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ORIGINAL ARTICLE

Healthcare Economics of Hydrocephalus After Aneurysmal Subarachnoid Hemorrhage in the United States

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Abstract

Hydrocephalus is one of the most common sequelae after aneurysmal subarachnoid hemorrhage (aSAH), and it is a large contributor to the condition's high rates of readmission and mortality. Our objective was to quantify the healthcare resource utilization (HCRU) and health economic burden incurred by the US health system due to post-aSAH hydrocephalus. The Truven Health MarketScan® Research database was used to retrospectively quantify the prevalence and HCRU associated with hydrocephalus in aSAH patients undergoing surgical clipping or endovascular coiling from 2008 to 2015. Multivariable longitudinal analysis was conducted to model the relationship between annual cost and hydrocephalus status. In total, 2374 patients were included; hydrocephalus was diagnosed in 959 (40.4%). Those with hydrocephalus had significantly longer initial lengths of stay (median 19.0 days vs. 12.0 days, $p < .001$) and higher 30-day readmission rates (20.5% vs. 10.4%, $p < .001$). With other covariates held fixed, in the first 90 days after aSAH diagnosis, the average cost multiplier relative to annual baseline for hydrocephalus patients was 24.60 (95% CI, 20.13 to 30.06; $p < .001$) whereas for non-hydrocephalus patients, it was 11.52 (95% CI, 9.89 to 13.41; $p < .001$). The 5-year cumulative median total cost for the hydrocephalus group was $230,282.38 (IQR, 166,023.65 to 318,962.35) versus $174,897.72 (IQR, 110,474.24 to 271,404.80) for those without hydrocephalus. We characterize one of the largest cohorts of post-aSAH hydrocephalus patients in the USA. Importantly, the substantial health economic impact and long-term morbidity and costs from this condition are quantified and reviewed.

Keywords Healthcare economics · Hydrocephalus · Subarachnoid hemorrhage · Ventriculoperitoneal shunt

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Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a common but devastating condition associated with case fatality rates ranging from 8 to 61% in the 1 month after diagnosis [1]. Of the various post-hemorrhage sequelae that contribute to this high mortality rate, hydrocephalus is one of the most common; its incidence ranges from 15–58.4% in the acute stage (48–72 h after SAH) to 4.3–37% in the chronic stage (> 14 days after SAH) [2]. Additionally, it has been shown that hydrocephalus is the second most common reason for 30-day readmission after aSAH and the third most common reason for 90-day readmission [3]. The two general explanations for the disruption in cerebrospinal fluid (CSF) flow in aSAH are as follows: (1) blood acting to create anatomic obstruction in the ventricles or cisterns and/or (2) impaired absorption by the arachnoid granulations [2].

Typical management of post-aSAH hydrocephalus includes placement of an extraventricular drain, sometimes followed by endoscopic third ventriculostomy or conversion to a permanent shunt. The most common shunt is the ventriculoperitoneal (VP) shunt, though ventriculoatrial and lumboperitoneal shunts are also possible.

In addition to the cost of these procedures, hydrocephalus is associated with longer hospital lengths of stay (LOS) [3–5]. Though there is this recognition of aSAH-associated hydrocephalus as a common and significant financial concern, there is scarce literature determining its actual monetary cost at the individual or systems level. Previous analyses include small single-institution studies regarding savings when VP shunts are placed at the same time as percutaneous endoscopic gastrostomy (PEG) tubes [5], changes in cost of treating aSAH over a 3-year period with VP shunting being a significant factor [4], and a comparison of cost between programmable and non-programmable shunts [6]. The only multi-institutional, large database study analyzed total cost associated with aSAH readmissions at 30 days and 90 days; hydrocephalus was one of the most common causes for readmission, though there was no analysis of costs associated specifically with hydrocephalus [3].

Timing of CSF diversion procedures may also be connected with the economic impact of post-aSAH hydrocephalus treatment. Previous groups have used discriminant analysis to predict soon after admission which patients will eventually need shunt operations, and they hypothesize that this capability may lead to shorter lengths of stay [7]. Others have also shown that earlier CSF shunting predicted improved recovery [8]. Though earlier CSF diversion procedures may be associated with reduced healthcare resource utilization, these potential savings have not yet been quantified. There are also a number of investigational clinical studies that have examined the potential for early blood removal post-aSAH and its impact on hydrocephalus, length of stay, and functional outcomes [9, 10].

The objective of this study was to quantify the additional healthcare resource utilization (HCRU) and health economic burden incurred by the US health system due to post-aSAH hydrocephalus.

Methods

Data Acquisition and Patient Population

The Truven Health Analytics MarketScan Research database (a national claims-based dataset covering inpatient admissions, outpatient services, and pharmacy costs, used in 1100+ publications since 1990 [11]) was utilized to retrospectively quantify both the prevalence and HCRU associated with hydrocephalus in patients who suffered aSAH and subsequently underwent either surgical clipping or endovascular coiling. All patients were at least 18 years old, treated in the USA between 2008 and 2015, and had continuous enrollment for at least 12 months before the aSAH diagnosis. Patients were identified by the primary International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for aSAH and the Current Procedural Terminology (CPT) codes for clipping or coiling. Additionally, patients were then classified as developing hydrocephalus or not based on ICD-9-CM codes. In the subset analysis of those who did develop hydrocephalus, *early* treatment was defined as a shunt procedure or third ventriculostomy done within 21 days of admission for aSAH, and *late* was between 22 and 90 days after admission. Patients with a CSF diversion procedure performed > 90 days after admission were excluded, as their hydrocephalus may not be directly related to aSAH; to isolate the effect of hydrocephalus specifically as a complication of aSAH, we focused on this acute 90-day period during which hydrocephalus most commonly develops. In all analyses, patients were excluded if they had ICD-9-CM codes for head trauma, arteriovenous malformations/fistulas, or a length of stay less than 2 days followed by a discharge home (to exclude superficial cortical and non-aneurysmal SAH). All codes may be found in Supplementary Tables 1 and 2.

Data were collected for the 1-year period prior to aSAH diagnosis to acquire a baseline and then through 5 years post-diagnosis (or 2 years for the subgroup analysis on early vs. late CSF diversion procedures). In addition to yearly tracking periods, costs were also tallied in the initial 90-day period immediately after diagnosis to better capture effects in the acute setting. Descriptive patient characteristics collected for the entire cohort include age at aSAH diagnosis, sex, insurance status, geographic region, employment status, and Charlson Comorbidity Index (CCI) score. CCI score was calculated using encounter services in the 1-year period before the initial diagnosis date.

