Intraventricular thrombolysis in intracerebral hemorrhage requiring ventriculostomy: a decade-long real-world experience

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Abstract

Background and purpose—Intraventricular thrombolysis (IVT) is a promising treatment in facilitating intraventricular clot resolution after intraventricular hemorrhage. We examined in-hospital outcomes and resource utilization after thrombolysis in patients with intraventricular hemorrhage requiring ventriculostomy in a 'real-world' setting.

Methods—Retrospective cohort. We identified adult patients with primary diagnosis of non-traumatic intracerebral hemorrhage requiring ventriculostomy from the Nationwide Inpatient Sample (NIS) from 2002–2011. We compared demographic and hospital characteristics, comorbidities, inpatient outcomes, and resource utilization measures between patients treated with IVT and those managed with ventriculostomy, but without IVT. Population estimates were extrapolated using standard NIS weighting algorithms.

Results—We included 34,044 patients in the analysis, of whom 1,133 (3.3%) received IVT. The thrombolysis group had significantly lower inpatient mortality (32.4% vs 41.6%, P=0.001) and it remained lower after controlling for baseline demographics, hospital characteristics, comorbidity, case severity and withdrawal of care status (adjusted odds ratio [OR]: 0.670; 95% confidence interval [CI]: 0.520–0.865; P=0.002). There was a trend toward favorable discharge (home or rehabilitation) among the thrombolysis cohort (adjusted OR: 1.335; 95% CI: 0.983–1.812, P=0.064). The adjusted rates of bacterial meningitis and ventricular shunt placement were similar between groups. The thrombolysis group had longer length of hospital stay (LOS) and higher inflation adjusted cost of care, but cost of care per day LOS was similar to the non-IVT group.

Conclusions—IVT for intracerebral hemorrhage requiring ventriculostomy resulted in lower inpatient mortality and a trend toward favorable discharge outcome with similar rates of inpatient complications compared to the non-IVT group.

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Keywords

intraventricular hemorrhage; intracerebral hemorrhage; hemorrhagic stroke; thrombolysis; intraventricular thrombolysis; ventriculostomy; shunting; meningitis; mortality; outcomes; real-world; nationwide inpatient sample

Introduction

Intraventricular extension of intracerebral hemorrhage (ICH) is common; occurring in 40% cases of non-traumatic ICH, and is a strong independent predictor of mortality after ICH.[1, 2] Intraventricular hemorrhage (IVH) is historically treated by insertion of a ventriculostomy catheter to allow for monitoring of intracranial pressure and drainage of hemorrhagic cerebrospinal fluid (CSF). However, ventriculostomy catheter alone does not promote clot resolution and may become obstructed by intraventricular blood. Intraventricular injection of fibrinolytic agents has been shown to facilitate clearing of ventricular blood clot, decrease the rate of hydrocephalus in animal models and improve mortality in case-series and meta-analysis.[3–6]

Efficacy of intraventricular thrombolysis (IVT) with recombinant tissue plasminogen activator (tPA) is being evaluated in a large multicenter clinical trial (Clot Lysis Evaluation of Accelerated Resolution of Intraventricular Hemorrhage, CLEAR III).[7] Efficacy in clinical trials may not always be reflected at a population level due to limited generalizability of trials using strict study protocols and variations in clinical practice. Moreover, clinical trials, due to their limited sample size, may not have enough power to study differences in infrequent treatment-related adverse events. Therefore, large-scale population studies are necessary to substantiate the results of clinical trials and evaluate the effectiveness of the delivery of treatment in clinical practice to a broader target. Although not yet approved by the United States (US) Food and Drug Administration, intraventricular tPA is already used off-label for the treatment of IVH associated hydrocephalus in the US.[8] Frequency of utilization and outcomes of such treatment outside the context of clinical trials is largely unknown. Therefore, we aimed to study in-hospital outcomes and resource utilization after IVT for ICH patients requiring ventriculostomy in a population-based, retrospective cohort study from a large national health database.

