Research Square

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Clinical prognosis of isolated anterior cerebral artery territory infarction: A retrospective study

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Abstract

Background

Isolated anterior cerebral artery territory (ACA) infarction is a rare phenomenon and had known to have distinctive clinical features. Little is known about the clinical prognosis of isolated ACA territory infarction with associated factors and its impact on dwelling and job status. We investigated the short- and long-term outcomes and associated factors involved in the development of the distinctive symptoms of anterior cerebral artery (ACA) territory infarction.

Methods

This retrospective study in a prospective cohort of acute ischaemic stroke patients included consecutively enrolled patients with isolated ACA territory infarction. We investigated the functional status using the modified Rankin scale (mRS) score at discharge, three months post-discharge, and one-year post-discharge. We also investigated the occlusion site of the ACA (proximal vs. distal); presence of distinctive symptoms of ACA territory infarction including behaviour changes, indifference, aphasia, and urinary incontinence; and the effect of these symptoms on dwelling and job status one year after discharge.

Results

From April 2014 to March 2019, 47 patients with isolated ACA territory infarction were included. Twenty-nine patients (61.7%) had good outcomes (mRS ≤ 2) at discharge; however, the mRS score increased at three months (40; 85.1%, $p < 0.001$) and one year (41; 87.2%) post-discharge. Occlusion of the ACA proximal segment was independently associated with the development of distinctive symptoms (adjusted odds ratio, 17.68; 95% confidence interval: 2.55–122.56, $p < 0.05$). Twenty-one (48.8%) patients with good outcomes at one year experienced a change in dwelling status and job loss; 20 (95.2%) of them had distinctive ACA territory symptoms with proximal ACA occlusion.

Conclusions

Short- and long-term outcomes of isolated ACA territory infarction were favourable. However, proximal segment occlusion was associated with the development of distinctive symptoms, possibly related to future dwelling and job status.

Background

Isolated anterior cerebral artery (ACA) territory infarction is a rare phenomenon [1]. It accounts for only 0.5–3% of all cerebral infarctions [2–4]. The relative rarity of isolated ACA territory infarction compared to middle cerebral artery (MCA) territory infarction may be related to the fact that the diameter of the A1 segment of the ACA is only about half that of the MCA; furthermore, the presence of the anterior communicating artery possibly plays an important role in emboli clearance [5].

Because of their rarity, there have been few reports about the natural prognosis of isolated ACA territory infarctions [2, 3, 6, 7]. Further, in most previous studies, ACA territory infarction was included in the group of hemispheric infarctions, despite its independent vascular topography [8]. ACA territory infarction also has diverse clinical features that are distinct from those of other cerebral vascular territory infarctions, which are not well defined by conventional functional outcome measures focusing on motor function [3, 4, 9, 10]. Therefore, neither the natural prognosis of isolated ACA territory infarction nor the influence of its distinctive symptoms on patients' outcomes has been revealed.

Thus, we aimed to retrospectively investigate the following: 1) the natural prognosis of patients with isolated ACA territory infarction in short (3-month) and long (1-year) time frames, 2) the factors associated with the development of distinctive symptoms in isolated ACA territory infarction, and 3) the influence of those symptoms of ACA territory infarction on dwelling and job status.

Materials And Methods

Study population

This study was a retrospective analysis of prospectively registered consecutive patients in a comprehensive stroke centre in Korea. All patients experienced an ischaemic stroke within seven days of symptom onset. They were managed according to a standardised protocol and care pathway, based on current guidelines. The inclusion criteria for this study were as follows: 1) isolated ACA territory infarction without involving any other cerebral vascular territory on magnetic resonance imaging (MRI); 2) modified Rankin Scale (mRS) ≤ 2 before the qualifying stroke; and 3) followed up at three months and one year after discharge.

During admission, brain MRI, computed tomography (CT) imaging, and cerebral angiography (magnetic resonance angiography, CT angiography, or digital subtraction angiography) were performed for all patients. Systemic evaluations, including 12-lead electrocardiography, chest radiography, standard blood test, and lipid profile, were performed. For detecting the cardiac embolic source, 24-h Holter monitoring or electrocardiographic monitoring was performed at the stroke unit. Based on these analyses, the stroke aetiology was retrospectively determined according to the Trial of ORG 10172 in Acute Stroke Management (TOAST) [11] using neuroradiologists' reports and the consensus of ≥ 2 stroke specialists in weekly stroke conferences.

