Stroke: Vascular and Interventional Neurology

## ORIGINAL RESEARCH

# Outcomes of Mechanical Thrombectomy in Patients With Ischemic Stroke and Heart Failure. A Systematic Review and Meta-analysis

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**BACKGROUND:** Patients with heart failure (HF) treated with mechanical thrombectomy (MT) for acute ischemic stroke were under-represented in clinical trials on MT. Our systematic review and meta-analysis aim to assess differences in outcomes between patients with HF and their counterparts without HF treated with MT for acute ischemic stroke.

**METHODS:** A systematic review of the English language literature from inception up to March 7, 2024, was conducted using PubMed, Embase, Cochrane Library, and Web of Science databases. Studies focused on patients with and without HF who were treated with MT for acute ischemic stroke were included. The primary outcome of interest was the rate of modified Rankin Scale scores of 0–2 at 90 days. Secondary outcomes of interest included rates of 90-day mortality, successful reperfusion, and symptomatic intracranial hemorrhage.

**RESULTS:** Of 5394 initially retrieved studies, 5 studies were included in the systematic review with a final population of 44 385 patients with ischemic stroke with and without HF treated with MT. Four studies were combined for the primary outcome and showed comparable rates of 0–2 modified Rankin Scale scores between patients with HF and patients without HF (odds ratio, 0.86 [95% CIs, 0.70–1.06]; $P = 0.15$). Ninety-day mortality was significantly higher in the HF group (odds ratio, 1.92 [95% CIs, 1.66–2.23]; $P<0.0001$) although the sample size was small (n of study = 3) and only unadjusted estimates were used. Successful reperfusion and symptomatic intracranial hemorrhage rates were similar between the groups.

**CONCLUSION:** In this systematic review and meta-analysis, patients with HF experienced worse 90-day mortality post-MT. Our data encourage further research on MT outcomes in patients with large vessel-occlusion ischemic stroke and concomitant HF.

**Key Words:** heart failure ■ ischemic stroke ■ mechanical thrombectomy



Heart failure (HF) is a clinical syndrome associated with high mortality and morbidity rates in survivors of stroke.[1–5] Indeed, up to 24% of patients with stroke present with HF, and acute ischemic stroke is reported to be caused by HF in at least 9% of stroke cases.[6,7] HF can increase the risk

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of stroke because of thromboembolic complications associated with reduced ejection fraction, progressive left ventricular dilatation, and cardiac remodeling.[8–10] In addition, HF and stroke share common risk factors such as hypertension, atrial fibrillation, coronary artery disease, obesity, and diabetes.[11–13] Mechanical thrombectomy (MT) is the gold standard of care to treat patients with acute ischemic stroke with large vessel occlusion (LVO), irrespective of the cause.[14] Previous studies showed conflicting data on outcomes of acute ischemic stroke patients with HF compared with patients without HF undergoing MT.[15–22] Additionally, patients with HF were generally underrepresented in the large clinical trials on MT (eg, ESCAPE [Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke], REVASCAT [Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting Within Eight Hours of Symptom Onset).[23,24] Therefore, understanding differences in outcomes between patients with HF versus without HF receiving MT is clinically relevant. Although individual studies have compared outcomes between patients with HF versus without HF receiving MT for acute ischemic stroke due to LVO, a systematic appraisal of the existing body of evidence to quantify these outcomes between these 2 populations is lacking.

We conducted a systematic review and meta-analysis of studies that reported outcomes among patients with HF and without HF who underwent MT for acute ischemic stroke due to anterior circulation LVO, aimed to compare procedural and functional outcomes between these 2 patient populations.



## Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **LVO** | large vessel occlusion |
| **mRS** | modified Rankin Scale |
| **MT** | mechanical thrombectomy |

## CLINICAL PERSPECTIVE

- This study underscores that while mechanical thrombectomy is equally effective in achieving functional independence (mRS 0–2) and successful reperfusion (mTICI $\geq$ 2b) in patients with ischemic stroke with and without heart failure (HF), patients with HF face significantly higher 90-day mortality.
- The findings highlight the need for heightened post-stroke care and tailored management strategies in patients with HF, as their higher mortality risk may stem from systemic complications, comorbidities, and HF-related pathophysiology. Despite their underrepresentation in major mechanical thrombectomy trials, these results affirm that mechanical thrombectomy is a viable treatment option for patients with HF with acute ischemic stroke.
- Future efforts should focus on prospective studies to better stratify risks by HF subtype and severity, while implementing multidisciplinary care pathways to address both cardiac and neurovascular complications. This integrated approach could improve survival and recovery outcomes in this high-risk population.