The primary outcome of interest was HCRU, comprising total LOS for the initial inpatient encounter, service costs, outpatient medication costs, total healthcare costs (inpatient costs + outpatient costs + medication costs), and 30-day readmission status. All costs were adjusted for inflation based on the US Bureau of Labor Statistics indices to the 2017 USD (http://www.usinflationcalculator.com/inflation/consumer-price-index-and-annual-percent-changes-from-1913-to-2008/). In order to assess the change in HCRU over time, patients who had continuous enrollment for at least 12 months before and 90 days after the initial diagnosis were included in the analysis. Note that patients who did not survive more than 90 days after the initial diagnosis were automatically excluded. Patients who did not have the prescription information captured by MarketScan were further excluded from the cohort. Finally, patients with total payments above the 99th percentile were removed as outliers.

To expand beyond these HCRU data, secondary outcomes of interest such as discharge status for the initial admission of aSAH and 1-year survival rates were also analyzed. For these variables, patients without continuous enrollment for at least 90 days after the diagnosis were not excluded.

Statistical Analysis

The Wilcoxon-Mann-Whitney tests and chi-square tests were used to compare continuous and categorical variables, respectively. Additionally, a multivariate longitudinal analysis was conducted to model the relationship between annual cost and hydrocephalus status over time using a generalized estimating equation (GEE) model with log link, adjusting for sex, insurance, clipping versus coiling procedures, and CCI. The survival rates of patients with and without hydrocephalus were compared by using the log-rank test and plotted as Kaplan-Meier curves (censoring patients lost to follow-up). All statistical analyses were performed using SAS (version 9.4; SAS Institute, Cary, NC, USA) (further details in the Supplementary Methods).

Results

Hydrocephalus Versus No Hydrocephalus

Incidence

Between 2008 and 2015, 3807 adult patients were diagnosed with aSAH and underwent either a clipping or coiling procedure, while also having 12 months of continuous enrollment prior to the diagnosis. Of these, 2374 patients also had continuous enrollment for at least 90 days after the initial diagnosis and had prescription information captured by MarketScan. In this subgroup, 959 (40.4%) were diagnosed with hydrocephalus. Figure 1 represents a flow diagram.

Patient Characteristics

Descriptive baseline characteristics for the 3807 patients stratified by hydrocephalus status are presented in Table 1. Overall, the two groups were highly similar, with only slight differences observable. By small margins, patients who developed hydrocephalus tended to be older (median age, 56 years vs. 55 years), female (74.0% vs. 70.0%), and retired (18.3% vs. 16.9%). Insurance status, geographic distribution, and CCI scores were similar between groups. In the subset of patients used for time-dependent cost analysis, these same slight demographic differences were found (Supplementary Table 3).

A slightly higher proportion of patients who eventually developed hydrocephalus had initially undergone endovascular coiling compared to surgical clipping (76.6% vs. 72.8%). With regard to the first discharge status after aSAH diagnosis, fewer patients developing hydrocephalus were discharged home (40.0% vs. 58.1%) (Table 2).

In the Kaplan-Meier survival analysis, there was no significant difference in 1-year survival between the patients with and without hydrocephalus ($p = .39$, Fig. 2). Note, however, that MarketScan only tracks inpatient deaths, and thus this survival analysis does not necessarily reflect the overall death rate for aSAH. The majority of the death events occurred within 30 days after aSAH diagnosis. The overall survival probability at 30 days post-aSAH diagnosis is 91.2% (95% CI, 90.2–92.1%), and it remains steady until 1 year post-aSAH diagnosis at 89.8% (95% CI, 88.8–90.8%).

Impact of Hydrocephalus on HCRU

Patients with hydrocephalus had significantly longer lengths of stay for both the initial aSAH encounter (median, 19.0 days [IQR, 14.0 days to 26.0 days] vs. 12.0 days [IQR, 8.0 days to 17.0 days]; $p < .001$) (Table 3) and the entire first 90 days after aSAH (median, 25.0 days [IQR, 16.0 days to 43.0 days] vs. 14.0 days [IQR, 9.0 days to 22.0 days]) (Table 3). Looking at the subset of patients who had at least 90 days of continuous enrollment after aSAH diagnosis, the hydrocephalus group also had a significantly higher 30-day readmission rate compared to the non-hydrocephalus group (20.5% vs. 10.4%, $p < .001$).

Total cost was calculated as the sum of service and outpatient medication costs (Table 4; see Supplementary Results for written breakdown). At baseline, the median cost for patients in the hydrocephalus group was $2374.5 (IQR, 619.3 to 6898.2), compared to $3661.0 (IQR, 846.2 to 11,087.6) for patients in the non-hydrocephalus group. In the 90 days after aSAH diagnosis, the overall median cost increased rapidly to $189,198.9 (IQR, 114,487.7 to 290,374.1) for those with hydrocephalus and $119,466.1 (IQR, 72,392.0 to 189,084.7) for those without. Total costs quickly fell back down in the 90-day to 1-year period to $14,867.4 (IQR, 5211.4 to 37,175.7) for the hydrocephalus group and to $10,601.0 (IQR, 3960.0 to 25,749.6) for the non-hydrocephalus group. The total cost continued to decline, and in year 5 after aSAH diagnosis, the median cost was $5058.6 (IQR, 1752.4 to 13,521.9) and $4826.9 (IQR, 2104.5 to 15,673.6) for patients with and without hydrocephalus, respectively (Table 4). The 5-year cumulative median total cost for the hydrocephalus group was $230,282.38 (IQR, 166,023.65 to 318,962.35), and the cumulative total cost for those without hydrocephalus was $174,897.72 (IQR, 110,474.24 to 271,404.80) (Fig. 3).

Note that because of the requirement of continuous enrollment and the availability of the database, the sample size drops significantly at these later years, and only

