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Investigation of Gender Differences and Exclusive Criteria in a Diabetic Acute Ischemic Stroke Population Treated with Recombinant Tissue-Type Plasminogen Activator (rtPA)

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Abstract

Background—Many studies have reported that women who survive stroke have less favorable outcomes than men in the use of rtPA, while others reported worse outcomes in men than women. The gender difference in the exclusion criteria in a diabetic stroke population is not fully understood. This issue was investigated in this study.

Method—In a diabetic stroke population from a stroke registry of data collected between January 2010 to June 30, 2016, the gender difference was determined using demographics and clinical factors. Comparison was determined using univariate analysis while multivariable model was used to adjust for the effect of confounding variables.

Results—In a diabetic stroke population of 439 patients, more females were excluded than males ($P < 0.0001$, OR = 2.323). The male exclusion was associated with atrial fibrillation ($P = 0.011$, OR = 3.697), carotid artery stenosis ($P = 0.023$, OR = 5.001), and cholesterol reducer ($P = 0.037$, OR = 0.409). In the female diabetic stroke population, exclusion from rtPA therapy was associated with language disturbances ($P = 0.039$, OR = 0.372), history of previous stroke ($P = 0.005$, OR = 3.276), antihypertensive medication use ($P = 0.013$, OR = 0.163), and antidiabetic medication use ($P = 0.031$, OR = 0.324).

Conclusion—In a stroke population, women have a worse outcome than men in an untreated acute ischemic stroke population, but when treated there is no significant difference, suggesting a better treatment outcome for women compared to men. In a diabetic stroke population, the clinical variables for the exclusion criteria for women and men are significantly different, even after adjustment for confounding variables.

Keywords

acute ischemic stroke; diabetes mellitus; gender; tissue-type plasminogen activator; exclusion

Introduction

Stroke is a leading cause of disability and mortality worldwide, making studies evaluating incidence, risk factor profiles, and treatment exclusions especially important to allow for appropriate prevention strategies to be employed in high-risk groups. Multiple studies have demonstrated differences in risk factors, stroke characteristics, and outcomes between men and women during acute ischemic stroke [1–8]. The literature to-date has shown that women that develop ischemic stroke are older, and have a worse prognosis than men [1,4,6]. These findings suggest that investigating gender differences in risk factor profiles as well as differences in treatment and treatment response may provide more information about active measures that could be taken to eliminate disparity and improve stroke care in the near future. Diabetes mellitus is a risk factor that contributes to 25–42% of all stroke cases and increases first-time stroke risk, subsequent stroke risk, risk of dementia, and cognitive decline after stroke [9–14]. Diabetic stroke patients have higher in-hospital mortality [10,15] as well as 3, 12, and 36 months post-stroke mortality compared to men [16]. In addition, diabetic women with stroke have an older age of onset, higher NIHSS scores, and higher modified ranking scale values than diabetic men

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[16]. In a stroke population, women have a worse outcome than men when untreated [17]. In contrast, there is no significant difference in treated patients, suggesting that thrombolysis maybe beneficial more to women than to men, as shown by some studies [17,18]. Whether this is the case in a diabetic stroke population is yet to be investigated. If thrombolysis is beneficial more to women than to men in a diabetic stroke population, one possibility is that clinical risk factors associated with thrombolysis efficacy are not present in the same proportion among women presenting with diabetic stroke than among men. Our first objective is to identify the different risk factors in rtPA excluded population of diabetic stroke, and determine whether these risk factors are different between male and female populations. Moreover, since males and females do not present the same exclusion criteria in a diabetic stroke population, our second objective is to determine the effect of gender in the exclusion criteria for rtPA using a prospective registry of data of diabetic acute ischemic stroke patients. The goal of this study is to identify the clinical variables for the exclusion criteria for women and men in a diabetic stroke population, and determine whether these variables are significantly different in men and women even after adjustment for confounding variables. In this study, we demonstrated the use of clinical and demographic variables in the inclusion and exclusion criteria as a promising approach to assist in the evaluation of gender differences in patients with a favorable risk-benefit profile for thrombolytic therapy in a 4.5-hour protocol.

