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Aneurysmal Subarachnoid Hemorrhage: Trends, Outcomes, and Predictions From a 15-Year Perspective of a Single Neurocritical Care Unit

BACKGROUND: Aneurysmal subarachnoid hemorrhage (aSAH) is associated with disproportionately high mortality and long-term neurological sequelae. Management of patients with aSAH has changed markedly over the years, leading to improvements in outcome.

OBJECTIVE: To describe trends in aSAH care and outcome in a high-volume single center 15-yr cohort.

METHODS: All new admissions diagnosed with subarachnoid hemorrhage (SAH) to our tertiary neuro-intensive care unit between 2002 and 2016 were reviewed. Trend analysis was performed to assess temporal changes and a step-wise regression analysis was done to identify factors associated with outcomes.

RESULTS: Out of 3970 admissions of patients with SAH, 2475 patients proved to have a ruptured intracranial aneurysm. Over the years of the study, patient acuity increased by Hunt & Hess (H&H) grade and related complications. Endovascular therapies became more prevalent over the years, and were correlated with better outcome. Functional outcome overall improved, yet the main effect was noted in the low- and intermediate-grade patients. Several parameters were associated with poor functional outcome, including long-term mechanical ventilation (odds ratio 11.99, CI 95% [7.15-20.63]), acute kidney injury (3.55 [1.64-8.24]), pneumonia (2.89 [1.89-4.42]), hydrocephalus (1.80 [1.24-2.63]) diabetes mellitus (1.71 [1.04-2.84]), seizures (1.69 [1.07-2.70]), H&H (1.67 [1.45-1.94]), and age (1.06 [1.05-1.07]), while endovascular approach to treat the aneurysm, compared with clip-ligation, had a positive effect (0.35 [0.25-0.48]).

CONCLUSION: This large, single referral center, retrospective analysis reveals important trends in the treatment of aSAH. It also demonstrates that despite improvement in functional outcome over the years, systemic complications remain a significant risk factor for poor prognosis. The historic H&H determination of outcome is less valid with today's improved care.

KEY WORDS: Subarachnoid hemorrhage, Cerebral aneurysm, Medical complications, Neurocritical care, Patient outcomes

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Although aneurysmal subarachnoid hemorrhage (aSAH) is a relatively uncommon cause of stroke, it is associated with disproportionately high mortality and morbidity. While there have been significant improvements in treatment for these patients

ABBREVIATIONS: AKI, acute kidney injury; aSAH, aneurysmal subarachnoid hemorrhage; CI, confidence interval; CPT, current procedural terminology; DCI, delayed cerebral ischemia; DSA, digital subtraction angiography; DVT, deep vein thrombosis; H&H, Hunt & Hess; ICD, international classification of disease; ICU, intensive care unit; IRB, Institutional Review Board; IQR, interquartile range; ISAT, International Subarachnoid Aneurysm Trial; LTCH, long-term care hospital; mRS, modified Rankin Scale; SAH, subarachnoid hemorrhage; SNF, skilled nursing facility

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over the last several decades, in-patient mortality remains around 20%.¹

At the time of Hunt and Hess's seminal work in 1968, mortality from aSAH was estimated to be 63%.^{2,3} Surgical treatment for aneurysms at that time was reserved for patients with minimal neurological injury, which was done weeks after the initial bleed. Two decades later, the mortality rate improved only to 43% in the first week.⁴ Only in the late 1980s did evidence emerge favoring early surgical intervention.⁵ The most significant advance in outcome was demonstrated with the development of endovascular coiling. The International Subarachnoid Aneurysm Trial (ISAT) revealed that early endovascular treatment is superior to surgical clipping for the first year following subarachnoid hemorrhage (SAH), with a mortality or dependency rate of 23.7%.⁶ Since then, early endovascular treatment has increasingly become the treatment approach in patients when it is technically feasible, and has been associated with a significant reduction in mortality.⁷ A recent analysis of Hunt & Hess (H&H) grade V aSAH cases compared the pre- and post-ISAT eras, demonstrating notable improvement in survival and favorable outcome.⁸

The medical management of aSAH has also evolved and focuses on prevention and treatment of both neurologic and systemic complications. Treatment and prevention of cerebral vasospasm and delayed cerebral ischemia (DCI) was historically based on the "triple H" combination of induced hypertension, hypervolemia, and hemodilution. Although there is some evidence suggesting a beneficial physiologic effect on cerebral perfusion,⁹ the various components were each the subject of dispute over the last several years.¹⁰⁻¹² The first effective medical intervention for the prevention of DCI was oral nimodipine, which was shown to reduce the rate of DCI and improve functional outcome.^{13,14}

The development of specialized teams and patient care units to treat severe acute neurological injuries has led to improvement in care and outcomes, not only in cases of SAH.¹⁵⁻¹⁸ Some evidence contradicting this finding also exists.¹⁹ To further investigate outcome trends and the contribution of surgical, endovascular, and critical care management, we performed an in-depth analysis of all cases of aSAH in a single, high-volume, neurocritical care unit.

This paper describes the changes in treatment, complications, and outcomes of patients with aSAH over the course of 15 years. We explore the factors contributing to outcomes and hypothesize the initial injury (as measured by the H&H score) is not as meaningful a prognostic factor as it was 15 yr ago.

METHODS

Following approval of the our University Institutional Review Board (IRB), all patients discharged from Emory University Hospital neurocritical care unit between January 1st, 2002 and December 31st, 2016 were screened on a quarterly basis through the University Health System Consortium and later through Vizient data repositories.²⁰ Given the retrospective nature of the study, consent was waived by the IRB.

