Epidemiology and Outcomes of Ischemic Stroke and Transient Ischemic Attack in the Adult and Geriatric Population

Allison Navis, MD, Rocio Garcia-Santibanez, MD, and Maryna Skliut, MD

Background: Rate of ischemic strokes and transient ischemic attacks (TIAs) increases with age. There is lack of evidence on how age affects treatment strategies and outcomes. Our aim is to compare epidemiology of ischemic strokes and TIAs in adult and geriatric populations including risk factors, treatment delivered, and outcomes. *Design:* We designed a retrospective cross-sectional review of patients admitted to neurology with diagnosis of stroke or TIA from 2010 to 2015. Obtained variables were: age, sex, risk factors, acute therapy, National Institutes of Health Stroke Scale on admission and discharge, and disposition. Means, confidence intervals, or percentages were calculated as appropriate. *Results:* Around 1,457 patients were divided into two groups: younger than 80 (n = 968) and 80 and older (n = 487). Rates of stroke and TIA were similar across younger and older groups (11% versus 12% TIA and 89% versus 88% stroke, respectively). Younger patients had lower admission National Institutes of Health Stroke Scale (mean 4.64 versus 7.84 in older group) and greater improvement on discharge (mean change −1.51 versus −1.29 accordingly). Older patients received tissue-type plasminogen activator (tPA) more often than younger patients, but no difference in rates of thrombectomy between groups. Older patients were more likely to have hypertension, atrial fibrillation, coronary artery disease, and less likely to be a smoker. On discharge, younger patients with stroke were discharged home or to acute rehab more frequently, regardless of tPA administration. *Conclusions:* Older patients had more comorbidities, received tPA more often, and had worse outcomes regardless of use of intravenous tPA or thrombectomy, and were more frequently institutionalized after discharge.

Key Words: Ischemic stroke—transient ischemic attack—epidemiology—elderly—older than 80—outcomes

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Introduction

In 1996, the Food and Drug Administration approved recombinant tissue-type plasminogen activator (tPA) for the acute treatment of ischemic stroke, with further expansion of treatment guidelines over the years.[1-4] There is now little question that tPA is an efficacious treatment for stroke and leads to improved outcomes in the studied populations; however, efficacy and outcomes within certain groups is still a source of much debate. One such group is patients aged 80 years and older (≥80), who are often excluded from current, as well as landmark trials. As a result, there is less quality evidence regarding stroke in this demographic. Given this lack of quality evidence, the Food and Drug Administration labeled advanced age (as defined by those ≥80 years old) as a potential risk factor for the administration of tPA especially within the 3- to 4.5-hour window[5,6]—a label which can perpetuate the notion that age increases risks and worsens outcomes in those affected by ischemic stroke.

While treatment of acute stroke should be based on medical considerations and guidelines, it is not uncommon for physicians to determine stroke treatment of the elderly with a degree of bias or personal beliefs on patient outcomes. This issue is further compounded by the lack of quality evidence. The elderly are more likely to present with poor functional status or dementia,

From the Mount Sinai Beth Israel, New York, New York.

Received May 17, 2018; revision received August 17, 2018; accepted September 3, 2018.

This work was supported in part through the resources and staff expertise provided by the Department of Vascular Neurology at Mount Sinai Beth Israel.

Address correspondence to Allison Navis, MD, Icahn School of Medicine at Mount Sinai, Department of Neurology, 1 Gustav L Levy Pl, New York, NY 1029. E-mail: Allison.Navis@mountsinai.org

1052-3057/$ - see front matter

Published by Elsevier Inc. on behalf of National Stroke Association.

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.09.013

conditions that may affect whether or not they are treated despite unclear evidence if those conditions affect outcomes.[7] Even a patient's age, without other risk factors, can give physicians concern despite no clear contraindication.[8] This may lead physicians to be less aggressive when treating elderly patients. Previous studies have looked at rates of complications in the elderly such as risk of intracerebral hemorrhage, but minimal research has gone into functional status after discharge or disposition, which is arguably more important measures than simply treatment complications. Given the ageing of the general population and the increased likelihood that more patients aged 80 years and older will present with stroke, it is clear that more research needs to be done in this area.

