

Background

Therapeutic hypothermia has been investigated as a promising intervention to improve outcomes in patients with acute neurotrauma, including traumatic brain injury (TBI)^{1,2}, ischemic stroke¹, and post-hemorrhagic conditions^{3,4}, due to its neuroprotective effects. However, conflicting evidence remains regarding its safety and efficacy across these neurological injuries. This review provides an updated synthesis of evidence, focusing on key clinical outcomes such as neurological recovery, complications, and mortality over a 6-month period.

Methodology

Search Strategy

Publications up to June 9, 2023, were searched in six databases, including Ovid MEDLINE, EMBASE, and the Cochrane Central Register for international studies, and KoreaMed, the Korean Medical Database, and the Korean Education and Research Information Service for South Korean research.

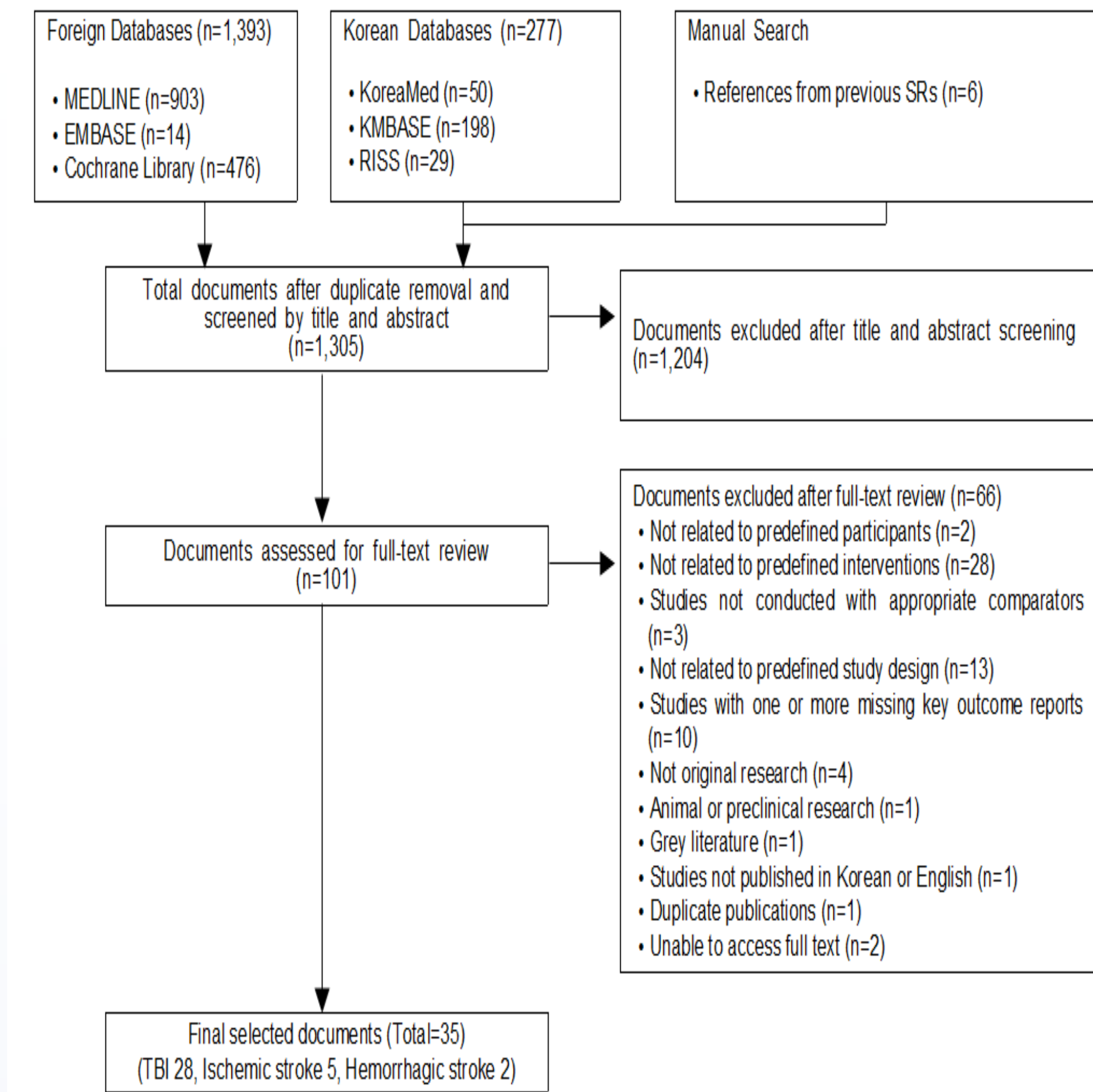
Study Inclusion

Only randomized controlled trials (RCTs) on therapeutic hypothermia in patients with TBI, ischemic stroke, or intracerebral hemorrhage, compared to normothermia, were included, with discrepancies resolved by consensus or third-party review.

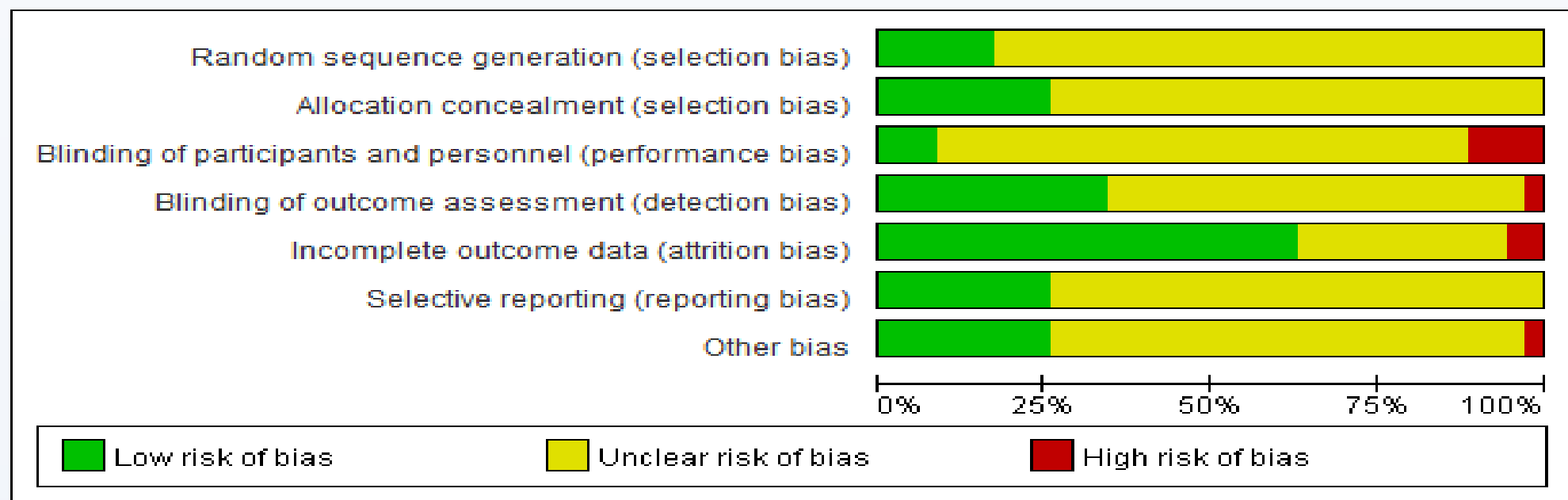
Bias Assessment and Data Synthesis

Bias was evaluated using the Cochrane Risk of Bias tool. Effect sizes were derived through the Mantel-Haenszel random-effects model as Relative Risk (RR), considering study heterogeneity. Heterogeneity was quantified using the I² statistic, with <50% indicating low and >75% high heterogeneity. Analyses were performed using RStudio 2022.12.0.

