Systematic Review and Meta-Analysis

Medicine

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Magnetic resonance imaging for predicting delayed neurologic sequelae caused by carbon monoxide poisoning

A systematic review and meta-analysis

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Abstract

Background: This study summarized and analyzed the prognostic value of magnetic resonance imaging (MRI) for delayed neurologic sequelae (DNS) caused by carbon monoxide (CO) poisoning.

Methods: PubMed, China National Knowledge Infrastructure, and Wanfang Database were searched to identify relevant articles from their inception to October 30, 2022. The pooled sensitivity and specificity were estimated to investigate MRI for predicting DNS.

Results: 6 studies comprising 635 participants were identified as eligible for the present analysis. The pooled sensitivity and specificity of MRI were 0.72 (95% CI: 0.62–0.81) and 0.80 (95% CI: 0.71–0.86), respectively. The findings of sensitivity analyses proved that the overall results were robust, and no publication bias was detected (P = .49).

Conclusion: Based on current evidence, MRI may be useful in determining DNS caused by acute CO poisoning.

Abbreviations: CO = carbon monoxide, DNS = delayed neurologic sequelae, MRI = magnetic resonance imaging.

Keywords: carbon monoxide, delayed neurologic sequelae, magnetic resonance imaging, prognosis

1. Introduction

Carbon monoxide (CO) is a gaseous molecule that occurs ubiquitously in nature as the product of organic combustion processes. CO poisoning is attributed to the affinity of CO and hemoglobin that is 250 times higher than that of oxygen and hemoglobin[1] and the highly stable carboxyhemoglobin that is not easily dissociated, resulting in hypoxia of the whole body. Acute CO poisoning causes symptoms, such as headaches, dizziness, nausea, and vomiting. In severe cases, it may cause unconsciousness, respiratory arrest, and death.[2–5] Delayed neurologic sequelae (DNS) caused by acute CO intoxication poses considerable treatment challenges for clinical practitioners. It was estimated that up to 30% of patients result in DNS complications after acute CO poisoning despite aggressive treatment.[6–9]

DNS is pathologically characterized by the demyelination of white matter with cytotoxic edema.[10,11] Novel magnetic resonance imaging (MRI) sequences such as diffusion-weighted imaging and diffusion tensor imaging can objectively and quantitatively indicate the magnitude and directionality of water molecular diffusion in tissues.[11] Cerebral edema changes occur early with the subsequent demonstration of globus pallidus lesions and white matter changes. Although MRI for predicting the development of DNS have been studied, no consistent results have been identified. Hence, a comprehensive systematic review and meta-analysis were performed to determine prognostic value of MRI for predicting DNS caused by CO poisoning.

2. Methods

2.1. Study design

The current meta-analysis was based entirely on previous published guidance for the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement[12] and no original clinical raw data were collected or utilized, and thus, ethical approval was not sought for this study.

2.2. Literature search

A systematic search was performed in PubMed, China National Knowledge Infrastructure, and Wanfang Database to identify relevant articles that investigated the clinical predictive

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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methods of DNS caused by CO poisoning from their inception to October 30, 2022. The search strategy included: "carbon monoxide [Title]," magnetic resonance imaging [Title/abstract], "sensitivity" and "specificity"). Additionally, the reference lists of relevant reviews and the articles selected for inclusion were further manually searched.

2.3. Inclusion and exclusion criteria

All the included studies were selected if they met the following criteria: research evaluated clinical predictive methods and delayed neurologic sequelae; and sufficient data were available for calculating pooled sensitivity and specificity with their 95% confidence interval (CI).

The exclusion criteria included: conference papers, meta-analysis, or review; duplicated data; not present the usable data; animal experiments; and unavailable full-text.

2.4. Data extraction and quality assessment

According to the unified inclusion and exclusion criteria, after the preliminary screening of the literature, the data of the included literature were extracted independently by 2 researchers and cross-checked to determine data accuracy. Baseline data extracted included first author and publication time, region, study type, sample size, age, prevalence of DNS, sensitivity, and specificity.

