

Return Home: A Practical Measure of IV-tPA Effectiveness?

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This poster is sponsored by the Cancer, Cardiovascular Disease, and Pulmonary Disease Grants Program at the Colorado Department of Public Health and Environment

Introduction/Hypothesis:

- Standard measures for the effectiveness of intravenous tissue plasminogen activator (tPA) in acute ischemic stroke (i.e. clinical outcomes at 3 months) are logistically & economically challenging. Alternative measures may be more practical (in hospital practice) for monitoring tPA's effectiveness.

Methods:

- Query ischemic strokes in the Colorado Stroke Registry¹ (CSR) to see whether tPA affects the likelihood of home discharge (DC-Home).
- Inclusion criteria: stroke onset in community setting; arrive from the scene by EMS or private means; data available on discharge destination & on tPA status (given or not).
- Exclusions: transfers between hospitals; received intra-arterial or research treatments.
- Recursive partitioning to select variables for a logistic model of DC-Home.

References:

- Smith DB, Murphy P, Phillips M, Paulsen M, Vislosky M, Wilde M. The Colorado Stroke Alliance. J Neurosci Nurs 2009. 41:106-114.
- Zhang J, Yu K. What's the Relative Risk? JAMA 1998. 280:1690-1691.

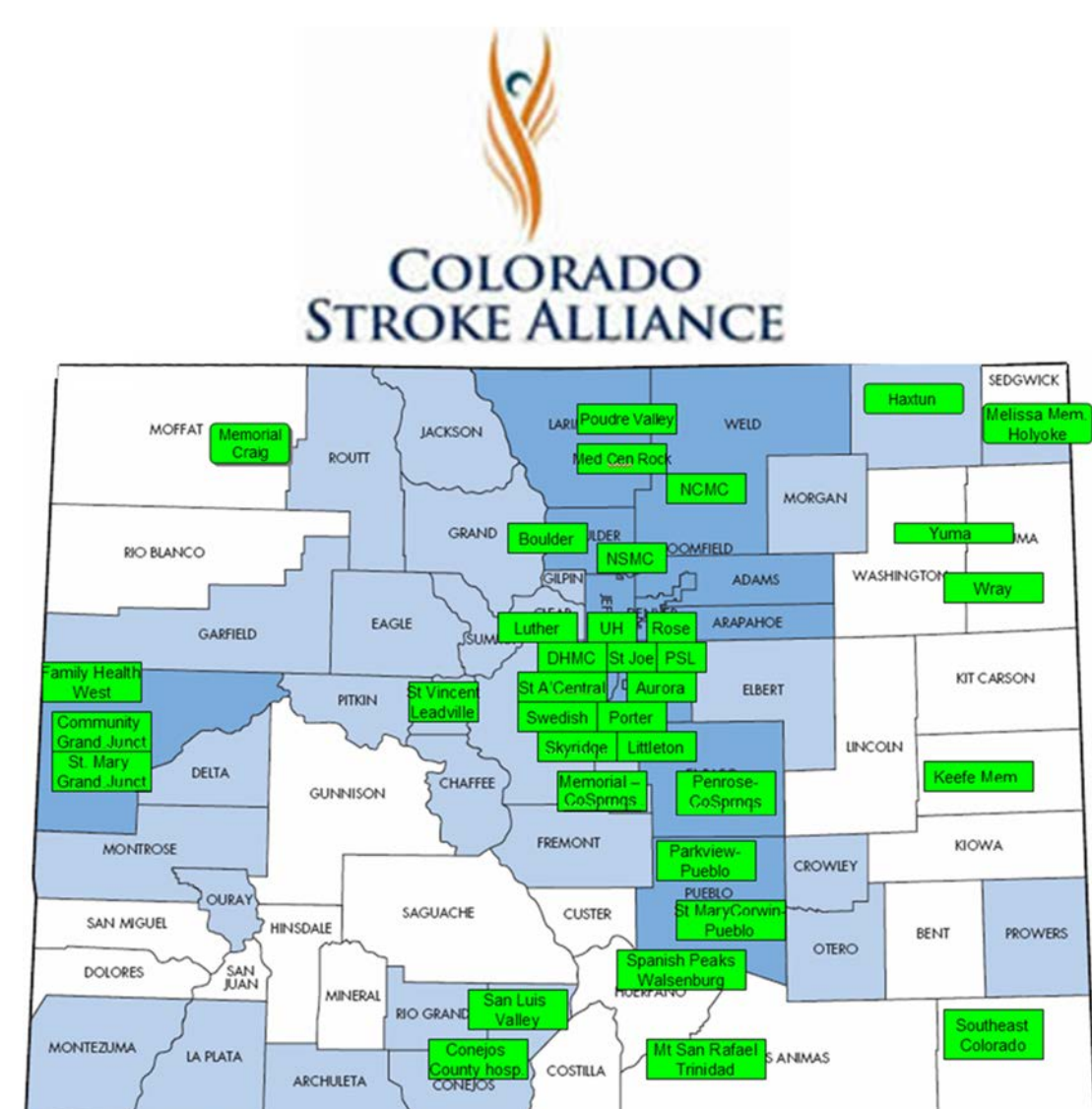


Figure 1: derivation of study population

Patients	Data Set
15,625.....	Database as of June, 2010
5,550.....	Met inclusion/exclusion criteria

↓
Logistic Model for DC Home (#, % missing data):
 Age (2, 0.04%)
 NIHSS (2737, 49%)
 Arrival mode (0, 0%)
 tPA status (0, 0%)

↓
2,812..... Complete data for all fields in model
 ↓
 415 (14.7%)..... Received tPA
 1443 (51.3%)..... DC-Home (tPA + non-tPA patients)

