

Evaluation of DeGIR registry data on endovascular treatment of cerebral vasospasm in Germany 2018–2021: an overview of the current care situation

Auswertung der DeGIR-Registerdaten zur endovaskulären Therapie von zerebralen Vasospasmen in Deutschland 2018–2021: Ein Überblick über die aktuelle Versorgungssituation

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Key words

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ABSTRACT

Background Evaluation of endovascular therapies for cerebral vasospasm (CVS) documented in the DeGIR registry from 2018–2021 to analyse the current clinical care situation in Germany.

Methods Retrospective analysis of the clinical and procedural data on endovascular spasm therapies (EST) documented anonymously in the DeGIR registry. We analysed: pre-interventional findings of CTP and consciousness; radiation dose applied, interventional-technical parameters (local medication, devices, angiographic result), post-interventional symptoms, complications and mortality.

Results 3584 patients received a total of 7628 EST (median age/patient: 53 [range: 13–100, IQR: 44–60], 68.2 % women) in 91 (2018), 92 (2019), 100 (2020) and 98 (2021) centres; 5388 (70.6 %) anterior circulation and 378 (5 %) posterior circulation (both involved in 1862 cases [24.4 %]). EST was performed once in 2125 cases (27.9 %), with a mean of 2.1 EST/patient. In 7476 times, purely medicated EST were carried out (nimodipine: 6835, papaverine: 401, nitroglycerin: 62, other drug not specified: 239; combinations: 90). Microcatheter infusions were documented in 1132 times (14.8 %). Balloon angioplasty (BA) (additional) was performed in 756 EST (9.9 %), other mechanical recanalisations in 154 cases (2 %) and stenting in 176 of the EST (2.3 %). The median dose area product during ET was 4069 cGycm² (drug: 4002/[+BA: 8003 [p < 0.001]). At least 1 complication occurred in 95 of all procedures (1.2 %) (drug: 1.1 %/[+BA: 4.2 % [p < 0.001]). Mortality associated with EST was 0.2 % (n = 18). After EST, overall improvement or elimination of CVS was found in 94.2 % of cases (drug: 93.8 %/[+BA: 98.1 % [p < 0.001]). In a comparison of the locally applied drugs, papaverine eliminated CVS more frequently than nimodipine (p = 0.001).

Conclusion EST have a moderate radiation exposure and can be performed with few complications. Purely medicated EST are predominantly performed, especially with nimodipine. With (additional) BA, radiation exposure, complication rates and angiographic results are higher or better. When considering drug EST alone, there is evidence for an advantage of papaverine over nimodipine, but a different group size has to be taken into account. In the analysis of EST, the DeGIR registry data are suitable for answering more specific questions, especially due to the large number of cases; for this purpose, further subgroupings should be sought in the data documentation.

Key points:

- In Germany, there are currently no guidelines for the endovascular treatment of cerebral vasospasm following spontaneous subarachnoid hemorrhage.
- In addition to oral nimodipine administration endovascular therapy is used to treat cerebral vasospasm in most hospitals.
- This is the first systematic evaluation of nationwide registry data on endovascular treatment of cerebral vasospasm in Germany.
- This real-world data shows that endovascular treatment for cerebral vasospasm has a moderate radiation exposure and can be performed with few complications overall. With (additional) balloon angioplasty, radiation exposure, complication rates and angiographic therapy results are higher or better.

Citation Format

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ZUSAMMENFASSUNG

Ziel Auswertung der 2018–2021 im DeGIR-Register dokumentierten endovaskulären Therapien von zerebralen Vasospasmen (ZVS) zur Analyse der aktuellen klinischen Versorgungssituation in Deutschland.

Material und Methoden Retrospektive Analyse der im DeGIR-Register anonymisiert dokumentierten klinischen und prozeduralen Daten zu endovaskulären Spasmustherapien (EST). Analysiert wurden: präinterventionelle Befunde der CTP und Bewusstseinslage; applizierte Strahlendosis, interventionell-technische Parameter (lokale Medikamente, Devices, angiografisches Ergebnis), postinterventionelle Symptomatik, Komplikationen und Mortalität.

Ergebnisse 3584 Patienten erhielten in 91 (2018), 92 (2019), 100 (2020) und 98 (2021) Zentren insgesamt 7628 EST (me-

dianes Alter/Patient: 53 [Range: 13–100, IQR: 44–60], 68,2 % Frauen); 5388 (70,6 %) vordere Zirkulation und 378 (5 %) hintere Zirkulation (in 1862 Fällen [24,4 %] beide beteiligt). In 2125 Fällen lediglich einmalige EST (27,9 %), der Mittelwert lag bei 2,1 Interventionen/Patient. 7476 EST erfolgten allein medikamentös (Nimodipin: 6835, Papaverin: 401, Nitroglycerin: 62, anderes Pharmakon ohne nähere Benennung: 239; Kombinationen: 90). Dauerbehandlungen mit einer Mikrokatheter-Infusion wurden 1132mal (14,8 %) dokumentiert. Die (zusätzliche) Ballonangioplastie (BA) wurde bei 756 EST (9,9 %) durchgeführt, andere nicht näher benannte mechanische Rekanalisationen in 154 Fällen (2 %) und ein Stenting in 176 der EST (2,3 %). Das Dosisflächenprodukt im Rahmen der EST betrug im Median 4069 cGycm² (medikamentös: 4002/[+BA: 8003 [p < 0,001]]). Mindestens 1 Komplikation trat in 95 aller Prozeduren auf (1,2 %) (medikamentös: 1,1 %/[+BA: 4,2 % [p < 0,001]]). Die mit EST verbundene Mortalität betrug 0,2 % (n = 18). Nach EST fanden sich insgesamt in 94,2 % der Fälle Besserungen oder Beseitigungen der ZVS (medikamentös: 93,8 %/[+BA: 98,1 % [p < 0,001]]). Im Vergleich der lokal applizierten Medikamente beseitigte Papaverin die ZVS häufiger als Nimodipin (p = 0,001).