## METHODS

Data can be shared upon reasonable request. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Meta-analysis of Observational Studies in Epidemiology guidelines[25,26] were used to draft the manuscript. The study protocol was pre-registered on the International Prospective Register of Systematic Reviews platform on April 17, 2024, under registration code CRD42024525773[https://www.crd.york.ac.uk/prospero/display_record.php?ID = CRD42024525773].

### Eligibility Criteria

Studies comparing outcomes of ischemic stroke due to LVO treated with MT (with or without intravenous thrombolysis) in patients with HF versus without HF, regardless of sex, age, etiology, and severity of HF were included. HF was defined when showing a reduced ejection fraction (EF) <55% in the echocardiography by Schnieder et al.[9]; Tan et al.[27] as a reduced ejection fraction <50% in the echocardiography; Gentile et al.[21] defined HF with preserved left ventricular EF (LVEF) if LVEF was ≥50%, with reduced LVEF if LVEF was <40%, and with mild-range LVEF if LVEF was in the range 40%–49%. Randomized controlled trials, observational studies (including cohort and case-control designs), and case series were considered, as we expected that patients with HF would be underrepresented in randomized controlled trials. Only studies reporting at least the primary outcome (ie, modified Rankin Scale [mRS] score at 3 months) were included, whereas no restriction was made for secondary endpoints.

### Search Strategy and Study Selection

PubMed, Embase, Cochrane Library, and Web of Science were searched from inception up to March 7, 2024. We developed the search query using a combination of 3 index terms ("ischemic stroke," "thrombectomy," and "heart failure") following an optimized method for systematic search creation[28]: briefly, the query was built using Embase-specific syntax, then refined based on initial results, and finally translated to the remaining databases (see also Table S1 for complete research strings). All publication types were included, and only manuscripts in English were considered. A backward and forward citation analysis was conducted after search completion using *citationchaser*.[29]

### Data Collection

Screening by title, abstract, and full text was conducted independently by 3 authors (L.A., F.B., and G.M.), and any discrepancy was resolved by consensus. Data extraction was piloted on 3 studies, and general study characteristics, primary, and secondary outcomes were collected where available.

### Risk of Bias and Quality of Evidence Assessment

Because only observational studies were finally included, risk of bias was evaluated by 2 authors (L.A., G.M.) independently using the Newcastle-Ottawa scale for observational studies (Table S2). Publication bias was assessed through funnel plots and Egger's test, and quality of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system. Given the exclusive inclusion of observational studies in our meta-analyses, we adopted the GRADE approach for prognostic studies.[30] A GRADE table was prepared using the GRADEPro tool.

### Outcome Measures

The primary outcome of interest was good functional independence at 90 days after stroke defined by a mRS score $\leq$2. Secondary outcomes included mortality at 90 days and successful reperfusion defined by a modified thrombolysis in cerebral infarction scale levels 2b, 2c, or 3. The occurrence of symptomatic intracranial hemorrhage post procedure was considered as the safety outcome according to the study definitions.[31–33]

### Statistical Analysis

We used a random-effects model to calculate the pooled treatment effect, and heterogeneity was assessed using the Cochran's *Q* ($P<0.05$) and $I^2$ statistic (<40% low, 40–60% moderate, >60% substantial). Effect estimates were expressed as odds ratios (ORs) with 95% CIs (95% CIs). Adjusted ORs were preferentially used where available, otherwise absolute counts and corresponding unadjusted OR were reported. Heterogeneity was explored through influence analysis, sequentially omitting each study. Statistical analysis was conducted using RStudio (version 2024.04) with *Meta* and *Metafor* packages. Significance level was set at 0.05.