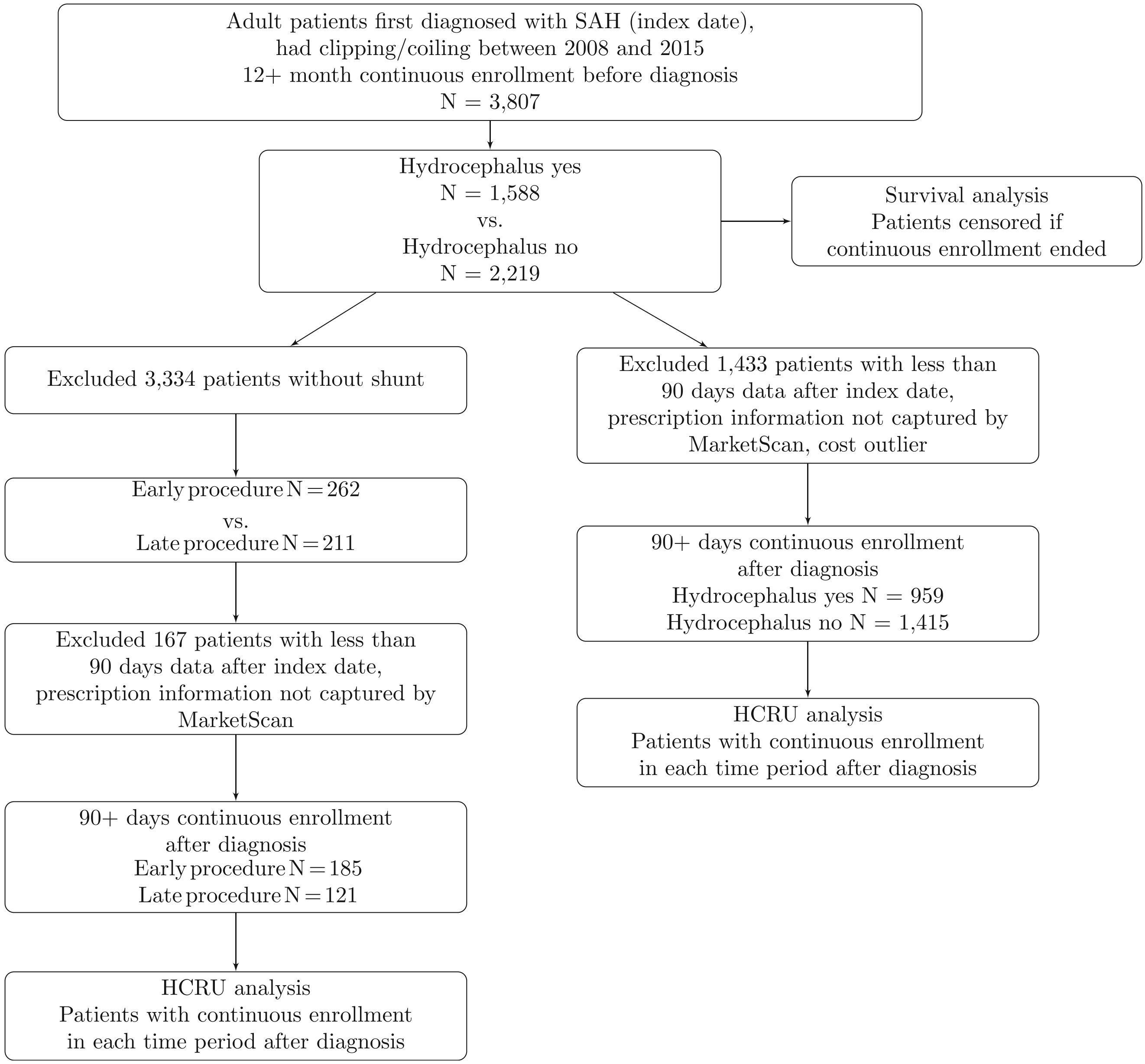

Fig. 1 Flow diagram of the inclusion/exclusion criteria for analysis

9.5% (225/2374) of the patients were used to assess 5-year post-diagnosis costs.

Multivariable Longitudinal Analysis for Total Cost

Table 5 presents the multivariable longitudinal analysis for total cost. Insurance status is a significant predictor ($p = .001$). The total cost for patients with Medicaid is 76.0% (95% CI, 0.64 to 0.90; $p = .001$) of that for patients with commercial claims. CCI is a significant predictor for the total cost ($p < .001$). With a 1-unit increase in CCI, the total cost will be 32% higher (95% CI, 26 to 38%; $p < .001$). Sex approached, but did not reach, significance ($p = .071$).

With other covariates held fixed, in the first 90 days after aSAH diagnosis, patients who developed hydrocephalus experienced, on average, a 24.60-times higher cost relative to their annual baseline (95% CI, 20.13 to 30.06; $p < .001$), whereas those without hydrocephalus experienced an average multiplier of 11.51 relative to baseline (95% CI, 9.89 to 13.41; $p < .001$). After 90 days post-diagnosis, the total cost decreased rapidly but was still significantly higher than at baseline. For patients with hydrocephalus, the average total cost in the 90–365-day period was 15.0% of that in the first 90-day period (95% CI, 0.13

Table 1 Baseline patient characteristics of the entire aSAH cohort, stratified by hydrocephalus status

	Hydrocephalus status		Total (*N* = 3807)
	No (*N* = 2219)	Yes (*N* = 1588)	
Age at SAH diagnosis			
Mean (SD)	54.7 (12.6)	55.7 (12.0)	55.2 (12.4)
Sex, *n* (%)			
Male	666 (30.0)	413 (26.0)	1079 (28.3)
Female	1553 (70.0)	1175 (74.0)	2728 (71.7)
Insurance, *n* (%)			
Commercial claims	1659 (74.8)	1141 (71.9)	2800 (73.5)
Medicaid	217 (9.8)	164 (10.3)	381 (10.0)
Medicare	343 (15.5)	283 (17.8)	626 (16.4)
Region, *n* (%)			
Northeast region	362 (16.3)	299 (18.8)	661 (17.4)
North central region	504 (22.7)	370 (23.3)	874 (23.0)
South region	805 (36.3)	527 (33.2)	1332 (35.0)
West region	287 (12.9)	203 (12.8)	490 (12.9)
Unknown region	44 (2.0)	25 (1.6)	69 (1.8)
Medicaid (no data)[a]	217 (9.8)	164 (10.3)	381 (10.0)
Employment status, *n* (%)			
Full time/part time	642 (28.9)	390 (24.6)	1032 (27.1)
Retiree	375 (16.9)	290 (18.3)	665 (17.5)
Other	985 (44.3)	744 (46.8)	1729 (45.4)
Medicaid (no data)[a]	217 (9.8)	164 (10.3)	381 (10.0)
Charlson Comorbidity Index score			
Missing	222	166	388
0, *n* (%)	1129 (56.5)	871 (61.3)	2000 (58.5)
1, *n* (%)	423 (21.2)	316 (22.2)	739 (21.6)
2, *n* (%)	237 (11.9)	142 (10.0)	379 (11.1)
3+, *n* (%)	208 (10.4)	93 (6.5)	301 (8.8)
Clipping/coiling, *n* (%)			
Clipping	603 (27.2)	371 (23.4)	974 (25.6)
Coiling	1616 (72.8)	1217 (76.6)	2833 (74.4)

SAH subarachnoid hemorrhage, *SD* standard deviation

[a] Medicaid data does not include region or employment status

to 0.17; $p < .001$), but 3.70 times of that in the baseline period (95% CI, 2.91 to 4.69; $p < .001$). For patients without hydrocephalus, the average total cost in the 90–365-day period was 17.0% of that in the first 90-day period

