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Brief Report

Brain multimodality monitoring in patients suffering from acute aneurysmal subarachnoid hemorrhage: clinical value and complications

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Brain multimodality monitoring measuring brain tissue oxygen pressure, cerebral blood flow, and cerebral near-infrared spectroscopy may help optimize the neurocritical care of patients with aneurysmal subarachnoid hemorrhage and delayed cerebral ischemia. We retrospectively looked for complications associated with the placement of the probes and checked the reliability of the different tools used for multimodality monitoring. In addition, we screened for therapeutic measures derived in cases of pathological values in multimodality monitoring in 26 patients with acute aneurysmal subarachnoid hemorrhage. Computed tomography scans showed minor hemorrhage along with the probes in 12 patients (46.2%). Missing transmission of values was observed in 34.1% of the intended time of measurement for cerebral blood flow probes and 15.5% and 16.2%, respectively, for the two kinds of probes measuring brain tissue oxygen pressure. We identified 744 cumulative alarming values transmitted from multimodality monitoring. The most frequent intervention was modifying minute ventilation (29%). Less frequent interventions were escalating the norepinephrine dosage (19.9%), elevating cerebral perfusion pressure (14.9%) or inspiratory fraction of inspired oxygen (7.5%), transfusing red blood cell concentrates (1.2%), initiating further diagnostics (2.3%) and neurosurgical interventions (1.9%). As well, 355 cases of pathological values had no therapeutic consequence. The reliability of the measuring tools for multimodality monitoring regarding a continuous transmission of values must be improved, particularly for cerebral blood flow monitoring. The overall high rate of missing therapeutic responses to pathological values derived from multimodality monitoring in patients with aneurysmal subarachnoid hemorrhage underlines the need for structured tiered algorithms. In addition, such algorithms are the basic requirement for prospective multicenter studies, which are urgently needed to evaluate the role of multimodality monitoring in treating these patients.

Keywords

Brain multimodality monitoring; Invasive neuromonitoring; Aneurysmal subarachnoid hemorrhage; Brain tissue oxygen ($PbtO_2$, PTO); Cerebral blood flow (CBF); Cerebral near-infrared spectroscopy (cNIRS); Neurocritical care

1. Introduction

Delayed cerebral ischemia (DCI) is the main contributor to poor patient outcomes with aneurysmal subarachnoid hemorrhage (SAH). DCI results in poor outcome or death in up to 30% of patients with SAH [1] and is thus directly correlated with clinical outcome [2]. DCI is caused by multiple processes, including vasospasm in cerebral arteries, ischemia, cortical spreading depolarization, microthromboembolism, loss of autoregulation, and capillary transit time heterogeneity [1, 3–6]. Besides peroral administration of nimodipine, patients developing severe and refractory cerebral vasospasm (CV) require close monitoring and adaption of mean arterial pressure (MAP) and cerebral perfusion pressure (CPP) to avoid extensive cerebral ischemia. A rescue strategy may be spasmolytic endovascular treatment with intra-arterial (IA) infusion of calcium channel antagonists to improve outcomes in such patients [7–12]. At our department, the standard treatment of refractory CV after aneurysmal SAH entails continuous long-term IA infusion of nimodipine (CIAN) [13], but this treatment is associated with hemodynamic side effects. Patients treated with CIAN need higher dosages of vasopressors than patients treated with oral nimodipine to maintain sufficient mean arterial pressure [14]. To optimize treatment during the challenging phase of serious CV and to detect any metabolic disorders and oxygenation crises before irreversible damage occurs, sedated patients can be additionally monitored with intracerebral probes for measuring brain tissue oxygen ($PbtO_2$, PTO) and cerebral blood flow (CBF) and with optodes for near cerebral near-infrared spectroscopy (cNIRS). Promising data on the outcome after severe traumatic brain injury (TBI) have been published for patients monitored with PTO probes [15]. Furthermore, a recently published study had suggested better outcomes in patients with poor-grade SAH when invasive neuromonitoring was used during episodes of DCI [16].

In this retrospective cohort study, we screened for any complications connected with the implantation of the probes

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for invasive neuromonitoring and to evaluate the reliability of the different tools of comprehensive cerebral multimodality (neuro-) monitoring (MMM) with a focus on missing values due to technical problems. In addition, we evaluated the clinical and therapeutic interventions initiated because of distinct pathological values detected during MMM in patients with serious CV after aneurysmal SAH.

