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Research Article

# Factors Influencing Acute Stroke Thrombolytic Treatments in Hispanics in the San Diego Region

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**Abstract**

**Background:** Since the introduction of recombinant tissue plasminogen activator (rt-PA) for acute ischemic stroke, rt-PA rate and number of stroke centers have increased. Despite this, studies have shown racial and ethnic disparities in stroke care especially in Black and Hispanic populations. What factors are related to the administration of rt-PA within the Hispanic population has to date been unclear.

**Methods:** We performed a retrospective review of IRB approved, prospectively collected data from the UC San Diego Stroke Registry from 7/2004-7/2016. Patients were included based on the primary diagnosis of Transient Ischemic Attack or Ischemic Stroke. Hispanic *vs.* non-Hispanic patients were compared to assess for overall rt-PA treatment rates and process of care intervals. For the Hispanic cohort itself, demographics and NIHSS scores were assessed to determine why some Hispanics received rt-PA while others were not.

**Results:** Overall, 1489 patients (300 hispanic *vs.* 1189 non-hispanic) were included. Comparing hispanics to non-hispanics, there was no difference in rt-pa rate (35.3% *vs.* 33.1%; p=0.49). In rt-pa treated patients, "onset to arrival" interval was higher in hispanics (1.03 *vs.* 0.88 hours; p=0.04), while the "arrival to treatment" interval was not different (1.13 *vs.* 1.02 hours; p=0.07). When looking at hispanic patients only, there was no difference in baseline characteristics except for initial nihss in treated *vs.* Non-treated patients (13.27 *vs.* 7.24; p<0.001).

**Conclusion:** Our analyses sought to determine the factors important to administration of rt-PA to Hispanic patients. These findings highlight the need for strategies to improve recognition and presentation pathways for Hispanics.

**Keywords:** Stroke; TPA; Hispanic; Regional stroke differences; Ethnic disparities

## Introduction

Since the introduction of recombinant tissue plasminogen activator (rt-PA) for acute ischemic stroke (AIS), we have seen the rate of rt-PA administrations and number of new primary and comprehensive stroke centers increase [1]. The recent positive endovascular trials have also further added to treatment options providers can provide in acute stroke care. Despite the rise of acute stroke treatment utilization, we continue to see racial and ethnic variations in stroke care in both urban and rural settings, especially in Hispanic populations. Among minority groups, Hispanic Americans are the fastest-growing group in the United States and are estimated to represent 15% of the US population [2]. Hispanics also have an increased prevalence of risks factors for strokes when compared to non-Hispanic whites [3].

Whether ethnicity and race is a major barrier for acute stroke care remains controversial. Some reports have shown that ethnic disparities trump other risk factors in determining the delay of rt-PA use in acute ischemic stroke [4]. Several studies have demonstrated Blacks presenting with AIS were significantly less likely to be treated with intravenous rt-PA than whites [5-7]. How Hispanic ethnicity affects rt-PA evaluations has had mixed results. Two large nationwide population studies found lower rates of rt-PA use in Hispanics while a separate study showed similar rates of rt-PA treatment in Hispanics *vs.* non-Hispanic whites [8-10].

Among rt-PA treated AIS Hispanic and non-Hispanic patients, differences in demographics, comorbidities, and interval of care processes in this cohort have not been clearly studied. In our patient population, we sought to present rt-PA rates for both Hispanics and non-Hispanics, but more so to report on factors that influence the administration of rt-PA to both Hispanics and non-Hispanics in our San Diego, California region.

## Methods

### Design

This IRB approved study is a retrospective review prospectively collected data from the UC San Diego Stroke Registry. We included all consecutive acute ischemic strokes patients presenting within 12 hours of symptom onset to our network hospitals from June 2004 to July 2016. 1 of the 3 hospitals is a Joint Commission certified Comprehensive Stroke center and the other 2 are certified Primary




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**Table 1:** rt-PA by Ethnicity.

| Ethnicity | | | | |
|---|---|---|---|---|
| | **Hispanic (n=300)** | **Non-Hispanic (n=1189)** | **Overall (n=1489)** | **p-value** |
| **rt-PA(+)** | 106 (35.3%) | 394 (33.1%) | 593 (33.6%) | 0.494 |
| **rt-PA(-)** | 194 (64.7%) | 795 (66.9%) | 1173 (66.4%) | |