Methods

Data collection

Retrospective data on daily admissions for acute ischemic stroke between January 1, 2010 and June 30, 2016 was obtained from the Greenville Health Care System (GHS) stroke registry. The GHS stroke registry data has been standardized according to the GWTG-stroke registry formed by the American Heart Association and American Stroke Association in a joint effort to improve the quality for acute ischemic stroke. A standardized data collection instrument was developed to obtain information on demographics (age and sex), admission date, medication use, clinical diagnosis, prehospital care, prestroke and post stroke ambulatory status, in-hospital procedures, past medical history, and information on patients that received or did not receive intravenous recombinant tissue plasminogen activator (rtPA). All data were collected at the time of the initial emergency department, stroke, or neurological units' evaluation. Documentations also included potential contraindications, patient history, stroke characteristics, physiologic status, and patient refusal for rtPA. Information on brain computed tomography or magnetic resonance imaging was also recorded in the database. Hospital admissions for ischemic stroke were identified according to the principal diagnosis. All data, including in-hospital procedures, treatments, contraindications to anticoagulant and antithrombotic treatment, and discharge instructions, were abstracted retrospectively. Collected data underwent an extensive series of quality and logic checks. All protocols were approved by the ethics committee.

Data analysis

All statistical analyses were computed using IBM SPSS version 15.0 (Statistical Analysis Software). Comparisons between men and women with respect to categorical variables were made by χ^2 test, while student *t*-test was used for continuous data. Comparisons of demographic and clinical characteristics of diabetic stroke patients who received rtPA were compared to a group of diabetic patients who did not receive the rtPA treatment. Following this, the diabetic stroke population was divided into male and female groups, and a multivariate binary logistic regression analysis was performed to control the confounding effect of clinical and demographic factors that influenced the exclusion of patients from the rtPA treatment. The effect confounding variables was controlled through adjustment and multivariable logistic modeling. In the multivariable logistic models, all demographic and clinical factors that differ by gender were analyzed. Since the relation of age with some variables may not be linear, older age groups were considered in all multivariable models and included if statistically significant. To test whether gender influenced rtPA treatment exclusion decisions, these analyses were repeated separately for diabetic male and diabetic female groups, respectively, with documented evidence of rtPA exclusion. Age and gender interaction effects on rtPA treatment were also explored. A partial proportional-odds model was developed for common OR based on cumulative logits across for all variables and parsimoniously adjusted such that covariates were only retained if they meaningfully confounded the association between gender and exclusion from rtPA. The significance level of all analysis was set to a probability level of 0.05

Results

Between January 2010 and June 2016, a total of 1446 stroke patients were identified. A total of 439 patients presented with a history of diabetes and stroke and comprised those that received rtPA versus those who did not

Table 1. Characteristics of stroke patients with diabetes, excluded and included for rtPA by gender

