

REVIEW ARTICLE

The Value of Serum CK in Predicting Traumatic Rhabdomyolysis Induced Acute Kidney Injury: A Systematic Review and Meta-Analysis

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Abstract:

Introduction: Creatine kinase (CK) has frequently been introduced as a predictive factor of rhabdomyolysis induced acute kidney injury (AKI) in several studies. However, its value, especially in traumatic and disaster settings, remains to be fully clarified. **Methods:** Online databases of Medline (via PubMed), Embase, Scopus, and Web of Science were systematically searched until May 15th, 2026 and studies evaluating the association between serum CK and AKI in traumatic rhabdomyolysis patients were included. Reports of CK were collected as mean differences between the AKI and non-AKI groups, odds ratios (ORs), and performance metrics such as sensitivity and specificity. Analyses were performed using STATA 17.0 statistical software. The study's protocol has been registered with PROSPERO (CRD420251250906). **Results:** 17 articles were included in this study. Twelve studies encompassing 3122 rhabdomyolysis patients (AKI: 30.94%) evaluated mean CK values in AKI and non-AKI patients with a pooled mean difference of 21770.75 (95% CI: 8987.39 to 34554.11) IU/L between groups. Four studies of 3549 patients (AKI: 20.29%) reported a pooled adjusted OR of 7.62 (95% CI 2.80 to 20.76). Ten articles, including 3421 patients (AKI: 18.42%), reported prediction accuracy measures. The pooled analysis showed an AUC of 0.73 (95% CI: 0.69 to 0.77), with sensitivity 0.68 (95% CI: 0.55 to 0.78) and specificity of 0.68 (95% CI: 0.54 to 0.78). **Conclusion:** Our findings indicate that, across traumatic rhabdomyolysis populations, AKI was associated with higher CK levels, with a more pronounced elevation observed in earthquake-related settings, although heterogeneity was high. CK alone demonstrated only fair discriminatory performance, suggesting its use as part of a broader clinical risk assessment rather than as a sole predictor of AKI.

Keywords:

Rhabdomyolysis; Creatine Kinase; Acute Kidney Injury; Trauma; Crush Syndrome

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1. Introduction

Rhabdomyolysis is a condition in which the breakdown of skeletal muscle cells leads to the release of intracellular contents, such as creatine kinase (CK), lactate dehydrogenase, and myoglobin into the bloodstream (1). Rhabdomyolysis can result from various causes, including trauma, intense physical activity, temperature changes, drugs, and toxins (2, 3). Patients experiencing rhabdomyolysis can show a wide range of symptoms, from no symptoms at all to organ failure, which makes it challenging to diagnose and prioritize high-risk patients. Typically, rhabdomyolysis is characterized by myalgia, muscle weakness, and tea-colored urine secondary to myoglobinuria (4). To the extent that muscle cell destruction occurs, the intracellular contents will be released, potentially causing several systemic complications (1, 5).

Acute kidney injury (AKI) is an important complication of rhabdomyolysis, which occurs in 10-67% of cases (4, 6). AKI,

as one of the main causes of mortality in patients with rhabdomyolysis, can lead to volume overload, worsening electrolyte imbalance, and, in the end stages, arrhythmia, multi-organ failure, and death (3). Therefore, predicting AKI and identifying at risk rhabdomyolysis patients is crucial for preventing complications.

Clinical and laboratory factors have been examined in several studies aimed at developing predictive models for AKI associated with rhabdomyolysis. However, the precise role of CK as a predictor of rhabdomyolysis related AKI, especially in traumatic and disaster settings, remains to be fully clarified.

Our previous systematic review and meta-analysis demonstrated a significant correlation between CK levels and AKI in all patients with rhabdomyolysis (7). The current study, in addition to providing an update to our previous study, aimed to specifically evaluate traumatic rhabdomyolysis patients to assess the value of CK in predicting AKI in traumatic and disaster conditions such as earthquakes.

2. Methods

2.1. Study design and search strategy

This systematic review and meta-analysis investigates the value of serum CK in predicting AKI in traumatic rhabdomyolysis patients. In this study, PIT (Patient, Index test, Target condition) was defined as P: Patients with traumatic

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rhabdomyolysis, I: Serum CK levels, T: AKI. For this purpose, online databases of Medline (via PubMed), Embase, Scopus, and Web of Science were systematically searched until May 15th, 2026. Keywords were chosen based on MeSH and Emtree terms, consultation with experts in the field, and review of relevant literature. Additionally, a manual search was performed in Google and Google Scholar search engines to acquire any missed papers. Supplementary Material 1 presents the utilized search strategy for each database. The study's protocol has been registered with PROSPERO (CRD420251250906).

2.2. Selection criteria and screening

All human studies evaluating CK levels and performance metrics for prediction of AKI in patients with traumatic rhabdomyolysis were included. Studies with mixed and non-traumatic etiology, in addition to rhabdomyolysis due to burn or electrical injuries, were excluded from this study. Case studies, series, letters, reviews, articles that did not report required information, and non-English articles were also excluded. Two researchers independently reviewed eligible articles, and relevant information was summarized in a checklist designed according to PRISMA guidelines (8).

2.3. Data collection and synthesis

Information on study characteristics (first author, publication year, country), study type, etiology, sample size, mean age, number of males, number of patients who developed AKI, AKI stage, type of CK (initial or peak), and reported cutoffs was gathered from included studies. Reports of CK were gathered as mean $\pm$ standard deviation (SD) in the AKI or non-AKI group, odds ratio (OR), and performance values, including true positive (TP), true negative (TN), false positive (FP), and false negative (FN). In studies reporting other measures such as median (IQR), sensitivity, and specificity, required values were calculated accordingly.

