INPLASY

Safety and efficacy of intravenous thrombolysis before mechanical thrombectomy in patients with acute ischemic stroke and atrial fibrillation

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202390015

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 September 2023 and was last updated on 06 September 2023.

INTRODUCTION

Review question / Objective The existing literature (randomized controlled trials or observational cohort studies) was systematically searched for compliance with the following PICO (patients, interventions, comparators and outcomes) criteria. P: AIS- LVO combined with AF. I: IVT before MT. C: Direct MT. O: 3-month good clinical outcome defined as an modified Rankin Score of 0-223, symptomatic intracerebral hemorrhage (sICH), successful reperfusion defined as thrombolysis in cerebral infarction (TICI) scores of 2b to 323, 3-month mortality.

Rationale Our objective was to assess whether bridging IVT is more beneficial than direct MT in AIS-LVO with AF patients.

Condition being studied Background: Intravenous thrombolysis (IVT) prior to mechanical thrombectomy (MT) is considered the standard treatment for patients with acute ischemic stroke caused by large vessel occlusion (AIS-LVO). However, the efficacy and safety of IVT prior to MT in AIS-LVO with atrial fibrillation (AF) patients remains controversial. Our objective was to assess whether bridging IVT is more beneficial than direct MT in AIS-LVO with AF patients. Method: We performed a systematic review and meta-analysis to investigate the outcomes of bridging IVT versus direct MT alone in AIS-LVO patients with AF. The outcomes included successful reperfusion (defined as thrombolysis in cerebral infarction scores of 2b to 3), symptomatic intracerebral hemorrhage (sICH), and 3-month good clinical outcome (defined as modified Rankin scale score≤2) and 3-month mortality. The protocol had been registered before data collection (INPLASY). Result: A total of 8 eligible observational studies were included, including 3827 patients with AIS-LVO complicated with AF treated with bridging IVT and 3171 patients treated with direct MT. Compared with direct MT, bridging IVT was associated with 3-month good clinical outcome (odd ratio [OR] 1.27,

95% confidence interval [CI] 1.05-1.54) and a lower 3-month mortality (OR 0.78, 95% CI 0.68-0.88). However, treatment modality was not associated with sICH (OR 1.26, 95% CI 0.91–1.75), or successful reperfusion (OR 0.98, 95% CI 0.83-1.17). Conclusion: In AIS-LVO with AF patients, bridging IVT may achieve better functional outcomes and lower mortality rates. Withholding bridging IVT on the sole ground of presenting with AF may not be justified.

METHODS

Search strategy

PubMed:
1. Stroke [MeSH Terms]
2. Brain Ischemia [MeSH Terms]
3. Intracranial Embolism and Thrombosis [MeSH Terms]
4. (stroke* or AIS or apople*) [Title/Abstract]
5. ((intracranial or carotid arter* or brain or cerebr*) and (isch*emi* or embolism or thrombosis or obstruct* or occlus* or block* or infarct* or clot*)) [Title/Abstract]
6. (cerebrovascular or cerebral arter*) and (accident or event* or disorder* or disease*) [Title/Abstract]
7. (anterior circulation or ACA) [Title/Abstract]
8. (large vessel occlusion* or large arter* occlusion* or LVO) [Title/Abstract]
9. or 1-8
10. (Atrial Fibrillation OR Auricular fibrillation* OR AF OR AFib) [Title/Abstract]
11. Thrombectomy [MeSH Terms]
12. Embolectomy [MeSH Terms]
13. (mechanical or endovascular) and (thromb* or embol*)[Title/Abstract]
14. (thrombectomy or embolectomy or EVT or MT) [Title/Abstract]
15. (bridg* or endovascular) and (therapy or treatment or intervention) [Title/Abstract]
16. ((clot* or thromb* or embol* or stent*) and (retriev* or disruption* or fragmentation)) [Title/Abstract]
17. (stent-retriever or aspiration or solitaire or trevo or preset or catch) [Title/Abstract]
18. or 11-17
19. (Fibrinolysin or Plasminogen or plasminogen activators or Thrombolytic Therapy or Fibrinolysis or Thrombosis/drug therapy or Thromboembolism/drug therapy or Intracranial Thrombosis/drug therapy or Intracranial Embolism/drug therapy or Intracranial Embolism and Thrombosis/drug therapy) [MeSH Terms]
20 (Fibrogammin or Thrombolysin or Plasmin or plasminogen activator* or Thrombolys* or Thrombolytic or Fibrinolytic or alteplase or tPA or t-PA or rtPA or rt-PA or Tenecteplase or TNK-tPA) [Title/Abstract]
21. or 19-20
22. 9 and 10 and 18 and 21