Table 2 Discharge statuses

Discharge status	Hydrocephalus status, *n* (%)			CSF diversion procedure type, *n* (%)		
	No (*N* = 2219)	Yes (*N* = 1588)	Total (*N* = 3807)	Early (*N* = 262)	Late (*N* = 211)	Total (*N* = 473)
Died	191 (8.6)	142 (8.9)	333 (8.7)	3 (1.1)	1 (0.5)	4 (0.8)
Home	1290 (58.1)	635 (40.0)	1925 (50.6)	94 (35.9)	61 (28.9)	155 (32.8)
Transferred to SNF, ICF, or other facilities	286 (12.9)	296 (18.6)	582 (15.3)	55 (21.0)	51 (24.2)	106 (22.4)
Other	452 (20.4)	515 (32.4)	967 (25.4)	110 (42.0)	98 (46.4)	208 (44.0)

ICF intermediate care facility, *SNF* skilled nursing facility

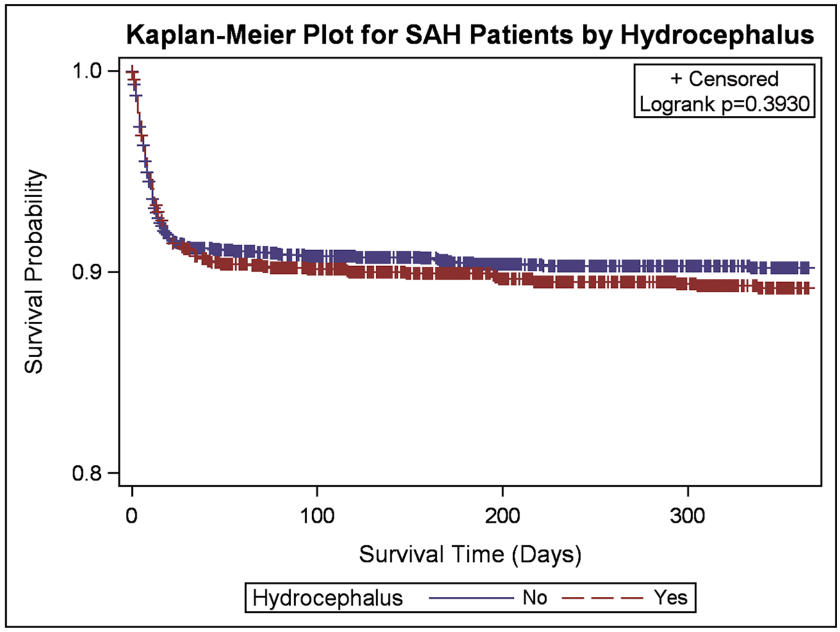

Fig. 2 Kaplan-Meier plots for aSAH patients with and without hydrocephalus (inpatient deaths only)

(95% CI, 0.15 to 0.19; $p < .001$), but 1.93 times of that in the baseline level (95% CI, 1.63 to 2.29; $p < .001$).

At baseline, the hydrocephalus group had an average total cost that was 70% that of the non-hydrocephalus group (95% CI, 0.55 to 0.89; $p = .004$). However, the cost for patients with hydrocephalus was 1.49 times (95% CI, 1.40 to 1.59; $p < .001$) and 1.34 times (95% CI, 1.12 to 1.59; $p = .001$) higher than those without the complication in the time periods of 1–90 days and 91–365 days after aSAH diagnosis, respectively. After year 1, the annual cost for both groups was not significantly different.

Early Versus Late CSF Diversion Procedures in Hydrocephalus

Incidence

Among 1588 patients who had hydrocephalus and continuous enrollment for at least 1 year prior to the diagnosis, 473 (29.8%) had CSF diversion procedures (shunts or third ventriculostomies). Of these, 262 (55.4%) had an early procedure (performed ≤ 21 days after aSAH admission) and 211 (44.6%) had a late procedure (performed > 21 days but <

Table 3 Length of stay, stratified by hydrocephalus status

	Hydrocephalus status		Total	*p* value
	No	Yes		
1-year period prior to diagnosis (baseline)				
N	1415	959	2374	
Median (Q1 to Q3)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	.001[a,b]
Initial SAH admission[c]				
N	2219	1588	3807	
Median (Q1 to Q3)	12.0 (8.0 to 17.0)	19.0 (14.0 to 26.0)	15.0 (10.0 to 22.0)	< .001[a]
90-day period post-diagnosis				
N	1415	959	2374	
Median (Q1 to Q3)	14.0 (9.0 to 22.0)	25.0 (16.0 to 43.0)	17.0 (12.0 to 31.0)	< .001[a]

SAH subarachnoid hemorrhage

[a] Wilcoxon test

[b] Due to the large sample size, even though the median is 0 for both groups, the distribution of lengths of stay in the two groups is still statistically different

[c] Note that for this secondary outcome, there is a larger *N* value because patients without continuous enrollment for at least 90 days after the diagnosis were not excluded

Table 4 Service, medication, and total cost breakdown by hydrocephalus status

	Hydrocephalus (no)	Hydrocephalus (yes)	Total
1-year period prior to diagnosis (baseline)			
N	1415	959	2374
Median HSC (Q1 to Q3)	2156.3 (460.2 to 8541.7)	1451.5 (340.8 to 4660.1)	1810.0 (420.3 to 6743.7)
Median medication cost (Q1 to Q3)	376.2 (22.8 to 1941.6)	321.7 (11.8 to 1582.1)	358.3 (17.6 to 1791.7)
Median total cost[a] (Q1 to Q3)	3661.0 (846.2 to 11,087.6)	2374.5 (619.3 to 6898.2)	2965.5 (751.2 to 9556.6)
90-day period post-diagnosis			
N	1415	959	2374
Median HSC (Q1 to Q3)	119,085.8 (71,671.8 to 188,252.1)	188,688.6 (114,124.4 to 290,192.3)	142,024.0 (84,787.5 to 232,493.5)
Median medication cost (Q1 to Q3)	356.4 (60.3 to 962.4)	211.6 (8.1 to 728.5)	285.1 (35.3 to 874.7)
Median total cost (Q1 to Q3)	119,466.1 (72,392.0 to 189,084.7)	189,198.9 (114,487.7 to 290,374.1)	142,801.1 (85,378.2 to 233,207.5)
90-day to 1-year period post-diagnosis			
N	948	589	1537
Median HSC (Q1 to Q3)	9016.5 (2834.4 to 22,984.5)	13,222.3 (4138.5 to 34,727.7)	10,677.1 (3258.0 to 26,916.6)
Median medication cost (Q1 to Q3)	672.2 (130.8 to 1941.8)	783.6 (158.5 to 1958.8)	712.4 (136.0 to 1942.5)
Median total cost (Q1 to Q3)	10,596.2 (3960.0 to 25,749.6)	14,867.4 (5211.4 to 37,175.7)	12,213.4 (4494.4 to 29,425.1)
2nd 1-year period post-diagnosis			
N	592	341	933
Median HSC (Q1 to Q3)	5273.0 (1816.1 to 15,578.0)	6274.2 (1751.1 to 17,821.5)	5606.5 (1803.0 to 16,259.2)
Median medication cost (Q1 to Q3)	745.8 (146.2 to 2767.1)	909.5 (234.3 to 2592.0)	826.0 (160.3 to 2692.4)
Median total cost (Q1 to Q3)	7120.1 (2582.8 to 18,591.3)	8740.7 (2825.4 to 20,586.7)	7615.9 (2670.0 to 19,531.3)
3rd 1-year period post-diagnosis			
N	422	241	663
Median HSC (Q1 to Q3)	3176.8 (1053.1 to 10,118.3)	3301.6 (1201.8 to 10,494.1)	3185.7 (1116.7 to 10,211.7)
Median medication cost (Q1 to Q3)	638.6 (138.3 to 2219.0)	834.6 (167.0 to 2237.9)	716.1 (156.4 to 2237.9)
Median total cost (Q1 to Q3)	4878.3 (1930.5 to 13,539.5)	4893.2 (2063.5 to 13,508.1)	4890.2 (2003.4 to 13,539.5)
4th 1-year period post-diagnosis			
N	258	136	394
Median HSC (Q1 to Q3)	3162.7 (782.0 to 9072.5)	3085.2 (1025.4 to 7835.4)	3123.5 (865.1 to 8769.2)
Median medication cost (Q1 to Q3)	675.0 (100.8 to 2430.9)	1199.1 (181.4 to 2400.2)	866.9 (124.5 to 2416.9)
Median total cost (Q1 to Q3)	4553.4 (1608.5 to 14,442.3)	4846.5 (2111.0 to 13,590.1)	4616.5 (1652.5 to 13,795.7)
5th 1-year period post-diagnosis			
N	144	81	225
Median HSC (Q1 to Q3)	3116.0 (1046.2 to 11,257.6)	2035.7 (872.8 to 7168.0)	2783.5 (974.6 to 10,188.9)
Median medication cost (Q1 to Q3)	939.0 (175.8 to 2671.5)	1171.1 (278.0 to 2860.7)	1011.7 (204.9 to 2681.7)
Median total cost (Q1 to Q3)	4826.9 (2104.5 to 15,664.7)	5058.6 (1752.4 to 13,521.9)	4944.0 (1964.4 to 14,555.6)