The quality assessment of diagnostic accuracy studies-2 (QUADAS-2)[13] checklist was used to assess the methodological quality of the included studies as recommended by the Cochrane Collaboration.

2.5. Statistical analysis

The data were analyzed using Stata version 11.0 (Stata Corporation, College Station, TX). Tests with $P \leq .1$ or $I2 > 50\%$ indicated significant heterogeneity. If there was obvious heterogeneity among the studies, a fixed-effect model was applied for analysis. Otherwise, a random-effect model was used. Sensitivity analysis was conducted to test the robustness of pooled outcomes of these studies by removing an individual study in sequence. Publication bias was examined by funnel plots, and Egger tests were employed for evaluating the degree of asymmetry. *P*-value < .05 was considered significant.

3. Results

3.1. Literature search and selection

The retrieval process for eligible studies is summarized in Fig. 1. According to the search strategy, 142 potentially relevant studies in the electronic databases and initially 34 duplicated publications were excluded. After the title, abstract, and full text were reviewed, 38 publications did not focus on MRI for predicting DNS and 14 had no unavailable data. Finally, 6 studies[14–19] were included according to the study inclusion and exclusion criteria.

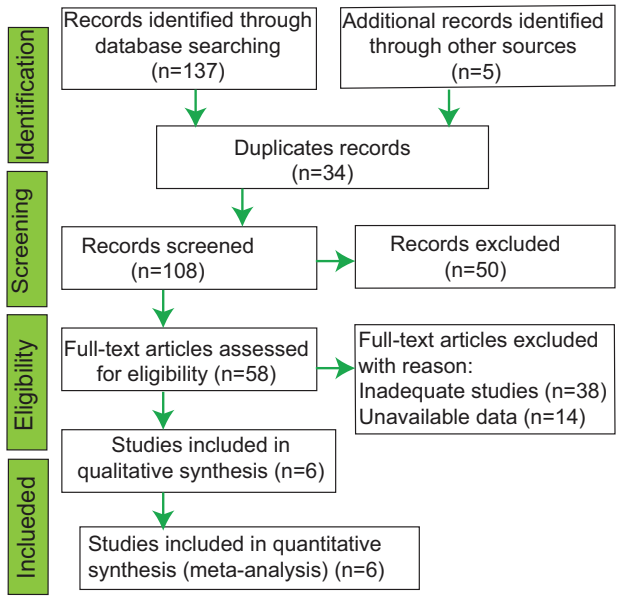

Figure 1. PRISMA flowchart of studies retrieved, screened, and selected for further analysis.

3.2. Characteristics of the included studies

The main information obtained from the included studies is shown in Table 1. All of the selected articles comprising 635 patients were published in English or Chinese with the posting time ranged from 2018 to 2021. All the studies were performed in Asia. Of these studies, 4 used diffusion-weighted imaging,[14–16,18] 1 used diffusion tensor imaging,[17] and 1 used diffusion kurtosis imaging.[19] The mean sample size of the studies was 106, ranging from 52 to 183. The total incidence of DNS was 32.6%.

3.3. Quality assessment

The quality assessment of the included studies is summarized in Fig. 2. With regard to patient selection, 4 (66.7%) patients were at a high or unclear risk of bias because they did not specify patient selection methodology (random or consecutive).[14,17–19] With regard to index text, 5 (83.3%) were at an unclear risk of bias with regard to the index text during blinding or not during sample analysis.[14,15,17–19] With regard to patient flow and time domains, 1 (66.7%) patients was at a high risk of bias, as not all selected patients received MRI.[14]

Table 1

Characteristics of the included studies.

