

Endovascular Rescue Therapy for Refractory Vasospasm: When and How?

Symptomatic vasospasm after subarachnoid hemorrhage is a common observation, with a considerable number of patients eventually failing conservative treatment (prophylactic nimodipine, induced hypertension). This subgroup of patients with refractory vasospasm remains particularly challenging¹ because critical hypoperfusion frequently culminates in delayed cerebral ischemia, cerebral infarction, and ultimately worsening of outcome. Consequently, clinical and experimental research effort focuses on timely detection of critical misery perfusion and identification of effective means to increase cerebral blood flow; on both issues, consensus is sparse and indications and technique of treatment remain a matter of individual experience and opinion.

The authors² present a retrospective analysis of 83 patients in whom endovascular rescue therapy (ERT) was initiated for refractory vasospasm in cases of neurologic or functional worsening (transcranial Doppler increase and MR/CT perfusion mismatch) despite maximal conservative treatment. ERT consisted of repeat, superselective bolus application of intra-arterial nimodipine (IAN) with or without concomitant percutaneous transarterial angioplasty (PTA). Patients were dichotomized according to the number of interventions performed (<3 interventions, ≥ 3 interventions); the central objective was a comparative analysis of safety and efficacy. The number of treatments, the number of vessels treated, and the need for PTA were associated with a higher risk of developing cerebral infarction. The risk of arterial dissection was significantly higher in patients requiring ≥ 3 ERTs. The complication rate for all other parameters, however, was comparable, and favorable functional outcome was observed in more than half of all patients, with no significant difference between the 2 treatment groups.

The study addresses an important aspect in the management of severely affected patients with SAH in whom conservative effort has been exhausted. Endovascular rescue therapies such as PTA or IAN represent treatment measures of last resort for refractory cerebral vasospasm³; in this context, recent studies were able to document improvement of cerebral oxygenation and metabolism after ERT.⁴⁻⁷ Unfortunately, a positive influence on outcome can only be assumed but not proved due to the vast heterogeneity of patients with SAH and the lack of a comparable control group

in which ERT is withheld. In view of this limitation but acknowledging the plausible hypothesis that functional improvement of oxygenation and metabolism is likely to contribute to better outcome, it is paramount to review and adhere to strict indications for ERT and to ensure a low periprocedural risk profile.

A detailed decision tree and escalating treatment—as implemented and followed by the authors—must be in place to identify and select those patients most likely to benefit from ERT. Angiographic narrowing of major cerebral vessels alone has been the basis for invasive spasmolytic treatment in the past, but the true hemodynamic relevance of angiographic findings within that compartment remains elusive. Without microcirculatory hypoperfusion, recently identified as a major contributor to territorial mismatch,⁸⁻¹⁰ treatment may not always be indicated and should not encourage possible accusations of overtreatment in patients who would have fared well regardless of any adjuvant treatment. Quantification of actual cerebral function, with CT or MR perfusion or continuous assessment of CBF, oxygenation (brain tissue oxygen), metabolism (lactate to pyruvate ratio on microdialysis), or electroencephalography/near-infrared spectroscopy are prerequisites for a selective, even restrictive but, at the same time, more substantiated implementation of ERT. Quantification of cerebral function should enable both timely detection of critical hypoperfusion and monitoring of treatment efficacy as a necessary next step to validate ERT and individually titrate the dose and duration of treatment.

The authors are commended for their expert performance and low overall complication rate. Indiscriminate application of ERT, no matter how expertly performed, inevitably increases the number of complications, possibly even negating any potential benefit on outcome. Even in the context of the refined treatment algorithm presented in this study, the rate of arterial dissection (16% in patients requiring ≥ 3 ERTs, clinically without relevant sequelae) is a sharp reminder of the causal relationship between the frequency of treatment and the complication rate.