Characteristic	rtPA		p-value	No rtPA		*P*-value
	Male	Female		Male	Female	
Total number of patients	100 (46.7)	70 (31.1)		114 (53.3)	155 (68.9)	0.001*
Age group: No. (%)						
<50 years	8 (8.0)	7 (10.0)	0.037*	7 (6.1)	4 (2.6)	0.007*
50–59	24 (24.0)	13 (18.6)		25 (21.9)	30 (19.4)	
60–69	31 (31.0)	14 (20.0)		32 (28.1)	28 (18.1)	
70–79	24 (24.0)	15 (21.4)		29 (25.4)	45 (29.0)	
≥80	13 (13.0)	21 (30.0)		21 (18.2)	48 (31.0)	
Mean ± SD	65.22 ± 11.4	69.54 ± 14.3		67.30±12.8	71.69 ± 13.5	
Race: No. (%)						
Caucasian	76 (76.0)	51 (72.9)	0.830	86 (75.4)	113 (72.9)	0.896
African–American	22(22.0)	18 (25.7)		26 (22.8)	39 (25.2)	
Other	2 (1.7)	1 (1.4)		2 (1.8)	3 (1.9)	
Medical history: No. (%)						
Hypertension	94 (94.0)	66 (94.3)	0.938	100 (87.7)	140 (90.3)	0.496
Coronary artery disease	52 (52.0)	21 (30.0)	0.004*	55 (48.2)	59 (38.1)	0.095
Dyslipidemia	64 (64.0)	48 (68.6)	0.536	76 (66.7)	105 (66.7)	0.853
Atrial fib/flutter	12 (12.0)	13 (18.6)	0.234	26 (22.8)	44 (28.4)	0.303
Previous stroke	34 (34.0)	14 (20.0)	0.046*	41 (36.0)	67 (43.2)	0.230
Previous TIA	15 (15.0)	7 (10.0)	0.339	17 (14.9)	22 (14.2)	0.869
Congestive heart failure	16 (16.0)	8 (11.4)	0.400	17 (14.9)	33 (21.3)	0.184
Carotid artery stenosis	4 (4.0)	1 (1.4)	0.329	10 (8.8)	12(7.7)	0.761
Peripheral vascular disease	5 (5.0)	8 (11.4)	0.121	9 (7.9)	19 (12.3)	0.247
History of smoking	28 (28.0)	15 (21.4)	0.332	28 (24.6)	24 (15.5)	0.062
Medication history: No. (%)						
Antiplatelet	73 (73.0)	35 (50.0)	0.002*	74 (64.9)	104 (67.1)	0.708
Antihypertension	85 (85.0)	65 (92.9)	0.118	89 (78.1)	130 (83.9)	0.227
Cholesterol reducer	67 (67.0)	39 (55.7)	0.135	63 (55.3)	101 (65.2)	0.100
Diabetes medication	74 (74.0)	60 (85.7)	0.066	85 (74.6)	112 (72.3)	0.673
Initial NIH stroke scale group: No. (%)						
0–9	69 (69.0)	35 (50.0)	0.036*	89 (78.1)	98 (69.5)	0.002*
10–14	18 (18.0)	15 (21.4)	0.838	7 (6.1)	18 (11.6)	0.127
15–20	6 (6.0)	9 (12.9)	0.329	13 (11.4)	24 (15.5)	0.033*
21–25	7 (7.0)	11 (15.7)	0.234	5 (4.4)	15 (9.7)	0.923
Mean ± SD	8.50 ± 5.7	10.63 ± 6.9		6.43 ± 6.0	8.90 ± 7.2	
Initial exam findings: No. (%)						
Weakness/paresis	95 (95.0)	66 (94.3)		88 (77.2)	131 (84.5)	
Altered level of consciousness	30 (30.0)	26 (37.1)		30 (26.3)	60 (38.7)	
Aphasia/language disturbance	72 (72.0)	56 (80.0)		72 (63.2)	97 (62.6)	
Risk of mortality GWTG ischemic stroke						
Mean ± SD	5.15 ± 5.2	6.92 ± 7.4	0.099	4.10 ± 4.6	5.99 ± 6.3	0.007*
Body mass index						
Mean ± SD	30.55±7.6	30.78±7.4	0.844	29.44± 5.6	31.67 ± 8.7	0.012*

by gender (Table 1). As shown in Table 1, more males than females were included for rtPA while more females (P = 0.001) than males were excluded for rtPA. The analysis revealed that females were older than males in both the rtPA receiving group (P = 0.037) and the group that was excluded (P = 0.007). More males than females with histories of coronary artery disease (P = 0.004) and previous stroke (P = 0.046) were included for rtPA, while there was no significant difference between males and females in all the clinical variables for the rtPA exclusive group. More males (P = 0.002) than females with antiplatelet medication received the rtPA, while there was no significant difference in the excluded group for diabetic stroke patients receiving antiplatelet medication. A significant gender difference was observed in the NIH stroke scale in both the rtPA (P = 0.036) and the no rtPA groups (P = 0.002). In the exclusion criteria group, more females than males were excluded from rtPA due to altered level of consciousness (P = 0.033), risk of mortality (P = 0.007), and body mass index (P = 0.012).

The confounding effect of variables was controlled through age-adjusted, and multivariable logistic modeling to identify the factors that were associated with rtPA exclusion in the diabetic stroke population (Table 2). A total of six variables were significantly associated with rtPA exclusion in the diabetic stroke population: weakness (OR = 0.233, P = 0.001), aphasia/language disturbance (OR = 0.521, P = 0.020), history of atrial fibrillation (OR = 2.587, P = 0.005), history of Carotid artery stenosis (OR = 3.358, P = 0.031), and history of stroke (OR = 1.984, P = 0.007). Even after adjustment, gender still had an effect among the diabetic stroke population (OR = 2.323, P =0.001) after controlling for confounding variables.