2.4. Definitions

The included studies used varying definitions and criteria for rhabdomyolysis and AKI. For this review, we defined rhabdomyolysis as a serum CK level $>1,000$ IU/L (or >3 times the upper limit of normal) and AKI as an increase in serum creatinine to ≥ 1.5 times the reference value (or AKI stage ≥ 1). In studies that included patients with CK values < 1000 IU/L, we either extracted only the subset with CK > 1000 IU/L or included the entire population if the number of patients with CK < 1000 IU/L was judged to be negligible. Thus, all included studies effectively represented patients with rhabdomyolysis.

2.5. Quality assessment and certainty of evidence

The risk of bias in studies was evaluated according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) guidelines (9). Two reviewers independently assessed the articles for risk of bias and applicability across the domains of participants (patient recruitment and selection), index test (context of use and interpretation), reference standard (definition, measurement, and interpretation), and flow and timing (missing data). Disagreements were resolved by consulting a third reviewer. Certainty of evidence and summary of findings were evaluated according to Grades of Recommendation, Assessment, Development and Evaluation (GRADE) framework (10).

2.6. Statistical analysis

Analyses were performed using STATA 17.0 statistical software. For studies reporting continuous data as mean $\pm$ SD values, we used "meta" package to pool the weighted mean differences in CK values between AKI and non-AKI groups. We conducted a predefined subgroup analysis comparing studies that reported initial CK values with those reporting peak CK values. In addition, a predefined sensitivity analysis restricted to studies of earthquake related rhabdomyolysis was performed to assess the robustness of the pooled mean difference in earthquakes. Studies reporting adjusted odds ratios (OR) for the association between CK and AKI were also analyzed using the "meta" package.

For studies reporting predictive performance indicators (TP, FP, TN, FN), we used the "midas" package to estimate pooled sensitivity, specificity, and the area under the summary receiver operating characteristic curve (AUC), in addition to negative and positive likelihood ratios. Due to the limited number of available studies, predefined subgroup and sensitivity analyses were not conducted for predictive accuracy or OR. Considering the high heterogeneity among studies, random-effects models were used in the analyses. Galbraith plot was used to evaluate possible outliers. Publication bias was evaluated using the asymmetry funnel plot and Egger's test.

3. Results

3.1. Study selection flow and characteristics

The systematic search yielded 23506 records, and after duplicate removal, 12080 records were screened, from which 106 articles were retrieved for full-text review. Ultimately, 17 articles were included in this study (11-27) (Figure 1). Nine articles were on disaster (i.e., earthquake) victims (11-19), eight articles evaluated non-disaster patients (six articles evaluated trauma patients (20, 22, 23, 25-27), and two articles were performed on ultramarathon (21) and exertional rhabdomyolysis (24)). Eight articles evaluated initial CK (11-16, 21, 25), while nine evaluated peak CK (17-20, 22-24, 26, 27). One study was conducted in pediatric population (11). Overall, the 17 included articles encompassed 6410 rhabdomyolysis patients, of whom 1683 developed AKI (26.26%). Table 1 demonstrates the characteristics of the included articles.

Twelve articles reported mean values for CK in AKI and non-AKI patients, four articles reported adjusted OR values, and ten articles reported predictive accuracy measures (such as sensitivity and true/false positive).

3.2. Difference in CK Levels Between AKI and Non-AKI Patients

Twelve studies (12-17, 19, 21, 23-26) encompassing 3122 rhabdomyolysis patients (AKI: $n=966$, 30.94%) evaluated mean values for CK in AKI and non-AKI patients. The pooled analysis demonstrated that patients who developed AKI had markedly higher CK values than those without AKI, with a mean difference of 21770.75 (95% CI: 8987.39 to 34554.11) IU/L (Figure 2). The included studies demonstrated high statistical heterogeneity ($I^2 = 99.65\%$, $p < 0.001$). Subgroup analysis for initial CK (12, 13, 15, 16, 21, 25) (7 studies, $N=2030$ [AKI: $n=573$, 28.23%]) vs peak CK (17, 19, 23, 24, 26) (5 studies, $N=1092$ [AKI: $n=393$, 35.99%]) showed no statistically significant differences between subgroups ($p = 0.86$) (Figure 3a; considering that peak CK crosses 0, but initial CK doesn't). In a sensitivity analysis on studies investigating earthquake-related rhabdomyolysis (12-17, 19) (7 studies, $N=1856$ [AKI:

n=640, 34.48%]), CK values were also higher in AKI group compared to non-AKI group (35432.90, 95% CI: 20062.48 to 50803.33) (Figure 3b).

Four studies (11, 15, 19, 20) on 3549 patients (AKI: n=720, 20.29%) reported adjusted OR, and our analysis demonstrated a pooled OR of 7.62 (95% CI 2.80 to 20.76). Brown et al. (20) reported an OR of 2.4 (95% CI: 1.7 to 3.4) for prediction of AKI at a CK cutoff of 5,000 IU/L. Najafi et al. (15) reported an OR of 23.7 (95% CI: 3.6 to 156.6) at a cutoff of 15,000 IU/L, and Bakaloglu et al. (11) reported an OR of 11.61 (95% CI: 7.51 to 17.95) at a CK threshold of 20,950 IU/L. Turgutalp et al. (19) reported an OR of 10.44 (95% CI: 2.75 to 39.67) for each 50,000 U/L increase in CK level. Additionally, two articles reported unadjusted ORs equal to 7.94 (95% CI: 1.60 to 39.42) (13) and 9.87 (95% CI: 3.76 to 25.86) (12).

3.3. Predictive accuracy of CK levels for prediction of AKI

Ten articles (12, 13, 18-20, 22-25, 27) including 3421 patients (AKI: n=630, 18.42%) reported predictive accuracy measures. The pooled analysis (Figure 4) showed an AUC of 0.73 (95% CI: 0.69 to 0.77), with a sensitivity of 0.68 (95% CI: 0.55 to 0.78) and a specificity of 0.68 (95% CI: 0.54 to 0.78) for value of CK in prediction of AKI. Positive likelihood ratio was calculated as 2.1 (95% CI: 1.4 to 3.1) and negative likelihood ratio as 0.48 (95% CI: 0.32 to 0.70) (Figure 5).