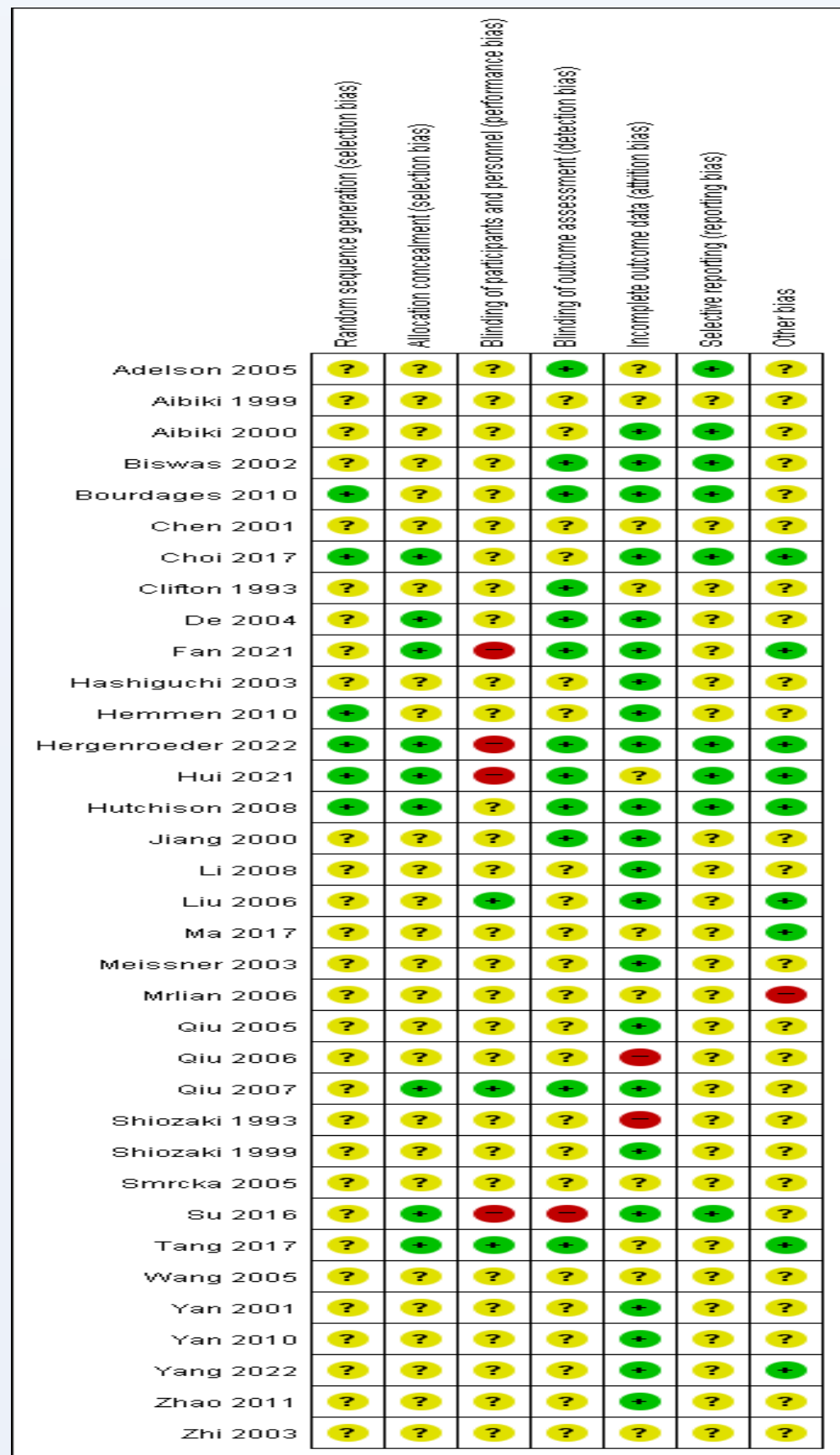
Key Findings



PRISMA Flowchart of Study Selection