TABLE 1. Demographic Information and Risk Factors

Risk factor	aSAH (n = 2540)
Age (mean ± SD)	53 ± 14
Gender (% female)	71.3% [69.5-73.1]
Race	
Caucasian	41.9% [40.0-43.9]
African American	30.5% [28.7-32.4]
Hispanic	1.3% [0.9-1.8]
Asian	0.8% [0.6-1.3]
Other/unknown	25.3% [23.6-27.0]
HTN	52.1% [50.1-54.0]
CAD	6.7% [5.7-7.7]
DM	9.4% [8.3-10.6]
Tobacco use	29.8% [28.0-31.6]
Hypercholesterolemia	10.1% [9.0-11.4]
H&H grade 1 and 2	40.8% [38.8-42.7]
H&H grade 3	35.7% [33.8-37.6]
H&H grade 4 and 5	23.5% [21.8-25.2]

HTN, hypertension; CAD, coronary artery disease; DM, diabetes mellitus.

Patients with a diagnosis of SAH (international classification of disease [ICD]9 430; ICD10 i608, i609, i611, i618) were included in the initial screen. From chart review, the etiology of the bleed was established and demographics, risk factors, and outcome measures were collected. Only patients with an aneurysmal source were included. Patients with SAH managed at other hospitals staffed by Emory University faculty were not included. The admission-related ICD and current procedural terminology (CPT) codes were collected and analyzed (**Supplemental Digital Content, Table S1**). The statistical analysis is detailed in the supplementary methods.

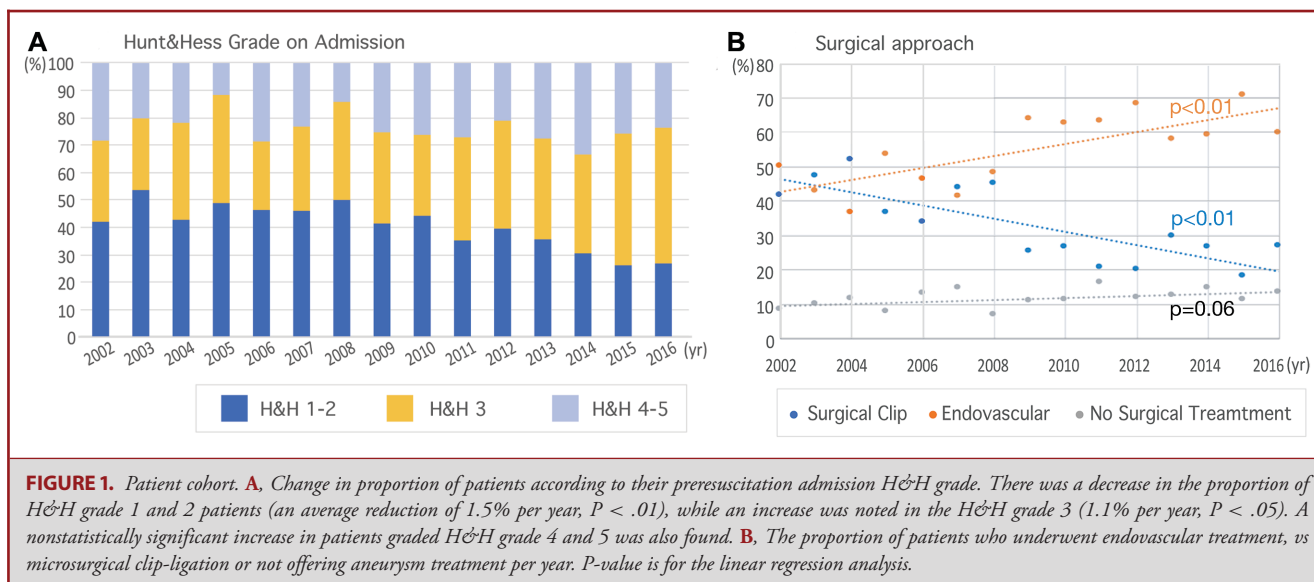
RESULTS

The Patient Cohort

Between 2002 and 2016, there were 3970 admissions with the diagnosis of SAH. All patients were treated according to the best available treatment guidelines at the time.²¹⁻²³ An aneurysmal etiology was determined in 2475 patients (62.3%); 684 admissions were due to idiopathic SAH (angio-negative, 17.2%); the remainder (811 patients, 20.4%) had other etiologies such as trauma, arteriovenous malformation, fistula, and cavernous malformation. Our analysis included only aneurysmal SAH cases (**Supplemental Digital Content, Figure S1**).

Demographic information and risk factors of the cohort are detailed in Table 1 and **Supplemental Digital Content, Figure S2**. Over time, the yearly number of patients remained similar (an average of 165 ± 33). However, patient groups by H&H changed with time (Figure 1A).

The method of securing the aneurysm changed over the years. There was a continuous and statistically significant increase in the rate of endovascular intervention and a decrease in the use of open microsurgical approaches (Figure 1B, **Supplemental Digital Content, Figure S3**). There was also a trend toward selection of withholding treatment of the aneurysm, usually as



a moribund admission status, often meeting criteria for brain death, suggesting that patient acuity has increased over the years (**Supplemental Digital Content, Table S2**).

Changes in the Utilization of Diagnostic Procedures

When examining the change in utilization of diagnostic procedures, an interesting trend appears: overall more imaging studies and electroencephalograms (Figure 2) were performed in the last 5 yr in comparison with the first 5 yr of our study; there is a statistically significant reduction in the number of patients undergoing repeat digital subtraction angiography (DSA) after an initial study performed at admission.

Changes in Neurological and Systemic Complications Secondary to SAH

When examining the rate of common diagnoses relevant for the intensive care unit (ICU) phase of treatment, several patterns appear. First, there is a noticeable increase in nearly all diagnoses in the last 10 yr (2007-2016) compared to the first 5 yr (2002-2006), suggesting a skew related to the comprehensive quality of hospital diagnostic coding. We therefore continued the analysis for the last 10 yr ($n = 1807$, **Supplemental Digital Content, Figures S4 and S5**). Although some of the patterns noted are probably a result of improved coding, we were able to demonstrate a reduction in the tracheostomy rates, and infectious complications. Other systemic complications increased in rate, such as acute kidney injury (AKI).

We further analyzed the prevalence of common systemic complications according to the surgical approach to the aneurysm (Table 2), excluding patients for whom no surgical treatment was offered. When analyzing the remaining 1586 patients, we found statistically significant higher rates of respiratory failure, long-term ventilation, tracheostomy, pneumonia, and deep vein

thrombosis (DVT) in the group that underwent an open surgical approach. Patients who were treated endovascularly, had higher rates of short-term (<96 h) ventilation, compared with the open surgical group.

