

Antegrade or Retrograde Approach for the Management of Tandem Occlusions in Acute Ischemic Stroke: Protocol for a Systematic Review and Meta-Analysis

Xiao Zhang

Department of Neurosurgery, Xuanwu Hospital, Capital Medical University

Xuesong Bai

Department of Neurosurgery, Xuanwu Hospital, Capital Medical University

Xue Wang

Medical Library, Xuanwu Hospital, Capital Medical University

Wuyang Yang

Department of Neurosurgery, Johns Hopkins University School of Medicine

Jie Wang

Department of Neurosurgery, Xuanwu Hospital, Capital Medical University

Tao Wang

Department of Neurosurgery, Xuanwu Hospital, Capital Medical University

Ran Xu

Department of Neurosurgery, Xuanwu Hospital, Capital Medical University

Xia Qian

Department of Medicine, University of Florida

Yan Wang

China Medical University

Kun Yang

Department of Evidence-Based Medicine, Xuanwu Hospital, Capital Medical University

Yao Feng

Department of Neurosurgery, Xuanwu Hospital, Capital Medical University

Yan Ma

Department of Neurosurgery, Xuanwu Hospital, Capital Medical University

Yanfei Chen

Department of Neurosurgery, Xuanwu Hospital, Capital Medical University

Liqun Jiao (✉ liqunjiao@sina.cn)

Xuanwu Hospital <https://orcid.org/0000-0003-4982-6295>

Protocol

Keywords: Acute ischemic stroke, Tandem occlusions, Mechanical thrombectomy, Antegrade or retrograde approach, Systematic review, Meta-analysis

Posted Date: December 8th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-121897/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

Acute ischemic stroke (AIS) is a major contributor to global morbidity and mortality, and mechanical thrombectomy (MT) is an effective treatment for AIS. AIS caused by tandem intracranial and extracranial occlusions are not rare. Evidence for optimal MT strategy regarding order of treatment, including antegrade (extracranial first) or retrograde (intracranial first) approach is lacking. Therefore, a systematic review and meta-analysis is necessary to compare the two approaches for optimal management of tandem lesions in AIS.

Methods

This study will be performed with accordance to the PRISMA statement. Major databases including PubMed, Web of Science, Embase, and the Cochrane Library will be used for literature search. Randomized controlled trials and high-quality observational studies will be included. Risk of bias will be assessed using the Cochrane Collaboration criteria or Newcastle–Ottawa Scale according to type of study. Two reviewers will independently screen for eligible studies and perform data extraction. The primary outcomes are successful recanalization at post-intervention, and favorable outcome at 3-month follow-up. Secondary outcomes include duration of onset to arrival, onset to puncture, onset to recanalization, intracerebral hemorrhage, procedure and device related complications and mortality at 3-month follow-up. We will assess heterogeneity using the I^2 statistic. Subgroup and sensitivity analyses will be performed to explore the sources of heterogeneity. Specific results will be described in narrative form when insufficient suitable studies are available for meta-analysis.

Discussion

This study will provide a reliable evidence base for antegrade or retrograde approach for the management of tandem lesions in AIS by synthesizing evidence from current pieces of literature comparing the two approaches, and also will provide updated clinical evidence of strategy selection and decision-making for this special group of patients.

PROSPERO registration number

CRD42020199093

Background

Acute ischemic stroke (AIS) is a major contributor of global morbidity and mortality [1]. Given similar pathophysiological mechanisms, AIS caused by tandem occlusions, including a proximal extracranial occlusion in conjunction with a intracranial occlusion is not rare, reported to consist of 10%-20% of all stroke patients [1-4].

The treatment for this unique subgroup of patients is challenging. Achieving successful recanalization is still the primary goal of treatment and will increase the likelihood of favorable functional outcomes. Previous studies have shown that the rate of recanalization via intravenous tissue plasminogen activator (IV tPA) alone may be unsatisfactory [4, 5]. Recently, the superiority of mechanical thrombectomy (MT) over IV tPA was established by clinical evidences from a series of randomized controlled trials (RCTs) [1, 6-8]. MT has been established as the primary care for intracranial occlusions out of IV tPA window, and recent study have shown MT alone is non-inferior to IV tPA even within 4.5-hour window [9].