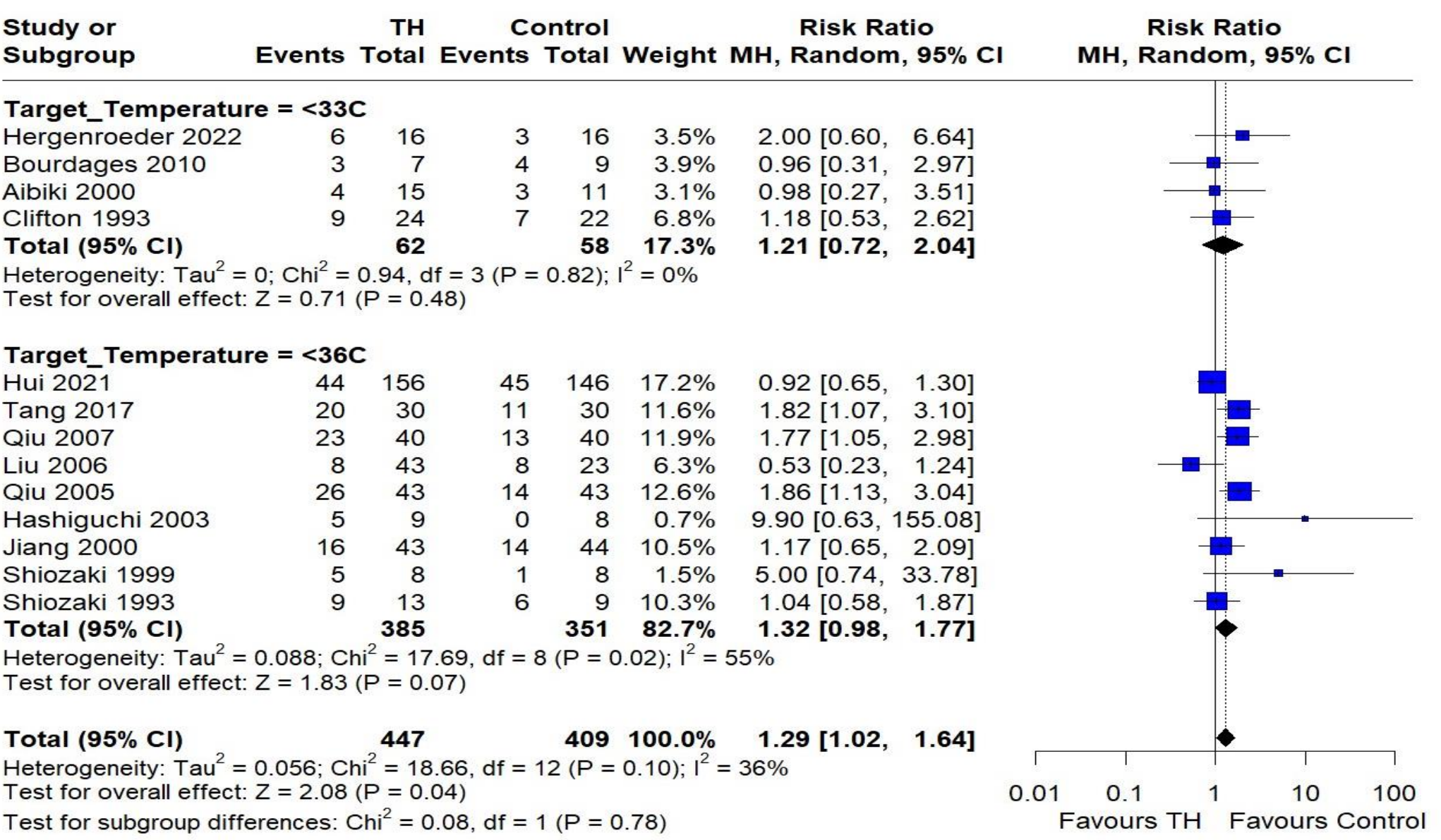
Risk of Bias (RoB) Assessment Graph



