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Original Article

The Predictors for Good Clinical Outcome in Acute Ischemic Stroke with Internal Carotid Artery Occlusion

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SUMMARY

Objectives: The evidence of intra-arterial thrombectomy (IAT) in acute ischemic stroke with internal carotid artery (ICA) occlusion was less solid than with middle cerebral artery occlusion. In this study, we aimed to investigate the predictors of good functional outcome of acute ischemic stroke with ICA occlusion after IAT in order to identify which characteristics were more associated with good functional outcome.
Methods: From June 2016 to November 2018, all subjects who received IAT for acute stroke in three hospitals were enrolled. Those who had angiographic evidence of arterial occlusion not at ICA were excluded. Presence of tandem lesions was also excluded. After review of images, subjects without available non-enhanced CT or multiphase CTA were also excluded. The modified Rankin Scale (mRS) was used to separate all subjects into good outcome (mRS: 0–2) and poor outcome (mRS: 3–6) groups. Statistical analysis was used to find between group differences, including epidemiological data, clinical characters, imaging results, and IAT results.
Results: The final enrolled subjects were 32 cases. The median and interquartile range of age was 74.5 [16.5] years old and there were 15 men. As compared with the poor outcome group, significant differences in the good outcome group included younger age ($p = 0.038$), higher percentage of usage of antithrombotic agents ($p = 0.019$), higher percentage of good or intermediate collateral ($p = 0.018$), and good reperfusion result ($p = 0.018$).
Conclusion: The benefit of IAT in acute ICA occlusion was stronger in patients with better collateral and the success of IAT was also a key to good clinical outcome.

1. Introduction

Intra-arterial thrombectomy (IAT) became a standard treatment for acute ischemic stroke with large vessel occlusion after the publication of the five large randomized trials in 2015.[1–5] For patients with acute ischemic stroke and large vessel occlusion, IAT was able to improve good outcomes, defined as a modified Rankin Scale (mRS) score from 0 to 2 within at 3 months, from 26.5% to 46.0% and there were no significant differences in intracerebral hemorrhage (ICH) or mortality as compared with control groups in a meta-analysis study.[6] The interventional group in these five large randomized trials mainly included an occlusion location in the middle cerebral artery (77%), especially at the M1 segment (69%) while the internal carotid artery (ICA) occlusion only occupied 21% of all cases, mainly at the distal ICA location. The evidence of IAT for acute M1 occlusion was more solid but for acute ICA occlusion was still questionable. A review study showed IAT increased recanalization rates and improved functional outcomes as compared with intra-arterial thrombolysis for acute ICA occlusion.[7] Another study supported the intravenous thrombolysis was more beneficial than IAT.[8] Afterward, the benefit of IAT for acute ICA occlusion was found to be different between intracranial and extracranial ICA and the role of IAT was more important in intracranial ICA occlusion but IAT might be not helpful in extracranial ICA, especially when there was patent intracranial ICA or M1.[9] Considering the heterogeneous evidence of IAT in ICA occlusion, more relevant studies were required.

In this study, we aimed to investigate the predictors of good functional outcome of acute ischemic stroke with ICA occlusion, including the clinical condition and imaging results, especially the technical result of IAT, in order to identify which characteristics in patients with acute ICA occlusion were more associated with good functional outcome and thereby, to help clinical practitioners in patient selection.

2. Material and methods

2.1. Study design and participants

From June 2016 to November 2018, all subjects who received

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IAT for acute stroke in three hospitals were enrolled. Those who had angiographic evidence of arterial occlusion not at ICA were excluded. Presence of tandem lesions was also excluded. After review of images, subjects without available non-enhanced CT or multiphase CTA were also excluded. The flowchart of enrollment was showed in Figure 1. This study had been approved by the institutional review boards in Mackay Memorial Hospital and Chang Gung Medical Foundation.

2.2. Data collection

The epidemiological data included age, sex, risk factors for stroke, and antithrombotic agent usage. The clinical parameters included initial National Institutes of Health Stroke Scale (NIHSS) scores, usage of tissue plasminogen activator (tPA) infusion, and mRS scores within 3 months. In this study, we defined a better outcome as an mRS score from 0 to 2, which meant a slight disability.

