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Accuracy of Pediatric Emergency Care Applied Research Network Rules in Prediction of Clinically Important Head Injuries; A Systematic Review and Meta-Analysis

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Abstract

Background: The present meta-analysis was designed to determine the value of Pediatric Emergency Care Applied Research Network (PECARN) rule in prediction of clinically important traumatic brain injury (ciTBI).

Materials and Methods: Extensive search was conducted in the databases of Medline, Embase, Scopus, Web of Sciences, Cinahl up to the end of August 2017. The search records were screened and summarized by two independent reviewers, and eventually the findings were presented as summary of receiver operating characteristics (SROC), sensitivity, specificity and diagnostic odds ratio with 95% confidence interval (95% CI).

Results: Data from 10 studies were included in this meta-analysis. Area under the curve (AUC) of SROC for PECARN model in prediction of ciTBI in children younger than 2 years old was 0.85 (95% CI: 0.82-0.88). Sensitivity, specificity and diagnostic odds ratio of this model were also calculated to be 0.98 (95% CI: 0.92-1.0), 0.56 (95% CI: 0.48-0.64) and 82.53 (95% CI: 16.23-419.63), respectively. AUC of SROC for this model in prediction of ciTBI in children aged 2-18 years old was also found to be 0.97 (95% CI: 0.95-0.98) with a sensitivity, specificity and diagnostic odds ratio of 0.98 (95% CI: 0.95-0.99), 0.60 (95% CI: 0.53-0.67) and 80.73 (95% CI: 30.59-213.05).

Conclusion: The findings of this study are indicative of a high screening value for PECARN model in prediction of ciTBI and classification of patients. So it is recommended that the decision rule be used in routine practice for children referring with mild traumatic brain injuries.

Key Words: Brain Concussion, Brain Injuries Technique, Decision Support, PECARN.

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1- INTRODUCTION

Mild traumatic brain injury (mTBI) is one of the most common reasons for emergency department referrals. Epidemiological studies have reported that 765 per 100,000 children experience traumatic brain injuries, of which 9 individuals expire. The reported disability for these injuries reaches up to 20% (1).

Computerized Tomography scan (CT scan) and magnetic resonance imaging are the gold standard methods for detection of brain injuries. However, studies have shown that in most mTBI cases undergoing CT scan and other imaging studies are unnecessary (2). For instance, in the study conducted by Kuppermann et al. on 42,412 children with mTBI, only 1% was found to have suffered a clinically important traumatic brain injury (ciTBI).

Accordingly, these researchers introduced a decision rule titled Pediatric Emergency Care Applied Research Network (PECARN) (3). The model was designed separately for two groups of children younger than 2 years old, and 2 to 18 years old, and helps classifying patients into three groups of low risk, moderate risk and high risk based on the level of consciousness according to Glasgow Coma Scale, presence of palpable skull fracture, altered mental status, scalp hematoma, loss of consciousness for more than 5 seconds, not acting normally per parent, severe injury mechanism, nausea, vomiting and symptoms of basilar skull fracture. In this regard, low risk patients do not require further imaging studies with CT scan, patients with moderate risk should undergo CT scan at their physician's discretion and imaging assessment is considered mandatory for high risk patients. These researchers showed that application of PECARN rule can reduce 58.3% of unnecessary CT scans (3). Further investigations also reported that using PECARN rule might be able to improve decision making in practice (4-6). However, the value of PECARN model could be affected by inter-population differences, and no general conclusion has been reached on the application of this instrument in clinical settings. One way to reach a consensus is conducting a systematic review and meta-analysis on this subject, which has not been done yet. In this regard, the present study aimed to assess the value of PECARN rule in classification of children with mTBI, using a meta-analytic approach.

2- MATERIALS AND METHODS

2-1. Study design and search strategy

In the present systematic review and meta-analysis an extensive search with no language restrictions was conducted in the databases of Medline (via PubMed), Embase, Scopus, Web of Sciences, Cinahl (via Ebsco), according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines, up to the end of August 2017. The search was performed based on the keywords related to traumatic brain injury (TBI) combined with Pediatric Emergency Care Applied Research Network OR decision rule. **Table.1** presents the search query for Medline database. It should be mentioned that the search in PubMed included records from PubMed Central as well. In addition, a manual search was also performed in the Google and Google Scholar search engines and the bibliographies of related articles. Finally, to find unpublished data on this topic, the authors of related articles were contacted via email (*Please see the table.1 in the end of paper*).

2-2. Inclusion and Exclusion criteria

Studies evaluating the diagnostic accuracy of PECARN rule for ciTBI in children younger than 18 years old were included in this systematic review. Based on the definition presented in the derivation study of PECARN rule, ciTBI was considered as death from TBI, need for neurosurgery, intubation more than 24 hours and TBI related admission to hospital for two or more nights, and so studies that have evaluated at least one of these outcomes were included. Exclusion criteria included review articles and unavailability of the results of the study presented as sensitivity, specificity, true positive (TN), true negative (TN), false positive (FP), and false negative (FN) values, even after two attempts of contacting the authors for acquiring their data. It should be mentioned that in two articles derivation and validation of the PECARN rule were reported simultaneously, from which data in the validation were included in this study to minimize heterogeneity.