For tandem occlusions occurring both at intracranial as well as extracranial locations (commonly the carotid artery), emergent carotid artery stenting-mechanical thrombectomy approach could achieve considerably high chance of recanalization and functional independence [10, 11], and is considered an acceptable treatment modality for treatment of tandem occlusions [12, 13]. Nevertheless, evidence for optimal strategy for order or treatment including antegrade (extracranial first) and retrograde (intracranial first) approach is lacking. Although comparable outcomes between the two approaches were found in previous meta-analysis by Wilson et al [14], the majority of recruited studies were single-armed, and many studies directly comparing the two approaches were published thereafter [15-18]. Some studies still showed comparable results between the two approaches [16, 17]. In contrast, a better outcome of retrograde approach was found in the study of Maus et al and Yang et al [15, 18]. Additionally, retrograde approach was adopted as the prior choice in some centers regarding its effectiveness and safety [17, 19]. Therefore, it is necessary to summarize the current literatures comparing the two approaches for the management of tandem lesions in acute ischemic stroke, thus to provide updated clinical evidence of strategy selection and decision-making for this special group of patients.

Methods

This protocol is drafted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols (PRISMA-P) guidelines (see online **Additional file 1**. PRISMA-P Checklist) [20]. The registration of this systematic review and meta-analysis is shown on the International Prospective Register of Systematic Reviews 'PROSPERO' database (CRD42020199093). If any modification is made to this protocol, the record will be updated in PROSPERO.

Search strategy

A literature search will be performed by two independent reviewers. We will search the following databases, including MEDLINE, EMBASE, Web of Science, and the Cochrane Library, for eligible studies. We will also search WHO trail register (<https://www.who.int/ictrp/en/>), for potential studies. The preliminary search terms, including stroke, large-vessel occlusion, acute ischemic stroke, tandem occlusion, internal carotid artery occlusion, and mechanical thrombectomy, will be utilized to capture all studies eligible for inclusion. The search strategy will be presented detailly on supplementary material (see online **Additional file 2**. Search strategy).

Study selection

The study selection will strictly follow criteria from the Population, Intervention, Comparison, Outcome (PICO) Model.

Eligibility criteria

Patient

Inclusion criteria: aged 18 years or older with AIS with $\geq 70\%$ stenosis or occlusion of the extracranial internal carotid artery (ICA) and concomitant occlusion of the intracranial ICA and/or proximal middle cerebral artery (MCA). Arterial stenosis or occlusion will be confirmed by imaging examinations such as computed tomographic angiography (CTA) or digital subtraction angiography (DSA). The grade of arterial stenosis will be measured according to NASCET (North American Symptomatic Carotid Endarterectomy) criteria.

Intervention

The intervention will be antegrade approach which is defined as proximal-to-distal recanalization, with angioplasty and/or stenting of the extracranial lesion first, followed by intracranial thrombectomy [15, 18]. For this technique, a microwire followed by a microcatheter will pass the proximal occlusion at first. If difficult to cross the extracranial occlusion site, intraarterial thrombolysis or balloon dilation will be performed to relieve occlusion and establish a narrow passage so that the microwire or the microcatheter could pass through the occlusion when necessary. Then angioplasty and/or stenting will be performed at the extracranial ICA lesion. The choice of stenting will be depended on the neurointerventionists. After extracranial occlusion is recanalized, intracranial thrombectomy will be conducted in terms of stent retrieval, intra-arterial thrombolysis, angioplasty and aspiration.

Comparator

The comparator will be retrograde approach, which is defined as distal-to-proximal recanalization, with treatment of the intracranial occlusion with mechanical thrombectomy first, followed by treatment of the extracranial ICA occlusion [15, 18]. Once the proximal occlusion site was crossed with a microwire, intracranial occlusion thrombectomy was applied subsequently. Stent placement or balloon angioplasty of the extracranial ICA lesion was then performed after intracranial thrombectomy.

