Original research

Cerebral aneurysms: Germany-wide real-world outcome data of endovascular or neurosurgical treatment from 2007 to 2019

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ABSTRACT

Background Evidence on clinical outcome after endovascular treatment (EVT) vs neurosurgical clipping of intracranial aneurysms (IAs) is based on one randomized and one pseudo-randomized trial for ruptured aneurysms. Herein, we analyze nationwide real-world hospital outcomes after EVT vs clipping of ruptured and unruptured IAs.

Methods This cohort study analyzed all EVT and clipping procedures for IAs in Germany between 2007 and 2019. The data basis was the billing-data of all German hospitals from the German Federal Statistical Office. EVT and clipping interventions, comorbidities, and in-hospital outcomes were identified using International Classification of Diseases (ICD) and Operation and Procedure (OPS) codes. Discharge type was used as a surrogate marker for functional independence. Poor clinical outcome at discharge was additionally defined by the dichotomous US National Inpatient Sample-Subarachnoid hemorrhage Outcome Measure score (NIH-SOM). Secondary outcomes included length of hospital stay, prolonged mechanical ventilation (>48 hour), and hospital reimbursement.

Results We analyzed 90 039 procedures (62.6% EVT, 35.52% clipping, 1.8% combined) for the treatment of IAs. After adjustment in-hospital mortality was equal after EVT compared with clipping, in ruptured IAs (adjusted OR (aOR) 0.98, p=0.707) and unruptured IAs (aOR 0.92, p=0.482). Functional independence was more likely after EVT for ruptured (aOR 0.81, p<0.001) and unruptured IAs (aOR 0.4, p<0.001). Poor clinical outcome was more likely after clipping for ruptured (aOR 0.67, p<0.001) and unruptured IAs (aOR 0.56, p<0.001).

Conclusions In German clinical practice, we observed higher rates of functional independence and lower rates of poor outcomes at discharge with equal mortality for EVT.

KEY MESSAGESWHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Comprehensive real-world data for the treatment of intracranial aneurysms is insufficient given the complexity of the disease with regards to the outcomes from the major therapeutic approaches of endovascular treatment vs neurosurgical clipping. Particularly the impact of treatment modality under real-world conditions needs to be monitored due to rapidly improving techniques, and is currently based largely on the National Inpatient Sample of the United States.

WHAT THIS STUDY ADDS

⇒ This study adds real-world outcome data from all German hospital in-patients with >90 000 procedures for ruptured and unruptured aneurysms between 2007–2019.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ There are clear differences in the real-world treatment situation between endovascular and neurosurgical treatment outcomes with regards to functional status at hospital discharge, length of hospital stay, and treatment costs that should be factored into the treatment decision.

INTRODUCTION

Endovscular treatment (EVT) and neurosurgical clipping (NSC) are the standard therapies for exclusion of ruptured and unruptured intracranial aneurysms (IAs) from the intracranial circulation to prevent bleeding.

Previous evidence supporting a better short-term, and midterm clinical outcome from EVT was based on the ISAT[1] (International Subarachnoid Aneurysm Trial) - a randomized controlled trial (RCT) that was performed in ruptured IAs, if the aneurysm was considered suitable for both clipping and EVT. Recently, long-term data (18 year follow-up) from ISAT and 6 year follow-up data from the Barrow Ruptured Aneurysm Trial (BRAT) which was a pseudo-randomized mono-institutional trial, were published.[2–4] However, generalizability of data from these trials for EVT for a broader range of ruptured IAs as well as for the use of newer EVT techniques has been questioned by recent studies. In particular, the external validity of ISAT may not be given as it included a lower proportion of patients with poor neurological grades (approximately 6%) than the general population of ruptured IA cases, aneurysms in ISAT were on average small and narrow-necked. Furthermore, EVT has since been developed using newer techniques and devices to approach aneurysms, which are wide-necked aneurysms or have other complex morphologies (eg,

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balloon remodeling technique, stent-assisted coiling, or flow-diverting stents) that were not used in ISAT.

Moreover, no RCT has been performed to compare EVT and NSC for treatment of unruptured aneurysms, and such study may be unlikely to occur in the future, as a long-term follow-up would be required to detect meaningful differences in outcome. Comprehensive recent meta-analyses comparing outcomes from both treatment modalities for unruptured and ruptured aneurysms from mostly nonrandomized observational studies with short- and long-term follow-up in the post-ISAT era, indicate a higher chance of independency and lower mortality after EVT.[5 6]

Hence, our study aims to assess real-world outcomes after aneurysm treatment free of restrictions derived from patient selection into clinical studies on the level of a nationwide cohort. To evaluate our hypothesis that EVT is associated with better outcomes than NSC in daily clinical practice, we studied in-hospital outcomes in the nationwide administrative dataset from an unselected series of patients admitted to a German hospital for IA treatment during an over ten-year interval (2007–2019).

METHODS

Data source, standard protocol approvals, registrations, and patient consents

Since 2005, the German Federal Statistical Office (DESTATIS) has provided anonymous, aggregated results on predefined requests on billing data using the diagnosis related group system of all hospital stays in Germany. This includes diagnoses (International Classification of Diseases, Tenth Revision, ICD-10) and procedures performed (according to “Operationen- und Prozedurenschlüssel”, a code of operations and procedures). On request, the data is available and can be used by anyone in accordance with the terms of use. In this study, only these public, aggregated routine health data were analyzed, consequently, no further approval by a local ethics committee or patient consent was required. The analysis is performed according to the RECORD guideline.[7]

Study population, treatment modalities, and group allocations

Inpatient cases with a billing code for treatment by EVT or NSC and a diagnosis of subarachnoid hemorrhage (SAH), intracerebral hemorrhage, or IA were identified during the years 2007–2019 (figure 1 and online supplemental table 1). To avoid erroneously including cases with other cerebrovascular diseases such as arteriovenous malformations or fistulas, which may also cause intracranial hemorrhage and may be treated with similar procedures, all cases with an additional coding for these diagnoses or an additional code for a typical treatment procedure for arteriovenous malformation such as embolization were excluded.