Clinical variables and imaging analysis

Data on demographics and stroke risk factors including hypertension, diabetes, smoking status, hyperlipidaemia, and history of coronary artery disease or stroke were obtained. The severity of stroke was determined using the National Institutes of Health Stroke Scale (NIHSS) score at admission.

Involved vascular territory was determined using high signal intensities on diffusion-weighted images from brain MRIs taken during admission. The location of occlusion or stenosis was also determined by CT angiography or MR angiography. ACA territory was determined according to previous studies [5, 12] (shown in Fig. 1). If cerebral infarction was only involved in the ACA territory without involving any other cerebral vascular territories, the case fulfilled the enrolment criteria. ACA territory was defined as follows: 1) rostrum, genu, and splenium of the corpus callosum, cingulate gyrus, and frontal pole supplied by the frontopolar and orbitofrontal arteries; 2) medial aspect of the superior frontal gyrus supplied by the anterior and middle internal frontal artery; 3) supplementary motor area supplied by the posterior internal frontal artery; and 4) paracentral lobule and cuneus supplied by the paracentral artery and superior parietal artery. To more clearly determine the differences that depend on the location, we divided the ACA region into proximal and distal portions. The proximal portion covered the A1 (precommunicating) to A3 segments (around the genu of the corpus callosum genu), shown as a red line (shown in Fig. 1), and the distal portion covered A4 (terminal branch of A4) and its distal part.

The ACA segment was defined according to Fischer's classification.

Outcome measurement

We obtained mRS at discharge, three months after discharge, and one year after discharge. The mRS at three months and one year were performed at the outpatient clinic. If the patient missed a scheduled visit, we obtained the information from them or their guardians via telephonic interviews based on a structured questionnaire about mRS. Good outcome was defined as mRS 0–2, which is considered to be functionally independent, at three months and one year after discharge. In ACA territory infarction, the cerebral infarction is often not severe; thus, we also investigated the functional status of patients with mRS 0–1. In addition, we also checked other distinctive symptoms related to ACA territory infarction, which could not be measured using mRS [3, 4, 10]. These symptoms included altered consciousness; features of indifference including abulia, akinetic mutism, and apathy; aphasia; behavioral changes such as utilisation, perseveration, and social inhibition; and urinary incontinence [3, 4]. We also investigated the dwelling and job status at three months and one year after discharge.

Statistical analyses

Data are presented as mean ± standard deviation, median (interquartile range), or a number (percentage), as appropriate. Differences according to the presence of distinctive symptoms were compared using the chi-square test, Fisher's exact test, Student's t-test, and Mann-Whitney U test, as appropriate. Temporal changes in mRS at discharge, three months after discharge, and one year after discharge were assessed using the chi-square test for trends. To determine the independently associated factors for the development of distinctive symptoms in isolated ACA territory infarction, binary logistic regression analysis was performed, and the results are summarised as odds ratio and 95% confidence interval. For multivariable analysis, variables with $p < 0.1$ in the univariate analyses were included in the multivariable analysis in the binary logistic regression. All tests were two-sided, and $p < 0.05$ was considered statistically significant. The final model was fitted using the Hosmer – Lemeshow goodness-of-fit analysis, and $p > 0.05$ was considered as the model fit to the binary logistic regression analysis. All statistical analyses were performed using R software version 3.6.1 (R foundation for Statistical Computing, Vienna, Austria).

Results

Patients' characteristics

From April 2014 to March 2019, a total of 219 patients with cerebral infarction in the ACA territory were admitted in our hospital. Among them, 166 patients had infarctions in multiple cerebral artery territories. After excluding those patients, 53 patients with isolated ACA infarction remained. Among these, five patients who were lost to follow-up and one with mRS 3 before onset of stroke were excluded. Finally, 47 patients who fulfilled the inclusion criteria were included in this study (shown in Fig. 2). Among included patients, none underwent endovascular thrombectomy or intravenous tissue plasminogen activator administration.

The mean age of the included patients was 71.7 ± 11.6 years, and 18 (38.3%) were male. The initial NIHSS score was 2 (1–5). The most common symptom was weakness of the extremities (33 patients, 70.2%). The median NIHSS sub-score for motor leg was 2.5, while the median NIHSS sub-score for the motor arm was 1. The most common stroke aetiology was large artery atherosclerosis (n = 17, 36.1%). Patients with distinctive symptoms of ACA infarction had higher initial NIHSS scores and more occlusion of the proximal ACA segment (Table 1).