2-3. Data synthesis and Quality control

Screening method and summarization of data have been further described in previous publications of the authors (7-22). Briefly, two independent reviewers screened the articles based on their titles and abstracts and then read the complete texts of the related studies, summarized their data and recorded them in a checklist. The checklist included information on the first author of the study, publication year, study design (prospective or retrospective), mean and range of the sample population's age, gender distribution, the specialty of the physician evaluating the patients, sample size, number of ciTBI cases and the evaluated outcomes in the study. Diagnostic value of the PECARN rule was also assessed according to the TP, TN, FP and FN figures. Quality control of the articles was performed based on the quality assessment of diagnostic accuracy studies version-2 (QUADAS-2) checklist (23).

2-4. Statistical analysis

Analyses were performed using "midas" command in the STATA 14.0 statistical software. Since two separate models have been introduced by the PECARN rule derivation study for two different age groups, analyses were also performed accordingly. However, three studies have presented their results regardless of the patients' age groups. So initially, the diagnostic value of PECARN rule was evaluated in all ages (0 to 18 years), and then the results were presented separately for the two groups of less than 2 year-olds and 2 to 18 year-olds. For this means, summary of receiver operating characteristics (SROC), sensitivity, specificity, diagnostic score and diagnostic odds ratio with 95% confidence interval (95% CI) were calculated. Deeks' funnel plot asymmetry test was also used to screen for publication bias. Heterogeneity was assessed using I-squared test and its corresponding p value.

3- RESULTS

3-1. Characteristics

The search yielded 934 records in the databases, of which 37 potentially relevant studies remained after primary screening and elimination of duplicates. After studying the full-texts of these articles, eventually 10 studies were included (3-6, 24-29) (**Figure.1**). Seven studies had presented their data according to age groups (less than 2 years old, 2 to 18 years old) (3-6, 24, 27, 29), while the data in the other 3 were presented for the whole age range of 0 to 18 years (25, 26, 28). These articles included data on a total of 54,785 children and adolescents aged 0 to 18 years, of which 755 (1.38%) had ciTBI. **Table.2** presents the summary of studies included in this systematic review (*Please see the table.2 in the end of paper*).

3-2. Quality assessment and risk of bias

Quality assessment of the articles based on Quadas-2 checklist showed that all the 7 items evaluated via this tool were at an acceptable level nearly in all the included studies. Only presence of selection bias in

2 articles was unclear. The quality status of these articles is presented in **Table.3**.

Deeks' funnel plot asymmetry test also found no significant publication bias in the present study (Coefficient= 9.49; 95% CI: -6.83 to 25.82; p=0.23) (**Figure.2**). However, considerable heterogeneity was observed between the included studies (I-squared values are presented in **Figures 3-6**) (*Please see the table.3 in the end of paper*).