In this study, we sought to determine the differences in baseline characteristics and risk factors between younger and elderly patients, as well as treatment delivered, overall improvement and outcomes for the elderly. We hope that by doing so, we can start to bridge the gap in physician bias toward treating elderly patients and ischemic stroke.

Methods

Subjects: We selected patients from Mount Sinai Beth Israel's stroke database. This database contains information on all patients admitted to our institution with the diagnosis of TIA, ischemic stroke, and intracerebral hemorrhage (ICH). The stroke log contains deidentified information, with each patient assigned a unique identification number during the data upload. The database fulfills the requirements of the New York State Department of Health and the Get with the Guidelines Stroke[9] program. All data was compliant with the Health Insurance Portability and Accountability Act (HIPAA) and the policies of the Institutional Board Review of Mount Sinai Beth Israel.

Inclusion/Exclusion criteria: We conducted a retrospective chart review of all patients admitted to our hospital between the years of 2010 and 2015 with a diagnosis of TIA or ischemic stroke. The only exclusion criterion was patients admitted with ICH. Patients were divided into two groups according to their age: patient who were aged 80 and older (the "older" group), and those who were younger than 80 (the "younger" group).

Clinical data: Variables obtained from the database included sex, age, risk factors for stroke (i.e. hypertension, hyperlipidemia, diabetes, atrial fibrillation, coronary artery disease, and smoking), presenting National Institutes of Health Stroke Scale (NIHSS), whether or not acute therapy was given (e.g., intravenous/intra-arterial tPA or mechanical thrombectomy), NIHSS on discharge, degree of disability at discharge as defined by a modified Rankin score (mRS), and to where the patient was sent after discharge from the hospital (e.g., disposition). The database did not include data on ICH rates in patients with ischemic stroke or TIA.

Statistical analysis: Statistical analysis was performed using statistical software (STATA, version 13.1). Percentages were calculated for categorical variables. Means and confidence intervals were calculated for continuous variables. Two-sample Wilcoxon rank-sum (Mann-Whitney) test was used to compare the NIHSS score change between groups. A P value of $<.05$ was considered significant.

Results

Demographics and Comorbidities

There were 1457 patients admitted to our institution for TIA or ischemic stroke between the years of 2010 and 2015; 968 were aged less than 80 years old and 487 patients were 80 years and older. There were a greater number of males in the younger group with 58% of younger patients being male and only 42% being female. In the older group, this proportion reversed and there were 68% females and only 32% males.

Data on comorbidities causing stroke such as hypertension, hyperlipidemia, diabetes, atrial fibrillation, coronary artery disease, smoking, and stroke were analyzed between both groups and results shown in Figure 1. The most common risk factor was hypertension, followed by hyperlipidemia. All comorbidities except for diabetes and smoking were higher in the older patients, and all comorbidities reached statistical significance except for hyperlipidemia.

Stroke Presentation and Treatment

There were a similar percentage of TIAs and strokes across younger and older groups (11% versus 12% TIA and 89% versus 88% stroke, respectively). The NIHSS score was higher for older patients at presentation (average 4.64 <80 and 7.84 in ≥80). Younger patients received IV tPA less than older patients (10% versus 16%, $P < .05$). However, rates of mechanical thrombectomy did not differ significantly between groups (5% in younger and 4% in older).

At discharge, younger patients had a greater improvement in their NIHSS, with an average change of −1.44 points, leading them to an average discharge score of 2.78. This differed significantly with their older counterparts, who only had an average change in score of −1.07 points and an average discharge score of 6 ($P < .05$) (Table 1). When both groups were compared to whether or not tPA was received, the younger group also showed greater improvement in NIHSS regardless of tPA administration. For the patients who did receive tPA, the results were significant favoring younger patients ($P < .05$) but for those patients who did not receive tPA there was no significance between groups (Fig 2).

