

The Role of Scoring Systems and Urine Dipstick in Prediction of Rhabdomyolysis-induced Acute Kidney Injury

A Systematic Review

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Introduction. During the past decade, using serum biomarkers and clinical decision rules for early prediction of rhabdomyolysis-induced acute kidney injury (AKI) has received much attention from researchers. This study aimed to broadly review the value of scoring systems and urine dipstick in prediction of rhabdomyolysis-induced AKI.

Materials and Methods. The study was designed based on the guidelines of the Meta-analysis of Observational Studies in Epidemiology statement. Search was done in electronic databases of MEDLINE, EMBASE, Cochrane Library, Scopus, and Google Scholar by 2 independent reviewers. Studies evaluating AKI risk factors in rhabdomyolysis patients with the aim of developing a scoring model as well as those assessing the role of urine dipstick in these patients were included.

Results. Of the 5997 articles found, 143 were potentially relevant studies. After studying their full texts, 6 articles were entered into the systematic review. Two studies had developed or validated scoring systems of the “rule of thumb,” and the AKI index, and the Mangled Extremity Severity Score. Four studies were on the predictive value of urine dipstick in risk prediction of rhabdomyolysis-induced AKI, with favorable results.

Conclusions. The findings of this systematic review showed that based on the available resources, using the prediction rules and urine dipstick could be considered as valuable screening tools for detection of patients at risk for AKI following rhabdomyolysis. Yet, the external validity of the mentioned tools should be assessed before their general application in routine practice.

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INTRODUCTION

Acute kidney injury (AKI) is a major preventable health problem all over the world. Its prevalence is high and rises about 8% annually. Kidney diseases take a toll on the finances of both health systems and families.¹ Unfortunately, it is usually asymptomatic until a big part of the kidney is

lost.² Existing studies show that using preventive strategies can dramatically reduce the burden of disease.³ Therefore, all physicians should be familiar with prevention, rapid diagnosis, and treatment of kidney diseases.

Rhabdomyolysis is one of the most important, yet preventable, causes of AKI. During the past decade,

using serum biomarkers and clinical decision rules for early prediction of rhabdomyolysis-induced AKI has received much attention from researchers.⁴⁻⁷ Urine dipstick, myoglobin and creatine kinase (CK) are among the most studied predictive factors.⁸⁻¹⁴ In addition, some studies have tried to develop scoring systems based on the related factors.¹⁵ One recently released systematic review on the role of urine myoglobin in prediction of AKI following rhabdomyolysis declared the lack of enough evidence regarding its value.¹⁶ Other factors have not been comprehensively studied either. Therefore, the present study aimed to broadly review the value of scoring systems and urine dipstick in prediction of rhabdomyolysis-induced AKI.

MATERIALS AND METHODS

Search Strategy

The present systematic review was designed based on the guidelines of Meta-analysis of Observational Studies in Epidemiology (MOOSE) statement.¹⁷ A thorough search was done in electronic databases of MEDLINE, EMBASE, Cochrane Library, Scopus, and Google Scholar without any time or language limitations by 2 independent reviewers. The keywords used for the search were extracted from the MeSH database (PubMed) and were related to rhabdomyolysis and kidney injury. These included “Crush syndrome” OR “crush injury” OR “rhabdomyolysis” AND “acute kidney injury” OR “acute renal failure” OR “renal insufficiency” combined with predictive factors and scoring models including “risk factors” OR “predictive factors” OR “urine dipstick” OR “urine analysis.” In addition, a hand search was done to find more articles.

Selection Criteria

Studies that had evaluated AKI risk factors in rhabdomyolysis patients with the aim of developing a scoring model, as well as those assessing the role of urine dipstick in this regard, were included. All observational studies (retrospective and prospective) with a clear definition of rhabdomyolysis and AKI based on standard scales were entered. Animal studies were excluded.

