# The effect of atrial fibrillation on functional outcomes in stroke patients: A meta-analysis

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## Abstract

*Backgound:* Although previous studies have evaluated the effects of atrial fibrillation (AF) on functional outcomes in stroke patients, due to the few previous studies and subjects included in each study, it is difficult to confirm the effect of AF on functional recovery after stroke. *Objective:* The aim of this study was to evaluate the effect of AF on functional outcomes in stroke patients. *Methods:* A systemic literature search was conducted using PubMed, Embase, Cochrane Library, and SCOPUS. We included studies that were published on July 15, 2021, or earlier and satisfied our inclusion criteria. We used the standardized mean difference (SMD) and 95% confidence interval (CI) to analyze the changes in functional state changes. The meta-analysis was performed using RevMan v.5.3. *Results:* Four studies were finally selected for the analysis, and they included 298 AF and 1089 non-AF post-stroke patients. The improvement in the Functional Independence Measure score was higher in the non-AF post-stroke patients (SMD = 0.17, 95% CI = 0.04 to 0.30). *Conclusions:* AF can affect functional recovery after stroke and minimally undermine functional

outcomes.

Keywords: Atrial fibrillation, function, stroke, recovery, meta-analysis

## INTRODUCTION

Stroke has functional sequelae, including motor weakness, spasticity, dysphagia, and neurogenic bladder. It leads to a deterioration in activities of daily living, such as dressing, bathing, and grooming.<sup>1,2</sup> Previous studies reported that lesion location, lesion volume, corticospinal tract (CST) interruption, and treatment strategies can affect the functional outcomes of stroke patients.<sup>3-7</sup> In addition, it has been reported that clinical factors, such as the presence of diabetes, depression, and old age, can hinder functional recovery in stroke patients.<sup>8,9</sup>

Atrial fibrillation (AF) is the most common arrhythmia in adults and a major risk factor for stroke.<sup>10,11</sup> Previous studies have evaluated the effects of AF on functional outcomes in stroke patients.<sup>12-15</sup> However, due to the few previous studies and subjects included in each study, it is difficult to confirm the effect of AF on functional recovery after stroke, if there is any. There is need for a review based on larger number of patients.

Here, we conducted a meta-analysis to evaluate the effect of AF on functional outcomes in stroke patients.

## METHODS

#### Search strategy

This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. We systematically searched for relevant literature in PubMed, Embase, Cochrane Library, and SCOPUS published earlier than or on July 15, 2021. The following keywords were used for the search: (atrial fibrillation) AND (stroke) AND (rehabilitation OR recovery).

#### Study selection

We used the following inclusion criteria for the selection of articles: (1) stroke patients were included; (2) initial functional state was evaluated during the acute stage; (3) the functional state was monitored during follow-up; (4) patients with AF and those with non-AF were compared. We excluded review articles, letters, and case reports. In addition, we excluded studies that reported no or incomplete results.

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## Data extraction

After discarding duplicate studies, two reviewers (K.H.C and M.C.C) independently evaluated the potentially eligible studies. They were screened for eligibility based on a review of the title and abstract, and disagreements were resolved through consensus. After screening, the full texts of the eligible articles were read independently by the two reviewers, and the eligibility of each article was re-assessed. The data, including the name of the first author, publication date, study type, number of patients, demographic information (age and sex), follow-up time point, and functional outcomes [Functional Independence Measure (FIM)], were extracted.

## Quality assessment

The methodological quality of the included studies was evaluated using the Newcastle-Ottawa scale (NOS).<sup>16</sup> It includes three domains: the selection of subjects, comparability of groups, and assessment of outcomes. The quality of each study was graded as low (0-3), moderate (4-6), or high (7-9). All divergences were resolved by consensus.

## Statistical analysis

The RevMan 5.3 software program (https://tech. cochrane.org/revman) was used for statistical analysis of the pooled data. For each analysis, a heterogeneity test was performed using I<sup>2</sup> statistics, which measures the extent of inconsistency among the results.  $I^2$  values of  $\geq$  50% represented substantial heterogeneity, and the random-effects model was used for analysis of the data. In contrast, when  $I^2$  was less than 50%, the pooled data were considered homogeneous, and a fixed-effect model was applied.

To analyze the changes in the functional state, we analyzed the standardized mean difference (SMD). In addition, a 95% confidence interval (CI) was used in the analysis. A p-value of <0.05 was considered statistically significant.

## RESULTS

#### Study selection

In total, 6,184 articles were searched and 883 duplicated articles were removed (Figure 1). After screening for eligibility, based on a review of the title and abstract, 10 articles were left for full-text reading. After a detailed assessment, six articles were excluded; four studies reported insufficient results and the other two studies did not evaluate functional outcomes. Accordingly, 4 studies were finally included in our meta-analysis (Table 1). All included studies were retrospective case-control studies. The four selected studies included 298 patients with AF and 1,089 non-AF patients. The detailed characteristics of each study are presented in Table 1.

