Sample two-page PECARN proposal concept

Clinical Decision Rules to Identify Children with Intra-abdominal Injuries

Background/Significance:

Intra-abdominal injury (IAI) is a leading cause of morbidity and mortality in children older than one year of age. Some IAIs are difficult to identify, and failure to identify such injuries may lead to preventable morbidity and mortality. More than 600,000 children with blunt abdominal trauma are evaluated annually in U.S. emergency departments (ED) and 23% undergo abdominal imaging. [1,2] Fewer than 10% of these imaging tests, however, identify an IAI and few patients with IAI require acute intervention. [3,4] Methods for diagnostic abdominal evaluation, including both abdominal CT scanning and exploratory laparotomy, have substantial drawbacks. The most important risk of abdominal CT scanning is radiation-induced malignancy with the risk of a fatal radiation-induced malignancy estimated to be one per 450 abdominal CT scans in infants and one per 1,000 abdominal CT scans for adolescents. [1,5-7] Therefore, both underuse and overuse of abdominal CT scanning have potential adverse effects. It is therefore essential that diagnostic abdominal evaluation of injured children be limited to children at risk for IAI based on high quality evidence and inappropriate diagnostic evaluations be minimized.

Despite the importance and frequency of blunt abdominal trauma in children, accurate data on which to derive evidence based guidelines for the diagnostic evaluation of children with blunt abdominal trauma are limited. Thus, the evaluation of children with blunt abdominal trauma varies widely from center to center. [2,4,8-10] We have derived a clinical decision rule for identifying children at high and very low risk for IAI using a readily available set of clinical criteria at the UC Davis Medical Center. [7] This suggests that an accurate clinical decision rule for identifying children at high and low risk for IAI can be derived using a readily available set of clinical criteria. However, the confidence intervals (CI) for the accuracy of the rule we derived were insufficiently narrow. [3] If we were able to derive/refine such a decision rule in a large and diverse population of children with abdominal trauma, the use of abdominal CT scanning could then be applied more appropriately, and the clinical care of injured children would be improved.

In this study, we will study a very large, diverse cohort of children with blunt abdominal trauma in PECARN. [69,70] This geographically and demographically diverse network sees more than 8,000 children evaluated for abdominal trauma, and more than 600 children with IAI each year, and will provide a large sample size on which to derive a highly accurate, generalizable decision rule, which we expect will generate narrow CI sufficient to impact clinical practice.

Specific Aims:

The long term objective of our research is to derive, refine, validate, disseminate and implement decision support tools to optimize the evaluation of children with blunt trauma, leading to reduced morbidity and mortality.

The current proposal has two specific aims:

1) To refine and internally validate a clinical decision rule that accurately and precisely identifies children at high risk of IAI in need of acute intervention. The sensitivity of this rule must be nearly 100%.
2) To refine and internally validate a clinical decision rule that accurately and precisely identifies those children at near-zero risk of IAI in need of acute intervention. The negative predictive value (NPV) of this rule must be nearly 100%.

We hypothesize that application of this refined decision rule would reduce the number of overall scans in the study population without missing an IAI requiring acute intervention. We will assess this by applying the final rule to the study population and comparing the actual CT scanning rate versus the rate of CT scanning recommended by the decision rule.

Research Design:

This will be a prospective observational cohort study of children with blunt abdominal trauma evaluated at select sites in the PECARN. [69, 70] Children with blunt abdominal trauma presenting to the participating EDs will be enrolled and followed prospectively to detect the outcomes of interest. Clinical data collected at the time of ED presentation on patients with blunt abdominal trauma will be analyzed and internally validated using binary recursive partitioning to generate clinical decision rule(s) for identifying children at high risk and near-zero risk of IAI. We will use three separate outcome variables and create decision rules for each. The three outcome measures of interest will be: 1) IAI that requires acute intervention, 2) clinically significant IAI, and 3) any IAI identified by a radiographic imaging study or at laparotomy. Therefore, we will utilize a patient oriented outcome as the primary outcome for our decision rule(i.e. IAI in need of acute intervention).

Sample size calculations for the sensitivity of the decision rule:

The most important risk of abdominal CT is the lifetime risk of fatal malignancy, with a conservative estimated risk of one death per 1,000 abdominal CT scans for a 1 year-old, one death per 1325 for a 5 year-old, and one death per 1,800 abdominal CT scans for a 15 year old.[5, 9, 53, 58] Moreover, the estimate of the ratio of non-fatal to fatal malignancy from abdominal CT scans is approximately 3:1.[54] Therefore, assuming one CT per child, we estimate that the risk of any malignancy (fatal and non-fatal) to be at least one per 350 CT-imaged children. In our pilot study, four of 1,095 patients had delayed diagnoses of their IAIs, although none required an acute intervention and no patient suffered increased morbidity or died from the delay.[7] Two prior studies on children with missed IAIs failed to demonstrate increased mortality related to a delayed diagnosis.[22, 23] For the purposes of sample-size calculation, we will balance the risk of a malignancy from CT to a missed IAI needing acute intervention.

Based on the above assumptions, the sample size must be sufficiently large such that we will have high confidence of missing no more than one IAI requiring acute intervention in 350 children who are hemodynamically-stable after blunt abdominal trauma. In our pilot study, IAI requiring acute intervention accounted for approximately 18% of the total IAIs in hemodynamically stable patients.[7] This estimate is consistent with prior studies which have demonstrated that 11 – 37% of children with IAI after blunt trauma will need acute intervention as we have defined.[152-155] Therefore, because one out of every six children with IAI will require acute intervention, the resulting clinical decision rule should not miss more than six children with IAI among 350 children undergoing abdominal CT scan due to risk of IAI (as one of the six will require acute intervention). We will, therefore, achieve a sufficient certainty if the lower boundary of the 95% CI around the sensitivity for the decision rule is no lower than 0.982 (i.e. 344/350). Assuming there are 164 hemodynamically-stable children in our study who have IAI in need of acute intervention, and that all 164 will be identified by the decision rule (i.e. 100% sensitivity), the lower boundary for the 95% one-sided exact binomial CI will be 0.982.

Under the assumption (based on the pilot data) that 18% of all hemodynamically stable patients with IAI will have IAI in need of acute intervention, an enrollment of approximately 877 (i.e. 164/0.187) hemodynamically stable patients with IAI of any type in the study will be needed. This translates into ~ 9,774 hemodynamically stable children with blunt abdominal trauma needed for this study, given the estimate from the pilot study that ~ 9% of eligible children will have IAIs. A total of 693 children with IAIs are evaluated at the participating site EDs on an annual basis, and ~ 5% of these 693 patients will be transferred to the participating centers with known diagnosis of IAI and thus ineligible, leaving 658 eligible patients with IAI annually. Assuming an enrollment rate of 70 – 80%, ~ 461 to 526 patients with IAI will be enrolled annually. Of these, 89% will be hemodynamically stable and, therefore, meet study criteria. Thus, 410 to 468 hemodynamically stable patients with IAI will be eligible and enrolled each year. Therefore, the study will require between 23 and 26 months of enrollment.