Author (Yr)	Region	Design	Mean age	Male (%)	Method	Sample size	DNS (%)	Sensitivity (%)	Specificity (%)
Jeon 2018	Korea	Prospective	42.0 (32.0–56.0)	63.0	Diffusion-weighted imaging	104	73.1	0.752	0.902
Kim 2018	Korea	Retrospective	55.5 (36.8–69)	57.8	Diffusion-weighted imaging	102	9.80	0.700	0.804
Kokulu 2020	Turkey	Prospective	38.0 (28.0–53.0)	60.1	Diffusion-weighted imaging	183	29.5	0.722	0.868
Liu 2019	China	Retrospective	48.5 ± 15.6	45.4	Diffusion tensor imaging	119	26.1	0.487	0.842
Suzuki 2021	Japan	Retrospective	46 (35–61)	69.0	Diffusion-weighted imaging	52	42.3	0.790	0.710
Zhang 2020	China	Prospective	47.4 ± 9.70	49.3	Diffusion kurtosis imaging	75	28.6	0.818	0.604

Categorical variables are expressed as numbers (%) and continuous variables are expressed as means, means ± standard deviations or medians (interquartile ranges), as appropriate.
DNS = delayed neurologic sequelae.

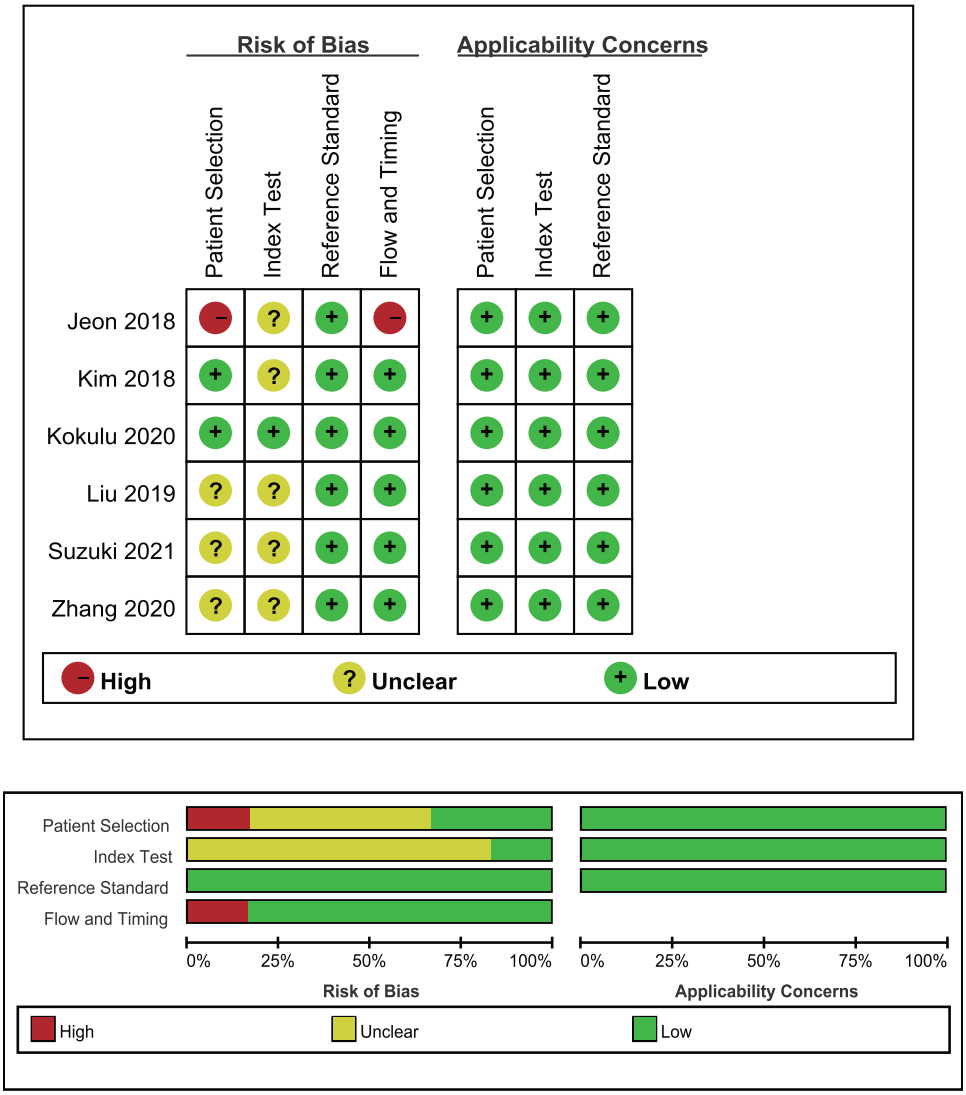

Figure 2. Summary of risk of bias and applicability concerns obtained from the QUADAS-2 tool for 6 studies included in meta-analysis. QUADAS-2 = quality assessment of diagnostic accuracy studies-2.

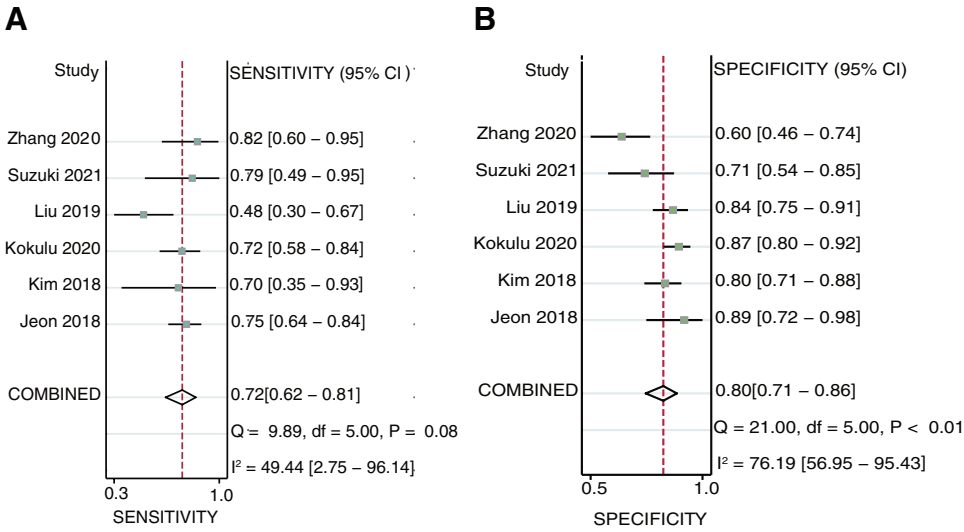

Figure 3. Forest plot of sensitivity and specificity of MRI for predicting DNS. (a) Sensitivity; (b) specificity. MRI = magnetic resonance imaging; DNS = delayed neurologic sequelae.

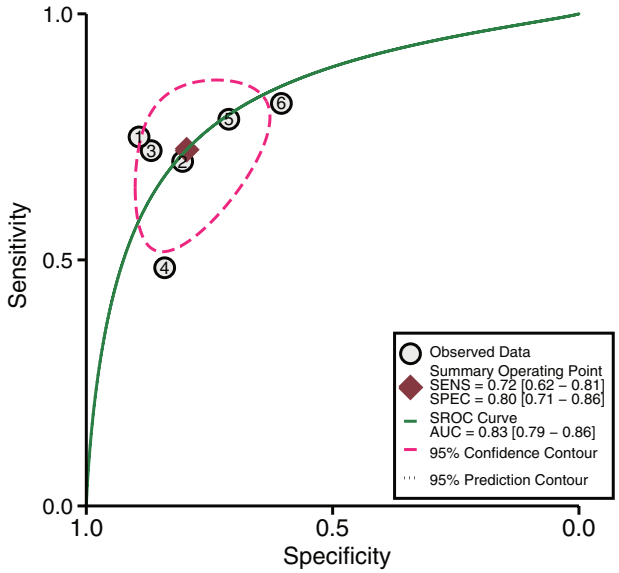

Figure 4. Summary receiver operating characteristic curve of MRI for predicting DNS. MRI: magnetic resonance imaging; DNS: delayed neurologic sequelae.

