Invasive neuromonitoring with an extended definition of delayed cerebral ischemia is associated with improved outcome after poor-grade subarachnoid hemorrhage

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OBJECTIVE The current definition of delayed cerebral ischemia (DCI) is based on clinical characteristics precluding its use in patients with poor-grade subarachnoid hemorrhage (SAH). Additional concepts to evaluate the unconscious patient are required. Invasive neuromonitoring (INM) may allow timely detection of metabolic and oxygenation crises before irreversible damage has occurred.

METHODS The authors present a cohort analysis of all consecutive SAH patients referred to a single tertiary care center between 2010 and 2018. The cohort (n = 190) was split into two groups: one before (n = 96) and one after (n = 94) the introduction of INM in 2014. A total of 55 poor-grade SAH patients were prospectively monitored using parenchymal oxygen saturation measurement and cerebral microdialysis. The primary outcome was the Glasgow Outcome Scale–Extended (GOSE) score after 12 months.

RESULTS With neuromonitoring, the first DCI event was detected earlier (mean 2.2 days, p = 0.002). The overall rate of DCI-related infarctions decreased significantly (from 44.8% to 22.3%; p = 0.001) after the introduction of invasive monitoring. After 12 months, a higher rate of favorable outcome was observed in the post-INM group, compared to the pre-INM group (53.8% vs 39.8%), with a significant difference in the GOSE score distribution (OR 4.86, 95% CI –1.17 to –0.07, p = 0.028).

CONCLUSIONS In this cohort analysis of poor-grade SAH patients, the introduction of INM and the extension of the classic DCI definition toward a functional dimension resulted in an earlier detection and treatment of DCI events. This led to an overall decrease in DCI-related infarctions and an improvement in outcome.

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KEYWORDS subarachnoid hemorrhage; invasive neuromonitoring; brain tissue oxygen saturation; cerebral microdialysis; delayed cerebral ischemia; vascular disorders

ANEURYSMAL subarachnoid hemorrhage (SAH) is a devastating disease with persistent high morbidity and mortality rates. Due to its high incidence in young patients, SAH carries a socioeconomic burden comparable to that of ischemic stroke.¹ Patients surviving the initial hemorrhage remain susceptible to further ischemic damage for up to 3 weeks. Ischemic complications occurring in this phase have been coined as delayed cerebral ischemia (DCI). The occurrence of DCI and DCI-related infarctions is the main contributor to SAH mortality and

morbidity.² Angiographic large-vessel cerebral vasospasm was historically considered to be the sole cause of DCI.³ Vasospasm, however, occurs in about two-thirds of SAH patients, of whom only half will develop actual DCI. The remaining half will remain asymptomatic without the development of infarctions despite considerable vessel narrowing. These observations are congruous with results from large randomized trials such as the CONSCIOUS trials in which effective reversal of vasospasm did not result in superior outcome. Conversely, nimodipine im-

ABBREVIATIONS CLINA = continuous local intraarterial nimodipine application; CMD = cerebral microdialysis; DCI = delayed cerebral ischemia; GOSE = Glasgow Outcome Scale–Extended; H&H = Hunt and Hess; iHTN = induced euvoletic arterial hypertension; INM = invasive neuromonitoring; p_tO₂ = brain tissue oxygenation; SAH = subarachnoid hemorrhage.

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proves clinical outcome with only a limited effect on angiographic vasospasm.^{4,5} Furthermore, cerebral infarction correlates with the territory of angiographic vasospasm in only 25%–81% of SAH cases.^{6,7} Additional vascular or tissue-specific mechanisms need to be involved either by reduced oxygen/energy deliverance or increasing demand. Possible explanations for reduced ischemic tolerance have been investigated in animal research and include failure of cerebral autoregulation, cortical spreading depolarization, microvascular spasms, and formation of microthrombi.^{8–11}

DCI has been defined as the occurrence of focal neurological impairment or a decrease in consciousness.¹² This definition is based on clinical characteristics and therefore only applicable to neurologically evaluable patients. This largely precludes its use in poor-grade SAH patients who are at the highest risk for ischemic complications.¹³ Sequential imaging such as CT perfusion imaging allows for a snapshot of brain perfusion, aiding in the diagnosis of DCI. Despite recent advancements, radiation exposure remains high.¹⁴ Also, the need for transportation of critically ill patients and the risk of delayed diagnosis of impending ischemia underline the need for other monitoring techniques.

