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Current trends in the acute treatment of ischemic stroke: analysis from the Paul Coverdell National Acute Stroke Program

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Abstract

Background—The intra-arterial treatment (IAT) of acute ischemic stroke (AIS) is now evidence-based and given the highest level of recommendation among eligible patients. Using a multi-state stroke registry, we studied the trend in IAT among patients with AIS over 11 years and its impact on the utilization of intravenous thrombolysis (IVT) within the same 11 years.

Methods—Using data from the Paul Coverdell National Acute Stroke Program (PCNASP), we studied trends in IVT and IAT for patients with AIS between 2008 and 2018. Trends over time were examined for rates of IVT only, IAT only, or a combination of IVT and IAT (IVT+IAT). Favorable outcome was defined as discharge to home.

Results—During the study period there were 595 677 patients (mean age 70.4 years, 50.4% women) from 646 participating hospitals with a clinical diagnosis of AIS in the PCNASP. Trends for IVT only, IAT only, and IVT+IAT all significantly increased over time (P<0.001). Total use of IVT and IAT increased from 7% in 2008 to 19.1% in 2018. The rate of patients discharged to home increased significantly over time among all treatment groups (P<0.001).

Conclusion—In our large registry-based analysis, we observed a significant increase in the use of IAT for the treatment of AIS, with continued increases in the use of IVT. Concurrently, the percent of patients with favorable outcomes continued to increase.

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BACKGROUND

The intra-arterial treatment (IAT) of acute ischemic stroke (AIS) is now proven to produce clinically meaningful improvements in outcomes among select patients and has been given the highest level of recommendation among eligible patients by the American Heart Association/American Stroke Association.[1] Perhaps due to the more definitive evidence supporting IAT, it has been reported that there has been a significant increase in the use of IAT among patients with AIS,[2] but its impact on trends of intravenous thrombolysis (IVT) remains unknown. In this study we used a multi-state stroke registry to examine the trend in IAT among patients with AIS over 11 years and its impact on the utilization of IVT during the same time period.

METHODS

Our study population included patients admitted with the clinical diagnosis of AIS from 2008 through 2018 within the Paul Coverdell National Acute Stroke Program (PCNASP). The PCNASP is an ongoing acute stroke quality improvement program funded by the Centers for Disease Control and Prevention (CDC) and provides feedback to states on adherence to guidelines of care to improve care quality for patients hospitalized with stroke and transient ischemic attack (TIA). Within our study period, hospitals across 12 states (Arkansas, California, Georgia, Iowa, Massachusetts, Michigan, Minnesota, New York, North Carolina, Ohio, Washington, and Wisconsin) participated in the PCNASP. Hospital participation within each state is voluntary. Trained abstractors from participating hospitals collect detailed information on stroke and TIA admissions concurrent with or soon after hospital discharge using standard data definitions provided by the CDC.[34] This study was approved by the CDC Institutional Review Board.

We defined the rates of IVT only, IAT only, or a combination of IVT and IAT (IVT + IAT) as percent of AIS admissions. Favorable outcome was defined as rate of discharge to home. Adverse outcome measures included rates of symptomatic intracranial hemorrhage (sICH) and in-hospital mortality. We also assessed the rate of ability to ambulate independently at discharge (with or without a walker) as an additional outcome measure. Categorical variables were compared across treatment groups using two-tailed Fisher's exact or χ^2 tests. Continuous variables were compared using the Wilcoxon–Mann–Whitney rank test or the Kruskal–Wallis test. We examined the trends and obtained the P values based on the Cochran-Armitage test. Statistical analyses were performed using SAS software Version 9.4 (SAS Institute, Cary, North Carolina, USA).

RESULTS

From 2008 to 2018 there were 595 677 patients (mean age 70.4 years, 50.4% women) with a clinical diagnosis of AIS from 646 participating hospitals in the PCNASP (table 1). The median National Institutes of Health Stroke Scale (NIHSS) scores decreased from 4 to 3 over time, while the median scores for those receiving any IAT were unchanged over time (range 15–18). The percent of patients with AIS receiving IVT only at participating hospitals increased from 4.6% in 2008 to 9.3% in 2018 (P<0.001), and the percent of patients with

AIS receiving IVT only prior to transferring to a participating hospital by way of the ‘drip and ship’ paradigm significantly increased from 1.5% in 2008 to 4.4% in 2018 (P<0.001). The percent of patients with AIS receiving IAT only significantly increased from 0.6% in 2008 to 4% in 2018 (P<0.001), and the percent of patients with AIS receiving IVT + IAT also significantly increased from 0.2% in 2008 to 1.5% in 2018 (P<0.001, table 2). Overall, the percent of patients receiving IVT (either alone or in combination with IAT) increased from 6.4% in 2008 to 15.2% in 2018 (P<0.001, figure 1). The percent of patients receiving IAT (either alone or in combination with IVT) increased from 0.8% in 2008 to 5.5% in 2018.

