Simulation-based training improves process times in acute stroke care (STREAM)

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INTRODUCTION

The benefits of recanalizing therapies in acute ischemic stroke are highly time-dependent [1,2]. Each minute lost reduces therapeutic efficacy [3,4]. Critical factors for the swift application of intravenous thrombolysis (IVT) and endovascular treatment (EVT) are a sensitive triage and a well-organized stroke team. Current guidelines recommend the establishment of stroke teams and education programs [5]. Improving process times in a multicentric design has been challenging. The French AVC II trial did not meet its primary goal to improve process times, but increased thrombolysis rates [6]. The interventions of the US INSTINCT trial and the Dutch PRACTISE trial had aimed primarily at triage and a well-organized stroke team. Current guidelines recommended the establishment of stroke teams and education programs [5].

Crew resource management (CRM) was coined in 1979 by NASA psychologist John Lauber [9]. CRM strengthens non-technical skills like communication and teamwork [10,11]. Similar to CRM, simulation training has been shown to enhance team operations and has been associated with improved clinical outcomes [12–14]. Recently, a significant alleviation of job strain for nurses on intensive care units by a simulation program has been reported [15]. There are several reports showing efficacy of simulation-based interventions directed at stroke teams of single hospitals [16,17], specific members of the stroke team [18,19] and regional stroke networks [20,21].

The STREAM Trial was directed at high-level stroke centers in a multicentric, prospective, interventional design to assess the effect of a multicomponent quality improvement program. We hypothesized that the implementation of a stroke team algorithm, applying the principles of CRM and stroke team simulation training would improve the process times of acute stroke care.

METHODS

The data that support the findings of this study as well as the stroke team training materials are available from the corresponding author.

Trial design

STREAM (Simulation-based Training of Rapid Evaluation and Management of Acute Stroke) was a single-arm, prospective, multicenter trial with a pre-test post-test design and central source data monitoring. The details of the study protocol were published previously [22]. Seven tertiary care neurocenters located at university hospitals in Germany jointly underwent the trial interventions in parallel and collected data on all direct-to-center patients receiving recanalizing therapies. This
trial had the approval of the ethics committee of Frankfurt University Hospital (ID 433/16) and secondary approvals were obtained from the ethics committees of all participating centers.

Patients

All adult (age ≥18 years) patients receiving IVT and/or EVT for stroke after direct referral by the emergency medical services (direct-to-center patients) were enrolled. Patients who were transferred from another hospital (e.g., for EVT) or patients with an in-hospital or walk-in stroke were excluded from the trial. The trial intervention itself, which was a guideline-based quality improvement program planned jointly by the participating centers and thus standard of care, did not require individual consent. Nevertheless, informed consent to the central data collection from patients or their legal representatives was sought by the trial teams in the days following the acute treatment.

Data collection

The trial intervention was flanked by two 3-month observation phases. All direct-to-center stroke patients receiving IVT and/or EVT were recorded in the 3 months before and after the intervention. During the 6 months of the intervention no patients were recruited. Monitored screening logs ensured adequate efforts at consecutive inclusion of all eligible patients. We collected data on individual patient case report forms as described previously [22]. The trial-specific simulation training was accompanied by a short questionnaire on the expectations (pre) and the rating (post) of the training that has been published previously [20].

Intervention

The intervention [22] consisted of five components:

1. Centers were asked to nominate three key persons of different professions and disciplines involved in acute stroke care to act as local champions of the STREAM intervention: emergency department/stroke unit nursing, neurology, neuroradiology and anesthesiology. These champions then attended one of two identically structured central 2-day site champion meetings comprising:
2. critical peer-to-peer review of their institutions’ stroke protocol with the aim of a critical revision and written adaptation (‘overhaul’) of the standard operating procedure (SOP) and
3. introduction to the concepts of simulation training as well as CRM, described in detail in the supplements online. The next step were
4. two full-day stroke team trainings at each trial site led by the principal investigator’s dedicated stroke team trainers, starting with a theoretical introduction focused on acute stroke therapies as well as CRM [23]. This theoretical primer was followed by in situ simulation for the entire interdisciplinary, multiprofessional stroke team with a high-fidelity manikin (Resusci Anne, Laerdal Medical, Puchheim, Germany) at the emergency department, computed tomography and angiography suite. The training was concluded by an intensive interdisciplinary debriefing focusing on CRM principles like closed-loop-communication [24,25]. Details concerning simulation training are described in detail in the supplemental material online.
5. The champions at each center were provided with teaching materials to establish independent stroke team trainings.