Invasive neuromonitoring (INM) allows for live, bedside assessment of brain oxygenation and metabolism. Brain tissue oxygenation ($p_{ti}O_2$) monitoring is strongly recommended for patients at risk of cerebral ischemia or hypoxia. Cerebral microdialysis (CMD) is recommended as an add-on to other monitoring modalities in SAH patients.¹⁵

In 2014, INM consisting of $p_{ti}O_2$ and CMD was introduced into our institutional treatment algorithm. In the context of endovascular rescue strategies, we were able to show that INM is a valuable tool to measure treatment efficacy.^{16,17} The purpose of this observational trial was to assess the impact of INM on the detection rate of DCI and its influence on patient outcome.

Methods

Patient Population and Study Design

This trial was designed as a cohort analysis from 2010 to 2018 in which we compare patients before (pre-INM) and after (post-INM) introduction of INM in 2014. All patients admitted to our institution with confirmed aneurysmal SAH in the respective time frame were screened for eligibility. We included all poor-grade SAH patients (Hunt and Hess [H&H] grades 3–5) who were between 18 and 90 years of age. The H&H scale was preferred over the World Federation of Neurosurgical Societies scale due to its easiness in use, as no steps are required to establish the grade. To correct for postictal reduced consciousness, grading was allocated as the best clinical grade within 24 hours after admission. Patients were excluded in cases of relevant angiographic vasospasm upon admission, admittance more than 5 days after the ictus, or early death (< 7 days postictus). Also excluded were patients with mycotic or trauma-induced pseudoaneurysms and aneurysms associated with arteriovenous malformations.

This observational trial was retrospectively registered at the ISRCTN registry (reference no. 16523175) on July

25, 2019 (<https://doi.org/10.1186/ISRCTN16523175>). The prospective data collection was registered on May 20, 2014, at ClinicalTrials.gov (NCT02142166).

The trial was conducted in accordance with the recommendations of the ethics committee of the medical faculty of RWTH Aachen University. Informed consent was obtained from all prospectively included patients.

Standard Treatment Algorithm

Our SAH treatment protocol has been published previously^{16,17} (Fig. 1). In brief, after establishing the diagnosis of the hemorrhage, aneurysms were secured within 48 hours via surgical clipping or endovascular coiling. All patients were monitored in our neurointensive care unit. Failing an initial wake-up test, poor-grade patients underwent INM probe placement. Contraindications were coagulation disorders and predictable early death (brainstem damage on imaging or bilateral fixed pupils). Brain tissue oxygen probes (NEUROVENT PTO, RAUMEDIC) and CMD catheters (71 High Cut-Off Brain Microdialysis Catheter, μ dialysis) were placed unilaterally on the side of the ruptured aneurysm or, in cases of midline aneurysms, on the side with higher subarachnoid blood load. To yield information from two vascular territories (middle and anterior cerebral arteries), probes were placed in the frontal watershed region, 4.5 cm lateral to the midline in front of the coronal suture.

The occurrence of DCI was determined based on two diagnostic entities: classic or functional DCI.

Classic DCI

The criteria set by Vergouwen et al. were used to define classic DCI as a new focal neurological deficit or a decrease in Glasgow Coma Scale score ≥ 2 for at least 1 hour, not ascribable to alternative diagnoses.¹²

Functional DCI

Perfusion CT scanning was used in the pre-INM group for functional DCI assessment in unconscious patients. In the post-INM group, its use was confined to the evaluation of refractory DCI and DCI treatment surveillance. DCI was defined as a perfusion deficit with typical territorial cerebral blood flow/mean transit time mismatch.