Figure 2: ROC for model

AUC, 95% CI = 0.81; 0.795-0.825

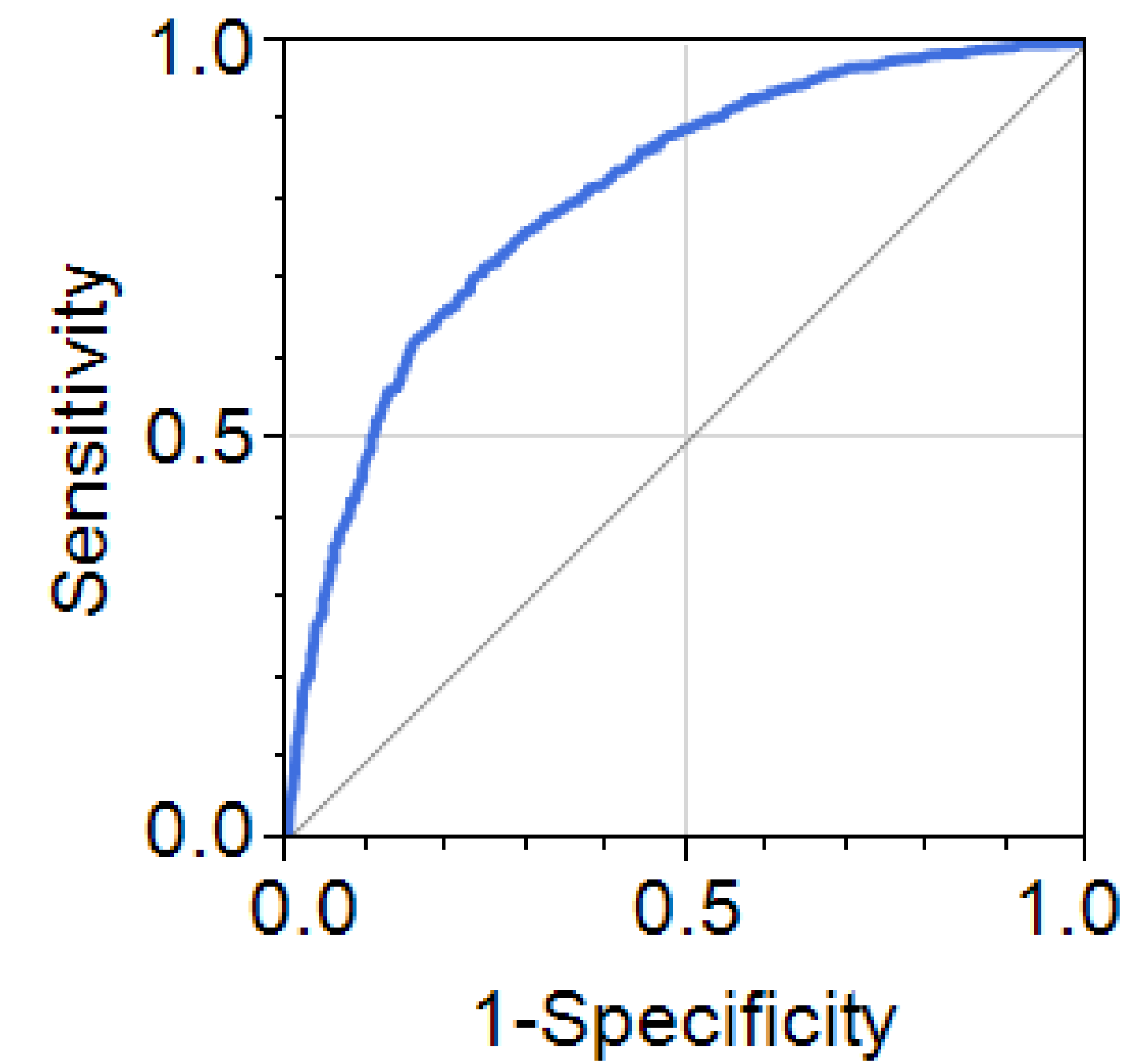


Figure 3: logistic models for DC-Home

Univariate Model (tPA only)			
Variable	Odds Ratio (DC Home)	95% CI	
		Lower	Upper
tPA = Yes	0.74	0.60	0.91
Multivariate Model			
Variable	Odds Ratio (DC Home)	95% CI	
		Lower	Upper
EMS = No	2.02	1.68	2.43
Age	0.96	0.95	0.97
NHSS	0.85	0.83	0.87
tPA = Yes	2.03	1.54	2.67

↓
 DC-Home Risk Ratio²: (tPA/no-tPA) = $\frac{OR}{(1-P_0)+(P_0*OR)} = 1.32$

Figure 4: calculating number needed to treat (NNT)

DC-Home (without tPA)		
No	Yes	%Yes
1140	1257	52.4%

- ↓
- 52.4% * 1.32 = 69.2% ($P_0 * Risk\ Ratio = P_1$)
 - 69.2% - 52.4% = 16.7% = Absolute difference ($P_1 - P_0$)
 - 100/16.7 = **5.99 = NNT**

↓
 This value is similar to the NNT of ~8, calculated using standard 3-month clinical outcomes as the measure of a "good outcome."

Results:

- 5,550 patients met inclusion/exclusion criteria
- Model included: Age, National Institutes of Health Stroke Scale (NIHSS), arrival mode (EMS or Private); and tPA status. (Figure 1)
- Model's discrimination: fairly good. (Figure 2)
- Missing data (almost all from NIHSS field) affected 49% of records. These were excluded from analysis; no values were imputed or assigned. (Figure 1)
- Final analysis was based on complete data of 2,812 patients. Of these, 415 (14.7%) received tPA & 1443 (51.3%) were DC-Home. (Figure 1)
- Unadjusted* analysis: tPA correlated negatively with DC-Home. *Multivariate model*: tPA correlated positively with DC-Home, and the risk ratio of DC-Home (tPA/no-tPA) = 1.32 . (Figure 3)
- Number-needed-to-treat (NNT) = 6. (Figure 3)

Conclusions:

- DC information is more readily available than are standard (clinical) measures of tPA effectiveness.
- DC-Home is a "good outcome," when the alternatives are rehabilitation, nursing facility, hospice, or death.
- When adjusted for arrival mode, age and stroke severity, the NNT for DC-Home is similar to the value for 3-month clinical outcomes, suggesting DC-Home may be a practical measure of tPA effectiveness.
- We encourage others to attempt to replicate our findings with independent data.