The imaging results of non-enhanced computed tomography (CT), multiphase CT angiography (CTA), and angiography for all subjects were retrospectively evaluated by two neuroradiologists with 4-year and 9-year experience. If there was discrepancy, the final result was concluded after discussion between the two neuroradiologists in order to diminish the inter-observer bias. The Alberta Stroke Program Early CT scores (ASPECTS) were measured using the non-enhanced CT and in general, ASPECTS with at least 6 points was considered to be related to a better outcome. A multiphase CTA has four series of images, including pre-contrast images and three arterial phase images. The collateral grading of the multiphase CTA was measured according to the original article of the development of multiphase CTA.[10] The collateral grading system included 0 to 5 collateral grades, where a grade of 4 and 5 represented an intermediate and good collateral, respectively. A grade between 0 and 3 represented a poor collateral. The final occlusion side of the ICA was recorded based on the angiographic findings and the ICA was divided into seven segments, including C1 (cervical segment), C2 (petrous segment), C3 (lacerum segment), C4 (cavernous segment), C5 (clinoid segment), C6 (ophthalmic segment), and C7 (communicating segment). The included data related to the IAT procedure were the relative use of general anesthesia, the usage of angioplasty for proximal cervical ICA, how many times of suction or stent-retrieving, onset-to-reperfusion time, and the modified thrombolysis in cerebral infarction (mTICI) grade. The mTICI grade was used to evaluate the reperfusion outcome after the IAT, ranging from grade 0, which meant no reperfusion, to grade 3, which meant complete reperfusion. Grade 1 was minimal reperfusion. Grade 2 meant obvious reperfusion, but there was still a presence of occluded branches, which was divided into grade 2a and 2b. Grade 2a was reperfusion of less than half of the affected territory, and grade 2b was reperfusion of more than half of the affected territory. The mTICI grade 2b or 3 was considered as a good reperfusion result. The occurrence of symptomatic ICH after IAT was also recorded.

2.3. Statistical analysis

The statistical analysis was performed using SPSS software, version 24.0 (IBM, Armonk, NY). A descriptive analysis for all parameters was conducted to display the number and percentage or the median and interquartile range (IQR). All subjects were divided into two groups: good outcome (mRS: 0–2) and poor outcome (mRS: 3–6). Nonparametric tests using the Mann-Whitney test were used to compare age, NIHSS, onset to reperfusion time between these two groups. Chi-square tests with the Fisher's exact test were used to compare the rest parameters between the two groups. A p-value less than 0.05 was considered statistically significant.

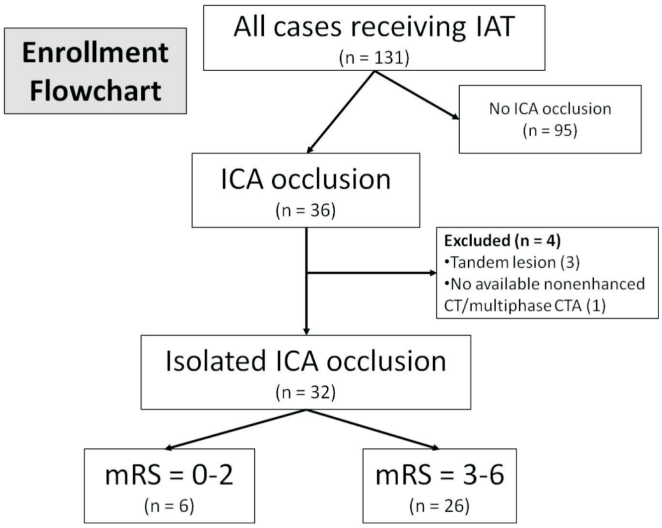

Figure 1. Flowchart of enrollment. IAT, intraaterial thrombectomy; ICA, internal carotid artery; CT, computed tomography; CTA, computed tomography angiography; mRS, modified Rankin Scale.

3. Results

3.1. Patient characteristics

The final enrolled subjects were 32 cases. The median [IQR] of age was 74.5 [16.5] years old and there were 17 women and 15 men. Among all, there were 23 cases with hypertension (71.9%), 11 cases with diabetes (34.4%), 20 cases with hyperlipidemia (62.5%), eight cases with a history of smoking (25.0%), 21 cases with atrial fibrillation (65.6%), and 17 cases being treated with antithrombotic agents (53.1%). The median [IQR] of the initial NIHSS scores was 18.5 [6.8]. The median [IQR] of the ASPECTS scores in the non-enhanced brain CTs was 9 [2.8] and 29 cases (90.6%) had a ASPECTS score of at least 6 points. Sixteen cases (50.0%) had received tPA treatment. There were 14 cases with right ICA occlusion and 18 cases with left ICA occlusion. According to the collateral grading method, there were six cases with intermediate collateral and six with good collateral. There are 13 cases (40.6%) receiving IAT under general anesthesia. Aniographic occlusion sites were 15 cases at C1, two cases at C2, four cases at C4, three cases at C5, four cases at C6 and four cases at C7. Sixteen cases (50.0%) had mTICI scores of 2b or 3. The median [IQR] of onset to reperfusion time was 323.50 [149.5] minutes. In the procedure of IAT, there was 3 cases (9.4%) receiving angioplasty for the proximal cervical ICA. For the suction technique, one case received 6 times, six cases received 4 times, five cases received 3 times, twelve cases received twice, three cases received once, and five cases did not receive this technique. For the stent-retrieving technique, one case received 4 times, two cases received 3 times, five cases received twice, seven cases received once, and seventeen cases did not receive this technique. According to the follow-up record for the 3-month mRS score, there were six cases (18.8%) with scores of 0 to 2. There were 7 cases (21.9%) with symptomatic ICH. The detailed information can be found in Table 1.