Schlussfolgerung EST weisen eine moderate Strahlenbelastung auf und sind insgesamt komplikationsarm durchführbar. Überwiegend werden rein medikamentöse EST durchgeführt, vor allem mit Nimodipin. Bei (zusätzlicher) BA sind Strahlenbelastung, Komplikationsraten und angiografisches Ergebnis höher bzw. besser. Bei alleiniger Betrachtung medikamentöser EST ergeben sich Hinweise für einen Vorteil von Papaverin gegenüber Nimodipin, jedoch ist die unterschiedliche Gruppengröße zu berücksichtigen. Bei der Analyse der EST sind die DeGIR-Registerdaten gerade aufgrund der großen Fallzahl geeignet, auch speziellere Fragestellungen zu beantworten, hierfür sind weitere Untergruppierungen bei der Datendokumentation anzustreben.

Introduction

Based on the described frequencies of subarachnoid hemorrhage (SAH), we can estimate the incidence of cerebral vasospasm (CVS) at around 9/100 000 annually [1]. Corresponding vascular constriction is a common secondary complication after SAH, with the risk of infarcts and potentially high morbidity and mortality. In intracranial aneurysmal hemorrhage, CVS typically occurs over the course of 4–10 days and occurs in approximately 50–90 % of all cases [2]. Pathophysiologically, the underlying cause is usually dysregulation and ultimately constriction of the arterial vessel walls as a result of the effects of blood degradation products distributed in the subarachnoid space [3]. However, since the processes leading to brain damage after SAH are extremely complex and are not solely a consequence of hemodynamic impairment,

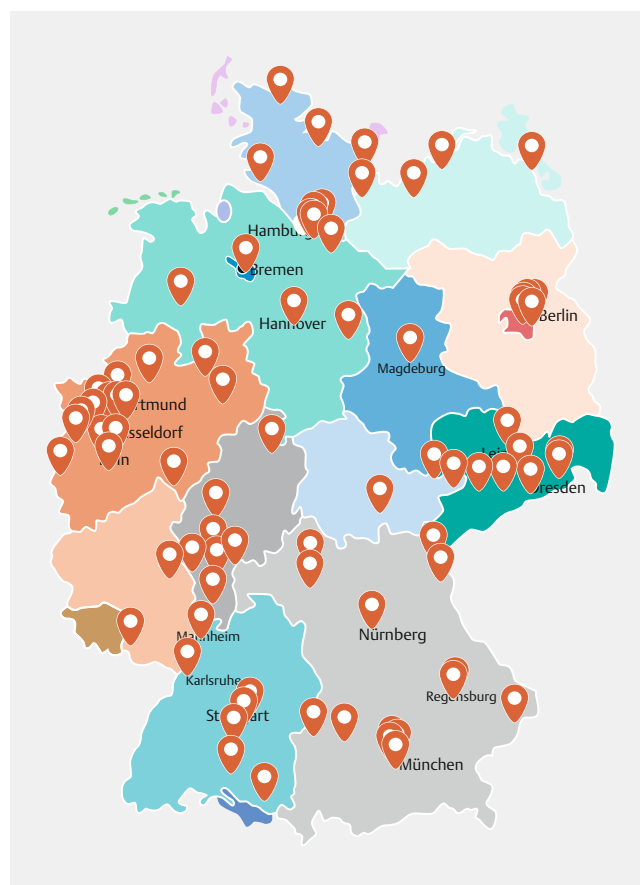
the term delayed cerebral ischemia (DCI) has also been adopted in recent years [4].

In addition to optimizing blood volume and cardiac performance, only the systemic, oral administration of the calcium channel antagonist nimodipine has been an evidence-based treatment for the prevention and treatment of CVS to date [3, 5, 6]. In contrast, there is a lack of prospective randomized trial results on the efficacy of endovascular vasospasm treatments (EVT); however, these are explicitly mentioned in, among others, guidelines of the American professional societies on additive treatment of CVS [5]. There is no doubt that angiographic interventions with topical application of vascular vasodilators as well as balloon angioplasty (BA) are performed in a very large number of institutions, including in Central Europe and especially Germany [3, 7, 8].