Quality Assessment and Data Extraction

The studies found in the systematic search were combined using the EndNote software (version X5,

Thomson Reuters, 2011) and after elimination of redundant ones, their abstracts were studied by 2 independent reviewers (MY and SS) and data of relevant articles were summarized using a checklist designed based on the MOOSE statement guidelines.¹⁷ Any disagreement between the reviewers was resolved by having a discussion involving a third reviewer (IN). Information related to study design, patient characteristics (age, sex, and rhabdomyolysis etiology), number of studied patients, and the study’s final conclusion were extracted.

Quality of the studies was evaluated using guidelines suggested by the Agency for Healthcare Research and Quality’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews.¹⁸ Studies were enrolled only if they had a good or fair quality rating. Scoring each article was done based on its design, selection bias, performance, and final outcome report (inter-rater reliability, 89%).

RESULTS

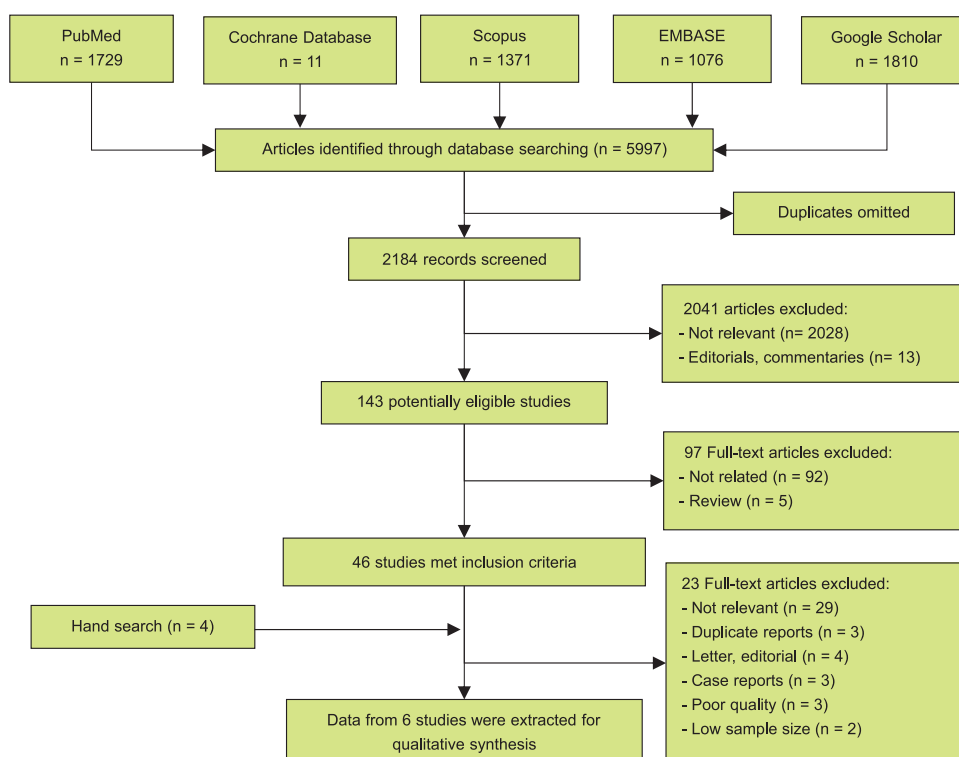
Study Characteristics

The flowchart of study selection is shown in the Figure. Out of the 5997 nonredundant retrieved articles, 143 were potentially relevant studies. After studying the full texts, 6 articles were entered into the systematic review.^{8,9,15,19-21} The characteristics of these studies are presented in the Table.

