

## Research Article

# Heart Failure Is Not Associated with a Poor Outcome after Mechanical Thrombectomy in Large Vessel Occlusion of Cerebral Arteries

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The impact of heart failure on outcome in stroke patients is not fully understood. There is evidence for an increased mortality and morbidity, but it remains uncertain whether thrombectomy in patients with large vessel occlusion (LVO) in the anterior circulation is less effective in patients with heart failure compared to patients without. Retrospectively, we analyzed echocardiographic data of all patients in our stroke database, who underwent mechanical thrombectomy (n=668) for the presence of heart failure. Furthermore, we collected baseline characteristics and neurological and neuroradiological parameters. In the analysis, 373 of the 668 patients of our stroke database underwent echocardiography. Of these 373 patients, 90 patients (24%) suffered from heart failure with reduced left ventricular ejection fraction measured by echocardiography according to the current guidelines. After adjustment for age, the Alberta stroke program early CT score (ASPECTS), and time from symptom onset to recanalization, the analysis revealed that thrombectomy in patients with heart failure and LVO is not associated with less favorable outcome measured by the modified Rankin Scale after 90 days (3 (0-6) vs. 3 (1-5); p=0.380). Moreover, we could not find a significant difference in mortality compared to patients without heart failure (11.0% vs. 7.4%; p=0.313).

## 1. Introduction

Heart failure is a disease associated with a high mortality and morbidity [1, 2]. Moreover, most of the patients with symptomatic heart failure suffer from comorbidities, such as peripheral artery embolism, pulmonary embolism, and stroke, leading to a higher mortality [3].

The risk of stroke in heart failure increases with the severity of heart failure, and patients with a moderate heart failure have an annual risk of stroke of approximately 1.5% [4], leading up to a risk of 4% in severe heart failure [5].

Because ischemic stroke and heart failure share common risk factors, such as diabetes and arterial hypertension [6], interactions between the two diseases are likely. Moreover, heart failure leads to a hypercoagulate state with rheological

alterations due to decreased blood flow [7] leading to a higher rate of stroke in patients with heart failure compared to the normal population [8]. These patients also have a higher incidence of atrial fibrillation and the risk of atrial fibrillation could vice versa increase the severity of heart failure [9]. It has been shown that, in patients with heart failure suffering from stroke, outcome is worse compared to those without heart failure, displayed by higher mortality, but also reduced neurological functional outcome [10]. Patients with heart failure may have a worse outcome after mechanical thrombectomy, since it could be shown that these patients have a poorer collateral-status regarding the blood supply of the brain compared to the patients without heart failure [11].

In contrast the analysis of the VISTA cohort could show that systemic thrombolysis with intravenous recombinant

TABLE 1: Baseline characteristics of patients with and without heart failure.

| Baseline characteristics and cardiovascular risk factors | Normal systolic LV-ejection fraction | Heart failure with reduced ejection fraction | p-value |
|--|--------------------------------------|--|---------|
| Age  | 73 (63-83)                           | 77 (70-84)                                   | 0.011   |
| Female   | 126 (53.8%)                          | 41 (48.8%)                                   | 0.428   |
| Male   | 108 (46.2%)                          | 43 (51.2%)                                   |         |
| Arterial Hypertension                                    | 182 (79.1%)                          | 71 (85.5%)                                   | 0.203   |
| Diabetes mellitus  | 53 (23.1%)                           | 27 (32.9%)                                   | 0.082   |
| Atrial fibrillation                                      | 81 (35.5%)                           | 50 (61.0%)                                   | < 0.001 |
| Obesity  | 71 (33.0%)                           | 33 (41.8%)                                   | 0.164   |
| Dyslipidemia   | 101 (43.9%)                          | 41 (50.6%)                                   | 0.298   |
| Smoking  | 46 (22.7%)                           | 12 (16.9%)                                   | 0.307   |
| Peripheral artery disease                                | 5 (2.2%)                             | 9 (11.0%)                                    | 0.003   |
| Coronary heart disease                                   | 41 (18.0%)                           | 44 (53.7%)                                   | <0.001  |
| Chronic renal failure                                    | 35 (18.2%)                           | 24 (35.8%)                                   | 0.003   |

tissue plasminogen activator (rt-PA) is as effective in patients with heart failure as in those without [12].

