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Low-dose versus standard-dose intravenous alteplase for octogenerian acute ischemic stroke patients: A multicenter prospective cohort study

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ABSTRACT

Background and purpose: The optimal dose of alteplase for acute ischemic stroke among geriatric patients is unclear. We aimed to assess the efficacy and safety of a low-dose (0.6 mg/kg) and standard-dose (0.9 mg/kg) alteplase for varying severity of Asian geriatric stroke patients.

Methods: The favorable functional outcome on day 90 after stroke onset, and the symptomatic intracranial hemorrhage (SICH) rate following 24–36 h of intravenous alteplase were measured. The baseline NIHSS of 4–8, 9–13, ≥14 were defined as mild, moderate, and high severity, respectively.

Results: Totally, 249 geriatric patients treated with low-dose (n = 108) and standard-dose (n = 141) alteplase. Compared to standard-dose alteplase, low-dose alteplase had decrease in favorable functional outcome (22.2% versus 34.8%), and no difference in SICH rates was observed. For mild severity patients, the mortality was significantly increased with standard-dose alteplase (the NNT/NNH = 22.9/8.0 for mild severity, the NNT/NNH = 15.0/14.7 for moderate severity, and the NNT/NNH = 13.5/19.6 for high severity).

Conclusions: Standard-dose and low-dose alteplase were comparable in reducing major disability, but low-dose alteplase for mild stroke showed much reduced mortality on day 90 for octogenarians.

1. Introduction

In 2006, the Japan Alteplase Clinical Trial (J-ACT) [1], a prospective, single-arm, open-label trial, proposed that low-dose (0.6 mg/kg) alteplase was as effective as standard-dose (0.9 mg/kg) alteplase in a Taiwanese population for recanalization of acute ischemic

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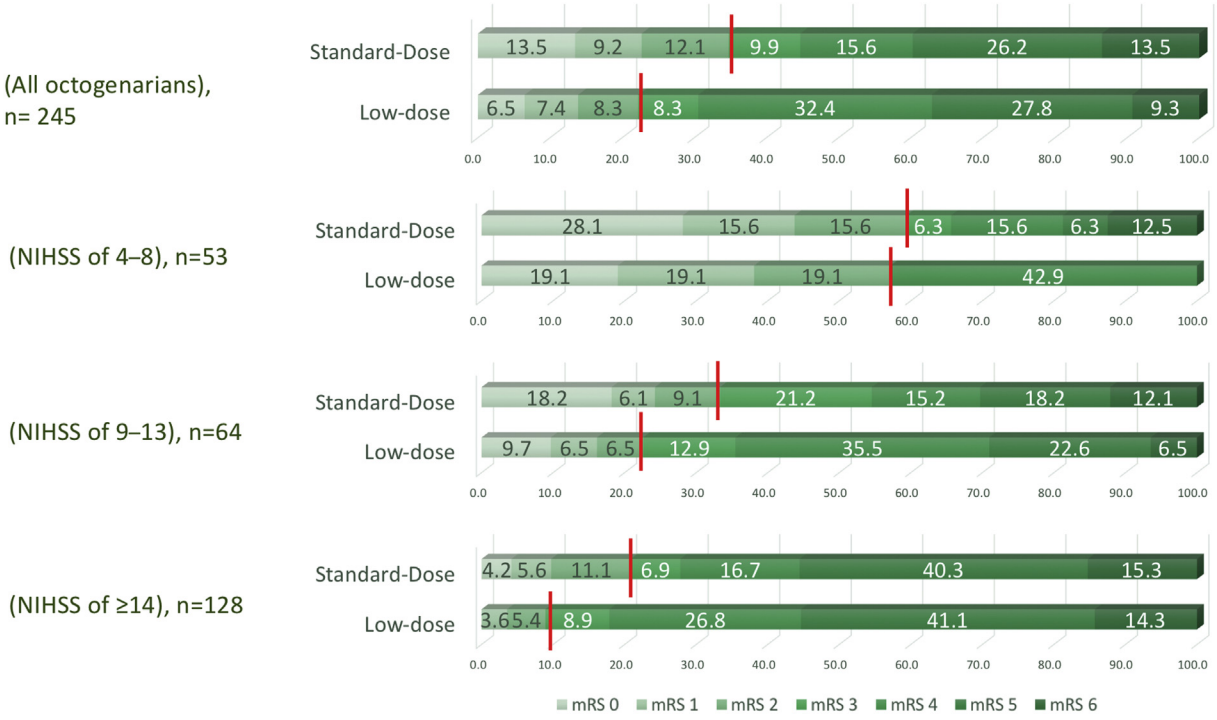