Limitations:

- Observational data
- Less-than-perfect model for DC-Home
- Missing NIHSS data limits applicability. Note, however, additional analysis shows that "NIHSS missingness" does not predict DC-Home: OR (95% CI) = 1.04 (0.93-1.15)

Hospital Patient Volume Correlates with the Likelihood, but not the Promptness or Risk of tPA

Don B Smith, Paul Murphy, William Jones - for the Colorado Stroke Alliance

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Introduction/Hypothesis:

A positive relationship between hospital patient-volume (HV) and outcomes is widely acknowledged. We asked whether this relationship holds between the HV for ischemic stroke and variables such as the likelihood, promptness, and risks of IV tissue plasminogen activator treatment (tPA).

Methods:

- Database: Colorado Stroke Registry¹ (38 hospitals)
- Inclusion criteria: ischemic stroke; onset in community setting; arrival from scene by EMS or private means, within 180 minutes.
- Exclusions: transfers between hospitals.
- Analysis: HV (inferred from # of included records from each hospital) vs. hospital-specific relative risks for: receiving tPA, receiving tPA within one hour, having a listed contraindication to tPA, and having symptomatic intracerebral hemorrhage (SICH) after tPA. We also compared HV to median arrival-to-CT and median arrival-to-tPA times.
- Statistical comparisons: linear regression, chi-square, Fisher's exact test, and Kruskal-Wallis, as appropriate.

Reference:

1. Smith DB, Murphy P, Phillips M, Paulsen M, Vislosky M, Wilde M. The Colorado Stroke Alliance. J Neurosci Nurs 2009. 41:106-114.

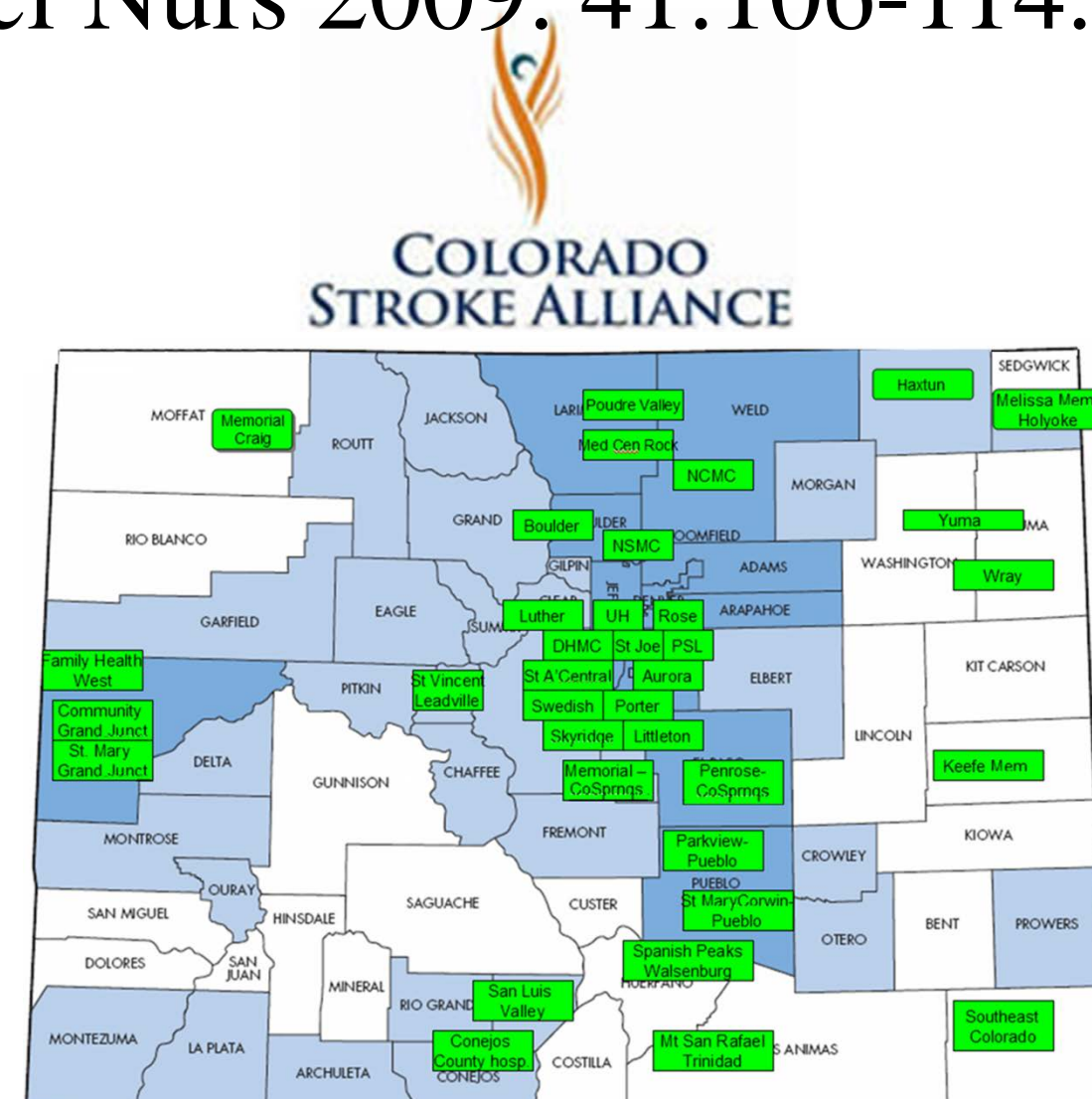


Figure 1: derivation of study population

Patients	Data Set
15,625	Database as of June, 2010
8,709	Ischemic Strokes
7,455	Complete Records
6,921	EMS or Private, from Scene
5,977	Community setting & not transferred
2,136	Arrival within 180 minutes of onset

32 Hospitals: median # patients = 31, range = 1-289
Analysis compares two hospital groups. Values in the shaded boxes are for #patients : mean (SD).