Table 1
Demographic features of patients with ACA territory infarction according to the presence of distinctive symptoms.

	Symptom (-) (N = 22)	Symptom (+) (N = 25)	
Demographics			
Age, years	69.1 ± 11.9	73.9 ± 11.2	0.165
Sex, men	9 (40.9)	9 (36.0)	0.964
Initial NIHSS score	1 [0.75–3.25]	4 [1–7]	0.013
Risk factors			
Hypertension	10 (45.5)	15 (60.0)	0.481
Diabetes mellitus	5 (22.7)	8 (32.0)	0.702
Hyperlipidemia	4 (18.2)	2 (8.0)	0.545
Atrial fibrillation	5 (22.7)	5 (20.0)	1.000
Smoking	7 (31.8)	8 (32.0)	1.000
Previous stroke	7 (31.8)	3 (12.0)	0.194
Coronary artery disease	3 (13.6)	7 (28.0)	0.399
Stroke etiology			0.565
Large artery atherosclerosis	6 (27.3)	10 (40.0)	
Cardioembolism	5 (22.7)	5 (20.0)	
Stroke of other determined etiology	1 (4.5)	0 (0)	
Stroke of undetermined etiology			
Two or more cause	1 (4.5)	0 (0)	
Negative evaluation	8 (36.4)	7 (28.0)	
Occlusion site, proximal	9 (40.9)	23 (92.0)	0.001
Infarction location			0.317
Right	13 (59.1)	10 (40.0)	
Left	9 (40.9)	14 (56.0)	
Bilateral	0 (0)	1 (4.0)	

Data are shown as n (%), mean ± standard deviation, or median [interquartile range]. ACA, anterior cerebral artery; NIHSS, National Institutes of Health Stroke Scale.

Outcomes at discharge, three months after discharge, and one year after discharge

The median mRS at discharge was 2 (1–2). At that point, 29 (61.7%) patients had good mRS. Short-term (three months) and long-term (one year) mRS after discharge were 1 (0–2) and 0 (0–1), respectively. The number of patients with good mRS increased to 40 (85.1%) at three months ($p < 0.001$), and one patient (2.1%) died within three months after discharge. Finally, 41 patients (87.2%) achieved a good outcome at one year. Compared to mRS 0–1 at three months (68.1%), the proportion of mRS 0–1 was 76.6% at one year. There were no additional deaths during this period. The temporal changes in mRS at discharge, three months after discharge (short-term), and one year after discharge (long-term) are shown in Fig. 3.

Associated factors for the development of distinctive symptoms in ACA territory infarction

Of the 40 patients with a good outcome at three months, 25 (62.5%) had distinctive symptoms in ACA territory infarction. Of these, 16 patients had features of indifference and nine had behavioural changes. In addition, two patients had aphasia, and one suffered from urinary incontinence and voiding difficulty. Among these patients, 23 (92.0%) had occlusion of the proximal ACA portion. No patient showed improvement of previously distinctive symptoms at three months or one year after discharge. For the development of distinctive symptoms in ACA territory infarction, the initial NIHSS score and proximal ACA segment occlusion were significantly associated. In multivariable analysis, occlusion of the proximal ACA portion (odds ratio, 12.37; 95% confidence interval, 2.63–92.04; $p < 0.05$) was independently associated with the development of distinctive symptoms in ACA territory infarction (Table 2).

Table 2
Factors associated with distinctive symptoms in anterior cerebral artery territory infarction

	Univariable analysis		**Multivariable analysis**	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.04 (0.99–1.10)	0.73		
Sex	0.81 (0.25–2.26)	0.17	2.43 (0.43–13.71)	0.32
Initial NIHSS score	1.26 (1.05–1.65)	< 0.05	1.20 (0.93–1.52)	0.16
Previous stroke	0.44 (0.77–2.55)	0.36		
Coronary artery disease	2.46 (0.59–12.82)	0.238		
Hypertension	1.80 (0.57–5.88)	0.28		
Diabetes mellitus	0.70 (0.19–2.59)	0.32		
Hyperlipidemia	0.39 (0.05–2.24)	0.31		
Atrial fibrillation	0.85 (0.20–3.54)	0.82		
Smoking	1.01 (0.29–3.52)	0.99		
Occlusion site				
Distal	Reference		Reference	
Proximal	16.61 (3.68–121.08)	< 0.05	17.68 (2.55–122.56)	< 0.05
Infarction location				
Left	Reference			
Right	2.02 (0.63–6.55)	0.24		
Bilateral	NA	NA		
Stroke etiology				
Large artery atherosclerosis	Reference			
Cardioembolism	2.50 (0.64–9.66)	0.18		
Stroke of other determined	NA	NA		
Undetermined	0.64 (0.13–3.25)	0.59		