Inpatient cases were then divided into two groups: ruptured and unruptured IAs, based on the principal and secondary diagnoses coded according to ICD-10 and the type of hospital admission according to the definition in § 301 SGB V as follows:

- The ruptured group was selected by inpatient cases undergoing IA treatment with coded diagnosis of SAH or intracranial hemorrhage.
- Inpatient cases with IA treatment that lacked the diagnosis of bleeding (intracerebral hemorrhage or SAH) were assigned to the unruptured group.

To minimize sample contamination of ruptured IA cases with unruptured cases that suffered from hemorrhagic procedural complications, the following additional step was added to the selecting algorithm: inpatient cases with elective admission for IA treatment (no emergency or transfer from another hospital within the first 24 hours) and coding of IA as the principal diagnosis and intracranial hemorrhage as secondary diagnosis were considered as hemorrhagic complications of the procedure and were thus assigned to the unruptured IA group. According to the German diagnosis-related group (DRG) system, periprocedural hemorrhage should not be coded as principal diagnosis in an elective procedure. The diagnosis coded as principal should be the one determined to be primarily responsible for the patient’s hospitalization.

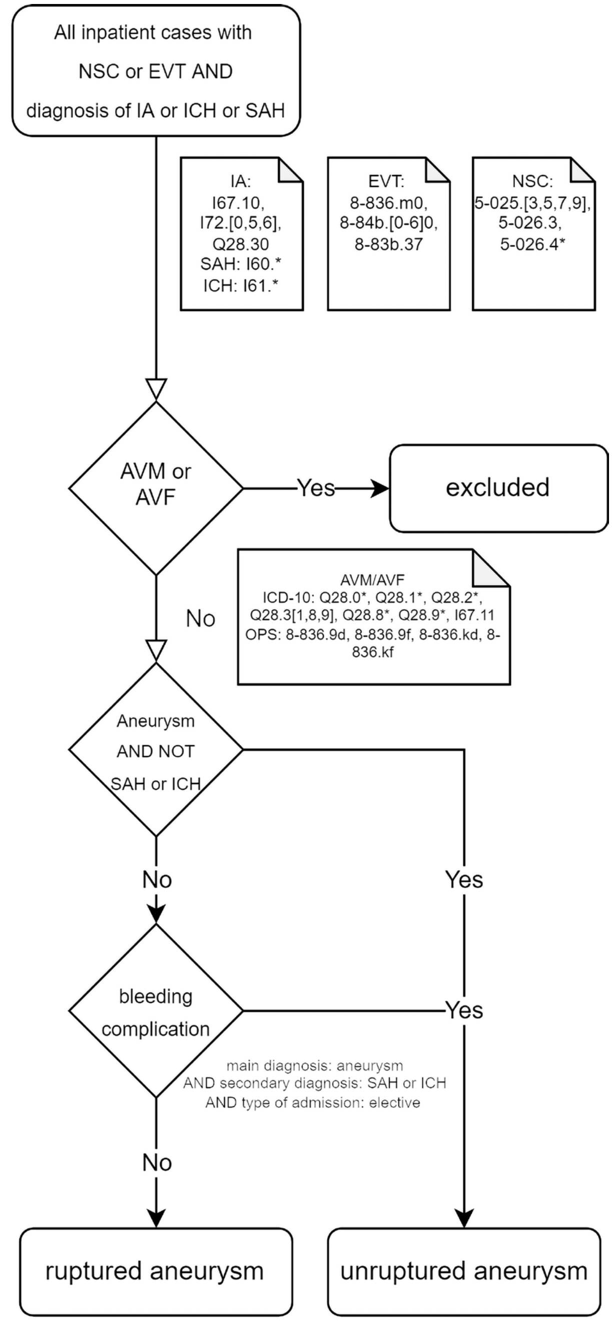

Figure 1 Flow chart for cohort definition of inpatient cases with ruptured and unruptured intracranial aneurysms. AVM, arteriovenous malformation; AVF, arteriovenous fistula (dural or pial); EVT, endovascular treatment; IA, intracranial aneurysm; ICH, intracranial hemorrhage; NSC, neurosurgical clipping; SAH, subarachnoid hemorrhage.

We used the Charlson Comorbidity Index (CCI) to determine the severity and number of comorbidities.[8]

Outcomes

The primary outcome was functional independence at hospital discharge and in-hospital mortality. These outcomes were derived from the type of hospital discharge according to §301 German Social Code V. As an ordinal measure of functional independence, the discharge types were further classified (online supplemental table 2) into three categories of functional outcome at hospital discharge:

1. Good outcome defined as discharge to home.
2. Intermediate outcome ("further therapy required").
3. Poor outcome (intrahospital death).

In addition to the functional outcome at discharge, the US National Inpatient Sample (NIS)-Subarachnoid hemorrhage Outcome Measure (NIS-SOM) score was derived as described by Washington *et al*.[9] This score additionally takes into account the placement of a tracheostomy tube and/or placement of a gastrostomy tube (online supplemental table 3), and was validated for SAH with 149000 cases from the National Inpatient Sample. The work shows a strong correlation between NIS-SOM as a dichotomous parameter for poor outcome and a modified Rankin Scale (mRS) >3 with an agreement and kappa statistic of 95% and 0.84, respectively.