Upon implementation of INM, the definition of DCI was extended to include oxygenation crises ($p_{ti}O_2 < 10$ mm Hg) or metabolic derangements (lactate/pyruvate ratio ≥ 40). After diagnosis, first-tier treatment was started, consisting of induced euvolemic arterial hypertension (iHTN; ≥ 180 mm Hg) by means of intravenous noradrenaline.

Cases refractory to iHTN were reevaluated by perfusion CT imaging. With persistent perfusion mismatch, second-tier endovascular rescue therapy was considered after interdisciplinary consensus. Transluminal balloon angioplasty was used in cases of proximal vasoconstriction and intraarterial spasmolysis in cases of diffuse vasospasm. Continuous local intraarterial nimodipine application (CLINA) was reserved as a third-/last-tier rescue therapy. Microcatheters (Excelsior SL-10, Stryker Neurovascular) were advanced into the internal carotid artery or vertebral artery. CLINA-treated patients received weight-adapted

FIG. 1. Differences in the diagnostic algorithm but identical treatment algorithm between the pre-INM and post-INM groups. In the post-INM group, the additional functional dimension of DCI (oxygenation crises or metabolic derangement) was introduced. Functional DCI, in addition to a perfusion deficit (radiological), was defined by an oxygenation crisis ($p_iO_2 < 10$ mm Hg) or metabolic derangement (lactate/pyruvate ratio ≥ 40) as measured by the INM probes. DSA = digital subtraction angiography; ERT = endovascular rescue therapy; i.a. = intraarterial; RR_{syst} = systolic blood pressure; TCD = transcranial Doppler.

intravenous tirofiban (Aggrastat, Correio Pharma) and remained sedated until catheter removal. Independent of the ongoing treatment tier, therapy was reevaluated daily and de-escalated as soon as possible. The de-escalation process was guided by imaging in the pre-INM group and by imaging and INM in the post-INM group.

Outcome

The primary outcome measure was the Glasgow Outcome Scale–Extended (GOSE) score at 12 months after ictus.¹⁸ The GOSE score was dichotomized into unfavorable outcome (GOSE scores 1–4) and favorable outcome (GOSE scores 5–8). In the pre-INM group, outcome data were collected prospectively during regular follow-up visits. Missing information was appended either by analysis of patient files or by a structured telephone interview conducted by a blinded assessor.¹⁹ In the pre-INM group, the GOSE score at 12 months had to be reconstructed retrospectively by investigation of patient files or by contacting the patient, his or her next of kin, or caregiver by telephone in a structured interview.

The secondary outcomes were the following: GOSE score at discharge and at 6 months, death, lag between ic-

tus and first treatment-triggering DCI event (days), number of CT investigations performed during the DCI time frame, prevalence of silent infarctions (i.e., the occurrence of a demarcated infarction as the first sign of ongoing DCI), rate of overall DCI-related infarctions, and DCI-related mortality.

Statistical Analysis

In the dichotomous outcome analysis, the GOSE data were compared between groups using chi-square testing. Nondichotomized data were tested with an ordinal logistic regression model. The GOSE score was collapsed to a 6-point ordinal scale in which death and vegetative state, as well as lower and upper good recovery, were combined. In both analyses, the modified Fisher scale, H&H grade, and DCI occurrence were added as predictor covariates. Sliding dichotomy was not considered due to its additional stratification based on expected prognosis, increasing the risk of information bias.²⁰ All data are presented as means and standard deviations for normally distributed continuous variables and as medians and interquartile ranges for nonnormally distributed continuous variables. Categorical variables are depicted as frequencies and proportions.

FIG. 2. Flowchart of patient recruitment.