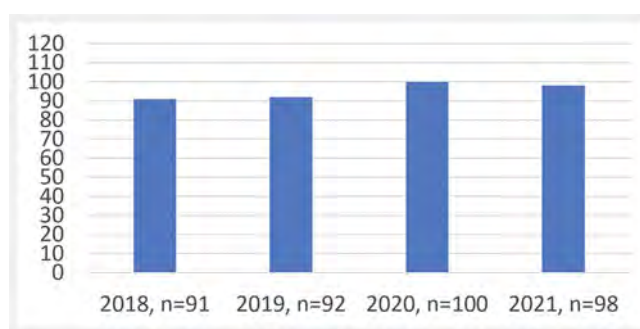
The group of intra-arterially administered substances with a vasodilating effect is dominated by nimodipine as a dihydropyridine blocker, which inhibits the flow of extracellular calcium through voltage-dependent L-type ion channels [9]. A temporary improvement in cerebral circulation has been described for nimodipine in the context of EVT [7]. In addition, for example, a recent study on CVS comparing systemic and additionally topically applied nimodipine has not shown any disadvantages in patients who are treated intraarterially and at the same time are initially in a clinically poorer state, suggesting a positive effect of such a local treatment [10]. Other substances used intra-arterially include papaverine, amrinone, milrinone, verapamil, nicardipine, fasudil hydrochloride, and forskolin derivative [11]. Balloon angioplasty is predominantly performed in addition to EVT with medication, with both non-compliant and compliant balloon catheters [12]. In addition, topical long-term drug therapies using micro-catheters and vascular dilatation with stent retrievers or other non-occlusive stents are used [13–15]. Furthermore, in the case of recurrent CVS, case series on long-term stent angioplasty can also be found [16]. In general, there is a lack of agreed recommendations on the indication and standardized implementation of EVT to date. The guidelines of the American Heart Association/American Stroke Association (AHA/ASA) describe the implementation of EVT as generally useful [5]. In contrast, the guideline of the German Society of Neurology (DGN), which was published in 2012, only suggests that EVT should be considered “on a case-by-case basis” [17].

In 2012, the German Society for Neuroradiology (DGNR) initiated a database for the purpose of the documentation and quality assurance of neuroradiological interventions, divided into neurovascular re-canalization (module E) and neurovascular embolization (module F) procedures on the vessels supplying the brain. Both modules were incorporated into the database of the German Society for Interventional Radiology and Minimally Invasive Therapy (DeGIR), which has documented general radiological interventions since 2005 (modules A–D). The main reasons for these web-based, voluntary registry data are to monitor and assure the quality of different interventional procedures; overall, there is an increasing number of participating hospitals in Germany and individual centers in Austria and Switzerland [18]. The registry data allow us to take a closer look at the reality of the care situation for endovascular procedures, as has already been demonstrated in publications on the treatment of acute ischemic stroke [19].

This study aimed to provide the first systematic evaluation of EVT which have been continuously recorded in Germany since 2018. For this purpose, the following categories were analyzed: pre-interventional findings of the CT perfusion and the patient's level of consciousness; with regard to EVT, the radiation dose applied, interventional parameters (topical medication, devices, angiographic result), and post-interventional symptomatology, any complications, and mortality.



► **Fig. 1** Map of DeGIR/DGNR centres (as of February 2023). Of 195 clinics/institutes, 96 are currently certified for Module E (“Vascular Opening Neuro-Interventions”) and thus potentially perform endovascular spasm therapies. Source map of Germany: Hell W. Bundesstaat. In: Hell W, Hrsg. Alles Wissenswerte über Staat, Bürger, Recht. 8., aktualisierte Auflage. Stuttgart: Thieme; 2018. doi:10.1055/b-005-145216.



► **Fig. 2** Endovascular spasm therapies: Participating centres.

Materials and methods

A retrospective analysis of the clinical and procedural data in the DeGIR registry (module E, neurovascular re-canalization) was carried out in anonymized form from 91 (2018), 92 (2019), 100 (2020), and 98 (2021) centers that documented EVT (► **Fig. 1, 2**). Prior to the intervention, the query points were abnormalities

in the CT perfusion as well as the state of consciousness of the patients (intubated/not assessable, focal neurologic deficit). In addition, the dose area product (DAP) as well as periprocedural complications (transient or long-term neurological deficit, dissection, acute thromboembolism, vascular occlusion, intraprocedural bleeding, material dislocation) and mortality associated with the intervention were inquired about for each individual Intervention. In addition to the localization of the vasospasm, the topically applied drug and devices used, as well as the angiographic treatment outcome (eliminated, improved, or unchanged), should be documented. Patients were also asked about their symptoms after the procedure.

The anonymized records from the registry database for module E (subcategory vasospasm) of each participating center were exported to a web-based spreadsheet program and viewed by several members of the DeGIR and DGNR. In the event of incomplete or inconsistent data, it was at the discretion of the authors to exclude implausible values in individual cases from the survey or not to evaluate individual categories. The statistical analysis was carried out after the data were transferred to IBM SPSS (version 28.0), calculating variation widths (= range) and means or median values as well as stating interquartile distances (= interquartile range [IQR]) for continuous values. The frequencies of categorical variables were presented in relation to the respective proportion of the total quantity. Independent samples with continuous values could be examined bilaterally using the Mann-Whitney U test; the chi-square test was used to compare independent samples of categorical values. In the case of dichotomous features, Fisher's exact test was used as an alternative. Statistical significance was assumed in each case with a probability of error of $p < 0.05$.

The examinations were subject to a positive ethics committee vote (file number 21-480).

