

RANDOMISED CLINICAL TRIAL

Hydrogen inhalation after cardiac arrest

A clear summary of the HYBRID II multicentre, double-blind, placebo-controlled trial published in *EClinicalMedicine* (2023).

The question

Could adding 2% molecular hydrogen to oxygen during intensive post-cardiac-arrest care improve neurological recovery or survival at 90 days?

Study at a glance

73 adults

Aged 20-80, comatose after out-of-hospital cardiac arrest of presumed cardiac cause.

15 hospitals

Prospective study conducted in Japan from February 2017 to September 2021.

Hydrogen group (n=39)

Mechanically ventilated with titrated oxygen plus 2% H₂ for 18 hours.

Control group (n=34)

Mechanically ventilated with titrated oxygen and blinded control gas.

What everyone received

All participants received multidisciplinary post-arrest intensive care, including targeted temperature management. Hydrogen was studied as an adjunct within hospital critical care - not as a home treatment or a replacement for resuscitation, ventilation or standard care.

Primary outcome

Good neurological outcome at 90 days, defined as Cerebral Performance Category (CPC) 1 or 2.

MAIN FINDINGS

Promising secondary outcomes - but the primary endpoint was inconclusive

56% vs 39%**GOOD NEUROLOGICAL OUTCOME**H2 vs control; primary endpoint,
P=0.15 - not statistically significant.**85% vs 61%****SURVIVAL**H2 vs control; secondary outcome,
P=0.02.**46% vs 21%****NO SYMPTOMS (mRS 0)**H2 vs control; secondary outcome,
P=0.03.

How to read these results

Primary endpoint: not confirmed

The proportion with CPC 1-2 was numerically higher with hydrogen, but the difference could have arisen by chance under the study threshold (P=0.15). The trial therefore did not prove its prespecified primary efficacy outcome.

Secondary outcomes: encouraging signals

Survival, the overall modified Rankin Scale distribution and symptom-free recovery favoured hydrogen in this small trial. Secondary findings can generate strong research interest, but they require confirmation in an adequately powered trial.

Safety observations

Adverse events were common in both groups, as expected in critically ill post-cardiac-arrest patients. The independent safety committee judged that no adverse event or serious adverse event was directly attributable to the trial intervention. This finding applies to the controlled hospital protocol studied.

Bottom line from the numbers

The results support further research into inhaled hydrogen after cardiac arrest. They do not establish routine clinical effectiveness, and they should not be used to infer benefits from consumer hydrogen equipment.

EVIDENCE IN CONTEXT

What this trial can - and cannot - tell us

Why caution is essential

- **Stopped early**
COVID-19 enrolment restrictions ended the study before its planned sample size was reached, leaving only 73 randomised participants.
- **Low statistical power**
The authors calculated post-hoc power of 0.21 for the primary outcome, increasing the risk of missing a real difference.
- **Primary endpoint not significant**
The CPC 1-2 result did not meet the conventional statistical threshold. Positive secondary outcomes remain hypothesis-supporting rather than definitive.
- **Selected ICU population**
Participants were comatose adults after cardiogenic out-of-hospital cardiac arrest and were mechanically ventilated. Results cannot be generalised to other patients or settings.
- **Baseline imbalances**
With such a small sample, clinically relevant differences between groups may influence outcomes despite randomisation.

Balanced conclusion

HYBRID II produced encouraging survival and functional-recovery signals and found the hospital protocol feasible and not directly linked to adverse events. Because the trial was small, stopped early and missed its primary endpoint, larger confirmatory trials are needed before inhaled hydrogen could become established post-cardiac-arrest therapy.

Original study

Tamura T, Suzuki M, Homma K, Sano M, HYBRID II Study Group. Efficacy of inhaled hydrogen on neurological outcome following brain ischaemia during post-cardiac arrest care (HYBRID II). *EClinicalMedicine*. 2023;58:101907. DOI: 10.1016/j.eclinm.2023.101907.

[READ THE FULL STUDY](#)[PubMed PMID: 36969346](#) | [Open-access full text available](#)

MEDICAL NOTE

This educational summary is not medical advice. Cardiac arrest is an emergency; call emergency services immediately. Hydrogen inhalation is not established self-care and must never delay or replace evidence-based treatment.