Thus, it remains uncertain whether mechanical thrombectomy in patients with large vessel occlusion is less effective in patients with heart failure compared to patients with normal systolic left ventricular heart function.

## 2. Methods

We retrospectively analyzed the echocardiographic data of patients of our prospectively kept stroke database, regarding the presence of heart failure. Patients were classified as suffering from heart failure when showing a reduced ejection fraction < 55% in the echocardiography.

The collected data includes neurological features as the National Institute of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS) and neuroradiological data such as the Alberta stroke program early CT score (ASPECTS) and the Collateral Status. The NIHSS and the mRS were assessed by experienced stroke neurologist and the ASPECTS and the collateral stroke by a senior neuroradiologist. The rate of symptomatic intracranial hemorrhage was collected as well. A symptomatic intracranial hemorrhage was defined as a deterioration of  $\geq 4$  in the NIHSS [13]. Furthermore, we collected the cardiovascular risk factors (CVRF) as well as long-term holter electrocardiographic data and duplex sonography of the brain-supplying arteries. Antiplatelet medication and anticoagulation were collected as well as heart failure medication.

Transthoracic echocardiography was performed by experienced cardiologists using a standard operating procedure (IE33, CX50 and X7-2t probe (Philips Medical Systems, Eindhoven, Netherlands) or Vivid E9 and 6VT-D probe (GE Healthcare, USA)). We collected echocardiography data such as the ejection fraction, the diameter of atrial and ventricle, wall motion abnormalities, patent foramen ovale, and valve insufficiencies and stenosis. The

valve insufficiencies and stenosis were further graduated into mild, moderate, and severe.

The statistical analysis was performed in IBM SPSS Statistics 24 package (IBM, Armonk, New York, USA). Descriptive analysis was described in relative frequencies using mean and median and standard deviation or the interquartile range. Group comparisons were performed using chi-square test. If they are not normally distributed, Mann-Whitney U-Test was performed. Multivariate regression analysis was performed to analyze the impact of the heart failure on the outcome of the patients. Possible baseline characteristics associated with the outcome ( $p < 0.1$ ) were included in the analysis. A backwards selection was then applied to find the best set of predictors. A p-value of < 0.05 was considered statistically significant.

## 3. Results

We screened 668 patients of our prospectively kept stroke database of patients with a large vessel occlusion who underwent mechanical thrombectomy for the presence of heart failure and further echocardiological characteristics. In total 373 (55.8%) patients underwent echocardiography. 90 (24%) of these patients suffered from heart failure with an impaired left ventricular systolic ejection fraction < 55%.

When comparing patients with and without heart failure, patients with heart failure are significantly older (77 (70-84) vs. 73 (63-83) years;  $p = 0.011$ ) and cardiovascular risk factors such as atrial fibrillation (50 (61.0%) vs. 81 (35.5%);  $p < 0.001$ ), peripheral artery disease (9 (11.0%) vs. 5 (2.2%);  $p = 0.003$ ), and coronary heart disease (44 (53.7%) vs. 41 (18.0%);  $p < 0.001$ ) were significantly more frequent as well as chronic renal failure (27 (35.8%) vs. 35 (18.2%);  $p = 0.003$ ) (Table 1). Interestingly there were no differences in rates of pretreatment antiplatelet medication (21 (34.4%) vs. 53 (33.1%);  $p = 0.874$ ) or oral anticoagulants (6 (17.1%) vs. 29 (18.1%);  $p = 0.153$ ) in patients with heart failure compared to those without.

TABLE 2: Echocardiological characteristics of patients with and without hear failure.