2. Methods

The research was approved by the Ethics Committee of the University of Regensburg (Approval Number 18-864-104) and conducted according to its respective guidelines. We included consecutive patients aged >18 years who had received MMM because of aneurysmal SAH and severe refractory CV at the neuro-intensive care unit (ICU) of the University Medical Center Regensburg between January 2012 and December 2017.

All patients were treated according to the institutional protocol [14]. All patients had been treated with external ventricular drainage within 24 hours after their admission to the ICU (Neurovent®, Raumedic AG, Helmbrechts, BY, Germany). Transcranial Doppler sonography (TCD) was conducted daily. CV was defined as an increase in mean flow velocity of >160 cm/s or >50% within 24 hours in the main branches of the anterior circulation arteries. After excluding other reasons, CV was also diagnosed if the neurological status of alert patients deteriorated despite normovolemic hypertension. If further neuro-imaging with computed tomography angiography (CTA) and digital subtraction angiography (DSA) confirmed a significantly reduced diameter of the artery, MMM was initiated immediately (Fig. 1).

For MMM, intracerebral probes measure brain tissue oxygen ($PbtO_2$, Integra Licox® Brain Tissue Oxygen Monitoring System, Integra LifeSciences, Princeton, NJ, USA) and CBF (Hemedex®, Promedics Medizinische Systeme GmbH, Düsseldorf, NRW, Germany) were implanted into the supposedly most affected area of the brain. A probe for measuring brain tissue oxygen (PTO, Neurovent-PTO®, Raumedic AG, Helmbrechts, BY, Germany) was installed on the contralateral side (Fig. 2). Probes should be placed into the frontal watershed area to yield information from two vascular areas (the middle and anterior cerebral arteries). In addition, optodes for cNIRS were attached bifrontally (SenSmart® Model X-100, Nonin Medical Inc, Plymouth, MA, USA). If values of MMM indicated DSA had previously confirmed persistent cerebral ischemic conditions and severe CV, CIAN therapy was initiated as described by Bele *et al.* [13].

According to the institutional protocol, pathological values for MMM were defined as follows: (1) ICP >20 cm H_2O, $PbtO_2$ and PTO <15 mmHg, CBF <15 mL/100 g/min, and saturation ($rScO_2$) in cNIRS <70%. For cNIRS, drops in $rScO_2$ of <70% were only considered serious events if $rScO_2$ values above this cut-off had remained stable for a longer period of time before.