Outcomes

At least one of the following items should be reported:

Primary outcomes:

1. Successful recanalization defined as modified Thrombolysis in Cerebral Infarction scale (mTICI) 2b and 3, determined by post-interventional DSA

2. Favorable outcome defined as the mRS (modified Rankin Score) ≤ 2 or equal to pre-stroke score at 3-month follow-up

Secondary outcomes:

1. Mean times of onset to arrival, onset to puncture, and onset to recanalization
2. Intracerebral hemorrhage (ICH) defined as intracranial hemorrhage on imaging and a minimum increase of 4 points on the National Institutes of Health Stroke Scale (NIHSS) within 24 hours post-intervention, in accordance with the second European Australasian Acute Stroke Study classification (ECASS II) [21]
3. Procedure and device related complications: arterial dissection, arterial perforation, stent fracture or stent deployment failure
4. Mortality at 3-month follow-up

Study type

RCTs and observational studies (cohort studies, case-control studies) will be included. The inclusion of observational studies is to gather sufficient data for outcome evaluation and to minimize the type-II errors that can result from the lack of statistical power found in sole RCTs [22].

Exclusion criteria

1. Patients' age less than 18 years old
2. Patients with intracranial hemorrhage, significant cerebellar mass effect, and acute hydrocephalus on computed tomography or magnetic resonance imaging before stroke.
3. No report about aforementioned outcomes or an inability to extract the exact number of complications.
4. Unsuitable study types, such as case series report, and studies with unavailable full text.

Data selection and analysis

Selection of studies

Two reviewers (RX and XQ) will screen and select the eligible studies, independently. First, the reviewers will screen titles, keywords, and abstracts among the initial searched studies, and the irrelevant studies will be excluded. We will then acquire the full texts of the rest of studies. Next, the reviewers will check the full-texted studies to evaluate their included eligibility and document the reasons for study exclusion. When data from the same trial are reported in more than one article, we will select the most recent study. A third reviewer (TW) will help to resolve any disagreements between the former two reviewers.

Data collection

Software of EndNote X9 (Clarivate Analytics, Philadelphia, USA) will be used for the management of included studies. A standardized form will be used for data extraction by two reviewers (YW and YF), independently. The extracted data will include the following information:

1. Study characteristics, such as type of study, authors, year of publication, sample size, and number of patients.
2. Patient characteristics, such as mean age, gender, medical history, site of occlusion, baseline NIHSS (National Institutes of Health Stroke Scale) score and the numbers of patients treated with IV thrombolysis.
3. Intervention characteristics, such as the time of onset to puncture or recanalization, numbers of patients treated with angioplasty or stent alone, numbers of patients treated antegrade or retrograde approach first.
4. The aforementioned primary and secondary outcomes.

Discrepancy in data extraction between two reviewers will be resolved by a third reviewer (TW) when it cannot be settled by discussion. For unclear or missing data, we will contact the corresponding authors via email. If no responses after two emails, we will exclude this study for meta-analysis and record this case in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow chart [23].

Risk of bias assessment

Two review authors (KY and YM) will independently assess risk of bias in each included study. Reviewers will use risk of bias 2.0 tool of the Cochrane Collaboration criteria for RCTs and quasi-experimental studies, the Newcastle-Ottawa Scale (NOS, see **Additional file 3**) for observational studies including cohort study and case control study, and the Methodological Quality and Synthesis of Case Series and Case Reports for case series, respectively [24-26]. The following seven domains will be used as criteria to assess the risk of bias for RCTs and quasi-experimental studies:

- Random sequence generation
- Allocation concealment
- Blinding of participants and personnel
- Blinding of outcomes assessments
- Incomplete outcome data
- Selective outcome report
- Other possible bias

The risk of bias for observational studies will be assessed by three domains including selection, compatibility and exposure. Each domain of included studies will be given a score based on the risk of bias. We will rank the level of risk of bias as low, unclear or high, and provide information from the study

report together with a justification for our judgment in the 'Risk of bias' tables [27]. If there is opinion disagreement between the two reviewers, initial face-to-face discussion will be performed. Also, further team group discussion will be held if necessary.