On a different note, continuous intra-arterial infusion may provide additional advantages compared with repeat bolus application.¹¹ The need for daily, oftentimes hazardous transportation¹² into the radiology department is substantially reduced in

patients who, at that time, are at their most critical and are vulnerable to many (cardiopulmonary) complications. In view of the average number of ERTs required (2.5 for all patients, 4.3 for patients with ≥ 3 ERTs, selected patients with up to 7–10 ERTs) and the short duration of treatment (usually <6–12 hours),¹³ continuous IAN can be an alternative. Limiting the number of repeat catheterizations may also reduce the incidence of arterial dissection.^{5,11} However, local experience, particularly in view of the immobilization of patients, handling of continuous anticoagulation, and invasive neuromonitoring are essential. It is our own observation that with continuous IAN, the complication profile can be reduced dramatically, with regard to both thrombosis or periprocedural hemorrhage, on an intensified anticoagulation regimen and dissection from an indwelling microcatheter (Weiss et al, unpublished data).

The authors are commended for adding valuable evidence for the feasibility of vigorous endovascular therapy; the present study convincingly demonstrates that when necessary, ERT can be escalated and that good outcome can be achieved, even in prolonged cases of refractory vasospasm.

The conclusion perfectly summarizes the *raison d'être* for ERT as an aggressive but effective last resort strategy to support patients when everything else has failed. Future studies will need to identify those patients most likely to benefit from ERT and to tailor treatment to the lowest possible risk with the highest efficacy.

REFERENCES

1. Francoeur CL, Mayer SA. **Management of delayed cerebral ischemia after subarachnoid hemorrhage.** *Crit Care* 2016;20:277 CrossRef Medline
2. Adereggen L, Beck J, Z'Graggen WJ, et al. **Feasibility and safety of repeated instant endovascular interventions in patients suffering from refractory cerebral vasospasms.** *AJNR Am J Neuroradiol* 2016 Dec 15. [Epub ahead of print] CrossRef Medline
3. Durrant JC, Hinson HE. **Rescue therapy for refractory vasospasm**

4. **after subarachnoid hemorrhage.** *Curr Neurol Neurosci Rep* 2015;15:521 CrossRef Medline
4. Pierot L, Aggour M, Moret J. **Vasospasm after aneurysmal subarachnoid hemorrhage: recent advances in endovascular management.** *Curr Opin Crit Care* 2010;16:110–16 CrossRef Medline
5. Bele S, Proescholdt MA, Hochreiter A, et al. **Continuous intra-arterial nimodipine infusion in patients with severe refractory cerebral vasospasm after aneurysmal subarachnoid hemorrhage: a feasibility study and outcome results.** *Acta Neurochir (Wien)* 2015;157:2041–50 CrossRef Medline
6. Jestaedt L, Pham M, Bartsch AJ, et al. **The impact of balloon angioplasty on the evolution of vasospasm-related infarction after aneurysmal subarachnoid hemorrhage.** *Neurosurgery* 2008;62:610–17; discussion 610–17 CrossRef Medline
7. Albanna W, Weiss M, Mueller M, et al. **Endovascular rescue therapies for refractory vasospasm after subarachnoid hemorrhage: a prospective evaluation study using multimodal, continuous event neuromonitoring.** *Neurosurgery*. In press
8. Terpolilli NA, Brem C, Bühler D, et al. **Are we barking up the wrong vessels? Cerebral microcirculation after subarachnoid hemorrhage.** *Stroke* 2015;46:3014–19 CrossRef Medline
9. Wagner M, Steinbeis P, Güresir E, et al. **Beyond delayed cerebral vasospasm: infarct patterns in patients with subarachnoid hemorrhage.** *Clin Neuroradiol* 2013;23:87–95 CrossRef Medline
10. Schubert GA, Seiz M, Hegewald AA, et al. **Acute hypoperfusion immediately after subarachnoid hemorrhage: a xenon contrast-enhanced CT study.** *J Neurotrauma* 2009;26:2225–31 CrossRef Medline
11. Musahl C, Henkes H, Vajda Z, et al. **Continuous local intra-arterial nimodipine administration in severe symptomatic vasospasm after subarachnoid hemorrhage.** *Neurosurgery* 2011;68:1541–47; discussion 1547 CrossRef Medline
12. Papon JP, Russell KL, Taylor DM. **Unexpected events during the intrahospital transport of critically ill patients.** *Acad Emerg Med* 2007;14:574–77 CrossRef Medline
13. Liu JK, Couldwell WT. **Intra-arterial papaverine infusions for the treatment of cerebral vasospasm induced by aneurysmal subarachnoid hemorrhage.** *Neurocrit Care* 2005;2:124–32 CrossRef Medline

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