Patient Outcomes

In terms of outcome, when analyzing the entire cohort, 46.0% (CI [43.7-48.3], $n = 832$) of the patients were discharged home, 12.8% (CI [11.2-14.3], $n = 231$) were discharged to an inpatient rehabilitation facility, 12.6% (CI [11.0-14.1], $n = 227$) were discharged to long-term care hospitals (LTCH), 5.2% (CI [4.2-6.2], $n = 94$) were discharged to a skilled nursing facility (SNF), 6.0% (CI [4.9-7.1], $n = 108$) were discharged to hospice and 6.8% (CI [15.1-18.5]) expired in hospital ($n = 304$).

The last 10 yr of the cohort, discharge disposition was analyzed according to admission H&H scores, as detailed in Figure 3. We found an increase in the proportion of patients who were discharged home, along with a decrease in the proportion of patients discharged to an inpatient facility, in the low- and intermediate-grade groups. An analysis of in-patient mortality and interventions demonstrated a beneficial correlation with the use of an endovascular approach (Table 3).

Functional outcome as measured by modified Rankin Scale (mRS) was assessed at discharge. These data were consistently available from 2007 (available for $n = 1772$). When dichotomizing the data to 5-yr periods, there was a statistically significant increase in the proportion of patients being discharged with good functional outcome ($mRS \leq 2$), for the low-grade and intermediate-grade groups (Figure 3). Interestingly, when examining functional outcome by the type of intervention, an endovascular approach was associated with a statistically significant advantage (Table 3). There was a trend toward an increase

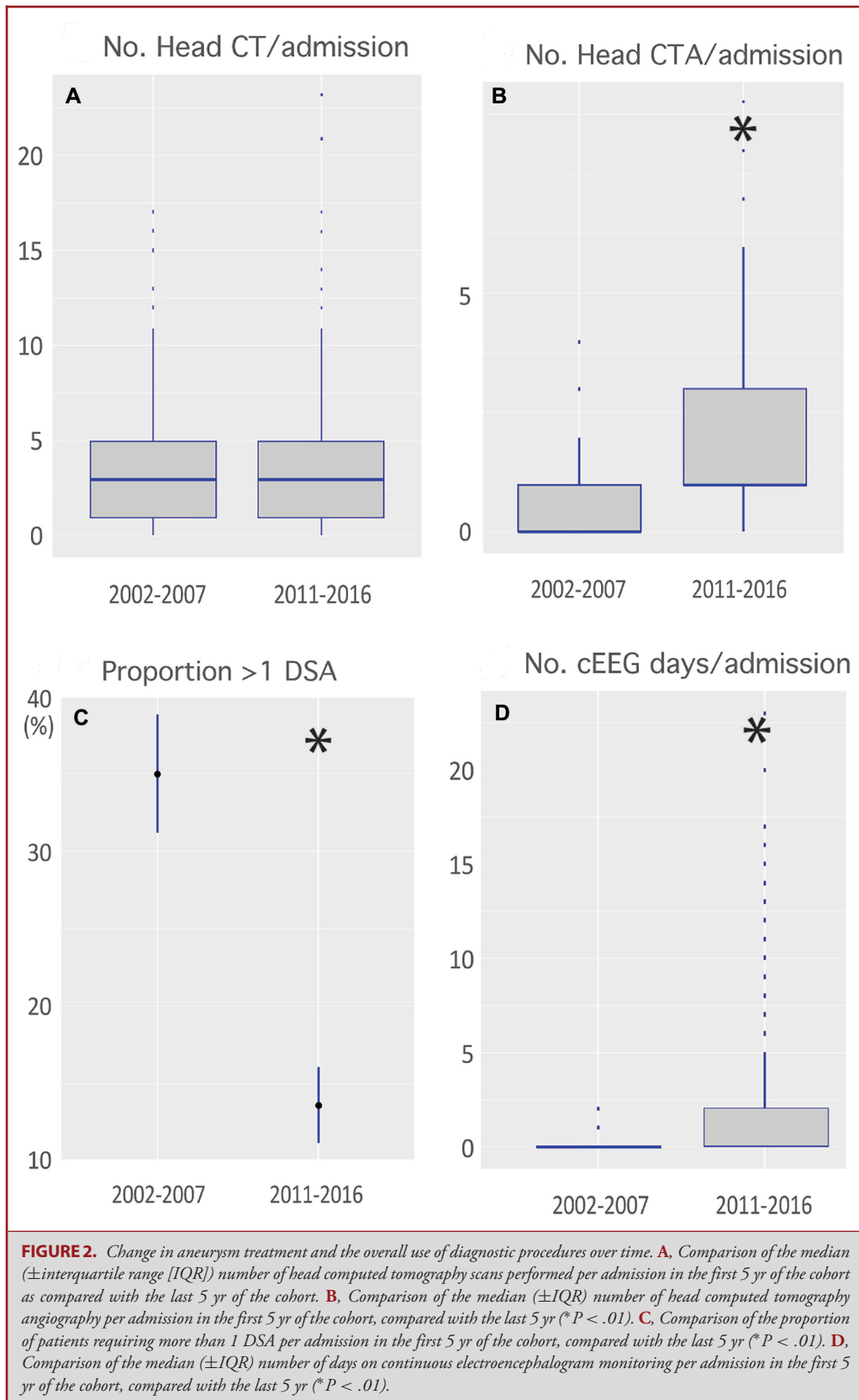


TABLE 2. Comparison of H&H Scale Between Patients Treated by an Endovascular vs Open Surgical Approach (Clip-ligation), and Overall Proportion of Patients With Common ICU Diagnoses According to the Method of Aneurysm Repair. Patients Who Had No Intervention Were Excluded From This Analysis

