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The Effect of T-Pa Administration In-Hospital Mortality in Hispanic Puerto Rican Patients with Acute Ischemic Stroke

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Abstract:
Introduction*: Stroke is the fourth leading cause of mortality in Puerto Rico. Tissue plasminogen activator (t-PA) improves acute ischemic stroke(AIS) outcomes when administered timely; however, there is limited information regarding the association of t-PA administration and mortality in Hispanics.*
Objective: To investigate if t-PA affects mortality rate among AIS patients in Puerto Rico.
Material And Methods*: We conducted a secondary data analysis of 1950 patients in the Puerto Rico Stroke Registry, a non-concurrent cohort study , during years 2007, 2009, and 2011.We reviewed medical record of adult patients with AIS .Patients with transient ischemic attacks (TIA) were excluded. We conducted initially a descriptive analysis of all variables; then, abi-variate analysis, and finally a logistic regression analyses to adjust for potential confounders in the relation between t-PA administration and mortality.*
Results*: t-PA was administered to 5.3% (104) of the patients. The association between t-PA administration and mortality was not significant (OR=1.97, 95%CI: 0.66-5.87).However, for every year of age increase, patients were 3% more likely to die, independently of any other covariates(OR=1.03, 95%CI: 1.01-1.06). Patients who received aspirin were 55% less likely to die after adjusting for age, gender, atrial fibrillation, body mass index, and lipid lowering agent (LLA).(OR=0.55, 95%CI: 0.31-0.97). The adjusted model showed that patients receiving LLA had 48% lower mortality (OR=0.52, 95% CI: 0.29-0.92).*
Conclusion*: Our findings suggest that the administration of t-PA during AIS does not impact in-hospital mortality. This may be due to the small number of stroke patients receiving t-PA in our study. The risk of dying after AIS increases with age, but decreases with the administration of aspirin and LLA, which should be used for all patients with AIS.*
Key Words*: stroke ,t-PA, mortality, Hispanic, Puerto Rico*

I. Introduction

Stroke is defined as a loss of blood supply to the brain which leads to damage of brain tissue that present as neurological defect. Stroke was previously called cerebrovascular accident (CVA) or stroke syndrome. It is the fourth cause of death in the U.S. killing 130,000 persons per year or 1 in every 19 Americans. (3) On average, every 4 minutes a person dies from stroke and every 40 seconds someone has a stroke in the U.S. The prevalence of stroke between ages 55 to 64 is 11% and the rate increases with age. The U.S.A spends almost $35.5 billion to treat stroke every year including health care services expenses, drug prescriptions, and absence from work. There are two types of stroke: ischemic and hemorrhagic. Acute Ischemic Stroke(AIS) is caused by obstruction of blood vessels due to thrombus. The occlusion causes a decrease of oxygen that ultimately will lead to adenosine triphosphate (ATP) depletion. ATP depletion will cause imbalance of ionic gradient across the cell membrane and cell action potential. This will increase influx of sodium and calcium ions and that will lead to cytotoxic cell edema. Recombinant human tissue-type plasminogen activator (t-PA) produces local fibrinolysis by converting plasminogen to plasmin which degrades fibrin and fibrinogen.(1) After the t-PA dissolves the clot, the blood circulation is restored, and the blood can deliver oxygen to the ischemic tissue. The majority of strokes are ischemic, and can be tr beneficial if it is diagnosed and treated early within the first 4½hours or the initiation of signs and symptoms t-PA for AIS was approved by the U.S. Food and Drug Administration (FDA) in 1996. Even after the approval, the use of t-PA was in small amount due to the concern about its safety and the restriction of t-PA use. Up to date, there are many studies supporting the use of t-PA; however, some studies deny any beneficial effect of t-PA. The aim of this study is to determine if a difference on in-hospital mortality rate exists among AIS patients from the Puerto Rican Stroke Registry according to t-PA administration.

II. Methodology

We used a secondary analysis of data collected by the Puerto Rico Stroke Registry, which had an observational, non-concurrent cohort design. The database consists of hospital discharge information collected during study years 2007, 2009, and 2011. Prior to releasing the data for research use, personal identifiers such as names and social security numbers were removed. Our inclusion criteria comprised patients 18+ years old hospitalized with AIS during the study period in all participating hospitals in Puerto Rico. We excluded patients with a transient ischemic attack (TIA). The purpose of this study is to determine if a difference on in-hospital mortality rate exists between patients with AIS (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 430 – 438) who received t-PA vs. those patients who didn't receive t-PA. Statistical analysis, we used SPSS statistical package v.20. Initially, we conducted a descriptive analysis of selected variables of interest such as age and sex. Also, then we analyzed the unadjusted association of t-PA administration (yes/no) and mortality (died/survived) using the chi-square test. After that we conducted a binominal logistic regression modeling to adjust for potential confounders in the relation between t-PA administration and mortality. Finally, we checked for collinearity among predictors in the multivariate model.