#### Risk of bias

All the included studies were rated 9 stars (selection of subjects: 4 stars; comparability of groups: 2 stars; assessment of outcome: 3 stars). Therefore, the quality of each included study, assessed using NOS, was considered high.

## Meta-analysis results

The fixed-effect model was used to analyze the change in FIM ( $l^2 = 0\%$ ). The improvement in FIM was significantly higher in the non-AF patients than in AF patients (standard mean difference [SMD] = 0.17, 95% CI = 0.04. 0.30) (Figure 2). A funnel plot analysis and Egger's test were performed for FIM (Figure 3). The p-value of Egger's test was 0.225, indicating that publication bias was not significant.

## DISCUSSION

In this study, we found that AF can disturb functional recovery after stroke. The effect size was 0.17. Based on Cohen's study<sup>17</sup>, this effect size suggests that AF minimally hinders functional recovery after stroke.

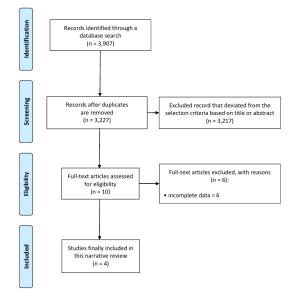


Figure 1. Flow chart showing the search results of the meta-analysis.

Study	Patients (N, AF %)	Age (yr, mean±SD)	Stroke type (Ischemic, %)	Outcome assessment time (day, mean±SD)
Giaquinto et al.12	185, 30.8%	68.4±11	15%	60±0.0
Karataş <i>et al</i> . <sup>13</sup>	196, 20.9%		AF group	
		65.0±9.9	95.1%	30.2±15.8
			Non-AF group	
		62.7±11.1	74.8%	35±19.4
Mizrahi <i>et al</i> . <sup>15</sup>	919, 19.6%		AF group	
		78.07±7.7	100%	49.6±27.8
			Non-AF group	
		75.1±7.9	100%	50.5±27.3
Kim et al. <sup>14</sup>	87, 23.0%		AF group	
		75.1±5.1	100%	91.1±22.6
			Non-AF group	
		71.8±8.8	100%	80.6±22.0

#### Table 1: Characteristics of the included studies

AF: atrial fibrillation; SD: standard deviation

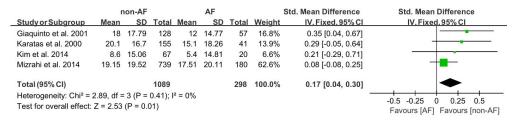


Figure 2. Results of Meta-analysis of Functional Independence Measures.

The mechanism by which AF hinders functional recovery after stroke has not been determined. The degree of recovery of neural tracts related to motor function is closely correlated with functional outcomes in stroke patients.<sup>18</sup> Previous studies demonstrated that AF induces hemodynamic instability and hypoperfusion in the brain, which can reduce brain volume and cause injury to neural tracts related to motor function.<sup>19-21</sup> Chronic hypoperfusion due to hemodynamic instability and changes in the brain can interrupt motor recovery after stroke. In addition, functional recovery after stroke is poor in older adults.8 The increase in the prevalence of AF with age is attributed to the lower recovery in stroke patients with AF than in non-AF patients.8,22 In the previous studies included in our meta-analysis, the average age of patients with AF was higher than that of patients with non-AF, although the difference was not statistically significant. These findings concur with the fact increase in the prevalence of AF with age. We think that this difference in the average age between patients with AF and those without AF could also contribute to the lower recovery in stroke patients with AF.

In conclusion, AF can minimally disturb the functional recovery of stroke patients. This is the

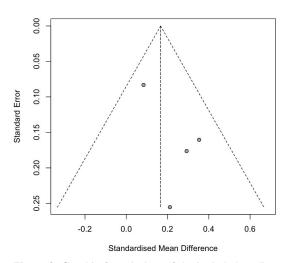


Figure 3. Graphic funnel plots of the included studies

first meta-analysis to evaluate the effect of AF on functional recovery after stroke. However, our study is limited, given that only FIM was used for the meta-analysis. The tools that previous studies used for assessing the functional state were heterogeneous, and only FIM was used in common. In addition, the included studies were few. Therefore, in the future, a meta-analysis to compensate for these limitations is needed.