Diagnosis during ICU stay	Proportion of patients – all (%[95% CI]) (n = 1586)	Proportion of patients – endovascular approach (n = 1067)	Proportion of patients – open surgical (clip) approach (n = 519)	P value (endovascular vs surgical clipping)
H&H 1 and 2	42.4% [40%-44.9%]	39.8% [36.9%-42.8%]	47.8% [43.5%-52.1%]	.003
H&H 3	40.1% [37.7%-42.5%]	42.5% [39.5%-45.4%]	35.26% [31.2%-39.4%]	.006
H&H 4 and 5	17.2% [15.4%-19.1%]	17.6% [15.3%-19.9%]	16.4% [13.2%-19.6%]	.571
Age (mean ± SD)	53 ± 13	53 ± 13	52 ± 13	.035
Sex (% woman)	72.1% [69.9%-74.3%]	71.2% [68.5%-73.9%]	74.0% [70.2%-77.8%]	.257
Respiratory failure/adult respiratory distress syndrome	47.6% [45.2%-50.1%]	44.6% [41.6%-47.6%]	53.8% [49.5%-58.1%]	.001
Short-term (<96 h) ventilation	14.5% [12.8%-16.2%]	15.9% [13.7%-18.1%]	11.8% [9.0%-14.5%]	.033
Hypotension/shock	24.7% [22.5%-26.8%]	23.6% [21.1%-26.2%]	26.8% [23.0%-30.6%]	.173
Bacterial central nervous system infection	5.4% [4.3%-6.5%]	5.4% [4.1%-6.8%]	5.4% [3.5%-7.3%]	1.000
Sepsis	8.6% [7.2%-10.0%]	7.7% [6.1%-9.3%]	10.4% [7.8%-13.0%]	.085
Pneumonia	29.7% [27.5%-31.9%]	26.1% [23.4%-28.7%]	37.2% [33.0%-41.3%]	.000
Urinary tract infection/pyelonephritis	36.2% [33.8%-38.6%]	35.0% [32.1%-37.8%]	38.7% [34.5%-42.9%]	.148
Long-term (>96 h) ventilation	32.4% [30.1%-34.7%]	27.6% [24.9%-30.3%]	42.4% [38.1%-46.6%]	.000
Tracheostomy	23.4% [21.3%-25.5%]	19.0% [16.7%-21.4%]	32.4% [28.3%-36.4%]	.000
AKI	5.5% [4.4%-6.6%]	5.3% [4.0%-6.7%]	5.8% [3.8%-7.8%]	.725
DVT	4.4% [3.4%-5.4%]	3.5% [2.4%-4.6%]	6.4% [4.3%-8.5%]	.013
PE	0.4% [0.1%-0.7%]	0.5% [0.1%-0.9%]	0.2% [-0.2%-0.6%]	.670

in 90-d survival over the years in all H&H scores, mostly noted in the H&H 3 group (Figure 3).

Outcome Prediction

A logistic regression analysis calculated the probability for unfavorable functional outcome over time according to H&H groups was performed to determine whether H&H grade remains a strong predictive measure for outcome. A downward trend of H&H as a predictive parameter was found, especially in the low and intermediate groups, suggesting that the contribution of the initial H&H grade to outcome is diminishing (Figure 4).

In order to identify other factors contributing to outcome, a logistic regression toward poor functional outcome at discharge (mRS > 2) was performed. Following the univariate regression analysis (**Supplemental Digital Content, Table S3**), a step-wise regression analysis is shown in Table 4. Of note, H&H grade on admission was not strongly correlated with overall outcome.

DISCUSSION

Key Findings

This study describes changes in the management and outcome of aSAH patients at a high-volume tertiary care center over a 15-yr period. We found that our cohort of aSAH patients had: increasing acuity, a significant change in the approach for aneurysmal repair favoring endovascular treatment, increased utilization of noninvasive imaging modalities with a concomitant decrease in cerebral angiography, and changes in the rates of common medical complications. Although overall mortality reduction did not meet statistical significance, there was a significant improvement in functional outcome for the low- and intermediate-grade aSAH patients. Unfortunately, high-grade patients did not demonstrate improved outcomes over time, regardless of the choice of aneurysm repair or critical care management.

