

INTRAVENOUS THROMBOLYSIS FOR YOUNG ISCHEMIC STROKE PATIENTS

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**Abstract**

Background: Intravenous thrombolysis (IVT) restores cerebral blood flow in patients with ischaemic stroke, potentially reversing neurological deficits. While IVT is well established in older patients, its safety and effectiveness in younger patients remain unexplored. This study aimed to evaluate the safety, functional outcomes, and complications of IVT in young ischaemic stroke patients (18–45 years) compared with older patients (>45 years). **Materials and Methods:** This retrospective observational study included 152 patients with ischaemic stroke treated with IVT at Madurai Medical College (2021–2024). Patients were categorised as young (18–45 years, n=38) and older (>45 years, n=114). Stroke severity was assessed using the NIHSS at admission and discharge, and functional outcomes were measured using the modified Rankin Scale (mRS) at three months. The incidence of symptomatic intracerebral haemorrhage (sICH) and mortality were compared between the groups. Demographic and clinical characteristics, including sex distribution and pre-existing comorbidities, were also analysed. **Result:** Among the 152 patients, 75% (n=114) were older and 73% (n=111) were men. The mean NIHSS at admission was 10.5 ± 3.2 in young vs. 12.8 ± 4.1 in older patients ($p=0.03$), improving at discharge to 3.4 ± 1.8 vs. 5.2 ± 2.6 ($p=0.02$). Good functional outcomes (mRS 0–2) occurred in 78.9% of young patients vs. 70.2% of older patients ($p=0.21$). Mortality was 5.3% versus 7%, and sICH was 2.6% versus 3.5% in young versus older patients, respectively. **Conclusion:** IVT was effective in younger patients, with better functional recovery and fewer complications. Older males exhibited higher sICH and mortality rates, necessitating closer post-thrombolysis monitoring.

INTRODUCTION

Stroke is the second or third most common cause of death worldwide. In 2005, it resulted in approximately 5.7 million deaths, with world mortality projections of 6.5 million in 2015 and 7.8 million in 2030. Important advances in this area include a greater focus on identifying cardiac and coagulation abnormalities, screening for new risk factors, enhancing advanced non-invasive brain imaging techniques, and using intravenous thrombolysis in acute ischaemic stroke cases. Stroke in young adults has a serious impact on their quality of life, work, and finances.^[1-3] Ischemic stroke in young people is a specific clinical entity with specific risk factors, prognosis, and challenges different from strokes in older adults.^[4]

Intravenous thrombolysis (IVT) is a therapeutic approach used to re-establish cerebral perfusion in patients with acute ischaemic stroke, potentially resulting in improved or reversed neurological deficits. The best treatment for preserving brain

tissue is recanalizing the blocked vessel through thrombolytic therapy.^[5] The National Institute of Neurological and Stroke (NINDS) trial established the safety and effectiveness of intravenous tissue plasminogen activator (tPA) in treating acute ischaemic stroke within three hours of the onset of symptoms. This is the first report of intravenous tPA improving survival and significantly decreasing disability. Prompt treatment gives the best results.^[6] The European Cooperative Acute Stroke Study III (ECASS 3) in 2008 raised the time limit for treatment to 4.5 hours, demonstrating that intravenous tPA significantly improved the proportion of successful outcomes at 90 days among a specific subgroup of patients with acute ischaemic stroke.^[7] Safe Implementation of Thrombolysis in Stroke Monitoring Study (SITS-MOST) data revealed that patients (aged less than 45 years) demonstrated improved recovery with a lower rate of complications.^[8]

Aim

This study aimed to examine the safety and effectiveness of IVT in treating ischaemic stroke in young patients (18-45 years) compared with its impact on older patients above 45 years.

MATERIALS AND METHODS

This retrospective observational study was conducted on 152 patients diagnosed with ischaemic stroke at Madurai Medical College over four years, from January 2021 to December 2024. The study was approved by the Institutional Ethics Committee prior to its conduct, and informed consent was obtained from all patients.

Inclusion Criteria

Patients diagnosed with ischaemic stroke and treated with intravenous alteplase (IV tPA) according to standard thrombolysis protocols were included.

Exclusion Criteria

- Age <18 yrs
- Head injury/ stroke in 3 months
- Malignancy Gastrointestinal/intracranial neoplasm

Methods

The patients were categorised into two groups: young group (18-45 years) and old (> 45 years). The outcomes and haemorrhage rates in young and older adults with stroke were analysed. The National Institutes of Health Stroke Scale (NIHSS) was used to assess stroke severity at admission and discharge.