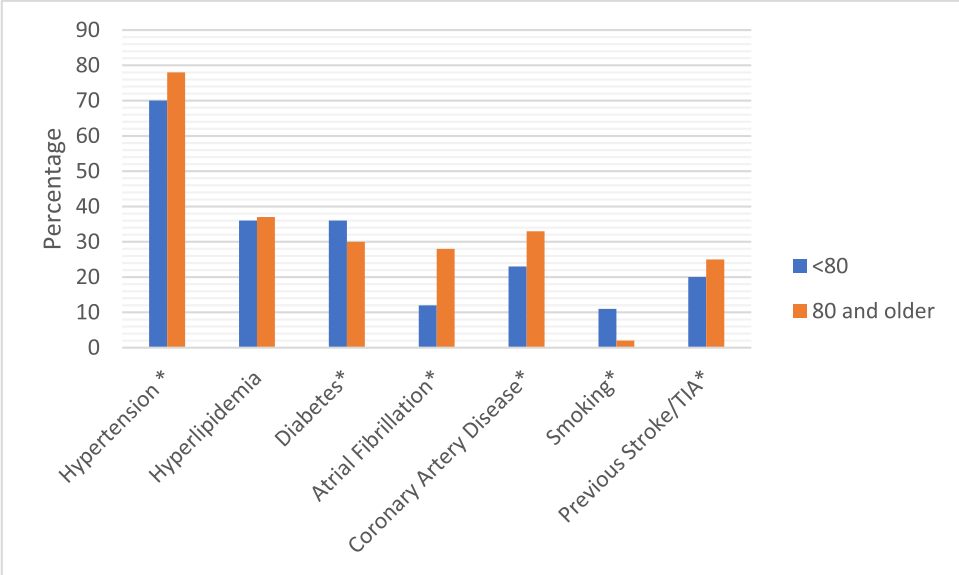

Figure 1. *Comorbidities (*P < .05).*

Table 1. *Stroke outcomes*

	<80	80 and older	
TIA	108 (11%)	57 (11%)	*P* = .807
Stroke	860 (89%)	430 (89%)	*P* = .807
IV tPA administration	95 (10%)	67 (16%)	*P* = .024
Thrombectomy	48 (5%)	19 (4%)	*P* = .458
NIHSS admission	4.64	7.84	
NIHSS discharge	2.78	6	

Abbreviations: IV, intravenous; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; tPA, tissue-type plasminogen activator.