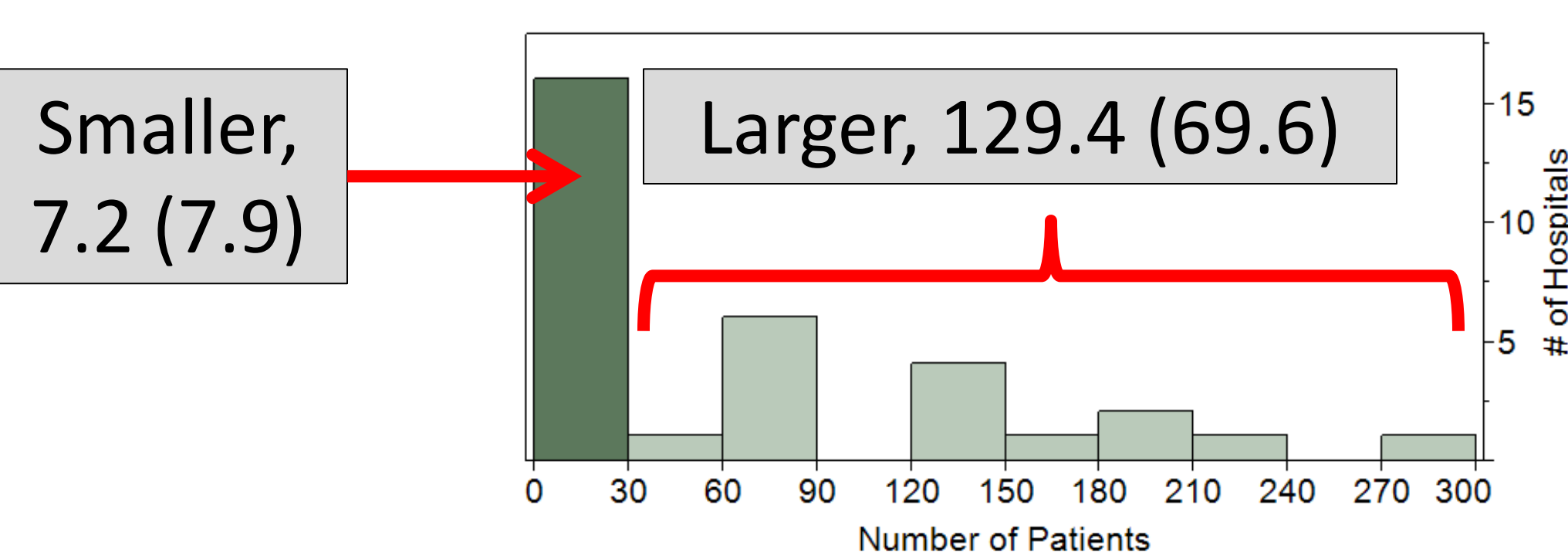
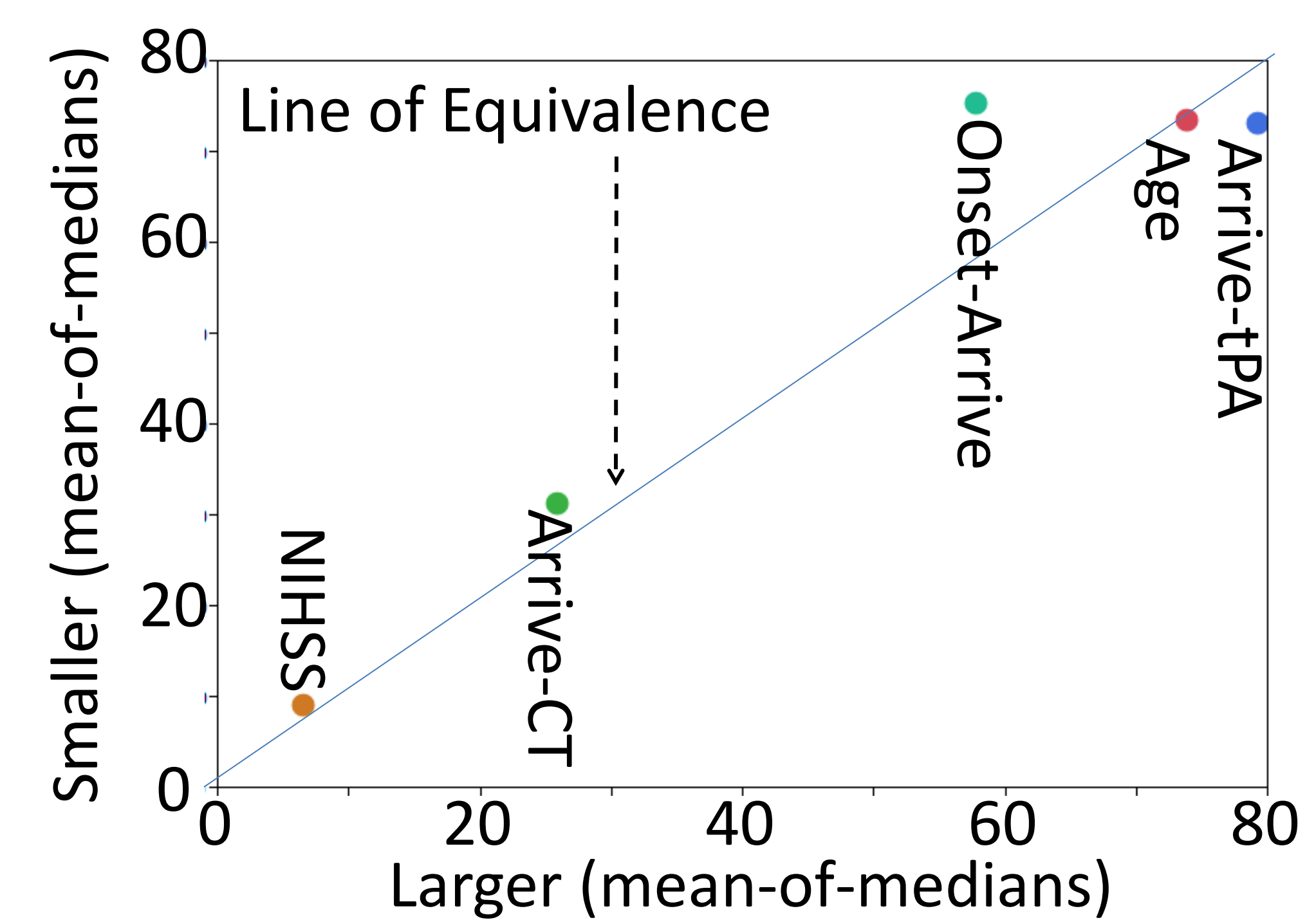
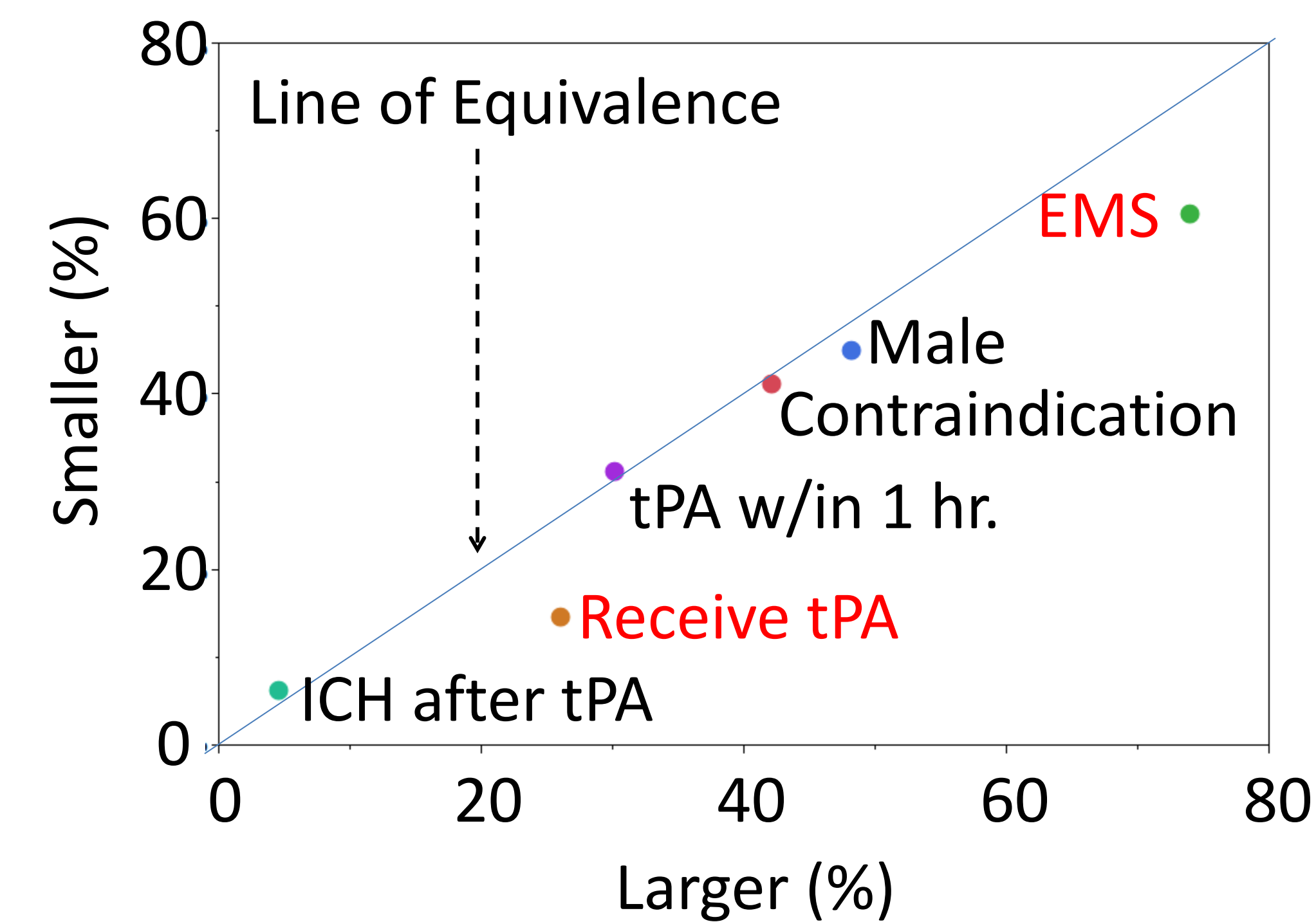