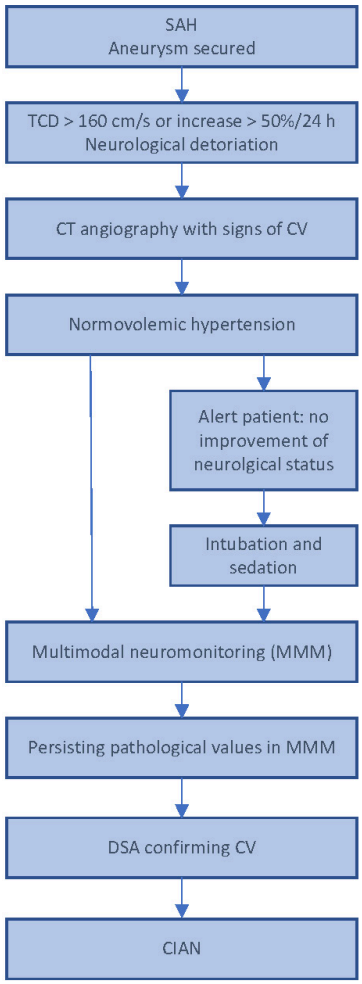

Fig. 1. Diagnostic and therapeutic algorithm in the case of cerebral vasospasm. Cerebral aneurysms identified as the source of bleeding are secured either by endovascular coiling or surgical clipping within 24 hours after the onset of subarachnoid hemorrhage. All patients are daily examined with Transcranial Doppler sonography. Serious cerebral vasospasm (CV) is assumed if the mean flow velocity increases to >160 cm/s or >50% within 24 hours or if the neurological status of alert patients deteriorate. Such patients first undergo computed tomography angiography (CTA). Patients with signs of severe CV in the CTA (arterial narrowing of the vessel diameter of >50% or irregularities in the vessel diameter) are immediately treated with euvolemic hypertension. Sedated patients receive multimodal (neuro-) monitoring (MMM) with additional bilateral measurement of brain tissue oxygen ($PbtO_2$/PTO) and cerebral near-infrared spectroscopy and measurement of cerebral blood flow (CBF) in the area supposed to be most affected. If neurological deterioration persists, patients who have not yet required sedation are also intubated and sedated and receive MMM. If MMM is suggestive of cerebral ischemia, patients undergo digital subtraction angiography (DSA). Continuous IA infusion of nimodipine (CIAN) is started in the case of confirmed CV (arterial narrowing of the vessel diameter of >50% or irregularities in the vessel diameter). Patients with distinct areas of cerebral infarction in previous CT scans are generally excluded from CIAN therapy because of the high risk of cerebral bleeding into the area affected by infarction.

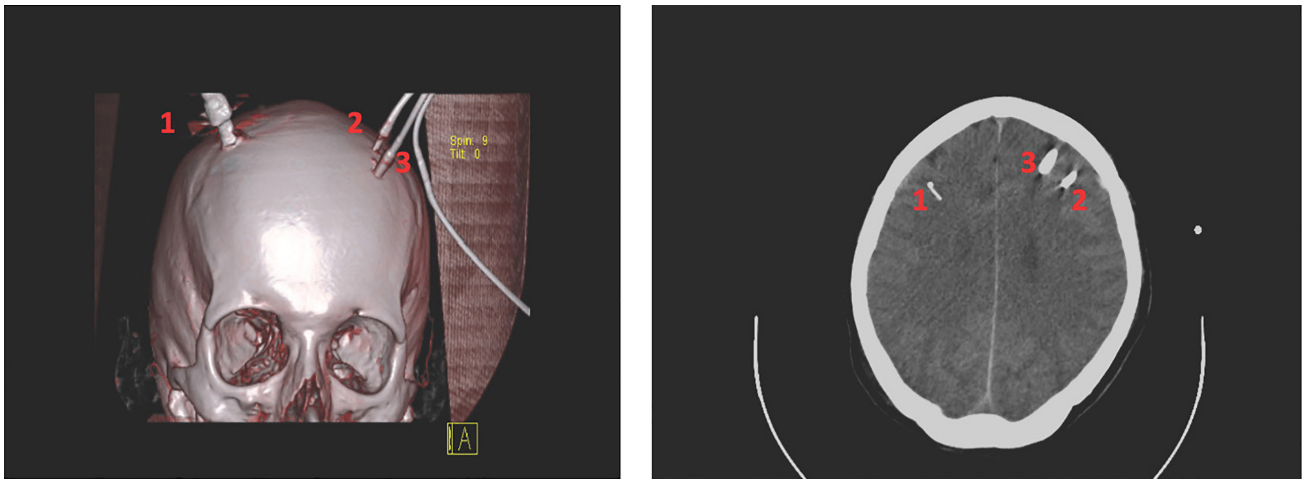

Fig. 2. Positions of the parenchymal probes for multimodal (neuro-)monitoring according to our institutional protocol. (1) A bundle of probes for measuring brain tissue oxygen (Integra Licox® Brain Tissue Oxygen Monitoring System, Integra LifeSciences, Princeton, NJ, USA) and cerebral blood flow (Hemedex®, Promedics Medizinische Systeme GmbH, Düsseldorf, NRW, Germany) inserted via a bolt kit screw system. (2) Probe for measuring brain tissue oxygen (Neurovent-PTO®, Raumedic AG, Helmbrechts, BY, Germany). (3) Eexternal ventricular drainage (Neurovent®, Raumedic AG, Helmbrechts, BY, Germany).