Trial outcomes

All time intervals were calculated centrally after central on-site data monitoring as described previously [22]. ‘Door-to-needle’ time (DTN), the interval from the patient’s arrival at the hospital until the start of IVT as the most important benchmark parameter for acute stroke therapy, was the primary endpoint. Secondary endpoints were the ‘door-to groin’ time (DTG) marking the interval from the patient’s arrival at the hospital to the start of the endovascular procedure (groin puncture). In patients receiving IVT prior to EVT, we collected the time interval from IVT initiation to the arrival in the angio suite (‘needle-to-angio’) reflecting the interdisciplinary decision-making process to proceed towards EVT, and the interval from the arrival at the angio suite to the start of the procedure (‘angio-to-groin’) reflecting the handover to and preparations by the anesthesiology and neuro-interventions team.

Since an acceleration of procedures may take its toll on patient safety (e.g., by overlooking possible contraindications to thrombolysis linked to a higher bleeding risk), we recorded intracranial hemorrhages on follow-up imaging as a safety outcome measure according to the Heidelberg Bleeding Classification [26] (classified as symptomatic or asymptomatic by the local investigators).

Data analysis

A priori sample size calculation based on a pilot trial in the regional stroke network INVN Rhein-Main yielded a minimal number of 110 patients in each observational phase for a statistical power of 80% and a type 1 error probability of < 0.05 to reduce door-to-needle time by 10 min [20]. Site feasibility questionnaires showed that the seven stroke centers performed 170 IVTs (mean, range 80–250) per year, and were thus able to recruit 200 patients in each intervention phase considering a potential dropout rate for missing reports or informed consent in one-third of the patients.

Statistical analysis was performed with SPSS version 27.0 (IBM) and GraphPad Prism 9.0 (GraphPad Software). Mean or median (depending on the presence of normal distribution, tested by quantile-quantile plots) and 25–75 percent interquartile ranges
RESULTS

Patient characteristics

A total of 378 stroke team operations from patient admission to the emergency department up to the initiation of a recanalizing therapy were evaluated in the trial (Figure 2). Pre- and post-interventional patient characteristics did not differ significantly in terms of age and pre-stroke disability (modified Rankin Score [mRS]; Table 1). Stroke severity was slightly higher in the post-interventional group (National Institutes of Health Stroke Scale [NIHSS] 5 vs. 6). We found a higher rate of large vessel occlusion (LVO) in the post-interventional phase (29% pre vs. 45% post, $p = 0.001$). Utilization of vessel imaging was not different (97% pre vs. 98% post, $p = 0.81$; Table 1). Selecting patients treated by simulation-experienced stroke teams (teams of whom at least one member had participated in the STREAM simulation training) did not lead to further significant imbalances in patient characteristics (Table 1).

Primary outcome

Mean DTN was not altered significantly in the primary analysis (Figure 1a; 38 min, IQR 25–43 min vs. 36 min, IQR 25–40 min, $p = 0.28$; Table 2). However, we observed an incomplete penetration of the stroke team simulation training to the entire stroke team workforce. Only 53% (89/169) of all patients who received IVT and 51% (30/59) of all patients who received EVT in the post-interventional observation phase were treated by a team in which at least one member had simulation experience. To estimate the putative effect of regular stroke team simulation trainings that reach the entire staff, we performed a secondary analysis capturing the combined effect of workflow overhaul and simulation training in the setting of optimal adherence to the trial intervention (Figure 1b) which
showed a significant decrease by 5 min in the post-interventional phase (38 min, IQR 25–43 min vs. 33 min, IQR 23–39 min, \( p = 0.03 \); Table 2). Patients had a non-significant greater likelihood of being treated within the first 20 min after hospital arrival (pre: 11% [18/171] vs. post: 17% [15/89], \( p = 0.15 \)) and there was a non-significant numerically smaller proportion of patients being treated beyond 60 min of admission (pre: 12% [20/171] vs. post: 6% [5/89], \( p = 0.12 \); Table 2). To evaluate the effect of the simulation training independent of the workflow overhaul, we compared process times achieved by teams with simulation experience versus simulation-naive teams exclusively in the post-interventional observation phase (Figure 1c). For simulation-experienced teams, we observed a reduction of the DTN by 6 min (39 min, IQR 25–44 vs. 33 min, IQR 23–39, \( p = 0.05 \); online supplemental Figure 1).