Table 1. Categorical Variables	%Yes		Total # Patients		P
	Larger	Smaller	Larger	Smaller	
Male	48.1%	45.0%	2027	109	0.515
Arrive by EMS	73.9%	60.6%	2020	109	0.002
Contraindication	42.1%	41.3%	2027	109	0.862
Treat w/in 1 hr.	30.1%	31.3%	522	16	0.920
Receive tPA	26.0%	14.7%	2027	109	0.008
Symptomatic ICH	4.5%	6.3%	534	16	0.530

Table 2. Continuous Variables	Mean of median value (95% CI)		# Hospitals		P
	Larger	Smaller	Larger	Smaller	
Age	73.8 (72.0-75.6)	73.5 (67.8-79.2)	16	16	0.850
NIHSS	6.4 (5.6-7.2)	9.1 (5.0-13.2)	16	10	0.151
Onset-Arrive	57.7 (54.7-60.7)	75.5 (55.4-95.7)	16	16	0.073
Arrive-CT Scan	25.8 (19.5-32.2)	31.3 (19.5-43.0)	16	16	0.865
Arrive-tPA	79.2 (71.8-86.5)	73.3 (46.5-100.0)	16	6	1

Figure 2: graphic comparison of variables.

Red text = statistically significant difference.



Results:

- 2,136 patients met inclusion/exclusion criteria. HV ranged from 1-289 patients, at 32 hospitals with data (Figure 1).
- Median HV (25-75 percentile) = 31 (4.5-127)
- For analysis, hospitals were grouped into those with < and those with > the median # of patients. (*Smaller vs. Larger*, Figure 1).
- HV not significantly correlated with: median age, gender, median NIHSS, median onset-to-arrival-time; tPA-in-1-hour, median arrival-to-CT-time, median arrival-to-tPA-time, contraindications to tPA, or post-tPA symptomatic intracerebral hemorrhage (ICH). (Tables 1-2 and figure 2)
- HV was correlated with the likelihood of receiving tPA and of arrival by EMS. (Table 1 and Figure 2)

Conclusions:

- Patients at larger hospitals are significantly more likely to receive tPA and more likely to arrive via EMS.
- Patients at smaller hospitals show a trend toward longer onset-arrival times.
- HV does not clearly correlate with the promptness of CT scanning or of tPA administration.
- HV does not clearly correlate with risk of SICH following tPA.