HSC hospital service cost (inpatient + outpatient)

[a] Total cost = service + medication cost

90 days after aSAH admission). Among these 473 patients, 306 (64.7%) had continuous enrollment for at least 90 days after aSAH admission and prescription data available in MarketScan, thus qualifying them for HCRU analysis.

Patient Characteristics

Descriptive baseline characteristics for the 473 patients stratified by procedure timing are presented in Table 6 (and Supplementary Table 4 for HCRU analysis subset). Overall, the two groups again exhibited only slight differences (see Supplementary Results for written breakdown).

Impact of CSF Diversion Procedure Timing on HCRU

Patients with late procedures had significantly longer lengths of stay for both the initial aSAH encounter (median, 32.0 days [IQR, 23.0 days to 43.0 days] vs. 22.0 days [IQR, 16.0 days to 27.0 days]; $p < .001$) and the entire first 90 days after aSAH (median, 47.0 days

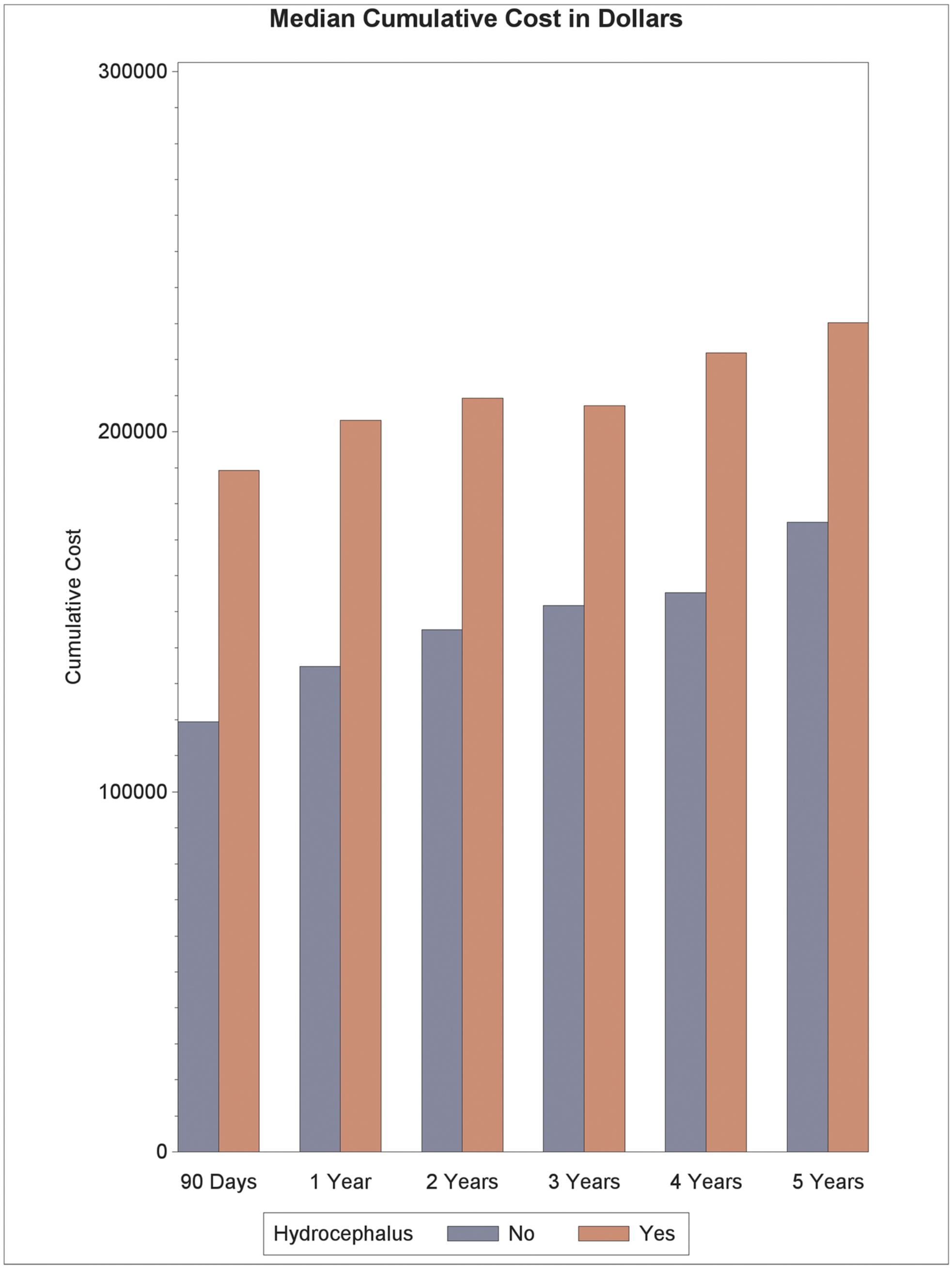

Fig. 3 Cumulative cost by hydrocephalus status

Note[1] that patients whose enrollment ended in each time window were excluded from the analysis. Therefore, the sample size in each time window is different, and the median cumulative cost for each time period was calculated with different sample sizes.