Fig. 1. Functional outcome at 90 Days after stroke onset for geriatric patients with acute ischemic stroke receiving different doses of alteplase. The red vertical line was marked for modified Rankin Scale of 2. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

stroke, with a decreased risk of intracranial hemorrhage. Since then, observational studies have shown inconsistent results as to whether low-dose (0.6 mg/kg) alteplase was as effective as standard-dose alteplase for acute ischemic stroke, although low-dose alteplase has been consistently reported to reduce the hemorrhagic risks for thrombolyzed stroke patients [2–10]. In 2016, the first randomized trial, the Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANTED) [11], was conducted to investigate the efficacy and safety of different doses of alteplase for acute ischemic stroke. The ENCHANTED trial enrolled patients with a broad range of ages and baseline severities (the interquartile ranges were 58–76 years of age and the National Institutes of Health Stroke Scale (NIHSS) of 5–14) [11]. The results of the ENCHANTED trial were limited in generalizing to an octogenarian or a more aged population, and to patients with acute ischemic stroke of a high severity (NIHSS of ≥14). No studies have specifically investigated which dose of alteplase is optimal for geriatrics over the age of 80 years in treating acute ischemic stroke of varied severity. Nowadays, a dilemma has ensued in choosing the appropriate dose of alteplase for geriatrics. In Taiwan, about half of all neurologists adopt the standard dose (0.9 mg/kg) of alteplase, while the other half use a lower dose (0.6–0.8 mg/kg) of alteplase for acute ischemic stroke within 3 h of stroke onset [2,5]. Our aim in the current study was to assess whether low-dose alteplase was as effective as standard-dose alteplase in treating acute ischemic stroke of varying severity in Taiwanese patients aged ≥80 years.

2. Methods

2.1. Study design and participants

This was a prospective, multicenter, observational study carried out in 30 hospitals throughout Taiwan using alteplase treatment for acute ischemic stroke. The study utilized an internet-based, interactive thrombolysis therapy registration platform. The investigators captured the total dose of alteplase used by physicians, time from stroke onset to needle administration as well as baseline demographic information including age, sex, and body weight. Medical comorbidities of hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, and atrial fibrillation, smoking status and alcohol use, blood pressure as alteplase was injected, lipid profiles on admission, and use of antiplatelet drugs and anticoagulants were also recorded. The contraindication of alteplase use for acute ischemic stroke was referred to that described in the European Cooperative Acute Stroke Study-II (ECASS-II) [12]. The subjects included in the study were aged ≥80 years, had an NIHSS score of ≥4, and had a door-to-needle time of ≤3 h. Patients administered an average dose of 0.6 mg/kg alteplase (range, 0.56–0.65 mg/kg) were categorized as the low-dose group, and those with an average of dose of 0.9 mg/kg (range, 0.86–0.95 mg/kg) were considered as the standard-dose group. The institutional review board of Kaohsiung Medical University Hospital (KMUH) approved the study proposal, and written informed consent was obtained from all patients. The data collection period ran between December 2004 and December 2016.

