INPLASY PROTOCOL

To cite: Bao et al. Implications of frailty in acute ischemic stroke receiving endovascular treatment: systematic review & meta-analysis. Inplasy protocol 202290013. doi: 10.37766/inplasy2022.9.0013

Received: 03 September 2022

Published: 03 September 2022

Corresponding author:
Mingfei Yang

iloveyoucmu@163.com

Author Affiliation:
Qinghai Provincial People's Hospital.

Support: **No. 2021-wjzd-01.**

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

Conflicts of interest:
None declared.

Implications of frailty in acute ischemic stroke receiving endovascular treatment: systematic review & meta-analysis

Bao, QJ[1]; Wu, XT[2]; Chen, SJ[3]; Zhang, JN[4]; Li, J[5]; Yang, MF[6].

Review question / Objective: **P: acute ischemic stroke patients I endovascular treatment C with frailty vs without frailty O mortality , poor function outcome S pro, restro.**
Condition being studied: **Frailty is a state of cumulative degradation of physical function that is consistently associated with poor outcomes following illness in older people. However, our knowledge about the relationship between frailty, stroke and stroke interventions outcomes is limited.**
Eligibility criteria: **Study inclusion criteria were as follows: 1) Studies reporting the relationship of frailty and AIS received EVT outcome; 2) Studies reporting patients who had suffered stroke (any stroke subtype, but not including hemorrhagic stroke, transient ischaemic attack, subarachnoid or subdural haemorrhage); 3) Studies focusing on human data; 4) Studies published in English.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 September 2022 and was last updated on 03 September 2022 (registration number INPLASY202290013).

INTRODUCTION

Review question / Objective: **P: acute ischemic stroke patients I endovascular treatment C with frailty vs without frailty O mortality , poor function outcome S pro, restro.**

Rationale: **We aimed to estimate the prevalence of frailty and examine associations with poor functional outcome and mortality in acute ischemic stroke (AIS) recevied endovascular treatment(EVT).**

Condition being studied: **Frailty is a state of cumulative degradation of physical function that is consistently associated**

with poor outcomes following illness in older people. However, our knowledge about the relationship between frailty, stroke and stroke interventions outcomes is limited.

METHODS

Search strategy: #1. (Frail[ti:ab]) OR (frailty[ti:ab]) 31027
#2. "Cerebrovascular Disorders"[MH]
#3. "Brain Ischemia"[MH] OR "Hypoxia-Ischemia, Brain"[MH] OR "Ischemic Attack, Transient"[MH]
#4. "Stroke"[MH] OR "Stroke, Lacunar"[MH] OR "Infarction, Posterior Cerebral Artery"[MH] OR "Brain Stem Infarctions"[MH] OR "Infarction, Middle Cerebral Artery"[MH] OR "Infarction, Anterior Cerebral Artery"[MH] 412140
#5. Stroke[ti:ab] OR cerebr* vascul* infarct*[ti:ab] OR cerebrovasc* infarct*[ti:ab] OR cerebr* vasc* event*[ti:ab] OR cerebrovasc* event*[ti:ab] OR cva [ti:ab] OR transient ischemic attack*[ti:ab] OR tia[ti:ab] 319513
#6. #2 OR #3 OR #4 OR #5 561608
#7. "Thrombolytic Therapy"[MH] OR thromboly* therap*[ti:ab] 39886
#8. "Fibrinolysis"[MH] OR fibrinoly*[ti:ab] 42154
#9. “tPA” [ti:ab] OR “t-PA”[ti:ab] OR “rtPA” [ti:ab] OR “rt-PA” [ti:ab] OR “IV-tPA” [ti:ab] OR “IV rt-PA” [ti:ab] 33088
#10. “alteplase” [ti:ab] OR “actilyse” [ti:ab] OR “activase” [ti:ab] OR “alteplasi” [ti:ab] OR “alteplasum”[ti:ab] OR “alteplasum” [ti:ab] OR “cathflo activase”[ti:ab] OR “GRTPA”[ti:ab] OR “SRT-PA”[ti:ab] OR “CAS Registry Number 105857-23-6”[ti:ab] OR “RN: 105857-23-6”[ti:ab] 3205
#11. #7 OR #8 OR #9 OR #10
102864
#12.Humans [MH] 20651871
#13. #1 AND #6 AND #11 AND #12
957
Embase:
#1 'frail elderly'/exp OR 'frailty'/exp 30741
#2. 'brain infarction'/exp OR 'brain ischemia'/exp OR 'cerebrovascular accident'/exp OR 'cerebral artery disease'/exp OR 'occlusive cerebrovascular disease'/exp 600023
#3. 'lacunar stroke'/exp OR 'middle cerebral artery occlusion'/exp OR ('brain artery'/exp AND 'artery occlusion'/exp) 32541
#4.'brain ischemia':ti,ab,kw OR 'cerebral ischemia':ti,ab,kw OR 'ischemic attack':ti,ab,kw OR 'transient ischemic attack':ti,ab,kw OR 'ischemic stroke':ti,ab,kw OR 'cerebral infarction':ti,ab,kw 167675
#5. #2 OR #3 OR #4 615873
#6. 'plasminogen activator'/exp OR 'fibrinolysis'/exp OR 'tissue plasminogen activator'/exp 145900
#7. 'fibrinolytic agents':ti,ab,kw OR 'anti thrombin':ti,ab,kw OR 'tissue plasminogen activator':ti,ab,kw OR 'intravenous tissue plasminogen activator':ti,ab,kw OR 'IV tissue plasminogen activator':ti,ab,kw OR 'IV recombinant tissue plasminogen activator':ti,ab,kw OR 'Recombinant human tissue-type plasminogen activator':ti,ab,kw 21886
#8. 'tPA':ti,ab,kw OR 't-PA':ti,ab,kw OR 'rtPA':ti,ab,kw OR 'rt-PA':ti,ab,kw OR 'IV-tPA':ti,ab,kw OR 'IV rt-PA':ti,ab,kw 46107
#9. 'alteplase':ti,ab,kw OR 'actilyse':ti,ab,kw OR 'activase':ti,ab,kw OR 'alteplasi':ti,ab,kw OR 'alteplasum':ti,ab,kw OR 'alteplasum':ti,ab,kw OR 'cathflo activase':ti,ab,kw OR 'SRT-PA':ti,ab,kw OR 'UNII-1RXS4UE564':ti,ab,kw 5593
#10. #6 OR #7 OR #8 OR #9 170468.