Limitations:

- Data are observational in nature and based on self-reporting from hospitals.
- Small numbers in some comparisons increase the risk of type II error.

Antiplatelet and Anticoagulation Therapy before an Ischemic Stroke Neither Precludes nor Complicates Intravenous Thrombolysis

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Background

•By American Heart and American Stroke Association guidelines, patients on anticoagulation (AC) with INR ≤ 1.7 are eligible for treatment with intravenous thrombolysis (tPA) in the absence of other contraindications.¹

•Aspirin or other antiplatelet (AP) therapy is not a published contraindication to tPA.¹

•There are limited data on safety of tPA in eligible patients on AP or AC therapy.

•There are limited data on whether otherwise eligible patients on AP or AC therapy are denied tPA due to fear of hemorrhagic complications.

Methods

•We queried the Colorado Stroke Registry, a shared database of 38 Colorado hospitals.

•This database tracks baseline use of antiplatelet medications and AHA/ASA contraindications to intravenous thrombolysis, including INR > 1.7 .

•We included patients with complete records of an outpatient ischemic stroke, presenting within 180 minutes of onset.

Reference:

1. Adams HP, del Zoppo G, Alberts MJ, *et al.* Guidelines for the early management of adults with ischemic stroke. *Stroke*. 2007;38:1655-1711.

Figure 1: Patients with a contraindication to IV tPA.

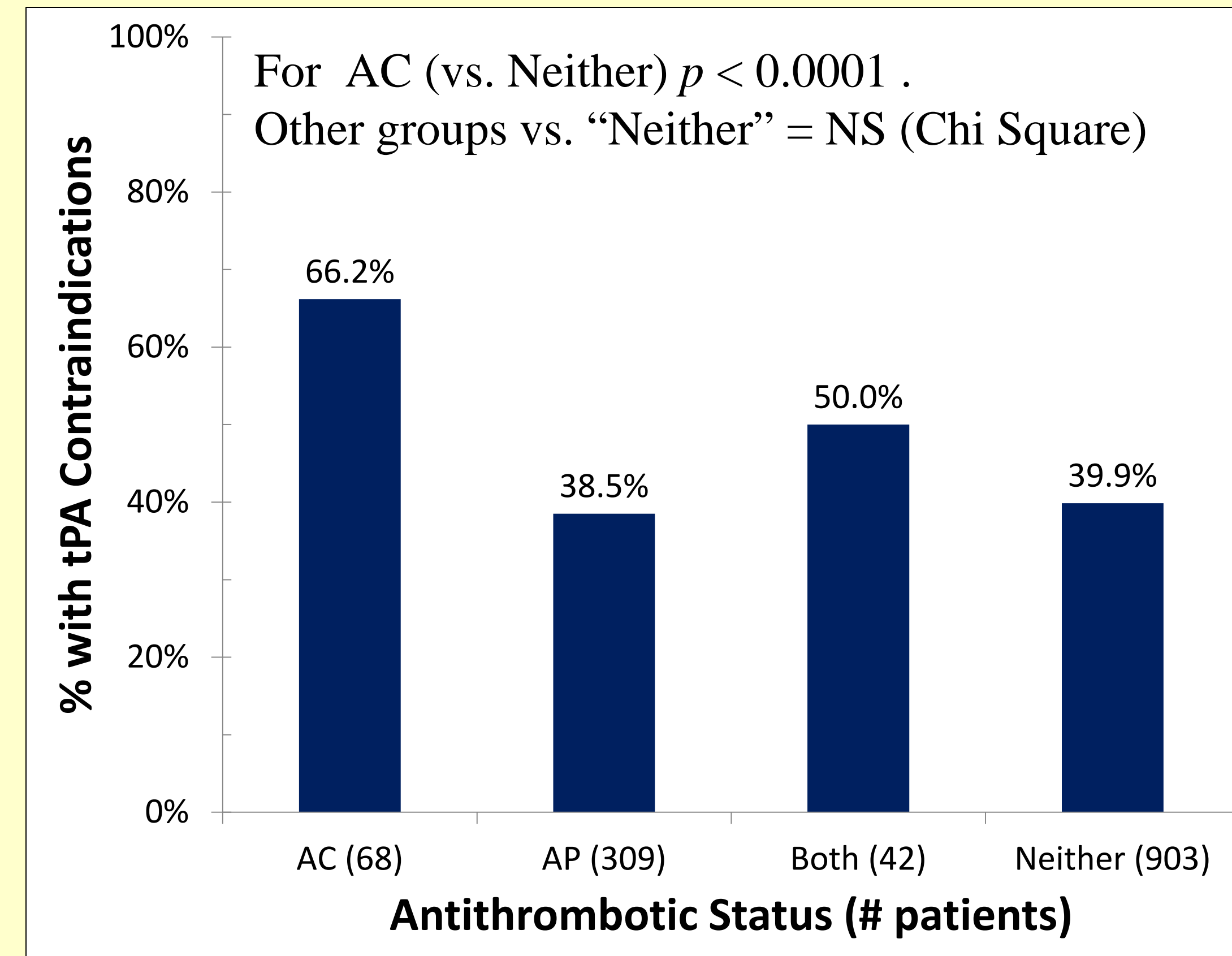


Figure 2: Eligible patients receiving IV tPA.