As a surrogate marker for the severity of subarachnoid hemorrhage because of the unavailability of clinical scores such as the Hunt & Hess or Fisher Grading Scale, the NIS-SAH Severity Score (NIS-SSS) was included as described by Washington *et al*,[9] which is derived from diagnoses and procedures performed (eTable 4). We did not adjust the outcomes of the ruptured group for the NIS-SSS since many of the diagnoses that are included in this score, could be related to the SAH itself but may also represent a complication from the aneurysm treatment, for example, coma, aphasia, or paralysis.

Secondary outcomes included the duration of inpatient stay, the duration of mechanical ventilation, and the rate of prolonged ventilation (more than 48 hours), as well as the treatment costs according to the German DRG system.

Statistical evaluations

To assess the impact of treatment strategies (NSC or EVT) of IAs, multivariable logistic regression analyses were carried out. In the multivariable logistic regression analysis, age, sex and CCI were included as potential confounders. Furthermore, year of treatment (2007 to 2019) was included as categorical covariate. These multivariable logistic regression analyses were conducted separately for the endpoints in-hospital mortality, the NIS-SOM score, and an ordinal endpoint with the three stage discharge home, further treatment required and death. For the ordinal endpoint, we applied ordered logistic regression analysis. Cluster-robust standard errors were used to account for the correlation of error terms of patients treated in the same hospital.

No imputation for missing values could be conducted due to the absence of codes indicating that data were missing. If a patient's electronic health record did not include information on a clinical characteristic, it was assumed that this characteristic was not present. Furthermore, no adjustment for multiple testing was carried out. Thus, p-values may not be interpreted as confirmatory but are descriptive in nature and inferences drawn from the 95% confidence intervals may not be reproducible. All analyses were performed with Stata 16 (StataCorp, College Station, Texas, USA) by a biostatistician experienced with the DESTATIS data.

RESULTS

We identified 90039 inpatient cases who had IA treatment between 2007 and 2019. Of these, 43097 cases (47.9%) were classified as unruptured, 46942 (52.1%) as ruptured. At 62%, EVT was significantly ahead of NSC at 35% of cases. Clipping was used more frequently in ruptured aneurysms (39.6% vs 31.0%). The combination treatment (NSC and EVT) was a very rare procedure (1.8%) and about four times more frequent in the treatment of ruptured aneurysms (3.0% vs 0.7%). Due to the limitations of the DESTATIS dataset, no statement can be made about the temporal order of the combined treatment within the same in-hospital stay when codes for clipping and for coiling are present. The proportion of female patients was higher both in the groups of unruptured aneurysms (72%) and in ruptured aneurysms (66%). The average age was about the same in all groups (55 years). The CCI was low for all treatment modalities. However, the lowest CCI value (0.27) was found in the group of clipped inpatients with an unruptured aneurysm, and the highest CCI value (0.43) in the group of combined treated ruptured aneurysms. Baseline characteristics (table 1) showed no relevant differences between EVT and NSC groups.

For ruptured IAs (table 2) the in-hospital mortality was approximately 17% (EVT 17.51% vs NSC 17.32%). The resulting OR was not significant, even after adjustment for age, sex, and CCI (0.98, 95% CI 0.9 to 1.07). In contrast, in-hospital mortality was low with 1.3% for unruptured aneurysms (table 3) for both techniques; the adjusted OR was not significant (0.92, 95% CI 0.73 to 1.16). No relevant trend in mortality over time (years 2007–2019; eFigure 1) was seen in both treatment modalities, neither for ruptured (NSC, 14.17–21.26%; EVT, 16.25–19.13%) nor unruptured aneurysms (NSC, 0.88–1.96%; EVT, 0.99–1.68%).

Combination therapy had a significantly increased risk in unruptured cases with in-hospital mortality of 6.45%.

While in-hospital mortality was roughly similar between both treatment modalities, there were marked differences in the NIS-SOM score as a dichotomous marker for poor outcomes. A NIS-SOM was present in the ruptured aneurysms (table 2) in 38.67% of cases treated with EVT and in 47.64% of cases treated with NSC. The adjusted odds ratio for this was 0.67 (0.61–0.74).

In unruptured IAs (table 3), a NIS-SOM was present in 2.7% of cases treated with EVT and in 4.4% of cases treated with NSC. The adjusted odds ratio for this was 0.56 (0.47–0.66). The analysis of hospital discharge type (ordinal endpoint) showed a significantly higher rate of patients that were discharged home: 35.94% after EVT vs 29.53% after NSC, and 92.39% after EVT vs 84.2% after NSC in ruptured and unruptured IAs, respectively, with similar mortality (see above). The corresponding aORs were significant at 0.4 (0.35–0.47, 95% CI) for unruptured and 0.81 (0.75–0.88, 95% CI) for ruptured aneurysms.

The increased need for further treatment after discharge in clipped patients was consistent with the increased intensity of treatment during the inpatient stay. These were longer on average: 27 vs 23 days for ruptured, 13 vs 7 days for unruptured IAs, and required longer mechanical ventilation (258 hours vs 193 hours for ruptured, 26 hours vs 11 hours for unruptured IAs). Among unruptured aneurysms, 7% of clipped patients and 3.3% of EVT patients required ventilation for longer than 48 hours.