**Secondary outcomes**

### EVT process times

Since the intervention was directed at all acute stroke patients receiving recanalizing therapies, EVT was applied in only 17.5% pre-interventional and 31.2% post-interventional. EVT process times were analyzed as secondary endpoints. The primary analysis of all patients in the pre- versus the post-interventional phase (Figure 1a) showed no significant difference of the door-to-groin time (DTG, pre: 76 min, IQR 52–95 vs. post: 84 min, IQR 55–96, \( p = 0.30 \); Table 2).

We performed two post-hoc secondary analyses. The first analysis captured the combined effect of workflow overhaul entailed by the peer-to-peer review during the central seminar and simulation training in the setting of optimal adherence to the trial intervention (Figure 1b). The difference between stroke team performances leading to EVT of simulation-naive teams in the pre-interventional phase versus those of simulation-experienced teams in the post-interventional phase was not significant (pre: 78 min, IQR 55–100 vs. 74 min, IQR 52–92, \( p = 0.70 \); Table 2).

The second analysis capturing the isolated simulation training effect by comparing stroke team operations of simulation-naive versus simulation-experienced teams exclusively in the post-interventional observation phase (Figure 1c) was independent of the significant differences in LVO prevalence and location (Table 1). We found a 21 min shorter DTG time by simulation-experienced teams (~21 min, simulation-naive: 95 min, IQR 69–111 vs. simulation-experienced: 74 min, IQR 51–92, \( p = 0.04 \); Figure 3).

### Safety outcomes

Intracerebral hemorrhage on follow-up imaging did not increase (pre: 15 (7.9%) vs. post: 14 (7.4%), \( p = 0.87 \)). Symptomatic hemorrhagic transformation occurred in 2.6% (\( n = 5 \)) of all patients during the pre-interventional phase and 1.6% (\( n = 3 \)) in the post-interventional phase, respectively (\( p = 0.41 \); Table 2).

### Workflow and behavioral changes

Baseline assessment in the pre-interventional phase showed that measures to accelerate IVT that have been described in a seminal paper by Meretoja et al. were already carried out in a considerable
TABLE 1  Patient characteristics of primary and secondary analyses

| Characteristic                        | Pre-intervention | Post-intervention | Workflow overhaul + simulation training | Simulation training |
|---------------------------------------|------------------|-------------------|------------------------------------------|---------------------|
|                                       | (n = 189)        | (n = 189)         | (n = 184)                                | (n = 90)            |
| Age, mean (SD), years                 | 72.8 (14.5)      | 71.9 (15.2)       | 73.0 (14.6)                              | 73.8 (12.46)        |
| Pre-stroke mRSa                        | 0 (0–1)          | 0 (0–1)           | 0 (0–1)                                  | 0 (0–2)             |
| NIHSSa                                | 5 (2–8)          | 6 (2–10)          | 5 (3–8)                                  | 7 (4–11)            |
| n (%): Symptom onset unknown          | 42 (22.2)        | 50 (26.5)         | 42 (22.8)                                | 24 (26.7)           |
| n (%): CT                             | 175 (92.6)       | 177 (93.7)        | 170 (92.4)                               | 85 (93.3)           |
| n (%): MRI                            | 18 (9.5)         | 20 (10.6)         | 18 (9.8)                                 | 6 (6.7)             |
| n (%): Vessel imaging                 | 184 (97.4)       | 185 (97.9)        | 179 (97.3)                               | 87 (96.7)           |
| n (%): LVO                            | 55 (29.1)        | 85 (45.0)         | 53 (28.8)                                | 41 (45.6)           |
| n (%): Non-M1/ICA                     | 28 (14.8)        | 49 (25.9)         | 27 (14.7)                                | 25 (27.7)           |
| n (%): IVT                            | 175 (92.6)       | 169 (89.4)        | 171 (92.9)                               | 80 (88.9)           |
| n (%): Off duty                       | 33 (17.5)        | 59 (31.2)         | 31 (16.8)                                | 29 (32.2)           |
| n (%): Off duty                       | 80 (42.3)        | 88 (46.6)         | 77 (41.8)                                | 41 (45.6)           |

