INPLASY

When to Initiate Anticoagulation in Atrial Fibrillation Patients with Stroke? A Network Meta-Analysis of Early, Intermediate, and Late Timing

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 6 February 2025 and was last updated on 6 February 2025.

INTRODUCTION

Review question / Objective Objective: The objective of this study is to evaluate the efficacy and safety of initiating anticoagulation therapy at different time intervals—early (≤4 days), intermediate (4-14 days), and late (>14 days)—following a stroke in patients with atrial fibrillation. This network meta-analysis aims to identify the optimal timing for initiating anticoagulation to prevent recurrent strokes while minimizing the risk of bleeding complications.

Condition being studied Atrial fibrillation (AF) increases the risk of ischemic stroke fivefold, with the highest risk of recurrence in the first 90 days after an acute stroke. However, the optimal timing for initiating oral anticoagulants (OACs) post-stroke remains uncertain. Traditionally, initiation timing was based on stroke severity (NIHSS score) and hemorrhagic transformation (HT). The 1-3-6-12-day rule suggested different initiation times based on stroke severity. Recent studies, such as the TIMING trial, showed that early DOAC initiation (≤4 days) was non-inferior to delayed initiation (5–10 days) in terms of recurrent stroke and intracranial hemorrhage. The OPTIMAS trial further supported early initiation within 4 days as non-inferior to delayed initiation for composite outcomes at 90 days, without stratifying by stroke severity.
Our study aims to evaluate the optimal timing for anticoagulation initiation in AF patients post-stroke using a Bayesian network meta-analysis. We compared early (≤4 days), intermediate (4–14 days), and late (>14 days) initiation strategies, integrating data from RCTs and cohort studies to assess risks of recurrent ischemic events and bleeding. This comprehensive approach provides insights into the relative efficacy and safety of different timing strategies, independent of stroke severity, and offers a more nuanced understanding for clinical practice.

METHODS

Participant or population Participant：Patients with stroke and atrial fibrillation.

Population : Atrial fibrillation (AF) is a major risk factor for ischemic stroke, with patients experiencing a fivefold increased risk of stroke compared to the general population. The risk of recurrent stroke and systemic embolism is particularly high in the first 90 days following an acute ischemic stroke associated with AF. Despite the established efficacy of anticoagulation in reducing the risk of recurrent stroke in patients with AF, there remains significant uncertainty regarding the optimal timing for initiating oral anticoagulants (OACs) after an acute ischemic stroke.

Intervention Anticoagulation initiated within ≤4 days.

Comparator Anticoagulation initiated between 4 and 14 days; Anticoagulation initiated after >14 days.

Study designs to be included Randomized controlled trials (RCTs), Cohort studies.

Eligibility criteria (1) Stroke patients with atrial fibrillation were included in the studies. (2) Patients were divided into three categories based on the timing of anticoagulant therapy initiation: within 14 days after stroke onset. (3) All studies included two or three arms.

Information sources A thorough manual search was conducted across the PubMed, Embase, Cochrane, and Web of Science databases to identify relevant studies. If necessary, the corresponding authors will be contacted to obtain additional research data.

Main outcome(s) Recurrent stroke, intracranial hemorrhage, major bleeding, All-cause mortality.

Quality assessment / Risk of bias analysis We evaluated the methodological quality of the individual studies using the Cochrane Risk of Bias tool for randomized controlled trials (RCTs), while cohort studies were evaluated using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I).

Strategy of data synthesis The estimates are expressed as Hazard ratio (HR) with a 95% confidence interval (CI).

Subgroup analysis In the context of stroke recurrence and bleeding, we considered subgroup analysis of different anticoagulants and antiplatelet agents.

Sensitivity analysis We performed sensitivity analyses to explore how a single study might affect the overall pooled estimate for each predefined outcome.

Country(ies) involved China.

Keywords Anticoagulation; Stroke; initiate.

Contributions of each author

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