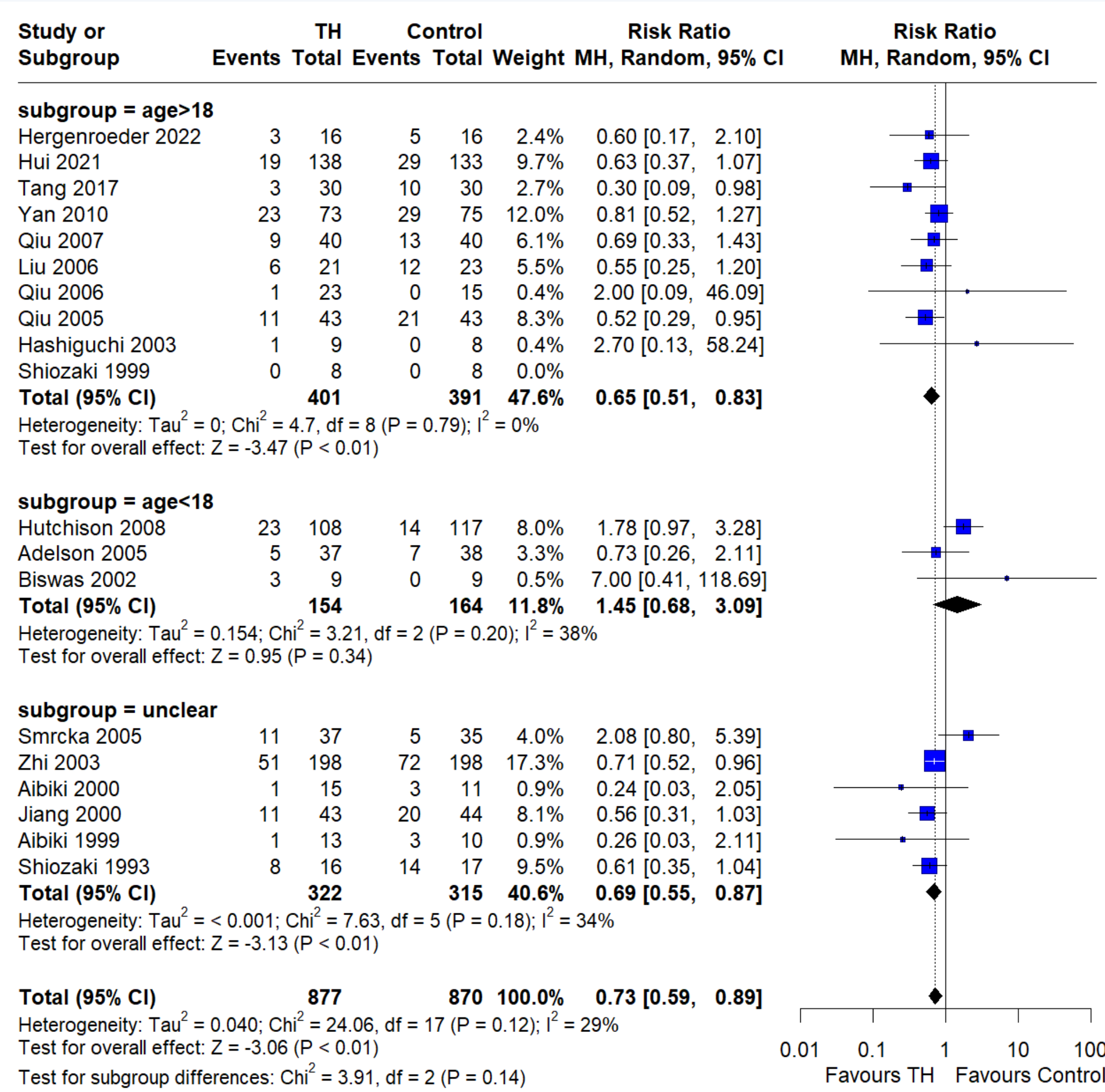
Summary Table of Results for RoB Assessment

Key Findings (Cont'd)