Measures of treatment effect and data synthesis

Data analysis for outcomes of antegrade or retrograde approach for the management of tandem lesions in AIS is practical when there are two or more studies accessible for a specific variable. The data analysis will be performed using Stata statistical software (version 15.0, Stata Corp, College station, Texas, USA). Treatment effect will be reported as relative risk (RR) with 95% CIs (confidence intervals) because most of the outcomes are dichotomous data. For continuous variables such as mean time of onset to recanalization, we will use mean differences (MDs) with 95% CIs. A narrative presentation of the study results will be provided under circumstance of lacking data.

Assessment of clinical and methodological heterogeneity

Assessment of heterogeneity

Heterogeneity will be measured with the I^2 statistic before any outcome is pooled. The heterogeneity of mild (<40%), moderate (40–60%), or substantial (>60%) will be graded depending on the pooled results. On condition that the results with substantial heterogeneity and sufficient number of included trials, we will use subgroup analysis to examine the reasonable origins of heterogeneity, which may include different study locations, patient characteristics, and endovascular treatments. Sensitivity analysis is also utilized to appreciate studies with high risk of bias through step-wise exclusion of studies and observation of combined bias in remaining studies.

Assessment of reporting biases

We will conduct a thorough protocol review of the included studies to evaluate reporting biases. Funnel plot and Egger's regression tests are suitable for assessing publication bias if the included studies exceed 10 [28]. If the included studies are less than 10, we will solely assess reporting bias qualitatively based on the characteristics of the included studies.

Assessment of pooled effect estimates

When the heterogeneity of results is high (>60%) in included studies, the DerSimonian and Laird method for random model will be applied; otherwise, the Mantel-Haenszel method for mixed model will be performed [29]. Statistical significance is defined at $p < 0.05$.

We will evaluate the quality of evidence contributing to pooled effect estimates of the main outcomes with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for observational studies and the principle of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for RCTs [30, 31]. We will use methods and recommendations described

in the *Cochrane Handbook for Systematic Reviews of Intervention* and the GRADEpro GDT software [27]. Eventually, we will construct a table summarizing the overall study results.

Discussion

The present study aims to provide a reliable evidence base for antegrade or retrograde approach for the management of tandem lesions in AIS by synthesizing evidence from current pieces of literature comparing the two approaches. Tandem vascular occlusions, including a proximal extracranial occlusion in conjunction with a downstream intracranial occlusion is not rare for patients with AIS. Currently, MT seems to be an effective technique for treating tandem vascular occlusions of AIS. However, tailored evidence for the optimal treatment order between antegrade and retrograde approach remain inconsistent and contradictory among studies and need to be clarified. However, some limitations may exist. For example, heterogeneity among studies may be inevitable. In addition, most studies may be observational in nature and RCTs are rare. However, this study will provide updated clinical evidence of strategy selection and decision-making for this special group of patients, and will definitely be helpful in summarizing the current clinical evidence and guiding future studies.

Abbreviations

AIS, acute ischemic stroke; IV tPA, intravenous tissue plasminogen activator; MT, mechanical thrombectomy; RCTs, randomized controlled trials; PRISMA-P, Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols; PICO, Population, Intervention, Comparison, Outcome; CTA, tomography angiography; MRA, magnetic resonance angiography; DSA, digital subtraction angiography; NASCET, North American Symptomatic Carotid Endarterectomy; ICA, internal carotid artery; MCA, middle cerebral artery; mTICI, modified Thrombolysis in Cerebral Infarction scale; mRS, modified Rankin Score; ICH, intracerebral hemorrhage; ECASS II, the second European Australasian Acute Stroke Study classification; NIHSS, National Institutes of Health Stroke Scale; NOS, Newcastle Ottawa Scale; RR, relative risk; CI, confidence interval; MDs, mean differences; GRADE, Grading of Recommendations Assessment, Development, and Evaluation

Declarations

Acknowledgements

NA

Authors' contributions

XZ, XB, YC and LJ contributed to the initial idea for this study. WT, XW, XZ, RX, XQ, YW and YF developed and revised the search strategy. XB, XZ, XW and WY completed the study design. YM, YC and LJ contributed to consults about clinical issues. XZ, XB, XW, WY, JW and LJ contributed to the original draft.