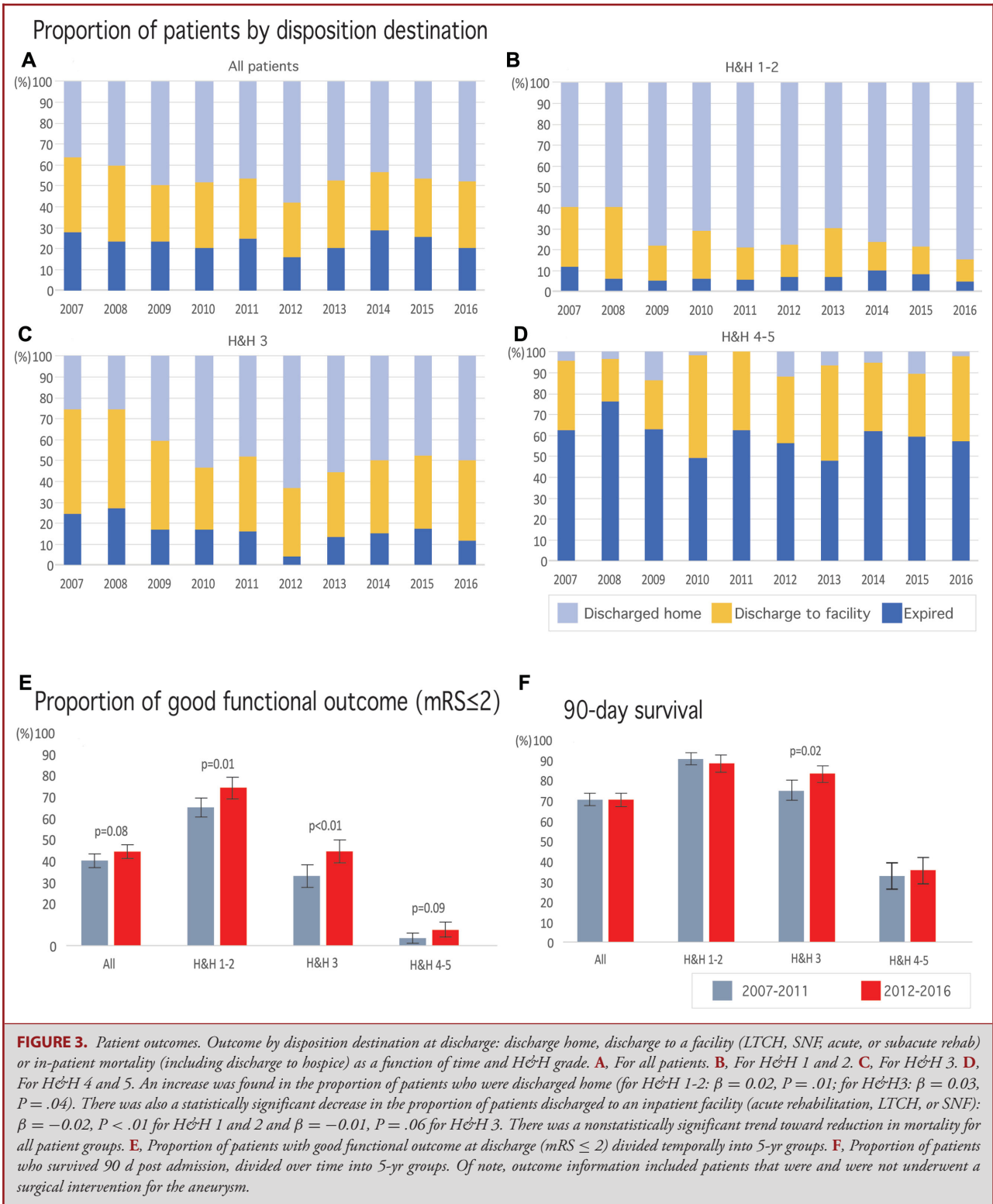


TABLE 3. Outcome Analyzed by Choice of Aneurysm Repair. Patients Who Received No Treatment for the Aneurysm Were Excluded (n = 1586)

Diagnosis during ICU stay	All patients	Endovascular approach	Open surgical (clip) approach	P value
In-patient mortality				
H&H 1 and 2	5.4% (n = 673)	3.5% (n = 425)	8.5% (n = 248)	<.01
H&H 3	11.5% (n = 636)	9.5% (n = 453)	16.4% (n = 183)	.02
H&H 4 and 5	37.0% (n = 273)	33.5% (n = 188)	44.7% (n = 85)	.08
Good functional outcome (mRS ≤ 2) at discharge				
H&H 1 and 2	69.1% (n = 673)	77.7% (n = 425)	54.4% (n = 248)	<.01
H&H 3	40.3% (n = 635)	47.6% (n = 452)	22.4% (n = 183)	<.01
H&H 4 and 5	8.4% (n = 273)	11.2% (n = 188)	2.4% (n = 85)	.02

Each result represents the proportion of patients within its group with the specified end point (in-patient mortality or good functional outcome at discharge). For each result, the population (n) is specified.

Limitations

This study has several limitations. It is a single-center, single hospital, and retrospective study, which makes generalizability and determining causation, problematic. Moreover, the results depend to some extent on the chart coding. Coding has the advantage of common language for analysis, but in order to avoid a bias, it requires uniformity among clinicians or coders to accurately and consistently select the code describing the condition. Over the 15 yr of our study, there were modifications made to the definitions of certain diagnoses, such as AKI²⁴ or sepsis.²⁵ Other diagnoses do not have a consensus definition outside the settings of a clinical trial, such as cerebral vasospasm.²⁶ We noted a drastic increase for some diagnoses between 2006 and 2008, which suggests that a new focus has occurred that led clinicians and coders to pay more attention to those specific diagnoses. This bias in the data is probably the reason for the “protective” effect cerebral edema has on outcome in the regression analysis. We chose to focus mainly on the last 10 yr, due to the improvement in coding.