# RESULTS

## Study Inclusion and Characteristics

The initial search identified 5394 articles, and after screening by title, abstract, and full text reading of eligible manuscripts, 5 studies were included in the systematic review (Figure 1); the backward-forward citation analysis based on the included studies did not add any new entry. We included 1 conference abstract,[34] considering the limited number of studies available on the topic and the conflicting results.[35] Overall, only observational studies were selected, with a final population of 44 385 patients with ischemic stroke with and without HF treated with MT. One study reported data from a national database in the United States.[20] There were 7901 patients with ischemic stroke with HF (age range 52.1–77.1 years old, 47.18% male patients) and 36 484 patients with ischemic stroke without HF (age range 61–73.8 years old, 48.76% male patients). As per Table , patients with acute ischemic stroke with HF had a higher prevalence of baseline cardiovascular comorbidities including hypertension, diabetes, atrial fibrillation, and coronary artery disease (Table). Study quality was good in 3 studies and low in the remainder: the scoring in this latter group was mainly reflective of low comparability between study arms (patients with HF versus without HF) and poor outcome reporting (Figure S1).

## Primary Outcome: 90-day mRS 0–2

Four studies[9,21,27,34] were combined for the primary outcome (mRS score $\leq$2) using adjusted estimates, with a pooled OR of 0.86 (95% CI, 0.70–1.06, $P=0.15$) for patients with HF versus controls, suggesting no difference between groups (Figure 2). Although the point estimate might be somehow indicative of a worse outcome for HF, the moderate to substantial heterogeneity

**Table.** **Baseline Characteristics and Outcomes of the Included Studies**

| Study | Schnieder et al. 2019[9] | Pana et al. 2021[19] | Tan et al. 2021[34] | Bhatt et al. 2022[32] | Gentile et al. 2023[20] |
|---|---|---|---|---|---|
| **Country** | Germany | United States | Singapore, Taiwan, Germany, Sweden, United Kingdom | United States | Italy |
| **Study design** | Retrospective analysis of a prospective stroke database | Retrospective analysis of a large national database with the ascertainment of exposure groups based on *ICD-9* | Retrospective analysis of 6 prospective stroke databases | Retrospective analysis of a prospective stroke database | Retrospective analysis of a prospective multicentric stroke registry |
| **Sample size** | | | | | |
| HF versus controls, n | 90 versus 283 | 6766 versus 26 407 | 101 versus 339 | 293 versus 1173 | 642 versus 8282 |
| **Median age (y)** | | | | | |
| HF versus controls, y | 77 versus 73 | 67 HF, 77 AF + HF versus 61 no AF-HF, 76 AF | 63.5 versus 67.0* | n.a. | 77.1 versus 73.8* |
| **Male sex** | | | | | |
| HF versus controls, n | 43 versus 108 | 3264 versus 13 448 | 69 versus 183 | n.a. | 344 versus 4052 |
| **Criteria for HF diagnosis** | An ejection fraction <55% in the echocardiography | An *ICD-9* code between 428.0 and 428.9 | | | |
| **Presence of patients with LVAD** | No | n.a. | No | n.a. | No |
| **Atrial fibrillation** | | | | | |
| HF versus controls, % | 61 versus 35.5 | 64.9 versus 40.9 | 42.6 versus 47.9 | n.a. | 48.4 versus 30.9 |
| **Hypertension** | | | | | |
| HF versus controls, % | 85.5 versus 79.1 | 79.2 versus 73.5 | 73.3 versus 61.1 | n.a. | 67.9 versus 64.7 |
| **Diabetes** | | | | | |
| HF versus controls, % | 32.9 versus 23.1 | 32.6 versus 22.6 | 39.6 versus 28 | n.a. | 26.5 versus 16.3 |
| **CAD** | | | | | |
| HF versus controls, % | 53.7 versus 18 | 44 versus 21.3 | 50.5 versus 19.8 | n.a. | 21.3 versus 9.9 |
| **Median NIHSS score at admission** | | | | | |
| HF versus controls | 15 versus 15 | n.a. | 19 versus 18 | n.a. | 18 versus 17 |
| **mRS score ≤2 at 3 months** | | | | | |
| HF versus controls, n | 32/90 versus 105/283 | n.a. | 32/101 versus 161/339 | 144/293 versus 486/1173 | 234/642 versus 3992/8282 |
| **Death at 3 months** | | | | | |
| HF versus controls, n | Sep-90 versus 17/283 | n.a. | n.a. | 87/293 versus 217/1173 | 197/642 versus 1530/8282 |
| **ICH** | | | | | |
| HF versus controls, n | Mar-90 versus 2/283 | n.a. | 15/101 versus 35/339 | n.a. | 45/642 versus 648/8282 |
| **mTICI ≥2b** | | | | | |
| HF versus controls, n | 63/90 versus 175/283 | n.a. | 87/101 versus 289/339 | n.a. | 488/642 versus 6398/8282 |

AF indicates atrial fibrillation; CAD, coronary artery disease; HF, heart failure; *ICD-9*, *International Classification of Diseases*, *Ninth Revision*; ICH, intracranial hemorrhage; LVAD, left ventricular assistance device; mRS, modified Rankin scale; mTICI, modified thrombolysis in cerebral infarction; n.a., not applicable; and NIHSS, National Institutes of Health Stroke Scale. United States of America

*Age reported as mean.

