ICU
MANAGEMENT & PRACTICE

Optimal Timing of Anticoagulation After Ischaemic Stroke and Atrial Fibrillation

Atrial fibrillation (AF) accounts for about 20–30% of ischaemic strokes. Direct oral anticoagulants (DOACs) are very effective for long-term secondary prevention of ischaemic stroke in AF patients, reducing the risk of intracranial haemorrhage by about half compared to vitamin K antagonists. However, the best timing to start anticoagulation after an acute ischaemic stroke in AF remains uncertain. Early DOAC treatment may lower the risk of stroke recurrence due to cardiac embolism, but there is concern that it could increase haemorrhagic transformation of the infarct, worsening outcomes.

Previous major DOAC trials excluded patients with recent acute ischaemic stroke (within 7–30 days). An earlier meta-analysis suggested early DOAC use might be safe but was limited by biases. Recently, four randomised controlled trials (TIMING, OPTIMAS, ELAN, and START) investigated early versus later initiation of DOACs. TIMING and OPTIMAS found early anticoagulation within 4 days was non-inferior to later start (5–14 days) for combined outcomes like recurrent stroke, symptomatic intracranial haemorrhage, or death. ELAN showed a numerically lower event rate with early DOAC use based on infarct size. START tested multiple timing strategies but did not definitively prove early DOAC treatment reduces recurrence without increasing bleeding risk.

To clarify this clinical question, researchers launched the CATALYST individual patient data meta-analysis (IPDMA), planned before trial results were known. Its primary goal was to assess if starting DOACs within 4 days is superior to starting on day 5 or later in reducing a composite outcome of recurrent ischaemic stroke, symptomatic intracerebral haemorrhage, or unclassified stroke at 30 days. Secondary aims included analysing individual outcome components up to 90 days and exploring differences in effect across subgroups such as stroke severity.

The primary outcome was a composite of recurrent ischaemic stroke, symptomatic intracerebral haemorrhage, or unclassified stroke within 30 days. Secondary outcomes were the individual components assessed at 30 and 90 days.

The meta-analysis included four trials (TIMING, ELAN, OPTIMAS, and START) with 5,441 participants (average age 77.7 years, 45.4% women, median stroke severity score of 5). Primary outcome data were available for 5,429 participants. The composite primary outcome occurred in 2.1% of those who started DOACs early (within 4 days) versus 3.0% who started later (day 5 or after), showing a significant 30% reduction in risk with early initiation. Early DOAC treatment also significantly reduced recurrent ischaemic stroke risk (1.7% vs 2.6%) without increasing symptomatic intracerebral haemorrhage rates (0.4% vs 0.4%).

Early DOAC initiation significantly reduced the composite outcome of recurrent ischaemic stroke, symptomatic intracerebral haemorrhage, or unclassified stroke at 30 days, with no variation in effect by stroke severity. Early treatment also lowered the risk of recurrent ischaemic stroke without increasing symptomatic intracerebral haemorrhage or major extracranial bleeding.

These results support the safety and efficacy of starting DOACs within 4 days post-stroke, challenging the common clinical practice of delaying anticoagulation due to haemorrhagic concerns. Early initiation may also improve patient adherence and reduce hospital stays. However, the benefit was most evident in the first two weeks; by 90 days, differences between early and later starts were no longer statistically significant, possibly due to other stroke mechanisms and both groups being on anticoagulation.

This analysis provides strong evidence favouring early DOAC initiation after ischaemic stroke with atrial fibrillation, except in patients with very severe strokes or large haemorrhagic complications where individualised decisions remain necessary. Early DOAC use should be considered routine to reduce early stroke recurrence risk within 30 days.

Source: The Lancet

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