Results

General information on endovascular vasospasm treatments in Germany 2018–2021

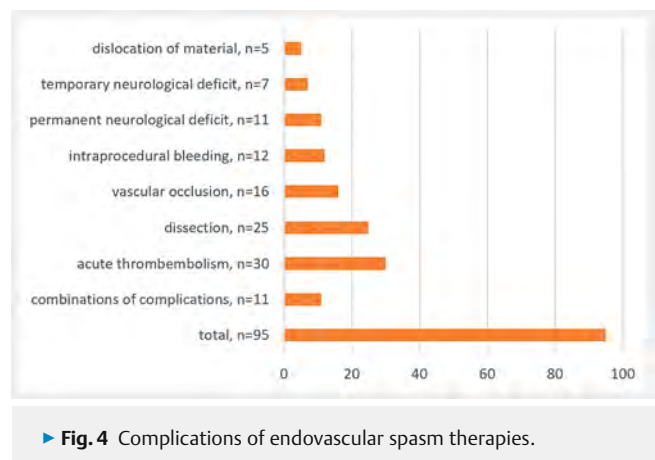
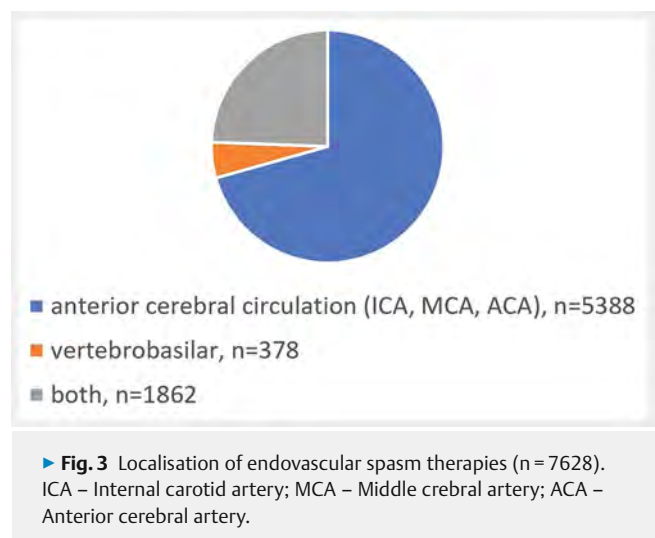
Between 1 January 2018 (00:00 am) and 31 December 2021 (24:00 am), a total of 3584 patients from 91 (2018), 92 (2019), 100 (2020), and 98 (2021) centers received a cumulative 7628 endovascular treatments for CVS.

The median age of patients was 53 years (range 13–100, IQR 44–60); 2443 patients were female (68.2%). Each patient received an average of 2.1 interventions.

Of all EVT, 5388 (70.6%) were performed in the anterior circulation (internal carotid artery, middle cerebral artery, and anterior cerebral artery) and 378 (5%) were performed in the vertebrobasilar system; in 1862 cases (24.4%) both areas were involved (► Fig. 3).

Single EVT were performed in 2125 (27.9%) of the procedures.

In 5593 procedures (73.3%), patients were intubated or could not be neurologically assessed for other reasons at the time of Intervention. A focal neurologic deficit was reported in 1675 cases (22%).

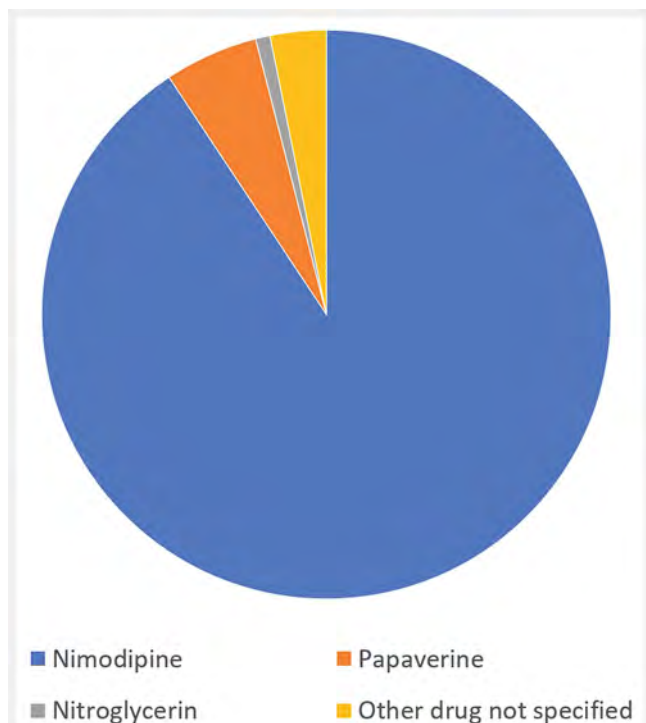


Prior to the EVT, abnormalities were observed in 2254 cases (29.6%) based on CT perfusion; however, these were not specified in more detail based on the registry query.

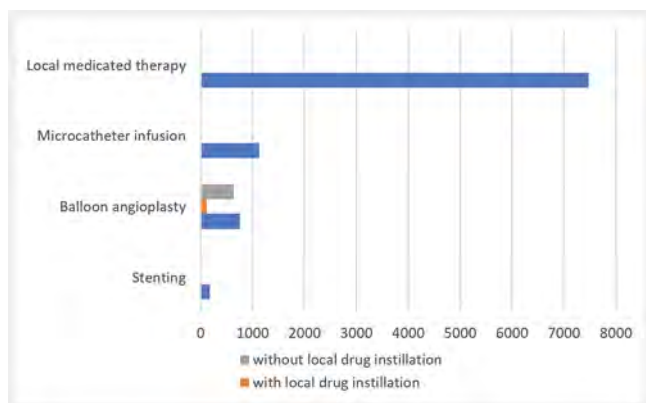
The median dose area product during the EVT was 4069 cGycm² (IQR 2451–7359) for the single intervention.

At least one complication was documented in 95 out of a total of 7628 (1.2%) EVT. Complications included, in particular: acute thromboembolism (n = 30), dissection (n = 25), vascular occlusion (n = 16), intraprocedural bleeding (n = 12), long-term neurological deficit (n = 11), transient neurological deficit (n = 7), material dislocation (n = 5); in 11 cases, combinations of complications were present. The mortality associated with EVT was 0.2% (n = 18) (► Fig. 4).