**Table 2:** Process of care intervals in Hispanics vs non-Hispanic whites treated with rt-PA. Data is reported as the mean hours (standard deviation).

| rt-PA(+) | | | |
|---|---|---|---|
| | **Hispanic (n = 102)** | **Non-Hispanic (n = 374)** | **p-value** |
| **Onset to Arrival** | 1.03 (0.08, 3.55) | 0.88 (0, 4.67) | 0.042 |
| **Arrival to Treatment** | 1.13 (0.47, 2.92) | 1.02 (0.02, 4.38) | 0.071 |
| **Onset to Treatment** | 2.42 (1.02, 4.38) | 2.13 (0.15, 4.67) | 0.004 |

Stroke Centers.

### Patient selection

Patients age ≥18 years were included based on the presentation and primary diagnosis of Transient Ischemic Attack (TIA) or Acute Ischemic Stroke (AIS). Transfer patients or in hospital stroke events were excluded from analysis for consistent reporting. Patient specific variables included age, gender, self-reported race/ethnicity, risk factors, blood pressure, National Institutes of Health Stroke Scale (NIHSS) score, and process of care intervals. Race/ethnicity is categorized as American Indian, Asian, Black, Hawaiian/Pacific Islander, Hispanic white, and non-Hispanic white.

### Statistical analysis

First, in order to assess rt-PA rates, Hispanic *vs.* non-Hispanic groups were compared. Second, care intervals were also assessed for the rt-PA subset comparisons and included onset-to-arrival time, arrival-to-decision-time, arrival-to-treatment time, and onset-to-treatment time. Times were reported as means and standard deviations (hours). Third, in order to assess the Hispanic population itself for rt-PA treatment differences, rt-PA+ *vs.* rt-PA- groups were compared within the Hispanic group itself. Baseline characteristics including risk factors, blood pressure, and presenting NIHSS were compared for Hispanics who received rt-PA (rt-PA+) to Hispanics who didn't receive rt-PA (rt-PA-). Significance was determined by a two sample t-test for continuous variables and Fisher's exact test for categorical variables.

## Results

We assessed 1,489 patients with a primary diagnosis of TIA or AIS. Among these patients, 300 were Hispanics (20% of the cohort) and 1189 were non-Hispanic. For the overall analysis, 33.6% of the assessed patients received rt-PA treatment. Among these patients, there was no difference in the rate of rt-PA utilization among Hispanic and non-Hispanic whites (35.3% *vs.* 33.1%; p=0.49) (Table 1).

In rt-PA treated patient subset, Hispanics and non-Hispanic whites had no significant difference in presenting NIHSS (mean 13.27 *vs.* 11.84; p=0.151). However, Hispanics had significant longer "onset to arrival" intervals (1.08 *vs.* 0.90 hours; p=0.024) and overall "onset to treatment" interval (2.42 *vs.* 2.13 hours p=0.003). Despite these differences, the "door to treatment" interval was not significantly different (1.13 *vs.* 1.02 hours; p=0.07) (Table 2).

**Table 3:** Subset Analysis of Hispanic Patients Only: Baseline demographics and exam difference by rt-PA. Blood pressure and NIHSS is reported as the mean (standard deviation).

| Subset Analysis: Hispanic Patients Only | | | |
|---|---|---|---|
| | **rt-PA(-)** n = 194 | **rt-PA(+)** n = 106 | **p-value** |
| **Age** | 65.7 | 67.02 | 0.510 |
| **Gender (Male)** | 112 (57.7%) | 53 (50%) | 0.225 |
| **Race (White)** | 190 (98.4%) | 102 (96.2%) | 0.266 |
| **Diabetes** | 80 (41.9%) | 44 (42.3%) | 1.000 |
| **Hypertension** | 136 (71.2%) | 75 (72.1%) | 0.893 |
| **Hyperlipidemia** | 56 (30.6%) | 31 (30.1%) | 1.000 |
| **Atrial Fibrillation** | 35 (18.3%) | 28 (27.7%) | 0.073 |
| **Coronary Artery Disease** | 35 (18.5%) | 23 (21.9%) | 0.541 |
| **Current Tobacco Use** | 43 (22.2%) | 16 (15.1%) | 0.172 |
| **Current Alcohol Use** | 26 (13.4%) | 16 (15.1%) | 0.729 |
| **Current SBP** | 153.36 (26.51) | 146.86 (26.1) | 0.091 |
| **Current DBP** | 82.02 (16.22) | 81.51 (13.41) | 0.775 |
| **Initial NIHSS (Total)** | 7.24 (9.05) | 13.27 (9.31) | <.001 |