| Echocardiographic characteristics                      | Normal systolic LV-ejection fraction | Heart failure with reduced ejection fraction | p-value |
|--|--------------------------------------|--|---------|
| Posterior wall thickness (mm, median, IQR)             | 12 (10.5-13.5)                       | 12 (10.5-13.5)                               | 0.559   |
| Left ventricular enddiastolic volume (ml, median, IQR) | 43 (39.5-46.5)                       | 46 (40-52)                                   | 0.001   |
| Left ventricular endsystolic volume (ml, median, IQR)  | 25 (21-29)                           | 31 (26-36)                                   | 0.001   |
| Left atrial diameter (mm, median, IQR)                 | 34 (29.5-38.5)                       | 42 (37.5-46.5)                               | <0.001  |
| Aortic sinus (mm, median, IQR)                         | 30 (26.5-33.5)                       | 30 (26.5-33.5)                               | 0.454   |
| Left ventricular ejection fraction (% ,median, IQR)    | 55 (55-55)                           | 44.5 (35.5-53.5)                             | <0.001  |
| Left ventricular hypertrophy                           | 138 (70.4%)                          | 49 (69.0%)                                   | 0.826   |
| Left ventricular dilatation                            | 2 (1%)                               | 15 (21.7%)                                   | <0.001  |
| Left atrial dilatation                                 | 103 (58.5%)                          | 64 (91.4%)                                   | <0.001  |
| Right ventricular dilatation                           | 12 (10.5%)                           | 14 (40%)                                     | <0.001  |
| Right atrial dilatation                                | 8 (19%)                              | 7 (77.8%)                                    | 0.001   |
| Wall motion abnormalities                              | 5 (2.6%)                             | 53 (72.6%)                                   | <0.001  |
| Congested inferior vena cava                           | 15 (8.8%)                            | 22 (34.4%)                                   | <0.001  |
| Aortic insufficiency                                   | 83 (42.1%)                           | 39 (61.9%)                                   | 0.009   |
| Aortic valve stenosis                                  | 25 (15.1%)                           | 10 (16.4%)                                   | 0.805   |
| Mitral valve sclerosis                                 | 30 (26.5%)                           | 10 (38.5%)                                   | 0.237   |
| Mitral valve insufficiency                             | 181 (81.2%)                          | 78 (95.1%)                                   | 0.003   |
| Pulmonary valve insufficiency                          | 47 (40.9%)                           | 14 (58.3%)                                   | 0.174   |
| Tricuspid valve insufficiency                          | 164 (74.5%)                          | 69 (90.8%)                                   | 0.003   |
| Thrombus in the Left atrial appendage                  | 4 (4.4%)                             | 2 (8.3%)                                     | 0.440   |
| Endocarditis   | 1 (2.8%)                             | 1 (10%)                                      | 0.391   |
| Patent foramen ovale                                   | 33 (18.9%)                           | 5 (11.4%)                                    | 0.275   |

As expected, patients with heart failure had more cardiac comorbidities. Using echocardiography, we found that patients with heart failure suffer more often from heart valve insufficiencies (aortic insufficiency (39 (61.9%) vs. 83 (42.1%);  $p=0.009$ ); mitral valve insufficiency (78 (95.1%) vs. 181 (81.2%);  $p=0.003$ ); tricuspid valve insufficiency (69 (90.8%) vs. 164 (74.5%);  $p=0.003$ )). When looking at the severity of valve insufficiencies especially, the difference becomes manifest. Patients with heart failure significantly suffer more often from severe mitral valve insufficiency (9 (90 %) vs. 1 (10 %);  $p < 0.001$ ) and severe tricuspid valve insufficiency (8 (72.7%) vs. 3 (27.3%);  $p < 0.001$ ).

Furthermore, dilatation of ventricles and atria were significantly more present in patients with heart failure comparing to those without (end diastolic left ventricular dilatation (15 (21.7%) vs. 2 (1%);  $p<0.001$ ); left atrial dilatation (64 (91.4%) vs. 103 (58.5%);  $p<0.001$ ); right ventricular dilatation (14 (40%) vs. 12 (10.5%);  $p<0.001$ ); right atrial dilatation (7 (77.8%) vs. 8 (19%);  $p=0.001$ )) (Table 2).

The neuroradiological characteristics did not differ between the two groups. There was no difference especially at the initial CCT-ASPECTS (8 (7-9) vs. 9 (8-10);  $p=0.155$ ) or the

collateral-status of the patients assessed by the Menon score (7 (5.5-8.5) vs. 7 (5-9);  $p=0.906$ ).

Looking closer at the neurological characteristics of the severity of the stroke, there is no difference of the NIHSS at admission (15 (10.5-19.5) vs. 15 (10.5-19.5);  $p=0.085$ ) and there is no difference regarding the NIHSS at discharge (6.5 (0-13) vs. 5 (0-10.5);  $p=0.324$ ) or in the mRS at discharge (3 (1-5) vs. 3 (1-5);  $p=0.238$ ) or at 90 days after stroke (3 (0-6) vs. 3 (1-5);  $p=0.380$ ). After dichotomizing the mRS in patients with a favorable outcome as mRS of 0-2 and an unfavorable outcome for mRS 3-6 there is still no difference in patients with heart failure and without (32 (43.8%) vs. 105 (48.2%);  $p=0.521$ ). We did not find a higher mortality either (9 (11.0%) vs. 17 (7.4%);  $p=0.313$ ) (Table 3).