2.2. Outcome measures

The primary outcome was the endpoint of major disability and death on day 90 of all stroke severities. Patients with an mRS of 0–2 were defined as having a favorable functional outcome, and an mRS of 3–6 as an unfavorable outcome of major disability and death. The secondary outcome was the symptomatic intracranial hemorrhage (SICH) rate at 90 days, with the criteria as defined in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) [12], in which local or remote parenchymal intracranial hemorrhage occurred with deterioration of the NIHSS score to ≥4 or death within 36 h, and the National Institute of Neurological Disorders (NINDS) study [13], in which any ICH occurred with deterioration of the NIHSS score by ≥1 or death within 36 h. The baseline NIHSS of 4–8, 9–13, ≥14 were defined as mild, moderate, and high severity, respectively, of acute ischemic stroke, with cut-off points in reference to

Table 1
Demographic characteristics of octogenarian acute ischemic stroke patients receiving a low or standard dose of alteplase.

Variable	Low dose 0.6 mg/kg (N = 108)	Standard dose 0.9 mg/kg (N = 141)	P value
Age, median (IQR)	83 (81–87)	82 (80–85)	0.2256
Age (year), n/total N (%)			0.0845
80–84	95/108 (67.4%)	59/141 (54.6%)	
85–89	31/108 (22.0%)	27/141 (25.0%)	
90–94	12/108 (8.5%)	20/141 (18.5%)	
95–100	3/108 (2.1%)	2/141 (1.9%)	
Sex (Female), n (%)	59 (54.6%)	66 (46.8%)	0.2212
Body weight (kilograms)	60.0 ± 11.8	60.0 ± 12.1	0.9709
Medical history, n/total N (%)			
Hypertension	89/108 (82.4%)	113/141 (80.1%)	0.6507
Diabetes mellitus	31/108 (28.7%)	43/141 (30.5%)	0.7590
Coronary artery disease	19/108 (17.6%)	21/141 (14.9%)	0.5654
Atrial fibrillation	59/94 (62.8%)	69/123 (56.1%)	0.3224
Hyperlipidemia	27/98 (27.6%)	61/131 (46.6%)	0.0034*
Smoking status n/total N (%)			0.4687
Never	89/108 (82.4%)	111/137 (78.7%)	
Smoker	19/108 (17.6%)	30/137 (21.3%)	
Alcoholism	8/108 (7.4%)	8/141 (5.7%)	0.5803
Blood pressure (mmHg)			
Systolic	159.3 ± 30.5	162.4 ± 31.0	0.4330
Diastolic	84.2 ± 16.9	87.3 ± 19.0	0.1827
Lipids (mg/dL)			
Total cholesterol	166.8 ± 39.8	180.9 ± 40.3	0.0103
LDL-C	103.3 ± 33.6	115.3 ± 35.2	0.0153
HDL-C	45.1 ± 11.6	49.2 ± 18.9	0.0733
TG	117.9 ± 132.3	112.3 ± 67.7	0.7086
Medications, n/total N (%)			
Aspirin	20/74 (27.0%)	22/107 (20.6%)	0.3110
Clopidogrel	5/74 (8.6%)	7/107 (7.1%)	0.9545
Ticlopidine	0/74 (0.0%)	1/107 (1.6%)	0.4043
Warfarin	1/74 (1.4%)	4/107 (3.7%)	0.3354
NIHSS scores			
NIHSS of all (N = 245)	14.6 ± 6.3	14.0 ± 6.7	0.4959
Number of patients in each category, n/total N (%)			0.2883
NIHSS of < 4 (N = 4)	0/108 (0%)	4/141 (2.8%)	
NIHSS of 4–8 (N = 53)	21/108 (19.4%)	32/141 (22.7%)	
NIHSS of 9–13 (N = 64)	31/108 (28.7%)	33/141 (23.4%)	
NIHSS of ≥14 (N = 128)	56/108 (51.9%)	72/141 (51.1%)	
Time to treatment—minute	134.4 ± 46.5	136.1 ± 47.3	0.7825

HDL-C, high-density lipoprotein cholesterol; N, number; NIHSS National Institutes of Health Stroke Scale; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides. Continuous variables are expressed as the mean ± standard deviation.

* Statistical significance as $p < .05$.

the lower and upper quantiles of NIHSS of the ENCHANTED study [11].