After normality testing via plotting and the Shapiro-Wilk test, the appropriate statistical test was selected. For nominal data, the chi-square test was used; for normally distributed continuous data, the unpaired t-test was used; and for nonnormally distributed data, the Mann-Whitney U-test was used. Missing outcome data were not imputed. All statistical analyses were performed using IBM SPSS Statistics version 25 (IBM Corp.). Statistical significance was defined as a two-sided $p < 0.05$.

Results

Patients

A total of 341 consecutive patients with aneurysmal SAH were admitted to our department between January 2010 and December 2018. Due to early, not DCI-related, deaths (death in < 7 days), 22 patients were excluded. Of the remaining 319 patients, 190 were clinically classified as having an SAH that was H&H grade 3 or higher. Ninety-six patients meeting the inclusion criteria were admitted before (pre-INM) and 94 patients after (post-INM) invasive monitoring became available (Fig. 2). Baseline characteristics of the two study groups, summarized in Table 1, were comparable, with a nonsignificant larger proportion of modified Fisher grade 3 hemorrhages in the post-INM group of 58 patients (61.7%) versus 44 patients in the pre-INM group (45.8%; $p = 0.068$). Additional variables were analyzed and are available in Supplementary Table 1. In the critical phase (days 7–14), 45 patients (46.9%) in the pre-INM group were neurologically assessable, compared to 47 patients (50.0%) in the post-INM group. INM was implemented in 55 patients (58.8%). Forty-four patients (46.8%) received dual monitoring (p_{iO_2} and CMD). INM was begun, on average, 2.0 ± 2.5 days after hemorrhage. The treatment algorithm for DCI remained unchanged from 2010 to 2018. In the pre-INM group, 51 patients (53.1%) were treated with iHTN versus 56 (59.6%) in the

post-INM group ($p = 0.370$). Endovascular rescue treatment was applied in 23 patients in the pre-INM group (24.0%) versus 29 patients (30.9%) in the post-INM group ($p = 0.266$).

Complications

A nonsignificant trend toward a higher rate of CSF infections was observed in the post-INM group (20.2% vs 11.5%; $p = 0.098$). No probes had to be removed due to signs of infection at the site of entry. A total of 10 hemorrhages were observed after probe implantation. Nine of the hemorrhages consisted of small bleeds along the trajectory of the probe. Operative evacuation was required in a single case. All of the hemorrhagic complications occurred under dual antiplatelet therapy after complicated or stent-assisted endovascular coiling. None resulted in permanent neurological deficits.

Primary Outcome Parameter

Twelve months after hemorrhage, a higher rate of favorable outcome was observed in the post-INM group compared to that of the pre-INM group (53.8% vs 39.8%), with more patients in upper moderate disability (15.4% vs 6.8%) and lower good recovery (14.3% vs 8.0%) categories (Table 2 and Fig. 3). The binary logistic regression model of dichotomized data showed a trend toward better outcome for patients in the post-INM group (OR 0.60, 95% CI 0.33–1.09, $p = 0.094$). Ordinal logistic regression analysis (with modified Fisher grade, H&H score, and DCI occurrence as predictor covariates) demonstrated a significant difference in the GOSE score distribution (OR 4.86, 95% CI -1.17 to -0.07 , $p = 0.028$).

Secondary Outcome Parameters

At discharge, the GOSE score distribution showed that a favorable outcome was achieved in 38% of patients in the post-INM group compared to 25% in the pre-INM group (OR 0.08, 95% CI -0.44 to 0.59 , $p = 0.776$). The GOSE distribution after 6 months is available in Supplementary Table 2. The overall mortality rate, as well as the overall incidence of DCI, remained unchanged after INM implementation. However, in the post-INM group, the first treatment-triggering DCI event was detected on average 2.2 days earlier compared to any event in the pre-INM group ($p = 0.002$). The rate of silent infarction decreased significantly from 33.3% to 12.8% ($p = 0.001$) after introduction of INM, as did the overall rate of DCI-related infarction (from 44.8% to 22.3%; $p = 0.001$). The DCI-caused mortality rate did not differ significantly between the groups (10.6% vs 14.6%; $p = 0.265$). As a secondary effect, the need for CT imaging during clinical decision-making was reduced from on average 8.4 to 6.8 images per patient ($p = 0.038$), resulting in a reduction in radiation exposure in the post-INM group.