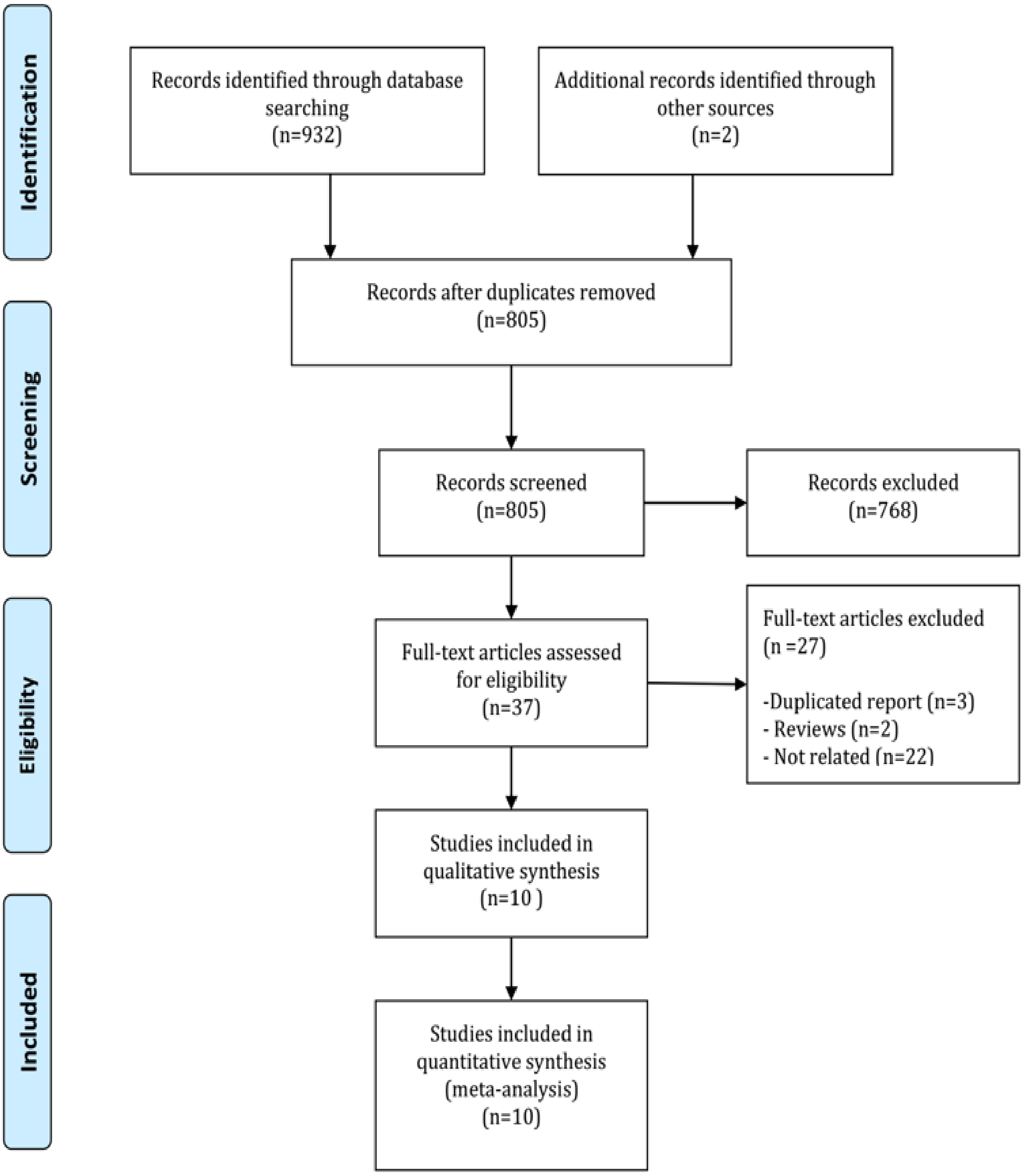


Fig.1: Flow diagram of study selection in present meta-analysis.

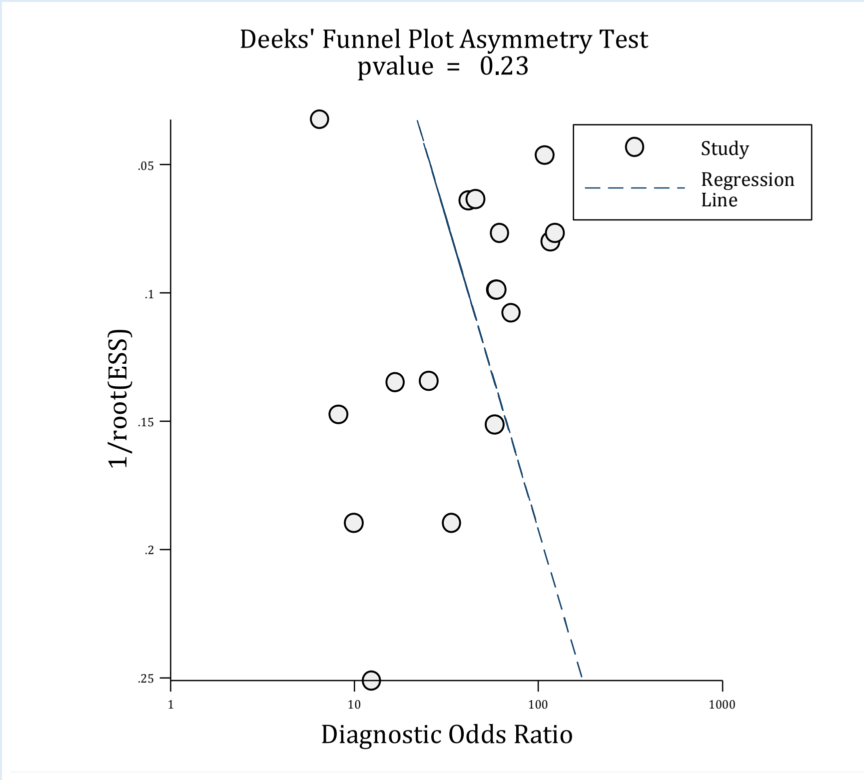


Fig.2: Assessment of publication bias based on Deeks' funnel plot asymmetry test.

3-3. Meta-analysis

3-3-1. All age groups

As mentioned, three studies had evaluated the value of PECARN rule in prediction of ciTBI in all age groups as a whole. Hence, yielded results from other studies were also pooled together and initially, the value of this model was assessed over the total age range of 0 to 18. Analyses showed that the AUC of SROC of PECARN rule in prediction of ciTBI was 0.97 (95% CI: 0.95 to 0.98) (**Figure.3A**). Sensitivity and specificity of this model were also found to be 0.98 (95% CI: 0.96 to 0.99) and 0.54 (95% CI: 0.45 to 0.63). The diagnostic odds ratio of PECARN in this section was also calculated to be 58.28 (95% CI: 24.95 to 136.14) (**Figure.4**).