3.4. Main results

The meta-analysis demonstrated a pooled sensitivity of 0.72 (95% CI: 0.62–0.81, Fig. 3A) and a pooled specificity of 0.80 (95% CI: 0.71–0.86, Fig. 3B). Figure 4 shows the summary receiver operating characteristic curve, and the AUC was 0.83 (95% CI: 0.79–0.86).

3.5. Sensitivity analysis and publication bias

Sensitivity analyses were conducted to determine whether modifications in the inclusion criteria of the meta-analysis affected the results, and the result was stable (Fig. 5). Deeks' tests indicated no evidence of significant publication bias after assessing the funnel plot for the studies included in our meta-analysis (P = .49; Fig. 6).

4. Discussion

In general, DNS caused by acute CO poisoning is characterized by a difficult early diagnosis and poor prognosis. The majority of patients are at a high risk of progressive stage at the time of diagnosis, indicating that brain function was impaired, and a poor prognosis follows. Precise prognostic forecast of patients with acute CO poisoning is critical for making further management decisions. In this study, DNS developed in 29.2% of our patients, which is consistent with previous research[6,14,20] Our findings showed that the AUC of MRI for predicting DNS caused by CO poisoning was 0.83 (95% CI: 0.79–0.86), with 72% sensitivity and 80% specificity, which indicate that MRI is a good prediction method.

The diagnosis of DNS is primarily made on the basis of the clinical features and radiological findings of CT and conventional MRI. Higher CO exposure levels and longer-duration exposure are associated with more severe symptoms and a greater likelihood of developing DNS. Unfortunately, determining which patients will develop DNS in a clinical setting is difficult with the use of CO exposure levels and exposure duration due to inaccuracies in establishing the exact exposure duration and the CO level at the time of exposure. Initial GCS scores were lower in patients who developed poor neurological outcomes than in patients who developed good neurological outcomes. However, it is important to consider that CO-poisoned patients could have taken drugs and/or alcohol, which can also affect their level of consciousness. As such, diagnosis requires objective indicators.

Brain lesions caused by CO poisoning can be seen using MRI in both acute and chronic phases. The pathological features of acute phase are characterized by altered signal intensity areas involving the globus pallidus bilaterally, which display T1WI low signal and T2WI high signal[21–24] DWI and apparent diffusion coefficient maps usually reveal areas of restricted diffusivity in the globus pallidus, as for cytotoxic edema[25] Follow-up MRI revealed extensive involvement of the basal ganglion structures, which displayed diffuse hypodense areas as a result of extensive