YM, YC, LJ and KY contributed to the revision of the draft. XZ, XB, and XW contributed equally to this article. All of the authors approved the final work prior to submission.

Funding

This work was supported by the Ministry of Science and Technology of the People's Republic of China (2016YFC1301700) and the Beijing Scientific and Technologic Project (Z201100005520019).

Availability of data and material

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

References

1. Goyal M, Menon BK, van Zwam WH, Dippel DWJ, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CBLM, van der Lugt A, de Miquel MA *et al*: Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *The Lancet* 2016, 387(10029):1723-1731.
2. Mpotsaris A, Kabbasch C, Borggrefe J, Gontu V, Soderman M: Stenting of the cervical internal carotid artery in acute stroke management: The Karolinska experience. *Interventional neuroradiology : journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences* 2017, 23(2):159-165.
3. Grau AJ, Weimar C, Bugge F, Heinrich A, Goertler M, Neumaier S, Glahn J, Brandt T, Hacke W, Diener HC: Risk factors, outcome, and treatment in subtypes of ischemic stroke: the German stroke data bank. *Stroke* 2001, 32(11):2559-2566.
4. Rubiera M, Ribo M, Delgado-Mederos R, Santamarina E, Delgado P, Montaner J, Alvarez-Sabin J, Molina CA: Tandem internal carotid artery/middle cerebral artery occlusion: an independent predictor of poor outcome after systemic thrombolysis. *Stroke* 2006, 37(9):2301-2305.
5. Christou I, Felberg RA, Demchuk AM, Burgin WS, Malkoff M, Grotta JC, Alexandrov AV: Intravenous tissue plasminogen activator and flow improvement in acute ischemic stroke patients with internal

- carotid artery occlusion. *J Neuroimaging* 2002, 12(2):119-123.
6. Campbell BCV, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, Yan B, Dowling RJ, Parsons MW, Oxley TJ *et al*: Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection. *New England Journal of Medicine* 2015, 372(11):1009-1018.
 7. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJ *et al*: A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015, 372(1):11-20.
 8. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, McTaggart RA, Torbey MT, Kim-Tenser M, Leslie-Mazwi T *et al*: Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging. *N Engl J Med* 2018, 378(8):708-718.
 9. Yang P, Zhang Y, Zhang L, Zhang Y, Treurniet KM, Chen W, Peng Y, Han H, Wang J, Wang S *et al*: Endovascular Thrombectomy with or without Intravenous Alteplase in Acute Stroke. *The New England journal of medicine* 2020, 382(21):1981-1993.
 10. Papanagiotou P, Haussen DC, Turjman F, Labreuche J, Piotin M, Kastrup A, Steglich-Arnholm H, Holtmannspotter M, Taschner C, Eiden S *et al*: Carotid Stenting With Antithrombotic Agents and Intracranial Thrombectomy Leads to the Highest Recanalization Rate in Patients With Acute Stroke With Tandem Lesions. *JACC Cardiovasc Interv* 2018, 11(13):1290-1299.
 11. Sadeh-Gonik U, Tau N, Friehmann T, Bracard S, Anxionnat R, Derelle AL, Tonnelet R, Liao L, Richard S, Armoiry X *et al*: Thrombectomy outcomes for acute stroke patients with anterior circulation tandem lesions: a clinical registry and an update of a systematic review with meta-analysis. *Eur J Neurol* 2018, 25(4):693-700.
 12. Zhu F, Bracard S, Anxionnat R, Derelle AL, Tonnelet R, Liao L, Mione G, Humbertjean L, Lacour JC, Hossu G *et al*: Impact of Emergent Cervical Carotid Stenting in Tandem Occlusion Strokes Treated by Thrombectomy: A Review of the TITAN Collaboration. *Front Neurol* 2019, 10:206.
 13. Anadani M, Spiotta AM, Alawieh A, Turjman F, Piotin M, Haussen DC, Nogueira RG, Papanagiotou P, Siddiqui AH, Lapergue B *et al*: Emergent Carotid Stenting Plus Thrombectomy After Thrombolysis in Tandem Strokes: Analysis of the TITAN Registry. *Stroke* 2019, 50(8):2250-2252.
 14. Wilson MP, Murad MH, Krings T, Pereira VM, O'Kelly C, Rempel J, Hilditch CA, Brinjikji W: Management of tandem occlusions in acute ischemic stroke - intracranial versus extracranial first and extracranial stenting versus angioplasty alone: a systematic review and meta-analysis. *Journal of neurointerventional surgery* 2018, 10(8):721-728.
 15. Yang D, Shi Z, Lin M, Zhou Z, Zi W, Wang H, Hao Y, Guo F, Liu W, Xu G *et al*: Endovascular retrograde approach may be a better option for acute tandem occlusions stroke. *Interventional neuroradiology : journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences* 2019, 25(2):194-201.
 16. Neuberger U, Moteva K, Vollherbst DF, Schönenberger S, Reiff T, Ringleb PA, Bendszus M, Pfaff JAR, Möhlenbruch M: Tandem occlusions in acute ischemic stroke - impact of antithrombotic medication