Discussion

In SAH patients, the occurrence of DCI and DCI-related infarction is directly correlated with clinical outcome.²¹ The current definition of delayed cerebral ische-

TABLE 1. Baseline characteristics in 190 patients with poor-grade SAH

Characteristic	Pre-INM (n = 96)	Post-INM (n = 94)	p Value
Mean age in yrs (range)	53.9 ± 12.2 (19–86)	56.5 ± 12.2 (32–87)	0.146
Female/male ratio	73:23	70:24	0.802
Risk factor			
Hypertension	39 (40.6%)	41 (43.6%)	0.676
Smoking	27 (28.1%)	30 (31.9%)	0.569
BMI in kg/m ² (± SD)	26 ± 4.5	26 ± 5.0	0.499
Aneurysm diameter max in mm (± SD)	7.6 ± 3.8	7.2 ± 4.7	0.564
H&H			0.068
Grade 3	44 (45.8%)	58 (61.7%)	
Grade 4	34 (35.4%)	20 (21.3%)	
Grade 5	18 (18.8%)	16 (17%)	
Aneurysm location			0.183
MCA	36 (37.5%)	31 (33.0%)	
ACoMA	24 (25.0%)	26 (27.7%)	
ICA	15 (15.6%)	11 (11.7%)	
PCoMA & AChA	9 (9.4%)	9 (9.6%)	
BA	5 (5.2%)	3 (3.2%)	
Others	7 (7.3%)	14 (14.9%)	
Anterior circulation	77 (80.2%)	73 (77.7%)	
Posterior circulation	19 (19.8%)	21 (22.3%)	
Clipping/coiling	49/47	45/48	
Modified Fisher scale			0.068
Grade 1	8 (8.3%)	11 (11.7%)	
Grade 2	9 (9.4%)	11 (11.7%)	
Grade 3	43 (44.8%)	20 (21.3%)	
Grade 4	35 (36.5%)	52 (55.3%)	
DCI surveillance			
Neurologically assessable (days 4–14)	45 (46.9%)	47 (50.0%)	0.667
INM	None	55 (58.8%)	
P _t O ₂	None	54 (57.4%)	
CMD	None	44 (46.8%)	

AChA = anterior choroidal artery; ACoMA = anterior communicating artery; BA = basilar artery; BMI = body mass index; ICA = internal carotid artery; MCA = middle cerebral artery; PCoMA = posterior communicating artery.
Values are presented as the number (%) of patients unless otherwise specified.

mia is solely based on clinical characteristics, precluding its use in poor-grade SAH patients. Additional concepts to evaluate the unconscious patient are therefore required. In a previous retrospective cohort analysis, we showed that INM is a powerful monitoring tool during endovascular DCI treatment.¹⁶ In this current two-group cohort analysis, the implementation of INM and the accompanying broadening of the classic DCI definition were associated with earlier detection of treatable DCI events. This resulted in earlier initiation of DCI treatment. Earlier treatment in the adequately selected patient resulted in a reduction of infarctions. This, in turn, translated into a higher rate of long-term favorable outcome in the post-INM group. At discharge, this difference is not yet apparent. However, a higher rate of upper and lower severe disability in the post-INM group was observed. These are patients with the rehabilitation potential of reaching a favorable out-

come (e.g., lower and upper moderate disability) after 12 months. Analysis of the dichotomized data confirmed this trend, and the ordinal regression model of GOSE score distribution after 12 months demonstrated significant differences between the groups. In a subgroup analysis, it became clear that patients with H&H grade 3 hemorrhages benefited the most from INM application because they are at high risk of DCI development and have the most to lose.