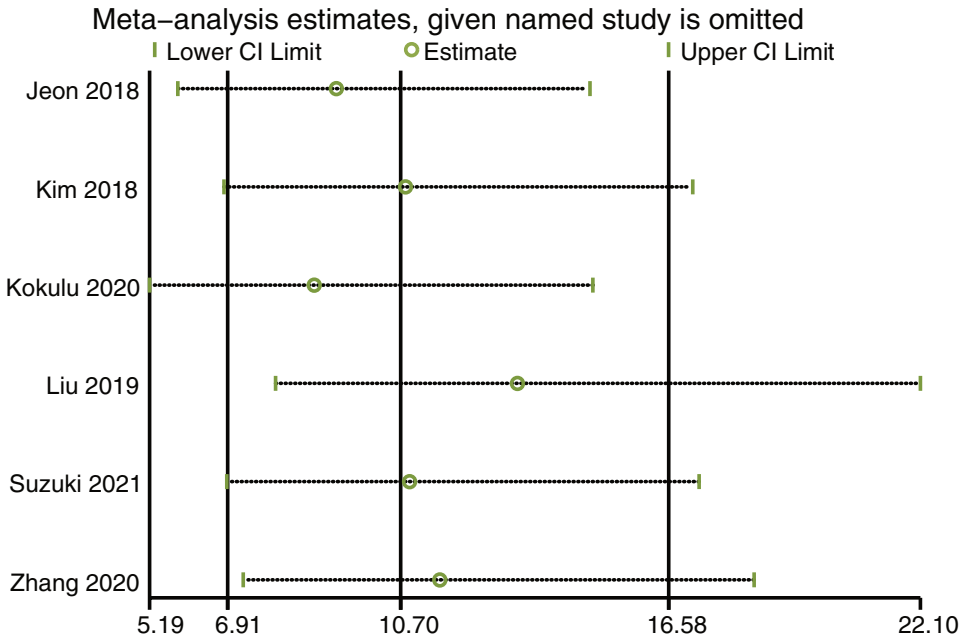

Figure 5. Sensitivity analysis of the association between MRI and DNS. MRI: magnetic resonance imaging; DNS: delayed neurologic sequelae.

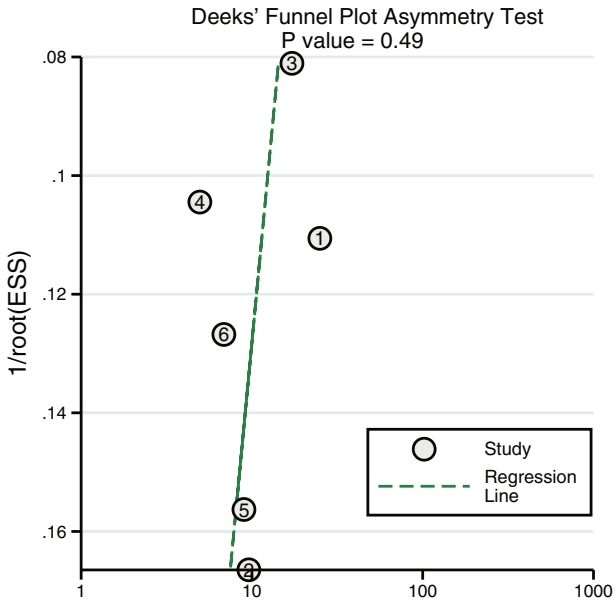

Figure 6. Deek's asymmetry plot showed no publication bias among the included studies.

demyelination. In more severe cases, these features can extend to involve the internal and external capsules, corpus callosum, and subcortical white matter.

To date, most investigations that used MRI have been focused on either diffusion-weighted imaging[14–16,18] or diffusion tensor imaging[17,26] as the sites of typical lesions after CO poisoning. However, pathological changes in the acute phase were too small to observe conventional MRI and diffusion-weighted imaging or diffusion tensor imaging in most patients. Novel MRI techniques are emerging, which enable doctors to detect subtle changes in cerebral tissue composition and cell metabolism. Xu et al demonstrated that the glutamate chemical exchange saturation transfer MRI non-invasively reflected the changes in glutamate content in the rat brain with higher sensitivity and spatial resolution and provided a pathogenetic and prognostic assessment of CO-associated encephalopathy.[27] Future studies would benefit from the use of latest technological developments to identify individuals at risk of dementia and new intervention strategies.

This meta-analysis has several limitations. Some signatures were designed to optimize sensitivity, while others were designed to optimize specificity. As such, bias may have been introduced in the pooled estimates of sensitivity and specificity in the meta-analysis. Our analysis might overestimate the prognostic significance of MRI to some degree due to the positive results reported in most of the included publications.

5. Conclusion

This systematic review and meta-analysis elucidated the prognostic value of MRI for DNS caused by carbon monoxide poisoning. The findings illustrate that MRI may serve as effective predictive tools for DNS. Future large-scale prospective and standard investigations should be conducted to confirm our results.

Author contributions

Conceptualization: Shun Yi Feng.
Software: Shun Yi Feng.
Writing – original draft: Shun Yi Feng.
Writing – review & editing: Shun Yi Feng.

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