This intensity of treatment is also reflected in the costs. These were 22% higher in the group of ruptured aneurysms for the clipped patients (€31 073±27686 vs €38 089±33044) and

Table 1 Inpatient cases with intracranial aneurysms – baseline demographics

	Ruptured aneurysms			Unruptured aneurysms		
	Neurosurgical clipping (NSC)	Endovascular Therapy (EVT)	EVT+NSC	Neurosurgical Clipping (NSC)	Endovascular Therapy (EVT)	EVT+NSC
N	18 601	26 955	1386	13 377	29 410	310
Age, year, mean±SD	54.72±13.56	55,39±13.63	54.05±13.03	54.77±11.23	55.75±12.20	54.17±12.40
Sex: female	65.65%	66.40%	69.26%	71.69%	72.22%	72.90%
Charlson Comorbidity Index	0.41±0.64	0.41±0.64	0.43±0.63	0.27±0.37	0.29±0.57	0.34±0.65
Myocardial infarction	0.07%	0.12%	XXX	0.15%	0.16%	0.00%
Congestive heart failure	0.38%	0.38%	0.29%	0.29%	0.39%	0.00%
Peripheral vascular disease	0.03%	0.02%	0.00%	0.11%	0.08%	0.00%
Cerebrovascular disease	29.87%	29.76%	32.03%	14.71%	16.83%	21.61%
Dementia	0.30%	0.34%	XXX	0.18%	0.21%	0.00%
Chronic pulmonary disease	1.06%	0.91%	1.52%	1.40%	1.00%	1.61%
Connective tissue / rheumatic disease	0.08%	0.08%	0.00%	0.19%	0.18%	0.00%
Peptic ulcer disease	0.02%	XXX	0.00%	XXX	XXX	0.00%
Mild liver disease	0.92%	0.76%	1.15%	0.68%	0.41%	0.97%
Diabetes without complications	0.63%	0.68%	0.58%	1.99%	1.65%	1.29%
Diabetes with complications	0.03%	0.03%	0.00%	0.07%	0.06%	XXX
Paraplegia and hemiplegia	1.71%	2.26%	2.24%	1.40%	1.54%	2.26%
Renal disease	0.73%	0.55%	0.65%	0.87%	0.69%	0.97%
Cancer	0.27%	0.27%	0.29%	0.51%	0.37%	XXX
Moderate or severe liver disease	0.28%	0.20%	XXX	0.10%	0.04%	0.00%
Metastatic carcinoma	0.03%	0.02%	0.00%	0.00%	0.01%	0.00%
AIDS/HIV	0.05%	0.05%	0.00%	XXX	0.05%	0.00%
NIS-SSS	15.46	14.78	17.49			
NIS-SSS>7	79.79%	63.64%	79.58%			

EVT, endovascular treatment; NIS-SSS National Inpatient Sample-Subarachnoid hemorrhage Severity Score, NSC, neurosurgical clipping; SD, standard deviation

26% higher in the group of unruptured aneurysms (€13 369 ± €12 553 vs €10 502 ± €8283).

DISCUSSION

Our analysis of German billing data for the treatment of ruptured and unruptured IAs from 2007 to 2019 provides evidence of less invasive treatment with a lower morbidity in the group of EVT patients. The inpatient stay was shorter; fewer patients required prolonged ventilation and hospitalization costs were lower. With comparable in-hospital mortality, more patients were discharged directly home and fewer patients had a poor clinical outcome as defined by NIS-SOM.

Short-term outcomes were better in favor of EVT for both ruptured and unruptured IAs, although it differed significantly between the two groups due to the differences in pathophysiology. The treatment effect was measurable in SAH patients despite the significant influence of severity of SAH and delayed cerebral ischemia on clinical outcomes. The absence of these parameters in the dataset prevents statistical adjustment.

In contrast, our dataset of unruptured IAs was adjusted using CCI for any comorbidities included that may have influenced treatment-related outcomes.

By adding the NIS-SOM[9] as a validated mRS-equivalent, dichotomous marker for poor SAH outcome, we could provide a comprehensive assessment of inpatient outcomes at hospital discharge derived from administrative datasets considering mortality, a 3-point ordinal measure of hospital discharge status, and poor mRS outcome (NIS-SOM).

We assume our results provide an adequate representation of the real-world treatment situation in Germany between 2007–2019, since the data derived from DESTATIS are comparable in baseline structure to recent figures from the NIS in the USA.[10] In the latter analysis of 243 754 patients with ruptured and unruptured IAs between 2004 and 2014, the proportion of women was 71.6% and the mean age was 55.4 (our sample 55.3) years. Indeed, 50% of the treated aneurysms were unruptured (our sample 47.9%), of which 65.3% (our sample 68.2%) were treated endovascularly and 34.7% (our sample 31.0%) surgically. For ruptured aneurysms, the rate of those treated endovascularly was 56.6% (our sample 57.4%).

For in-hospital outcomes, our results reproduce earlier data from the NIS from 2001 to 2008 with observed lower morbidity and shorter hospital stay after EVT.[11] Regarding in-hospital mortality, Luther *et al*. presented more recent comparable data from the NIS that was derived from 1 14 137 ruptured and 1 22 916 unruptured IA cases between 2004 and 2014.[12] They found mortality rates in unruptured IAs of 0.49% (our sample 1.26%) after EVT and 0.68% (our sample 1.25%) after clipping. Moreover, the in-hospital mortality decreased in their clipping cohort from 1.6% in 2004 to 0.4% in 2014 and remained stable for EVT (0.59% vs 0.52%). In their ruptured cohort, in-patient mortality also decreased between 2004 and 2014 for clipped

Table 2 Primary and secondary outcomes in inpatient cases with ruptured intracranial aneurysms

