Influence of Age on Thrombolysis Outcome in Wake-Up Stroke

Dulka Manawadu, MRCP; Shankaranand Bodla, MD; Jeff Keep, FCEM; Lalit Kalra, PhD

Background and Purpose—Thrombolysis in patients >80 years remains controversial; we hypothesized that >80-year-old patients with wake-up ischemic stroke (WUIS) will benefit from thrombolysis despite risks because of poor outcomes with no treatment.

Methods—The study included 68 thrombolysed patients with WUIS (33 [48%] >80 years), 54 nonthrombolysed patients with WUIS (21 [39%] >80 years), and 117 patients (>80 years old) thrombolysed within 4.5 hours of symptom onset (reference group). Mortality and modified Rankin Scale (mRS) were assessed at 90 days.

Results—Baseline characteristics of thrombolysed and nonthrombolysed >80 and ≤80-year-old patients with WUIS were comparable. Thrombolysis outcomes in >80-year-old patients with WUIS were better than in nonthrombolysed >80-year-old patients with WUIS (90-day mortality: 24% versus 47%, P=0.034; mRS 0–2: 30% versus 5%, P=0.023; mRS 0–1: 15% versus 5%, P=0.24) and comparable with thrombolysed ≤80-year-old patients with WUIS. Thrombolysis was associated with odds ratio 0.27 (95% confidence interval, 0.05–0.97) for mortality and odds ratio 28.6 (95% confidence interval, 1.8–448) for mRS 0 to 2 at 90 days in >80-year-old patients with WUIS after adjusting for stroke severity and risk factors.

Conclusions—Thrombolysis may be associated with greater benefit in >80-year-old patients with WUIS but a selection bias favoring thrombolysis in those most likely to benefit may significantly reduce interpretability of these findings. (Stroke. 2013;44:2898-2900.)

Key Words: aging ■ outcomes ■ stroke management ■ thrombolysis ■ wake-up stroke

Patients who are ≥80 years old constitute a third of strokes but are excluded from clinical trials and recombinant tissue-type plasminogen activator license.1 Although >80-year-old patients with stroke have 2-fold higher mortality and morbidity even with thrombolysis compared with ≤80-year-old patients,2,3 pooled results of thrombolysis and neuroprotection trials suggest potential for benefit with thrombolysis in >80-year-old patients.4 This may be important for patients wake-up ischemic stroke (WUIS), who are significantly older, constitute 14% of acute presentations, and 36% may be eligible for thrombolysis.5 We have shown that thrombolysis improves outcomes in patients with WUIS6 and hypothesize that >80-year-old patients with WUIS benefit more from thrombolysis than ≤80-year-old patients because of worse outcomes without treatment.

Methods

We compared outcomes in thrombolysed and nonthrombolysed >80- and ≤80-year-old patients with WUIS, sampled consecutively from a prospective register between January 2009 and December 2010. Selection criteria were the following: (1) last seen normal ≤0–1: 15% versus 5%, P=0.24) and comparable with thrombolysed ≤80-year-old patients with WUIS. Thrombolysis was associated with odds ratio 0.27 (95% confidence interval, 0.05–0.97) for mortality and odds ratio 28.6 (95% confidence interval, 1.8–448) for mRS 0 to 2 at 90 days in >80-year-old patients with WUIS after adjusting for stroke severity and risk factors.

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Thrombolysis Benefits >80-Year-Old Patients With WUIS

Favorable functional outcomes at 90 days and bleeding rates were comparable between >80- and ≤80-year-old patients with WUIS and the reference group. The reference group had higher mortality but also higher NIHSS score and Alberta Stroke Program Early CT Score (ASPECTS).

Twenty-one patients (39%) of the 54 nonthrombolysed patients with WUIS were >80 years old and comparable with nonthrombolysed ≤80-year-old patients with WUIS and thrombolysed >80-year-old patients with WUIS (Table). Nonthrombolysed >80-year-old patients with WUIS had significantly worse functional outcomes and mortality compared with younger patients (Table).

Thrombolysed >80-year-old patients with WUIS had lower mortality (24% versus 47%; \( P=0.034 \)), better mRS 0 to 2 (30% versus 5%; \( P=0.023 \)) and mRS 0 to 1 (15% versus 5%; \( P=0.24 \)) at 90 days than nonthrombolysed patients >80 years old (Table). There were no significant differences in outcomes between thrombolysed and nonthrombolysed ≤80-year-old patients with WUIS. Thrombolysis was associated with an odds ratio of 0.27 (95% confidence interval, 0.05–0.97), \( P=0.034 \) for mortality and 28.6 (95% confidence interval, 1.8–448), \( P=0.017 \) of mRS 0 to 2 at 90 days in >80-year-old patients with WUIS (n=54), after adjusting for baseline NIHSS score, diabetes mellitus, and atrial fibrillation. Thrombolysis was not an independent predictor of mortality or mRS 0 to 2 at 90 days in ≤80-year-old patients with WUIS (n=68).

Discussion

Patients with stroke, who were >80 years old, have higher morbidity and mortality because of prestroke disability or comorbidities and may have more to gain with thrombolysis despite the risks (Figure). This study showed that >80-year-old patients with WUIS who are eligible but not thrombolysed...
had significantly worse outcomes than nonthrombolysed patients \( \leq 80 \) years, and the benefits of thrombolysis were greater in this age group (Figure). The independent association between thrombolysis and good outcomes in \( >80 \)-year-old patients with WUIS persisted after adjusting for stroke severity and other prognostic covariates in multiple logistic regression. The bleeding risk with thrombolysis in \( >80 \)-year-old patients with WUIS was comparable with \( \leq 80 \)-year-old patients with WUIS and the reference group.

The study is a nonrandomized comparison in a small sample, and thrombolytic therapy in WUIS is not proven. The sample consisted of consecutive patients meeting predefined criteria for thrombolysis but selection bias in thrombolysis favoring those likely to benefit reduces interpretability. The potential effect of baseline differences in covariates was accounted for in the multiple logistic regression; the effect of thrombolysis was statistically significant in patients \( \geq 80 \) but not \( \leq 80 \) years. Although baseline data did not show any statistical difference between the groups, the findings of this study need to be interpreted cautiously because subjective bias in selection for thrombolysis and unmeasured age–related confounders remain unknown.

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**Disclosures**

None.

**References**

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