Methods

Data-source

We analyzed data from the Nationwide Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project (HCUP) from 2002–2011. NIS is a 20% stratified random sample of all admissions to non-federal hospitals in the US. It contains information regarding demographics, hospital characteristics, primary and secondary diagnoses, inpatient procedures, comorbidities and case-severity measures. All diagnoses and procedures are recorded using International Classification of Diseases version 9 Clinical Modification (ICD-9-CM) codes. Discharge weights are provided to permit extrapolation of population

estimates from the sampled cases. Detailed information regarding the design and the contents of NIS is available at the HCUP website.[9]

Case-selection

We first identified cases with primary diagnosis of non-traumatic ICH with or without IVH by using ICD-9-CM code 431.[10, 11] Only patients with IVH requiring ventriculostomy were selected, using procedure code 02.2 (prior to October, 1, 2011) and 02.21 (from October, 1, 2011).[12] We excluded cases with age <18 years, traumatic brain injury, brain malignancy, cerebral vascular malformations and those undergoing aneurysm clipping or coiling to restrict our population to those with primary ICH. Thrombolytic treatment was ascertained by procedure code 99.10. As the ICD-9-CM code does not distinguish the indication and route of thrombolytic treatment delivery, cases with acute stroke, myocardial infarction, pulmonary embolism, and end-stage renal disease requiring dialysis with possibility of access catheter thrombosis were excluded to minimize the uncertainty of indication for thrombolytic treatment. As the unit of the NIS database is discharge after hospitalization, rather than an individual patient, cases transferred to another hospital were excluded to prevent double counting of the same patient. Patients enrolled in a clinical trial (ICD-9-CM code V70.7) were also excluded. (Figure 1)

Comorbidity and severity adjustment

We calculated the modified Charlson comorbidity index,[13] a weighted score of 17 different comorbidities validated for outcome adjustment for analyses of administrative datasets using ICD-9-CM codes.[14] Case severity was determined using the all patient refined diagnosis-related groups (APR-DRGs) to assess risk of mortality using an algorithm developed by 3M™ Health Information Systems. This proprietary 4 point ordinal scale (minor, moderate, major and extreme risk of mortality) is derived from age, primary and secondary diagnoses, and procedures.[15, 16] The APR-DRG methodology has been validated to predict mortality more reliably than other severity measures using administrative datasets and has been used as a severity indicator in prior studies, including those relating to hemorrhagic stroke.[17–19]

Outcomes measures

The primary outcome of interest was inpatient mortality. Secondary outcomes studied were a composite favorable outcome of discharge to home/self-care or rehabilitation, and a composite unfavorable outcome of discharge to skilled nursing facility, hospice or death. Discharge disposition has been shown to correlate with 90-day and 1-year modified Rankin Scale with discharge to home or rehabilitation indicating higher functional potential than discharge to skilled nursing facility.[20] Other safety outcomes studied were rates of bacterial meningitis, permanent ventricular shunting, gastrointestinal bleeding, gastrostomy and tracheostomy. Resource utilization measures used in the study were length of stay (LOS), overall cost of care and cost of care per day LOS. Cost of care was obtained by using hospital charges and HCUP cost-to-charge ratios, and was adjusted for inflation to obtain 2013 US dollar values by using yearly inflation rates published by US Department of Labor-Bureau of Labor statistics.[21]

We also compared the outcomes between the IVT group and the non-IVT group among the following sub-cohorts to assess robustness of the primary results: (1) cases excluding withdrawal of care (ICD-9-CM code V66.7),[22] (2) survival beyond 48 hours from admission, (3) high ICH case volume hospitals (>47 cases/year comprising top 2 quartiles), (4) coding for obstructive hydrocephalus, (5) prolonged mechanical ventilation (>96 hours), (6) transferred in from another hospital.

Statistical analysis

Comparisons were made using Chi-square and Wilcoxon rank sum tests for categorical and continuous variables respectively. Multivariate logistic regression was used to adjust for available potential confounders in assessing the effect of IVT on outcomes. The following covariates were included in all regression models: age, sex, race/ethnicity, inter-institutional transfer, hospital characteristics (location, teaching status, geographic region, bedsize and ICH case volume quartile), modified Charlson comorbidity index, 3M™ APR-DRG risk of mortality subclass, coronary artery disease, diabetes mellitus, hypertension, atrial fibrillation, dyslipidemia, anemia, valvular disease, anticoagulation associated hemorrhage, thrombocytopenia, blood components transfusion, performance of cerebral angiography, craniectomy and craniotomy, prolonged mechanical ventilation and withdrawal of care status. We studied 10-year temporal trends of utilization of ventriculostomy in ICH and of IVT among the cases included in the analysis using Chi-square test for linear association. As recommended by HCUP, population estimates were obtained by complex sample analyses that consider weights, clustering, and stratification used for NIS sampling.[23] All analyses were performed by using IBM SPSS version 20 (IBM Corporation, NY, USA) with statistical significance set at $P < 0.05$. No adjustment was made for multiple comparisons due to the exploratory nature of the analysis.