Table 3 identified four variables associated with rtPA exclusion among the male diabetic stroke population: weakness (OR = 0.186, P = 0.009), history of atrial fibrillation (OR = 3.697, P = 0.011), and carotid artery stenosis (OR = 5.001, P = 0.023). Following adjustment, the effect of aphasia and the history of stroke disappear in the male diabetic stroke rtPA exclusion population, while the use of cholesterol reducing medication was significantly associated with rtPA exclusion in the

Table 2. Patient-level factors associated with rtPA exclusion in a diabetic stroke population

	P Value	Odds ratio	95% C.I. Lower	For OR Upper
Age	0.079	1.020	0.998	1.042
BMI	0.551	1.010	0.977	1.044
NIH stroke scale	0.455	0.965	0.878	1.060
Presentation of weakness	0.001*	0.233	0.096	0.567
Altered level of consciousness	0.563	1.202	0.645	2.241
Aphasia/language disturbance	0.020*	0.521	0.301	0.903
Risk of mortality GWTG	0.991	1.001	0.907	1.104
Female gender	0.001*	2.323	1.426	3.785
Ethnicity	0.250	1.338	0.815	2.198
Atrial fibrillation	0.005*	2.587	1.338	5.002
Coronary artery disease	0.864	0.956	0.571	1.600
Carotid artery stenosis	0.031*	3.358	1.117	10.095
Dyslipidemia	0.739	1.093	0.647	1.847
Congestive heart failure	0.818	0.925	0.476	1.798
Hypertension	0.678	0.818	0.317	2.112
Previous stroke	0.007*	1.984	1.205	3.265
Previous TIA	0.390	0.741	0.375	1.467
Peripheral vascular disease	0.701	1.177	0.513	2.698
History of smoking	0.417	0.778	0.425	1.425
Antiplatelet medication	0.408	0.794	0.460	1.370
Cholesterol reducer	0.084	0.508	0.236	1.095
Antihypertensive medication	0.879	0.958	0.555	1.656
Antidiabetic medication	0.274	0.726	0.409	1.288

Table 3. Patient-level factors associated with rtPA exclusion in a diabetic stroke male population

	P Value	Odds ratio	95% C.I. Lower	For OR Upper
Age	0.726	1.006	0.973	1.040
BMI	0.533	0.982	0.927	1.040
NIH stroke scale	0.212	0.904	0.771	1.059
Presentation of weakness	0.009*	0.186	0.052	0.662
Altered level of consciousness	0.636	1.273	0.469	3.451
Aphasia/language disturbance	0.456	0.736	0.329	1.646
Risk of mortality GWTG	0.838	1.019	0.854	1.215
Ethnicity	0.569	1.244	0.587	2.638
Atrial fibrillation	0.011*	3.697	1.342	10.187
Coronary artery disease	0.484	0.773	0.377	1.587
Carotid artery stenosis	0.023*	5.001	1.243	20.117
Dyslipidemia	0.139	1.780	0.829	3.821
Congestive heart failure	0.614	0.771	0.281	2.118
Hypertension	0.510	0.610	0.140	2.653
Previous stroke	0.358	1.418	0.673	2.985
Previous TIA	0.511	0.731	0.287	1.862
Peripheral vascular disease	0.208	2.509	0.599	10.510
History of smoking	0.582	0.792	0.345	1.817
Antiplatelet medication	0.067	0.464	0.204	1.055
Cholesterol reducer	0.818	1.142	0.368	3.537
Antihypertensive medication	0.037*	0.409	0.177	0.946
Antidiabetic medication	0.643	1.223	0.522	2.867

male diabetic population (OR = 0.409, $P = 0.037$). A similar adjustment on the female population (Table 4) reveals that four variables were also associated with rtPA exclusion: Aphasia/language disturbance (OR = 0.372, $P = 0.039$), history of previous stroke (OR = 3.313, $P = 0.005$), the use of antihypertension medication (OR = 0.163, $P = 0.013$), and the use of antidiabetic medication (OR = 0.324, $P = 0.031$).