Rates of sICH significantly decreased in patients receiving IVT only and IVT + IAT (P<0.001 and P = 0.038, respectively, table 3). A significant trend was not found among patients receiving IAT only. Rates of in-hospital mortality significantly decreased in patients receiving IVT only and those receiving IVT + IAT (P<0.001 and P = 0.005, respectively); the same trend was not noted for patients receiving IAT only. The rate of life-threatening complications significantly decreased in patients receiving IVT only (P=0.002), and the rates of such complications were too low among those receiving IAT only or IVT + IAT to identify a trend. The percent of patients able to ambulate independently at discharge and the percent discharged to home increased significantly over time among all treatment groups (P<0.001).

DISCUSSION

The rates of IVT only, IAT only, and IVT + IAT utilization significantly increased during our study period from 2008 to 2018. With increases in IAT we noted a continued increase in IVT, which is likely related to updated guidelines.[1] Concurrent with the increased use of all acute reperfusion treatment options in AIS, we noted a significant increase in favorable outcomes as defined by the percent discharged to home. When compared with the percent of patients who required assistance from another person to ambulate or were unable to ambulate, the percent of patients who were able to ambulate independently significantly increased during the study period.

Through the years of this study we found that the increasing use of these treatment modalities was accompanied by decreases in serious bleeding complications in the setting of community-based hospital care. There was a significant trend towards a lower rate of sICH among patients with AIS receiving IVT + IAT. The rate of sICH in our study among those receiving IVT only in 2018 (2.8%) is lower than in earlier analyses.[56] The rates of sICH among those receiving IAT only and IVT + IAT in 2018 are similar to those reported in the pivotal IAT trials (4.4%) and much lower than other studies.[7–10]

Previous studies have reported steady increases in IAT for AIS over time,[28–10] which we also report in our analysis. However, only one study addressed this trend and its impact on the use of IVT, but was limited to an analysis spanning only 2 years.[8] In our 11-year analysis we show that, in addition to the increased rates of IAT, there were also increasing rates of IVT. Our study shows that over time the trend for increased utilization of IVT was not impacted by increased utilization of IAT. With the generous expansion of the time window for IAT in recent trials,[11,12] we would expect continued increases in the proportion of patients receiving IAT.

Our observed trends are similar to that observed within the cardiology literature. After the introduction of percutaneous coronary intervention (PCI) decades ago, there was a noted increased trend in PCI among patients with coronary artery disease. However, this trend has recently declined and considered to be the result of advances in prevention strategies.[13] Other studies have demonstrated that PCI centers may have developed risk avoidance behaviors, where treatment is withheld from higher-risk patients in order to avoid having to publicly report increased mortality rates. States with public reporting of outcomes have been found to perform fewer PCI procedures that disproportionately affect higher-risk patients.[14] As we enter a new era for AIS intervention that includes IAT, the long-term implications of the trends we observed in our study remain unknown. We should define metrics that best reflect stroke quality of care in order to minimize risk avoidance behavior that could impact acute stroke treatment trends in the future.[14]

Important strengths of our study include the large number of patients and the multi-state data from a variety of hospitals collected during regular care delivery. An important limitation of our study is the inability to assess selection criteria for those receiving IAT. Baseline NIHSS scores were documented in 79% of patients in our study (improving from 37.9% in 2008 to 91.8% in 2018), which creates difficulties in ascertaining baseline disability in a noteworthy proportion of patients. However, neither of these limitations should affect the main observation of the study. Ambulatory status at time of discharge has not been shown to be predictive of long-term outcomes; as such we could not define independent ambulatory status at time of discharge as a favorable outcome. Favorable outcomes were defined by discharge destination rather than formal outcome scales such as the modified Rankin Scale score; it has been shown that discharge destination can act as a surrogate for standard outcome scales and be highly predictive in determining rates of death and disability.[15,16]

In our large registry-based analysis, we report a significant trend towards the use of IAT in standard practice for the treatment of AIS. This coincides with continued increases in the utilization of IVT, decreases in serious bleeding events, and reduced in-hospital mortality. The proportion of patients with favorable outcomes continued to increase. IAT for AIS in community practice is as safe and clinically effective as what has been shown in recent clinical trials.