In the Hispanic-only subset, comparing rt-PA (+) to rt-PA (-) among Hispanics patients only, there was no difference for male sex (56%), Hypertension (71%), Hyperlipidemia (29%), Diabetes (43%), a trial Fibrillation (23%), Smoking (20%), and blood pressure. However, rt-PA (+) Hispanic patients differed from rt-PA (-) patients by presenting NIHSS at arrival (mean 13.27 *vs.* 7.24; p<0.001) (Table 3).

## Discussion

Our analyses sought to determine the factors important to administration of rt-PA to Hispanic patients. We compared Hispanics to non-Hispanics, assessed the rt-PA (+) subset, and finally analyzed the Hispanic cohort itself for relevant factors. Our primary finding was that the rate of rt-PA treatment overall was not significantly different between Hispanics and non-Hispanics in our patient population. Some studies have reported on overall differences in rt-PA rates. A population study performed by Nasr, et al. demonstrated that white patients with AIS received rt-PA at a significantly higher rate than Hispanics (2.3% *vs.* 2%) [8]. Another study by A paricio, et al. showed that Hispanics still received rt-PA less often at both primary stroke center and non-primary stroke centers [9]. The major difference between our findings and other reports are both Hispanics and whites had high rt-PA treatment rates with no significant difference in treatment rates. It is affirming to the overall system that rt-PA treatment rates do not differ based on self-report of Hispanic ethnicity. While the national average rt-PA treatment rate is between 3.0% and 8.5% of all stroke admissions with some centers reporting a treatment rate up to 35%, we found that 33.5% of patients in our study received rt-PA [11,12]. Our dataset includes only acutely presenting stroke code patients within 12 hours of symptom onset, and does not report a percentage based on number of discharges. This is limitation to our study and may be a reason why the reported treatment rates are higher than the national average.

Our study also found that for rt-PA treated patients, although "door to treatment" intervals were not significantly different between Hispanics and non-Hispanics, "onset to treatment" intervals were longer, with this finding likely being driven by longer "onset to door" times. The reason for this difference is speculative, but may be due to poorer recognition, cultural differences, EMS activation differences, or even dispatch differences. Few studies have looked at the treatment intervals and delays in arrivals among Hispanics with AIS. Our study adds to the literature in that despite similar rt-PA treatment rates and "door to treatment" intervals, Hispanics patients with AIS are likely to have significant delay in hospital arrival time compared to whites. One hypothesis for this delay in arrival time is the mode of transportation Hispanic patient's use. Neil, et al. showed Hispanics utilized EMS services less often compared to non-Hispanic whites [13]. However, that analysis did not show significant differences in onset to arrival intervals in Hispanics compared to non-Hispanic whites. Our study may have found a different result due to having a larger sample size. Another study found that Hispanic patients were more likely to present to larger hospitals. This was likely attributed to the urban location of hospitals [14]. Given this notable delay, more research should target the process of outside hospital factors that delay TPA treatment. We point out a need for clinician and policy maker investigation into possible regional and ethnic specific differences in stroke treatment access.

In our cohort of Hispanics only, there were no differences in demographic or co-morbidities between those treated with rt-PA and those who were not treated. This homogeneity is reassuring, showing that there were no systematic reasons why some Hispanics were treated and others were not. We did note that the presenting NIHSS was higher for those treated with rt-PA, which is in many ways an expected finding. Disabling deficits are generally treated to a greater degree than milder deficits [15]. When looking at the non-Hispanic white population, the percentage was similar (33.1%) showing that there was not a disproportionately lower treatment per NIHSS scale score for Hispanics. We plan to further assess this ratio in other race and ethnicity groups in subsequent analyses.

With the expected continued growth of the Hispanic American population, identifying the relevant factors (demographics, comorbidities and potential barriers) that contribute to rt-PA use in the Hispanic population, may improve the delivery of acute stroke care to this population. Our study supports the need to develop culturally relevant education programs to focus on treatment delays and differences in order to optimize rt-PA treatments. We are in the planning stages for tailored interventions which may work to minimize these barriers and optimize acute stroke treatment for this population.

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