3-3-2. Age < 2 years old

AUC of SROC of PECARN model for prediction of ciTBI in children younger than 2 years old is presented in **Figure.3B**, which was measured to be 0.85 (95% CI: 0.82 to 0.88). Sensitivity, specificity and diagnostic odds ratio of the model were also calculated to be 0.98 (95% CI: 0.92 to 1.0), 0.56 (95% CI: 0.48 to 0.64), and 82.53 (95% CI: 16.23 to 419.63) (**Figure.5**).

3-3-3. Aged 2 to 18 years old

Analyses in this section found the AUC of this model for prediction of ciTBI in the age group of 2-18 years old to be 0.97 (95% CI: 0.95 to 0.98). Sensitivity, specificity and diagnostic odds ratio of PECARN rule in prediction of ciTBI were also found to be 0.98 (95% CI: 0.95 to 0.99), 0.60 (95% Ci: 0.53 to 0.67), and 80.73 (95% CI: 30.59 to 213.05), respectively (**Figure.6**).

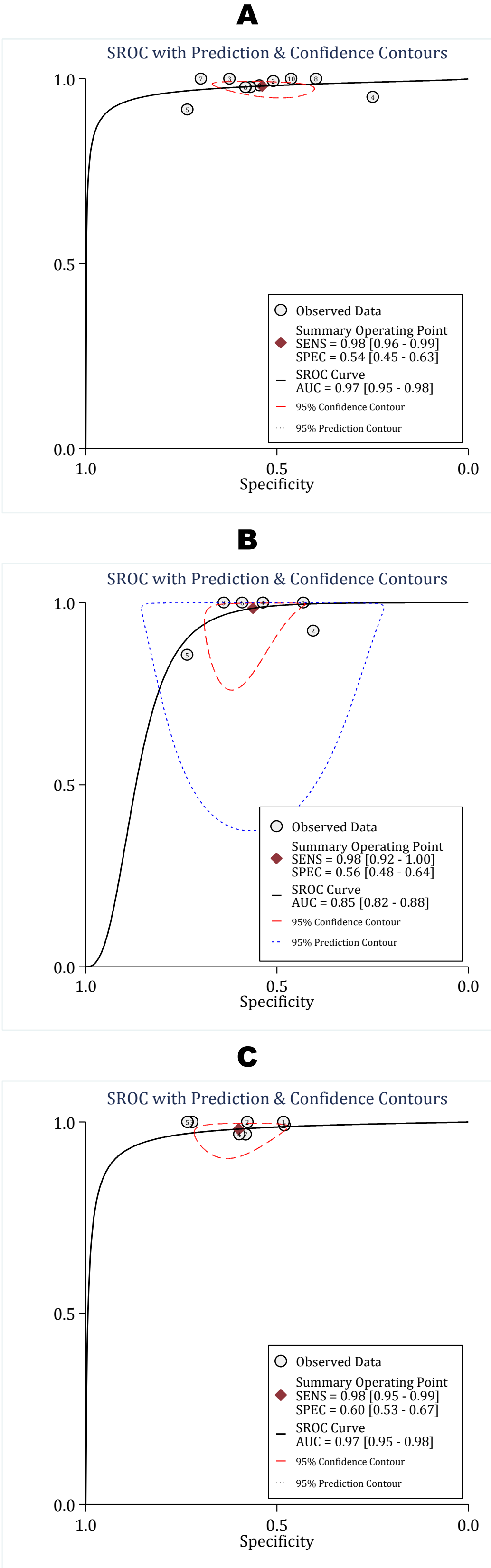


Fig.3: Summary receiver operating characteristics of PECARN rule in detection of clinically important traumatic brain injury in all ages (A), ages lower than 2 years (B) and ages between 2 to 18 years (C).