Abbreviations: CT, computed tomography; EVT, endovascular treatment; ICA, internal carotid artery with involvement of terminal bifurcation; IVT, intravenous thrombolysis with alteplase; LVO, large vessel occlusion on initial brain imaging; M1, middle cerebral artery M1; MRI, magnetic resonance imaging; mRS, modified Rankin Score; NIHSS, National Institutes of Health Stroke Scale; off duty, admission of the patient between 5 pm and 8 am on Monday to Friday and the entire weekend; SD standard deviation.

*aModified Rankin Score (mRS) before stroke and National Institutes of Health Stroke Scale (NIHSS) at admission (median and IQR).

Tested via Wilcoxon–Mann–Whitney test.
# Table 2

Primary and secondary analyses of acute stroke care process times

| Characteristic | Pre-intervention | Post-intervention | Workflow overhaul + simulation training | Simulation training |
|----------------|------------------|-------------------|-----------------------------------------|---------------------|
|                | (n = 189)        | (n = 189)         | Naive (n = 184) | Implemented (n = 99)        | Naive (n = 90) | Implemented (n = 99) |
| DTN mean (SD), min | 38.3 (21.3) | 35.9 (19.8) | 0.28 | 38.4 (21.5) | 33.3 (16.1) | 0.03 | 38.7 (23.1) | 33.3 (16.1) | 0.05 |
| DTN, n (%) | | | | | | | |
| ≤20 min | 18 (10.3%) | 24 (14.2%) | 0.27 | 18 (10.5%) | 15 (16.9%) | 0.15 | 9 (10.0%) | 15 (16.9%) | 0.30 |
| ≤30 min | 73 (41.7%) | 86 (50.9%) | 0.09 | 72 (42.1%) | 48 (53.9%) | 0.07 | 38 (42.2%) | 48 (53.9%) | 0.41 |
| ≥60 min | 20 (11.4%) | 14 (8.3%) | 0.33 | 20 (11.7%) | 5 (5.6%) | 0.12 | 9 (10.0%) | 5 (5.6%) | 0.19 |
| DTG, mean (SD), min | 76.0 (34.1) | 84.0 (36.6) | 0.30 | 78.2 (34.1) | 74.1 (27.0) | 0.61 | 94.5 (42.7) | 74.1 (27.0) | 0.04 |
| IVT-to-angio, mean (SD), min | 20.4 (23.0) | 26.6 (34.7) | 0.43 | 21.3 (23.3) | 16.8 (16.6) | 0.51 | 37.5 (45.6) | 16.8 (16.1) | 0.07 |
| Angio-to-groin, mean (SD), min | 26.5 (11.1) | 25.9 (12.0) | 0.83 | 27.3 (11.0) | 26.6 (13.3) | 0.83 | 25.6 (10.7) | 26.2 (13.2) | 0.87 |
| HT, n (%) | 15 (7.9%) | 14 (7.4%) | 0.87 | 14 (7.6%) | 6 (6.1%) | 0.20 | 9 (10.0%) | 6 (6.1%) | 0.32 |
| Asymptomatic | 10 (5.3%) | 11 (5.8%) | 0.43 | 9 (4.9%) | 4 (4.1%) | 0.99 | 8 (8.9%) | 4 (4.1%) | 0.53 |
| Symptomatic | 5 (2.6%) | 3 (1.6%) | 0.41 | 5 (2.7%) | 2 (2.0%) | 0.81 | 1 (1.1%) | 2 (2.0%) | 0.83 |

Abbreviations: DTG, door-to-groin time; DTN, door-to-needle time; HT, hemorrhagic transformation according to the Heidelberg Bleeding Classification and classified as symptomatic or asymptomatic by the local investigator; IVT, intravenous thrombolysis; SD, standard deviation.

