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**The thrombolytic therapy for wake-up stroke base on neuroimaging: Yes or no? A meta-analysis of comparative studies**

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**Background & Aim:** Intravenous recombinant tissue plasminogen activator (rt-PA) is a preferred therapy for patients with acute ischemic stroke within 4.5 hours. But patients with unknown stroke onset usually excluded from the standard thrombolytic therapy. Although some existing studies which evaluated conducted the thrombolytic therapy for patients with unknown stroke onset or wake-up stroke, there have been no comprehensive meta-analyses of the effect of thrombolytic therapy for these patients. We performed the first meta-analysis to evaluate the effect of thrombolytic therapy for patients with wake-up stroke or unknown stroke onset.

**Methods:** Articles were screened from electronic database in September 2017 and all randomized controlled trials and retrospective comparative studies were included.

**Results:** Two randomized controlled trials, three retrospective studies, one prospective, multicenter, single-arm study, one case-controlled study and one open-label pilot study including 964 patients were included. The control group had lower National Institutes of Health stroke scale score (95% CI 0.62-4.26;  $p=0.009$ ). For excellent clinical outcome (mRS, 0-1), no significant difference was found between experiment group and control group (OR 1.76; 95% CI 0.71-4.35;  $p=0.22$ ). There was no statistically significant difference when we compared the favorable clinical outcome (mRS, 0-2) between both groups (OR 1.42; 95% CI 0.85-2.36;  $p=0.18$ ). Intracranial hemorrhage of control group were lower than experiment group (OR 1.81; 95% CI 1.00-3.37;  $p=0.05$ ). But the mortality between both groups was not statistically significant (OR 1.29; 95% CI 0.64-2.59;  $p=0.47$ ).

**Conclusion:** Intravenous rt-PA in patients with WUS based on neuroimaging did not improve clinical prognosis. However the ICH rate was statistically significant higher for experiment group than control group. More well-designed RCTs are needed to evaluate the effect of intravenous rt-PA for WUS.

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