- and complementary heparin on clinical outcome and stent patency. *Journal of neurointerventional surgery* 2020.
17. Eker OF, Bühlmann M, Dargazanli C, Kaesmacher J, Mourand I, Gralla J, Arquizan C, Fischer UM, Gascou G, Heldner M *et al*: Endovascular Treatment of Atherosclerotic Tandem Occlusions in Anterior Circulation Stroke: Technical Aspects and Complications Compared to Isolated Intracranial Occlusions. *Frontiers in neurology* 2018, 9:1046.
 18. Maus V, Borggrefe J, Behme D, Kabbasch C, Abdullayev N, Barnikol UB, Yeo LLL, Brouwer PA, Söderman M, Möhlenbruch M *et al*: Order of Treatment Matters in Ischemic Stroke: Mechanical Thrombectomy First, Then Carotid Artery Stenting for Tandem Lesions of the Anterior Circulation. *Cerebrovascular diseases (Basel, Switzerland)* 2018, 46(1-2):59-65.
 19. Rodrigues M, Cunha A, Figueiredo S, Carvalho A, Veloso M, Barros P, Gregório T, Paredes L, Pinho J, Castro S *et al*: Emergent carotid artery stenting in atherosclerotic disease of the internal carotid artery with tandem intracranial occlusion. *Journal of the neurological sciences* 2018, 387:196-198.
 20. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ (Clinical research ed)* 2015, 350:g7647.
 21. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, Larrue V, Bluhmki E, Davis S, Donnan G *et al*: Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian Acute Stroke Study Investigators. *Lancet (London, England)* 1998, 352(9136):1245-1251.
 22. Bai X, Feng Y, Yang K, Wang T, Luo J, Wang X, Ling F, Ma Y, Jiao L: Extracranial-intracranial bypass surgery for occlusive atherosclerotic disease of the anterior cerebral circulation: protocol for a systematic review and meta-analysis. *Systematic reviews* 2020, 9(1):70.
 23. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *International journal of surgery (London, England)* 2010, 8(5):336-341.
 24. Lo CK, Mertz D, Loeb M: Newcastle-Ottawa Scale: comparing reviewers' to authors' assessments. *BMC medical research methodology* 2014, 14:45.
 25. Murad MH, Sultan S, Haffar S, Bazerbachi F: Methodological quality and synthesis of case series and case reports. *BMJ evidence-based medicine* 2018, 23(2):60-63.
 26. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ (Clinical research ed)* 2011, 343:d5928.
 27. Higgins J, Green S: *Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0*. The Cochrane Collaboration. 2013.
 28. Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, Carpenter J, Rücker G, Harbord RM, Schmid CH *et al*: Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ (Clinical research ed)* 2011, 343:d4002.

29. Zhang X, Yu Y, Yang K, Bai X, Wang T, Feng Y, Xu R, Yang B, Wang X, Jiao L *et al*: Clinical outcomes of radiation-induced carotid stenosis: A systematic review and meta-analysis. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association* 2020, 29(8):104929.
30. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ (Clinical research ed)* 2007, 335(7624):806-808.
31. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ: GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ (Clinical research ed)* 2008, 336(7650):924-926.