Results Interpretation

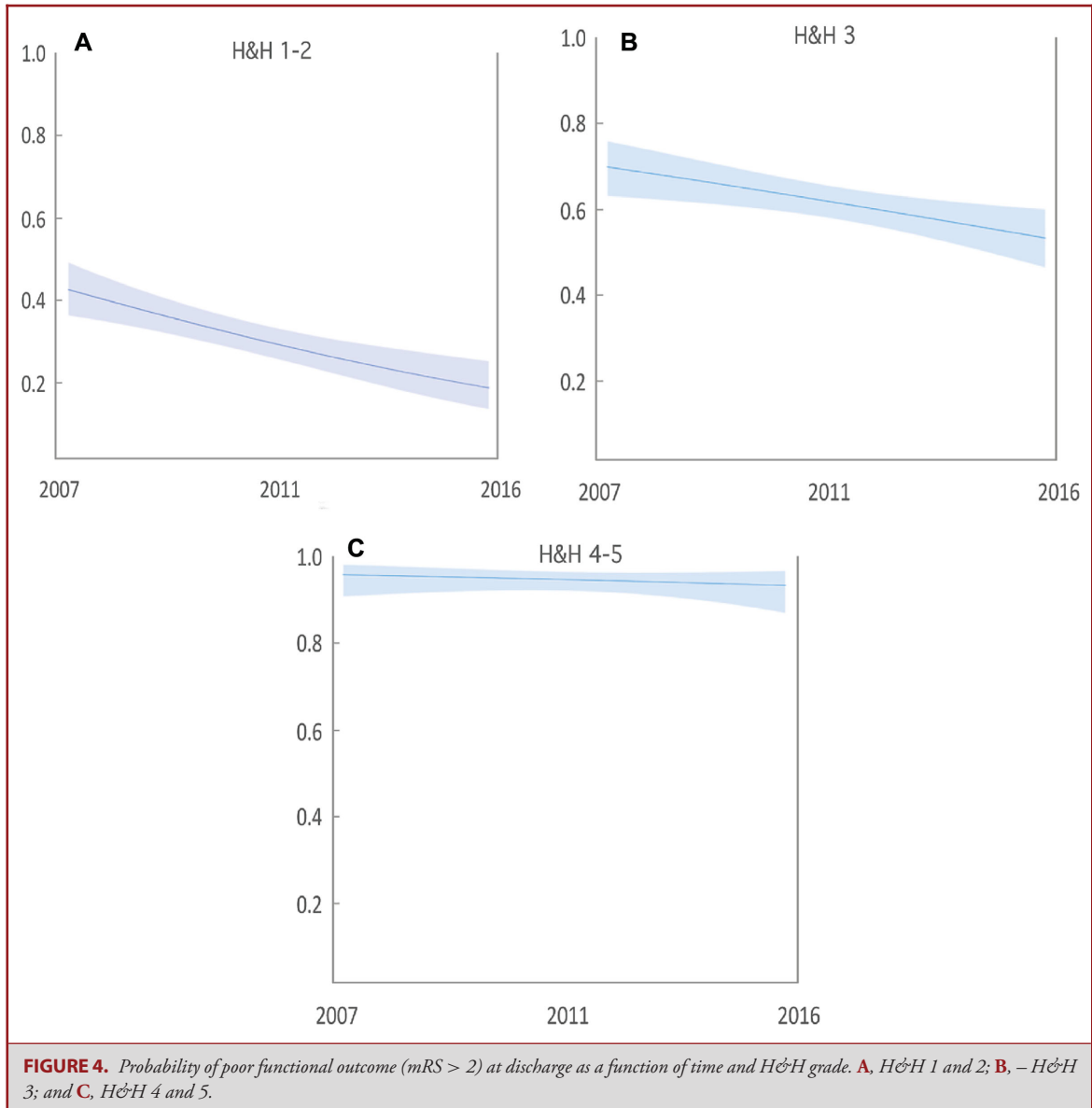
Looking at neurological complications, our cohort showed an increased rate of vasospasm diagnosis, the rate of DSA use decreased, and noninvasive computed tomography angiography has become more commonly used. Since DSA is often used for the diagnosis and therapeutic intervention for cerebral vasospasm,²⁷ the reduction in the rate of DSAs performed in our cohort may suggest that factors in the management of aSAH patients are becoming more effective; however, the retrospective nature of this study limits further delineation.

Review of common neurologic and critical care-related diagnoses in the cohort revealed several interesting trends. Although mechanical ventilation rates remained stable, there was a decrease in tracheostomy; suggesting that over time, the improved ICU care led to a higher rate of successful extubation. There was a decrease in rates of infectious complications, mainly bacterial ventriculitis. There was also a surprising increase in

the rate of AKI, which might be related to increased acuity or improvement in detection.

Three outcome parameters: discharge disposition, functional state at discharge, and 90-d mortality were available for analysis in the cohort. Mortality, either in-hospital or at 90 d, overall remained stable. However, a significant improvement was observed in the H&H 3 group. From a functional standpoint, a more robust improvement was seen both in the low-grade and intermediate-grade groups in both discharge mRS and rates of discharged home. There was a ceiling effect for the high-grade patients, since there was only a nonsignificant trend in improved outcome for this group. Interestingly, this ceiling effect was similarly demonstrated in another large cohort of SAH patients.¹⁹ There was an increasing proportion of the high-grade patients, who did not undergo a surgical intervention of the aneurysm (see **Supplemental Digital Content, Supplementary Data**). However, a large proportion of these patients arrived in a state of brain death, and only a minority was discharged to hospice, suggesting this is part of the increased acuity trend, rather than a self-fulfilling prophecy of high-grade injuries. These findings highlight both the successes and failures of 15 yr of management of patients with aSAH at a tertiary neurovascular center. While this large cohort analysis clearly demonstrates the positive impact of the advancements in the management of patients with mid-acuity (H&H 3) aneurysmal SAH, high-grade aSAH demonstrated only modest improvements.

The approach for aneurysmal treatment, although not randomized, demonstrated a significant impact on the development of later complications and correlated independently with outcome. Endovascular approaches became more frequently used, to the point that an endovascular approach became almost the default option for aneurysm repair. Currently, clip-ligation is utilized for patients in whom endovascular approach is either technically not feasible, or not safe, or in cases in which an emergent surgical hematoma evacuation is also required. The ISAT,⁶ and later studies,⁸ set the grounds for this shift, although others did not find a similar advantage for the endovascular treatment.²⁸ Our data showed increased rates of mechanical



ventilation, pneumonia, tracheostomy, and DVT in patients treated surgically, compared with an endovascular approach. The interplay among the factors leading to the choice of therapeutic procedure, the effect of craniotomy in the face of acute SAH, and related complications that would explain the disadvantage of craniotomy over an endovascular approach remains unclear. Further research is needed to better understand the postoperative physiological changes to allow for more precisely tailored treatment for this specific patient group.

Among the most impactful clinical issues influencing outcome in the regression analysis were respiratory failure with the need for mechanical ventilation and AKI. Respiratory complications were more frequent in the surgical group, and co-correlation

appears. AKI has been a well-known poor prognostic factor in general medical-surgical critically ill patients, and more recent data suggest AKI is of particular importance in neurocritical care as a potentially modifiable risk factor.^{29,30} An unexpected findings in the cohort was that AKI, pneumonia, or >96 h ventilation are better predictors of outcome than the initial H&H grade. This further demonstrates the ongoing significant impact and contribution to outcome of medical factors in SAH. Moreover, a risk analysis showed that the effect of H&H on functional outcome has decreased over time for all grades. These results reinforce prior data demonstrating that up to 40% of SAH patients suffer from a life-threatening medical complication during their ICU admission.³¹

TABLE 4. Multiple Regression Analysis Toward Poor Functional Outcome at Discharge (mRS > 2)