	Endovascular therapy (EVT)	Neurosurgical clipping (NSC)	EVT+NSC	OR (EVT vs NSC)	aOR* (EVT vs NSC)
Inpatient cases with ruptured aneurysms, N	26 955	18 601	1386		
Primary endpoints					
Functional outcome at discharge (ordinal endpoint)				0.83 (95% CI 0.76 to 0.90, p<0.001)	0.81 (95% CI 0.75 to 0.88, p<0.001)
Good (discharge to home)	35.94%	29.53%	26.70%		
Intermediate (further hospital /rehab/nursing home)	46.54%	53.15%	57.14%		
Poor (intrahospital death)	17.51%	17.32%	16.16%		
In-hospital mortality	17.51%	17.32%	16.16%	1.01 (95% CI 0.93 to 1.11, p .767)	0.98 (95% CI 0.90 to 1.07, p .707)
NIS-SOM (modified Rankin Scale>3)	38.67%	47.64%	51.23%	0.69 (95% CI 0.63 to 0.76, p<0.001)	0.67 (95% CI 0.61 to 0.74, p<0.001)
Secondary endpoints					
Length of stay (in days), mean±SD	23.62±18.52	27.45±23.22	32.36±24.62		
Ventilation (in hours), mean±SD	193.38±276.37	257.86±297.61	324.14±349.29		
Ventilation>48 hour	49.34%	62.19%	70.20%		
Reimbursement (in €), mean±SD (available since 2010)	31 073±27 686	38 089±33 044	46 283±37 427		
n=refers only to reimbursement (2010–2017)	20 947	13 846	1082		

*Primary endpoints were adjusted for age, sex, comorbidity (Charlson Comorbidity Index), and year of treatment (2007 to 2019) as potential confounders
aOR, adjusted OR; CI, confidence interval; EVT, endovascular treatment; NIS-SOM, National Inpatient Sample-Subarachnoid hemorrhage Outcome Measure; NSC, neurosurgical clipping; OR, odds ratio; SD, standard deviation.

patients (13.0% vs 11.8%; our sample: 17.31%) as well as for endovascularly treated patients (15.7% vs 12.7%; our sample: 17.51%). Compared with NIS data,[10 12] in-hospital mortality was generally increased in our cohorts.

For the unruptured cases, the different algorithm for group assignment between the NIS and our sample could be causal for the differences in mortality rates. Whereas in the NIS sample all cases with ICD 9 code for SAH/ICH and aneurysm were assigned to the ruptured group,[10] the principal diagnosis and type of admission were additionally regarded for group allocation in our study. Thus, the unruptured group in our sample includes unruptured aneurysms (coded with IA as principal diagnosis and with elective admission status) with bleeding complications, which usually have a poor prognosis and may potentially have a fatal outcome. In addition, primary SAH cases that were incorrectly assigned by miscoding (when the IA but not the SAH was coded as primary diagnosis) may have been falsely included into the unruptured group. However, this error could affect both clipping and EVT cohorts equally.

Regarding the ruptured aneurysms, differences in mortality might be related to an increased severity of SAH/comorbidity at baseline in our sample compared with the NIS sample, that is, mean NIS-SSS was 15.46 (NIS-SSS >7 corresponding to Hunt & Hess score of 4–5, 79.79%) in NSC patients and 14.78 (NIS-SSS >7, 63.64%) in EVT patients from our ruptured cohort compared with 1.66 (NIS-SSS >7, 42.2%) in clipped patients and 1.74 (57.8%) in EVT patients from the NIS analysis.[9 12 13] Reasons for such imbalances may relate to a potential underrepresentation of severe SAH cases in the NIS, which represents a random 20% sample of US inpatient hospital records. Thereby, certain subspecialties may be potentially undersampled due to hospital preferences, thus rates from high-volume institutions for either treatment modality may be thus underrepresented in the NIS cohorts. Whereas our samples were taken from a nationwide database representing all German hospital inpatients.

By contrast, Lindgren *et al* reported an increased 14-day mortality after endovascular coiling (8.2% vs 6.4% after clipping) in acute SAH patients derived from an administrative dataset of 7658 patients (22 tertiary care hospitals from Europe, USA, Australia; 2007–2013).[14] Although they could correlate these results with outcomes from 1501 aneurysmal SAH patients derived from two European high volume centers, their findings may not be generalized and as representative as our analysis derived from a complete nationwide hospital sampling, or as the NIS data with overall by-far larger numbers of inpatient cases. Moreover, in the analysis by Lindgren at al. patients treated with other EVT techniques than coils were excluded.

When comparing treatment modalities for IAs, other outcome factors must be considered that are not included in the study data. Higher recanalization rates after EVT and the associated need for reinterventions may negate the advantage of a shorter hospital stay, depending on the extent.

The lower rate of discharge to home after clipping may not simply be equated with a worse outcome as following intensive rehabilitation treatment a favorable mRS outcome after 3 months may still be achievable. Moreover, improved neuropsychological outcomes following EVT in patients after aneurysmal SAH were not addressed in our data.[15]

Consistent analysis of existing routine data can make an important contribution to elaborate clinical trials and smaller case series with specific, rich datasets derived from nationwide hospital inpatient sampling, especially if the routine data are a

Table 3 Primary and secondary outcomes in inpatient cases with unruptured intracranial aneurysms

	Endovascular therapy (EVT)	Neurosurgical clipping (NSC)	EVT+NSC	OR (EVT vs NSC)	aOR* (EVT vs NSC)
Inpatient cases with unruptured aneurysms, N	29 410	13 377	310		
Primary endpoints					
Functional outcome at discharge (ordinal endpoint)				0.44 (95% CI 0.38 to 0.52, p<0.001)	0.40 (95% CI 0.35 to 0.47, p<0.001)
Good (discharge to home)	92.39%	84.20%	60.32%		
Intermediate (further hospital /rehab/nursing home)	6.35%	14.55%	33.23%		
Poor (intrahospital death)	1.26%	1.25%	6.45%		
In-hospital mortality	1.26%	1.25%	6.45%	1.01 (95% CI 0.80 to 1.27, p .947)	0.92 (95% CI 0.73 to 1.16, p .482)
NIS-SOM (modified Rankin Scale>3)	2.69%	4.40%	17.74%	0.60 (95% CI 0.51 to 0.71, p<0.001)	0.56 (95% CI 0.47 to 0.66, p<0.001)
Secondary endpoints					
Length of stay (in days), mean±SD	7.06±7.21	13.60±10.48	23.15±17.96		
Ventilation (in hours), mean±SD	11.31±77.44	26.19±120.00	107.28±230.46		
Ventilation >48 hour	3.28%	7.09%	25.48%		
Reimbursement (in €), mean±SD (available since 2010)	10 567±8283	13 369±12 553	24 425±24 638		
n=refers only to reimbursement (2010–2017)	24 987	11 006	*228*		