We retrospectively gathered information on complications associated with the placement of parenchymal probes and the reliability of the obtained measurements. For this purpose, we screened all available data obtained from MMM and stored in the patient data management system of the ICU (PDMS, MetaVision Suite®, iMDsoft, Tel Aviv, Israel) to obtain information about technical problems with the probes, thus leading to discontinuous monitoring and missing values. In addition, we examined all CT scans for any hemorrhage due to probe insertion. Due to missing interfaces between the monitors of MMM on the one side and the PDMS on the other side, an automatic and continuous transfer from data from the MMM monitors to the PDMS is not possible yet except for ICP. Thus, values of MMM are added manually to the PDMS every full hour. The first 24 hours of the measuring period were generally not considered valid because—according to the probe manuals and our perception, the most critical moment concerning accuracy is the time immediately after probe insertion.

In addition, the clinical interventions because of pathological values during MMM were examined retrospectively. To evaluate therapeutic interventions, we considered an escalation of the norepinephrine dosage, elevation of cerebral perfusion pressure (CPP) or inspiratory fraction of inspired oxygen (FiO_2), decrease or increase of minute ventilation, escalation of the IA nimodipine dosage in patients with CIAN therapy, transfusion of red blood cell concentrates, and initiation of further diagnostics or interventions (e.g., CT scan, DSA, neurosurgical treatment) to be adequate reactions to pathological values during MMM. We classified three different types of events of pathological values derived from probes measuring $PbtO_2$, PTO, CBF, and cNIRS (Table 1):

Event A: Pathological value(s) derived from only one probe for at least 2 subsequent hours. Single pathological values lasting for only 1 hour did not trigger an event.

Event B: Pathological values from two different probes at the same time for at least 1 hour.

Event C: Pathological values from three different probes at the same time for at least 1 hour.

Statistical analysis was conducted using IBM SPSS Statistics® 26 (IBM, Armonk, NY, USA). Data are presented as mean and standard deviation if normally distributed and as median and interquartile range if not.

3. Results

Twenty-six patients (21 women, 5 men; mean age 53.6 ± 7.8 years) with aneurysmal SAH had received MMM because of refractory CV. These patients were included in the study. Baseline data and cornerstones of neurocritical care therapy are summarized in Table 2.

MMM was initiated 5.9 ± 2.9 days after ICU admission. The mean duration of MMM was 14.5 ± 6.8 days.

Minor bleeding at the tip of the probes or along the probe's trajectory occurred in 12 patients (46.2%). These hemorrhages did not require any neurosurgical therapy. Still, they replaced the respective probe in 7 patients. 1 patient developed a major complication and required emergency decompressive craniectomy and evacuation of the bleeding because of serious intracerebral hemorrhage after probe implantation. No infectious complications due to the insertion of probes were observed.

Data on the cumulative frequencies of missing values for all patients in relation to each type of probe and measuring tool are shown in Table 3. Considering all patients, a cumulative time of MMM of 8865 hours was intended.

Table 1. Example for the classification of events.

$PbtO_2$	PTO	cNIRS on the right side	cNIRS on the left side	CBF	Event
40	35	70	73	32	
40	33	69	71	26	No event
41	35	70	72	28	
35	26	69	71	33	
36	28	69	70	31	A
32	25	71	71	29	
11	22	68	70	29	B
17	23	71	72	20	
29	12	68	71	13	C

$PbtO_2$, brain tissue oxygen pressure measured with the Integra Licox® Brain Tissue Oxygen Monitoring System; PTO, brain tissue oxygen pressure measured with the Neurovent-PTO® probe; cNIRS, cerebral near-infrared spectroscopy; CBF, cerebral blood flow measured with the Hemedex® probe.

Table 2. Demographic data and cornerstones of neurocritical care therapy.