*Tested via two-tailed Student’s t-test or Wilcoxon–Mann–Whitney test.
proportion of the acute stroke treatments [30]. Between the pre- and the post-interventional phase, an increase of the involvement of emergency medical services (EMS) in the acute stroke workflow (pre: 25.9% vs. post: 38.4%, \( p = 0.01 \); online supplemental Table 1) and a trend towards an increase in the administration of the IVT bolus on the computed tomography (CT)/magnetic resonance imaging (MRI) table (pre: 56.1% vs. post: 64.7%, \( p = 0.07 \)) was found. In patients with simulation experience compared to simulation-naive teams, we observed a significant increase of initiation of IVT directly in the scanner (pre: 55.4% vs. post: 69%, \( p = 0.02 \); online supplemental Table 1).

**Staff participation and acceptance**

We carried out two in situ stroke team simulation trainings at each center with in total 186 participants of the seven centers’ stroke teams. Before the study intervention, 5 participants had previous experience with stroke simulation; these were excluded from subgroup analysis targeting the effect of simulation training (Table 1). Different teams participated in the two on-site simulation trainings at each trial site. No participant received more than one training. The training was rated as useful by 95.5% (105/110) of all participants and this perception did not differ significantly by profession or – in the subgroup of physicians – by formative level. Most participants (93.6%, 103/110) would welcome a regular training and the suggested interval for repetition was 1 year (online supplemental Figure 3).

**DISCUSSION**

In spite of the neutral results of the primary analysis, our trial provides strong indicators for a beneficial effect of stroke team simulation training on process times of both IVT and EVT if this intervention is made accessible to a relevant share of employees from all involved disciplines. The STREAM trial evaluated the effects of a multicomponent intervention consisting of recruitment of champions from the crucial disciplines at each site and introduction to simulation training as a vehicle to improve technical and non-technical aspects of stroke team operations followed by the delivery of two centrally designed stroke team simulation trainings at each trial site. In two independent secondary analyses taking into account the actual simulation exposure of at least one member of the stroke team, we observed a modest but statistically significant reduction of the DTN by 5 min (38 min, IQR 25–43 min vs. 33 min, IQR 23–39 min, \( p = 0.033 \)) and of the DTG by 21 min (95 min, IQR 69–111 vs. 4 min, IQR 51–92, \( p = 0.04 \)) without an increase in symptomatic or asymptomatic intracerebral hemorrhage. Concerning clinical endpoints, this is one of the first trials demonstrating efficacy of simulation training on procedural time metrics in real-life clinical practice.