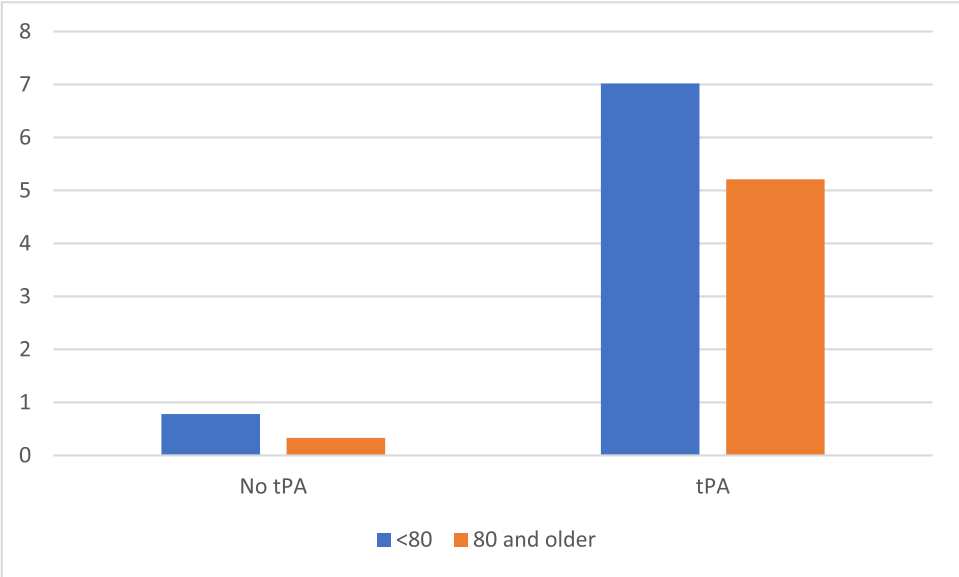

Figure 2. *Change in NIHSS depending on treatment in younger and older patients. Abbreviation: NIHSS, National Institutes of Health Stroke Scale.*

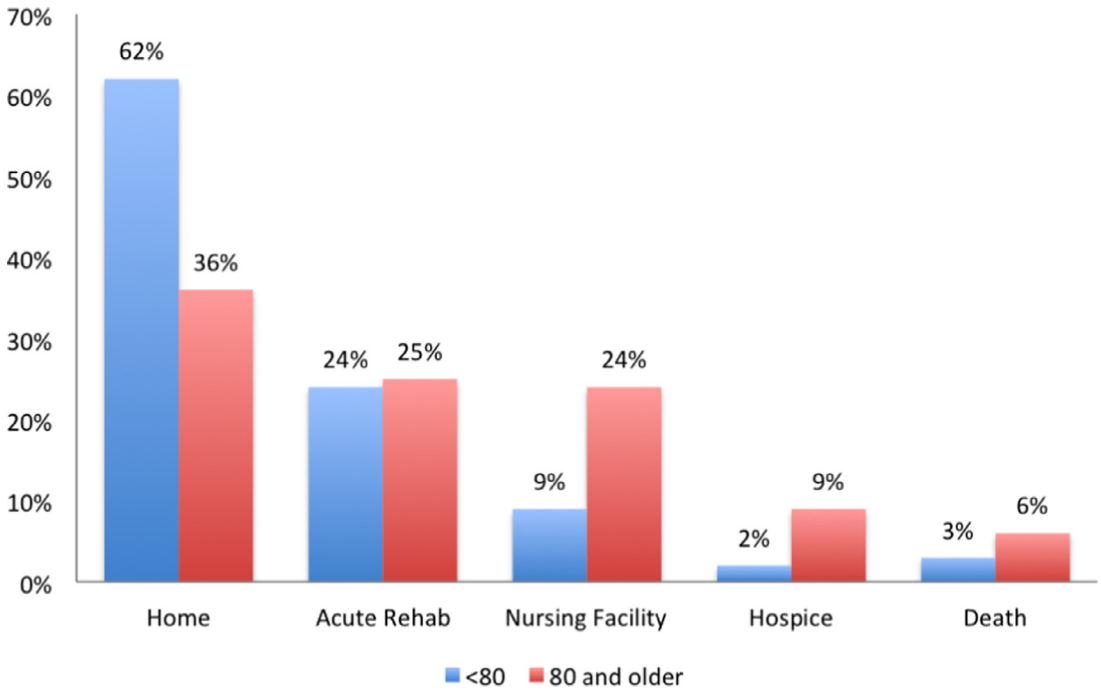

Figure 3. *Disposition on discharge between age groups for patients with ischemic stroke who did not receive intravenous tPA. Abbreviation: tPA, tissue-type plasminogen activator.*

Figures 3 and 4 show the disposition of patients with ischemic stroke, broken down between patients who received tPA and those who did not. Younger patients were statistically more likely to go either home or to an acute rehab after their hospital stay and older patients were more likely to go to a nursing facility, hospice or die in the hospital ($P < .0001$) regardless of whether they received tPA or not.