3.4. Quality assessment

The included studies were evaluated for risk of bias and applicability across the domains of patient selection, index test, reference standard, and flow and timing. In patient selection, four studies were rated as unclear due to no mention of sampling method (12-14, 23), and two studies were rated as unclear due to not providing a clear definition for rhabdomyolysis (18, 26). In the domain of index test, seven studies with post-hoc cutoffs were evaluated as high in risk of bias (11-13, 19, 20, 23, 25). One study was rated as unclear in the reference standard domain due to the lack of a clear definition of AKI (18). Three studies were rated as unclear in flow and timing due to possible missing data (13, 20, 26). All studies were rated as low concern regarding their applicability (Table 2). Overall, studies were judged not to have a significant risk of bias.

3.5. Publication bias and certainty of evidence

No publication bias was found between the included studies ($p = 0.941$) (Figure 6). The included articles were observational studies, and accordingly, the base level of evidence was set at high (28, 29). The articles did not demonstrate any significant imprecision or indirectness. Given the high heterogeneity, the overall level of evidence was reduced by one and rated as moderate (Table 3).

4. Discussion

The results of our study demonstrate that serum CK levels were markedly higher among patients who developed AKI compared with those who did not, with a pooled mean difference of 21,770 IU/L. The pooled mean difference was even higher in earthquake related rhabdomyolysis patients (35432.90 IU/L). Across studies reporting adjusted OR, higher CK was associated with higher odds of AKI (pooled adjusted OR 7.62). CK had an overall fair AUC (0.73) with balanced sensitivity and specificity (both 0.68). Collectively, these results

further support CK as a marker of AKI risk stratification in traumatic rhabdomyolysis, while underscoring its limited performance as a sole marker of AKI risk. Trauma consensus guidance emphasizes that rhabdomyolysis ranges from asymptomatic enzyme elevations to life-threatening AKI and electrolyte derangements, and that CK is commonly used to monitor the muscle injury burden and trajectory in this context. Markedly elevated CK values should heighten vigilance for AKI and prompt renal protective care (30). However, CK is best positioned as a triage and prognostic enrichment tool, not a definitive predictor that can substitute for kidney function assessment (30, 31).

A notable finding in our analyses is the substantial mean difference in CK levels between the AKI and non-AKI groups. This between group difference was even more pronounced in earthquake related rhabdomyolysis studies, which could be due to prolonged continuous compression, delayed extraction, and delayed initiation of effective volume resuscitation. Our findings suggest that in traumatic rhabdomyolysis, and particularly in disaster and earthquake settings, only markedly elevated CK levels (e.g. rises exceeding 10000 IU/L) translate into clinically meaningful risk of AKI, whereas commonly cited lower thresholds such as 5000 IU/L may not adequately capture risk in these settings. These inferences should be interpreted cautiously, given the reported heterogeneity.

The building material (concrete vs mud brick) is also a credible driver of between disaster heterogeneity in crush severity and therefore CK distributions. Building construction influences collapse patterns and the formation of survivable void spaces, thereby affecting the intensity and duration of entrapment. More void spaces may remain after collapse of well-constructed reinforced concrete and steel buildings than in mud brick walls; the latter tend to compact and form fewer void spaces (32). This supports that building materials and code compliance can shift the observed CK-AKI relationship across earthquakes in various regions. Studies comparing renal disaster outcomes across events have emphasized that local circumstances (including structural and systems factors) affect renal casualty profiles and outcomes (32, 33).

Our moderate pooled predictive accuracy is also consistent with well-recognized limitations of CK as an indirect surrogate for the nephrotoxic burden. CK reflects muscle membrane disruption and enzyme release, whereas the proximate mediator of nephropathy is myoglobin; the relationship between these biomarkers is imperfect and time-dependent (23). Trauma consensus guidance highlights that the diagnosis and management of rhabdomyolysis depend on clinical context, serial evaluation, and electrolyte and renal monitoring rather than on any single laboratory threshold (30). In addition, CK is confounded by factors such as injury severity and systemic shock, variables that independently increase AKI risk through ischemic and inflammatory pathways. The practical implication is that CK should be interpreted as part of a multidimensional risk profile rather than as a stand-alone prognostic instrument. This perspective is consistent with the development of multi-variable risk tools for rhabdomyolysis outcomes (31).

4.1. Limitations

Our study has its limitations. Definitions of both rhabdomyolysis and AKI varied across studies, and studies applied a wide range of CK cut-offs, which contributes to the heterogeneity of our analysis. Additionally, the timing of sampling relative to injury and resuscitation was inconsistently reported. Etiologic

heterogeneity remained considerable even within traumatic rhabdomyolysis (earthquake crush, conventional blunt trauma, mixed ICU populations, exertional), and contextual factors (construction type, rescue delays, prehospital care) plausibly modify both CK levels and renal risk. Finally, disaster research is uniquely vulnerable to data-quality threats. The immediate post-disaster period is chaotic, and retrospective and even prospective data collected may be unreliable. Future work should focus on utilizing unified definitions for rhabdomyolysis and AKI, as well as evaluating the best cut-off value for CK. Additionally, standardizing measurement windows and reporting CK trajectories rather than single values would enrich findings.

5. Conclusions

Our findings indicate that, across traumatic rhabdomyolysis populations, higher serum CK is associated with increased risk of AKI, with a more pronounced elevation observed in earthquake related rhabdomyolysis; although with high heterogeneity. CK's standalone performance appears limited, with a fair AUC. Future studies should focus on utilizing unified definitions for rhabdomyolysis and AKI, as well as evaluating the best cut-off value for CK.

6. Declarations

6.1. Acknowledgments

None.