Results

Of the 655,078 cases with primary diagnosis of ICH, 42,422 (6.5%) underwent ventriculostomy. Among 34,044 patients meeting eligibility criteria, 1,133 (3.3%) patients received IVT. Patients receiving IVT were slightly younger [median (interquartile range, IQR) age: 58 (51–70) vs 61 (51–72) years, $P < 0.001$]. Sex and racial distributions were similar between the IVT and non-IVT groups. The IVT group had proportionately higher rates of inter-institutional transfer and patients were more likely to be treated in a teaching hospital and in the western US. Annual hospital ICH case volume was also higher among the treatment group. (Table 1)

Patients receiving IVT were more likely to have history of hypertension ($P = 0.030$) and anemia ($P < 0.001$). IVT group also had a higher modified Charlson comorbidity index ($P = 0.038$), a higher rate of undergoing cerebral angiography ($P < 0.001$), and a lower rate of craniotomy ($P = 0.003$). Overall case severity as assessed by 3M™ APR-DRGs risk of mortality was higher in the thrombolysis group (extreme likelihood of dying: 56.6% vs. 41.5%, $p < 0.001$). The rates of prolonged mechanical ventilation and obstructive hydrocephalus were also higher in thrombolysis group ($P < 0.001$ and $P = 0.003$ respectively). (Table 2)

The rate of ventriculostomy utilization in ICH increased from 5.7% in 2002–2003 to 7.0% in 2010–2011 (trend P<0.001) and the rate of IVT among the cases included in this analysis also showed an upward trend from 0.6% to 5.6% across the same interval (trend P<0.001). (Figure 2)

The thrombolysis group had lower unadjusted inpatient mortality compared to the non-IVT group (32.4% vs 41.6%, odds ratio [OR]: 0.671; 95% confidence interval [CI]: 0.528–0.854, P=0.001). Adjusted inpatient mortality (adjusted OR: 0.670; 95% CI: 0.520–0.865, P=0.002) and the rate of composite unfavorable discharge was lower (adjusted OR: 0.670; 95% CI: 0.502–0.894, P=0.007) in the IVT group after controlling for available potential confounders. There was a trend toward higher rate of favorable discharge in the treatment group (adjusted OR: 1.335; 95% CI: 0.983–1.812, P=0.064). The adjusted rates of bacterial meningitis, permanent ventricular shunting, gastrostomy and tracheostomy were similar between the two groups. The outcome comparisons between the IVT and non-IVT groups after excluding withdrawal of care were comparable to the primary results as shown in Table 3. The outcomes of the other sub-cohorts were also largely consistent with the primary results that included all cases and are shown in Table I in the online-only Data Supplement. It is noteworthy that the proportions of patients with favorable outcome was higher for IVT vs. non-IVT patients for patients treated in high ICH case volume hospitals (adjusted OR: 1.497; 95% CI: 1.075–2.086, P=0.017) and for patients transferred from another hospital (adjusted OR: 2.159; 95% CI: 1.190–3.918, P=0.011). Overall inpatient mortality improved from 43.3% during 2002–2007 to 38.7% during 2008–2011 (P<0.001). IVT cohort had lower mortality during 2002–2007 (31.9% vs 43.5%, OR: 0.606; 95% CI: 0.398–0.924, P=0.019) and a trend toward lower mortality during 2008–2011 (32.6% vs 39.0%, OR: 0.757; 95% CI: 0.555–1.031, P=0.076).

Patients receiving IVT had longer LOS [median (IQR): 18 (10–26) vs 14 (6–25) days, P<0.001]. The IVT group also incurred higher inflation adjusted cost of care [58,770 (33,379–88,434) vs 42,052 (21,757–71,481) USD, P<0.001]. These rates remained higher in the IVT group after excluding cases with withdrawal of care. The cost of care per day LOS was similar between the two groups (P=0.285 for all cases and P=0.270 after excluding withdrawal of care) (Table II in the online-only Data Supplement). LOS was similar between the two groups among the survivors [21 (15–29) vs 21 (14–31) days, P=0.931]. Resource utilization measures stratified by risk of mortality subclass revealed higher cost of care and LOS in IVT cohort only among cases with major or extreme likelihood of dying (Table III in the online-only Data Supplement).