Data on disability at discharge as defined by the mRS was only available for 965 patients, of these 838 had an ischemic stroke (65% younger patients and 35% older patients). In the ischemic stroke cohort, at discharge, younger patients were more likely than older patients to have none to slight disability (scores 0-2) [63% versus 30%] and older patients were more likely than younger patients to have severe disability to death (scores 3-6) [70% versus 37%]; $P < .0001$. In the TIA stroke cohort (127 patients) there was no difference in the discharge mRS between the younger and older group; 94% of the younger group and 86% of the older group had none to slight disability at discharge ($P = .11$). Of the patients with mRS data, 106 received tPA (65% younger patients and 35%

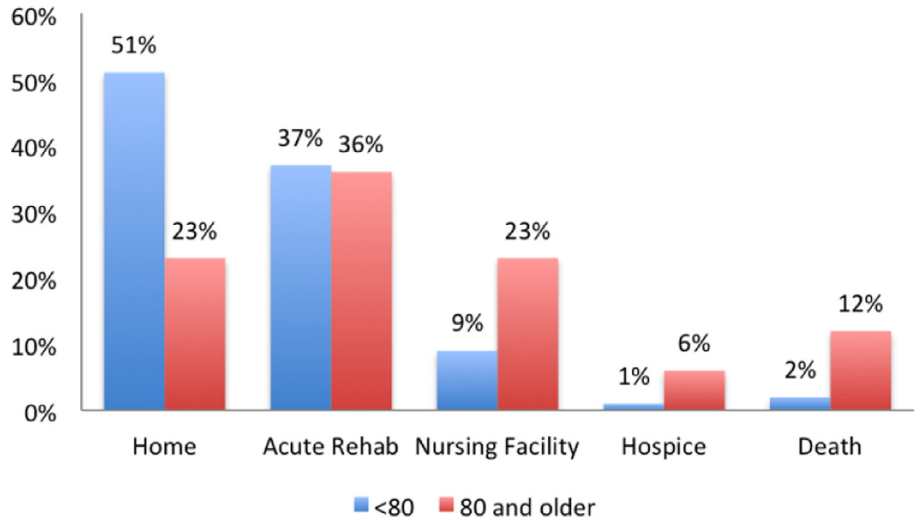

Figure 4. *Disposition on discharge between age groups for patients with ischemic stroke who did receive intravenous tPA. Abbreviation: tPA, tissue-type plasminogen activator.*

older patients), at discharge, younger patients were more likely than older patients to have none to slight disability (scores 0-2) [62% versus 22%] and older patients were more likely than younger patients to have severe disability to death (scores 3-6) [78% versus 38%]; $P < .0001$

Discussion

Approximately 1500 patients were admitted to our institute for transient ischemic attack or stroke during the years of 2010 and 2015. The demographics for that group in terms of reversal of men and women between older and younger groups were expected given the longer lifespan of women compared to their male counterparts. The higher average NIHSS for older patients may be in part explained by higher rates of atrial fibrillation and coronary artery disease, which predisposes patients to thromboembolic events and large vessel occlusions with worse initial presentations—a similar finding to other studies looking at stroke and elderly patients.[10,11] Our study did not look at door to needle (DTN) time for tPA administration but there is evidence that older patients with higher presenting NIHSS have longer DTN time, particularly with NIHSS > 10.[12] This occurred without clear factors contraindicating treatment, raising concern that delayed decision making may have been due to reasons other than the defined criteria for tPA administration. In addition, older patients had less of an improvement in their NIHSS than their younger counterparts, which may be in part explained by larger strokes being more resistant to treatment. While younger patients on average left the hospital with an NIHSS of 2 and minimal residual deficits, patients ≥80 were more likely to have more deficits and thus increased need for services and care after discharge.

Older patients also improved less with treatment compared to their younger counterparts. However, they still had an average change in NIHSS of approximately 5 points when given tPA. While that was significantly less than the 7 points in younger patients, when taken in a clinical context it is still a sizeable change in exam and could make the difference between needing a nursing home versus acute rehab at discharge. In addition, there was not a significant difference in NIHSS change throughout hospital stay in both younger and older patients who did not receive tPA. Therefore, it is reasonable to assume that the higher NIHSS at discharge of the older patients is primarily related to worse presenting NIHSS and not due to decompensation in the hospital.