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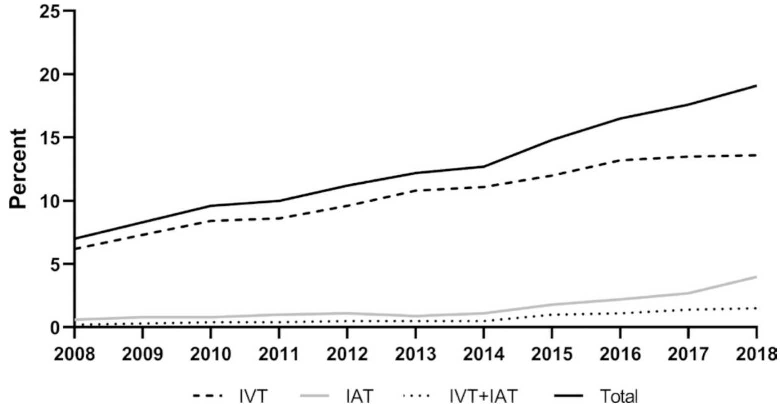

Figure 1.

Trends in type of treatment by year (%) among patients with acute ischemic stroke, PCNASP 2008–2018. IAT, intra-arterial therapy; IVT, intravenous thrombolysis.

Table 1

Demographic and baseline characteristics among patients with acute ischemic stroke, 2008–2018

Variables	2008 (n=22 086)	2009 (n=27 963)	2010 (n=35 320)	2011 (n=40129)	2012 (n=41121)	2013 (n=59 395)	2014 (n=68 925)	2015 (n=66944)	2016 (n=70 657)	2017 (n=80 681)	2018 (n=82 456)
Mean (SE) age, years	70.4 (0.1)	70.6 (0.1)	70.0 (0.1)	70.0 (0.1)	70.0 (0.1)	70.2 (0.1)	70.5 (0.1)	70.4 (0.1)	70.6 (0.1)	70.5 (0.1)	70.4 (0.1)
No (%) of women	11 608 (52.6)	14 509 (51.9)	18 137 (51.4)	20 684 (51.5)	20 879 (50.8)	30 108 (50.7)	34 590 (50.2)	33 810 (50.5)	35 241 (49.9)	39 997 (49.6)	40 835 (49.5)
Race, n (%)											
White	16 388 (74.2)	20 760 (74.2)	25 616 (72.5)	29 220 (72.8)	30 168 (73.4)	44 499 (74.9)	51 413 (74.6)	49 793 (74.4)	52 460 (74.2)	58 966 (73.1)	59 680 (72.4)
Black	4388 (19.9)	5570 (19.9)	7672 (21.7)	8576 (21.4)	8610 (20.9)	11 280 (19.0)	12 753 (18.5)	12 084 (18.1)	12 749 (18.0)	14 537 (18.0)	14 358 (17.4)
Other race	1310 (5.9)	1633 (5.8)	2032 (5.8)	2333 (5.8)	2343 (5.7)	3616 (6.1)	4759 (6.9)	5067 (7.6)	5448 (7.7)	7178 (8.9)	8418 (10.2)
Median (IQR) admission NIHSS score											
IVT*	12 (7–18)	11 (7–17)	11 (6–17)	10 (6–16)	9 (5–16)	9 (5–16)	8 (5–15)	7 (4–13)	7 (4–12)	6 (3–12)	6 (3–11)
IAT*	17 (12–22)	14 (7–20)	15 (8–21)	15 (8–21)	16 (10–21)	16 (10–21)	14 (8–21)	16 (9–21)	15 (8–21)	15 (9–21)	15 (8–21)
IVT+IAT*	16 (13–20)	17 (13–19)	17 (13–22)	18 (13–21)	17 (12–21)	16 (12–21)	17 (11–21)	16 (10–21)	16 (11–21)	16 (10–21)	16 (10–22)

*Treatment given at a participating hospital.

IAT, intra-arterial treatment; IVT, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale.

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Table 2

Trends in type of treatment by year, 2008–2018

Type of treatment	2008 (n=22 086)	2009 (n=27 963)	2010 (n=35 320)	2011 (n=40129)	2012 (n=41121)	2013 (n=59 395)	2014 (n=68 925)	2015 (n=66944)	2016 (n=70 657)	2017 (n=80 681)	2018 (n=82 456)	P for trend
IVT* (3.5%)	339 (1.5)	553 (2.0)	817 (2.3)	1022 (2.5)	1194 (2.9)	1707 (2.9)	2112 (3.1)	2591 (3.9)	3066 (4.3)	3733 (4.6)	3616 (4.4)	<0.001
IVT† (7.8%)	1026 (4.6)	1481 (5.3)	2160 (6.1)	2431 (6.1)	2760 (6.7)	4709 (7.9)	5540 (8.0)	5423 (8.1)	6245 (8.8)	7197 (8.9)	7639 (9.3)	<0.001
IAT† (1.9%)	139 (0.6)	212 (0.8)	284 (0.8)	416 (1.0)	446 (1.1)	552 (0.9)	771 (1.1)	1227 (1.8)	1578 (2.2)	2186 (2.7)	3263 (4.0)	<0.001
IVT+IAT† (0.8%)	47 (0.2)	74 (0.3)	124 (0.4)	160 (0.4)	216 (0.5)	289 (0.5)	354 (0.5)	646 (1.0)	784 (1.1)	1091 (1.4)	1272 (1.5)	<0.001

*IVT given at a referring facility and received in transfer to participating hospital.