2.3. Statistical analysis

Characteristics of the low-dose and standard-dose alteplase groups were compared using the Student's t-test for means, Mann–Whitney U test for medians, and Pearson's Chi-squared test or Fisher's exact tests were employed for discrete variables. Regarding the primary and secondary outcomes, multiple logistic regressions were employed to derive unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs). For the multivariate logistic regression analyses, the model 1 was performed without covariate adjustment, model 2 was adjusted for the covariate which was significantly imbalanced between the low- and standard-dose groups, and the model 3 was employed to adjust for both the imbalanced covariate and stroke severity. Stratification analyses of all severity categories of acute ischemic stroke were performed. The number needed to treat (NNT) and the number needed to harm (NNH) were defined as the favorable outcome (mRS of 0–2) and mortality (mRS of 6), respectively. Two separate analyses were performed in this investigation to examine (1) whether the three stroke severity groups had different covariates distribution, and (2) the characteristics of the patients died of mild or moderate to high severities. The analysis of variance (ANOVA) was performed in the separate analysis. The statistical significance level was defined as a p value < .05. All analyses were conducted using SAS version 9.4 (SAS, Cary, NC, USA).

3. Results

3.1. Patients

From December 2004 to December 2016, a total of 249 patients fulfilled the inclusion criteria for the study; 108 patients were in the low-dose group, and 141 were in the standard-dose group (Fig. 1). These two groups were generally comparable according to the measured criteria (Table 1). Though more aged population in the standard-dose group, the age distribution between the low-dose and the standard-dose groups were comparable. Most of the enrolled geriatric patients had acute ischemic stroke of moderate to high severity. In these cohorts, the mean baseline NIHSS were 14.6 ± 6.3 in the low-dose group and 14.0 ± 6.7 in the standard-dose group. For the mild, moderate, and high severity acute ischemic stroke patients, the ratios of stroke severity between the low-dose and standard-dose groups were comparable. On the other hand, we found 4 patients in our registry with extremely mild symptoms of acute ischemic stroke (baseline NIHSS < 4) received the intravenous thrombolysis. The stroke onset-to-needle times in the two cohorts were also comparable: 134.4 ± 46.5 min in the low-dose cohort and 136.1 ± 47.3 min in the standard-dose cohort. These two cohorts differed slightly in comorbidity of hyperlipidemia. Significantly higher total cholesterol levels (180.9 ± 40.3 mg/dl vs 166.8 ± 39.8 mg/dl) and low-density lipoprotein cholesterol (115.3 ± 35.2 mg/dl vs 103.3 ± 33.6 mg/dl) were observed in the standard-dose cohort than in the low-dose cohort.

3.2. Outcome measures

For the primary outcome, the proportion of patients with a favorable outcome of 0–2 on the mRS was greater in the standard-dose group (34.8%) than the low-dose group than (22.2%) of alteplase (Table 2). Generally, a reduction in favorable outcome with low-dose alteplase was observed compared to that with the standard dose in model 1 (OR: 0.54, 95% CI: 0.30–0.95, p = .0326), but there were no significant differences after adjusting for hyperlipidemia in model 2 (OR: 0.57, 95% CI: 0.32–1.05, p = .0692) and adjusting for hyperlipidemia and stroke severity in model 3 (OR: 0.58, 95% CI: 0.31–1.11, p = .1016). For the secondary outcome, SICH according to the SITS-MOST criteria was observed in 4 of 108 patients (3.7%) in the low-dose cohort and 5 of 141 patients (3.6%) in the standard-dose cohort (unadjusted OR: 1.05, 95% CI: 0.27–3.99, p = .9474; adjusted OR in model 2: 0.64, 95% CI: 0.15–2.78, p = .5463; adjusted OR in model 3: 0.63, 95% CI: 0.14–2.77, p = .5412). According to the NINDS criteria, SICH occurred in 7 of 108 patients (6.5%) in the low-dose group and 6 of 141 patients (4.3%) in the standard-dose group (unadjusted OR: 1.56, 95% CI: 0.51–4.79, p = .4371; adjusted OR in model 2: 1.14, 95% CI: 0.35–3.70, p = .8912; adjusted OR in model 3: 1.14, 95% CI: 0.34–3.76, p = .8329).