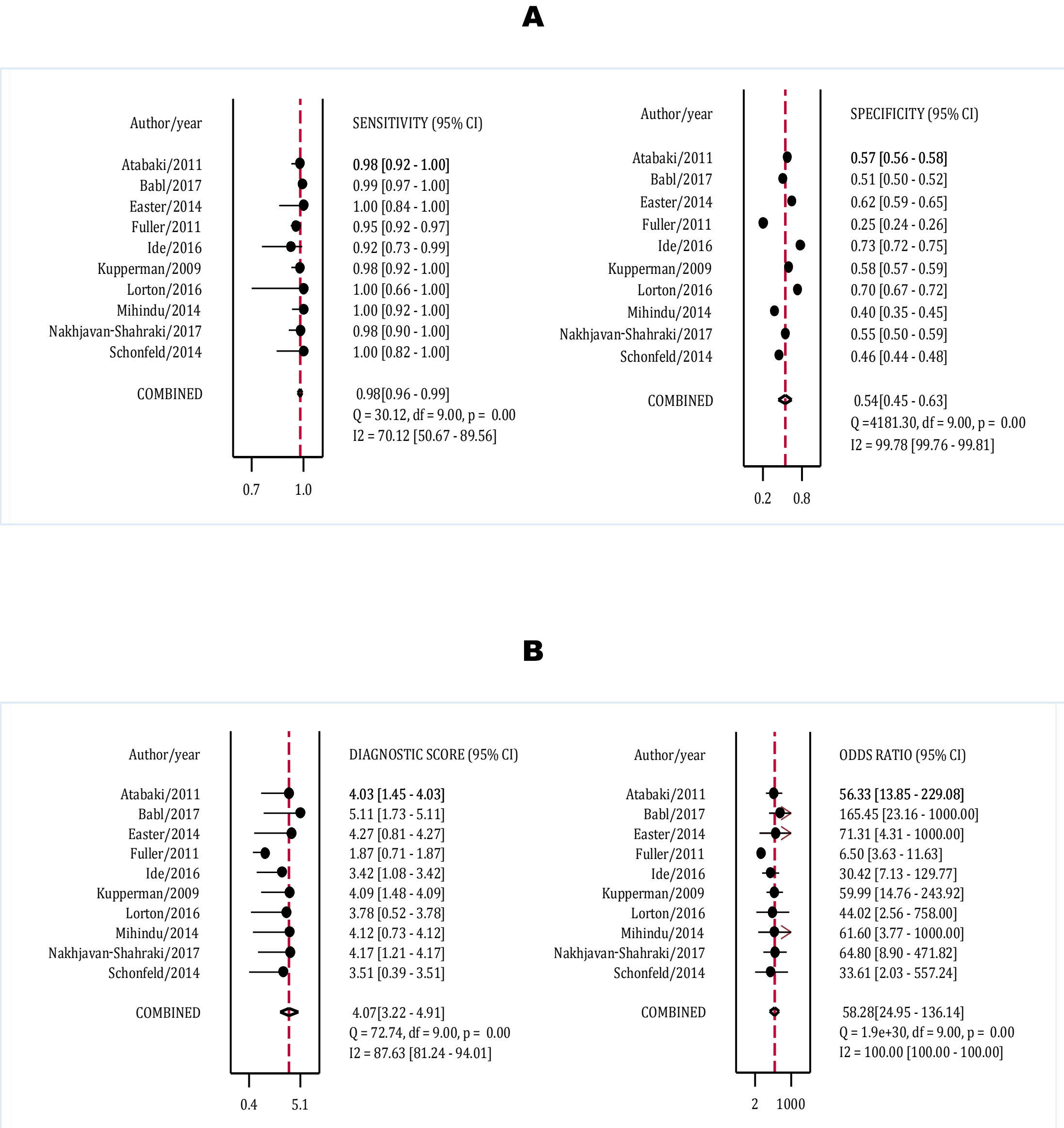
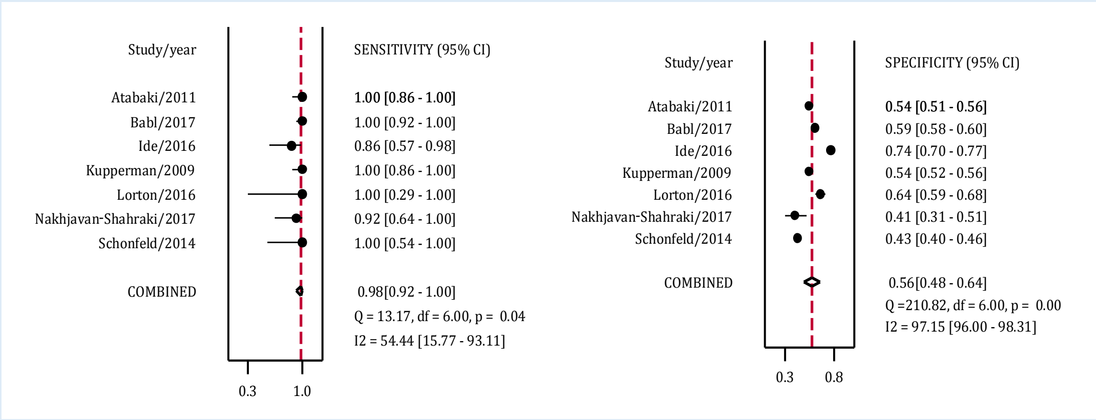


Fig.4: Sensitivity, specificity (A) and diagnostic odds ratio (B) of PECARN rule in detection of clinically important traumatic brain injury in all ages.