Participant or population: Acute ischemic stroke.

Intervention: Endovasculartreatment.

Comparator: With frailty vs without frailty

Study designs to be included: We conducted a systematic review of the relationship between frailty and AIS recevied EVT. Paired researchers searched 3 databases (Pubmed, EMBASE, and Cochrane) from inception until August 2022. The effect value was evaluated by random-effects meta-analyses, pooled Odds Ratio (OR) and 95% confidence intervals (95%CI).

Eligibility criteria: Study inclusion criteria were as follows: 1) Studies reporting the

relationship of frailty and AIS received EVT outcome; 2) Studies reporting patients who had suffered stroke (any stroke subtype, but not including hemorrhagic stroke, transient ischaemic attack, subarachnoid or subdural haemorrhage); 3) Studies focusing on human data; 4) Studies published in English.

Information sources: Two independent researchers(Bao QJ and Wu XT) systematically retrieved three databases (PubMed, EMBASE, and Cochrane).

Main outcome(s): We finally included 10 studies comprising 3662 non-overlapping participants. Six studies used a clinical frailty scale(CFS),two studies used Hospital Frailty Risk Scores(HFRS), two studies used frailty index. The frailty prevalence ranged (HFRS: 21%; 95% CI, -0.01-0.42; CFS: 38%; 95% CI, 0.28-0.47; low quality evidence, downgraded due to heterogeneity, bias). In unadjusted analyses, poor functional outcome (5 studies, odds ratio[OR] 1.456, 95% CI 1.161-1.827), mortality (11 studies, OR 2.653, 95% CI 1.878-3.748) were significantly associated with frailty. In adjusted analyses, poor functional outcome (4 studies, ORadj 1.182, 95% CI 1.033-1.351), mortality (3 studies, ORadj 1.154, 95% CI 1.001-1.331) were significantly associated with frailty.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa scale was assessed risk of bias of the cohort studies. The risk of outcome bias was considered as moderate. The overall score of Newcastle-Ottawa scale was considered to represent an overall high quality. The detailed were displayed in supplementary materials 3. Funnel plot inspection revealed no evidence of asymmetry in studies reporting the unadjusted outcomes (supplementary materials 4).

Strategy of data synthesis: To calculate the summary revalence estimates, frailty was classified by us as a binary variable. Where a Hospital Frailty Risk Score(HFRS) used hierarchical categorisation, we classified the most severe as frail. We also collected data on pre-frailty, indicators of outcome after receiving intravenous thrombolysis odds ratios (OR) and different frailty tool. Where OR receiving intravenous thrombolysis was not reported in the original paper, we derived a 95% confidence interval (95%CI) and OR using sample size. We used random effects models to perform the analysis with Comprehensive Meta-Analysis (CMA version 3.0) and Reviwe manager (Revman 5.3) and generate a summary estimate of frailty prevalence, adverse outcomes risk(unadjusted, adjusted data) pooled across the included studies using random effects models. We considered a 2-tailed value of $p < 0.05$ as statistically significant. For the qualitative interpretation of heterogeneity, $I2 > 50\%$ and $I2 > 75\%$ were considered substantial and considerable heterogeneity, respectively[11]. A funnel plot was evaluated publication bias across individual studies, while funnel plot asymmetry was assessed using the Egger linear regression test with a $p < 0.10$ significance level.

Subgroup analysis: We additionally evaluated those studies based on different death time. We found that frailty was associated with 1 month mortality(5 studies; OR 1.998, 95% CI, 1.290–3.094, p = 0.002, I2 =69.072%), 3 month mortality(3 studies; OR 4.719, 95% CI, 2.652–8.398, p = 0.000, I2 =46.271%) No significant associations were observed for 12 month mortality(3 studies; OR 3.812, 95% CI, 0.780–18.623, p = 0.098, I2 =80.511%) Unfortunately, no statistical significance was observed for a lower odds of pooled mortality in 12 month (supplementary materials 5).

Sensitivity analysis: We performed additional analyses for the adjusted associations, stratified by assess frailty tool (CFS, HFRS, frailty index). We removed a study[14] from mortality and poor function outcome group. The heterogeneity of mortality and poor function outcome was reduced, which was 0% and 14.663%, respectively. The results indicated statistically significant difference. We believe that the results of the removed

articles may be different due to the different frailty assess tool, which can lead to the differences in results (Supplementary materials 6).

Language restriction: English.

Country(ies) involved: Qinghai Provincial People's Hospital, China.

Keywords: stroke, frailty, endovascular treatment, outcome, metaanalysis.

Contributions of each author:

Author 1 - QiangJi Bao.
Email: b94960218@163.com
Author 2 - XinTing Wu.
Email: 1582123670@qq.com
Author 3 - ShuJun Chen.
Email: 2627073402@qq.com
Author 4 - JingNi Zhang.
Email: zhangjingni1985@163.com
Author 5 - Jing Li.
Email: 1043249788@qq.com
Author 6 - MingFei Yang.
Email: iloveyoucmu@163.com