The EVT was performed with medication in 7476 cases (98%). The topical application of only one active ingredient was with nimodipine in 6835 procedures (91.4%), with papaverine in 401 procedures (5.4%), with nitroglycerin in 62 procedures (0.8%), and with another non-specified pharmaceutical in 239 cases (3.2%). In 90 cases (1.2%), topically combined drug administrations were documented (nimodipine + papaverine n = 71, nimodipine + nitroglycerin n = 16, and papaverine + nitroglycerin n = 3) (► Fig. 5).



► **Fig. 5** Substances used in endovascular spasm therapies with medication alone (n = 7476).

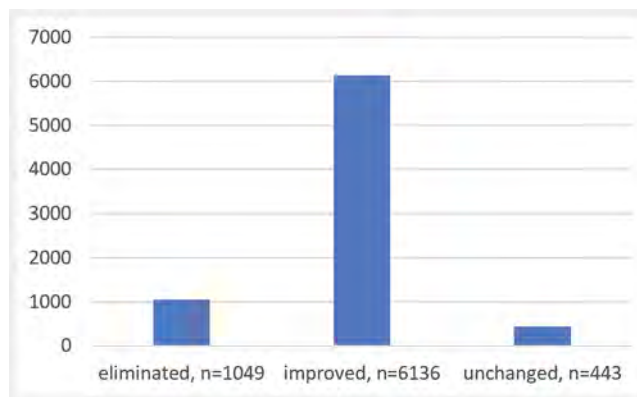


► **Fig. 6** Type of all endovascular spasm therapies (n = 7628).

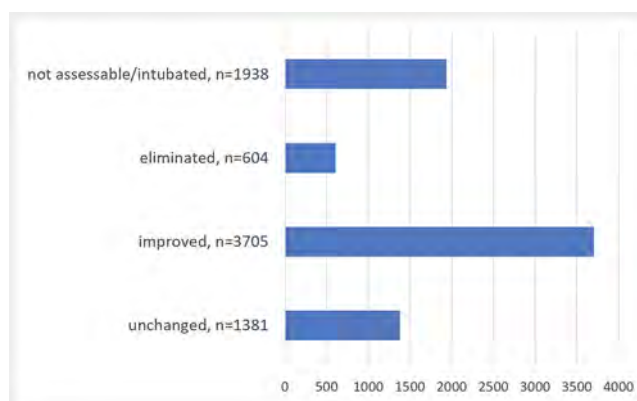
Long-term drug treatment with a microcatheter infusion was reported in 1132 EVT (14.8%). The median DAP was 5598 cGycm² (IQR 3296–10389), and at least one complication (2.7%) occurred in 30 of these procedures.

BA was performed in 756 cases (9.9%) (of which 638 were combined with local drug administration). Other unspecified mechanical recanalizations were performed in 154 EVT (2%). Intracranial stenting was documented in 176 cases (2.3%) (► **Fig. 6**).

For all EVT, CVS was eliminated angiographically in 1049 cases (13.8%), improved in 6136 cases (80.4%), and unchanged in 443 cases (5.8%) (► **Fig. 7**).



► **Fig. 7** Angiographic outcome after endovascular spasm therapies (n = 7628).



► **Fig. 8** Symptomatology of patients after endovascular spasm therapies (n = 7628).

After the EVT, the symptomatology of the patients was documented as follows: n = 1381 unchanged (18.1%), n = 3705 improved (48.6%), n = 604 eliminated (7.9%), n = 1938 unassessed/intubated (25.4%) (► **Fig. 8**).

Focused analyses of endovascular vasospasm treatments in Germany 2018–2021

Comparison of periprocedural radiation exposure and complications, as well as angiographic results after endovascular vasospasm treatments with medication and (additional) balloon angioplasty:

The median DAP was 4002 cGycm² (IQR 2554–6982) for the single EVT with medication and 8003 cGycm² (IQR 4772–12785) for an (additional) BA. This difference was statistically significant ($p < 0.001$).

In EVT with medication alone (n = 6838), at least one complication occurred in 67 cases (1.1%). If a BA was (additionally) implemented (n = 756), at least one complication (4.2%) was documented 28 times. There was a statistically significant difference between the two groups ($p < 0.001$).

When comparing the angiographic results, CVS was eliminated in 814 cases (11.9%), improved in 5599 cases (81.9%), and unchanged in 425 cases (6.2%) after EVT with medication alone.

► **Table 1** Comparison of periprocedural radiation exposure(s) and complications as well as angiographic outcomes after drug-only endovascular spasm therapies and (additional) balloon angioplasty.

	Medicated endovascular spasm therapies (n = 6838)	(Additional) Balloon angioplasty (n = 756)	p-value
Dose area product (IQR)	4002 (2554–6982)	8003 (4772–12 785)	< 0.001
Complications	n = 67 (1.1 %)	n = 28 (4.2 %)	< 0.001
Angiographic result			
▪ Spasm eliminated	n = 814 (11.9 %)	n = 224 (29.6 %)	
▪ Spasm improved	n = 5599 (81.9 %)	n = 518 (68.5 %)	
▪ Spasm unchanged	n = 425 (6.2 %)	n = 14 (1.9 %)	< 0.001

► **Table 2** Comparison of angiographic results after endovascular spasm therapies with nimodipine and papaverine alone and related to the individual intervention depending on gender.