Embase:
1. 'brain infarction'/exp or 'brain infarction':ab,ti or 'cerebrovascular accident'/exp or 'occlusive cerebrovascular disease'/exp
2. 'stroke*':ab,ti or 'AIS':ab,ti or 'apople*':ab,ti
3. ('intracranial':ab,ti or 'carotid arter*':ab,ti or 'brain':ab,ti or 'cerebr*':ab,ti) and ('isch*emi*':ab,ti or 'embolism':ab,ti or 'thrombosis':ab,ti or 'obstruct*':ab,ti or 'occlus*':ab,ti or ' block*':ab,ti or 'infarct*':ab,ti or 'clot*':ab,ti)
4. ('cerebrovascular':ab,ti or 'cerebral arter*':ab,ti) and ('accident':ab,ti or 'event*':ab,ti or 'disorder*':ab,ti or 'disease*':ab,ti)
5. 'large vessel occlusion*':ab,ti or 'large arter* occlusion*':ab,ti or 'anterior circulation occlusion*':ab,ti or 'LVO':ab,ti
6. or 1-5
7. 'Atrial Fibrillation':ab,ti or 'AF':ab,ti or 'AFib':ab,ti
8. 'thrombectomy'/exp or 'embolectomy'/exp
9. 'thrombectomy':ab,ti or 'embolectomy':ab,ti
10. ('mechanical':ab,ti or 'endovascular':ab,ti) and ('thromb*':ab,ti or 'embol*':ab,ti)
11.('bridg*':ab,ti or 'endovascular':ab,ti) and ('therapy':ab,ti or 'treatment':ab,ti or 'intervention':ab,ti)
12.'stent-retriever':ab,ti or 'aspiration':ab,ti or 'solitaire':ab,ti or 'trevo':ab,ti or 'preset':ab,ti or 'catch':ab,ti
13. or 8-12
14. 'plasmin'/exp or 'plasminogen'/exp or 'plasminogen activator'/exp or 'fibrinolytic therapy'/exp or 'fibrinolysis'/exp
15. 'fibrinolysin':ab,ti or 'fibrogammin':ab,ti or 'thrombolysin':ab,ti or 'plasmin':ab,ti or 'plasminogen activator*':ab,ti or 'thrombolys*':ab,ti or 'thrombolytic':ab,ti or 'fibrinolytic':ab,ti or 'thrombosis/drug therapy':ab,ti or 'thromboembolism/drug therapy':ab,ti or 'intracranial thrombosis/drug therapy':ab,ti or 'intracranial embolism/drug therapy':ab,ti or 'intracranial embolism thrombosis/drug therapy':ab,ti
16. 'alteplase':ab,ti or 'tpa':ab,ti or 't pa':ab,ti or 'rtpa':ab,ti or 'rt pa':ab,ti or 'Tenecteplase':ab,ti or 'TNK-tPA':ab,ti
17. 14-16
18. 6 and 7 and 13 and 17