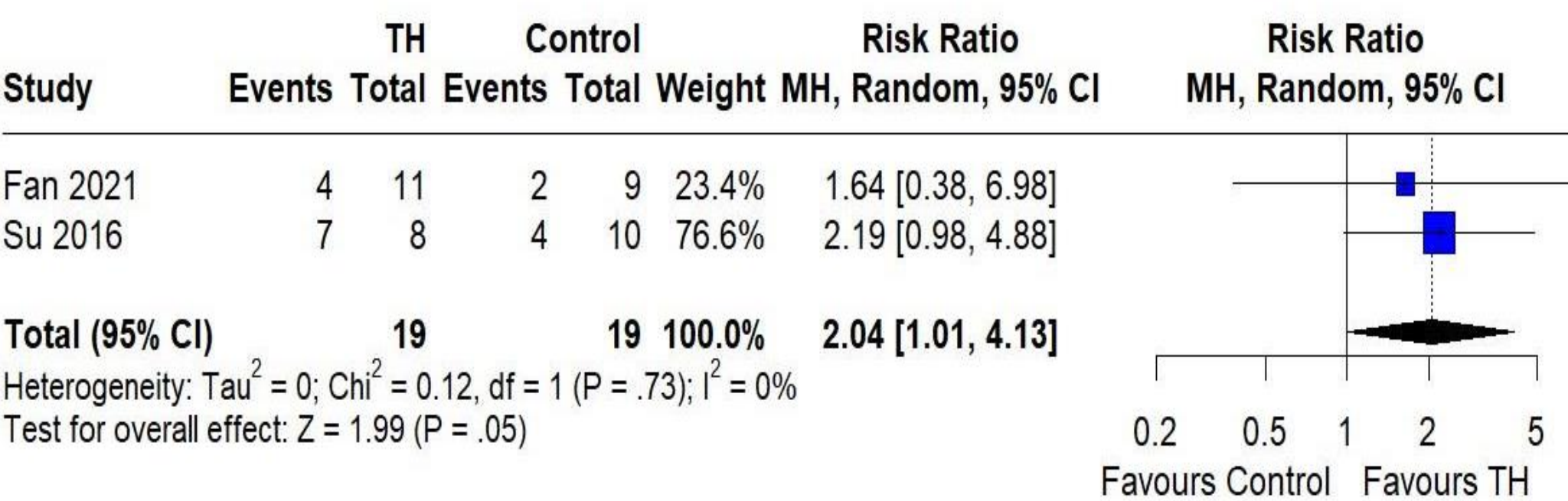
In our review of 35 studies with 2,639 patients, therapeutic hypothermia was associated with more complications such as pneumonia (RR 1.29, 95% CI 1.02-1.64; I²=36%), coagulopathy (RR 1.74, 95% CI 1.39-2.18; I²=18%), and electrolyte imbalances (RR 1.29, 95% CI 1.06-1.56; I²=23%) in TBI cases. However, it notably reduced mortality (RR 0.73, 95% CI 0.59-0.89; I²=29%) in TBI patients and improved neurological outcomes at 6 months in ischemic stroke cases (RR 2.04, 95% CI 1.01-4.13; I²=0%).



Pneumonia Incidence (%) in TBI Patients by Target Temperature, Forest Plot



Long-Term Mortality in TBI Patients by Age Group: 6-Month Follow-Up, Forest Plot



Long-Term Neurological Outcomes (mRS) in Acute Ischemic Stroke (AIS) Patients: 6-Month Follow-Up, Forest Plot

Takeaways

This study confirmed that therapeutic hypothermia significantly reduces mortality in traumatic brain injury (TBI) patients and improves neurological outcomes in ischemic stroke cases. Despite increased complications, the therapy showed clinical value in enhancing neurological function and survival among critically ill patients. Further research is needed to manage complications and refine cooling parameters. These findings highlight therapeutic hypothermia as a valuable option for severe brain injuries not responsive to standard treatments.

Citations

- Clifton GL, Coffey CS, Fourwinds S, Zygun D, Valadka A, Smith KR, et al. Early induction of hypothermia for evacuated intracranial hematomas: a post hoc analysis of two clinical trials. J Neurosurg. 2012;117(4):714-20.
- Erecinska M, Thoresen M, Silver IA. Effects of hypothermia on energy metabolism in mammalian central nervous system. J Cereb Blood Flow Metab. 2003;23(5):513-30.
- Zhao J, Mao Q, Qian Z, Zhu J, Qu Z, Wang C. Effect of mild hypothermia on expression of inflammatory factors in surrounding tissue after minimally invasive hematoma evacuation in the treatment of hypertensive intracerebral hemorrhage. Exp Ther Med. 2018;15(6):4906-10.
- Staykov D, Wagner I, Volbers B, Doerfler A, Schwab S, Kollmar R. Mild prolonged hypothermia for large intracerebral hemorrhage. Neurocrit Care. 2013;18:178-83.

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