*Primary endpoints were adjusted for age, sex, comorbidity (Charlson index), and year of treatment (2007 to 2019) as potential confounders
aOR, adjusted OR; CI, confidence interval; EVT, endovascular treatment; NIS-SOM, National Inpatient Sample-Subarachnoid hemorrhage Outcome Measure; NSC, neurosurgical clipping; OR, odds ratio; SD, standard deviation.

good match. With regards to our sample taken from German administrative data, the finding of higher rates of functionally independent outcome after EVT is in line with the results from randomized and non-randomized trials with short and long-term outcome as reported in recent meta-analyses.[5 6]

Strengths and Limitations

Our study draws strength from its utilization of a large nationwide database intended to represent the German inpatient population accurately. The DESTATIS analysis also remains retrospective and provides no information regarding post-discharge course or readmissions, making analysis of long-term outcomes or re-hemorrhage rates impossible. Moreover, because of the sampling algorithm any patient admitted for retreatment of a recurrent/partially occluded aneurysm or transferred from another hospital would be analyzed as a new patient. This inherent bias prevents analysis of patients undergoing multiple treatments or crossing over from one treatment to another on separate admissions, and likely leads to an overestimation of the rates of EVT and an inability to account for the additive effects of repeat treatments on morbidity and mortality. It also provides no characteristics of aneurysm morphology or location, which are known to significantly affect clinical decision-making. Although there is no ICD-10 code for intraoperative aneurysm rupture, we utilized a dedicated algorithm to regroup cases with elective admission status and coding of SAH or intracranial hemorrhage as secondary diagnoses into the cohort of unruptured aneurysms to account for this complication. Correct coding of primary and secondary diagnoses is an important prerequisite to avoid false group allocations of cases. Any analyses performed on DESTATIS data rely on accurate ICD-10 and OPS coding which is inherently error-prone. These errors were well described in the literature early on, so the usability of billing data depends on the scientific question.[16] For cerebrovascular disease in Spanish billing data, for example, the basic suitability for statistical analysis has been demonstrated.[17]

Generally, our study design has several distinct limitations compared with retrospective registry studies that have to be taken into account. In contrast, traditional registries allow more clinical details, especially with regards to the patient's clinical admission status (ie, Hunt & Hess grades in ruptured IAs), aneurysm characteristics (size, morphology, and vessel location), operators' experience, and long-term functional (mRS) outcome.

Thus, our data does not enable to inform individual decision making which may rely on these factors. However, the analysis of a nationwide administrative dataset has several other advantages and can avoid limitations frequently encountered in traditional registries. As data transfer to Research Data Centers of the Federal Bureau of Statistics is mandatory in Germany, our cohort is virtually complete and avoids selection bias by individual investigators, which tends to result in an underestimation of risk in traditional studies. Compared with previous administrative analysis that only considered coiling procedures,[14] we also included cases treated by novel endovascular technologies, such as flow-diversion or WEB devices, which are increasingly being utilized as IA treatments.

However, incidental aneurysms are usually grouped together in traditional studies, our category of unruptured IAs also included symptomatic aneurysms that were not conspicuous by hemorrhage but, for example, by mass effect or cranial nerve compression.

The utilized administrative data are primarily collected for billing purposes and are therefore subject to optimization artifacts such as upcoding for revenue optimization. At the same time, medically relevant secondary diagnoses are unreliably coded if they play no role in the evaluation of the comorbidity index or if, due to special DRGs, the revenue is essentially defined by ventilation times or other measures. These effects are probably equally pronounced in both treatment modalities and should therefore not influence the comparison of the treatment groups, even if the absolute rate in both groups deviates from reality as a result.

CONCLUSIONS

In a nationwide comparison of 90 039 procedures for the treatment of IAs derived from German hospital in-patient administrative data, we found an advantage for EVT with regards to discharge to home, poor outcome at discharge, duration of inpatient treatment and ventilation, and costs. The demonstrated advantages of EVT relate exclusively to the period of inpatient treatment and allow no conclusion on long-term clinical course or radiological outcome regarding aneurysm exclusion. Thus, a well-balanced treatment decision should only be made by experienced neurovascular teams incorporating all individual patient's clinical and imaging data as well as long-term outcome data of the treatment modalities.

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Supplemental Material

Haverkamp C, Kaier K, Shah MJ, et al.: Cerebral Aneurysms: Germany-Wide Real-World Outcome Data of Endovascular or Neurosurgical Treatment from 2007 to 2019