6.2. Conflict of interests

None.

6.3. Funding and supports

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6.4. Authors' contributions

Study design: SS, MY Data gathering: SR, KA, SD, NK Analysis: KA, MY Interpretation of results: SS, MY, KA Drafting and revising: all authors.

6.5. Ethical statement

This study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1402.383).

6.6. Informed consent

Not applicable.

6.7. Availability of supporting data

The gathered dataset is available from the corresponding author upon reasonable request.

6.8. Using artificial intelligence chatbots statement

ChatGPT (OpenAI) was used solely for the final refinement of the manuscript's language and readability. All output was critically reviewed and edited by the authors, who take full responsibility for the accuracy, integrity, and content of the manuscript.

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Table 1: Characteristics of included studies

First author, Year	Country	Study design	Disaster/ Non-disaster*	Sample size	Age#	AKI n (%)	Type of CK	Cutoff CK	AKI definition
Bakkaloglu, 2024 (11)	Turkey	POS	Disaster	675	NR	314 (46.52)	Initial	20950	Cr > 2x upper limit
Hu, 2012 (12)	China	ROS	Disaster	101	26.16 ± 21.43	42 (41.58)	Initial	14494.4	Cr > 2.0
Koroglu, 2024 (13)	Turkey	ROS	Disaster	33	28	19 (57.58)	Initial	14300	KDIGO
Kurt, 2024 (14)	Turkey	ROS	Disaster	377	33.51 ± 0.89	87 (25.82)	Initial	NR	KDIGO
Najafi, 2011 (15)	Iran	ROS	Disaster	638	NR	134 (21.00)	Initial	15000	Cr ≥ 1.6
Omrani, 2020 (16)	Iran	ROS	Disaster	54	39.59 ± 19.95	10 (18.52)	Initial	1656	Cr ≥ 1.6
Sever, 2001 (17)	Turkey	POS	Disaster	500	31.3	292 (58.4)	Peak	NR	Cr > 2.0
Sezer, 2024 (18)	Turkey	ROS	Disaster	37	NR	18 (48.65)	Peak	10000	NR
Turgutalp, 2024 (19)	Turkey	ROS	Disaster	153	NR	56 (36.60)	Peak	6967	Cr > 2.0
Brown, 2004 (20)	USA	ROS	Non-disaster	2083	37 ± 17	217 (10.42)	Peak	5000	Cr > 2.0
Hoffman, 2016 (21)	USA	ROS	Non-disaster	596	NR	196 (32.89)	Initial	NR	RIFLE
Nielsen, 2017 (22)	USA	ROS	Non-disaster	77	39 ± 17	24 (31.17)	Peak	10000	Cr > 2.0
Raju, 2017 (23)	India	POS	Non-disaster	90	34.21 ± 13.64	14 (15.55)	Peak	12388	AKIN
Sabouri, 2024 (24)	USA	ROS	Non-disaster	200	30.5 ± 8.5	17 (8.5)	Peak	40000	KDIGO
She, 2025 (25)	China	ROS	Non-disaster	231	43.82	85 (36.80)	Initial	4511	KDIGO
Skinner, 2017 (26)	South Africa	ROS	Non-disaster	149	NR	14 (9.40)	Peak	NR	KDIGO
Vasquez, 2020 (27)	USA	POS	Non-disaster	416	NR	144 (34.61)	Peak	5000	AKIN

*Disaster = Earthquake, Non-disaster = Trauma, Exertional, Ultramarathon. #Age reported as mean ± SD in years. Cr: Creatinine (mg/dl), CK: Creatine kinase, NR: Not reported, POS: Prospective observational study, ROS: Retrospective observational study.

Table 2. Risk of bias assessment

Study, year	Risk of Bias				Applicability			Overall
	Patient selection	Index test	Reference Standard	Flow and timing	Patient selection	Reference Standard	Outcome	
Bakkaloglu, 2024 (11)	Low	High	Low	Low	Low	Low	Low	Some concern
Hu, 2012 (12)	Unclear	High	Low	Low	Low	Low	Low	Some concern
Koroglu, 2024 (13)	Unclear	High	Low	Unclear	Low	Low	Low	Some concern
Kurt, 2024 (14)	Unclear	Low	Low	Low	Low	Low	Low	Some concern
Najafi, 2011 (15)	Low	Low	Low	Low	Low	Low	Low	Low
Omrani, 2020 (16)	Low	Low	Low	Low	Low	Low	Low	Low
Sever, 2001 (17)	Low	Low	Low	Low	Low	Low	Low	Low
Sezer, 2024 (18)	Unclear	Low	Unclear	Low	Low	Low	Low	Some concern
Turgutalp, 2024 (19)	Low	High	Low	Low	Low	Low	Low	Some concern
Brown, 2024 (20)	Low	High	Low	Unclear	Low	Low	Low	Some concern
Hoffman, 2016 (21)	Low	Low	Low	Low	Low	Low	Low	Low
Nielsen, 2017 (22)	Low	Low	Low	Low	Low	Low	Low	Low
Raju, 2017 (23)	Unclear	High	Low	Low	Low	Low	Low	Some concern
Sabouri, 2024 (24)	Low	Low	Low	Low	Low	Low	Low	Low
She, 2025 (25)	Low	High	Low	Low	Low	Low	Low	Some concern
Skinner, 2017 (26)	Unclear	Low	Low	Unclear	Low	Low	Low	Some concern
Vasques, 2020 (27)	Low	Low	Low	Low	Low	Low	Low	Low