Predictors	Odds ratio and 95% CIs	P value
Age*	1.06 [1.05-1.07]	.000
H&H grade on admission*	1.67 [1.45-1.94]	.000
Endovascular treatment vs surgical clip*	0.35 [0.25-0.48]	.000
No treatment vs surgical clip*	5.60 [2.42-14.40]	.000
CAD*	0.44 [0.23-0.84]	.013
DM*	1.71 [1.04-2.84]	.035
Hyperlipidemia	0.63 [0.39-1.01]	.058
Respiratory failure/adult respiratory distress syndrome*	1.67 [1.14-2.45]	.009
Short-term ventilation (<96 h)*	1.58 [1.02-2.44]	.039
Long-term ventilation (>96 h)*	11.99 [7.16-20.64]	.000
Pneumonia*	2.89 [1.90-4.42]	.000
Urinary tract infection/pyelonephritis	1.28 [0.95-1.72]	.110
Bacterial central nervous system Infection	1.83 [0.96-3.53]	.069
AKI*	3.55 [1.64-8.24]	.002
Hydrocephalus*	1.80 [1.24-2.63]	.002
Cerebral edema/brain compression*	0.59 [0.37-0.93]	.022
Seizure*	1.70 [1.07-2.70]	.025

HTN, hypertension; CAD, coronary artery disease; DM, diabetes mellitus; *P < .05.

Generalizability

Although this is a single-center study, it does have detailed, patient-level data that are often missing in larger cohorts,^{19,32} allowing for thorough, in-depth analysis. In the era of “big-data,” this type of in-depth analysis could be expanded into a multi-center effort. This and similar databases could also allow preliminary investigations using “off the shelf” comparison control groups.^{32,33} Having a detailed repository, could aid in identification of systemic complications and not just neurological ones, since, as has been shown in our study and by others,³⁴ the systemic portion of the critical care is a highly important determinant of outcome.

CONCLUSION

This is the largest single-center cohort to describe temporal changes in the treatment and outcome of aSAH. Although limited by its retrospective nature, our analysis demonstrated that an endovascular approach is more prevalent and is associated with better outcome, regardless of the initial severity of the neurological injury. The data also showed an increase in the overall rate of use of diagnostic tests, with the exception of DSA. Finally, we found admission H&H score to be less predictive of outcome over time.

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REFERENCES

- Rincon F, Rossenwasser RH, Dumont A. The epidemiology of admissions of nontraumatic subarachnoid hemorrhage in the United States. *Neurosurgery*. 2013;73(2):217-223.
- Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg*. 1968;28(1):14-20.
- Pakarinen S. Incidence, aetiology, and prognosis of primary subarachnoid haemorrhage. A study based on 589 cases diagnosed in a defined urban population during a defined period. *Acta Neurol Scand*. 1967;43(Suppl 29):1-28.
- Bonita R, Thomson S. Subarachnoid hemorrhage: epidemiology, diagnosis, management, and outcome. *Stroke*. 1985;16(4):591-594.
- Ohman J, Heiskanen O. Timing of operation for ruptured supratentorial aneurysms: a prospective randomized study. *J Neurosurg*. 1989;70(1):55-60.
- Molyneux A, Kerr R, Stratton I, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet (London, England)*. 2002;360(9342):1267-1274.
- Worthington JM, Goumas C, Jalaludin B, Gattellari M. Decreasing risk of fatal subarachnoid hemorrhage and other epidemiological trends in the era of coiling implementation in Australia. *Front Neurol*. 2017;8:424.
- Konczalla J, Seifert V, Beck J, et al. Outcome after Hunt and Hess grade V subarachnoid hemorrhage: a comparison of pre-coiling era (1980-1995) versus post-ISAT era (2005-2014). *J Neurosurg*. 2018;128(1):100-110.
- Engquist H, Rostami E, Ronne-Engström E, Nilsson P, Lewén A, Enblad P. Effect of HHH-therapy on regional CBF after severe subarachnoid hemorrhage studied by bedside xenon-enhanced CT. *Neurocrit Care*. 2018;28(2):143-151.
- Sakr Y, Dünisch P, Santos C, et al. Poor outcome is associated with less negative fluid balance in patients with aneurysmal subarachnoid hemorrhage treated with prophylactic vasopressor-induced hypertension. *Ann Intensive Care*. 2016;6(1):25.
- Kissoon NR, Mandrekar JN, Fugate JE, Lanzino G, Wijidicks EFM, Rabinstein AA. Positive fluid balance is associated with poor outcomes in subarachnoid hemorrhage. *J Stroke Cerebrovasc Dis*. 2015;24(10):2245-2251.