Discussion

One of the most common biological explanations for a gender difference in stroke is that women have greater chances of inheriting ischemic stroke than men, especially if they have a maternal history of stroke [19]. The fact that women are more likely to be significantly older than men when stroke occurs, more likely to suffer cardioembolic stroke, and have atrial fibrillation as a risk factor for stroke [19–21] indicates that gender difference is not only linked to genetic factors but also clinical and demographic factors are involved [8,22,23]. In our study, diabetic women with stroke have an older age of onset and higher NIHSS scores than diabetic men [16]. This finding indicates that an understanding of the gender differences in the treatment outcome of a diabetic stroke population could help improve stroke treatment outcome in diabetic stroke populations, irrespective of gender. Our data reveals that in a diabetic stroke population, women are more likely than men to be excluded from rtPA treatment. This result is supported by previous findings [1,6,24,25] indicating that there is a significant gender difference in an acute ischemic stroke popu-

Table 4. Patient-level factors associated with rtPA exclusion in a diabetic stroke female population

	P value	Odds ratio	95% C.I. Lower	For OR Upper
Age	0.264	1.020	0.985	1.055
BMI	0.380	1.024	0.972	1.078
NIH stroke scale	0.330	0.931	0.806	1.075
Presentation of weakness	0.312	0.468	0.108	2.040
Altered level of consciousness	0.250	1.762	0.671	4.625
Aphasia/language disturbance	0.039*	0.372	0.146	0.950
Risk of mortality GWTG	0.682	1.029	0.897	1.181
Ethnicity	0.538	1.276	0.587	2.771
Atrial fibrillation	0.345	1.594	0.606	4.196
Coronary artery disease	0.298	1.618	0.653	4.007
Carotid artery stenosis	0.225	4.070	0.423	39.203
Dyslipidemia	0.324	0.639	0.262	1.557
Congestive heart failure	0.737	1.199	0.417	3.445
Hypertension	0.598	1.496	0.336	6.667
Previous stroke	0.005*	3.313	1.444	7.601
Previous TIA	0.234	0.482	0.145	1.603
Peripheral vascular disease	0.378	0.601	0.193	1.866
History of smoking	0.606	0.760	0.267	2.162
Antiplatelet medication	0.771	1.137	0.478	2.705
Cholesterol reducer	0.013*	0.163	0.039	0.680
Antihypertensive medication	0.195	1.746	0.751	4.054
Antidiabetic medication	0.031*	0.324	0.116	0.903

lation, and that women are less likely than men to receive rtPA treatment than men.

In unadjusted analyses, we found that some variables were significantly or not significantly different in males and females that were excluded from rtPA treatment in diabetic stroke population. For example, more men than women with previous history of stroke, carotid artery disease, and antiplatelet medication received rtPA. More women than men were excluded from rtPA due to risk of mortality and body mass index. Both men and women in the diabetic stroke population were excluded because of the initial NIH scores on evaluation and age. Men that were included for rtPA treatment were an average of 65.22 years old, while women were 69.54 years old. In the excluded group, men were an average of 67.30 years old, and women were an average of 71.69 years old. This data shows that diabetic women with ischemic stroke were significantly older than diabetic men with stroke, regardless of their treatment group. Old age in women probably comes with a range of effects, including mitigating circumstances related to comorbid conditions and patient preferences. Our data also found that diabetic stroke women had higher NIH Stroke Scale scores when compared to diabetic stroke men, with rtPA included patients having average scores of 10.63 compared to 8.50, respectively, and rtPA excluded patients having average scores of 8.90 and 6.43, respectively. The initial NIHSS score represents an evaluation tool for assessing the efficacy of rtPA treatment. The higher NIH Stroke Scale scores in the women excluded from rtPA suggests that the severity of stroke combined with risk of mortality, body mass index and altered level of consciousness as well as differences in risk factor profiles contribute to the exclusive treatment effect observed in the diabetic female stroke population.

More men with coronary artery disease and a history of previous stroke were treated with rtPA compared to women with those same risk factors. Similar findings have been reported by other studies [6,26]. There were no gender differences in risk factor distribution in the group that was excluded from rtPA treatment. More diabetic men receiving anti-platelet medication were treated with rtPA compared to diabetic women receiving this medication in our data set, but this gender difference was not present in the population excluded from rtPA treatment. These findings indicate that more men with a history of prior stroke were likely to receive rtPA, because patients with this history would be more likely to be treated with antiplatelet agents in order to decrease their risk of recurrence. A gender difference was observed in the rtPA excluded population with respect to altered level of consciousness, mortality risk, and BMI; these differences were not observed in the rtPA-treated population. Moreover, women with altered level of consciousness were more likely to be excluded from rtPA treatment when compared to men, and women in the rtPA excluded group have a higher body mass index on average and higher mortality risk when compared to men in the rtPA excluded group. The altered level of consciousness could be related to higher NIHSS values and higher stroke severity women compared to men when they are excluded from rtPA treatment [16]. In the rtPA excluded group, men had an average BMI of 29.44, whereas women had an average BMI of 31.67. This result is supported by previous studies [3,16,27,28] that women with stroke, as a general population but also with diabetes as a comorbid factor, had higher rates of obesity and metabolic syndrome when compared to men. After adjustment for confounding variables, our results reveal that diabetic stroke patients were more