Case	Sex	Age	Site of aneurysm	Treatment of aneurysm	Hunt and Hess grade	Duration of ICU therapy (days)	GOS at ICU discharge	GOS at 6 months after bleeding	CIAN therapy
1	f	51	ACOM	ET	3	52	3	4	yes
2	f	64	BA	ET	4	24	3	3	no
3	m	55	ACOM	ET	4	25	3	3	yes
4	f	48	ACOM	ST	4	34	3	5	yes
5	m	41	ACOM	ST	1	31	4	5	no
6	f	46	ACOM	ET	5	45	2	3	yes
7	f	62	MCA	ET	2	34	3	4	yes
8	f	52	MCA	ST	4	5	1	-	yes
9	f	51	PICA	ET	4	32	3	4	no
10	f	69	ACOM	ET	4	29	2	3	no
11	f	57	CMA	ET	2	24	3	5	yes
12	f	53	ACOM	ET	1	36	3	4	yes
13	f	45	MCA	ST	3	31	2	2	yes
14	m	61	ACOM	ET	1	40	2	not available	yes
15	f	52	MCA	ST	5	42	4	4	yes
16	f	63	AOM	ST	5	39	2	not available	no
17	f	43	PCOM	ET	4	45	3	4	yes
18	f	60	ACOM	ET	4	29	2	not available	yes
19	f	52	PCOM	ET	4	30	3	5	no
20	m	53	ACOM	ET	3	12	1	-	yes
21	f	50	BA	ET	1	29	3	5	no
22	f	61	ICA	ET	5	9	1	-	no
23	f	53	ICA	ET	5	28	2	3	yes
24	m	55	ICA	ST	1	44	3	5	yes
25	f	61	AICA	ET	2	31	2	2	no
26	f	36	ICA	ET	5	45	3	5	yes

F, female; m, male; ACOM, anterior communicating artery; BA, basilar artery; MCA, middle cerebral artery; PICA, posterior inferior cerebellar artery; CMA, callosomarginal artery; PCOM, posterior communicating artery; ICA, internal carotid artery; AICA, anterior inferior cerebellar artery; ET, endovascular treatment; ST, surgical treatment; GOS, Glasgow outcome scale.

Overall, we could identify 744 events (227 "Events A", 383 "Events B", and 134 "Events C"). Simultaneously elevated ICP was recorded in 7.9% of all cases for "Event A", in 5.5% for "Event B", and in 6.7% for "Event C". The most frequent interventions were modifications in minute ventilation as a therapeutic consequence of pathological MMM values (29% of the cases in which pathological values led to therapeutic intervention). Less frequent were an escalation of the norepinephrine dosage (19.9%), elevation of CPP (14.9%) or FiO_2 (7.5%), transfusion of red blood cell concentrates (1.2%), or

Table 3. Missing values of all patients.

Probe	Probe in situ (hours)	Probe in situ related to the intended period of measurement	Transmission of values (hours)	Missing values related to the intended period of measurement	Missing values related to the period with probe in situ
ICP	8865	100.0%	8767	1.1%	1.1%
$PbtO_2$	7827	88.3%	7490	15.5%	4.3%
PTO	7745	87.4%	7432	16.2%	4.0%
CBF	6785	76.5%	5842	34.1%	13.9%

Overall, a cumulative MMM time of 8865 hours was intended. ICP measured with the Neurovent® probe; $PbtO_2$ brain tissue oxygen pressure measured with the Integra Licox® Brain Tissue Oxygen Monitoring System; PTO, brain tissue oxygen pressure measured with the Neurovent-PTO® probe; CBF, cerebral blood flow measured with the Hemedex® probe.

Table 4. Summary of pathological brain multimodality monitoring.

Event	Cumulative events	No intervention initiated	1 intervention initiated	2 interventions initiated	≥3 interventions initiated
A	227 (30.5%)	122 (53.7%)	83 (36.6%)	15 (6.6%)	7 (3.1%)
B	383 (51.5%)	163 (42.6%)	137 (35.8%)	66 (17.2%)	17 (4.4%)
C	134 (18.0%)	70 (52.2%)	45 (33.7%)	16 (11.9%)	3 (2.2%)
All events	744 (100.0%)	355 (47.7%)	265 (35.7%)	97 (13.0%)	27 (3.6%)

the initiation of further diagnostics (2.3%) and neurosurgical interventions (1.9%). The dosage of IA nimodipine was only escalated in 0.8% of all cases. 355 out of 744 cumulative events (47.7%) had no therapeutic consequence. A detailed summary of pathological MMM values is provided in Table 4.

4. Discussion

The placement of parenchymal probes for invasive neuromonitoring does not per se positively affect outcome after aneurysmal SAH. A beneficial effect will only arise if values reflecting a real problem in cerebral oxygen supply are regularly and reliably provided through the probes and if the detected pathological values result in structured treatment modification, thus optimizing therapy. In addition, it has to be demanded that serious complications are only rarely observed.