Discussion

This study, the first to our knowledge exploring the outcomes of IVT for IVH requiring ventriculostomy at the population level, showed that patients treated with intraventricular thrombolytics had lower inpatient mortality compared to those given standard care without thrombolysis. This finding is consistent with randomized studies showing decreased mortality in patients treated with IVT compared to those with standard treatment.[4, 24, 25] The 33% mortality seen in the treatment group in this study is higher than that reported in the thrombolytic trials[4, 25] but the thrombolysis trials excluded patients with predicted poor

prognosis such as hematoma volume >30cc, age> 80 years and midbrain compression; the mortality rates in prior observational studies from clinical chart abstraction are similar to those found in the current study.[26, 27] The effect size of survival benefit with thrombolytic treatment (33% lower odds of mortality) is also close to that found in a previous meta-analysis of observational studies showing decrease in odds by 56% (95% CI: 21%-75%) with IVT versus ventriculostomy alone.[3] We also found a higher rate of favorable discharge among the thrombolysis group which reached statistical significance in the subgroups of high ICH case volume hospitals and transfer-in from another hospital. This finding may indicate a potential benefit of the treatment on functional outcome in addition to improved survival, especially in hospitals with experience in this procedure. It is well known, however, that functional recovery continues for months after hemorrhagic stroke [28] and a well-validated follow up functional assessment such as 180-day modified Rankin scale (not available in NIS database) is needed to confirm or refute the treatment effect on functional outcome.

The adjusted rates of permanent ventricular shunt placement were similar between the two comparison groups (adjusted OR: 1.358; 95% CI: 0.929–1.984, P=0.114). This result may indicate that thrombolytics do not prevent communicating hydrocephalus despite faster clearance of intraventricular blood. Alternatively, this finding may be driven by a higher survival rate of patients with more severe disease in IVT compared to non-IVT patients. Of note, consistent with the current study, a prior meta-analysis found no evidence that IVT reduces the need for ventricular shunting procedures.[3] Prior studies have shown no increase in infectious complications with IVT.[3] This was also found in our study showing similar rates of bacterial meningitis in both groups.

This is also the first large study analyzing the hospital characteristics and resource utilization measures associated with IVT. Teaching hospitals and hospitals with larger annual ICH case volume were more likely to utilize IVT, possibly due to teaching hospitals having greater availability of resources and technical expertise, higher full time in-hospital staffing and overall more experience with resultant higher comfort level of treating physicians for using this infrequent treatment. Higher overall cost associated with IVT is largely explained by longer LOS in the thrombolysis group, as the cost of care per day of hospitalization was not higher. We speculate that preferential improvement in survival of the most severe cases may have contributed to comparative higher cost of care and longer LOS in the IVT group. Patients in the non-treatment group had higher rates of craniotomy. This may reflect differences in the population considered for surgery and thrombolysis with larger ICH more likely receiving the surgical treatment and larger IVH more likely to receive thrombolysis.

The results of this study should be interpreted with caution due to inherent limitations of administrative databases, the retrospective and exploratory nature of the analysis, and a lack of well-validated ICH severity measures, and follow up data. For severity measures, the NIS database does not have critically important prognostic elements such as Glasgow coma scale and ICH/IVH volume and location. We have used a previously-validated DRG based risk of mortality algorithm to partially overcome this limitation and found APR-DRG risk of mortality to be a strong predictor of mortality in a dose-response fashion (Table IV in the online-only Data Supplement). The primary limitation in assessing any treatment effect from

a non-randomized study is the risk of confounding by indication (i.e., that the choice to treat with thrombolysis was tied to the final outcomes in a non-causal way) and survivor bias (i.e. patients surviving initial days after ICH had more time to be selected for IVT thus causing spurious association of IVT with survival).[29] In this case, however, patients given thrombolysis had higher APR-DRG severity scores, arguing against our findings being solely due to confounding. Additionally, more than 2/3 patients in the IVT group received thrombolysis within 2 days after ventriculostomy. Therefore, survivor bias in this study though possible, is less likely to impact the mortality significantly as suggested by lower mortality in IVT group among patients surviving at least 2 days from admission. Our method of case selection is also an important limitation. ICD-9-CM code 431 is validated to have high positive predictive value for diagnosing primary ICH from administrative datasets, but its accuracy in identifying IVH has not previously been studied.[10, 11] Similarly, procedure code 99.10 has high specificity for intravenous thrombolysis in stroke.[30] However, no prior study has validated the use of the code for ascertaining IVT. In order to increase the accuracy of case ascertainment, we excluded the cases with confounding diagnoses for thrombolysis indication such as ischemic stroke, myocardial infarction, pulmonary embolism, and those on hemodialysis with possibility of clotted access lines requiring thrombolytic agents. The temporal trend in the fraction of treated cases is coincident with development and publication of research data supporting the use of thrombolysis in IVH, lending some credibility to our case selection method. Nevertheless, it remains possible that our cases were not all cases of IVH and that some 'treated' cases were given thrombolytic agents via some other route than intraventricular. Although diagnosis coding is imperfect, random ICD-9 coding errors would bias the results toward the null, so are unlikely to account for the measured differences in mortality rates found in this study. Despite these limitations, we believe that large scale studies to analyze the effects of infrequently used treatments such as IVT by chart abstraction is not feasible and national administrative databases such as the NIS provides a more readily accessible tool to validate the effectiveness of this treatment at the population level in routine clinical practice.

