Risk of traumatic brain injury in infants younger than 3 months after minor blunt head trauma

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A. **Study Purpose and Rationale**

Head trauma is common in young children, accounting for approximately 81,000 emergency department (ED) visits annually in children younger than 1 year.[1] Among the challenging decisions facing clinicians is whether to obtain head CTs in very young infants after minor head trauma, particularly in those younger than 3 months of age. These younger infants pose the difficulty of having potentially subtle symptoms such as irritability or not acting normally and/or have minimal physical examination findings to suggest the presence of clinically-important traumatic brain injury.[2] However, clinicians must balance the risk of missing important intracranial injuries with risk of radiation-induced malignancy from CTs, with the radiation risk higher as age decreases.[3]

Prior studies have typically combined the youngest infants with the group of children younger than 1-2 years, [4-11] with little data specifically addressing those younger than 3 months. In retrospective and prospective observational studies, youngest infants with minor head trauma have been described who have had seemingly minor mechanisms of injury (e.g. falls from low heights) and minimal physical finding (e.g. only small scalp hematomas), yet important findings on head CT such as extra-axial hematomas.[6] In the Pediatric Emergency Care Applied Research Network's (PECARN's) cohort of 2,998 children younger than 24 months with minor blunt head trauma whose only clinical findings were scalp hematomas, those younger than 3 months were at higher risk of TBI on CT as compared to older children.[6] However, details of all those younger than 3 months of age were not presented in prior studies. Therefore, in order to inform decision-making in these young infants, we aim to determine the risk of and risk factors associated with skull fractures, intracranial injuries on CT, and the need for interventions in infants younger than 3 months who sustain minor blunt head trauma.

B. **Study Design and Statistical Analysis**

We will conduct a secondary analysis of the PECARN head trauma public use dataset, a multicenter prospective observational study. If available and appropriate, we will combine the PECARN dataset with a similar dataset from the Paediatric Research in Emergency Departments International Collaborative.[12]

Study Design

This is a secondary analysis of the parent study, which was a multicenter prospective observational study.

Statistical Analysis

The first part of this study will be a descriptive analysis of the patients younger than 3 months in

our dataset, including demographic characteristics and mechanisms of injury. We will then analyze bivariate relationships between physical signs/symptoms, including those that are included in the PECARN head trauma clinical decision rule,[4] and risk of clinically important TBI, TBI on CT, and skull fracture among infants 0-3 months using chi-squared tests. If the data allows, we will examine these relationships among smaller subsets of infants, namely those 0-1 months, 1-2 months, and 2-3 months. We will be using SAS v. 9.4 for all analyses. Outcomes are defined as described in Kuppermann et al.[4] Of particular interest are minimal physical examination findings not included in the PECARN criteria but which may be important in young infants, including abrasions or lacerations. Proposed preliminary tables are shown below.

Characteristics of Infants <90 Days with Minor Blunt Head Trauma

	Do not meet PECARN low risk criteria	Meet low risk criteria and have no other findings	Meet low risk criteria but have abrasions/lacerations
Age 0-29 days 30-59 days 60-89 days			
Female			
Mechanism of injury Falls < 3 ft 3-5 ft > 5 ft Other			
Symptoms and signs Vomiting Acting abnormally Signs of skull fracture Scalp hematoma			

Risk of Skull Fracture, Intracranial Injury and cITBI based on clinical findings

	A. <u>Do not</u> meet PECARN low risk criteria	B. Meet low risk criteria and have no other findings	C. Meet low risk criteria but have abrasions/lacerations
ciTBI	X/N % (CI)	0/N % (CI)	0/N % (CI
Skull fracture only	X/N % (CI)	X/N % (CI)	X/N % (CI)
Intracranial injury on CT but not ciTBI	X/N % (CI)	X/N % (CI)	X/N % (CI)

Sample Size Determination and Power Analysis

The sample has approximately 10,000 subjects under age 2, and approximately 180 patients age 0-3 months who have an isolated scalp hematoma.[6] The total number of subjects aged 0-3 months - not just those with isolated scalp hematomas - is currently unknown. To detect an association between an laceration/abrasion and TBI on CT at an $\alpha = 0.05$ level with a power of 80% using a χ^2 test, assuming a 15% risk of TBI on CT among those with laceration/abrasion compared to 5% risk with no findings, and 25% prevalence of laceration/abrasion in the sample group requires 113 subjects with a laceration/abrasion and 339 subjects with no findings.

C. Study Procedure

This is a secondary data analysis using de-identified data collected for a multicenter observational study of children with blunt head trauma. It does not involve any active participation of subjects. For procedures related to the parent study from which the data is obtained, see Kuppermann et al.[4]

D. Study Drugs

No study drugs, approved or investigational, will be used.

E. Medical Device

No medical devices are being employed in this study.

F. Study Questionnaires

No questionnaires will be utilized in the current study. In the parent study, trained site investigators and other emergency department physicians recorded patient history, injury mechanism, and symptoms and signs on a standardized data form.[4]

G. Study Subjects

The study subjects are children younger than 3 months with minor blunt head trauma in the PECARN head trauma public use dataset.

H. Recruitment of Subjects

No subjects will be actively recruited as all data has already been collected.

I. Confidentiality of Study Data

All data is de-identified and publicly available.

J. Potential Conflict of Interest

None of the investigators have any conflicts of interest to report.

K. Location of the Study

The current study will take place at Morgan Stanley Children's Hospital/Columbia University Medical Center. It will use data from the PECARN network, which is comprised of 25 emergency departments across the United States.

L. Potential Risks

There are no potential risks of the current study as all data has already been collected.

M. Potential Benefits

The benefit from this study is that we will gain evidence on which to base decisions about CT scan use in infants younger than 3 months.

N. Alternative Therapies

There are no alternatives to participating in this study as it is a publicly available de-identified dataset.

O. Compensation to Subjects

No compensation will be provided.

P. Costs to Subjects

There is no cost to subjects.

Q. Minors as Research Subjects

The parent study involved collecting data about minors, but did not require their active participation. The parent study requested and received a waiver from written informed consent. It met criteria for the waiver under 5 CFR 46.116 (d), because it involved 1) no more than minimal risk to the patient, 2) the waiver did not adversely affect the rights and welfare of the subjects, 3) the research could not have been practicably carried out without the waiver, and 4) the subjects (guardians) will be provided with study information (at the time of the ED visit).

R. Radiation or Radioactive Substances

This study will not employ radiation or radioactive substances.

References

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