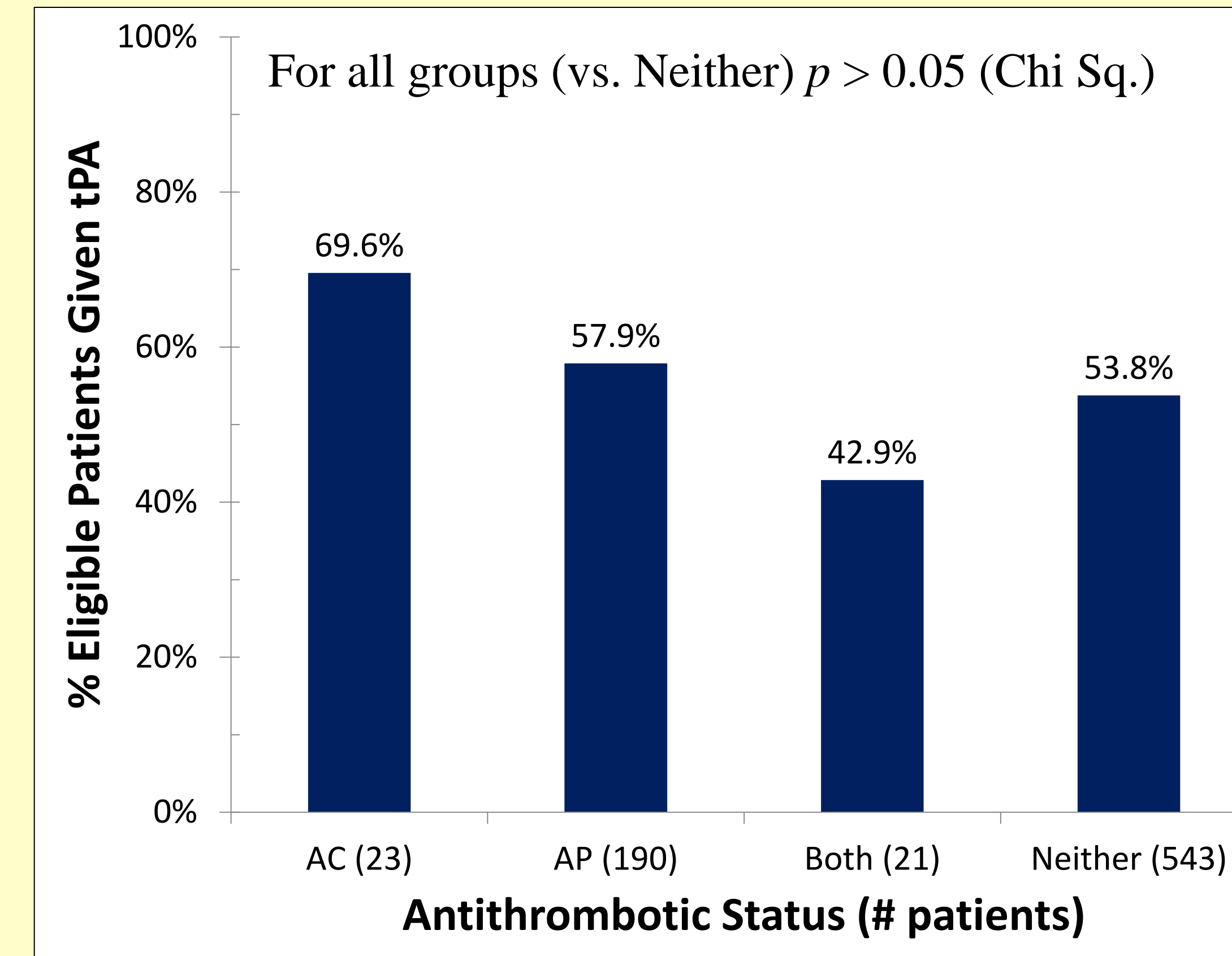


Figure 3: Baseline National Institutes of Health Stroke Scale (NIHSS) scores.