Almost 50% of our patients showed minor bleeding around the tip or along the trajectory of the probes. From the neurosurgeon's point of view, such bleeding is harmless and does per se not contribute to higher morbidity but may lead to unreliable and wrong pathological values that subsequently result in the initiation of unnecessary and maybe hazardous interventions. This issue has to be considered in the interpretation of pathological values derived from MMM. Veldeman *et al.* [16] reported 9 out of 94 patients with minor bleeding along the probe's trajectory, and that operative evacuation was required by 1 patient with critical bleeding. All complications occurred in patients who had received dual antiplatelet therapy after complicated or stent-assisted endovascular coiling. Compared to this, the number of bleeding complications in our study seems to be rather high. However, all our patients with MMM during CIAN therapy had received therapeutic anticoagulation with unfractionated heparin. Only 1 of our 26 patients had developed a major procedure-related complication, i.e., intracerebral hemorrhage after the placement of a parenchymal probe, that required neurosurgical treatment. In addition, no infectious complication associated with MMM had occurred.

We observed different rates of untransmitted values from the probes to the monitors. In particular, measurement of ICP was continuously possible in almost all patients. A remarkable finding was that CBF could not be measured in about one-third of the intended time. From the pathophysiological point of view, the measurement of CBF would be the most important parameter for treating patients with SAH and serious CV. Our findings, however, suggest that the reliability of the probes measuring CBF needs to be further improved and that this tool does not fulfill the requirements for reasonable invasive neuromonitoring yet.

To evaluate the therapeutic consequences of pathological values derived from MMM, we looked for special interventions as reasonable distinct consequences during episodes of DCI in patients with aneurysmal SAH. In the case of elevated ICP and hypercapnia, a reasonable intervention would be increasing minute ventilation. On the other hand, decreasing minute ventilation may also be beneficial because it leads to cerebral arterial vasodilatation. Therefore, depending on the underlying problem, an adequate intervention may increase or decrease minute ventilation. Elevation of FiO_2 is reasonable in patients with low arterial oxygen tension (paO_2). If paO_2 values are in the upper normal range or above, further elevation of FiO_2 may be critical. No relevant increase in arterial oxygen content (CaO_2) can be expected as long as normal values for hemoglobin (Hb), and arterial oxygen saturation (SaO_2) are guaranteed. In addition, in contrast to normoxia, arterial hyperoxia has been described to be independently associated with in-hospital death in ventilated stroke patients [17]. The authors of that study concluded

that unnecessary oxygen delivery should be avoided in ventilated stroke patients. In patients with ventilated traumatic brain injury (TBI), arterial hyperoxia was also independently associated with higher in-hospital case mortality [18]. Yet, both findings result from retrospective studies and could not be confirmed in a recent retrospective cohort study [19] and can surely not be transferred one-to-one to the situation of patients with SAH and DCI.

Nevertheless, the uncritical elevation of FiO_2 in patients with normoxia has to be assessed carefully. Derived from pathophysiological considerations, the transfusion of red blood cell concentrates, however, seems to be an expedient and important measure in cases of low Hb to increase CaO_2 and cerebral oxygen delivery. The same importance applies to escalating the norepinephrine dosage and elevating CPP, which are integral and established methods of treating DCI and CV [20–22].

In the present retrospective study, almost 50% of pathological values during MMM did not lead to corresponding therapeutic interventions. It can be assumed that the lack of a clear treatment algorithm could have been the main reason for this. A feasible approach could be implementing a clear, tiered intervention protocol similar to that used in the BOOST II study [15]. The authors of that study observed a trend towards lower mortality and more favorable outcomes in patients with TBI when comparing patients who had undergone measurement of brain tissue oxygenation and treatment according to the intervention protocol with patients who had only undergone measurement of ICP. However, the confirmation of the results in the phase III study BOOST III is still awaited. In line with the intervention protocol used for the BOOST II study, the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC) has recently published a management algorithm for patients monitored for both brain oxygen and intracranial pressure [23]. However, the provided management recommendations do not reflect high-level evidence but are based on expert opinion. In addition, the situation of patients with TBI may differ from that of patients with aneurysmal SAH. Furthermore, some instructions of the interventional protocol, such as hyperventilation or a liberal increase in FiO_2, may be critical and even harmful for patients with SAH during episodes of DCI and CV.