Table 3: Summary of findings and certainty of evidence

Outcome	Studies, Sample size, Number of AKI	Calculated measures	Factors that may decrease certainty of evidence					Quality of evidence
			Risk of bias	Heterogeneity	Indirectness	Imprecision	Publication bias	
Mean CK in AKI and non-AKI rhabdomyolysis patients	12 studies N=3122 n AKI=966 (30.94%)	Mean difference: 21770.75 (8987.39 to 34554.11) IU/L	Not serious	Serious	Not serious	Not serious	None	Moderate
Risk association between CK and AKI	4 studies N=3549 n AKI=720 (20.29%)	Pooled adjusted OR: 7.62 (2.80 to 20.76)	Not serious	Serious	Not serious	Not serious	None	Moderate
Accuracy of CK in prediction of AKI	10 studies N=3421 n AKI=630 (18.42%)	AUC: 0.73 (0.69 to 0.77) Sensitivity: 0.68 (0.55 to 0.78) Specificity: 0.68 (0.54 to 0.78)	Not serious	Serious	Not serious	Not serious	None	Moderate

AKI: Acute Kidney Injury, AUC: Area under the summary receiver operating characteristic curve, CI: Confidence interval, CK: Creatine kinase, OR: Odds ratio.

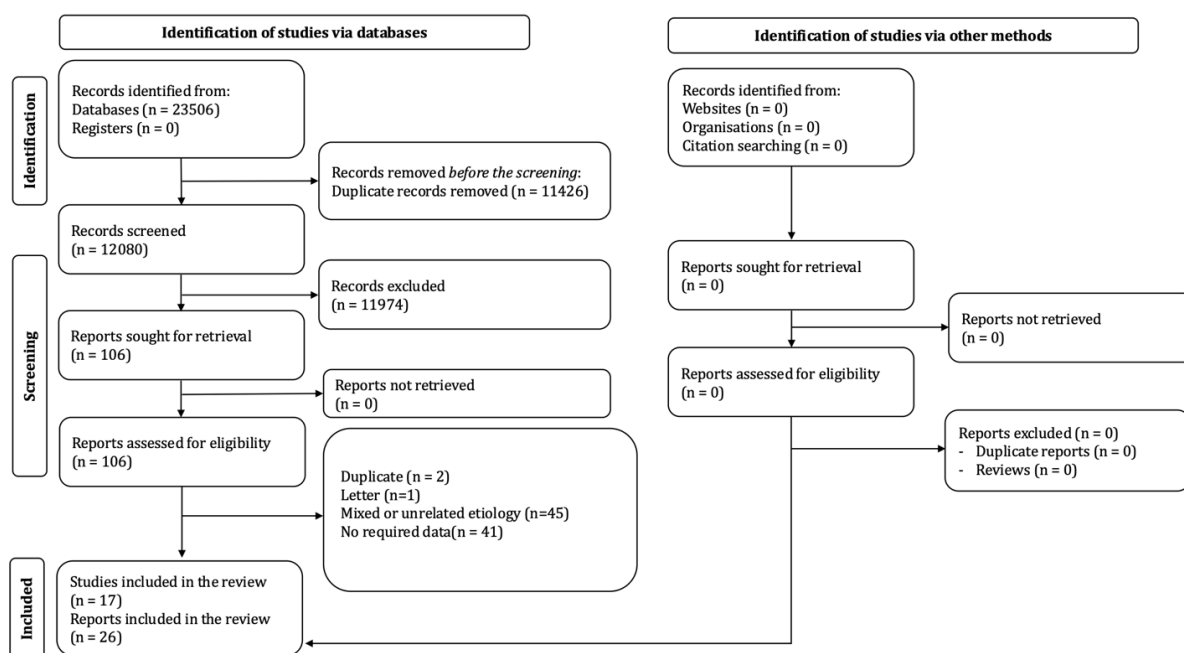


Figure 1. PRISMA flow diagram for article selection and inclusion.

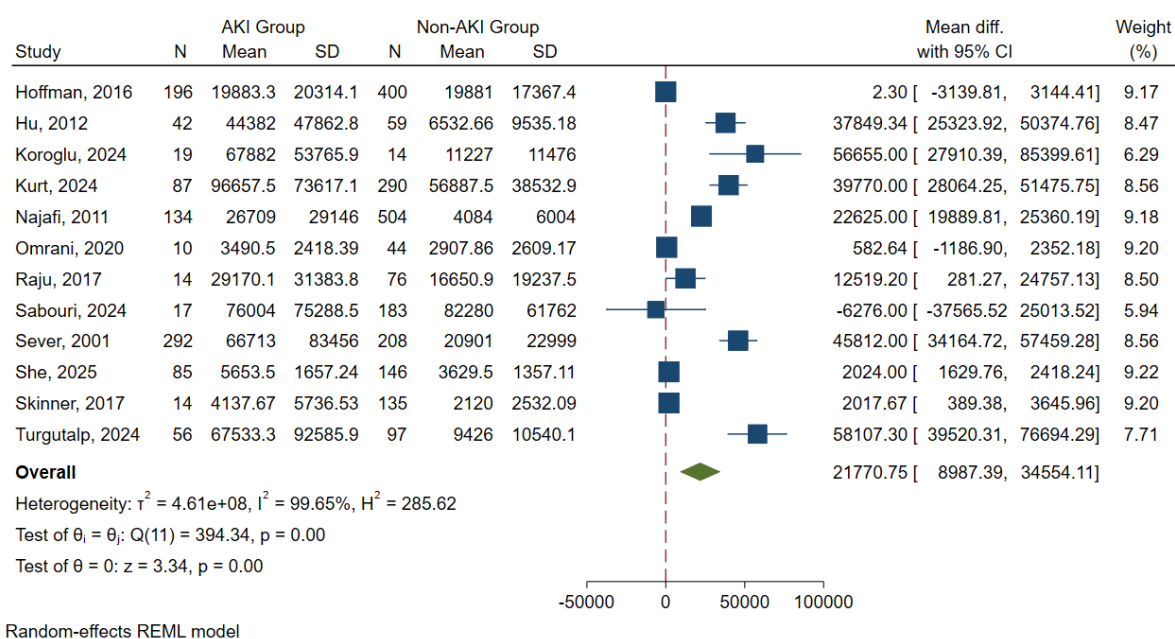


Figure 2: Forest plot for weighted mean differences between acute kidney injury and non-acute kidney injury groups in traumatic rhabdomyolysis patients.