likely to be excluded from rtPA treatment if they were female, have atrial fibrillation, display weakness of motor functions, and have language deficits, have a history of carotid artery stenosis, or have a history of previous stroke. After adjustment, most of the associations with age were attenuated and became nonsignificant. However, the effect of female gender was significant such that female diabetic stroke patients were more likely to be excluded from rtPA. This finding indicates that women had higher odds of being excluded from rtPA, even after adjustment for contraindications. The result of this study reveals that the diabetic stroke population faces higher rates of exclusion from rtPA treatment when certain comorbid conditions, such as carotid artery stenosis and history of stroke, are present. Similar findings have been demonstrated in the general stroke population [29].

In the adjusted male diabetic stroke population, four variables were found to be significantly associated with exclusion of males from rtPA treatment: presentation with weakness, history of atrial fibrillation, carotid artery stenosis, and treatment with cholesterol lowering medications. Adjustment in the male diabetic stroke population did not eliminate the effect of atrial fibrillation and carotid artery stenosis such that both factors were significantly associated with the exclusion of male diabetic stroke patients from rtPA treatment. Diabetic stroke women have higher rates of atrial fibrillation, compared to diabetic men [15]. The finding that diabetic male stroke patients with atrial fibrillation have a higher odd of being excluded from rtPA indicates the complexity of the comorbidity profile underlying the increased risk of stroke in diabetic men. Carotid artery stenosis is a risk factor demonstrated to be more prevalent in the male stroke population compared to females [6,16], and our data demonstrates that this risk factor increases rtPA exclusion in men. Treatment with cholesterol lowering medications was also found to be associated with exclusion of diabetic male stroke patients from rtPA treatment. It is possible that men had higher rates of hyperlipidemia [1,5,6].

Four variables were significantly associated with female exclusion from treatment following adjustment: aphasia or language disturbance, history of previous stroke, use of antihypertensive medications, and use of anti-diabetic medications. It is interesting that the history of previous stroke significantly increased exclusion in females but not in the male population, whereas the effect of atrial fibrillation, which was significant in the male population, was eliminated in the adjusted female diabetic stroke population. The finding that aphasia or language disturbance increases rtPA exclusion in the female diabetic population suggests that these women may be demonstrating increased severity in strokes. This idea is supported by previous studies, which found that women have more severe strokes on admission [30–33] whereas others studies report no gender differences in stroke severity [34,35]. It is not clear whether stroke severity would confound our data in this study. The finding that the use of antihypertensive and antidiabetic medications led to higher rates of exclusion for rtPA treatment in diabetic females is an interesting new finding for the diabetic stroke population. It could be that women may have had uncontrolled hypertension [36], and were therefore excluded from rtPA.

There are many limitations that require a cautious interpretation of the findings of this study. This is a retrospective study, so there is a tendency for a measurement bias in NIHSS. Moreover, the specific treatments for the diabetic subtypes in the stroke population and how they were treated after the onset of stroke were not known. This is a single institution study; therefore, selection bias could have affected the selection of patients. However, the strengths of this study lie in the opportunity investigate gender difference in a diabetic stroke population using data from a large stroke center in the state designed to monitor treatment of rtPA. Our data illustrated interesting new risk factors that were associated with men and women in their respective treatment groups, as well as clinical variables that were found to be associated with higher rates of rtPA exclusion in the overall diabetic population as well as for male and female populations, respectively.

Conclusion

In conclusion, in a diabetic stroke population, women who were excluded from rtPA are more likely to have aphasia or language disturbance, history of previous stroke, use of antihypertensive medications, and use of anti-diabetic medications. Men excluded for rtPA were more likely to have weakness, history of atrial fibrillation, carotid artery stenosis, and treatment with cholesterol lowering medications. The observed gender differences in the exclusive criteria for the unadjusted analyses were directly associated with the increasing age, higher NIH stroke scale scores, and risk of mortality in women. Improving the low rates of rtPA treatment in diabetic stroke patients, irrespective of gender, can improve treatment outcomes in this patient population.

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