OR, odds ratio; CI, confidential interval; NIHSS, National Institutes of Health Stroke Scale

Dwelling, job status, and distinctive symptoms in ACA territory infarction

Before the qualifying stroke, all patients enrolled in this study dwelled in their home with family and 12(25.5%) had a job. Among the 41 (87.2%) patients classified as having good mRS at one year, 17 (36.2%) moved into chronic care facilities and four (33.3%) lost their jobs. Of the 21 patients who moved their residence or lost their jobs, 20 (95.2%) had distinctive symptoms of ACA territory infarction, and all of them had proximal ACA segment occlusion.

Discussion And Conclusion

This study showed that (1) short- and long-term prognosis in isolated ACA territory infarction were good, (2) proximal ACA segment occlusion was an independently associated factor for developing distinctive symptoms in ACA territory infarction, and (3) the distinctive symptoms related to proximal ACA segment occlusion influenced dwelling and job status, regardless of positive mRS.

Short-term mortality after isolated ACA territory infarction can range between 0 and 8%, which is much lower than the 17.3% short-term mortality after MCA territory infarction [3, 8, 13]. Consistent with previous studies, only one patient (2.1%) died during the follow-up period in our study. Regarding functional outcomes, approximately 70% of patients achieved functional independence at three months in previous studies [13, 14]. In our study, 85.1% of patients had a good outcome at three months in isolated ACA territory infarction. Thus, short-term outcomes after isolated ACA territory infarction seemed to be favourable, and in line with previous research. However, little is known about the long-term prognosis after isolated ACA territory infarction. We investigated the long-term outcomes, with 87.2% of patients showing good outcomes at one year after discharge. Thus, similar to the short-term outcomes, the long-term outcomes in isolated ACA territory infarction also seem to be favourable.

The most common symptom in isolated ACA territory infarction was motor deficit, typically involving the lower extremity contralateral to the infarction site [3, 4, 8]. In our study, the median NIHSS sub-score for the leg was also higher than that for the arm [3]. Similar to previous studies, the symptoms in our patients also involved the lower extremity more than the upper extremity. This dominance of the involvement of the lower extremity originates in the paracentral lobule located in the ACA territory. On the contrary, the cortical area for the hand and arm is located in the MCA territory, and the corona radiata, where the projection fibres from the cortex were merged, is also located in the MCA territory. Therefore, developing hemiparesis is relatively uncommon in isolated ACA territory infarction, and preserving motor function in the arm may help achieve functional independence. In addition, motor function of the lower extremity usually recovers faster and more completely than that of the upper extremity [15]. This may be the reason why patients with isolated ACA territory infarction showed favourable functional independence as measured by mRS.

Distinctive symptoms in ACA territory infarction include altered mental status, abulia, mutism, decreased verbal fluency, aphasia, and urinary incontinence [3, 4]. Abulia and mutism are associated with cingulate gyrus and supplementary motor area involvement, which are important for human behaviour [16–18], while aphasia is associated with involvement of the supplementary motor area located in the superior medial frontal lobe [19, 20]. Urinary incontinence suggests involvement of the superior frontal gyrus, cingulate, and large infarction lesions affecting the superior and medial parts of the frontal lobe [21]. In terms of distinctive symptom development in ACA territory infarction, infarction size may be an influencing factor. Moreover, the structures associated with distinctive symptoms in the ACA territory are located at least above the A3 segment and classified as the proximal portion in our study. Thus, the risk of developing distinctive symptoms in the ACA territory seems to be high in cases of proximal ACA segment occlusion. As mentioned above, proximal ACA segment occlusion was an independent factor for the development of distinctive symptoms in ACA territory infarction.

Furthermore, the presence of distinctive symptoms in ACA territory infarction was closely associated with dwelling and job status in patients with good mRS.