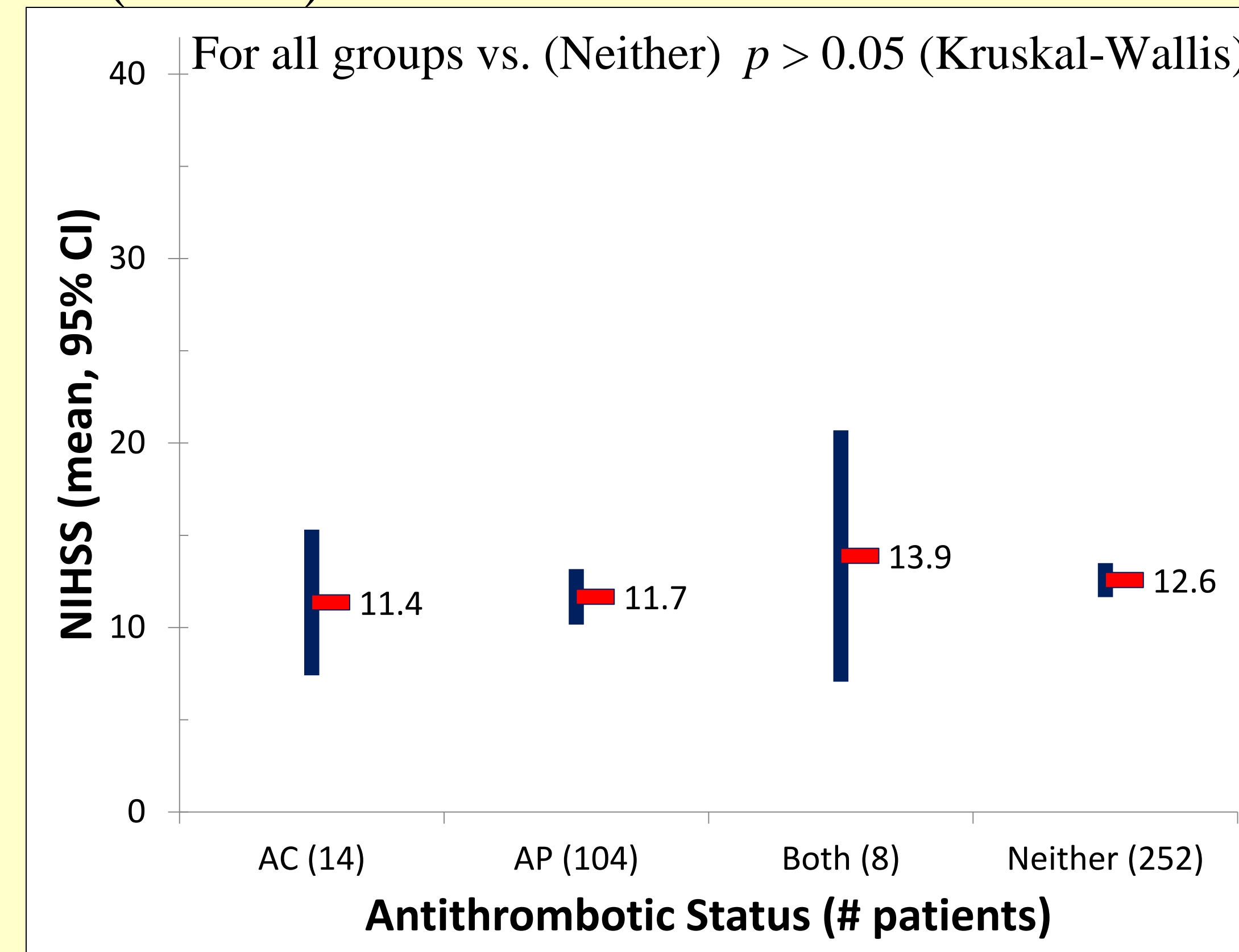
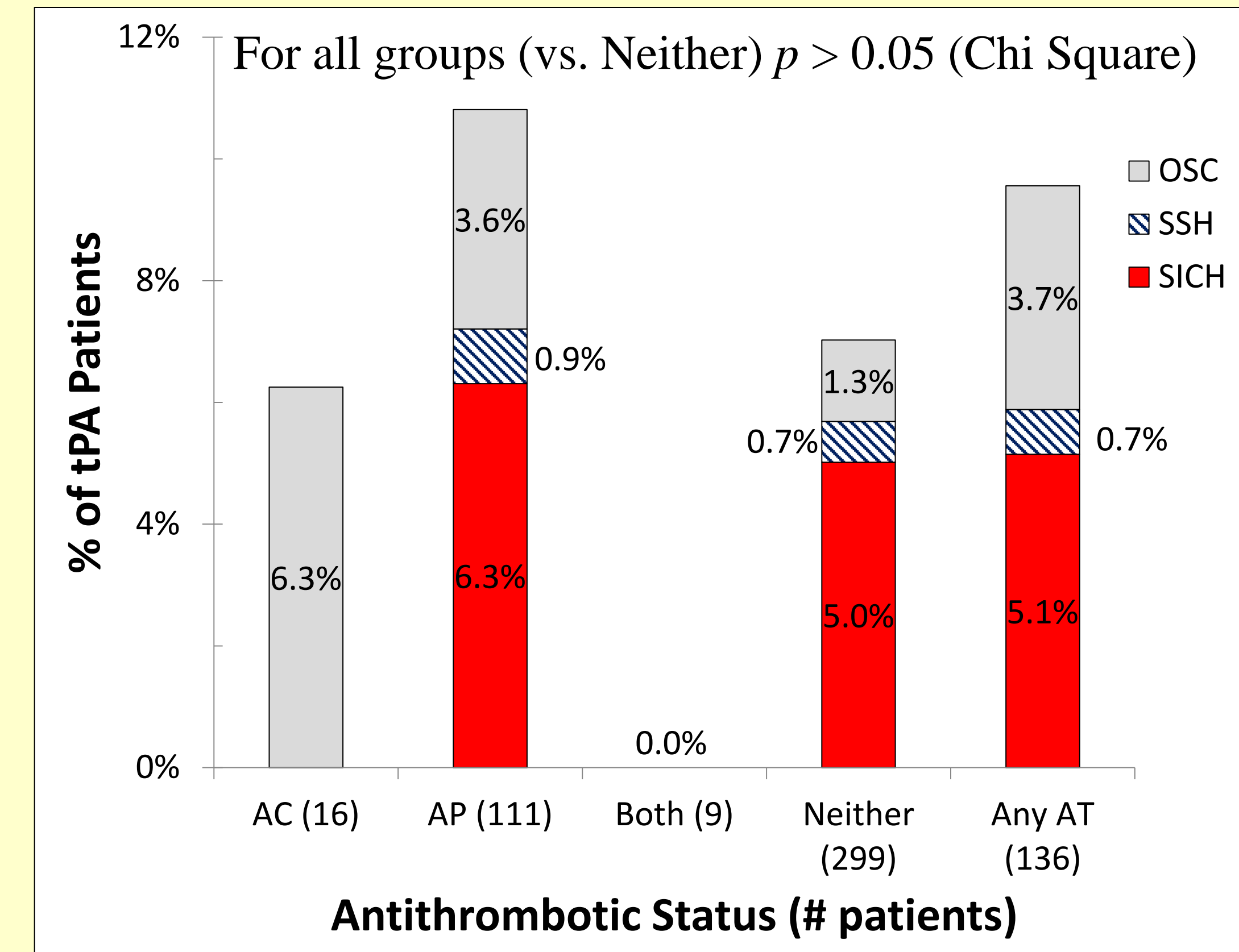


Figure 4: Complications from IV tPA.



Key to Figures: AP = antiplatelet therapy; AC = anticoagulation therapy; AP + AC = both therapies

Any AT = antiplatelet and/or anticoagulant therapy; **Neither** = no antithrombotic therapy.

SICH = symptomatic intracerebral hemorrhage; **SSH** = serious systemic hemorrhage; **OSC** = other serious complication

Results

•Of 15,625 records, 1,322 (8.5%) met inclusion criteria.

•Of included patients, 777 (59%) were eligible for tPA.

•Of the tPA eligible patients, 427 (55%) were treated.

•Only AC patients were more likely (than those not on antithrombotics) to have tPA contraindications (Fig.1).

•Eligible patients were equally likely to receive tPA, regardless of antithrombotic status (Fig.2).

•Treated patients had similar NIHSS scores (Fig 3).

•There was no significant difference in complications of IV tPA therapy among the groups (Fig. 4).

Conclusions

•Pre-stroke antiplatelet, anticoagulation, or combination therapy does not seem to preclude the likelihood of IV tPA thrombolysis in Colorado patients with ischemic stroke, in the absence of published contraindications.

•To date, our monitoring suggests that neither antiplatelet, nor anticoagulation, nor combination therapy appears to increase risk of complications after IV tPA. However, a type II error cannot be excluded. To have 80% confidence of detecting an increase in symptomatic intracerebral hemorrhage from 5% with no antithrombotic to 10% with any antithrombotic requires approximately 432 patients in each group. Our numbers of 299 (Neither) and 136 (Any Antithrombotic) give a confidence level of only 43% of not missing a difference of this magnitude at the $p < 0.05$ level. We continue to monitor this issue in the Colorado Stroke Registry.