We recognize that the time gains of the DTN for IVT (–5 min) are modest but probably clinically relevant [2,3]. However, the time gains of the DTG for EVT by simulation-experienced teams (–21 min) are substantial [31]. We hypothesize that this discrepancy is caused by the more complex decision process and a number of handovers which both benefit from interdisciplinary fine-tuning and training. Accordingly, the ‘needle-to-angio’ interval between IVT and the handover to the angio suite in patients undergoing EVT, reflecting the period of interdisciplinary therapeutic decision-making, was shortened most notably by the STREAM intervention. Noteworthy, regarding all stroke team operations leading to EVT, we counterintuitively found faster DTGs in the pre-interventional observation phase. Since LVO was substantially more frequent in the post-interventional phase despite only a small increase in stroke severity as measured by the NIHSS, we assume that the definition of LVO that could be treated by EVT gradually expanded during the trial. This is reflected by considerably more non-M1/internal carotid artery (ICA) occlusions in the EVT cohort of the post-interventional phase (pre: 14.5% vs. post: 25.9%, \( p = 0.22 \)). It seems plausible that these cases involved longer decision-making times of the interdisciplinary teams. To avoid this confounder, we concentrated our analysis on the comparison of DTGs achieved by simulation-experienced versus simulation-naive teams exclusively in the post-interventional phase.
In addition to and in continuation of the INSTINCT [7], PRACTISE [8] and AVC II [6] trials, which were based on similar concepts but could not show effects of the trial interventions on process times, we captured the actual reach of the trial intervention by recording for each individual acute stroke team operation whether at least one member of the stroke team had participated in the STREAM simulation training. This allowed us to generate a main hypothesis why the result of the pre-planned primary analysis was neutral. Our data indicate that despite training 186 clinicians (neurologists, neuroradiologists, anesthesiologists, nurses and radiology technicians) at seven trial sites, the on-site stroke team simulation training was “underdosed” since only 53% of all stroke team operations in the post-interventional phase were carried out by teams in which at least one team member had participated in one of the simulation trainings. Our secondary analysis, capturing both workflow overhaul and simulation training (Figure 1b), allows an estimate of the effectiveness of the trial interventions under optimal institutional adherence to continued simulation training. This comparison has to be pondered with care since we cannot fully exclude a bias-by-participation (motivated colleagues would be more likely to participate in the trial-specific simulation training and – possibly independent of this – achieve faster process times). The comparison of process times achieved by simulation-naïve compared to simulation-experienced teams exclusively in the post-interventional phase (Figure 1c) corroborates our hypothesis of exposure to simulation training as the main driver of improvement. Since the training was rated as useful by the vast majority of the participants and most participants would welcome a regular training (online supplemental Figure 3), we conclude that even stroke teams of high-volume centers with ample practical experience benefit from stroke-specific team trainings. However, a follow-up inquiry on team training routines at the end of the trial revealed that only one center had intensified their previously occasional team trainings whereas the other six centers had not managed to perpetuate independent team trainings. Professional societies could promote a more widespread use of simulation training by providing materials, certification criteria for trainers and programmes, and requirement of a structured team-based education program in the certification process for stroke centers. Simulation training is often viewed as time-consuming and costly, but recent comprehensive studies have shown a positive cost-benefit relationship in terms of staff retention, reduction of absenteeism and staff satisfaction [15,32,33]. Therefore, future research needs to focus on barriers and enablers of simulation training for stroke teams in order to promote a more widespread use.

We acknowledge the following limitations of our trial. First, a pre-versus post-interventional comparison is definitely problematic as it strictly does not allow one to distinguish an effect of the intervention from a natural history of improvement. Nevertheless, randomization or a stepped-wedge design was not appropriate due to the limited number and heterogeneity of centers. Besides that, we found two robust indicators for improvements beyond general trends towards faster treatment times in acute stroke care: (1) the secondary analysis of process times achieved by simulation-experienced versus simulation-naïve stroke teams exclusively in the post-interventional period and (2) the significant difference in time trend slopes of the interrupted time series analysis (online supplemental Figure 2).

Second, it may be discussed whether an increased treatment of stroke mimics entailing unnecessary treatment risks and costs would have been a more valid safety endpoint than hemorrhagic transformation on follow-up brain imaging. We decided against this in favor of an unequivocal endpoint and argue that similar patient numbers in the pre- and post-interventional observation period argue against an uncritical application of IVT. Third, including only tertiary care university hospital neurocenters in Germany limits the generalizability of our results. But since the mean pre-interventional DTN of our cohort is significantly faster than the mean DTN reported from prospective registries of several other countries [34,35], our results most probably even underestimate the treatment effect that could be possible in less-effective centers where even larger time gains can be made. We would expect that the effects of workflow optimization would be even more pronounced in these centers with simulation training exerting an independent additive effect as a team-specific measure. Fourth, it must be pointed out that our data cannot show an influence on clinical outcomes because we decided to relinquish a 90 days follow-up evaluation for the benefit of practicability and data completeness. Finally, it is not entirely possible to discern the impact of each of the five components of our intervention, but the robust effects especially on the stroke team performances in the post-interventional phase comparing simulation-naïve to simulation-experienced teams argue for a simulation-specific effect.