[IQR, 36.0 days to 68.0 days] vs. 28.0 days [IQR, 18.0 days to 45.0 days]) (Table 7). Looking at the subset of patients who had at least 90 days of continuous enrollment after aSAH diagnosis, the late procedure group had a significantly higher 30-day readmission rate compared to the early procedure group (42.2% vs. 21.5%, $p < .001$).

Total cost was calculated as the sum of service and outpatient medication costs (see Supplementary Results for written breakdown). At baseline, the median cost for patients in the early procedure group was $3288.2 (IQR, 811.0 to 7205.0) compared to $2801.8 (IQR, 851.1 to 6408.7) for patients in the late procedure group. In the 90 days after aSAH diagnosis, the overall median cost increased dramatically to $201,136.9 (IQR, 124,038.7 to 292,087.2) for those with early procedures and to $271,383.3 (IQR, 169,392.6 to 391,879.6) for those with late procedures. Total costs quickly fell back down after

Table 5 Multivariable longitudinal analysis for cost

Covariate	Level	Cost ratio (95% confidence interval)	*p* value
Sex of patient	Male	1.13 (0.99, 1.30)	.071
	Female	Reference	
Charlson Comorbidity Index score		1.32 (1.26, 1.38)	< .001
Insurance type	Medicaid	0.76 (0.64, 0.90)	.001
	Medicare	0.84 (0.71, 1.01)	.059
	Commercial claims	Reference	
Baseline: coiling vs. clipping	Coiling	1.13 (1.02, 1.26)	.024
	Clipping	Reference	
Days 1–90 vs. baseline: hydrocephalus (yes)	1–90 days	24.60 (20.13, 30.06)	< .001
	Baseline	Reference	
Days 1–90 vs. baseline: hydrocephalus (no)	1–90 days	11.52 (9.89, 13.41)	< .001
	Baseline	Reference	
Days 90–365 vs. days 1–90: hydrocephalus (yes)	90–365 days	0.15 (0.13, 0.17)	< .001
	1–90 days	Reference	
Days 90–365 vs. days 1–90: hydrocephalus (no)	90–365 days	0.17 (0.15, 0.19)	< .001
	1–90 days	Reference	
Days 90–365 vs. baseline: hydrocephalus (yes)	90–365 days	3.69 (2.91, 4.69)	< .001
	Baseline	Reference	
Days 90–365 vs. baseline: hydrocephalus (no)	90–365 days	1.93 (1.63, 2.29)	< .001
	Baseline	Reference	
Baseline: hydrocephalus (yes vs. no)	Hydrocephalus (yes)	0.70 (0.55, 0.89)	.004
	Hydrocephalus (no)	Reference	
1–90 days: hydrocephalus (yes vs. no)	Hydrocephalus (yes)	1.49 (1.40, 1.59)	< .001
	Hydrocephalus (no)	Reference	
90–365 days: hydrocephalus (yes vs. no)	Hydrocephalus (yes)	1.34 (1.12, 1.59)	.001
	Hydrocephalus (no)	Reference	
1–2 years: hydrocephalus (yes vs. no)	Hydrocephalus (yes)	0.94 (0.75, 1.18)	.59
	Hydrocephalus (no)	Reference	
2–3 years: hydrocephalus (yes vs. no)	Hydrocephalus (yes)	0.96 (0.66, 1.38)	.81
	Hydrocephalus (no)	Reference	
3–4 years: hydrocephalus (yes vs. no)	Hydrocephalus (yes)	0.98 (0.60, 1.60)	.95
	Hydrocephalus (no)	Reference	
4–5 years: hydrocephalus (yes vs. no)	Hydrocephalus (yes)	1.16 (0.73, 1.85)	.54
	Hydrocephalus (no)	Reference	

The number of observations used in the regression was 7441

the 90-day period; in year 2 after aSAH diagnosis, the median cost was $12,827.7 (IQR, 4131.3 to 24,371.3) and $10,877.9 (IQR, 5183.4 to 23,645.1) for patients with early and late procedures, respectively (Table 8). The 2-year cumulative median total cost for the early procedure group was $241,086.3 (IQR, 148,417.3 to 340,615.1) versus $285,836.2 (IQR, 182,570.5 to 443,474.5) for those with late procedures (Fig. 4).

Note that because of the requirement of continuous enrollment and the availability of the database, the sample size drops by year 2 so that 37.3% (114/306) of the patients were used to assess 2-year post-diagnosis costs.

Discussion

To our knowledge, we herein present the first large-scale analysis of the economic and healthcare resource burden of post-aSAH hydrocephalus. By several metrics, this common complication of aSAH takes a significant toll on patients and the US healthcare system. Previous studies have investigated predictors for the development of hydrocephalus after aSAH [2, 7, 12–14], but none have quantified the impact of the complication on HCRU.

In the first 90 days after aSAH diagnosis, comparing patients going on to develop hydrocephalus versus those who did not, the difference in median total cost was

Table 6 Baseline patient characteristics, stratified by timing of CSF diversion procedure

	Early (N = 262)	Late (N = 211)	Total (N = 473)
Age at SAH diagnosis			
Mean (SD)	57.2 (12.0)	56.5 (10.6)	56.9 (11.4)
Sex, *n* (%)			
Male	64 (24.4)	57 (27.0)	121 (25.6)
Female	198 (75.6)	154 (73.0)	352 (74.4)
Insurance, *n* (%)			
Commercial claims	182 (69.5)	157 (74.4)	339 (71.7)
Medicaid	20 (7.6)	15 (7.1)	35 (7.4)
Medicare	60 (22.9)	39 (18.5)	99 (20.9)
Region, *n* (%)			
Northeast region	50 (19.1)	40 (19.0)	90 (19.0)
North central region	62 (23.7)	59 (28.0)	121 (25.6)
South region	92 (35.1)	61 (28.9)	153 (32.3)
West region	35 (13.4)	34 (16.1)	69 (14.6)
Unknown region	3 (1.1)	2 (0.9)	5 (1.1)
Medicaid (no data)[a]	20 (7.6)	15 (7.1)	35 (7.4)
Employment status, *n* (%)			
Full time/part time	69 (26.3)	61 (28.9)	130 (27.5)
Retiree	58 (22.1)	47 (22.3)	105 (22.2)
Other	115 (43.8)	88 (41.7)	203 (42.9)
Medicaid[a]	20 (7.6)	15 (7.1)	35 (7.4)
Charlson Comorbidity Index score			
Missing	28	29	57
0, *n* (%)	143 (61.1)	110 (60.4)	253 (60.8)
1, *n* (%)	49 (20.9)	42 (23.1)	91 (21.9)
2, *n* (%)	25 (10.7)	16 (8.8)	41 (9.9)
3+, *n* (%)	17 (7.3)	14 (7.7)	31 (7.5)
Clipping/coiling, *n* (%)			
Clipping	73 (27.9)	52 (24.6)	125 (26.4)
Coiling	189 (72.1)	159 (75.4)	348 (73.6)

SAH subarachnoid hemorrhage, *SD* standard deviation

[a] Medicaid data does not include region or employment status

$69,732.8. The annual cost differential disappeared 1 year after aSAH diagnosis. With all other factors held constant in multivariable analysis, having hydrocephalus resulted in a nearly 25-fold increase in cost over baseline just during the first 90 days after aSAH, compared to only a 12-fold increase in those who did not develop hydrocephalus.