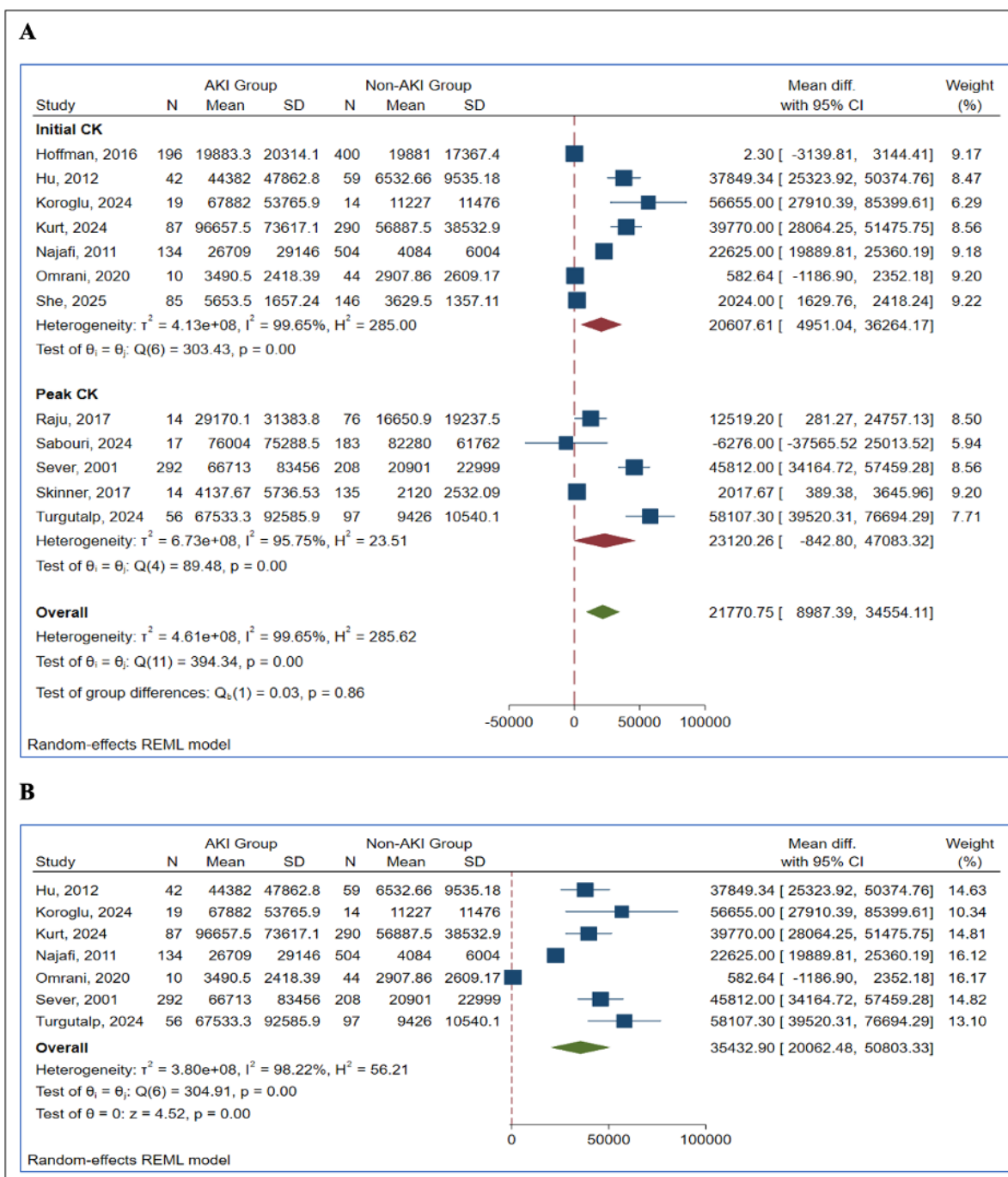


Figure 3: Forest plot for weighted mean differences between acute kidney injury and non-acute kidney injury groups in traumatic rhabdomyolysis patients for (a) studies with initial CK compared to peak CK and (b) studies performed on earthquake patients.