Haverkamp C, *et al. J NeuroIntervent Surg* 2023;0:1–7. doi: 10.1136/jnis-2023-020181

eTable 1: Billing codes used for cohort definition

Category	System	Code	Description
AVM/AVF	ICD10	G28.0-	Arteriovenous malformation of precerebral vessels
AVM/AVF	ICD10	G28.00	Congenital arteriovenous aneurysm of precerebral vessels
AVM/AVF	ICD10	G28.01	Congenital arteriovenous fistula of precerebral vessels
AVM/AVF	ICD10	G28.08	Other congenital arteriovenous malformations of precerebral vessels
AVM/AVF	ICD10	G28.09	Congenital arteriovenous malformation of precerebral vessels, unspecified
AVM/AVF	ICD10	G28.1-	Other malformations of precerebral vessels
AVM/AVF	ICD10	G28.10	Congenital aneurysm of precerebral vessels
AVM/AVF	ICD10	G28.11	Congenital fistula of precerebral vessels
AVM/AVF	ICD10	G28.18	Other congenital malformations of precerebral vessels
AVM/AVF	ICD10	G28.19	Congenital malformation of precerebral vessels, unspecified
AVM/AVF	ICD10	G28.2-	Arteriovenous malformation of cerebral vessels
AVM/AVF	ICD10	G28.20	Congenital arteriovenous aneurysm of cerebral vessels
AVM/AVF	ICD10	G28.21	Congenital arteriovenous fistula of cerebral vessels
AVM/AVF	ICD10	G28.28	Other congenital arteriovenous malformations of cerebral vessels
AVM/AVF	ICD10	G28.29	Congenital arteriovenous malformation of cerebral vessels, unspecified
AVM/AVF	ICD10	G28.3-	Other malformations of cerebral vessels
AVM/AVF	ICD10	G28.31	Congenital fistula of cerebral vessels
AVM/AVF	ICD10	G28.38	Other congenital malformations of cerebral vessels
AVM/AVF	ICD10	G28.39	Congenital malformation of cerebral vessels, unspecified
AVM/AVF	ICD10	G28.8-	Other congenital malformation of the circulatory system, unspecified
AVM/AVF	ICD10	G28.80	Other congenital aneurysm
AVM/AVF	ICD10	G28.81	Other congenital fistula of the circulatory system
AVM/AVF	ICD10	G28.88	Other specified congenital malformations of the circulatory system
AVM/AVF	ICD10	G28.9	Congenital malformation of the circulatory system, unspecified
AVM/AVF	ICD10	I67.11	Cerebral arteriovenous fistula (acquired)
AVM/AVF	OPS	8-836.9d	Percutaneous transluminal vascular intervention: selective embolization with embolizing fluids: Vascular malformations
AVM/AVF	OPS	8-836.9f	Percutaneous transluminal vascular intervention: selective embolization with embolizing fluids: Vessels spinal
AVM/AVF	OPS	8-836.kd	Percutaneous transluminal vascular intervention: selective embolization with particles: Vascular malformations
AVM/AVF	OPS	8-836.kf	Percutaneous transluminal vascular intervention: selective embolization with particles: Vessels spinal
SAH	ICD10	I60	Subarachnoid hemorrhage
ICH	ICD10	I61	Intracerebral hemorrhage
IA	ICD10	I67.10	Cerebral aneurysm (acquired)
IA	ICD10	I72.0	Aneurysm and dissection of carotid artery
IA	ICD10	I72.5	Aneurysm and dissection of other precerebral arteries
IA	ICD10	I72.6	Aneurysm and dissection of vertebral artery
IA	ICD10	Q28.30	Congenital aneurysm of cerebral vessels
EVT	OPS	8-836.m0	Selective embolization with metal coils: Vessels intracranial

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EVT	OPS	8-84b.00	Percutaneous transluminal implantation of stents for flow lamination in aneurysms: one stent, vessels intracranial
EVT	OPS	8-84b.10	Percutaneous transluminal implantation of stents for flow lamination in aneurysms: two and more stents, vessels intracranial
EVT	OPS	8-84b.20	Percutaneous transluminal implantation of stents for flow lamination in aneurysms: 2 stents, vessels intracranial
EVT	OPS	8-84b.30	Percutaneous transluminal implantation of stents for flow lamination in aneurysms: 3 Stents, vessels intracranial
EVT	OPS	8-84b.40	Percutaneous transluminal implantation of stents for flow lamination in aneurysms: 4 Stents, vessels intracranial
EVT	OPS	8-84b.50	Percutaneous transluminal implantation of stents for flow lamination in aneurysms: 5 Stents, vessels intracranial
EVT	OPS	8-84b.60	Percutaneous transluminal implantation of stents for flow lamination in aneurysms: 6 or more stents, vessels intracranial
EVT	OPS	8-83b.37	Intraaneurysmal closure device for intracranial aneurysms
NSC	OPS	5-025.3	Incision, excision, destruction, and closure of intracranial blood vessels: Dissection and clipping, intracerebral
NSC	OPS	5-025.5	Incision, excision, destruction, and closure of intracranial blood vessels: Dissection and destruction, intracerebral
NSC	OPS	5-025.7	Incision, excision, destruction, and closure of intracranial blood vessels: Clipping
NSC	OPS	5-025.9	Incision, excision, destruction, and closure of intracranial blood vessels: other combined procedures
NSC	OPS	5-026.3	Reconstruction of intracranial blood vessels: Combined procedures
NSC	OPS	5-026.4*	Reconstruction of intracranial blood vessels: Number of clips on intracranial blood vessels

AVF: arteriovenous fistula, AVM: arteriovenous malformation, EVT: endovascular treatment, IA: intracranial aneurysm, ICD10: International Statistical Classification of Diseases and Related Health Problems 10, ICH: intracranial hemorrhage, NSC: neurosurgical clipping, OPS: “Operationen- und Prozedurenschlüssel” = key of operations and procedures, SAH: subarachnoid hemorrhage

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eTable 2: Ordinal functional outcome according to type of hospital discharge

Ordinal outcome at discharge	Type of discharge	Discharge codes according to §301german social code V*
1: Good outcome = discharge to home	Discharge to home	01, 02, 03, 04
2: Intermediate Outcome = Further hospital care, rehabilitation, or nursing required	Discharge to other hospital	06, 08
	Discharge to rehabilitation	09
	Discharge to nursing facility	10
	Discharge to hospice	11
3: Poor outcome = Intrahospital death	Intrahospital death	7

* Source: *http://fhir.de/CodeSystem/dkgev/EntlassungsgrundErsteUndZweiteStelle*

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eTable 3: Definition of National Inpatient Sample-Subarachnoid hemorrhage Outcome Measure (NIS-SOM)*

Good outcome: discharge to home or a rehabilitation facility and/or other hospital.