This is also reflected in the multivariate regression analysis where no influence of heart failure on outcome of the patients could be demonstrated (RR - 0.001; 95% CI: (-0.011-0.009);  $p=0.860$ ) (Table 4).

#### 4. Discussion

We could show that mechanical thrombectomy is as effective in patients with heart failure as in those without. Heart

TABLE 3: Neurological characteristics of patients with and without heart failure.

| Neurological and neuroradiological characteristics | Normal systolic LV-ejection fraction | Heart failure with reduced ejection fraction | p-value |
|--|--------------------------------------|--|---------|
| <i>Neurological Characteristics</i>                |                                      |  |         |
| NIHSS at admission (median, IQR)                   | 15 (10.5-19.5)                       | 15 (10.5-19.5)                               | 0.085   |
| NIHSS at discharge (median, IQR)                   | 5 (0-10.5)                           | 6.5 (0-13)                                   | 0.324   |
| mRS at admission (median, IQR)                     | 5 (4-6)                              | 5 (4-6)                                      | 0.174   |
| mRS at discharge (median, IQR)                     | 3 (1-5)                              | 3 (1-5)                                      | 0.238   |
| mRS after 90 days (median, IQR)                    | 3 (1-5)                              | 3 (1-5)                                      | 0.380   |
| Favorable Outcome                                  | 105 (48.2%)                          | 32 (43.8%)                                   | 0.521   |
| Intravenous rt-PA                                  | 160 (68.7%)                          | 51 (60.7%)                                   | 0.185   |
| Hemicraniectomy                                    | 9 (4.7%)                             | 7 (10.3%)                                    | 0.098   |
| Symptomatic Intracranial Hemorrhage                | 2 (1%)                               | 3 (4.4%)                                     | 0.080   |
| Mortality  | 17 (7.4%)                            | 9 (11%)                                      | 0.313   |
| <i>Toast criteria</i>                              |                                      |  | <0.001  |
| Macroangiopathy                                    | 23 (12.2%)                           | 4 (5.9%)                                     |         |
| Cardio-embolic                                     | 82 (43.6%)                           | 53 (77.9%)                                   |         |
| other  | 11 (5.9%)                            | 1 (1.5%)                                     |         |
| unknown  | 44 (23.4%)                           | 5 (7.4%)                                     |         |
| ESUS   | 28 (14.9%)                           | 5 (7.4%)                                     |         |
| <i>Neuroradiological Characteristics</i>           |                                      |  |         |
| <i>TICI-Scale</i>                                  |                                      |  | 0.177   |
| 0  | 15 (6.6%)                            | 5 (6.0%)                                     |         |
| 1  | 8 (3.5%)                             | 8 (9.6%)                                     |         |
| 2a   | 31 (13.5%)                           | 7 (8.4%)                                     |         |
| 2b   | 117 (51.1%)                          | 39 (47%)                                     |         |
| 3  | 58 (25.3%)                           | 24 (28.9%)                                   |         |
| CT-ASPECTS (median, IQR)                           | 9 (8-10)                             | 8 (7-9)                                      | 0.155   |
| Collateral Status (median, IQR)                    | 7 (5-9)                              | 7 (5.5-8.5)                                  | 0.906   |
| Symptom onset to recanalization (min, median, IQR) | 220 (159-281)                        | 246 (176-316)                                | 0.341   |
| <i>Occlusion site</i>                              |                                      |  | 0.326   |
| Proximal carotid artery                            | 8 (3.4%)                             | 2 (2.4%)                                     |         |
| Distal carotid artery                              | 39 (16.8%)                           | 17 (20.5%)                                   |         |
| M1   | 135 (58.2%)                          | 41 (49.4%)                                   |         |
| M2   | 25 (10.8%)                           | 14 (16.9%)                                   |         |
| Basilar artery                                     | 24 (10.3%)                           | 7 (8.4%)                                     |         |
| Posterior cerebral artery                          | 1 (0.4%)                             | 1 (1.2%)                                     |         |
| Anterior cerebral artery                           | 0 (0.0%)                             | 1 (1.2%)                                     |         |

IQR: interquartile range, rt-PA: recombinant tissue plasminogen activator, NIHSS: National Institute of Health Stroke Scale, mRS: modified Rankin Scale, ESUS: embolic stroke of unknown source, TICI: thrombolysis in cerebral infarction, and CT-ASPECTS: computer tomography-Alberta Stroke program early CT score.