	Spasm eliminated	Spasm improved	Spasm unchanged	p-value
Local medication				
▪ Nimodipine (n = 6748)	n = 892 (13.2 %)	n = 5462 (80.9 %)	n = 394 (5.9 %)	
▪ Papaverine (n = 401)	n = 71 (17.7 %)	n = 320 (79.8 %)	n = 10 (2.5 %)	0.001
Gender				
▪ Female (n = 5086)	n = 668 (13.1 %)	n = 4138 (81.4 %)	n = 280 (5.5 %)	
▪ Male (n = 2542)	n = 381 (15 %)	n = 1998 (78.6 %)	n = 163 (6.4 %)	0.016

In the case of BA, either in addition to topical medication or on its own, the baseline findings of CVS were eliminated after 224 EVT (29.6 %), improved in 518 (68.5 %), and remained unchanged in 14 (1.9 %). These differences between the groups were also statistically significant ($p < 0.001$) (► **Table 1**).

Comparison of angiographic results after endovascular vasospasm treatment with nimodipine and papaverine and with respect to individual intervention depending on age:

When looking at the angiographic results after EVT with the two most commonly used substances nimodipine (n = 6748) and papaverine (n = 401) alone, papaverine showed better results in terms of the complete elimination of the vasospasm (in 71/401 cases [17.7 %] compared to nimodipine in 892/6748 cases [13.2 %]). There was a statistically significant difference between the two groups ($p = 0.001$).

Also focusing on the endpoint of angiographic results, a comparison of the group was made by sex (female n = 5086, male n = 2542) with regard to the single EVT. In 381 cases (15 %), men were more likely to have complete elimination of the vasospasm than women (n = 668, 13.1 %). Again, the differences between the groups were statistically significant ($p = 0.016$) (► **Table 2**).

Discussion

During this study, the endovascular treatments for CVS, which have been continuously recorded in the DeGIR registry since 2018, were systematically evaluated for the first time. In this regard, the results of this “real-world” analysis showed an average of more than one neuroradiological intervention for each patient (mean 2.1), which underscores the clinical significance of EVT. Recurrent vasospasms are also frequently reported in the existing literature, and it has been shown that multiple EVT are worthwhile even in initially clinically poorer patients, as favorable courses can be achieved with a locally supported treatment strategy [20].

The radiation exposure associated with the individual EVT (median DAP 4069 cGycm²) appears to be moderate overall. This is consistent with recently published results from a working group from Essen that described EVT (with nimodipine) compared to other therapeutic interventions such as thrombectomy or aneurysm coiling as having a substantially lower radiation exposure [21].

Overall, evaluations of registry data showed very few complications in the context of EVT (1.2 %, predominantly acute thromboembolisms and dissections). This is consistent with previously published results from smaller cohorts in which evaluations had only rarely shown periprocedural complications [22]. Mechanical vasospasm treatment with BA, on the other hand, showed a

slightly higher complication rate (4.2%), but this can be considered low in comparison with individual published papers from German hospitals [23].

Endovascular vasospasm treatments were performed with medication in 7476 cases (98%); the use of nimodipine alone was clearly dominant (91%). This active ingredient is attributed superiority over other substances for its vasodilating effect in catheter angiographic images [24]. In addition, the registry data showed an EVT with the combination of different medications in 90 cases (1.2%). Analyses on their specific efficacy have already been the subject of dedicated studies by individual centers [25]. Long-term drug treatment with a microcatheter infusion was found in the cohort studied in 1132 (14.8%) of all interventions. This procedure has already been described with a relatively high overall number of side effects and at least an increased rate of catheter-associated thromboembolism [13]. Even after our evaluation, the complication rate was 2.7% higher than the total number of EVT (1.1%).

Based on the evaluated registry data, BA was relatively rarely used for EVT (in almost 10% of all documented interventions). If it was used, this was predominantly in combination with topical medication (84.4%). This is consistent with previously published studies describing mechanical angioplasty as an additive procedure in EVT [12].

Unspecified mechanical recanalizations were performed in 154 cases of all EVT (2%). Although the exact name of the materials is missing in the queries, the use of stent retrievers for temporary vasodilation is primarily to be assumed here based on the existing literature [14]. As part of the evaluation of this method, an opinion procedure was initiated in January this year before a final decision on a policy for testing the material is made by the Federal Joint Committee (GBA) [26]. In addition, other non-occlusive stents are also used [15]. The frequency of stenting in 176 cases of all EVT (2.3%) also seems interesting. In the literature, such implantations have been described as “bail-out” options [16].

In addition, the focused analysis of the registry data looked at the comparison of EVT performed with medication alone and (additional) BA. With regard to periprocedural radiation exposure (median DAP 8003 vs. 4012 cGycm²), of complication rates (4.2 vs. 1.1%) and angiographic treatment outcome (vasospasm eliminated or improved in 93.8% vs. 88.1%), the values were each statistically significantly higher or better after using mechanical vascular dilatation. This supports BA as a more effective but also significantly more invasive procedure. However, the different group size must be mentioned in this comparison (ratio of EVT with medication alone/[+]BA is approximately 10:1).