The modified Rankin Scale (mRS) score was assessed at the 3-month follow-up.

Statistical analysis

Statistical analyses were performed using IBM SPSS version 25.0. Categorical variables (e.g. sex, symptomatic intracerebral haemorrhage, mortality, and functional outcomes) were compared using the chi-square test or Fisher's exact test, while continuous variables were analysed using the independent t-test or Mann-Whitney U test, as appropriate. Binary logistic regression was conducted to assess predictors of good functional outcomes (mRS 0-2) and mortality, adjusting for age, sex, NIHSS score, and symptomatic intracerebral haemorrhage (sICH). Statistical significance was set at $p < 0.05$.

RESULTS

The majority of patients were older than 45 years, accounting for 114 (75%) patients, while 38 (25%) were younger than 45 years. Males constituted the majority of the study population, with 111 (73%), whereas females comprised 41 (27%). Symptomatic intracerebral haemorrhage was the least frequent complication, occurring in 5 (3%) patients, whereas 147 (97%) did not experience this condition. Mortality was recorded in 10 (7%) patients, while 142 (93%) survived. A good functional outcome (mRS 0-2) was observed in 110 (80%) patients, while 27 (20%) did not achieve a favourable recovery [Table 1].

Table 1: Patient demographics and clinical outcomes.

		Frequency (%)
Age in years	< 45	38 (25%)
	> 45	114 (75%)
Sex	Male	111 (73%)
	Female	41 (27%)
Symptomatic intracerebral haemorrhage	Yes	5 (3%)
	No	147 (97%)
Mortality	Yes	10 (7%)
	No	142 (93%)
Good functional outcome (mRS 0-2)	Yes	110 (80%)
	No	27 (20%)

Among the thrombolysed patients (n=152), the majority were from the older age group (> 45 years), with 83 (74.8%) men and 31 (75.6%) women. In the younger age group (18-45 years), there were 28 (25.2%) males and 10 (24.4%) females. Symptomatic intracerebral haemorrhage was observed in five patients, with three (75%) males and one (100%) female in the older group, while one (25%) male in the younger group was affected.

A good functional outcome (mRS 0-2) was achieved by 62 (71.3%) older men and 18 (78.3%) older women, whereas in the younger group, 25 (28.7%) men and 5 (21.7%) women had a favourable recovery. Mortality was recorded in 10 patients, with 7 (77.8%) older men and 1 (100%) older woman, while 2 (22.2%) younger men had fatal outcomes. No mortality was observed in younger females [Table 2].

Table 2: Age and sex-wise distribution of clinical outcomes

	Sex	Young group (18-45 years)	Old age group (> 45 years)
Patients thrombolysed (n=152)	Male	28 (25.2%)	83 (74.8%)
	Female	10 (24.4%)	31 (75.6%)
Symptomatic intracerebral haemorrhage (n=5)	Male	1 (25.0%)	3 (75%)
	Female	0 (0.0%)	1 (100%)
Good functional outcome (mRS 0-2) (n=110)	Male	25 (28.7%)	62 (71.3%)
	Female	5 (21.7%)	18 (78.3%)

Mortality (n=10)	Male	2 (22.2%)	7 (77.8%)
	Female	0 (0.0%)	1 (100%)

DISCUSSION

The thrombolysis outcomes indicated that the prognosis of patients largely depends on their age and sex. Thrombolysis in acute ischaemic stroke is a vital procedure that is highly reliant on patient demographics, namely age and sex. Research has found that the prognosis following thrombolysis and the efficacy of thrombolysis itself are finely interwoven with these dimensions, reflecting recognised trends in prevalence and risk of stroke. Knowledge of these demographic subtleties is critical for maximising treatment plans and enhancing patient outcomes.

Disparities observed in thrombolysis outcomes among and between sexes and age groups might be a result of a combination of clinical, lifestyle, and biological factors. Older patients, usually with increased comorbidities such as hypertension, diabetes, and cardiovascular disease, can have a decreased response to thrombolysis. Similarly, sex-related variability in hormonal patterns, vascular morphology, and baseline health status may contribute to differences in the effectiveness of treatment and overall prognosis.^[5,8] An in-depth understanding of such factors is imperative for personalizing thrombolytic treatment in accordance with the patient's unique characteristics and averting potential outcome disparities.^[9,10]

A comparative study by Mishra et al. revealed that thrombolysis is beneficial in elderly patients, which is consistent with our results that older patients are also benefited by IVT despite having a greater risk of complications.^[9] Likewise, Pego et al. compared 512 patients and revealed that IVT is effective in patients aged > 80 years, even with a greater risk of complications.^[10] Our research is in line with these results, as we found that even though older patients had greater sICH and mortality rates, IVT was still effective in enhancing functional outcomes.