3.3. Stratification by stroke severity, NNT (mRS of 0–2) and NNH (mRS of 6) analyses

Characteristics of mild, moderate, and serious stroke severities were shown (Supplemental Table I) and these three groups were generally similar in covariates distribution. In all severity categories, the NNT and NNH for the standard dose of alteplase were 12.3 and 16.9, respectively (Table 3). Upon stratification by stroke severity (Fig. 2), the difference in favorable outcome between the standard- and low-dose groups were

Table 2
Primary and secondary outcomes at 3 months.

Dose of alteplase use	Standard dose 0.9 mg/kg (ref.)	Low dose 0.6 mg/kg	Model 1 OR (95% CI)	*P value*	Model 2 OR (95% CI)[a]	*P value*	Model 3 OR (95% CI)[b]	*P value*
Primary outcome at 90 days, *n*/total *n* (%)								
Favorable Outcome (mRS of 0–2)	49/141 (34.8%)	24/108 (22.2%)	0.54 (0.30–0.95)	0.0326*	0.57 (0.32–1.05)	0.0692	0.58 (0.31–1.11)	0.1016
Secondary outcome (SICH), *n*/total *n* (%)								
By NINDS standard	6/141 (4.3%)	7/108 (6.5%)	1.56 (0.51–4.79)	0.4371	1.14 (0.35–3.70)	0.8912	1.14 (0.34–3.76)	0.8329
By SITS-MOST standard	5/141 (3.6%)	4/108 (3.7%)	1.05 (0.27–3.99)	0.9474	0.64 (0.15–2.78)	0.5463	0.63 (0.14–2.77)	0.5412
Score on the mRS at 90 days, *n*/total *n* (%)								
mRS 0 (No symptoms)	19/141 (13.5%)	7/108 (6.5%)						
mRS 1 (No substantive disability)	13/141 (9.2%)	8/108 (7.4%)						
mRS 2 (Slight disability)	17/141 (12.1%)	9/108 (8.3%)						
mRS 3 (Moderate disability)	14/141 (9.9%)	9/108 (8.3%)						
mRS 4 (Moderate to severe disability)	22/141 (15.6%)	35/108 (32.4%)						
mRS 5 (Severe disability)	37/141 (26.2%)	30/108 (27.8%)						
mRS 6 (Death)	19/141 (13.5%)	10/108 (9.3%)	0.66 (0.29–1.48)	0.3068	0.54 (0.20–1.55)	0.2205	0.54 (0.19–1.41)	0.1979

CI, confidence interval, mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; NINDS, National Institute of Neurological Disorders and Stroke; OR, odds ratio; SITS-MOST, Safe Implementation of Thrombolysis in Stroke-Monitoring Study; ref., reference group.

* Statistical significance ($p < .05$).

[a] The model 2 adjusted for hyperlipidemia.

[b] The model 3 adjusted for hyperlipidemia and the stroke severity by NIHSS categories of < 4, 4–8, 9–13, and ≥14.

Table 3
Primary and secondary outcomes of risk difference, NNT and NNH.

Variables	Standard dose 0.9 mg/kg	Low dose 0.6 mg/kg (ref.)	Model 1 Absolute Risk Reduction (95% CI)	Model 2 Absolute Risk Reduction (95% CI)[a]	Adjusted NNT (mRS of 0–2)	Adjusted NNH (mRS of 6)
Patients of all severity						
Favorable Outcome (mRS of 0–2)	49/141 (34.8%)	24/108 (22.2%)	12.5% (1.4%–23.6%)*	8.2% (−3.0%–19.3%)	12.3	
Mortality (mRS of 6)	19/141 (13.5%)	10/108 (9.3%)	4.2% (−3.6%–12.1%)	5.9% (−1.9%–13.7%)		16.9
Patients of NIHSS of 4–8 (mild severity)						
Favorable Outcome (mRS of 0–2)	19/32 (59.4%)	12/21 (57.1%)	2.2% (−24.9%–29.4%)	4.4% (−22.8%–31.5%)	22.9	
Mortality (mRS of 6)	4/32 (12.5%)	0/21 (0.0%)	12.5% (1.0%–24.0%)*	–		8.0[b]
Patients of NIHSS of 9–13 (moderate severity)						
Favorable Outcome (mRS of 0–2)	11/33 (33.3%)	7/31 (22.6%)	10.8% (−11.0%–32.6%)	6.7% (−15.1%–28.5%)	15.0	
Mortality (mRS of 6)	4/33 (12.1%)	2/31(6.5%)	5.7% (−8.4%–19.8%)	6.8% (−7.3%–20.9%)		14.7
Patients of NIHSS of ≥14 (high severity)						
Favorable Outcome (mRS of 0–2)	15/72 (20.8%)	5/56 (8.9%)	11.9% (0.0%–23.9%)*	7.4% (−4.6%–19.4%)	13.5	
Mortality (mRS of 6)	11/72 (15.3%)	8/56 (14.3%)	1.0% (−11.4%–13.4%)	5.1% (−7.3%–17.5%)		19.6