III. Result :

Total of 1950 patients who had stroke only 104 patient receive t-pa . At baseline there is no significant difference in hypertension (HTN), diabetes mellitus (DM), body mass index (BMI), atrial fibrillation (AF), current smocking (CS), aspirin administration, lipid lowering agent (LLA), alcohol consumption between patients who were administered t-PA and patients who were not administered t-PA. The inability to find significant differences at baseline may be due tothe small number of stroke patient who receive t-PA. Males (61.5%) are significantly more likely to receive t-PA than females (38.5%).

Table 1: Characteristics of patients with ischemic stroke treated with intravenous tissue plasminogen activator (t-PA) in Puerto Rico 2007, 2009, 2011.

Characteristics	t-PA No N (%)	Yes N (%)	Sig
Age in years - mean (SD)	70.96(13.3)	71.51 (16.1)	0.684
Gender			0.004
Female	977 (52.9%)	40 (38.5%)	
Male	869 (47.1%)	64 (61.5%)	
Diabetes mellitus			0.801
Yes	891(55.5%)	46(54.1%)	
No	714(44.5%)	39(45.9%)	
BMI category			0.438
Underweight	96(6.8%)	3(3.9%)	
Normal	485(34.3%)	30(39.5%)	
Overweight	490(34.7%)	29(38.2%)	
Obese	343(24.3%)	14(18.4%)	
Alcoholism/excessive alcohol use			0.116
Yes	100(6.5%)	2(2.3%)	
No	1437(93.5%)	85(97.7%)	
Atrial fibrillation			0.787
Yes	124(8.0%)	6(7.1%)	
No	1434(92.0%)	78(92.9%)	
Aspirin			0.234
No	1033(56.0%)	52(50.0%)	
Yes	813(44.0%)	52(50.0%)	
Lipid lowering agent			0.238
No	944(51.1%)	47(45.2%)	
Yes	902(48.9%)	57(54.8%)	
Current smoker			0.455
Yes	156(9.3%)	11(11.6%)	
No	1525(90.7%)	84(88.4%)	
Hypertension			0.355
Yes	1488(87.3%)	79(84.0%)	
No	216(12.7%)	15(16.0%)	
Hyperlipidemia			0.750
Yes	492(31.2%)	26(29.5%)	
No	1087(68.8%)	62(70.5%)	

We couldn't find a significant association between t-PA administration and mortality rates among patients with ischemic stroke in Puerto Rico.This may be due to the fact that we had a small number of patients who were administered t-PA.The odds of dying increased with age by 6% per year. Males are 39% (OR=0.61, 95% CI:0.39-0.96) less likely to die than females. Overweight patients were 58%less likely to die than patients with normal weight. In addition, patients who took aspirin were 55%(OR=0.45, 95% CI: 0.27-0.73) less likely to die

than patient who did not take aspirin. Patients with atrial fibrillation were 2.4 (OR=2.44, 95% CI: 1.34-4.47) times more likely to die than patients without atrial fibrillation

Table 2:Association between mortality rate and predictor variables among stroke patients in Puerto Rico 2007, 2009, 2011

Characteristics	Diedbefore discharge Yes N (%)	No N (%)	OR (95% CI)	p-value
Age in years - mean (SD)	70.7(13.4)	77.6(13.1)	1.06(1.03-1.06)	<0.001
t-PA				0.803[1]
No	80(4.3%)	1766(95.7%)	Reference	
Yes	5(4.8%)	99(95.2%)	1.11(0.44-2.81)	
Gender				0.032
Female	54(5.3%)	963(94.7%)	Reference	
Male	31(3.3%)	902(96.7%)	0.61(0.39-0.96)	
Hypertension				0.490
No	13(5.6%)	218(94.4%)	Reference	
Yes	72(4.6%)	1495(95.4%)	0.80(0.44-1.48)	
BMI				0.018
Normal	27(5.2%)	488(94.8%)	Reference	
Underweight	8(8.1%)	91(91.9%)	1.58(0.70-3.60)	
Overweight	12(2.3%)	507(97.7%)	0.42(0.21-0.85)	
Obese	19(5.3%)	338(94.7%)	1.02(0.55-1.85)	
Hyperlipidemia				0.412
No	62(5.4%)	1087(94.6%)	Reference	
Yes	23(4.4%)	495(95.6%)	0.81(0.49-1.33)	
DiabetesMellitus				0.303
No	42(5.6%)	711(94.4%)	Reference	
Yes	42(4.5%)	895(95.5%)	0.79(0.51-1.23)	
CurrentSmoker				0.064
No	80(5.0%)	1529(95.0%)	Reference	
Yes	3(1.8%)	164(98.2%)	0.35(0.10-1.12)	
Alcoholism				0.141
No	80(5.3%)	1442(94.7%)	Reference	
Yes	2(2.0%)	100(98.0%)	0.36(0.08-1.48)	
AtrialFibrillation				0.003
No	71(4.7%)	1441(95.3%)	Reference	
Yes	14(10.8%)	116(89.2%)	2.44(1.34-4.48)	
Aspirin				0.001
No	62(5.7%)	1023(94.3%)	Reference	
Yes	23(2.7%)	842(97.3%)	0.45(0.27-0.73)	
Lipid Lowering Agents				0.085
No	51(5.1%)	940(94.9%)	Reference	
Yes	34(3.5%)	925(96.5%)	0.67(0.43-1.05)	

