Increasing time to thrombolysis is associated with worse long-term outcomes in patients with ischaemic stroke: a nationwide study

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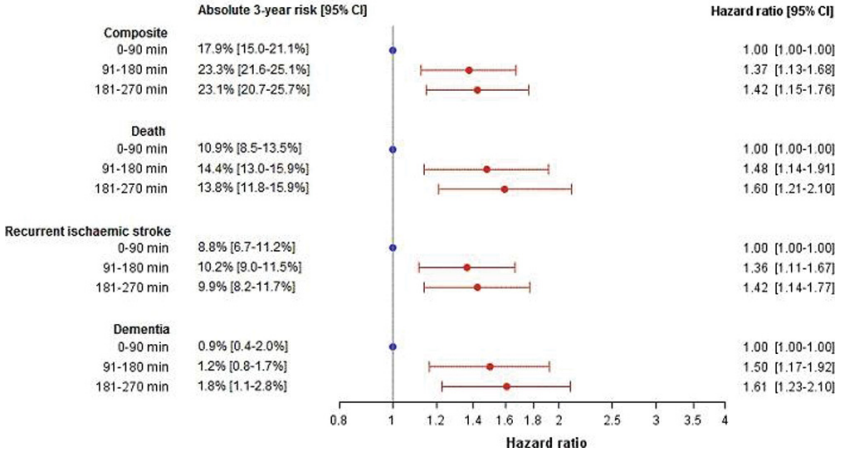
Background: It is well-established that the short-term benefits of intravenous thrombolytic therapy are reduced with increasing treatment delay in patients with acute ischaemic stroke. However, there is a paucity of contemporary data on the association between time from symptom onset to initiation of thrombolysis and long-term outcomes. With improving post-stroke survival in the Western world, data on time to thrombolysis and subsequent long-term outcomes are warranted in order to provide further insight into the importance of time to treatment.

Purpose: To examine the long-term risk of adverse outcomes according to time from symptom onset to intravenous thrombolytic therapy in patients with acute ischaemic stroke.

Methods: In this observational cohort study, we identified all patients with first-time ischaemic stroke treated with intravenous thrombolysis between 2011–2015 and alive at discharge through the Danish National Stroke Registry. Patients who received thrombolysis after >270 min were excluded. Using multivariable Cox regression, we examined associations between time from symptom onset to thrombolysis and risks of the composite of death, recurrent ischaemic stroke, and dementia, as well as each of these components separately. Patients were followed until the outcome of interest, emigration, or December 31, 2017.

Results: Of the 4,313 patients with first-time ischaemic stroke treated with intravenous thrombolysis, 4,119 were alive at discharge (median age 69 years [25th-75th percentile 59–78 years], 60% males). The median follow-up was 3.3 years (25th-75th percentile 2.3–4.7 years). The median time from symptom onset to initiation of thrombolytic therapy was 140 min (25th-75th percentile 106–187 min), and the median National Institutes of Health Stroke Scale score at presentation was 5 (25th-75th percentile 3–10). The unadjusted absolute 3-year risks of the composite outcome, death, recurrent ischaemic stroke, and dementia according to time to thrombolysis are displayed in the figure. Compared with thrombolysis within 90 min, time to thrombolysis >90 min was associated with a higher relative risk of the composite outcome (91–180 min: adjusted hazard ratio [HR] 1.37 [95% confidence interval [CI], 1.13–1.68]; 181–270 min: adjusted HR 1.42 [95% CI 1.15–1.76]). The risks of each component of the composite outcome according to time to thrombolysis were similar to results for the composite endpoint, as illustrated in the figure.

Conclusions: In this nationwide cohort of patients with acute ischaemic stroke treated with thrombolysis, increasing time from symptom onset to initiation of intravenous thrombolytic therapy was associated with higher long-term risks of the composite of death, recurrent ischaemic stroke, and dementia, as well as all three outcomes separately. These data indicate that long-term outcomes of patients with ischaemic stroke treated with intravenous thrombolysis can be greatly improved by reducing treatment delay.



Time to thrombolysis and outcomes