Poor outcome: in-hospital mortality; discharge to a nursing facility, extended care facility, or hospice (as defined above); placement of a tracheostomy tube (OPS codes: 5-311, 5-312), and/or placement of a gastrostomy tube (OPS codes: 5-431.2)

OPS: “Operationen- und Prozedurenschlüssel” = key of operations and procedures

** Washington CW, Derdeyn CP, Dacey RG, Dhar R, Zipfel GJ. Analysis of subarachnoid hemorrhage using the Nationwide Inpatient Sample: the NIS-SAH Severity Score and Outcome Measure: Clinical article. Journal of Neurosurgery. 2014;121:482–489*

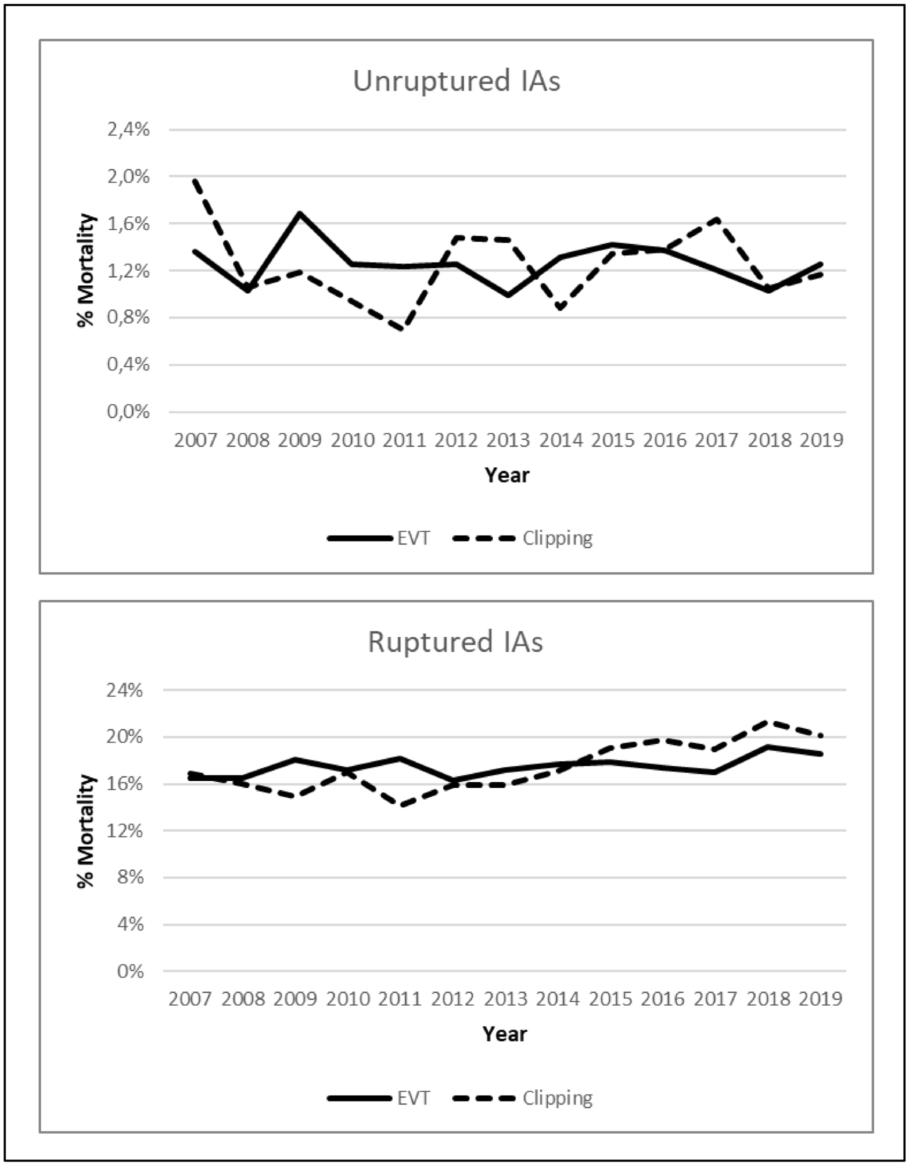
eTable 4: Definition of National Inpatient Sample-Subarachnoid hemorrhage Severity Score (NIS-SSS)*

Item	ICD-10	OPS	multivariate logistic regression coefficient (B) as described by Washington et al.*
mechanical ventilation	directly contained in the DRG dataset		2,023
hydrocephalus	G91.[0-1]		-0,073
treatment of hydrocephalus		5-022.00, 5-023	0,223
coma	R40.1		1,793
cranial nerve palsy	H49, H57.1		-1,139
paralysis/paraparesis	G8.[1-3]		0,507
aphasia	R47		0,445
Score	$\text{NIS-SSS} = e^{\left(\sum_{i=1}^{7} B_i \cdot x_i\right)}$ where $x_i = 1$ when the item is present and 0 if absent		

ICD-10: International Statistical Classification of Diseases and Related Health Problems 10, OPS: "Operationen- und Prozedurenschlüssel" = key of operations and procedures, DRG: diagnosis related groups

** Washington CW, Derdeyn CP, Dacey RG, Dhar R, Zipfel GJ. Analysis of subarachnoid hemorrhage using the Nationwide Inpatient Sample: the NIS-SAH Severity Score and Outcome Measure: Clinical article. Journal of Neurosurgery. 2014;121:482–489*

eFigure 1: Time course of in-hospital mortality in treatment of intracranial aneurysms (years 2007-2019)



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