Cochrane Central Register of Controlled Trials
1. MeSH descriptor: [Stroke] explode all trees
2. "Cerebrovascular event" or Stroke or apoplex or CVA or "cerebrovascular accident" or "brain vascular accident" or "brain isch*" or "brain infarc*" or "cerebral infarc$" or "cerebral isch$" or ”large vessel occlusion” or "intracranial isch*" or "intracranial infarction" or "intracranial vessel occlusion" or "brain vessel occlusion"

3. 1 or 2
4. MeSH descriptor: [Thrombectomy] explode all trees
5. Thrombectomy or thrombectomie$ or mechanical or endovascular or embolectomy
or "intracranial intervention" or Stent-retriever or stentretriever or preset or solitaire or
trevo or catch
6. 4 or 5
7. MeSH descriptor:Atrial Fibrillation
(Atrial Fibrillation OR Auricular fibrillation* OR AF OR AFib) [All Fields]
8. (thrombolysis OR tPA OR tissue plasminogen activator)[All Fields]
9. 3 and 6 and 7 and 8.

Participant or population AIS- LVO combined with AF.

Intervention AIS- LVO combined withAF.

Comparator Direct MT.

Study designs to be included The existing literature (randomized controlled trials or observational cohort studies) was systematically searched for compliance with the following PICO (patients, interventions, comparators and outcomes) criteria.

Eligibility criteria The existing literature (randomized controlled trials or observational cohort studies) was systematically searched for compliance with the following PICO (patients, interventions, comparators and outcomes) criteria.P: AIS- LVO combined with AF.I: IVT before MT.C: Direct MT. O: 3-month good clinical outcome defined as an modified Rankin Score of 0-223, symptomatic intracerebral hemorrhage (sICH), successful reperfusion defined as thrombolysis in cerebral infarction (TICI) scores of 2b to 323, 3-month mortality.

Information sources PubMed, EMBASE, and Cochrane.

Main outcome(s) O: 3-month good clinical outcome defined as an modified Rankin Score of 0-223, symptomatic intracerebral hemorrhage (sICH), successful reperfusion defined as thrombolysis in cerebral infarction (TICI) scores of 2b to 323, 3-month mortality.

Additional outcome(s) No.

Data management Noteexpress and excel.

Quality assessment / Risk of bias analysis The risk of bias of each study was critically assessed by two independent raters (BQJ and HXD) using the Newcastle-Ottawa scale24. All studies were scored for selection, comparability and outcomes. A score of 7 or above on the Newcastle-Ottawa scale is considered to be of high quality. Any discrepancies between raters were resolved by discussion, and differences were reached by consensus after discussion with the corresponding author (ZXQ).

Strategy of data synthesis n pairwise meta-analyses, we calculated the corresponding odds ratios (ORs) and 95% confidence intervals (95% CIs) for the outcome events in patients who received direct MT and those who received bridging IVT. Pooled estimates were calculated using a meta-analysed random-effects model (DerSimonian and Laird)25. Heterogeneity was assessed using the I2 statistic. For qualitative interpretation of heterogeneity, I2 values >50% and I2>75% were considered to represent significant and considerable heterogeneity, respectively26. Publication bias was assessed using funnel plots. All statistical analyzes were performed using Reviewer Manager (RevMan v.5.3) software.

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Country(ies) involved Department of Neurosurgery, People's Hospital of Guang'an City, Guang'an, Sichuan, China.

Keywords ischemic stroke, large vessel occlusion, atrial fibrillation, intravenous thrombolysis, mechanical thrombectomy.

Contributions of each author

Author 1 - Qiangji Bao - QiangJi Bao and Xiaodong Huang collected and analyzed the data and wrote the paper; QiangJi Bao and Pengxia Wang analyzed the data; QiangJi Bao and XiaoDong Huang conceived and designed this study, analyzed the data, and wrote the paper.
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Author 2 - Xiaodong Huang - QiangJi Bao and Xiaodong Huang collected and analyzed the data and wrote the paper; QiangJi Bao and XiaoDong Huang conceived and designed this study, analyzed the data, and wrote the paper.
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