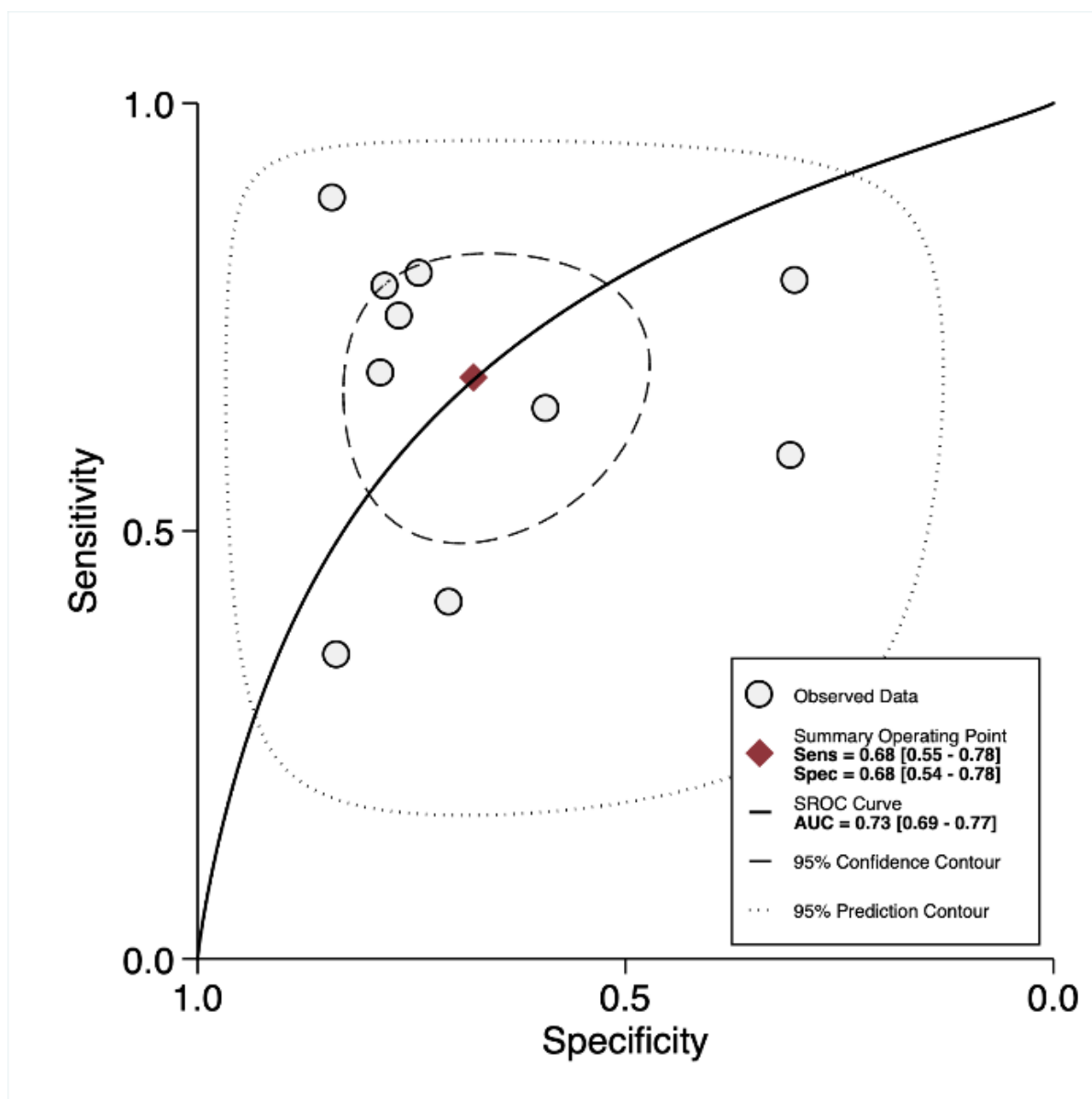
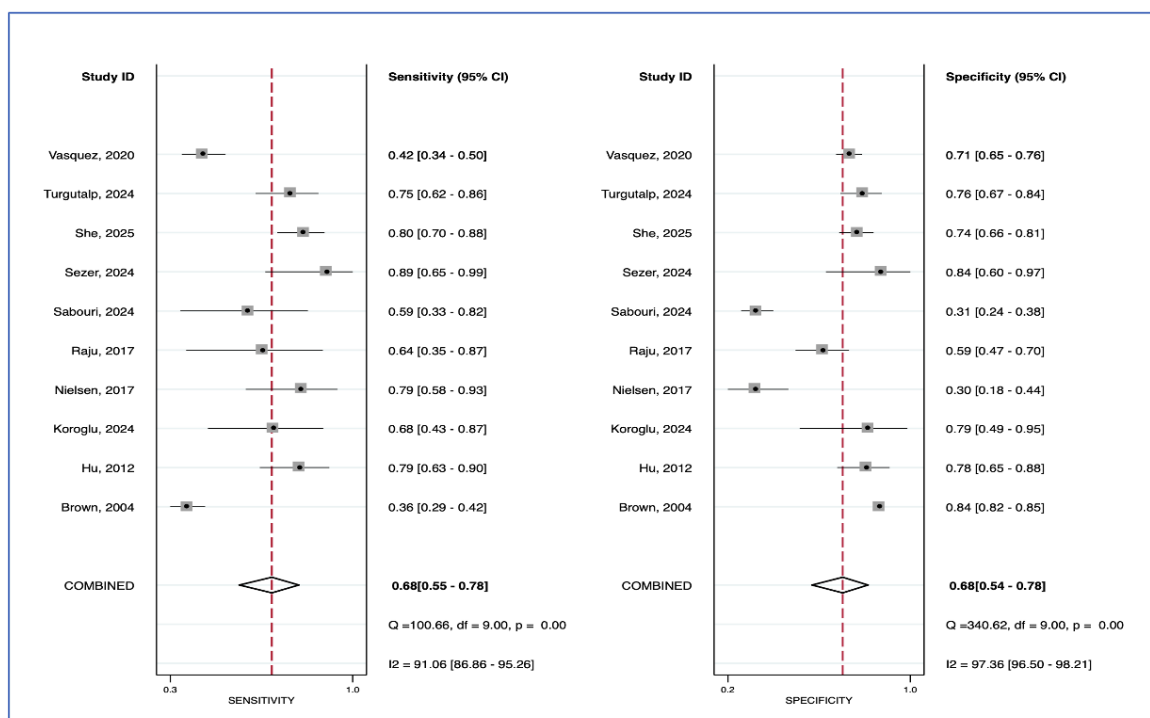


Figure 4: Receiver operating characteristics curve (AUC) for value of CK in prediction of acute kidney injury in traumatic rhabdomyolysis patients.

