SCORING SYSTEMS FOR PREDICTING OUTCOMES OF NEONATAL SEIZURE

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Abstract: *Clinicians are dealing with considerable information's from clinical records (medical history, symptoms) and different investigations (ultrasound examinations, functional explorations, MRI).They have to integrate these data in difficult decisions related to the diagnosis and treatment of infants with neonatal seizures and their subsequent complications. Different scoring systems were developed for predicting and quantifying outcomes after neonatal seizures (mental development, motor dysfunction, epilepsy, cerebral palsy). In this paper we propose a review of the existing scoring systems underlining their developing/validation methods (univariate analysis, logistic regression analysis, sensitivity, specificity) and their identified independent risk factors (for each scoring system).*

INTRODUCTION

Recognizing neonatal seizures in newborns can be a very challenging task for clinicians, because of the variability of symptoms. Many studies consider that etiologic factors are responsible for injuries of newborn's central nervous system.(1,2,3,4,5,6,7,8,9,10,11,12,13) Clinicians are dealing with considerable informations from clinical records (medical hystory, symptoms) and different investigations (ultrasound examinations, functional explorations, laboratory tests, MRI). They have to integrate these data in difficult decisions related to the diagnosis and treatment of infants with neonatal seizures and their subsequent complications.

Different scoring systems were developed for predicting and quantifying outcomes after neonatal seizures. These approaches involved the study of adequate accumulated data from newborns with seizures (at the admission and after the admission). A comprehensive analysis was conducted on the risk factors related to different outcomes prognostic after neonatal seizure (mental development, motor dysfunction, epilepsy, cerebral palsy) with a high risk model proposal in neonatal groups.

PURPOSE

This review highlights the existing scoring systems of predicting outcome after neonatal seizure.

MATERIALS AND METHODS

We undertook a literature review of existing scoring systems for outcome predictions after neonatal seizures using the combination of specific searching keywords: scoring system, outcome, neonatal seizures. Five scoring systems proposed by Ellison & all (1981) (14,15), Pisani & all (2009) (16), Garfinkle & Shevell (2011) (17) , Salmon & all (2014) (18), Hur & Chung (2016) (19) were identified.

RESULTS

Ellison & all (1981) (14,15) presented a scoring system based on initial and after 3 months evaluation of clinical records (EEG abnormality, neurologic examination, etiology of seizures, length of seizure, type of seizure, and birth weight), concluding that the proposed scoring system is accurate for the outcome following neonatal seizure.

Pisani & all (2009) (16), (20) analysed data from clinical examination of the seizures, considering ultrasound examination of the brain (cerebral ultrasound and video EEG). Two scoring systems were design (with variable background EEG and without). The discriminatory ability of two scoring system was nonsignificantly diferent (score 1 AUC: 0.917, score 2 AUC: 0.919).

Garfinkle and Shevell (2011) (17) developed a scoring system considering information from clinical examination but also EEG, imaging findings (EEG background findings, EEG epileptiform activity, EEG burst suppression pattern) and treatment (anticonvulsant therapy efficacy).

Salmon & all (2014) (18) in their research focused on identifying the risk factors only for epilepsy after neonatal seizure. Firstly, they validated Garfinkle's scoring system, then they tested five independent factors from Garfinkle's scoring system and other factors reported in literature. The authors considered that seizures time interval is a factor that acts different on prognosis in combination with gestational age. As a consequence, a limitation of interaction factors was recommended when developing the scoring systems for epilespy outcome after neonatal seizures.

Hur & Chung (2016) (19) proposed an arithmetic composite scoring system including seven predictors. Their approach identified some of the risk factors described in the systems presented by other authors, emphasizing the association between 3 months follow-up EEG normalization or persistent normal findings and adverse outcomes.

Table no. 1. Outcome Scoring Systems: Description

Scoring systems Year / Country Author Study type	Research period Predicting Data particularities
1981 / Albany (N.Y) Ellison & all Pilot study	1975-1976, 1978 adverse outcome mental development,

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	motor dysfunction 96 infants
2009 / Parma (Italy) Pisani & all Retrospective /hospital-based study	1999-2004 adverse outcome (neurologic outcome) 106 preterm infants
2011 / Montreal Garfinkle & Shevell Retrospective /hospital-based study	1991-2007 adverse outcome cerebral palsy, global development delay epilepsy mortality 124 borne at time infants
2014 / Ljubljana Salmon & all Retrospective /hospital-based study	1999-2009 adverse outcome epilepsy 176 newborns
2016 / Haeundae Hur & Chung Retrospective /hospital-based study	2010-2015 adverse outcome cerebral palsy, global development delay epilepsy 174 newborns

Identified risk factors from studied scoring systems were: method of delivery, time of seizure onset, duration of seizures, seizure type, seizure severity, EEG findings, neurologic examination, cerebral ultrasound, neuroimaging results, status epilepticus, etiology, gestational age, birth weight, Apgar score at 1 minute, anticonvulsant therapy, other risk factors. These factors and developing methods are presented in the table no. 2 for each of the studied scoring systems.