In conclusion, using population-based data, we have shown that IVT in patients with primary ICH requiring ventriculostomy may be associated with higher survival to discharge and perhaps even improved favorable discharge disposition. We found no evidence that IVT increased the rate of bacterial meningitis. This finding is consistent with the results from prior randomized pilot trials and small observational studies. A more definitive conclusion regarding the effect of the treatment on outcomes requires confirmation by large randomized studies, such as the ongoing CLEAR III trial.[7]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Disclosures

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Primary diagnosis
intracerebral hemorrhage
n=655,078

No ventriculostomy
n=612,656 (93.5%)

Underwent ventriculostomy
n=42,422 (6.5%)
(screened for eligibility)

Excluded cases n=8,378* (19.7%)
- Age <18 years (639)
- Traumatic brain injury (163)
- Arteriovenous malformation (759)
- Aneurysm treatment (988)
- Brain malignancy (415)
- Ischemic stroke (1,087)
- Myocardial infarction (1,244)
- Pulmonary embolism (650)
- Hemodialysis (1,196)
- Transferred out (2,129)
- Clinical trial enrollment(125)

Included in the study
n=34,044 (80.3%)

Intraventricular thrombolysis
n=1,133 (3.3%)

No intraventricular thrombolysis
n=32,911 (96.7%)

Withdrawal of
care
n=113 (10.0%)

No withdrawal of
care
n=1,020 (90.0%)

Withdrawal of
care
n=2,330 (7.1%)
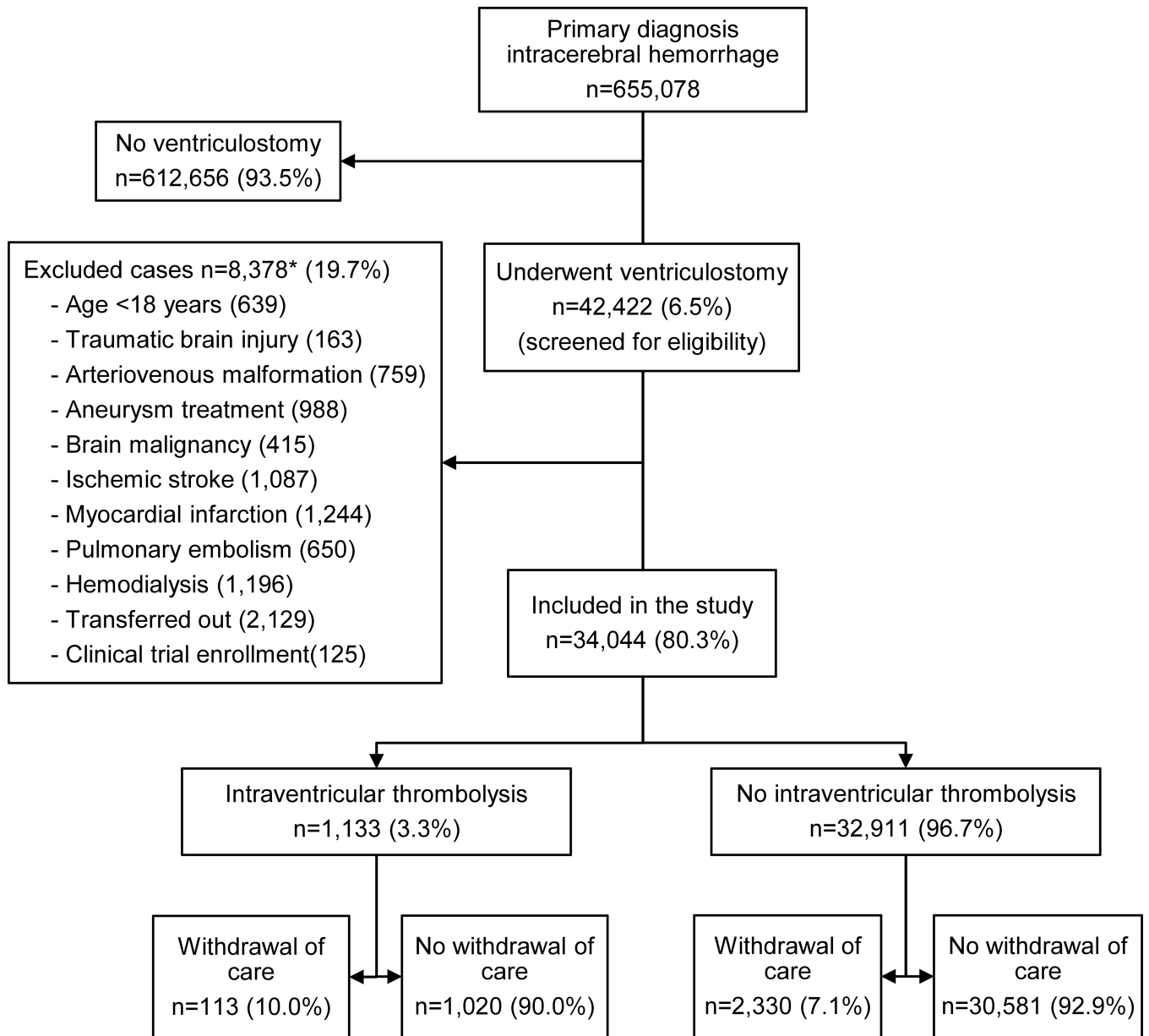
No withdrawal of
care
n=30,581 (92.9%)