In a single-center cohort analysis comparing 190 patients treated with and without invasive neuromonitoring (parenchymal oxygen saturation measurement and cerebral microdialysis), Veldeman *et al.* [16] observed a higher rate of a favorable outcome in patients with poor-grade SAH and invasive neuromonitoring 12 months after bleeding. The design of our retrospective study does not allow any conclusions regarding the influence of MMM on patient outcomes. An interesting aspect, however, is the way Veldeman *et al.* [16] used invasive neuromonitoring, which, in part, differed from our institutional standard. In their study, invasive neuromonitoring of patients with poor-grad SAH was established very early in the course of treatment after an initial wake-up test had failed. In our population, MMM was initiated later, on average, one week after ICU admission. Veldeman *et al.* [16] saw the main advantage of invasive neuromonitoring in the early recognition of the onset of DCI. Interventions because of pathological values (brain tissue oxygen tension <10 mmHg or metabolic derangements with lactate/pyruvate ratio ≥ 40) were euvolemic arterial hypertension by escalating the norepinephrine dosage and consideration of initiating endovascular rescue therapy. The authors did not propose any special intervention protocol beyond these interventions to react to pathological values during invasive neuromonitoring. According to our institutional standard, we usually initiate MMM when the presence of serious CV is already most likely with the intention to optimize the therapeutic regime during this critical phase of treatment, and especially to monitor the effect and to adapt the dosage of IA nimodipine during CIAN therapy when patients are sedated, as any clinical neurological examination is impossible.

Our study has some limitations. First, we conducted a retrospective analysis in a selected population with a low number of patients. In addition, we cannot provide any control group to compare patients with and without MMM. However, it was not the aim of the present study to gather information about the influence of MMM on the outcome of patients with aneurysmal SAH. For this purpose, the first and crucial step is implementing a clear intervention protocol because, otherwise, reliable multicenter studies will not be realizable. Second, the missing interfaces between the MMM monitors and the PDMS values for neuromonitoring except for ICP are only recorded manually for every full hour in the PDMS. Thus, only these values are available for the present retrospective analysis. However, in context with a treatment protocol, a much higher resolution of values (e.g., 5-minute intervals) and a much faster triggering of a therapeutic reaction must be demanded. Third, we defined interventions that seem reasonable from a pathophysiological point of view in the context of pathological values derived from MMM in patients with SAH and can be easily obtained from the patient data management system as "initiation of therapeutic interventions".

In some cases, simple interventions such as optimizing the position of the head, which cannot be documented in the PDMS, may have been sufficient to achieve normalization of the values. Here, the consequence of the intervention would not have been realized and thus not been documented. Fourth, our institutional standard provides an absolute lower limit for cNIRS values. To our knowledge, validated lower limits for $rScO_2$ for the cNIRS system used at our department do not yet exist. It could be reasonable and is an often-used approach in kind of cNIRS monitoring in an intraoperative setting to prefer considering the trend of $rScO_2$ overstating an absolute lower limit (e.g., drop-in $rScO_2$ below 20% of the baseline value). According to our institutional standard, drops in $rScO_2$ below 70% are only considered pathological

if values for $rScO_2$ above this cut-off remained stable for a long time before, thus avoiding unnecessary interventions. Finally, in many neurocritical units, cerebral microdialysis is used for monitoring patients with acute cerebral damage. As we do not use this tool, our data cannot provide any information on the practicability of using cerebral microdialysis and potential problems associated with this technique.

5. Conclusions

MMM with the placement of parenchymal probes is a feasible and safe technique for gathering information beyond the parameters derived from standard monitoring of patients with serious CV and aneurysmal SAH. However, the reliability of the probes, in particular of the CBF probes, has to be improved. A tiered algorithm for treating these patients in pathological values detected during MMM will be necessary to optimize therapy. In addition, such algorithms are a basic requirement for initiating prospective multicenter studies to evaluate the effect of MMM on the outcome. The reliability of probes for measuring CBF needs to be improved.

Author contributions

MK, KM and KS designed the research study. MK and KM performed the research. MK, KM and KS analyzed the data. MK and KS wrote the manuscript, SB, EB, BG and NOS were responsible for manuscript revisions. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The research was approved by the Ethics Committee of the University of Regensburg (Approval Number 18-864-104) and conducted according to its respective guidelines.

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Conflict of interest

The authors declare no conflict of interest.

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