Our finding that hydrocephalus is associated with higher 30-day readmission rates supports previous findings using the Nationwide Readmissions Database; in fact, hydrocephalus was the only SAH-related complication that was actually related to readmission [15]. Our work also provides more concrete numbers illustrating the economic impact of hydrocephalus.

In single-institution studies of SAH, the need for VP shunt was predictive in multivariable analysis of longer LOS [4], and predictors for early versus late shunting have been identified [16]. Our study complements both ideas, as it is the first to quantify differences in HCRU depending on the timing of CSF diversion procedures. Comparing late versus early procedures, the difference in median total cost was $70,246.4 in the first 90 days after aSAH. The most likely explanation for this dramatic difference is the increased LOS for the late procedure group; their median LOS in the first 90 days post-aSAH was 1.68 times longer (47 days vs. 28 days), and their total first 90-day cost was 1.35 times higher ($271,383.3 vs. $201,136.9). Of course, there may be several other factors contributing to the difference. In 2013, Becker's Hospital Review estimated that one inpatient day in a US non-profit hospital costs an average of $2289 [17]; using this as a rough, conservative estimate (since state/local government hospitals and for-profit hospitals were associated with lower costs), the 19-day difference in median LOS for the late procedure versus early procedure groups should contribute to a cost difference of $43,491 (not inflation adjusted)—far short of the $70,426 seen here.

Table 7 Length of stay for initial SAH admission by timing of CSF diversion procedure

	Early	Late	Total	*p* value
1-year period prior to diagnosis (baseline)				
N	185	121	306	
Median (Q1, Q3)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.8538[a]
Initial SAH admission[b]				
N	262	211	473	
Median (Q1, Q3)	22.0 (16.0, 27.0)	32.0 (23.0, 43.0)	25.0 (18.0, 36.0)	< .0001[a]
90-day period post-diagnosis				
N	185	121	306	
Median (Q1, Q3)	28.0 (18.0, 45.0)	47.0 (36.0, 68.0)	37.0 (22.0, 52.0)	< .0001[a]

SAH subarachnoid hemorrhage

[a] Wilcoxon test

[b] Note that for this secondary outcome, there is a larger *N* value because patients without continuous enrollment for at least 90 days after the diagnosis were not excluded

Table 8 Service, medication, and total cost breakdown by timing of CSF diversion procedure

	Total costs		
	Early	Late	Total
1-year period prior to diagnosis (baseline)			
N	185	121	306
Median HSC (Q1 to Q3)	1801.4 (455.0 to 4833.6)	1390.1 (297.9 to 3905.3)	1690.2 (372.6 to 4425.0)
Median medication cost (Q1 to Q3)	451.2 (20.6 to 1898.3)	317.2 (13.2 to 1703.9)	413.0 (13.2 to 1883.1)
Median total cost[a] (Q1 to Q3)	3288.2 (811.0 to 7205.0)	2801.8 (851.1 to 6408.7)	2907.9 (811.0 to 6987.9)
90-day period post-diagnosis			
N	185	121	306
Median HSC (Q1 to Q3)	200,792.9 (123,280.2 to 291,619.2)	271,109.0 (168,994.4 to 391,879.6)	227,452.4 (133,744.1 to 339,569.6)
Median medication cost (Q1 to Q3)	202.1 (25.5 to 704.8)	55.2 (0.0 to 286.2)	142.8 (0.0 to 502.6)
Median total cost (Q1 to Q3)	201,136.9 (124,038.7 to 292,087.2)	271,383.3 (169,392.6 to 391,879.6)	228,458.4 (134,846.6 to 339,992.6)
90-day to 1-year period post-diagnosis			
N	120	74	194
Median HSC (Q1 to Q3)	18,612.5 (6090.8 to 35,087.2)	24,409.6 (7495.9 to 54,648.5)	19,698.2 (6794.2 to 42,725.7)
Median medication cost (Q1 to Q3)	1069.3 (282.2 to 2264.4)	1102.4 (571.2 to 2307.3)	1093.6 (315.7 to 2276.3)
Median total cost (Q1 to Q3)	21,617.7 (6618.0 to 38,018.2)	25,764.9 (10,493.0 to 56,365.3)	22,315.5 (8317.9 to 47,090.7)
2nd 1-year period post-diagnosis			
N	74	40	114
Median HSC (Q1 to Q3)	8635.8 (2199.9 to 21,347.2)	8941.3 (3273.6 to 21,456.9)	8635.8 (2725.8 to 21,347.2)
Median medication cost (Q1 to Q3)	1194.3 (321.8 to 3206.9)	1593.4 (380.1 to 2629.0)	1213.8 (342.3 to 2953.5)
Median total cost (Q1 to Q3)	12,827.7 (4131.3 to 24,371.3)	10,877.9 (5183.4 to 23,594.3)	12,114.2 (4918.4 to 24,371.3)

HSC hospital service cost (inpatient + outpatient)

[a] Total cost = service + medication cost

Future analyses may aim to repeat the comparisons made here with larger sample sizes, and the effect of procedure timing on HCRU should be analyzed in multivariable fashion to better understand the many factors that may play into total cost. Ultimately, the goal should be to accurately identify patients at risk of developing procedure-requiring hydrocephalus and treat them early; with the data presented here, we now know how much burden could be lifted from the US healthcare system if this was possible. A recent meta-analysis identified several risk factors for eventual shunting after aSAH, including high Fisher grade, high Hunt and Hess scale score, presence of intraventricular blood, re-hemorrhage, posterior circulation location of the aneurysm, and age ≥ 60 years [18]. The Chronic Hydrocephalus Ensuing from SAH Score (CHESS) incorporates some of these variables into a simple tool to predict which patients are most likely to become shunt-dependent after aSAH; scoring is based on Hunt and Hess grade ≥ 4 (1 point), location of the ruptured aneurysm in the posterior circulation (1 point), acute hydrocephalus (4 points), the presence of intraventricular hemorrhage (1 point), and early cerebral infarction on follow-up CT scan (1 point). A score ≥ 6 was associated with a 6.74-fold higher risk of shunt dependency compared to those with < 6 points [19]. Our results suggest that the increased use of this tool and others like it may improve patient outcomes and reduce HCRU after aSAH if it enables earlier treatment.