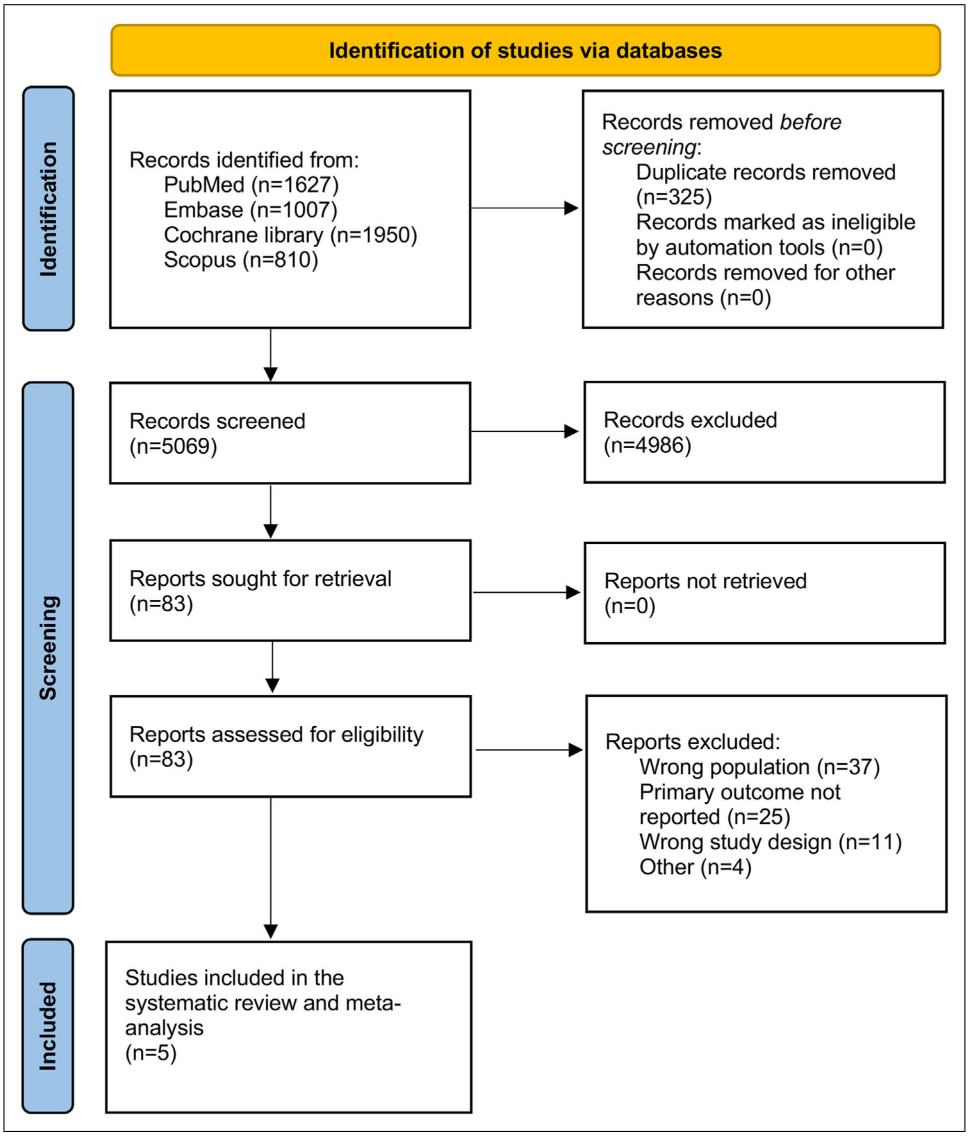


**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart for study selection.



($Q = 8.2$, $P = 0.04$; $I^2 = 63\%$) and the limited number of studies do not allow a definitive interpretation of this finding. When using unadjusted estimates, the single study OR interpretation changed in 2 cases[21,34]; nevertheless the final pooled results interpretation remained unchanged, although with a wider CI (OR, 0.80 [95% CI, 0.52–1.25], $P = 0.3$), possibly reflecting the increased between-study heterogeneity ($Q = 29.5$, $P<0.001$; $I^2 = 90\%$).

