results do not sum to 100% because some subjects had >1 injury identified.

definitive testing and 74 (4.8%) were diagnosed with an intraabdominal injury (Fig 1). Definitive testing included 276 subjects with abdominal CT, 35 with autopsy, 6 with abdominal MRI, and 3 with diagnostic laparotomy. Some subjects had >1 type of definitive testing.

Of the 1352 subjects who did not undergo transaminase testing, 28 (2.1%) underwent definitive testing and 8 (0.6%) had intraabdominal injuries identified. Eighteen subjects underwent abdominal CT or laparotomy directly because of their history and symptoms, and 10 arrived dead and underwent autopsy.

Test characteristics of hepatic transaminases were similar to the previous cohort.[13] The ROC curve for the higher of the 2 initial transaminases (AST or ALT) had an area under the curve (AUC) of 0.87 for the identification of intraabdominal injury (Fig 2). A threshold of 80 IU/L, chosen on the basis of the results of the previous study, had a sensitivity of 83.8%, a specificity of 83.1%, a positive likelihood ratio of 4.9, and a negative likelihood ratio of 0.20.

## Abdominal CT

Abdominal CT was performed in 292 subjects, including 73 (25.0%) with intraabdominal injuries. Abdominal CT was obtained in 95 subjects with concerning clinical findings who did not have transaminase testing or who had transaminases ≤80 IU/L. Intraabdominal injuries were identified in 13 (13.7%) of such subjects and in 60 of 197 (30.5%) subjects when initial transaminases were >80 IU/L.

## Pancreatic Enzymes

Lipase was measured in 990 subjects, including 216 who also had definitive testing for intraabdominal injury and 65 in whom an intraabdominal injury was identified. The AUC for lipase to identify an intraabdominal injury was 0.71 (Fig 2). By using threshold of 100 U/L, lipase had a sensitivity of 61.5% and a specificity of 79.2%.

There were 143 subjects who did not have elevated transaminases in whom lipase was >100 U/L, including 7 (4.9%) subjects with intraabdominal injuries identified. The use of this threshold of 100 U/L to identify abdominal injury in the population without elevated transaminases yielded the following test characteristics: sensitivity of 58.3%, specificity of 88.8%, and a positive predictive value of 4.9%. However, only 22 subjects (15.4%) in this group underwent definitive testing for intraabdominal injury; the true positive predictive value may be higher if occult intraabdominal injuries were missed in children who did not undergo definitive testing.

Amylase was measured in 1043 subjects, including 220 who also had definitive testing for intraabdominal injury and 64 in whom an intraabdominal injury was identified. The AUC for amylase to identify an intraabdominal injury was 0.67. By using a threshold of 50 U/L, amylase had a sensitivity of 62.5% and a specificity of 77.9%. Amylase was not elevated in any of the subjects with intraabdominal injury that was missed by both hepatic transaminases and lipase.

**TABLE 2** Types of Intraabdominal Injuries Identified

| Injured Organ | Initial Transaminases, *n* (%) | | No Transaminases Obtained, *n* (%); (*n* = 8) | Total, *n* (%); (*n* = 82) |
|---|---|---|---|---|
| | >80 IU/L (*n* = 62) | ≤80 IU/L (*n* = 12) | | |
| Liver | 37 (59.7) | 2 (16.7) | 1 (12.5) | 40 (48.8) |
| Bowel/mesentery | 18 (29.0) | 6 (50.0) | 5 (62.5) | 29 (35.4) |
| Renal/adrenal | 14 (22.6) | 1 (8.3) | 1 (12.5) | 16 (19.5) |
| Pancreas | 13 (21.0) | 2 (16.7) | 1 (12.5) | 16 (19.5) |
| Spleen | 5 (8.0) | 1 (8.3) | 2 (25.0) | 8 (9.8) |
| Other[a] | 2 (3.2) | 3 (25.0) | 0 (0.0) | 5 (6.1) |

The number of injuries may be more than the number of patients because some patients had multiple injuries.

[a] Other injuries included 2 subjects with hematoperitoneum of unclear origin, 2 subjects with retroperitoneal bleeding, and 1 subject with an injury to the inferior vena cava.

## DISCUSSION

In this multicenter cohort of children <10 years old who were evaluated for physical abuse, 2.8% had an intraabdominal injury identified. Among children with an initial AST or ALT >80 IU/L, the posttest probability for intraabdominal injury was 20.0% (62 of 310) assuming that none of the subjects without definitive testing had an occult intraabdominal injury. These data support the use of a transaminase threshold of 80 IU/L as an indicator for further definitive