A



B

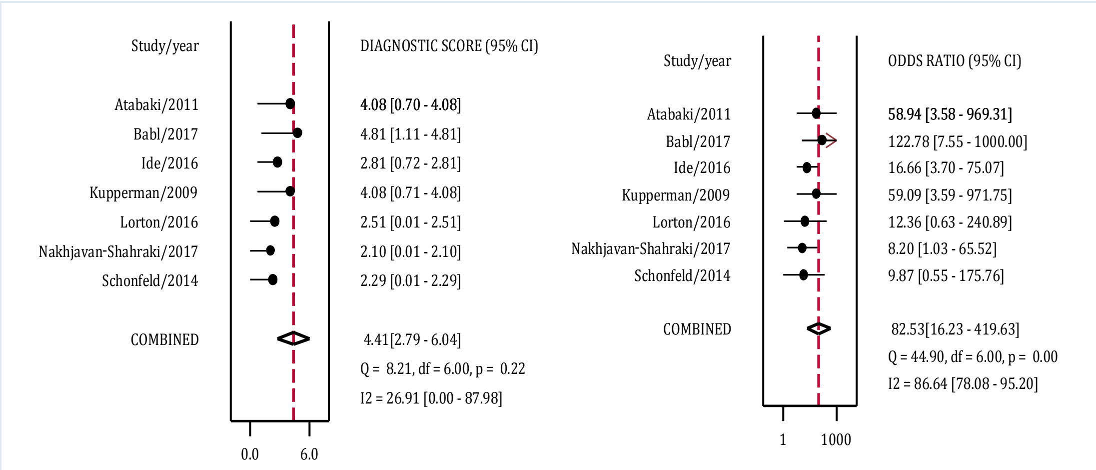


Fig.5: Sensitivity, specificity (A) and diagnostic odds ratio (B) of PECARN rule in detection of clinically important traumatic brain injury in ages lower than 2 years.

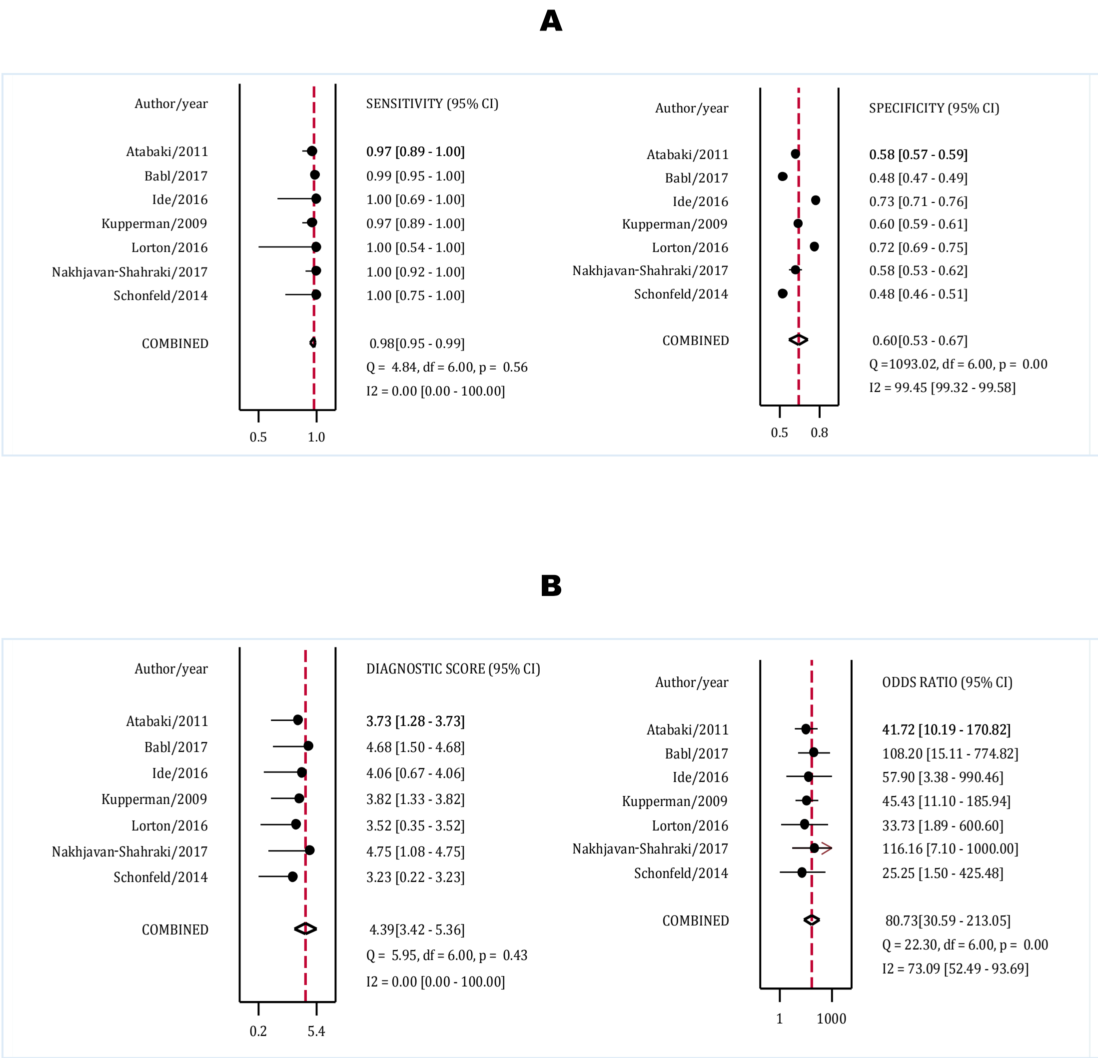


Fig.6: Sensitivity, specificity (A) and diagnostic odds ratio (B) of PECARN rule in detection of clinically important traumatic brain injury in ages between 2 to 18 years.