CI, confidence interval; NIHSS, National Institutes of Health Stroke Scale; NINDS, National Institute of Neurological Disorders and Stroke; NNT, number needed to treat; NNH, number needed to harm, and SITS-MOST Safe Implementation of Thrombolysis in Stroke-Monitoring Study. The low-dose (0.6 mg/kg) was defined as the reference group since the standard dose group was observed with greater number of patients with favorable outcome and mortality.

* Statistical significance ($p < .05$).

[a] Adjustment for hyperlipidemia.

[b] The unadjusted NNH for mild severity was showed because the logistic model cannot be applied here.

very small, and no mortality was reported in the low-dose cohort in mild stroke patients of NIHSS 4–8. The NNT and NNH were 22.9 and 8.0, respectively for mild acute stroke. For patients with moderate and high severity stroke (NIHSS of 9–13 and ≥14), a greater proportion of favorable outcomes and a lower incidence of mortality was observed in the standard-dose group. In patients with moderate severity stroke (NIHSS 9–13), the NNT and NNH were 15.0 and 14.7, respectively. In patients with high severity stroke (NIHSS ≥14), the NNT of 13.5 was lower than the NNH of 19.6. The characteristics for patients who were dead of mild severity and moderate to high severity were shown in supplemental materials (Supplemental Table II).

4. Discussion

This study was motivated by our concern that deficiency of previous studies had considered both the optimal dose of alteplase and baseline severity of acute ischemic stroke in octogenarian patients. For the patients with acute ischemic stroke of moderate to high severity, our results showed that a standard dose (0.9 mg/kg) of alteplase tended to be beneficial, taking into consideration both efficacy and safety.

The distribution of mRS scores in the two dose groups on day 90 in our octogenarian patients (Fig. 1) indicated that the standard-dose group had an increased proportion of favorable functional outcomes (22.2% in the low-dose group vs 34.8% in the standard-dose group with an mRS of 0–2), but in association with a rise in mortality (9.3% in the low-dose group vs 13.5% in the standard-dose group with an mRS of 6). In fact, these results showed a similar trend to those of the ENCHANTED trial; an increased proportion of favorable outcomes in the standard-dose group (62.4% in the low-dose group vs 63.0% in the standard-dose group with an mRS of 0–2) and an increase in mortality in the standard-dose group (8.7% in the low-dose group vs 10.6% in the standard-dose group with an mRS of 6) [11]. Nevertheless, a wider range of favorable outcomes of mRS of 0–2 between the low-dose and standard-dose groups was found in our octogenarians, which directed