The findings presented here complement a single-institution cost analysis regarding the increased HCRU associated with cerebral vasospasm after aSAH [20]. In this study of 198 patients, linear regression models showed that patients experiencing symptomatic vasospasm incurred costs that were 1.27 times higher and

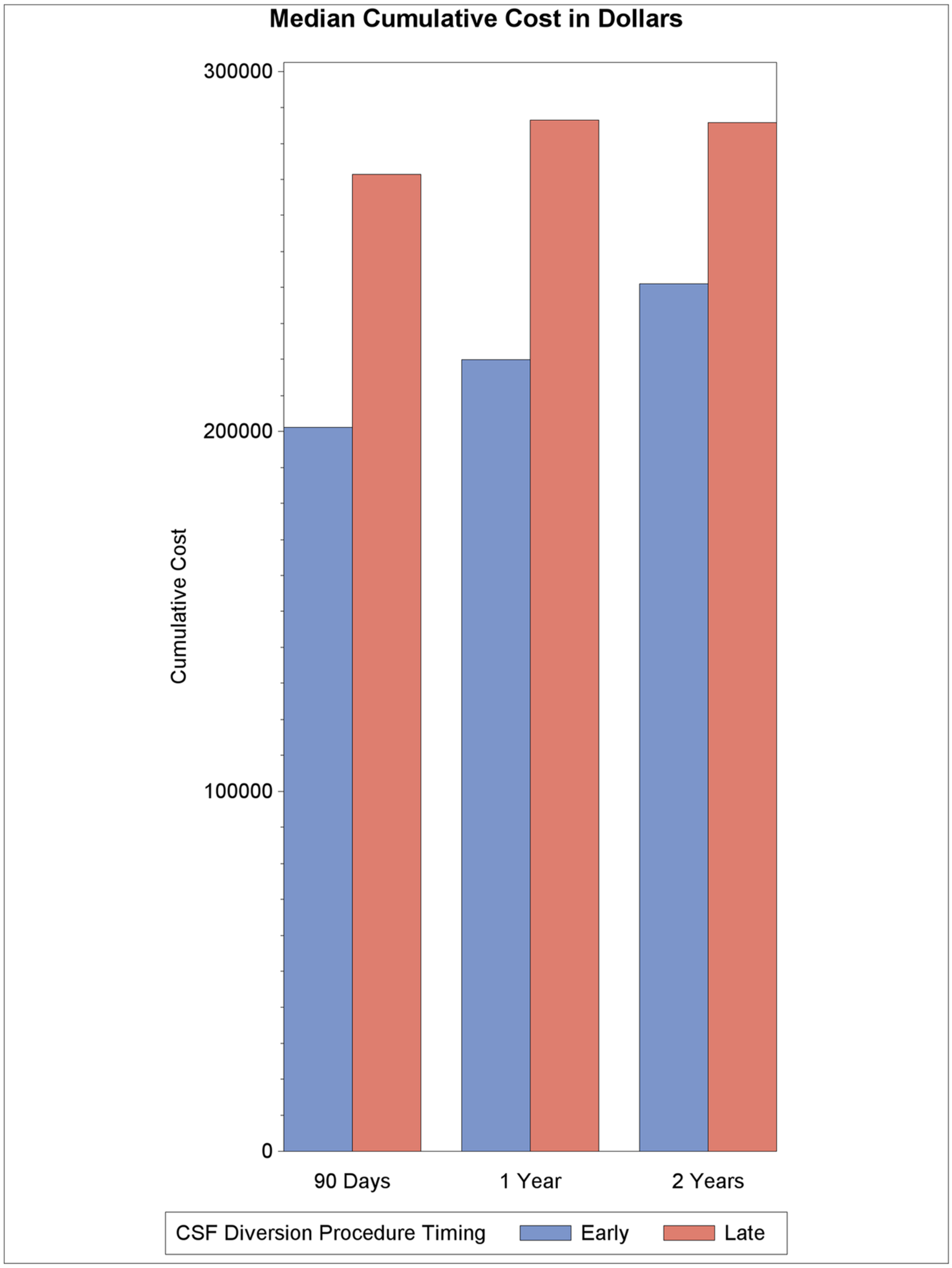

Fig. 4 Cumulative cost by CSF diversion procedure timing.

Note[1] that patients whose enrollment ended in each time window were excluded from the analysis. Therefore, the sample size in each time window is different, and the median cumulative cost for each time period was calculated with different sample sizes.

endured lengths of stay 1.24 times longer than those without vasospasm. With a better understanding of the resource burden of post-aSAH sequelae such as vasospasm and hydrocephalus, we will be better equipped to target future efforts towards those factors that most affect both patients and healthcare systems.

Though not the primary aim of the current study, as a clinical point, there were similar proportions of patients who underwent either clipping or coiling in both the hydrocephalus and non-hydrocephalus groups. One may hypothesize that because clipping is an open procedure, there may be a smaller chance of hydrocephalus development, but this gestalt is not supported by our descriptive data. This finding is in line with a previous observational study using the National Inpatient Sample database [21]. On the other hand, though not targeting the same question, a 2017 study of California's non-federal emergency departments and acute care hospitals found microsurgical clipping to be associated with the development of delayed hydrocephalus (without a clear definition of *delayed*) in multivariable analysis [22].

This study is limited by its retrospective nature and inherent shortcomings of the MarketScan database. Incorrect or incomplete coding, in addition to patient exclusion due to death before 90 days or non-continuous enrollment either before or after aSAH, could potentially bias results. Additionally, only a small subset of hydrocephalus patients had complete data available for HCRU analysis of the effect of CSF diversion procedure timing, and it is uncertain whether or not our sample was representative of the broader patient population. Finally, the 21-day cutoff for early versus late is somewhat arbitrary; we chose it to align with the window of time commonly used in the treatment of vasospasm after SAH, as it serves as the checkpoint for clinicians to begin scaling back medications and other protections. Thus, though our selection of 21 days is one choice among many, having consistent temporal checkpoints may lead to greater ease of application of our findings in the clinical setting.

Conclusion

Our study characterizes one of the largest cohorts of aSAH patients in the USA. Importantly, the health economic impact and long-term morbidity due to post-aSAH hydrocephalus are quantified and reviewed. The healthcare resource utilization of post-aSAH hydrocephalus in the USA is substantial.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Ethical Approval This article does not contain any studies with human participants performed by any of the authors.

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