Older patients received tPA at higher rates than their younger counterparts at our institution. This may be in part due to the higher presenting NIHSS raising more concern and prompting treatment. It also contrasts with the assumption that younger patients receive more aggressive treatment for their neurological deficits. While rates of tPA differed significantly between groups, rates of thrombectomy did not at 4%-5% between both groups. Of note, the time frame of this study does not reflect the current guidelines on indication for thrombectomy.[13]

Analysis of stroke risk factors in the younger versus elderly is important in determining risk modification. Not surprisingly, older patients had a much higher rate of atrial fibrillation; however, they also had higher rates of hypertension, coronary artery disease and previous stroke. All these conditions can be thought of as cumulative throughout the life, which may explain their higher rates in older patients. Atrial fibrillation is especially important in elderly patients as it drastically increases the risk of embolic phenomena if not treated with anticoagulation, often times leading to devastating strokes. Our study showed that slightly less than one third of patients presented with known atrial fibrillation but other studies have shown even higher rates up to 43%.[14,15] Conversely, diabetes and smoking were the only risk factors that were higher in younger patients. This is likely due to the fact that they can arise younger in life, and if severe enough will cause other life-threatening complications much earlier than stroke. These risk factors should remind clinicians of the importance of tailoring preventative treatment appropriately as too often older patients with known atrial fibrillation are not placed on anticoagulation out of concern for risk of bleeding.[16,17] However, atrial fibrillation is an important risk factor and placing patients on anticoagulation can help prevent large strokes that cause severe disability and long term deficits.

Finally, we analyzed disposition for patients in both groups in order to see if elderly patients were more likely to be discharged to long-term care regardless of intervention. In both the treated and untreated groups, the disposition on discharge remained about the same between younger and older patients. Younger patients were more likely to either go home or to a short-stay acute rehab, likely due to the minimal deficits that were present on discharge. Whereas the patients ≥80 were more likely to either go to a nursing facility, hospice or die in the hospital. In the treatment category, patients ≥80 were 4 times more likely to die than their younger counterparts. Disability at discharge was worse (mRS of 3 or above) in the older group with ischemic stroke regardless of whether tPA was given or not. We did not have data readily available regarding reason for mortality for this study so we cannot comment on the causes of death. However, recent research shows that tPA does not increase risk of intracranial hemorrhage in the elderly,[9,18-22] but there may be an associated increase in mortality for the elderly likely related to other iatrogenic factors from being hospitalized (i.e., infection, deep vein thrombosis), which are more prevalent in the elderly while in the hospital.[9,12,18,19]

Our study has several limitations, among which is its retrospective nature. The hospital stroke database contains a plethora of information, but data on premorbid functioning, stroke etiology or stroke volume, and causes for death were not available. More information on

premorbid functioning and stroke size would allow us to determine if poor response to tPA or higher NIHSS on discharge were related to a poor baseline or larger stroke and not simply age. It is likely that poor functional status regardless of age is a greater predictor of outcome than age itself. Future research should focus on stratifying risk factors and determining which play the greatest role in certain outcomes.

Conclusion

Tissue-type plasminogen activator is the only approved treatment for ischemic stroke, and despite guidelines warning of potential risks to patients over 80 years of age, this should not prevent them from receiving appropriate and timely treatment. While it may be important to discuss certain risks with patients and their families, namely long-term neurological deficits and the need for continued care, the conversation should not center around the risks of age and tPA itself. More research is needed in order to appropriately stratify older patients' risks based on premorbid functional status and size of stroke. However, age alone should not deter physicians from providing them with appropriate care.

Acknowledgments: The authors would like to thank David Lucido for his assistance in data analysis. The authors report no conflicts of interest.

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