## Secondary Outcomes: 90-day Mortality, Good Reperfusion, and Symptomatic Intracranial Hemorrhage

For secondary outcomes, only unadjusted estimates were available, and 3 studies for each outcome were combined.[9,21,34] As regards 90-day mortality, the pooled OR was 1.92 (95% CI, 1.66–2.23, $P<0.0001$) for patients with HF versus controls, with null heterogeneity ($Q = 0.1$, $P = 0.9$; $I^2 = 0\%$); however, the lack of adjustment and the small sample size (n = 3 studies) significantly limit the interpretation of this result as indicative of possible a true effect in the group with HF. No significant difference was found for successful recanalization post MT (OR, 1.05 [95% CI, 0.80–1.37], $P = 0.7$) and for symptomatic intracranial hemorrhage (OR, 1.29 [95% CI, 0.68–2.44], $P = 0.4$) with low ($Q = 2.5$, $P = 0.3$; $I^2 = 20\%$) and moderate to substantial ($Q = 5.0$, $P = 0.08$; $I^2 = 60\%$) heterogeneity respectively; however, these results should be interpreted in a framework lacking estimate adjustment (Figure 3).

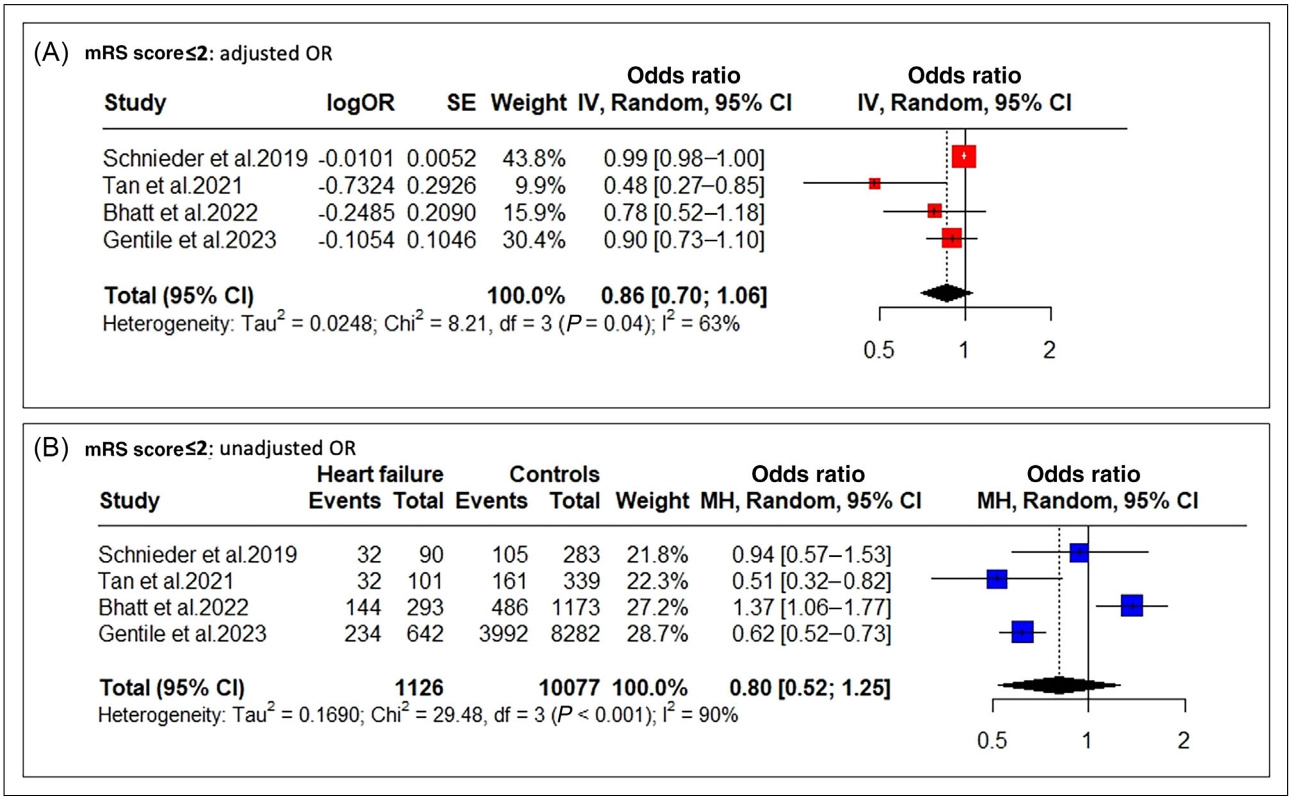


**Figure 2. Forest plots of the pooled adjusted (panel A) and unadjusted (panel B) odds ratio for 90-day modified Rankin Scale score ≤2 comparing patients with and without heart failure.** IV indicates information value; MH, Mantel–Haenszel; mRS, modified Rankin Scale; and OR, odds ratio.



## Sensitivity Analysis

Influence (ie, "leave-one-out") analysis of the primary outcome (mRS score ≤2) revealed no influential studies, but some relevant insights were obtained. In fact, we found a disproportionate influence on the pooled estimate of the study by Schnieder et al.[9] after its removal, showing a relative increase in the effect size (OR, 0.76 [95% CI, 0.56–1.04], $P = 0.08$) alongside a small reduction of heterogeneity ($I^2 = 52\%$ versus initial 63%). However, the removal of the study by Tan et al.