3.2. Comparison between good and poor outcome groups

The comparison between good and poor outcome groups was

Table 1
Patient demographics, clinical and imaging data.

Variable	Median [Interquartile range] or No. (%) (N = 32)
Age (years)	74.5 [16.5]
Female	15 (46.9)
Risk factors	
Hypertention	23 (71.9)
Hyperlipidemia	20 (62.5)
Atrial fibrillation	21 (65.6)
Diabetes	11 (34.4)
Smoking	8 (25.0)
Antithrombotic agent usage	17 (53.1)
NIHSS	18.5 [6.8]
tPA treatment	16 (50.0)
ASPECTS	9 [2.8] (≥ 6: 90.6%)
Occlusion side	
Right	14 (43.8)
Left	18 (56.2)
Collateral grade	0: 0, 1: 8, 2: 8, 3: 4, 4: 6, 5: 6 (4–5: 37.5%)
General anesthesia	13 (40.6)
Occlusion site	C1: 15, C2: 2, C3: 0, C4: 4, C5: 3, C6: 4, C7: 4
Angioplasty for proximal cervical ICA	3 (9.4)
Suction	0: 5, 1: 3, 2: 12, 3: 5, 4: 6, 5: 0, 6: 1
Stent-retrieving	0: 17, 1: 7, 2: 5, 3: 2, 4: 1
Onset to reperfusion time (min)	323.5 [149.5]
mTICI	0: 13, 1: 1, 2a: 2, 2b: 7, 3: 9 (2b–3: 50.0 %)
Symptomatic ICH	7 (21.9)
3month_mRS	0: 1, 1: 3, 2: 2, 3: 5, 4: 9, 5: 2, 6: 10 (0–2: 18.8%)

NIHSS, National Institutes of Health Stroke Scale; tPA, tissue plasminogen activator; ASPECTS, Alberta Stroke Program Early CT Score; ICA, internal carotid artery; mTICI, modified thrombolysis in cerebral infarction; ICH, intracerebral hemorrhage; mRS, modified Rankin Scale.

detailed in Table 2. There were 6 cases with good outcome while 26 cases with poor outcome. The statistically significant results favoring good outcome included younger age (68.5 [18.0]) vs. 79.0 [16.8], p-value = 0.038), taking antithrombotic agent (100% vs. 42.3%, p-value = 0.019), having good or intermediate collateral (83.3% vs. 27.0%, p-value = 0.018), and having mTICI results of 2b or 3 (100% vs. 38%, p-value = 0.018). As compared with proximal ICA occlusion (C1 to C5) and distal ICA occlusion (C6 and C7), the good functional outcome ratio was not significantly different (p-value = 0.148).

Table 2
Comparison between good and poor outcome.

Variable	Median [interquartile range] or No. (%)		p-value
Group (case number)	3month_RS: 0–2 (6)	3month_RS: 3–6 (26)	
Male	5 (83.3)	10 (38.5)	0.076
Age	68.5 [18.0]	79.0[16.8]	0.038*
Hypertension	4 (66.7)	19 (73.1)	1.000
Diabetes	3 (50.0)	8 (30.8)	0.390
Hyperlipidemia	5 (83.3)	15 (57.7)	0.370
Smoking	2 (33.3)	6 (23.1)	0.625
Atrial fibrillation	3 (50.0)	18 (69.2)	0.390
Antithrombotic agent	6 (100)	11 (42.3)	0.019*
NIHSS	17.0 [3.8]	19.0 [7.8]	0.285
ASPECTS	10 [1]	9 [3]	0.652
tPA	4 (66.7)	12 (46.2)	0.654
Lesion side			0.365
Left	2	16	
Right	4	10	
Good/Intermediate collateral	5 (83.3)	7 (27.0)	0.018*
General anesthesia	1 (16.7)	12 (46.2)	0.361
Onset to reperfusion (min)	268.5 [81.5]	331.5 [137.5]	0.062
Symptomatic ICH	0 (0.0)	7 (26.9)	0.296
mTICI (2b–3)	6 (100)	10 (38.5)	0.018*

mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; tPA, tissue plasminogen activator; ICH, intracerebral hemorrhage; mTICI, modified thrombolysis in cerebral infarction.
* p-value < 0.05.