Figure 1.
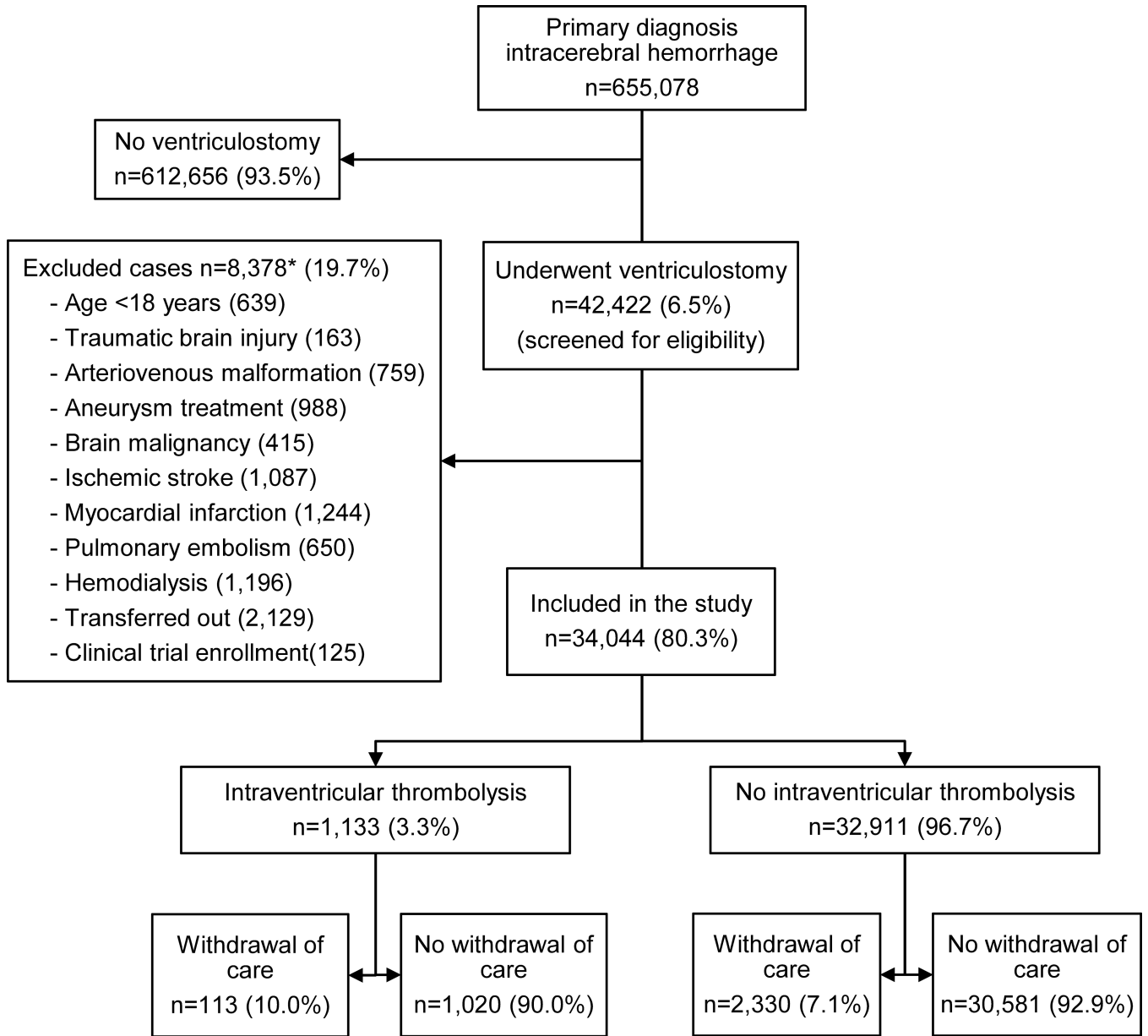Case selection
* Not mutually exclusive