## DISCLOSURE

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Confict of interest: None

#### REFERENCES

- 1. Teasell RW. Long-term sequelae of stroke: How should you handle stroke complications? *Can Fam Physician* 1992;38:381-8.
- Veerbeek JM, Kwakkel G, van Wegen EE, Ket JC, Heymans MW. Early prediction of outcome of activities of daily living after stroke: a systematic review. *Stroke* 2011;42(5):1482-8. DOI: 10.1161/ STROKEAHA.110.604090.
- Yassi N, Churilov L, Campbell BC, *et al*. EPITHET Investigators; DEFUSE Investigators. The association between lesion location and functional outcome after ischemic stroke. *Int J Stroke* 2015;10(8):1270-6. DOI: 10.1111/ijs.12537.
- Jang SH, Choi BY, Chang CH, Kim SH, Chang MC. Prediction of motor outcome based on diffusion tensor tractography findings in thalamic hemorrhage. *Int J Neurosci* 2013;123(4):233-9. DOI: 10.3109/00207454.2012.752364.
- Lam TK, Binns MA, Honjo K, *et al.* Variability in stroke motor outcome is explained by structural and functional integrity of the motor system. *Sci Rep* 2018;8(1):9480. DOI: 10.1038/s41598-018-27541-8.
- Lin DJ, Cloutier AM, Erler KS, *et al*. Corticospinal tract injury estimated from acute stroke imaging predicts upper extremity motor recovery after stroke. *Stroke* 2019;50(12):3569-77. DOI: 10.1161/ STROKEAHA.119.025898.
- Wollenweber FA, Tiedt S, Alegiani A, *et al*. Functional outcome following stroke thrombectomy in clinical practice. *Stroke* 2019;50(9):2500-6. DOI: 10.1161/ STROKEAHA.119.026005.
- Alawieh A, Zhao J, Feng W. Factors affecting poststroke motor recovery: Implications on neurotherapy after brain injury. *Behav Brain Res* 2018;340:94-101. DOI: 10.1016/j.bbr.2016.08.029.
- Moon JS, Chung SM, Jang SH, Won KC, Chang MC. Effects of diabetes on motor recovery after cerebral infarct: A diffusion tensor imaging study. J *Clin Endocrinol Metab* 2019:jc.2018-02502. DOI: 10.1210/jc.2018-02502.

- Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics-2020 update: A report from the American Heart Association. *Circulation* 2020;141(9):e139-e596. DOI: 10.1161/ CIR.000000000000757.
- Sposato LA, Cipriano LE, Saposnik G, Ruíz Vargas E, Riccio PM, Hachinski V. Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol* 2015;14(4):377-87. DOI: 10.1016/S1474-4422(15)70027-X.
- 12. Giaquinto S, Ferrara I, Muscherà R, Pagano G, Nolfe G. The effects of atrial fibrillation on functional recovery in post-stroke patients. *Disabil Rehabil* 2001;23(5):204-8. DOI: 10.1080/09638280151080603.
- Karataş M, Dilek A, Erkan H, Yavuz N, Sözay S, Akman N. Functional outcome in stroke patients with atrial fibrillation. *Arch Phys Med Rehabil* 2000;81(8):1025-9. DOI: 10.1053/apmr.2000.6981.
- Kim JY, Lee SJ, Kim JH, Choi CM, Yoon SR, Jung KI. Effects of atrial fibrillation on the outcome of the rehabilitation in patients with cerebral infarction. *Ann Rehabil Med* 2014;38(6):766-74. DOI: 10.5535/ arm.2014.38.6.766.
- Mizrahi EH, Fleissig Y, Arad M, Adunsky A. Short-term functional outcome of ischemic stroke in the elderly: a comparative study of atrial fibrillation and non-atrial fibrillation patients. *Arch Gerontol Geriatr* 2014;58(1):121-4. DOI: 10.1016/j. archger.2013.07.015.
- Ottawa Hospital Research Institute. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Available: http://www.ohri.ca/programs/clinical\_epidemiology/ oxford. asp 2011.
- 17. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale: Erlbaum; 1988.
- Jang SH. A review of motor recovery mechanisms in patients with stroke. *NeuroRehabilitation* 2007;22(4):253-9. DOI: 10.3233/NRE-2007-22401.
- Gardarsdottir M, Sigurdsson S, Aspelund T, et al. Atrial fibrillation is associated with decreased total cerebral blood flow and brain perfusion. *Europace* 2018;20(8):1252-8. DOI: 10.1093/europace/eux220.
- Petersen P, Godtfredsen J. Risk factors for stroke in chronic atrial fibrillation. *Eur Heart J* 1988;9(3):291-4. DOI: 10.1093/oxfordjournals.eurheartj.a062499.
- Stefansdottir H, Arnar DO, Aspelund T, et al. Atrial fibrillation is associated with reduced brain volume and cognitive function independent of cerebral infarcts. *Stroke* 2013;44(4):1020-5. DOI: 10.1161/ STROKEAHA.12.679381.
- 22. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. *Arch Intern Med* 1995;155(5):469-73. DOI:10.1001/archinte.1995.00430050045005.