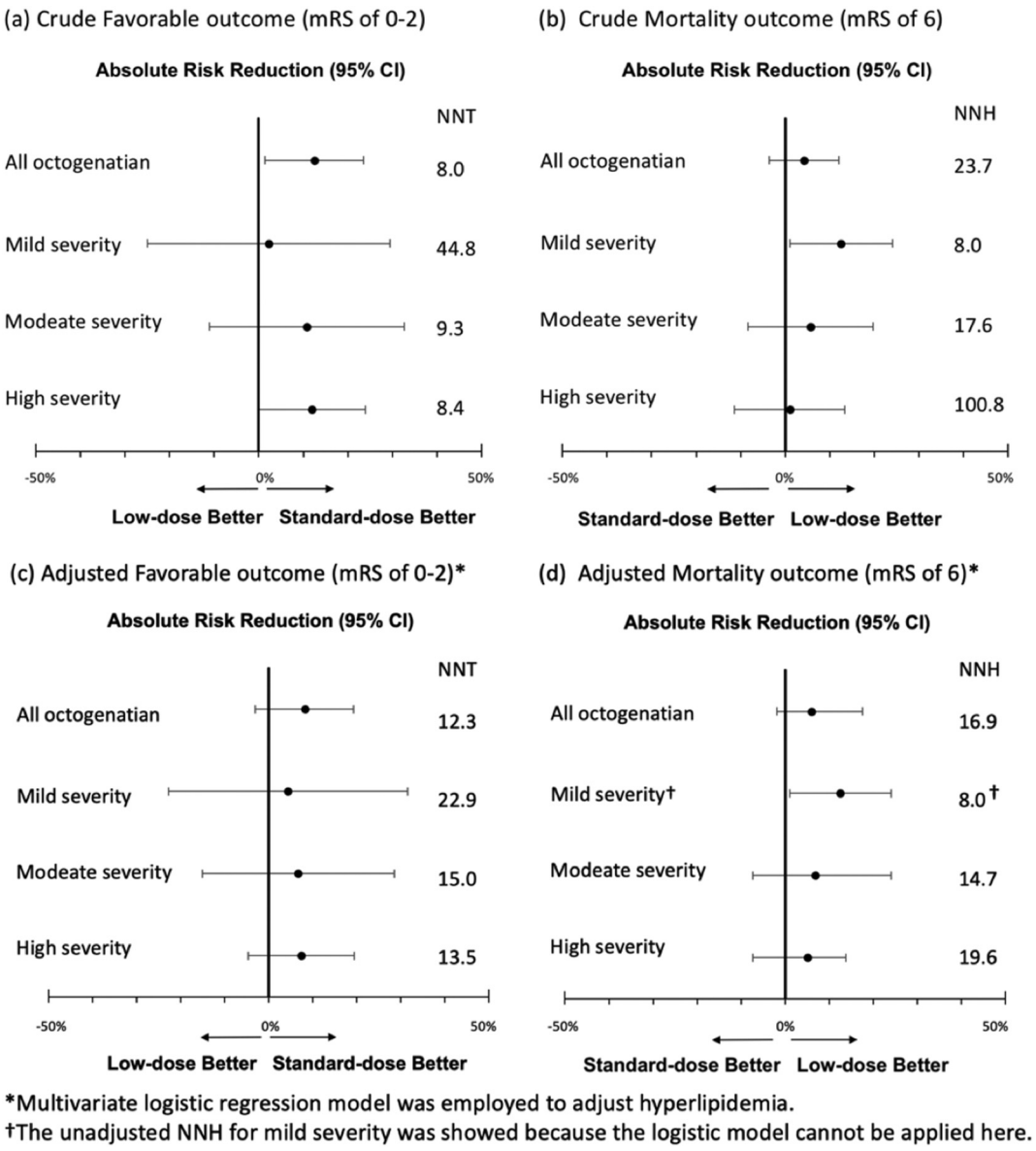

Fig. 2. Number Needed to Treat (NNT) and to Number Needed Harm (NNH) Comparison between.
Standard- and Low-dose Alteplase Group. (a) Crude favorable outcome (mRS of 0–2). (b) Crude mortality outcome (mRS of 6). (c) Adjusted favorable outcome (mRS of 0–2). (b) Adjusted mortality outcome (mRS of 6).

our stratified analysis of baseline severities.