Figure 2.
Temporal trends
Error bar indicates standard error of the population estimate

TABLE 1

Baseline patient and hospital characteristics

	No IVT (N=32,911)		IVT (N=1,133)		P value
	n	(%)	n	(%)	
Age, year					**0.013**
18–64	19325	(58.7)	751	(66.3)	
65–79	10169	(30.9)	271	(23.9)	
80	3417	(10.4)	111	(9.8)	
Female sex	14365	(43.7)	502	(44.3)	0.806
Race/ethnicity					0.102
Caucasian	13970	(42.4)	434	(38.3)	
Black	6712	(20.4)	235	(20.7)	
Hispanic	2638	(8.0)	131	(11.6)	
Asian or Pacific Islander	1469	(4.5)	85	(7.5)	
Other	1160	(3.5)	48	(4.2)	
Missing information	6961	(21.2)	200	(17.6)	
Transfer from another hospital	5763	(17.5)	311	(27.4)	**<0.001**
Hospital geographic region					**0.020**
Northeast	5690	(17.3)	182	(16.0)	
Midwest	5760	(17.5)	180	(15.9)	
South	14282	(43.4)	383	(33.8)	
West	7179	(21.8)	388	(34.2)	
Hospital location					0.133
Rural	584	(1.8)	10[*]	(0.0)	
Urban	32006	(98.2)	1122	(100.0)	
Teaching hospital	24266	(74.5)	995	(88.7)	**<0.001**
Hospital bed size					0.428
Small	1031	(3.2)	28	(2.5)	
Medium	5829	(17.9)	160	(14.2)	
Large	25730	(79.0)	935	(83.3)	
Hospital ICH case volume quartile (cases/year)					**<0.001**

	No IVT (N=32,911)		IVT (N=1,133)		
	n	(%)	n	(%)	P value
1st (1–23)	2754	(8.4)	46	(4.1)	
2nd (24–47)	7558	(23.0)	170	(15.0)	
3rd (48–84)	9869	(30.0)	305	(26.9)	
4th (85)	12730	(38.7)	612	(54.0)	

* NIS data use agreement prohibits reporting of cells with n 10. ICH=intracerebral hemorrhage, IVT=intraventricular thrombolysis