12. Gathier CS, van den Bergh WM, van der Jagt M, et al. Induced hypertension for delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage: a randomized clinical trial. *Stroke*. 2018;49(1):76-83.
13. Allen GS, Ahn HS, Preziosi TJ, et al. Cerebral arterial spasm—a controlled trial of nimodipine in patients with subarachnoid hemorrhage. *N Engl J Med*. 1983;308(11):619-624.
14. Pickard JD, Murray GD, Illingworth R, et al. Effect of oral nimodipine on cerebral infarction and outcome after subarachnoid haemorrhage: British aneurysm nimodipine trial. *BMJ*. 1989;298(6674):636-642.
15. Samuels O, Webb A, Culler S, Martin K, Barrow D. Impact of a dedicated neurocritical care team in treating patients with aneurysmal subarachnoid hemorrhage. *Neurocrit Care*. 2011;14(3):334-340.
16. Patel HC, Menon DK, Tebbs S, Hawker R, Hutchinson PJ, Kirkpatrick PJ. Specialist neurocritical care and outcome from head injury. *Intensive Care Med*. 2002;28(5):547-553.
17. Elf K, Nilsson P, Enblad P. Outcome after traumatic brain injury improved by an organized secondary insult program and standardized neurointensive care. *Crit Care Med*. 2002;30(9):2129-2134.
18. Lerch C, Yonekawa Y, Muroi C, Bjeljac M, Keller E. Specialized neurocritical care, severity grade, and outcome of patients with aneurysmal subarachnoid hemorrhage. *Neurocrit Care*. 2006;5(2):85-92.
19. Udy AA, Vlastic C, Saxby ER, et al. Subarachnoid hemorrhage patients admitted to intensive care in Australia and New Zealand: a multicenter cohort analysis of in-hospital mortality over 15 years. *Crit Care Med*. 2017;45(2):e138-e145.
20. Vizient. <https://www.vizientinc.com>. Last Accessed July 2017.
21. Bederson JB, Sander CE, Hunt BH, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage. *Stroke*. 2009;40(3):994-1025.
22. Connolly ES, Rabinstein AA, Carhuapoma JR, 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.
23. Mayberg MR, Barjer HH, Dacey R, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage. A statement for healthcare professionals from a special writing group of the stroke council, American Heart Association. *Circulation*. 1994;90(5):2592-2605.
24. Kellum JA, Lameire N, Aki K, Work G. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). *Crit Care*. 2013;17(Part 1): 1-15.
25. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):762-774.
26. Vergouwen MDI. Vasospasm versus delayed cerebral ischemia as an outcome event in clinical trials and observational studies. *Neurocrit Care*. 2011;15(2):308-311.
27. Findlay JM, Nisar J, Darsaut T. Cerebral vasospasm: a review. *Can J Neurol Sci*. 2016;43(1):15-32.
28. Mocco J, Ransom ER, Komotar RJ, et al. Preoperative prediction of long-term outcome in poor-grade aneurysmal subarachnoid hemorrhage. *Neurosurgery*. 2006;59(3):529-538; discussion 529-38.
29. Sadan O, Singbartl K, Kandiah PA, Martin KS, Samuels OB. Hyperchloremia is associated with acute kidney injury in patients with subarachnoid hemorrhage. *Crit Care Med*. 2017;45(8):1382-1388.
30. Sadan O, Singbartl K, Kraft J, et al. Low-chloride- versus high-chloride-containing hypertonic solution for the treatment of subarachnoid hemorrhage-related complications: the ACETatE (a low chloride hypertonic solution for brain edema) randomized trial. *J Intensive Care*. 2020;8(1):32.
31. Solenski NJ, Haley EC, Kassell NF, et al. Medical complications of aneurysmal subarachnoid hemorrhage: a report of the multicenter, cooperative aneurysm study. Participants of the multicenter cooperative aneurysm study. *Crit Care Med*. 1995;23(6):1007-1017.
32. Macdonald RL, Cusimano MD, Etminan N, et al. Subarachnoid Hemorrhage International Trialists data repository (SAHIT). *World Neurosurg*. 2013;79(3-4):418-422.
33. Parra A, Kreiter KT, Williams S, et al. Effect of prior statin use on functional outcome and delayed vasospasm after acute aneurysmal subarachnoid hemorrhage: a matched controlled cohort study. *Neurosurgery*. 2005;56(3):476-484; discussion 476-84.
34. Wartenberg KE, Schmidt JM, Claassen J, et al. Impact of medical complications on outcome after subarachnoid hemorrhage. *Crit Care Med*. 2006;34(3): 617-623.

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Supplemental Digital Content. Supplementary Methods. Figure S1: Patient flow chart describing the cohort.

Supplemental Digital Content. Figure S2: Temporal trends in risk factors diagnoses for patients with aSAH. **A**, Temporal changes in the proportion of patients admitted with past medical history of hypertension. Of note, the trend is increasing in a statistically significant manner ($P < .05$) for all patients, as well as when separated into low-, intermediate-, and high-grade hemorrhage. **B**, Temporal changes in the proportion of patients admitted with a past medical history of diabetes mellitus. Overall, the trend remained stable for all patients, and when dissected by H&H grade. **C**, Temporal changes in the proportion of patients admitted with a past medical history of coronary artery disease. Overall, the trend remained stable for all patients and when dissected by H&H grade. **D**, Temporal changes in the proportion of patients admitted with a past medical history of active smoking. Overall, the trend remained stable for all patients and when dissected by H&H grade. **E**, Temporal changes in the proportion of patients admitted with a past medical history of dyslipidemia. Of note, the trend has increased in a statistically significant manner ($P < .05$) for all patients, and when separated into low-, intermediate-, and high-grade hemorrhage.

Supplemental Digital Content. Figure S3: Temporal changes in surgical approach for the ruptured aneurysm by low-, intermediate-, and high-grade hemorrhage. **A**, Surgical clipping. **B**, Endovascular approach. **C**, No treatment offered. P -value is for the linear regression analysis.

Supplemental Digital Content. Figure S4: Trends in common ICU complications and procedures over the years. P -value is calculated for each linear regression line. **A**, Rate of hydrocephalus; **B**, rate of cerebral vasospasm; **C**, rate of seizures; **D**, rate of bacterial central nervous system infections; **E**, rate of short-term mechanical ventilation; **F**, rate of long-term ventilation; **G**, rate of tracheostomy; **H**, rate of respiratory failure and/or adult respiratory distress syndrome; **I**, rate of hypotension and/or shock; **J**, rate of sepsis; **K**, rate of pneumonia; **L**, rate of urinary tract infection and/or pyelonephritis; **M**, rate of acute kidney injury; **N**, rate of DVT.

Supplemental Digital Content. Figure S5: Trends in common ICU complications and procedures over the years, analyzed using nonlinear methodology.

Supplemental Digital Content. Table S1: ICD/CPT codes found in the cohort and their separation into groups of diagnoses.

Supplemental Digital Content. Table S2: Details regarding patients who did not undergo a surgical procedure to secure their ruptured aneurysm during the acute admission. Not securing the aneurysm was not necessarily associated with withdrawal of care. To some degree, it resulted from the high acuity of the patients. Of note, the majority of these patients were admitted with a H&H 5. However, over a third of those patients were brain dead, and less than 10% were transitioned to hospice. In the lower-grade patients, the reasons for not offering an acute surgical intervention were diverse and included progression to brain death, withdrawal of care but also mortality due to critical illness and surgical preferences (for example, planning a delayed flow diverter in complex aneurysms). Proportion of brain dead patients is calculated per H&H group, and these patients are included in the in-patient mortality group.

Supplemental Digital Content. Table S3: Univariate logistic regression toward mRS > 2 at discharge ($n = 1793$)