TABLE 4: Regression analysis regarding predictors of a good outcome (mRS 0-2) in patients with mechanical thrombectomy in LVO.

| Outcome                         | RR     | 95% Confidence Interval | Interval | p-value |
|---------------------------------|--------|-------------------------|----------|---------|
| Age                             | 0.10   | 0.004                   | 0.017    | 0.004   |
| Occlusion side                  | -0.037 | -0.178                  | 0.104    | 0.606   |
| Intravenous rt-PA               | 0.135  | -0.059                  | 0.328    | 0.171   |
| Coronary heart disease          | 0.146  | -0.066                  | 0.357    | 0.174   |
| Chronic renal failure           | -0.109 | -0.345                  | 0.126    | 0.359   |
| NIHSS at admission              | 0.016  | 0.000                   | 0.032    | 0.044   |
| Symptom onset to recanalization | 0.001  | 0.000                   | 0.002    | 0.021   |
| TICI Scale                      | -0.125 | -0.229                  | -0.021   | 0.019   |
| CT-ASPECTS                      | -0.015 | -0.085                  | 0.054    | 0.665   |
| Collateral Score                | -0.027 | -0.072                  | 0.017    | 0.222   |
| HFrEF                           | -0.001 | -0.011                  | 0.009    | 0.860   |
| Left ventricular hypertrophy    | -0.020 | -0.206                  | 0.165    | 0.828   |

RR: relative risk, rt-PA: recombinant tissue plasminogen activator, NIHSS: National Institute of Health Stroke Scale, TICI: thrombolysis in cerebral infarction, CT-ASPECTS: computer tomography-Alberta Stroke program early CT score, HFrEF: heart failure with reduced ejection fraction, mRS: modified Rankin Scale, and LVO: large vessel occlusion.

failure does not have an impact on neurological outcome after large vessel occlusion when treated with mechanical thrombectomy. These findings are coherent to the analysis of the VISTA cohort, in which it was shown that systemic thrombolysis is effective, regardless of the presence of heart failure [12]. Even though it had been shown that patients with heart failure experience a higher mortality and morbidity after stroke [14]. One possible explanation might be the impaired cerebral perfusion due to the compromised ejection fraction, leading to poorer baseline collateral status, which is associated with worse outcome in patients with LVO [11]. In our study, we could not find an impact of heart failure on the cerebral collateral status of the patients; patients with heart failure did show similar collateral status, measured by the Menon score, compared to patients without heart failure. Another factor often blamed for possible worse outcome of HF patients after stroke is that symptomatic intracranial bleedings after systemic thrombolysis are more common in patients with heart failure [15]. In contrast, we did not detect a higher rate of symptomatic intracranial bleedings after mechanical thrombectomy and the proportion of patients also receiving systemic thrombolysis was not different in either group. One statistical drawback might be that the rate of intracranial bleedings after mechanical thrombectomy was very low and potential differences may not have been detected due to the small number of intracranial bleedings.

The strength of this study is the sample size and the well characterized patient cohort with comprehensive data especially regarding the neurological and neuroradiological parameters, as well as a 90-day followup examination. A limitation is the retrospective character of the study. Furthermore, we only included patients with a reduced ejection fraction, and we did not include patients with heart failure with a preserved ejection fraction and diastolic dysfunction. Thus, there is a probability of inclusion of some of those patients into the control group, which might influence our results.

## 5. Conclusion

In our study heart failure is not associated with a poorer outcome or higher mortality after mechanical thrombectomy in LVO. The NIHSS at discharge and mRS at 90 days as well as the mortality are similar in the two groups of patients. Even though patients with heart failure suffer from a high morbidity and mortality in stroke, they seem to benefit from cerebral artery recanalization therapy just as patients without heart failure.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Disclosure

A part of the data was presented at the European Stroke Organisation Conference in 2018.