TABLE 2

Comorbidities, inpatient procedures and case severity

	No IVT (N=32,911)		IVT (N=1,133)		
	n	(%)	n	(%)	P value
Modified Charlson comorbidity index					0.038
0	16742	(51.3)	539	(47.5)	
1	8699	(26.7)	286	(25.2)	
2	4155	(12.7)	207	(18.2)	
3	3042	(9.3)	102	(9.0)	
Hypertension	24669	(75.6)	925	(81.6)	0.030
Diabetes mellitus	6749	(20.7)	280	(24.7)	0.071
Dyslipidemia	4724	(14.4)	186	(16.4)	0.303
Coronary artery disease	3798	(11.5)	135	(11.9)	0.829
Congestive heart failure	2609	(8.0)	101	(8.9)	0.579
Atrial fibrillation	4309	(13.1)	142	(12.6)	0.774
Valvular disease	1154	(3.5)	55	(4.8)	0.291
Anemia	5311	(16.1)	286	(25.2)	<0.001
Thrombocytopenia	1610	(4.9)	55	(4.8)	0.961
Alcohol abuse	2873	(8.8)	97	(8.6)	0.902
Drug abuse	1923	(5.9)	85	(7.5)	0.288
Chronic kidney disease	1852	(5.6)	83	(7.3)	0.185
Transfusion of packed red blood cells	2812	(8.5)	122	(10.7)	0.315
Transfusion of platelets	1758	(5.3)	58	(5.1)	0.884
Transfusion of fresh frozen plasma	2837	(8.6)	124	(10.9)	0.199
Cerebral angiogram	3498	(10.6)	217	(19.2)	<0.001
Craniotomy	1113	(3.4)	10*	(0.4)	0.003
Craniectomy	515	(1.6)	10*	(0.5)	0.164
Mechanical ventilation >96hrs	14773	(44.9)	662	(58.4)	<0.001
Obstructive hydrocephalus	20189	(61.3)	801	(70.7)	0.003
3M™ APR-DRG risk of mortality					<0.001

	No IVT (N=32,911)		IVT (N=1,133)		
	n	(%)	n	(%)	P value
Minor likelihood of dying	399	(1.2)	10 [*]	(0.9)	
Moderate	1235	(3.8)	45	(3.9)	
Major	17449	(53.5)	437	(38.6)	
Extreme	13555	(41.5)	641	(56.6)	

[*] NIS data use agreement prohibits reporting of cells with n 10. APR-DRG = all patient refined diagnosis related groups, IVT=intraventricular thrombolysis

TABLE 3

Discharge outcomes and inpatient complications

	No IVT % (N=1,133)	IVT % (N=32,911)	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
All cases						
Inpatient mortality	41.6	32.4	0.671 (0.528–0.854)	**0.001**	0.670 (0.520–0.865)	**0.002**
Favorable discharge *	23.2	28.1	1.292 (0.969–1.724)	0.080	1.335 (0.983–1.812)	0.064
Unfavorable discharge†	61.3	54.1	0.745 (0.575–0.965)	**0.026**	0.670 (0.502–0.894)	**0.007**
Bacterial meningitis	3.0	2.0	0.674 (0.266–1.708)	0.402	0.525 (0.202–1.362)	0.185
Ventricular shunting	7.8	11.1	1.470 (1.027–2.103)	**0.034**	1.358 (0.929–1.984)	0.114
Gastrointestinal bleeding	1.7	1.3	0.731 (0.262–2.037)	0.547	0.591 (0.204–1.719)	0.334
Tracheostomy	2.3	2.9	1.230 (0.537–2.817)	0.624	1.401 (0.592–3.317)	0.442
Gastrostomy	26.0	33.3	1.422 (1.069–1.893)	**0.015**	1.250 (0.947–1.650)	0.116
Withdrawal of care excluded	(N=1,020)	(N=30,581)				
Inpatient mortality	38.7	26.9	0.583 (0.445–0.764)	**<0.001**	0.614 (0.460–0.821)	**0.001**
Favorable discharge *	24.6	30.9	1.365 (1.022–1.825)	**0.035**	1.333 (0.983–1.807)	0.064
Unfavorable discharge†	58.8	49.7	0.693 (0.528–0.909)	**0.008**	0.677 (0.505–0.906)	**0.009**
Bacterial meningitis	3.1	2.2	0.720 (0.285–1.823)	0.487	0.560 (0.217–1.449)	0.232
Ventricular shunting	8.3	11.1	1.388 (0.948–2.033)	0.091	1.248 (0.847–1.841)	0.263
Gastrointestinal bleeding	1.8	1.4	0.774 (0.276–2.169)	0.625	0.610 (0.209–1.784)	0.367
Tracheostomy	2.5	2.6	1.041 (0.490–2.213)	0.917	1.142 (0.522–2.497)	0.739
Gastrostomy	27.3	34.5	1.404 (1.054–1.871)	**0.020**	1.183 (0.902–1.552)	0.224

*
Discharge to home/self-care or rehabilitation.

†
Discharge to skilled nursing facility, hospice or death.

Sum of favorable and unfavorable discharge rates is not 100% as other less common specified (such as home health care, law enforcement, intermediate care center) and unspecified discharge dispositions were not included in the definitions.
IVT=intraventricular thrombolysis

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