**CONCLUSIONS**

The pragmatic and rigorously controlled STREAM Trial demonstrates potential efficacy of the intervention on acute stroke care process times. Very high acceptance among the trained teams and the willingness for regular training make simulation-based training an effective tool for the education of interdisciplinary and multiprofessional stroke teams.

**CONFLICT OF INTEREST**

F.O.B., H.R., P.S. and W.P. report speakers honoraria from LAERDAL, a distributor of simulation equipment and simulation course concepts. K.G.H. reports grants and personal fees from Bayer, personal fees from BMS, personal fees from Daiichi Sankyo, personal fees from Sanofi, personal fees from Pfizer, personal fees from AstraZeneca, personal fees from Medtronic, personal fees from Biotronik, personal fees from WL Gore & Associates, personal fees from Edwards Lifesciences, personal fees from Boehringer Ingelheim and personal fees from Abbott outside the submitted work. S.N. reports personal fees from Brainomix, personal fees from Boehringer Ingelheim, personal fees from BMS Pfizer and grants from Cerenovus outside the submitted work. J.P. reports personal fees from Stryker outside the submitted work. W.P. reports personal fees from LAERDAL and grants from Stryker Neurovascular during the conduct of the
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AUTHOR CONTRIBUTIONS
Ferdinand O. Bohmann: Conceptualization (lead); Data curation (lead); Formal analysis (lead); Funding acquisition (lead); Investigation (lead); Methodology (lead); Project administration (lead); Resources (lead); Software (lead); Supervision (lead); Validation (lead); Visualization (lead); Writing-original draft (lead); Writing-review & editing (lead). Katharina Gruber: Data curation (equal); Formal analysis (equal); Investigation (equal); Writing-original draft (equal). Natalia Kurka: Investigation (equal); Writing-original draft (equal). Laurent M. Willems: Formal analysis (equal); Investigation (equal); Methodology (equal); Writing-original draft (equal). Eva Herrmann: Formal analysis (equal); Methodology (equal); Writing-original draft (equal). Richard du Mesnil de Rochemont: Investigation (equal); Writing-original draft (equal). Peter Scholz: Investigation (equal); Writing-original draft (equal). Heike Rai: Data curation (equal); Investigation (equal); Writing-original draft (equal). Philipp Zickler: Investigation (equal); Writing-original draft (equal). Michael Ertl: Investigation (equal); Writing-original draft (equal). Ansgar Berlis: Investigation (equal); Writing-original draft (equal). Sven Poli: Investigation (equal); Writing-original draft (equal). Annerose Mengel: Investigation (equal); Writing-original draft (equal). Peter Ringleb: Investigation (equal); Writing-original draft (equal). Simon Nagel: Investigation (equal); Writing-original draft (equal). Johannes Pfaff: Investigation (equal); Writing-original draft (equal). Frank A. Wollenweber: Investigation (equal); Writing-original draft (equal). Lars Kellert: Investigation (equal); Writing-original draft (equal). Moritz Herzberg: Investigation (equal); Writing-original draft (equal). Luzie Koehler: Investigation (equal); Writing-original draft (equal). Karl Georg Haeseler: Investigation (equal); Writing-original draft (equal). Anna Alegiani: Investigation (equal); Writing-original draft (equal). Charlotte Schubert: Investigation (equal); Writing-original draft (equal). Caspar Brekenfeld: Investigation (equal); Writing-original draft (equal). Christoph Kebabch: Investigation (equal); Writing-original draft (equal). Tanja Manser: Formal analysis (equal); Investigation (equal); Methodology (equal); Writing-original draft (equal). Helmut Steinmetz: Conceptualization (equal); Funding acquisition (equal); Supervision (equal); Writing-original draft (equal). Waltraud Pfleischf: Conceptualization (lead); Data curation (lead); Formal analysis (lead); Funding acquisition (lead); Investigation (lead); Methodology (lead); Project administration (lead); Resources (lead); Software (lead); Supervision (lead); Validation (lead); Visualization (lead); Writing-original draft (lead); Writing-review & editing (lead).

DATA AVAILABILITY STATEMENT
Data, methods and materials used to conduct the research in the article were carefully documented. The data that support the findings of this study are available from the corresponding author on reasonable request.

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