Table no. 2. Outcome Scoring Systems: Factors

Scoring systems	Developing methods	Identified independent risk factors
Ellison & all	Chi square, Product moment correlations, Multiple regression analyses	abnormality of EEG, neurologic examination, etiology, length of seizure, type of seizure, birth weight
Pisani & all	Univariate analysis Logistic regression analysis six-point scoring system score: by addition of scores of the 6 variables scoring system range from 0 to 12 for cutoff of >=4: sensitivity 85.7% specificity 80.6%	birth weight, Apgar score at 1 minute, seizure onset, cerebral ultrasound, anticonvulsant therapy, status epilepticus
Garfinkle & Shevell	Univariate analysis Logistic regression analysis scoring system range from 0 to 5 for cutoff of >=4: sensitivity 81.1% specificity 84.0%	method of delivery (cesarean section), time of seizure onset (first 24 h of life), seizure type (other than focal clonic), EEG findings (moderately or severely abnormal EEG), etiology
Salmon & all	Bivariate analysis Logistic regression analysis	etiology, gestation, mode of delivery, duration of seizures, other risk factors
Hur & Chung	Multivariate logistic regression analysis	birth weight, time of onset, EEG findings, neuroimaging results, seizure type, seizure severity, etiology
	Seven predictors Score ranging from 0 to 7 cutoff score ≥ 3 sensitivity 84.2% specificity 82.1%	

DISCUSSIONS

The identified and presented scoring systems should be easily applicable and simple. Moreover, they should be based on admission units data regarding the routinely available risk factors measurements such as basic birth information's, data collected at the admission and after, rapid (early prognostic) and accurate identification of neonatal seizures that eventually would yield both short-term or long-term adverse outcomes from the early life. The scores were derived using data analysis techniques such as univariate analysis (Student T test to compare mean value of continuous variables or/and chi-square/Fisher's exact test for nominal variables) usually in combination with multiple logistic regression analysis. Score validating methods (training/test, calibration, recalibration, etc.) and score performance evaluation indicators (accuracy, sensitivity, specificity, Receiver operating characteristic (ROC) curves, area under curve (AUC), 95% confidence interval (CI)) were also performed. However, there were differences between studies regarding methodological aspects such as cases inclusion criteria / study limitations and follow up period.

In case of Ellison & all (1981) scoring system the inclusion criteria of patients were based on clinical findings while in case of Pisani & all (2007, 2009) they included data from clinical examination of the seizures and ultrasound examination of the brain (video EEG and cerebral ultrasound) and Garfinkle and Shevell (2011) included data from clinical findings with or without EEG findings. Differnt by Pissani's approach (2007, 2009), Garfinkle included only infant with recurrent neonatal EEG confirmed seizure.

Pisani & all (2009) scoring system included only preterm infants, Garfinkle and Shevell (2011) term infants and Salmon & all (2014) both preterm and term infants.

Recognition of seizure, etiology types and abnormal outcomes establishing protocols were also underlining some selection bias between studies. Hur & Chung (2016) scoring system considered the following adverse outcomes naming cerebral palsy, global development delay and/or epilepsy while Garfinkle & Shevell (2011) mentioned also mortality as adverse outcome. Salmon & all (2014) proposed the scoring system only for epilepsy. This kind of inclusion criteria or study limitations affects the number of selected patients leading to incidence overestimation/underestimation and variability between studies.

Only in the case of Ellison & all (1981) the authors scored the variables from the beginning and used chi square analysis for confirmation of the proposed scoring system. In the other remaining scoring systems the approach started with identifying potential predictors of adverse outcome using univariate analysis for all the variables included in the study (a relation between the target variable and adverse outcome). Multiple logistic regression methods were implemented subsequently using significant variables from univariate analysis. Then, a scoring system was proposed based on assignation of binary or greater scores for the significant variables from the multiple logistic regression analysis. Usually both minimum and maximum of the computed score is presented and a cutoff point is determined (the value of the score that provides the best compromised for sensitivity and specificity). The performance of the presented scoring systems (were specify) was greater than 80% for both sensitivity and specificity performance measures.

CONCLUSIONS

The use of scoring systems for predicting outcome after neonatal seizure could be useful tools for clinicians (neonatologists, paediatricians, neurologists), health-providers, patients, legal representatives and researchers. Their intrinsic values reside in the explanation, understanding, guiding treatment, data comparison between hospitals, identifying factors that can be predicted in the situation of a wide variation and differences of neonatal seizure mortality and adverse outcomes scenarios. Nonetheless we should consider the accuracy of the model, models limitations, clinical complexity, etc.

Desired properties of a universal scoring system for predicting outcomes after neonatal seizure are very hard to accomplish. Further models on uniform populations, appropriately sized, considering new factors, may confirm the existing scores, remedying shortcomings or achieving more accurate ones.

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