The frequency of sICH in the present study was 3%, which is within the reported range of 2–6% in large thrombolysis trials, including the ECASS and NINDS trials. We also noted that sICH was more common in older men, a finding corroborated by Nosedá et al., who reported increased post-thrombolysis haemorrhage frequencies in elderly men. This would imply that the greater vascular fragility and increased incidence of vascular comorbidities in older men could be responsible for their increased risk of complications.^[11]

Our research also revealed that favourable functional outcomes (mRS 0–2) were observed in 80% of patients, corroborating the work of Nybondas et al., who proved that younger patients (18–49 years) receiving IVT for acute ischaemic stroke have significantly greater opportunities for successful functional recovery. This could be explained by increased neuroplasticity, lower comorbidities, and

lower baseline severity of stroke in the younger population.^[12] Interestingly, our results are consistent with Khedr et al., who found that even though male and female patients with stroke improved similarly in terms of mRS following thrombolysis, there could be some unmeasured variables like socioeconomic status and length of hospital stay contributing to the variability.^[13]

In contrast, Alsheklee et al. reported that older stroke patients, particularly those >80 years, had significantly higher mortality rates (12.8%) and an increased risk of sICH (16.9%) compared with younger patients. Their study suggested that the presence of intracerebral haemorrhage post-thrombolysis was strongly associated with mortality (OR: 2.24, 95% CI: 1.89–2.65).^[14] Although our study did not observe such high mortality rates, we found that older males had a higher risk of mortality than younger patients, suggesting that age remains a key determinant of post-thrombolysis outcomes.

Our study also suggests that sex differences may influence IVT outcomes. While younger women exhibited better functional recovery than younger men, older men were more prone to complications. This may be due to hormonal influences, stroke severity at baseline, and pre-existing vascular conditions of the patients. However, Abdu and Seyoum found no significant sex differences in mortality post-thrombolysis, indicating that factors such as stroke severity, access to post-stroke care, and rehabilitation may play a more substantial role in outcomes than sex alone.^[15,16]

The mortality rate in our study was 7%, consistent with previous reports estimating post-thrombolysis mortality between 6% and 10%. Similar to prior studies, mortality was higher in older patients, particularly males, which may be attributed to a higher burden of vascular comorbidities and greater stroke severity.^[17] However, the absence of mortality in younger females suggests a potential protective effect of female sex hormones, as described in the stroke literature. In contrast, Cai et al. reported higher mortality in females post-thrombolysis, indicating potential variations based on population characteristics and study settings.^[18]

These findings highlight the importance of age- and sex-specific risk stratification when selecting IVT candidates. Given the observed benefits in younger patients, IVT should be considered a viable treatment option for this age group. However, older men require closer post-thrombolysis monitoring to mitigate complications. Future research should focus on individualised thrombolysis protocols tailored to patient demographics, comorbidities, and stroke severity to optimise the treatment outcomes.

Limitations

The small sample size may limit the statistical power, and the retrospective design introduces potential biases, including missing data. The lack of detailed

information on comorbidities, stroke severity beyond the NIHSS, and post-stroke care may have influenced the outcomes. Additionally, the study did not account for socioeconomic status, education level, or hospital length of stay, which could have affected recovery. As this was a single-centre study, the findings may not be generalisable. Larger multicentre prospective studies are needed to validate these results and further assess the impact of age, sex, and comorbidities on IV thrombolysis outcomes.

CONCLUSION

Although most thrombolysed patients were older, our study suggests that IVT can be safely and effectively administered in younger patients. Although older patients, particularly males, more frequently experience symptomatic intracerebral haemorrhage and mortality, younger patients demonstrate favourable functional outcomes following IVT, comparable to or even exceeding those of older patients in some studies. These findings underscore the importance of considering IVT as a viable treatment option for eligible young patients with stroke. However, further research with larger, prospective, multicentre studies is needed to confirm these findings and explore the complex interplay of age, sex, comorbidities, stroke severity, and post-stroke care in influencing IVT outcomes.

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