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Aneurysmal subarachnoid hemorrhage: remote ischemic preconditioning to prevent delayed cerebral ischemia/vasospasm

Hemorragia subaracnoidea aneurismática: acondicionamiento isquémico remoto para prevenir isquemia cerebral retardada/vasoespasmo

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Aneurysmal subarachnoid hemorrhage (aSAH) remains one of the most biologically unstable conditions in vascular neurology. Even after aneurysm securing, the clinical course is often shaped by secondary injury rather than by the index hemorrhage alone [1]. Delayed cerebral ischemia (DCI) continues to account for a substantial proportion of preventable disability, and its pathogenesis extends beyond angiographic vasospasm to include microcirculatory dysfunction, inflammation, impaired autoregulation, endothelial injury, and reperfusion-related damage [2]. Current guideline-based care still relies heavily on nimodipine, which underscores how limited the therapeutic armamentarium remains once early aneurysm treatment has been achieved [3].

That therapeutic gap is precisely where remote ischemic conditioning (RIC) deserves renewed attention. The biological rationale is unusually compelling [4]. In cerebrovascular disease, RIC has been associated with multimodal protective signaling involving neural, humoral, endothelial, and immune pathways; in stroke more broadly, it has been explored as a low-cost strategy capable of modulating ischemia-reperfusion injury and vascular resilience [2]. Recent critical reviews suggest that the concept remains biologically credible, even if clinical translation has been uneven across indications [4].

In aSAH, the appeal of RIC is not difficult to understand. DCI is dynamic, delayed, and at least partly ischemia-driven, which makes a conditioning strategy conceptually attractive [2]. Early human studies established feasibility and safety. The phase Ib study by Koch et al. [5] found limb preconditioning to be safe and well tolerated in critically ill patients with subarachnoid hemorrhage. Subsequent pilot and cohort studies suggested potential signals in relation to vasospasm, DCI, stroke, or functional outcomes, but these studies were small and methodologically heterogeneous [5]. More importantly, they were not strong enough to settle the clinical question [5].

The more recent literature sharpens the issue rather than resolves it. A 2025 randomized, rater-masked trial by Albrecht et al. [6] did not show a significant reduction in symptomatic vasospasm, cerebral infarction, or in-hospital mortality with upper-limb remote ischemic preconditioning delivered for 10 days after aSAH. That negative result matters. It argues against simplistic enthusiasm. At the same time, it should not be read as the end of the field [6]. The intervention dose, timing, limb selection, target

population, and chosen surrogate endpoints remain unsettled, and these variables are not trivial in a conditioning therapy whose effect is likely to be context dependent [6].

That is why the ongoing trial landscape is more important than it may first appear. The REPAIR protocol, is a multicenter, randomized, double-blind, sham-controlled trial planning to enroll about 500 patients with aSAH within 72 hours of onset, using twice-daily lower-limb RIC for 7 days and 90-day functional outcome as the primary endpoint [7]. In parallel, a protocol is testing postoperative lower-limb RIC after microsurgical clipping in a smaller evaluator-blinded pilot trial, explicitly acknowledging that the evidence base remains insufficient and that safety, feasibility, and signal detection still need clarification in surgically treated patients [7].

What follows from this is a narrower but more defensible claim: RIC should not yet be framed as an established therapy for preventing DCI or vasospasm after aSAH, but neither should it be dismissed as another negative neurocritical care idea [7]. Its real promise lies in its profile: noninvasive, inexpensive, repeatable, and mechanistically broader than a pure anti-vasospasm intervention [7]. That distinction is central. If RIC works, it will probably do so not by abolishing vasospasm alone, but by modifying the broader ischemic vulnerability that links early brain injury, disturbed autoregulation, endothelial dysfunction, and delayed infarction [7].

The next phase of research should therefore be more precise. Trials should move beyond asking whether RIC prevents vasospasm and instead determine in whom, when, and with which protocol it meaningfully alters DCI-related injury [8]. Functional outcome will remain essential, but mechanistic endpoints, infarction burden, and subgroup analyses by treatment modality and baseline severity may be just as informative. Until those data mature, RIC in aSAH should be regarded as a serious investigational strategy, one with a stronger biological footing than many failed adjuncts, but not yet the evidentiary certainty required for routine adoption.

Conflicts of interest

The authors declare no conflict of interest.

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Data, Materials, and Code Availability

Not applicable.

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of the original draft, writing, revision and editing, approval of the final version. Juan Felipe Briceño Quevedo: conceptualization, research, writing of the original draft, writing, revision and editing, approval of the final version. Mario Andrés Severiche Martínez: conceptualization, research, writing of the original draft, writing, revision and editing, approval of the final version. Melissa Rivera Menjura: conceptualization, research, writing of the original draft, writing, revision and editing, approval of the final version.

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REFERENCES

1. Göttsche J, Piffko A, Pantel TF, Westphal M, Dührsen L, Czorlich P, et al. Aneurysm Location Affects Clinical Course and Mortality in Patients With Subarachnoid Hemorrhage. Front Neurol. 2022 Mar 14;13:846066. doi: 10.3389/fneur.2022.846066

2. Shah VA, Gonzalez LF, Suarez JI. Therapies for Delayed Cerebral Ischemia in Aneurysmal Subarachnoid Hemorrhage. Neurocrit Care. 2023 Aug;39(1):36-50. doi: 10.1007/s12028-023-01747-9

3. Hoh BL, Ko NU, Amin-Hanjani S, Chou SH-Y, Cruz-Flores S, Dangayach NS, et al. 2023 Guideline for the Management of Patients With Aneurysmal Subarachnoid Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2023 Jul;54(7):e314-e370. doi: 10.1161/STR.0000000000000436

4. Keevil H, Phillips BE, England TJ. Remote ischemic conditioning for stroke: A critical systematic review. Int J Stroke. 2024 Mar;19(3):271-279. doi: 10.1177/17474930231191082.

5. Koch S, Katsnelson M, Dong C, Perez-Pinzon M. Remote ischemic limb preconditioning after subarachnoid hemorrhage: a phase Ib study of safety and feasibility. Stroke. 2011 May;42(5):1387-91. doi: 10.1161/STROKEAHA.110.605840

6. Albrecht C, Silvestri T, Wostrack M, Maegerlein C, Janssen I, Martin J, et al. Remote Ischemic Preconditioning to Prevent Delayed Cerebral Ischemia Due to Vasospasm in the Treatment of Patients with Aneurysmal Subarachnoid Hemorrhage. Neurocrit Care. 2025 Dec;43(3):960-967. doi: 10.1007/s12028-025-02324-y

7. Jin T, Niu H, Liu L, Yin Y, Zhao W, Feng X, et al. Remote ischaemic conditioning for efficacy in patients with aneurysmal subarachnoid haemorrhage (REPAIR): protocol for a multicentre, randomised, double-blind, sham-controlled, parallel-group trial. BMJ Open. 2025 Aug 11;15(8):e101350. doi: 10.1136/bmjopen-2025-101350

8. Veldeman M, Rossmann T, Haeren R, Vossen LV, Weiss M, Conzen C, et al. Delayed Cerebral Infarction After Aneurysmal Subarachnoid Hemorrhage: Location, Distribution Patterns, Infarct Load, and Effect on Outcome. Neurology. 2024 Aug 13;103(3):e209607. doi: 10.1212/WNL.0000000000209607.