[27] reduced substantially the heterogeneity ($I^2 = 6\%$) leading to a more precise estimate (OR, 0.97 [95% CI, 0.90–1.05]), confirming the absence of functional outcome difference in patients with HF versus without HF found in the main analysis. Overall, no outlier was evident for the secondary outcomes (Figure S2).

## Publication Bias and Quality of Evidence Assessment

Visual appraisal of the funnel plots for primary outcome revealed a right asymmetry, with a trend for significance ($P = 0.08$) on Eggers's test, possibly reflective of a publication bias for studies with worse functional outcome in patients with HF (Figure S4). Secondary outcomes did not reveal substantial asymmetries (Figure S4), as confirmed by the Egger test ($P>0.05$ for all outcomes), although the limited number of studies could not exclude a publication bias. The quality of evidence was assessed using the GRADE system applied to prognosis,[30] given the observational nature of the studies included, and was considered low (Table S3).

# DISCUSSION

In this systematic review and meta-analysis, we observed comparable rates of 90-day functional outcome, symptomatic hemorrhagic transformation, and successful recanalization in patients with HF compared with their counterparts without HF undergoing MT for acute ischemic stroke due to LVO. However, we acknowledge that there was a trend for a worse functional outcome in patients with HF; therefore, it is possible that a true effect is masked by the substantial between-studies heterogeneity. Conversely, patients with acute ischemic stroke and HF had significantly higher rates of 3-month mortality after MT compared with patients without HF, although due to the lack