According to the mRS, patients with a slight disability who were able to look after their own affairs without assistance, but unable to perform all previous activities, were given a score of 2. However, if, for example, patients had mild aphasia or abulia with a mild degree of motor deficit, they could still take care of their own affairs since motor function was relatively good. In such cases, their outcome may have been classified as good, even if the patient's family suffered from the after-effects of the distinctive symptoms of ACA territory infarction. Thus, the real prognosis after ACA territory infarction might not be correctly assessed by mRS alone, and it might be wrong to conclude, based on mRS, that patients with isolated ACA territory infarction had favourable outcomes.

Currently, mechanical thrombectomy (MT) is recommended as primary treatment for MCA and carotid artery occlusion [22, 23]. Because of its rarity, there are few studies of MT in ACA occlusion. The average A2 and A3 diameters were > 2.0 mm [24]. Thus, considering the minimal stent retriever diameter (3.00 mm), the proximal ACA segment was suitable for MT [25]. In a retrospective study of 30 patients, MT on ACA occlusions led to a good recanalization rate with few complications [26]. In addition, recent studies have shown that the presence of ACA occlusion by secondary embolism during MT for MCA without recanalization was associated with poor functional outcomes [27, 28]. Thus, if patients with proximal ACA segment occlusion arrived within the right therapeutic window of time, MT could be considered because proximal segment occlusion was associated with the development of distinctive symptoms in ACA territory infarction, which could affect future patient's true prognosis, which could not be assessed with mRS alone.

This study had several limitations. First, this was a retrospective single-centre study with a small sample size. We did not use a validated questionnaire or examination to check for distinctive symptoms in ACA territory infarction. To circumvent these limitations, we plan to perform a prospective study with a validated questionnaire for the prognosis in ACA territory infarction.

Both short- and long-term prognoses based on mRS in isolated ACA territory infarction were favourable. However, despite good mRS, proximal ACA segment occlusion was associated with the development of distinctive symptoms in ACA territory infarction, which could affect the patients' dwelling and job status.

Acute treatment such as endovascular thrombectomy or administration of intravenous tissue plasminogen activator might be beneficial to patients with proximal occlusion.

List Of Abbreviations

ACA: anterior cerebral artery

CT: computed tomography

MCA: middle cerebral artery

MRI: magnetic resonance imaging

MT: mechanical thrombectomy

NIHSS: National Institutes of Health Stroke Scale

TOAST: Trial of ORG 10172 in Acute Stroke Management

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board of Keimyung University Dongsan Hospital, which waived the requirement for informed consent from the patients due to the retrospective nature of this study. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due them containing information that could compromise research participant privacy/consent but are available from the corresponding author on reasonable request.

Competing interests

The authors declare no conflict of interest.

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Author's contributions

Conceptualization, H.P. and J.Y.; Methodology, Y.S.J. and S.H.L.; Formal analysis, H.P. and J.Y.; Investigation: H.P., Y.S.J., S.H.L., D.H.K., S.H.J., J-H.H., S-I.S., and J.Y.; Writing-original draft preparation, H.P. and J.Y.; Writing-review and editing: H.P., Y.S.J., S.H.L., D.H.K., S.H.J., J-H.H., S-I.S., and J.Y.; Read and approved the final manuscript, all authors.

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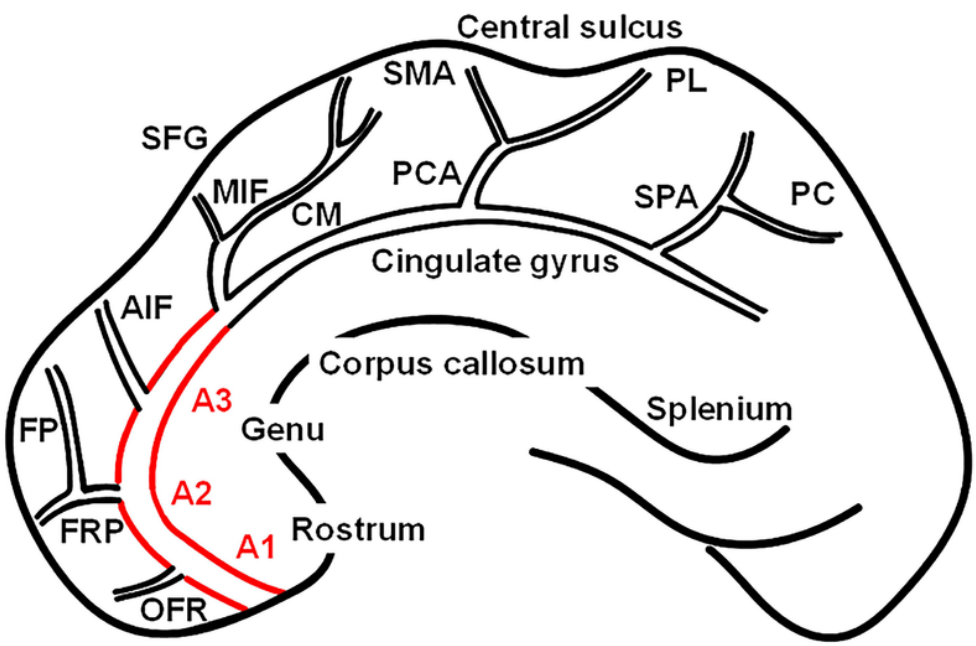
Figures