4- DISCUSSION

The findings of the present study showed that PECARN rule has a high value as a screening tool for classification of children with mTBI. Sensitivity of this decision instrument in children younger than 2 years and in children older than 2 years of age were 0.98 and 0.97, respectively. The diagnostic odds ratio calculated for this model is also very high, which confirms the high effectiveness of PECARN rule in routine practice. Nowadays, major attention has been drawn to application of scoring systems and biomarkers for classification of patients (30, 31). PECARN is one of these tools whose value was confirmed in this study using a meta-analytic approach.

Comparable to the present study, Lyttle et al. had also conducted a systematic review in 2012 and showed that this model is designed based on a high methodological standard and provides an acceptable predictive value for mTBI (32). Similarly, in their systematic review published in 2011, Pickering et al. showed that the model has a high sensitivity in prediction of ciTBI (33). However, the results of two mentioned reviews were merely based on one study which was the derivation study of PECARN rule (3), and so there were debates on whether their findings could be generalized to other populations or not.

There are models for this means other than the PECARN rule as well, such as the Canadian assessment of tomography for childhood head injury (CATCH), and children's head injury algorithm for the prediction of important clinical events (CHALICE) whose validity and reliability have been confirmed by various studies (4, 32, 34-37). However, the PECARN rule is superior to them as it has classified children into two age groups of less and greater than 2 years old. Since the trend of brain development is quite different between these two age groups, brain injuries would elicit different clinical signs and symptoms in the two populations and so assessment of patients with two different approaches is considered an advantage for the PECARN model.

In the present systematic review and meta-analysis 10 studies were included who were found to have low risk of bias in their methodologies during quality assessment. Hence, the findings of this study have acceptable validity. Moreover, no publication bias was detected in this survey, which is strength of the study. Presence of significant heterogeneity between included studies is one of this systematic review's limitations. Further analyses were also performed to identify the source of this heterogeneity, but they were unsuccessful. Accordingly, to minimize the effect of this limitation, bivariate mixed-effects binary regression modelling framework was used, which is a type of random effect model.

5- CONCLUSIONS

For the first time, the present study applied a meta-analytic approach to combine the results all available literature on the diagnostic value of PECARN rule for prediction of ciTBI. The findings were indicative of a high prognostic value for this model in prediction of these injuries and classification of patients according to their need for imaging studies. On this basis, the decision rule is recommended for application in practice.

6- CONFLICT OF INTEREST

All the authors declare that they have no conflict of interest.

7- ACKNOWLEDGMENTS

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Table-1: Search query in PubMed