Figures

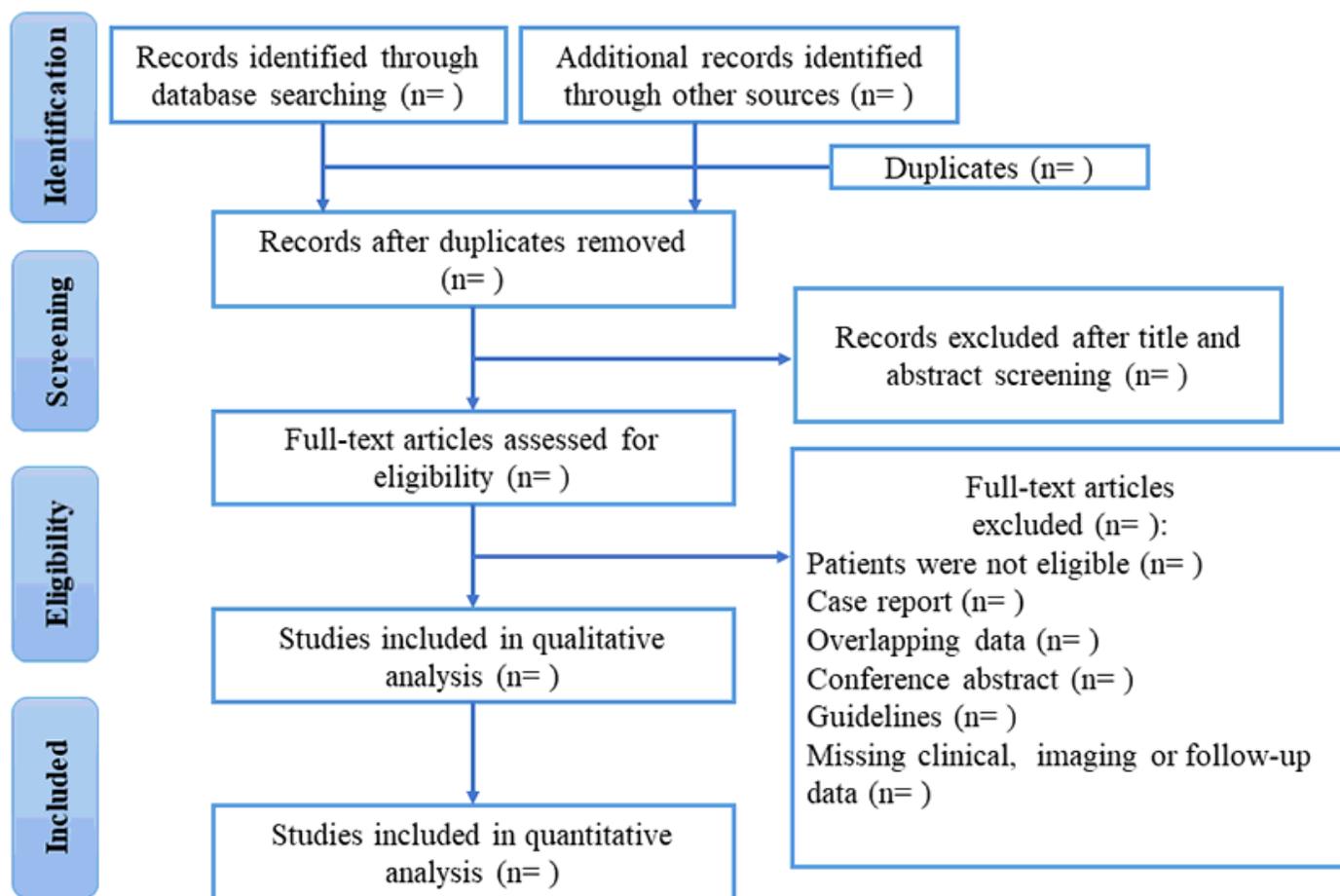


Figure 1

Flow diagram of literature for systematic review and meta-analysis.