In addition, the angiographic outcome of topically treated CVS was considered in more detail as an endpoint. In EVT performed with medication alone, the two most commonly used substances nimodipine (n = 6838) and papaverine (n = 401) were compared. Here, a better therapeutic effect of papaverine in terms of eliminating the vasospasm could be shown, and the difference between the groups was statistically significant, although again a very different group size had to be considered (in total, nimodipine were instilled intraarterially more than 15 times more often than papaverine). In principle, these results are consistent with work by Kerz et al., who had seen better angiographic results

with EVT with papaverine, but did not include effects on the outcome [27]. A further analysis of the angiographic result was performed for the individual EVT in relation to the sex of the patients (female n = 5086, male n = 2542). Men were more likely to show complete elimination of the vasospasm (15% vs. 13.1%) and the difference between the two groups was statistically significant. These results encourage further studies with the dedicated assessment of factors influencing the course of therapy in CVS.

Limitations

The large number of all EVT documented anonymously in the DeGIR registry in the years 2018–2021 results in a considerable amount of data and the corresponding complexity of evaluation. This is a large case series without a comparator group.

The registry data show some fundamental deficiencies. In some cases, we found extreme values that were implausible to us, and which were excluded from the analysis in individual cases. Thus, our evaluation is subject to a certain degree of preselection, the overall influence of which we consider to be low. It is difficult to rule out incorrect entries overall; this problem has already been highlighted in publications of evaluations of other DeGIR registry data [28].

In general, there is a lack of queries about the initial clinical condition as well as the potential source of bleeding and its treatment (endovascular embolization or neurosurgical operation) of the examined patients with CVS. Furthermore, the data do not allow us to determine whether there was an underlying subarachnoid hemorrhage due to an aneurysm or another reason, and what was the cause of the CVS. Corresponding influences on the clinical course are also the subject of recently published papers [29].

Another limitation is the non-unified, presumably semi-quantitative evaluation of angiographic results after EVT. There is also a lack of information on the dosage of the topically used drugs. In addition, due to the BA, which is often used in combination with medications, its exact influence on the angiographic result and further course remains unclear (confusion effects). In addition, the information on the initial distribution of CVS is inaccurate, so that the influences of the exact vasospasm distribution (if only roughly subdivided into anterior and posterior circulation) cannot be clarified in detail. This specific topic complex was also the focus of a recent study, and the results were published [30].

Only part of the documented information on the course of clinical symptomatology is available, as this is not a mandatory query in the DeGIR registry data. For example, in 5595 cases after EVT, patients were described as intubated or otherwise unable to be assessed, compared to only 1938 patients before the procedure. Queries about individual outcome parameters are completely missing.

Conclusion

This analysis of a very large data set (7628 interventions, 3584 patients) from many different centers (91 [2018], 92 [2019], 100 [2020] and 98 [2021]) provides a valuable overview of the current

care situation for EVT in Germany. In general, the DeGIR registry data are suitable for answering more specific questions in an interventional context, especially because of the large number of cases.

However, it is clear that further improvements in the documentation of data must be pursued for this purpose. The overarching goal must be to improve both the query points and the input quality. The first is the responsibility of the professional associations; the type of registry management should be systematically reviewed together with the persons entering the data. Information on the initial clinical condition, on the pre-interventional diagnosis, and possibly also on the outcome in the future is only possible with specialist and detailed knowledge. The goal should be to ensure a greater obligation to enter data and to place a stronger emphasis on the clinical outcome.

In order to improve the treatment of CVS in Germany, it is desirable to combine clinical and interventional registry data and to establish agreed treatment guidelines for the future. In addition, targeted studies on quality differences between individual centers and on the value of newer devices in mechanical angioplasty should be promoted, among other things.

It would be desirable to supplement the database with information on the initial clinical situation, source of bleeding and its treatment procedures, as well as outcome.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