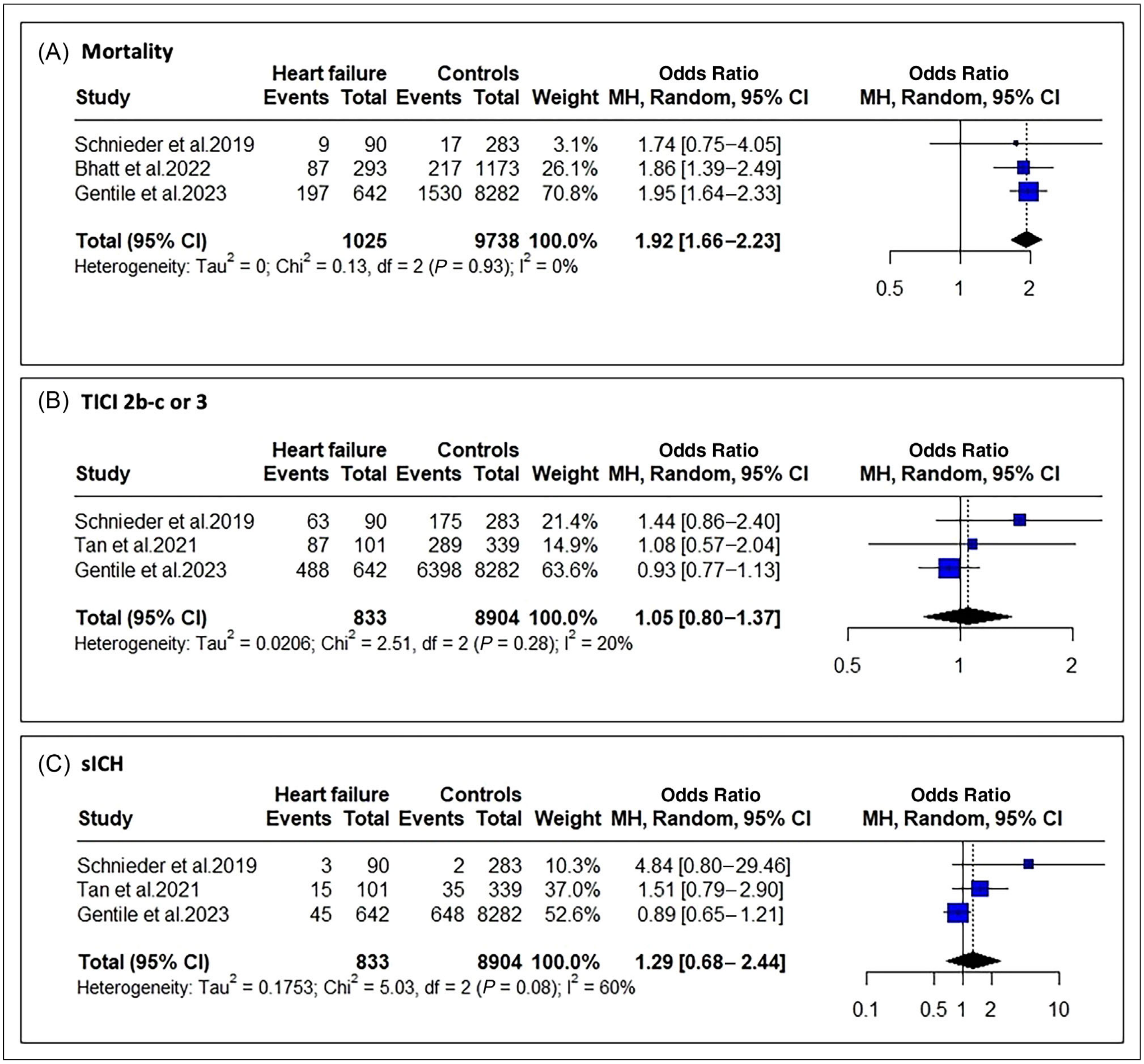


**Figure 3. Forest plots of the pooled adjusted odds ratio for 90-mortality, modified thrombolysis in cerebral infarction scale levels 2b, 2c, or 3, and symptomatic intracranial hemorrhage comparing patients with and without heart failure.** MH indicates Mantel–Haenszel; mTICI, modified thrombolysis in cerebral infarction; sICH, and symptomatic intracranial hemorrhage.

of adjustment and limited study number this finding must be interpreted with caution. Of note, in our study population, patients with acute ischemic stroke with HF showed a generally higher prevalence of baseline cardiovascular comorbidities, including hypertension, diabetes, atrial fibrillation, and coronary artery disease. Therefore, the higher 90-day mortality rate in patients with HF could be interpretable as related to the higher burden of cardiovascular risk factors and the fact that HF may serve as a prognostic indicator in this population.

Our findings provide initial systematic evidence regarding the impact of HF in patients with acute ischemic stroke undergoing endovascular recanalization treatment. In fact, to date there are diverging results in the literature about the impact of HF on functional outcome and mortality in patients undergoing MT.[22] Data from the multicenter IRETAS (Italian Registry of Endovascular Treatment in Acute Stroke) showed that patients with acute ischemic stroke with HF suffered from higher 3-month mortality and unfavorable outcome.[21] However, Schnieder et al. in their single-center study of 373 patients reported that HF was not associated with poorer outcome or higher mortality. The 2 studies differ not only in the study design but also in patients' inclusion criteria. The IRETAS registry study[21] included patients with HF and preserved, mild-range, and reduced LVEF whereas the analysis by Schnieder et al.[9] considered only patients with reduced LVEF. Differences between the 2 studies might have influenced the outcome results.