As fewer CT scans were obtained in patients who underwent invasive monitoring, we believe that the technique can help to safely reduce the rate of imaging and thus exposure to ionizing radiation and potentially hazardous patient transports.²²

Because treatment approaches to DCI vary among centers, our results cannot be readily extrapolated. Apart from prophylactic oral nimodipine, not a single treatment has been proven to be beneficial in a randomized trial on

TABLE 2. Overview of results

Outcome	Pre-INM (n = 96)	Post-INM (n = 94)	p Value
DCI diagnostics			
DCI incidence	55 (57.3%)	60 (63.8%)	0.357
Median lag 1st DCI event in days ($\pm$ SD)	7.5 $\pm$ 5.3	5.3 $\pm$ 2.9	0.002
Silent infarction	32 (33.3%)	12 (12.8%)	0.001
DCI-related infarction	43 (44.8%)	21 (22.3%)	0.001
Overall mortality	20 (20.8%)	19 (20.2%)	0.916
DCI-related deaths	14 (14.6%)	10 (10.6%)	0.265
DCI treatment			
iHTN	51 (53.1%)	56 (59.6%)	0.370
ERT	23 (24.0%)	29 (30.9%)	0.266
Angioplasty	15 (15.6%)	10 (10.6%)	
Spasmolysis	32 (33.3%)	34 (36.2%)	
Patients w/ multiple ERTs	14 (14.6%)	15 (16.0%)	
Total no. of ERTs	39	45	
	Pre-INM (n = 96)	Post-INM (n = 94)	
Discharge GOSE result			0.776
Death	21 (21.9%)	19 (20.2%)	
Vegetative state	9 (9.4%)	11 (11.7%)	
Lower severe disability	31 (31.3%)	36 (38.3%)	
Upper severe disability	19 (19.8%)	10 (10.6%)	
Lower moderate disability	12 (12.5%)	10 (10.6%)	
Upper moderate disability	4 (4.2%)	6 (6.4%)	
Lower good recovery	0 (0.0%)	2 (2.1%)	
Upper good recovery	0 (0.0%)	0 (0.0%)	
Median score (IQR)	3 (2–4)	3 (2–4)	
Favorable outcome, scores 5–8	16 (25%)	18 (38%)	0.559
	Pre-INM (n = 88)	Post-INM (n = 91)	
12-mo GOSE result			0.028
Death	25 (28.4%)	22 (24.2%)	
Vegetative state	7 (8.0%)	5 (5.5%)	
Lower severe disability	8 (9.1%)	6 (6.6%)	
Upper severe disability	13 (14.8%)	9 (9.9%)	
Lower moderate disability	17 (19.3%)	15 (16.5%)	
Upper moderate disability	6 (6.8%)	14 (15.4%)	
Lower good recovery	7 (8.0%)	13 (14.3%)	
Upper good recovery	5 (5.7%)	7 (7.7%)	
Median score (IQR)	4 (1–5)	5 (2–6)	
Favorable outcome, scores 5–8	35 (39.8%)	49 (53.8%)	0.094

ERT = endovascular rescue therapy.

Values are presented as the number (%) of patients unless otherwise specified. Boldface type indicates statistical significance. The GOSE outcome categories are defined as follows: 1 = death; 2 = vegetative state (unable to obey commands); 3 = lower severe disability (dependent on others for care); 4 = upper severe disability (independent at home); 5 = lower moderate disability (independent at home and outside the home but with some physical or mental disability); 6 = upper moderate disability (independent at home and outside the home but with some physical or mental disability, with less disruption than lower moderate disability); 7 = lower good recovery (able to resume normal activities with some injury-related problems); 8 = upper good recovery (no problems).

FIG. 3. Stacked bar chart of GOSE results after 12 months in the pre-INM and post-INM groups.

outcome in SAH patients. The HIMALAIA study has questioned the use of induced hypertension but was terminated due to a lack of recruitment. The application of euvoletic hypertension remains largely based on observational data.²³ With this in mind, there is still no class I evidence to support our current practice. The evidence for endovascular rescue treatment is even more scarce and mostly based on case series. We have shown in the past that endovascular rescue therapy can be safe and effective in highly selected patients.¹⁷ The evaluation of long-term clinical outcome will be the topic of future analyses. The improvement of diagnostic abilities is only as valuable as the efficacy of the treatment approaches used. Nevertheless, with our treatment algorithm itself remaining unchanged between groups, the improvement in the detection rate of DCI and in outcome can be appreciated and attributed to the change in monitoring.