## Conflicts of Interest

Marios N. Psychogios received honoraria and travel from grants Penumbra Inc., honoraria from Phenox GmbH, is a consultant to Stryker Neurovascular and Siemens Healthineers, and has a research agreement with Siemens Healthineers. Jan Liman received Speaker or Advisory Board fees from Pfizer, BMS, Bayer Healthcare, Stryker, and Daichii Sankyo.

## References

- [1] J. S. Gottdiener, "Outcome of Congestive Heart Failure in Elderly Persons: Influence of Left Ventricular Systolic Function: The Cardiovascular Health Study," *Annals of Internal Medicine*, vol. 137, no. 8, p. 631, 2002.

- [2] P. S. Jhund, K. MacIntyre, C. R. Simpson et al., "Long-Term Trends in First Hospitalization for Heart Failure and Subsequent Survival Between 1986 and 2003," *Circulation*, vol. 119, no. 4, pp. 515–523, 2009.
- [3] G. Y. H. Lip and C. R. Gibbs, "Antiplatelet agents versus control or anticoagulation for heart failure in sinus rhythm: A Cochrane systematic review," *QJM: Monthly Journal of the Association of Physicians*, vol. 95, no. 7, pp. 461–468, 2002.
- [4] B. J. Witt, A. S. Gami, K. V. Ballman et al., "The Incidence of Ischemic Stroke in Chronic Heart Failure: A Meta-Analysis," *Journal of Cardiac Failure*, vol. 13, no. 6, pp. 489–496, 2007.
- [5] E. Shantsila and G. Y. H. Lip, "Antiplatelet versus anticoagulation treatment for patients with heart failure in sinus rhythm," *Cochrane Database of Systematic Reviews*, vol. 2016, no. 9, 2016.
- [6] R. S. Freudenberger, A. S. Hellkamp, J. L. Halperin et al., "Risk of Thromboembolism in Heart Failure," *Circulation*, vol. 115, no. 20, pp. 2637–2641, 2007.
- [7] G. Y. H. Lip and C. R. Gibbs, "Does heart failure confer a hypercoagulable state? Virchow's triad revisited," *Journal of the American College of Cardiology*, vol. 33, no. 5, pp. 1424–1426, 1999.
- [8] A. H. Katsanos, J. Parissis, A. Frogoudaki et al., "Heart failure and the risk of ischemic stroke recurrence: A systematic review and meta-analysis," *Journal of the Neurological Sciences*, vol. 362, pp. 182–187, 2016.
- [9] J. P. Ferreira, N. Girerd, S. Alshalash, M. A. Konstam, and F. Zannad, "Antithrombotic therapy in heart failure patients with and without atrial fibrillation: update and future challenges," *European Heart Journal*, vol. 37, no. 31, pp. 2455–2464, 2016.
- [10] P. Appelros, I. Nydevik, and M. Viitanen, "Poor Outcome After First-Ever Stroke," *Stroke*, vol. 34, no. 1, pp. 122–126, 2003.
- [11] D. S. Liebeskind, T. A. Tomsick, L. D. Foster et al., "Collaterals at Angiography and Outcomes in the Interventional Management of Stroke (IMS) III Trial," *Stroke*, vol. 45, no. 3, pp. 759–764, 2014.
- [12] A. H. Abdul-Rahim, R. L. Fulton, B. Frank, J. J. McMurray, and K. R. Lees, "Associations of chronic heart failure with outcome in acute ischaemic stroke patients who received systemic thrombolysis: analysis from VISTA," *European Journal of Neurology*, vol. 22, no. 1, pp. 163–169, 2015.
- [13] N. Wahlgren, N. Ahmed, A. Dávalos et al., "Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study," *The Lancet*, vol. 369, no. 9558, pp. 275–282, 2007.
- [14] B. J. Witt, R. D. Brown, S. J. Jacobsen et al., "Ischemic stroke after heart failure: A community-based study," *American Heart Journal*, vol. 152, no. 1, pp. 102–109, 2006.
- [15] W. N. Whiteley, K. B. Slot, P. Fernandes, P. Sandercock, and J. Wardlaw, "Risk Factors for Intracranial Hemorrhage in Acute Ischemic Stroke Patients Treated With Recombinant Tissue Plasminogen Activator," *Stroke*, vol. 43, no. 11, pp. 2904–2909, 2012.