†Treatment given at a participating hospital.

IAT, intra-arterial treatment; IVT, intravenous thrombolysis.

Table 3

Comparison of outcomes among patients receiving acute treatments for stroke

		2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	P value
Symptomatic ICH	IVT*	60 (5.8)	76 (5.1)	83 (3.8)	107 (4.4)	97 (3.5)	166 (3.5)	185 (3.3)	161 (3.0)	200 (3.2)	234 (3.3)	215 (2.8)	<0.001
	IAT*	8 (5.8)	14 (6.6)	18 (6.3)	13 (3.1)	18 (4.0)	25 (4.5)	27 (3.5)	49 (4.0)	61 (3.9)	82 (3.8)	159 (4.9)	0.72
	IVT+IAT*	6 (12.8)	3 (4.1)	14 (11.3)	14 (8.8)	15 (6.9)	10 (3.5)	14 (4.0)	37 (5.7)	46 (5.9)	54 (4.9)	69 (5.4)	0.038
Life-threatening complications	IVT*	14 (1.4)	12 (0.8)	19 (0.9)	18 (0.7)	19 (0.7)	36 (0.8)	32 (0.6)	33 (0.6)	39 (0.6)	39 (0.5)	43 (0.6)	0.002
	IAT*	1 (0.7)	1 (0.5)	2 (0.7)	5 (1.2)	2 (0.4)	2 (0.4)	4 (0.5)	6 (0.5)	7 (0.4)	5 (0.2)	25 (0.8)	NA
	IVT+IAT*	1 (2.1)	3 (4.1)	3 (2.4)	2 (1.3)	0	5 (1.7)	5 (1.4)	7 (1.1)	4 (0.5)	10 (0.9)	15 (1.2)	NA
In-hospital mortality	IVT*	72 (7.0)	121 (8.2)	174 (8.1)	170 (7.0)	156 (5.7)	326 (6.9)	324 (5.8)	269 (5.0)	304 (4.9)	314 (4.4)	297 (3.9)	<0.001
	IAT*	17 (12.2)	37 (17.5)	45 (15.8)	77 (18.5)	61 (13.7)	75 (13.6)	80 (10.4)	180 (14.7)	231 (14.6)	288 (13.2)	441 (13.5)	0.09
	IVT+IAT*	4 (8.5)	20 (27.0)	21 (16.9)	29 (18.1)	24 (11.1)	36 (12.5)	34 (9.6)	64 (9.9)	92 (11.7)	132 (12.1)	137 (10.8)	0.005
Able to ambulate independently at discharge	IVT*	341 (33.2)	529 (35.7)	747 (34.6)	902 (37.1)	1111 (40.3)	1868 (39.7)	2349 (42.4)	2609 (48.1)	3021 (48.4)	3801 (52.8)	4078 (53.4)	<0.001
	IAT*	29 (20.9)	44 (20.8)	49 (17.3)	85 (20.4)	95 (21.3)	127 (23.0)	225 (29.2)	373 (30.4)	453 (28.7)	638 (29.2)	948 (29.1)	<0.001
	IVT+IAT*	15 (31.9)	11 (14.9)	20 (16.1)	37 (23.1)	60 (27.8)	73 (25.3)	128 (36.2)	233 (36.1)	276 (35.2)	403 (36.9)	485 (38.1)	<0.001
Discharge home	IVT*	248 (24.2)	423 (28.6)	755 (35.0)	894 (36.8)	1030 (37.3)	2000 (42.5)	2469 (44.6)	2685 (49.5)	3123 (50.0)	3749 (52.1)	4151 (54.3)	<0.001
	IAT*	23 (16.5)	42 (19.8)	54 (19.0)	78 (18.8)	85 (19.1)	123 (22.3)	218 (28.3)	301 (24.5)	375 (23.8)	559 (25.6)	800 (24.5)	<0.001
	IVT+IAT*	7 (14.9)	8 (10.8)	16 (12.9)	37 (23.1)	50 (23.1)	75 (26.0)	117 (33.1)	221 (34.2)	259 (33.0)	360 (33.0)	457 (35.9)	<0.001

* Treatment given at a participating hospital.

IAT, intra-arterial treatment; ICH, intracranial hemorrhage; IVT, intravenous thrombolysis.