Treatment guidance with invasive monitoring has three main potential pitfalls: the limited spatial resolution of local information, the problem of a cutoff value, and technical difficulties. Implanted probes only provide information from brain tissue in their immediate proximity. We have observed patients developing distinct contralateral or posterior fossa ischemia without registration of aberrant measurements. Whether a p_{iO_2} sensor or microdialysis probe in the anterior watershed region is able to detect impending ischemia in the posterior portion of the middle cerebral artery territory is unclear. However, a threshold-based approach as such is an oversimplification, not taking into account the dynamic and more complex nature of the underlying pathophysiological mechanisms. The relative changes toward baseline values and the slopes of parameter curves may be of greater importance and will be part of a future analysis. Technical difficulties with p_{iO_2} sensors, and especially microdialysis probes, are not uncommon. Erroneous measurements can lead to prejudicial treatment decisions, and unreliable probes have to be identified early.

Complications of probe implantation are seldom serious. We observed 9 microbleeds that required no further treatment and 1 hemorrhage necessitating surgical evacuation. No neurological sequelae were observed. All patients with hemorrhagic complications were under double antiplatelet treatment, emphasizing the need for placement before endovascular aneurysm closure. The higher rate of

CSF infections in the post-INM group needs to be critically addressed. These were patients with a positive CSF culture and an increased cell count collected from an external ventricular drain. It is difficult to assess the contribution of adding an additional port of contamination by INM as all patients also had an external ventricular drain. It is worth noting, however, that no probe had to be removed due to local signs of infection at the site of entry.

This trial is part of a broader effort to extend the classic definition of DCI by including functional aspects of perfusion, oxygenation, and metabolism.

Limitations

Despite having one of the largest and most comprehensively recorded cohorts of SAH patients, this study is limited by an observational design where both study groups are separated in time. Individuals were included according to the predefined inclusion and exclusion criteria. However, outcome data of the pre-INM group had to be collected retrospectively. This introduces an information bias that cannot be corrected. Reports of clinical SAH grading and the documentation of INM application have been very rigorous in minimizing any selection bias. However, there are still multiple potential confounders and sources of effect modification that cannot be corrected. Also, simply inclusion into the study of post-INM patients creates a context of general higher vigilance, potentially contributing to earlier DCI detection independent of invasively collected data and therefore creating detection bias. Finally, outcome data assessment could not be blinded, creating potential observer and information bias. Comparability between the groups was, however, tested extensively and was confirmed without significant differences, negating the need for additional matching.

Conclusions

In this study, INM with a resulting extension of the classic DCI definition toward a functional dimension enabled earlier detection of treatable DCI events in poor-grade SAH patients. This translated into a reduction of silent and overall DCI-related infarctions and an improvement in outcome after 12 months.

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Author Contributions

Conception and design: Veldeman, Albanna, Schubert. Acquisition of data: all authors. Analysis and interpretation of data: Veldeman, Schubert. Drafting the article: Veldeman, Albanna. Critically revising the article: all authors. Reviewed submitted version of manuscript: Veldeman, Albanna, Weiss, Conzen, Schmidt, Wiesmann, Clusmann, Schubert. Approved the final version of the manuscript on behalf of all authors: Veldeman. Statistical analysis: Veldeman. Administrative/technical/material support: Veldeman, Albanna, Weiss, Conzen, Schmidt, Schulze-Steinen, Clusmann, Schubert. Study supervision: Clusmann, Schubert.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplementary Tables 1 and 2. <https://thejns.org/doi/suppl/10.3171/2020.3.JNS20375>.

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