A



B

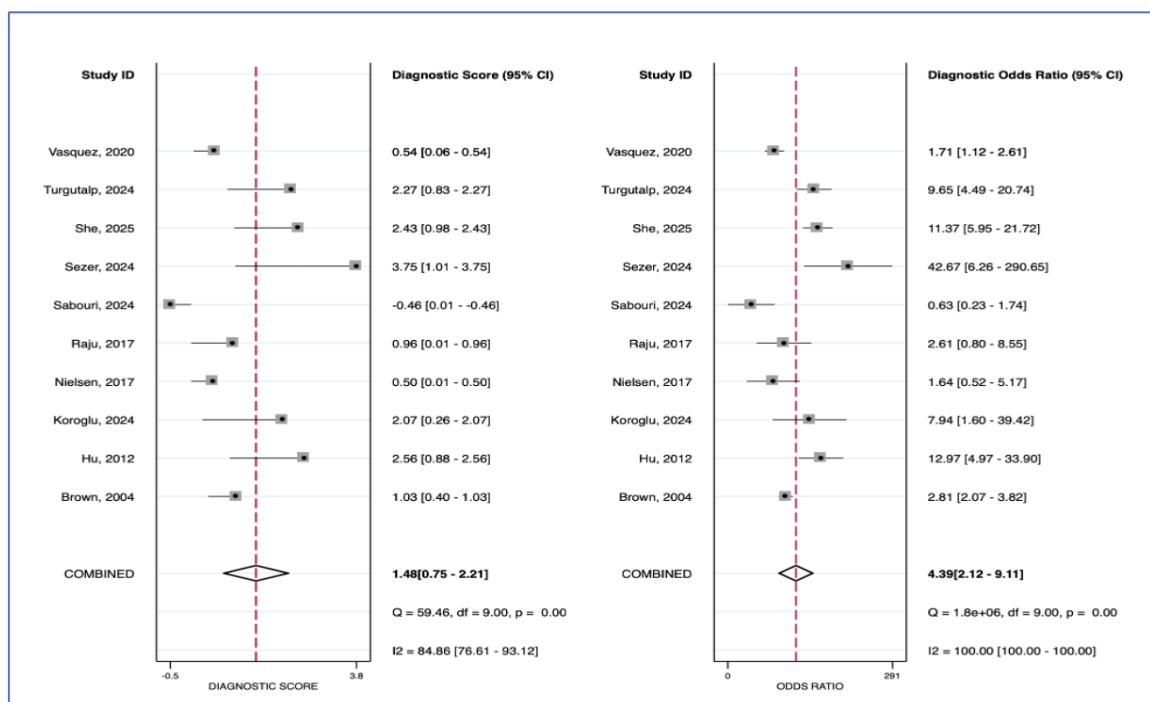


Figure 5: Performance indicators for value of CK in prediction of acute kidney injury in traumatic rhabdomyolysis patients.

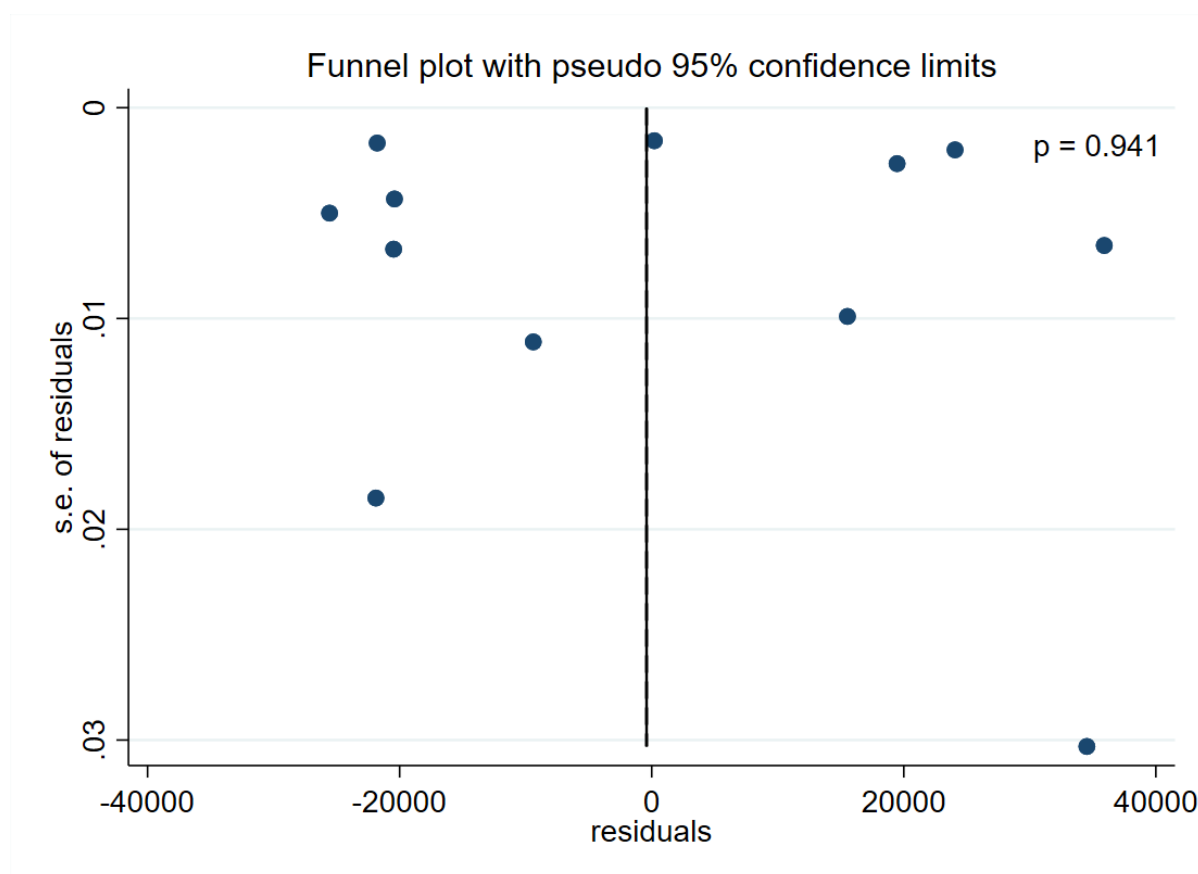


Figure 6: Publication bias for the included studies.