[1] fisher test was used instead of chi square

While adjusting for age, gender, alcohol consumption,atrial fibrillation (AF),aspirin administration, body mass index (BMI), diabetes mellitus (DM), hypertension (HTN), current smocking, lipid lowering agent (LLA), we didn't find a significant association between t-PA administration and mortality rate.
In the adjusted model the association between atrial fibrillation and mortality disappeared (OR=1.57, 95% CI: 0.69-3.55). However, in the same adjusted model people who took aspirin were still significantly less likely to die than people who didn't take aspirin (OR=0.55, 95% CI: 0.31-0.97)

Table 3: Unadjusted and adjusted risk of mortality among stroke patients in Puerto Rico 2007, 2009, 2011.

Characteristics	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age in years - mean (SD)	1.04(1.025-1.064)	<0.001	1.03(1.01-1.06)	0.012
t-PA		0.803		0.221
No	Reference			
Yes	1.11(0.44-2.81)		1.97(0.66-5.87)	
Gender		0.032		0.475
Female	Reference			
Male	0.61(0.39-0.96)		0.80(0.44-1.45)	
Hypertension		0.49		0.817
No	Reference			
Yes	0.80(0.44-1.48)		0.90(0.38-2.10)	
BMI		0.018		0.065
Normal	Reference			
Underweight	1.5(0.70-3.60)		1.53(0.64-3.63)	
Overweight	0.42(0.21-0.85)		0.58(0.28-1.20)	
Obese	1.02(0.55-1.85)		1.53(0.76-3.06)	
Hyperlipidemia		0.412		0.117
No	Reference			
Yes	0.81(0.49-1.33)		1.6(0.88-2.91)	
DiabetesMellitus		0.303		0.656
No	Reference			
Yes	0.79(0.51-1.23)		1.13(0.65-1.97)	
CurrentSmoker		0.064		0.789
No	Reference			
Yes	0.35(0.10-1.12)		0.84(0.24-2.93)	
Alcoholism		0.141		0.919
No	Reference			
Yes	0.36(0.08-1.48)		1.08(0.23-4.98)	
AtrialFibrillation		0.003		0.273
No	Reference			
Yes	2.44(1.34-4.47)		1.57(0.69-3.55)	
Aspirin		0.001		0.042
No	Reference			
Yes	0.45(0.27-0.73)		0.55(0.31-0.97)	
	Lipid Lowering Agents	0.085		0.025
No	Reference			
Yes	0.67(0.43-1.05)		0.52(0.29-0.92)	

VI. Discussion:

The aim of This study is to find association between t-PA administration in AIS and mortality among Hispanic population in Puerto Rico.in this non-concurrent cohort study 1950 patients with AIS were enrolled,104 (5.3%) received treatment with intravenous t-PA .

Administration of t-PA need to match specific criteria for example, the time of administration t-PA and stroke attack must be within 4 hours and a half, No history of active bleeding , No major surgery within 14 days and not currently taking any anticoagulants or receiving heparin within 48 hours preceding stroke. So that the small number of AIS patients in this study could be due to the absence of one of these criteria, this can be the reason we couldn't find a significant association between t-PA administration and mortality. However the reason for whether the patient were eligible to receive t-PA or didn't were not available.

865 patient who receive aspirin 23 (2.7%) of them die before discharge in another hand patient who didn't receive aspirin and die before discharge 62 (5.7%). Patient who took aspirin were 45% less likely to die than patient who weren't on aspirin. Because aspirin prevent blood clot by inhibit platelets aggregation after ruptured atherosclerosis by acting on cyclooxygenase (COX) and that will prevent release thromboxane A2.