OFR = orbitofrontal; FRP: Frontopolar; FP: frontal pole; AIF: anterior internal frontal artery; SFG: superior frontal gyrus; MIF: middle internal frontal artery; CM: callosomaginal artery; PCA: paracentral artery; SMA: supplementary motor area; PL: paracentral lobule; SPA: superior parietal artery; PC: precuneus

Figure 1. A schematic drawing of anterior cerebral artery and branches of ACA

Figure 1

A schematic drawing of anterior cerebral artery (ACA) territory and branches of ACA

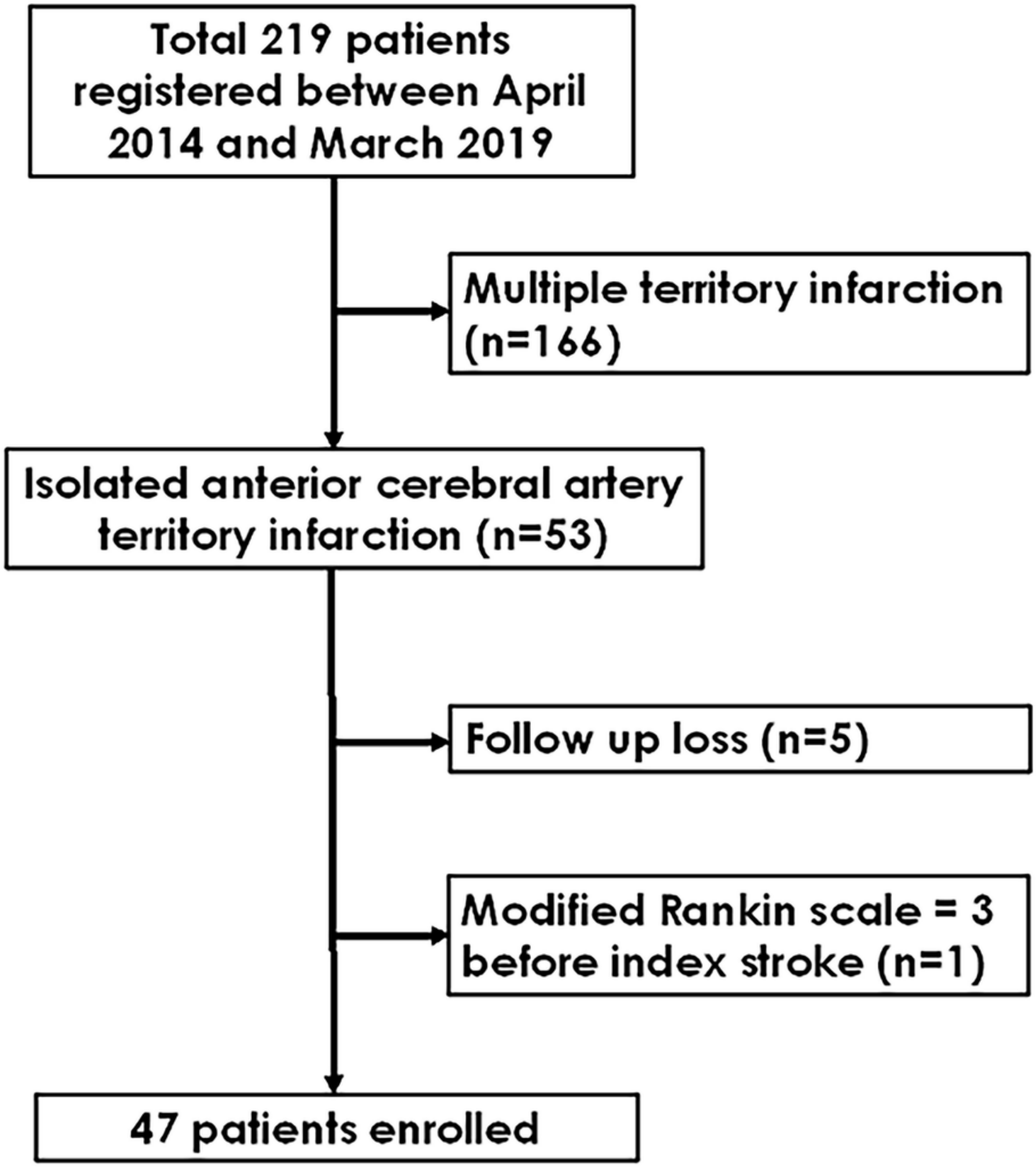


Figure 2. Flow chart of patients' selection

Figure 2

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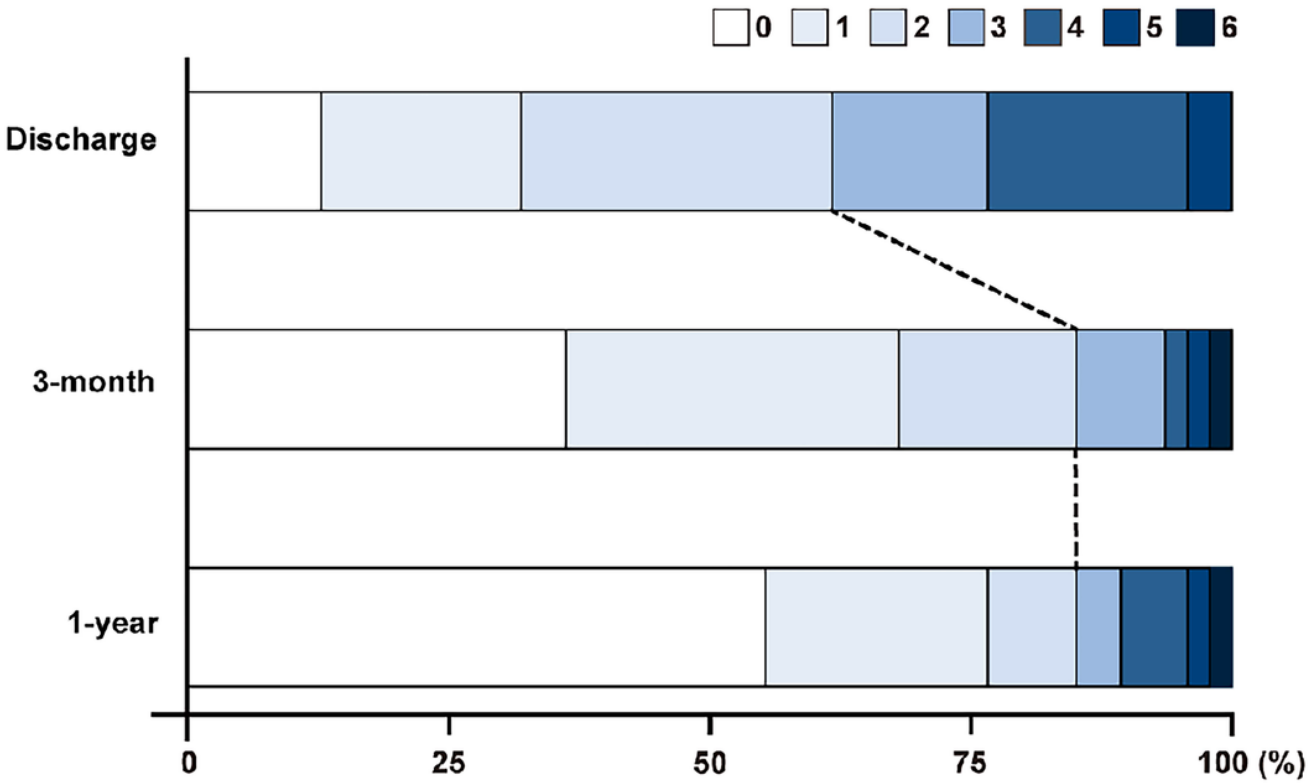

Figure 3. Modified rankin scale at discharge, 3 months and 1 year after dicharge

Figure 3

Modified Rankin scale at discharge, 3 months after discharge, and 1 year after discharge