Scoring Systems

Two studies had developed (1 study) or validated (1 study) scoring systems in risk prediction of rhabdomyolysis-induced AKI.^{15,21} In a study of Bam earthquake, in Iran, by Najafi and colleagues, 2 scoring models (the “rule of thumb” and the AKI index) were designed to predict the risk of rhabdomyolysis-induced AKI in crush injury cases.¹⁵ In the rule of thumb model, the level of serum lactate dehydrogenase on the 1st day, uric acid level, and serum creatinine level were predictive factors of AKI occurrence on the 3rd day. If the level of serum creatinine was less than 2 mg/dL, lactate dehydrogenase was less than 2000 IU, and uric acid was less than 6 mg/dL, the risk of development of AKI was almost zero. In the AKI index model, creatinine level of the 3rd day could be estimated using the following formula:

$$\text{Serum creatinine on day 3} = (0.45 \times \text{CK} + 2.5 \times$$



Flowchart of the selection of the articles.

lactate dehydrogenase + 2700 × serum potassium – 14 000) / 10 000

The area under the receiver operating characteristic (ROC) curve calculated for this formula was 0.99.

The value of the Mangled Extremity Severity Score (MESS) in predicting AKI occurrence following trauma was assessed by Paul and coworkers.²¹ This scoring system was originally designed for determining the risk of extremity amputation after trauma. The study showed the higher MESS of AKI patients and concluded its acceptable ability in predicting kidney outcome of trauma patients.²¹

Urine Dipstick

Four studies had evaluated the predictive value of urine dipstick in kidney outcome of the rhabdomyolysis patients. Two were done on the patients affected by crush syndrome,^{8,9} 1 on marathon runners¹⁹, and 1 on patients with rhabdomyolysis due to various causes.²⁰ All the four studies demonstrated a high value of urine dipstick in prediction of AKI occurrence. Amini and colleagues showed the equal value of urine dipstick and CK in prediction of rhabdomyolysis-induced AKI.⁹ Alavi-Moghadam and coworkers

also expressed the higher screening performance indexes of urine dipstick in prediction of traumatic rhabdomyolysis-induced AKI compared to serum CK level. They concluded that urine dipstick could be used as an appropriate tool in management of these patients.⁸ Hoffman and associates studied marathon runners and revealed that urine dipstick had a 100% sensitivity and a 76% specificity in predicting AKI occurrence.¹⁹

Mannix and coworkers studied 191 pediatric rhabdomyolysis patients and showed a 100% sensitivity and a 73.6% specificity of urinary heme dipstick of 2+ and greater in prediction of at-risk patients for development of AKI following rhabdomyolysis with different causes.²⁰

DISCUSSION

The present systematic review comprehensively summed up the articles trying to evaluate the role of scoring models and urine dipstick in predicting rhabdomyolysis-induced AKI. We could find only 6 relevant studies for the systematic review. The limited number of available studies can be explained by complications of research in disaster settings, which is the major source of traumatic rhabdomyolysis patients. The lesson learned from

Characteristics of the Studies on Rhabdomyolysis-induced Acute Kidney Injury (AKI) Included in the Systematic Review*

Study	Patients		Age*	Male, %	Cause of Rhabdomyolysis	Evaluated Factor	Main Conclusion	Comment
	With AKI	Without AKI						
Mannix et al ²⁰	9	182	11 (6 to 16)	67	Multiple	Urinary dipstick	Urinary heme dipstick < 2+ indicated a lower risk of developing AKI.	Low proportion of AKI patients
Najafi et al ¹⁵	94	1374	≥ 15	52	Crush injury	Rule of Thumb; AKI index	The rule of thumb yielded a sensitivity and specificity of 100% and 96.1%, respectively. These values were 96.6% and 95.7% for AKI index, respectively.	Retrospective design; missing data
Paul et al ²¹	5	50	37.4 (11 to 91)	...	Trauma	MESS	A Mangled Extremity Severity Score ≥ 7, higher age, shock, and increased myoglobin levels in urine and serum correlated with a greater risk of developing AKI.	Low sample size
Amini et al ⁹	8	71	26 (1 to 90)	68	Crush injury	Urine dipstick	Urine dipstick was a highly sensitive and easy screening tool for identification of patients at risk of developing AKI.	Low sample size; possibility of selection bias; retrospective design
Alavi-Moghaddam et al ⁸	200	2762	28.4 (1 to 90)	60	Crush injury	Urine dipstick	Urine dipstick could be considered as an early screening tool for detection and triage of patients at risk of developing AKI.	Missing data; varied time interval between crush injury and urine dipstick; retrospective design
Hoffman et al ¹⁹	9	198	42.5 ± 9.5	80	Crush injury	Urine dipstick	Urine dipstick successfully identified individuals meeting injury criteria for AKI.	Low proportion of AKI patients

*Values are presented as mean ± standard deviation (range) or range minimum.

the previous studies can be a guide for future ones. Therefore, reviewing the few existing studies can be helpful in this regard.