- [1] de Rooij NK, Linn FH, van der Plas JA et al. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. *J Neurol Neurosurg Psychiatry* 2007; 78 (12): 1365–1372
- [2] Dorsch NW, King MT. A review of cerebral vasospasm in aneurysmal subarachnoid haemorrhage Part I: Incidence and effects. *J Clin Neurosci* 1994; 1 (1): 19–26
- [3] Li K, Barras CD, Chandra RV et al. A Review of the Management of Cerebral Vasospasm After Aneurysmal Subarachnoid Hemorrhage. *World Neurosurg* 2019; 126: 513–527
- [4] Vergouwen MD, Vermeulen M, van Gijn J et al. Definition of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage as an outcome event in clinical trials and observational studies: proposal of a multidisciplinary research group. *Stroke* 2010; 41 (10): 2391–2395
- [5] Connolly ES Jr, Rabinstein AA, Carhuapoma JR. American Heart Association Stroke Council; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; Council on Cardiovascular Surgery and Anesthesia; Council on Clinical Cardiology et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2012; 43 (6): 1711–1737
- [6] Francoeur CL, Mayer SA. Management of delayed cerebral ischemia after subarachnoid hemorrhage. *Crit Care* 2016; 20 (1): 277
- [7] Hänggi D, Turowski B, Beseoglu K et al. Intra-arterial nimodipine for severe cerebral vasospasm after aneurysmal subarachnoid hemorrhage: influence on clinical course and cerebral perfusion. *AJNR Am J Neuroradiol* 2008; 29 (6): 1053–1060
- [8] Mielke D, Döring K, Behme D et al. The Impact of Endovascular Rescue Therapy on the Clinical and Radiological Outcome After Aneurysmal Subarachnoid Hemorrhage: A Safe and Effective Treatment Option for Hemodynamically Relevant Vasospasm? *Front Neurol* 2022; 13: 838456
- [9] Carlson AP, Hänggi D, Macdonald RL et al. Nimodipine Reappraised: An Old Drug With a Future. *Curr Neuropharmacol* 2020; 18 (1): 65–82
- [10] Walter J, Grutza M, Möhlenbruch M et al. The Local Intraarterial Administration of Nimodipine Might Positively Affect Clinical Outcome in Patients with Aneurysmal Subarachnoid Hemorrhage and Delayed Cerebral Ischemia. *J Clin Med* 2022; 11 (7): 2036
- [11] Hasegawa S, Hasegawa Y, Miura M. Current Therapeutic Drugs Against Cerebral Vasospasm after Subarachnoid Hemorrhage: A Comprehensive Review of Basic and Clinical Studies. *Curr Drug Deliv* 2017; 14 (6): 843–852
- [12] Schacht H, Kuchler J, Boppel T et al. Transluminal balloon angioplasty for cerebral vasospasm after spontaneous subarachnoid hemorrhage: A single-center experience. *Clin Neurol Neurosurg* 2019; 188: 105590
- [13] Kapapa T, König R, Mayer B et al. Adverse Events and Complications in Continuous Intra-arterial Nimodipine Infusion Therapy After Aneurysmal Subarachnoid Hemorrhage. *Front Neurol* 2022; 12: 812898
- [14] Hensler J, Wodarg F, Madjidyar J et al. Efficacy and safety in the use of stent-retrievers for treatment of cerebral vasospasms after subarachnoid hemorrhage. *Interv Neuroradiol* 2022. doi:10.1177/15910199221086389
- [15] Salem MM, Khalife J, Desai S et al. COManeci MechANical dilation for vasospasm (COMMAND): multicenter experience. *J Neurointerv Surg* 2022. doi:10.1136/jnis-2022-019272 Epub ahead of print.
- [16] Khanafer A, Cimpoca A, Bhogal P et al. Intracranial stenting as a bail-out option for posthemorrhagic cerebral vasospasm: a single-center experience with long-term follow-up. *BMC Neurol* 2022; 22 (1): 351
- [17] Deutsche Gesellschaft für Neurologie (DGN). S1-Leitlinie Subarachnoidalblutung (SAB) (Version 4.0 der [online]), 30.09.2012. Verfügbar unter (Zugriff am 24.02.2023): <https://register.awmf.org/de/leitlinien/detail/030-073>
- [18] Berlis A, Morhard D, Weber W. On the Basis of the DeGIR/DGMR Register Nationwide Care for Acute Ischemic Stroke Patients in 2016 and 2017 Using Mechanical Thrombectomy by Radiologists and Neuroradiologists. *Fortschr Röntgenstr* 2019; 191 (7): 613–617
- [19] Rohde S, Weber W, Berlis A et al. Acute Endovascular Stroke Treatment in Germany in 2019. *Clin Neuroradiol* 2021; 31: 11–19
- [20] Ditz C, Neumann A, Wojak J et al. Repeated endovascular treatments in patients with recurrent cerebral vasospasms after subarachnoid hemorrhage: a worthwhile strategy? *World Neurosurg* 2018; 112: e791–e798
- [21] Opitz M, Zensen S, Bos D et al. Radiation exposure in the intra-arterial nimodipine therapy of subarachnoid hemorrhage related cerebral vasospasm. *J Radiol Prot* 2022; 42 (1). doi:10.1088/1361-6498/ac32a2
- [22] Jabbarli R, Pierscianek D, Rölz R et al. Endovascular treatment of cerebral vasospasm after subarachnoid hemorrhage: More is more. *Neurology* 2019; 93 (5): e458–e466
- [23] Adami D, Berkefeld J, Platz J et al. Complication rate of intraarterial treatment of severe cerebral vasospasm after subarachnoid hemorrhage with nimodipine and percutaneous transluminal balloon angioplasty: Worth the risk? *J Neuroradiol* 2019; 46 (1): 15–24
- [24] Jentzsch J, Ziganshyna S, Lindner D et al. Nimodipine vs. Milrinone – Equal or Complementary Use? A Retrospective Analysis. *Front Neurol* 2022; 13: 939015
- [25] Sherif C, Wambacher B, Loyoddin M et al. Repeated combined endovascular therapy with milrinone and nimodipine for the treatment of severe vasospasm: preliminary results. *Acta Neurochir Suppl* 2015; 120: 203–207
- [26] <https://www.g-ba.de/bewertungsverfahren/methodenbewertung/264/> (Zugriff am 24.02.2023).

- [27] Kerz T, Boor S, Beyer C et al. Effect of intraarterial papaverine or nimodipine on vessel diameter in patients with cerebral vasospasm after subarachnoid hemorrhage. *Br J Neurosurg* 2012; 26 (4): 517–524
- [28] Nadjiri J, Geith T, Wiggershauser T et al. Comparison of radiation exposure in common hepatic interventions: A retrospective analysis of DeGIR registry data. *Radiologe* 2021; 61 (1): 80–86. doi:10.1007/s00117-020-00737-8 German. PMID: 32816049; PMCID: PMC7810650.
- [29] Göttische J, Piffko A, Pantel TF et al. Aneurysm Location Affects Clinical Course and Mortality in Patients With Subarachnoid Hemorrhage. *Front Neurol* 2022; 13: 846066
- [30] Cole TS, Rudy RF, Faridmoayer E et al. Relationship between cerebral vasospasm vascular territory and functional outcome after aneurysmal subarachnoid hemorrhage. *J Neurointerventional Surg* 2022. doi:10.1136/jnis-2022-019016 Epub ahead of print.