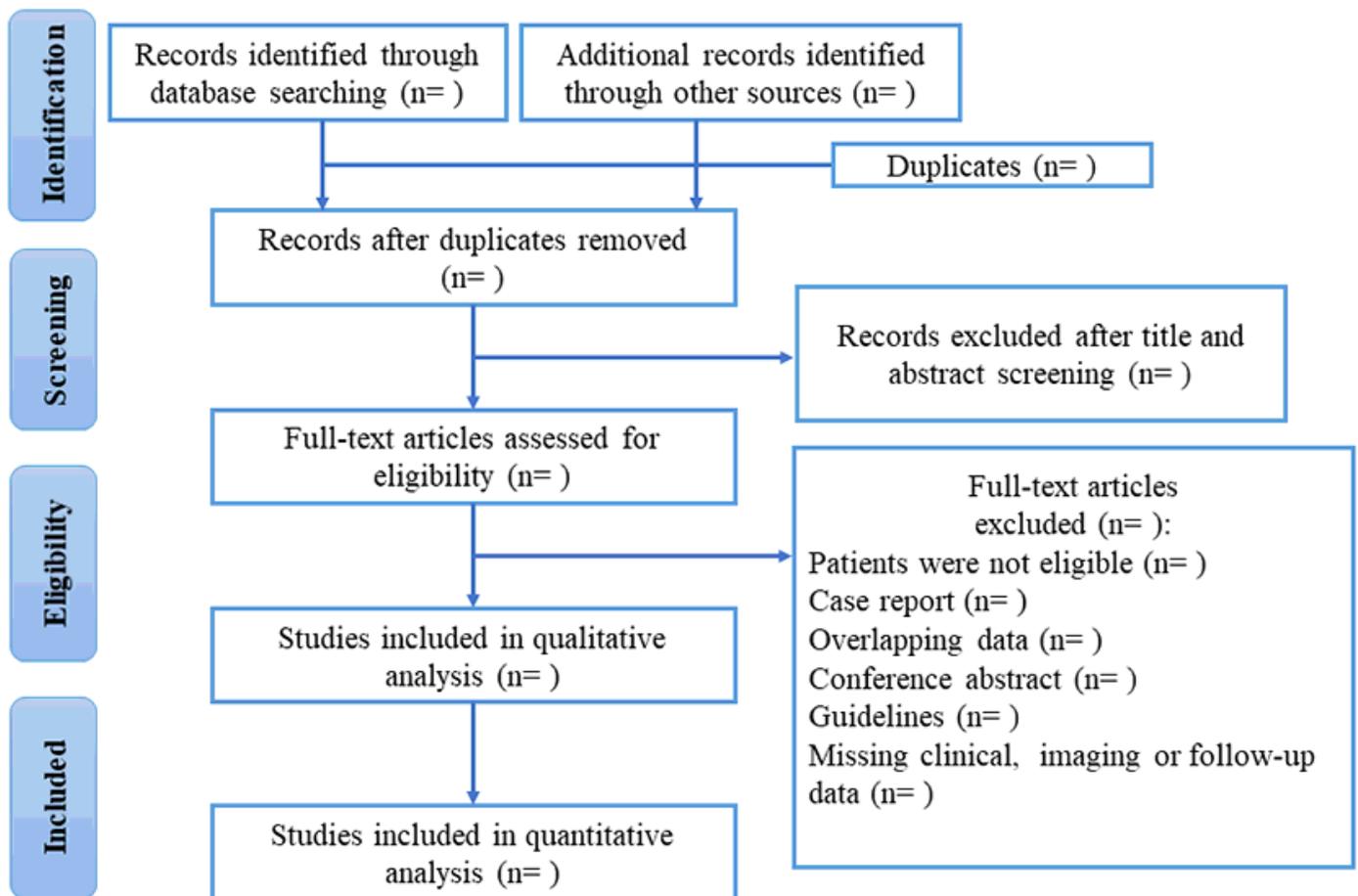


Figure 1

Flow diagram of literature for systematic review and meta-analysis.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Additionalfile1.PRISMAPchecklist.docx](#)
- [Additionalfile1.PRISMAPchecklist.docx](#)
- [Additionalfile2.Searchstrategy.docx](#)
- [Additionalfile2.Searchstrategy.docx](#)
- [Additionalfile3.NOS.docx](#)
- [Additionalfile3.NOS.docx](#)