**TABLE 3** Characteristics of Children With and Without Transaminase Testing

| Characteristic | Transaminases Obtained (*n* = 1538) | Transaminases Not Obtained (*n* = 1352) | *P* |
|---|---|---|---|
| Age in months, median (IQR) | 7 (3–18.9) | 20 (7–48) | <.001 |
| Male, *n* (%) | 793 (51.6) | 894 (66.1) | <.001 |
| Race/ethnicity, *n* (%) | | | .09 |
| White/non-Hispanic | 658 (42.8) | 628 (46.4) | |
| Nonwhite or Hispanic | 835 (54.3) | 679 (50.2) | |
| Unknown/not reported | 45 (2.9) | 45 (3.3) | |
| Identified injuries, *n* (%) | | | |
| Fractures | 800 (52.0) | 408 (30.2) | <.001 |
| TBI | 478 (31.1) | 108 (8.0) | <.001 |
| Cutaneous injury | 792 (51.5) | 815 (60.3) | <.001 |
| ICU admission, *n* (%) | 311 (20.2) | 73 (5.4) | <.001 |
| Death | 55 (3.6) | 18 (1.3) | <.001 |
| Ultimate level of concern for abuse | | | <.001 |
| 1 (definitely not) | 51 (3.3) | 99 (7.3) | |
| 2 (no concern) | 226 (14.7) | 387 (28.6) | |
| 3 (mild concern) | 210 (13.7) | 227 (16.8) | |
| 4 (intermediate concern) | 174 (11.3) | 167 (12.4) | |
| 5 (very concerning) | 209 (13.6) | 146 (10.8) | |
| 6 (substantial evidence) | 286 (18.6) | 114 (8.4) | |
| 7 (definitely inflicted) | 382 (24.8) | 212 (15.7) | |
| ULTRA center[a] | 856 (55.7) | 547 (40.5) | <.001 |
| Non–ULTRA center[a] | 682 (44.3) | 805 (59.5) | |

IQR, interquartile range; TBI, traumatic brain injury; ULTRA, using liver transaminases to recognize abuse research network.
[a] ULTRA centers had previously endorsed screening transaminases as a part of their standard of care in the evaluation of potentially abused children.

testing for abdominal injury in children with concern for physical abuse.

Subjects with intraabdominal injuries identified were older than other subjects, which is similar to results from our previous cohort.[13] Intraabdominal injuries may be more common in older children if anatomic differences make them more likely to be victims of blunt trauma to the abdomen. Alternatively, intraabdominal injuries may be identified more frequently in children who are able to communicate about the presence of abdominal pain or tenderness or who are able to report trauma to the abdomen.

Testing was performed less commonly in this cohort than in our previous cohort of centers that endorsed transaminase screening as standard of care.[13] One likely reason for this difference is the inclusion of centers that had not participated in the previous cohort and which may not have considered transaminase testing to be their standard of care. Centers that had participated in the previous cohort tested at higher rates than those that had not (856/1403 [61.0%] vs 682/1487 [45.9%]; OR: 1.85; 95% CI: 1.59–2.15). However, even centers that had previously endorsed routine testing tested at a lower rate than did the previous ULTRA cohort (61.0% vs 75.9%; OR: 0.50; 95% CI: 0.42–0.58), suggesting that the Hawthorne effect may have increased screening in the first study, even though both studies were meant to be observational. Although not as rigorous as a randomized trial, these 2 cohorts can serve as a comparison between routine testing (the previous cohort) and testing at the discretion of the clinical team (the current cohort).

When compared with the routine testing cohort, subjects in the discretionary cohort who had transaminases measured were more likely to have elevated transaminases (20.2% vs 15.4%), and those with elevated transaminases were more likely to undergo definitive imaging (68.1% vs 53.3%; OR: 1.87; 95% CI: 1.31–2.67). Physicians may have been more willing to pursue definitive testing because of the publication of the previous cohort's suggested threshold for screening or

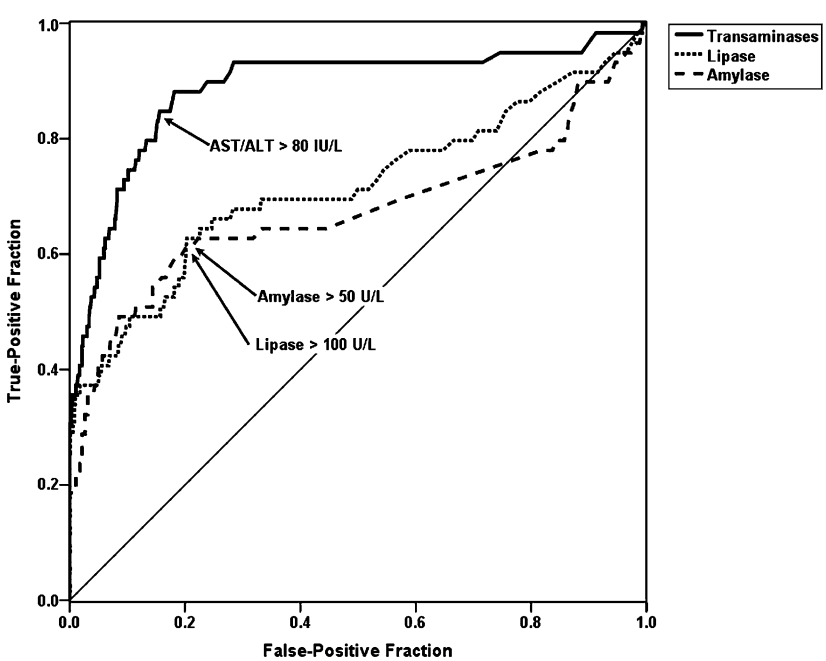


**FIGURE 2**
ROC curves for hepatic transaminases, amylase, and lipase and any identified abdominal injury. The AUCs for transaminases, lipase, and amylase were 0.87, 0.72, and 0.67, respectively.

because their initial clinical gestalt was higher in subjects they chose to test relative to subjects tested by protocol.