Database	Query
Medline (via PubMed)	(("Pediatric Emergency Care Applied Research Network"[tiab] OR "PECARN"[tiab] OR "decision rule"[tiab] OR "Decision Support Techniques"[Mesh] OR "Decision Support Techniques"[tiab] OR “Decision Support Technique”[tiab] OR “Technique, Decision Support”[tiab] OR “Techniques, Decision Support”[tiab] OR “Decision Support Technics”[tiab] OR “Decision Support Technic”[tiab] OR “Technic, Decision Support”[tiab] OR “Technics, Decision Support”[tiab] OR “Decision Aids”[tiab] OR “Aid, Decision”[tiab] OR “Aids, Decision”[tiab] OR “Decision Aid”[tiab] OR “Models, Decision Support”[tiab] OR “Decision Support Model”[tiab] OR “Decision Support Models”[tiab] OR “Model, Decision Support”[tiab] OR “Decision Analysis”[tiab] OR “Analyses, Decision”[tiab] OR “Decision Analyses”[tiab] OR “Analysis, Decision”[tiab] OR “Decision Modeling”[tiab] OR “Modeling, Decision”[tiab] OR “Clinical Prediction Rule”[tiab] OR “Clinical Prediction Rules”[tiab] OR “Prediction Rule, Clinical”[tiab] OR “Prediction Rules, Clinical”[tiab] OR “Rule, Clinical Prediction”[tiab] OR “Rules, Clinical Prediction”[tiab])) AND ("Brain Concussion"[Mesh] OR "Brain Injuries"[Mesh] OR "Brain Injuries, Traumatic"[Mesh] OR "Brain Concussion"[tiab] OR "Brain Injuries"[tiab] OR "Brain Injuries, Traumatic"[tiab] OR “Brain Concussions”[tiab] OR “Concussion, Brain”[tiab] OR “Commotio Cerebri”[tiab] OR “Cerebral Concussion”[tiab] OR “Cerebral Concussions”[tiab] OR “Concussion, Cerebral”[tiab] OR “Concussion, Intermediate”[tiab] OR “Intermediate Concussion”[tiab] OR “Intermediate Concussions”[tiab] OR “Concussion, Severe”[tiab] OR “Severe Concussion”[tiab] OR “Severe Concussions”[tiab] OR “Concussion, Mild”[tiab] OR “Mild Concussion”[tiab] OR “Mild Concussions”[tiab] OR “Mild Traumatic Brain Injury”[tiab] OR “Injuries, Brain”[tiab] OR “Brain Injury”[tiab] OR “Injury, Brain”[tiab] OR “Injuries, Acute Brain”[tiab] OR “Acute Brain Injuries”[tiab] OR “Acute Brain Injury”[tiab] OR “Brain Injury, Acute”[tiab] OR “Injury, Acute Brain”[tiab] OR “Brain Injuries, Acute”[tiab] OR “Brain Lacerations”[tiab] OR “Brain Laceration”[tiab] OR “Laceration, Brain”[tiab] OR “Lacerations, Brain”[tiab] OR “Brain Injuries, Focal”[tiab] OR “Brain Injury, Focal”[tiab] OR “Focal Brain Injury”[tiab] OR “Injuries, Focal Brain”[tiab] OR “Injury, Focal Brain”[tiab] OR “Focal Brain Injuries”[tiab] OR “Brain Injury, Traumatic”[tiab] OR “Traumatic Brain Injuries”[tiab] OR “Trauma, Brain”[tiab] OR “Brain Trauma”[tiab] OR “Brain Traumas”[tiab] OR “Traumas, Brain”[tiab] OR “TBI (Traumatic Brain Injury)”[tiab] OR “Encephalopathy, Traumatic”[tiab] OR “Encephalopathies, Traumatic”[tiab] OR “Traumatic Encephalopathies”[tiab] OR “Injury, Brain, Traumatic”[tiab] OR “Traumatic Encephalopathy”[tiab] OR “TBIs (Traumatic Brain Injuries)”[tiab] OR “TBI (Traumatic Brain Injuries)”[tiab] OR “Traumatic Brain Injury”[tiab] OR “TBI”[tiab])).

Table-2: Summary of included studies

Author, Year; Country	Design of study	Severity of injury	Mean age (year)	Male gender (n)	Assessor	Sample size	
						Total	No CiTBI / CiTBI
Atabaki, 2011; US (24)	Prospective	Minor	6.8	5322	Clinician	8627	8540 / 87
Babl, 2017; Australia and New Zealand (4)	Prospective	Minor	5.7	NR	EP	18913	18753 / 160
Easter, 2014; US (25)	Prospective	Minor	6.1	650	Clinician	981	960 / 21
Fuller, 2011; England (26)	Retrospective	Minor	5.7	6770	NR	10415	10169 / 246
Ide, 2016; Japan (27)	Retrospective	Minor	3.3	1398	NR	2208	2184 / 24
Kupperman, 2009; US (3)	Prospective	Minor	7.1	NR	EP	8627	8539 / 88
Lorton, 2016; France (5)	Prospective	Minor	3	955	Clinician	1499	1490 / 9
Mihindu, 2014; US (28)	Retrospective	Minor	2 to 17	NR	NR	493	447 / 46
Nakhjavan Shahraki, 2017; Iran (6)	Prospective	Minor	7.9	471	EP	594	539 / 55
Schonfeld, 2014; US and Italy (29)	Prospective	Minor	0 to 18	1439	Clinician	2428	2409 / 19

CiTBI: Clinically important traumatic brain injury, including death from traumatic brain injury (TBI), need for neurosurgery, intubation more than 24 hours and TBI related admission to hospital for two or more nights; EP: Emergency physician; NR: Not reported.

Table-3: Quality assessment of included studies

Author, Year	Risk of bias				Applicability		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Atabaki, 2011	🙂	🙂	🙂	🙂	🙂	🙂	🙂
Babl, 2017	🙂	🙂	🙂	🙂	🙂	🙂	🙂
Easter, 2014	🙂	🙂	🙂	🙂	🙂	🙂	🙂
Fuller, 2011	🙂	🙂	🙂	🙂	🙂	🙂	🙂
Ide, 2016	😐	🙂	🙂	🙂	🙂	🙂	🙂
Kupperman, 2009	🙂	🙂	🙂	🙂	🙂	🙂	🙂
Lorton, 2016	😐	🙂	🙂	🙂	🙂	🙂	🙂
Mihindu, 2014	🙂	🙂	🙂	🙂	🙂	🙂	🙂
Nakhjavan Shahraki, 2017	🙂	🙂	🙂	🙂	🙂	🙂	🙂
Schonfeld, 2014	🙂	🙂	🙂	🙂	🙂	🙂	🙂

🙂, Low risk of bias; 😐, Unclear risk of bias.