Chronic HF adversely affects the physiological homeostasis in patients with stroke resulting in arterial and venous hemodynamic disturbances, body fluid imbalances, worsening of cerebral tissue oxygenation, endothelial dysfunction, as well as proinflammatory and prothrombotic responses.[1,10,12,36,37] Thus, it was hypothesized that HF might have an impact on the efficacy of recanalization therapies in acute ischemic stroke. In our analysis, we found that the recanalization rates after MT use in patients with HF were comparable to patients with normal cardiac function, and the clinical response to MT, reflected by the comparable rates of 90-day functional outcome, was equal. Therefore, these results suggest that the HF negative impact on recanalization therapies might be at least lower than initially postulated. Supporting this view, the rate of intracranial bleeding complications was not significantly higher in patients with HF. Previous studies did not detect a higher rate of symptomatic intracranial bleeding after MT although this might be due to the very low rate of intracranial bleeding after MT, and therefore potential differences may not have been detected due to the small number of events.[9,21] In the large prospective clinical trials on MT in stroke, patients with HF were generally underrepresented because of strict selection criteria; indeed, in the ESCAPE trial, only 15% of patients were experiencing congestive HF, and HF was not systematically assessed in other trials.[23,24,38–42] Therefore, the applicability of these results to a real-world setting with a higher prevalence of HF might be limited. Our results provide an initial step toward the implementation of real-world evidence for endovascular therapy in patients with stroke with HF, suggesting its feasibility.

Finally, stroke subtype may play a significant role in influencing outcomes in patients undergoing MT.[43,44] Patients with HF are more likely to experience cardioembolic strokes, which are typically associated with larger clot burdens and poorer collateral circulation.[45] However, evidence from the SITS (Safe Implementation of Treatment in Stroke) thrombectomy register suggests that large artery atherosclerosis strokes may result in lower chances of reperfusion and worse outcomes despite more favorable baseline characteristics compared with cardioembolic strokes.[46] Future studies should incorporate patient-level data to stratify outcomes by stroke subtype and explore their interaction with HF to inform tailored treatment strategies.

## Limitations

This study has several limitations. First, we included a small number of studies (n = 5), although the final population was overall sufficiently large. Second, the lack of adjusted estimates for secondary endpoints might eventually mask true treatment effects. Third, the pooling of study populations with different definitions and levels of HF and stroke severity and the overall low quality of evidence limit the external applicability of the results. Fourth, unpublished negative results might have led to the exclusion of studies with worse outcomes. We acknowledge that our decision to include only studies published in English may have introduced a language bias, potentially excluding relevant data from non-English publications. Finally, administrative coding of patients included in a national database study may have been at risk for misclassification coding.[20] Moreover, we did not have a control group of patients with HF who were not treated with MT. Considering the time sensitivity of MT, physicians often do not know details of the cardiac status of the patient when screening a patient for MT. These limitations notwithstanding, our results provide initial evidence supporting further studies on this patient population.

# CONCLUSIONS

This systematic review and meta-analysis showed limited information on the prognosis of patients with acute ischemic stroke with HF treated with MT. The literature data point to similar functional outcomes considering the presence or absence of HF in this population although to worse 90-day mortality in the group with HF. However, this latter finding should be cautiously interpreted considering the limited number of studies and the lack of unadjusted estimates. No differences were found in successful reperfusion and symptomatic hemorrhagic transformation. Further randomized controlled trials or observational evidence targeting this patient population with stroke are, therefore, needed to clarify prognosis.

## ARTICLE INFORMATION

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## Conflicts of Interest Statement

None declared.

## Supplemental Materials

**Table S1**: Detailed search query in each database. Search date was March 16th, 2024.

**Table S2**: Newcastle-Ottawa scale for cohort studies adapted to study outcomes (source https://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf).

**Table S3**: GRADE assessment.

**Figure S1**: Traffic light plot for risk of bias using the Newcastle Ottawa scale (NOS). Images were realized using the robvis shinyapp.

**Figure S2**: Influence analysis of primary (panel a) and secondary outcomes (panels b–d). Study rows within each panel show the pooled odds ratio omitting the relative study ($p < 0.05$).

**Figure S3**: Contour-enhanced funnel plot for primary endpoint (mRS $\leq 2$).

**Figure S4**: Funnel plots for primary endpoint (mRS $\leq 2$).

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