Whereas subjects who were of nonwhite race or Hispanic ethnicity were slightly more likely to be tested in this cohort, the converse was true in the previous cohort in which testing was considered to be standard of care (73.9% tested for nonwhites versus 78.8% for whites; OR: 0.76; 95% CI: 0.60–0.96), suggesting that an approach that relies on clinician discretion may be more subject to unconscious bias and more likely to result in racial disparities in testing.

The overall difference in the proportion of subjects with identified intraabdominal injuries (3.2%; 95% CI: 2.4%–4.1%, in the routine testing cohort versus 2.8%; 95% CI: 2.3%–3.5%, in the discretionary testing cohort) was not significant (OR: 1.14; 95% CI: 0.79–1.64), but if the slightly higher rates in the routine cohort were confirmed in a larger sample, it would suggest that using a routine approach for intraabdominal injury screening would require measuring an average of 47 additional sets of hepatic transaminases and 10 to 11 abdominal CTs to identify 1 additional abusive intraabdominal injury.

Several experts have recommended using amylase and lipase to increase the sensitivity of hepatic transaminases for occult intraabdominal injury, perhaps because pancreatic injuries are overrepresented among abused children relative to those with other sources of trauma.[14,17,20] In our cohort, amylase failed to identify injuries missed by both transaminases and lipase, and the threshold suggested by ROC inspection was well within the normal range. A lipase threshold of 100 U/L identified injuries missed by transaminases, but our low estimate of the test's positive predictive value was limited by the fact that most subjects with elevated lipase did not undergo definitive testing.

We did not determine the time of transaminase testing relative to the episode of abuse or to the time the child presented for evaluation. Because transaminases normalize over days or weeks,[21] intraabdominal injury screening must be undertaken in the early phases of an investigation for physical abuse and is not likely to be useful in children who have been in a protected environment for several weeks before their evaluation. Test characteristics may have been better than we report here if a significant number of our subjects had delayed testing.

Consultants were not asked to record their abdominal examination findings before knowing the results of hepatic transaminases or other testing for abdominal imaging. If clinicians were prompted to perform a more thorough physical examination after an intraabdominal injury was identified, or if physical examination findings evolved over time, then the sensitivity of abdominal bruising, tenderness, distention, or abnormal bowel sounds may be overestimated.

Definitive testing was omitted for the vast majority of subjects with normal tests and for a significant fraction of those with elevated transaminases, amylase, or lipase. If intraabdominal injuries were present in a significant number of subjects without elevated markers, our reported test sensitivities are overestimated. Conversely, if a significant number of injuries were present, but missed among subjects with elevated markers, then our specificity is underestimated.

One reason for omitted definitive studies may be the attention to increased use of CT among pediatric patients, with the associated increase in exposure to ionizing radiation. We feel that the rate of intraabdominal injuries identified in subjects with elevated transaminases justifies imaging in this cohort, although clinicians may consider MRI as an alternative to reduce exposure to radiation.[22] Because abnormal transaminases will rapidly normalize in almost every case, even when an intraabdominal injury is present, serial transaminase testing is not a substitute for imaging.[21]

Clinicians may also have chosen to forego definitive testing in children with elevated transaminases if the child was clinically stable and if the evidence of abuse was strong, even without the identification of an intraabdominal injury. Because most occult abdominal injuries are clinically self-limited, this may be 1 reasonable approach.[16] However, the identification of injury to an additional organ system may help establish the diagnosis of abuse in a contentious legal environment.[23]

Because of the reported low sensitivity for intraabdominal injury, we did not consider abdominal ultrasound to be a definitive test for intraabdominal injury.[24] This is consistent with expert guidelines that support abdominal CT as the first-line test in children with concerns for abusive abdominal injury.[22,25] No subject was diagnosed with an intraabdominal injury by ultrasound that was not confirmed by another definitive study.

Our comparison of these data with those from our previous cohort is limited because inclusion criteria for the 2 cohorts were slightly different. Whereas this cohort included children as old as 120 months (10 years), the previous cohort was restricted to children $<60$ months old (5 years). Our cohort included a relatively small proportion (281; 9.7%) of subjects aged $\geq 60$ months. Although rates of transaminase testing (46; 16.4%) were significantly lower in this cohort ($P <$ .001), we did not identify a significant difference in rates of transaminase elevation between subjects who were tested (11/46; 23.9%) or in injury identification among those with elevated transaminases (5/11; 45.5%).

## CONCLUSIONS

Intraabdominal injuries are uncommon among children evaluated for physical abuse, but they carry significant mortality. Hepatic transaminases can increase sensitivity for occult intraabdominal injury relative to the clinical examination alone in children with concern for physical abuse. Children with elevated transaminases ($>$80 IU/L) should undergo definitive testing for abdominal injury, such as CT scan.


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