As we stratified the baseline severities into three categories of mild, moderate, and high, we found that the increased mortality for the standard-dose alteplase group was not attributed to the patients with high severity stroke (Table 3). For patients with high baseline severity (NIHSS of ≥14), the difference between an NNT of 13.5 and an NNH of 19.6 favored standard-dose alteplase use. On the other hand, the standard-dose group had 12.5% of mortality cases and the low-dose group showed completely no mortality cases for mild severity acute stroke (NIHSS of 4–8), and the NNH showed significant low value of 8.0. These results suggest that low-dose alteplase was more appropriate for mild severity stroke patients, and a standard-dose was considered safe for moderate to high severity acute ischemic stroke octogenarian patients.

Our results support physicians not to hesitate with standard-dose alteplase for moderate and high severity acute ischemic stroke octogenarian patients. Even though an increase in a small proportion of mortality cases with the standard dose of alteplase was observed, mortality rates between the low-dose and standard-dose groups in neither our study nor the ENCHANTED trial showed significant differences. A low dose of alteplase decreased the number of death cases, but it may have caused the number of moderate to high severity geriatric patients to fall. Besides, in our SICH criteria as specified by the SITS-MOST and NINDS studies, the low-dose and standard-dose groups showed no significant difference between them. Physicians should therefore not be concerned about hemorrhagic transformation and/or hemorrhagic infarction with a standard dose of alteplase, since the occurrence of SICH was comparable between the low and standard doses of alteplase used for stroke in our safety analysis.

These results do not contradict our previous findings that a standard dose of 0.9 mg/kg was not optimal for all patients according to TTT-AIS [5] and TTT-AIS II [2]. In the present study, we divided patients into three baseline severity categories: mild (4–8), moderate (9–13), and high (≥14) severity of NIHSS. For octogenarian patients, low-dose alteplase was supposed to be enough to recanalize the artery in mild severity stroke patients, whereas standard-dose alteplase was still required to dissolve the clots in high severity stroke patients.

In clinical practice, physicians should discuss the pros and cons of

different doses of alteplase with patients and their families. From a public health viewpoint, low-dose alteplase treatment for geriatric acute ischemic stroke increases socioeconomic burden, since a greater proportion of geriatric patients will only obtain partial treatment and will experience moderate disabilities or be bedridden for the rest of their lives. Those patients will also require further post-acute stroke care in nursing homes, which represents increasing costs of post-acute stroke care due to increased stroke severity [14]. To reduce major disabilities in geriatric patients with moderate to severe stroke, to ensure the quality of life of geriatric patients, and to reduce costs of post-acute stroke care, we propose that the standard dose of alteplase for geriatric patients with moderate to high severity acute ischemic stroke should be recommended.

Our study has some limitations. This was an observational study. Though baseline characteristics between the low-dose and standard-dose groups were comparable, the residual confounding still existed. The dose of alteplase was decided by each physician's judge in the real-world practice. In Taiwan, the stroke guideline had no strong recommendation of either low-dose and standard-dose alteplase use for octogenarians. The physician's judge was considered to be affected by the previous TTT-AIS and TTT-AIS II studies, which reported that low-dose alteplase was associated with better outcomes in the range of 71 to 80 years [2,5]. On the other hand, the National Health Insurance in Taiwan did not cover the costs of intravenous thrombolytic therapy for octogenarian with acute ischemic stroke. Sometimes, the large price discrepancy between low-and standard-dose may also interfere physician's judge. The expenses for intravenous alteplase was around 1200 United States Dollars (per alteplase vial use) in Taiwan, and each vial of alteplase contained a total amount of 50 mg. With a patient of 70 kg as a concrete example, the patient was costed with double expenses with standard-dose regimen ($70 \times 0.9 = 63$ mg). Our investigation, however, was truly reflected the “real-world” use of alteplase for Asian population and each patient was assessed by trained neurologists in the TTT-AIS study group. Lastly, our study results still need to be confirmed via systematic, randomized controlled trials in the future.

In conclusion, our study supports a low dose of alteplase for geriatric patients aged ≥ 80 years with acute ischemic stroke of mild severity, and standard dose of alteplase was considered to have comparable efficacy and safety to low dose alteplase to treat geriatric acute ischemic stroke of moderate to high severity (with a baseline NIHSS score of at least > 9).

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Disclosures

No conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2019.01.047.

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