Nowadays, using clinical decision rules as one of the powerful sources of estimating pretest probability is getting more attention in daily practice of physicians. The results of this study showed that to date, only 3 models (the rule of thumb, AKI index, and Mangled Extremity Severity Score) have been designed or validated in prediction of AKI occurrence. The rule of thumb and AKI index were designed using a big pool of data from rhabdomyolysis patients of Bam earthquake in 2003. Although the accuracy of these models in AKI prediction has been reported to be high, their external validity has not been evaluated in another study, yet. The rule of thumb model claims that AKI occurrence on the 3rd day can be predicted on the 1st day using the level of serum creatinine, uric acid, and lactate dehydrogenase. In addition, with the aid of AKI index formula, one can estimate the probable level of serum creatinine on the 3rd day. The importance of this ability is highlighted when one is confronted with a large number of mass disaster victims and limited resources. Therefore, one has to triage and screen patients based on their severity of injury and allocate the limited available resources to those who are actually in need.

On the other hand, it can also be helpful in making decisions regarding patient transfer to other more resourceful centers, such as those having dialysis machines. The important point is that the data needed for these models are available on the disaster scene and in unequipped local hospitals. Paul and colleagues validated the MESS and showed its ability in prediction of AKI occurrence.²¹ This model was designed for prediction of the need for amputation following traumatic extremity injuries. In this model, each patient is given a score based on their age, shock state, injury mechanism, and grading and time of limb ischemia. Since the most important source of rhabdomyolysis and the subsequent AKI are the large bulk of extremity muscles, it seems that this scoring can be applicable in prediction of AKI. Paul and colleagues showed that its score is significantly higher for patients with rhabdomyolysis-induced AKI.²¹

Urine is another source of data regarding patients at risk for development of AKI following

rhabdomyolysis. Four studies were done in this regard. Mannix and colleagues and Hoffman and associates showed proper screening performance characteristics of urine dipstick in this regard for marathon runners and pediatric patients, respectively.^{19,20} Using Bam earthquake data, 2 studies by Amini and colleagues and Alavi-Moghadam and colleagues evaluated the value of urine dipstick in screening of crush injured victims at risk for development of AKI.^{8,9} Both studies demonstrated that urine dipstick could be considered as a helpful screening tool for triage of crush injured patients regarding AKI development risk. Considering its simple application, urine dipstick could be done even by the patients themselves. All the patient has to do is dip a urine dipstick in urine sample and compare the color change to the reference standard on the package. In case of color changing to alarming ones, they can inform their physician in charge.

It seems that using a combination of the abovementioned methods can increase their reliability. One of the most important limitations of these prediction tools is lack of external validation studies. Taking into account the chaotic situation after mass disaster, running the validation studies seems to be difficult. Therefore, we have to run these validation studies on similar situations such as marathon races, sport injuries, and bombing disasters, and rely on their results.

One of the strong points of this study is the comprehensive search in various databases for finding the most articles possible, but a systematic review on descriptive studies has some limitations in nature. First, descriptive studies cannot evaluate all confounding factors as a result of their intrinsic limitation. Therefore, they cannot assertively prove the causality relationships. We should not forget that this limitation can never be completely eliminated.

CONCLUSIONS

The findings of this systematic review showed that based on the available resources, using the prediction rules and urine dipstick could be considered as valuable screening tools for detection of patients at risk for AKI following rhabdomyolysis. Yet, the external validity of the mentioned tools should be assessed before their general application in routine practice.

CONFLICT OF INTEREST

None declared.

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