4. Discussion

In this study, the benefit of IAT in acute ICA occlusion was not significantly different between proximal and distal ICA occlusion. The predictors for good functional outcome included younger age, usage of antithrombotic agent, better collateral result in multi-phase CTA, and better IAT result.

In the baseline characteristics of the enrolled subjects, there were two significant differences related to good outcome group, including younger age and usage of antithrombotic agents. The gender effect in this study did not show significantly different in this study, which was compatible with the results of previous large-scale meta-analysis studies.[6,11] The good outcome group had relatively younger age. Although the benefit of IAT was present regardless of age on previous the same large-scale meta-analysis studies, it was reasonable that young age can be associated with a better outcome because the recovery ability of central nervous system after injury was found to decline with aging and aged individuals regained function less well than young individuals after stroke.[12,13] The antithrombotic agents were used to against clot formation by several different pathways, including inhibiting platelet aggregation (antiplatelet drugs), inhibiting formation of fibrin strands (anticoagulants), and dissolving existing clots (fibrinolytics).[14] After identifying the most possible mechanism of ischemic stroke, the corresponding kind of antithrombotic agent was able to decrease the severity and recurrence rate of ischemic stroke.[15] Our study found the antithrombotic agent was also of potential to decrease the severity of acute ischemic stroke due to ICA occlusion.

There was a main favorable imaging finding in the CT studies.

The percentage of good or intermediate collateral grade was significantly higher in the good outcome group. Multiphase CTA was designed to evaluate anterior circulation collateral supply in acute ischemic infarction with large vessel occlusion. The ability of predicting clinical outcome was found to be better using multiphase CTA than using perfusion scan.[10] A higher collateral grade meant a more profound collateral supply to the ischemic area after the occlusion site and therefore, the ischemic area would be of potential to tolerate the ischemic insult longer or to decrease the severity of ischemic insult. Our results also supported this phenomenon in acute ischemic stroke with ICA occlusion. ASPECTS did not reveal significant difference between the two groups. However, previous meta-analysis studies for the anterior circulation large vessel occlusion showed a trend that the benefit of IAT was more significant when the ASPECTS was higher.[6,11] ASPECTS was established to quantify low density regions from acute stroke on nonenhanced brain CT and could be used to predict clinical outcome.[16] More hypodense regions resulted in lower ASPECTS, which meant more aggressive injury of ischemic stroke and poorer clinical outcome. Our study did not find that predictor effect of ASPECTS for clinical outcome in acute ischemic stroke with ICA occlusion, probably due to small sample size or relatively high scores in the majority of enrolled cases in both groups.

The result of IAT was also significantly related to the clinical outcome with good reperfusion (mTICI 2b or 3) ratio being much higher in the good outcome group. More specifically, the good outcome only happened when IAT achieved good reperfusion result. This finding strongly supported the beneficial effect of IAT in acute ischemic stroke with ICA occlusion. The functional outcome was not different between proximal and distal ICA occlusion. Thus, the benefit of IAT might be both evident for any location of ICA occlusion.

Symptomatic ICH was not significantly different between the control group and the IAT group on previous studies.[6,11] However, the occurrence of symptomatic ICH would increase risk of early neurological deterioration and 3-month mortality.[17] Our results did not display symptomatic ICH was a predictor of poor prognosis in acute ischemic stroke with ICA occlusion after IAT. However, there seemed to be a trend in our study. There was no case with symptomatic ICH in the good outcome group and the occurrence of symptomatic ICH only happened in poor prognosis group. However, the negative effect of symptomatic ICH required a larger scale study to prove in the future. In addition, the occurrence rate of symptomatic ICH was 21.9%, which is much higher than previous study for overall IAT cases. There might be some possible reasons. First, the cases with poor collateral occupied the majority in our ICA occlusion cases. Second, the successful rate of technique with good mTICI score was merely 50%, probably due to relatively more difficult to achieve adequate reperfusion for ICA occlusion. Third, the ICA occlusion might affect larger territory of intracranial blood supply, including anterior and middle cerebral arterial territories. As a result, the infarction might be worse in this ICA occlusion group and thereby the rate of symptomatic ICH was higher.

There are some limitations of this study. First of all, the total number of enrolled cases is relatively small and generalization requires a further large-scale study. In addition, there is no straightforward evaluation method for some imaging results, including ASPECTS and collateral grading, which might cause some interpretive bias. Furthermore, univariate statistical analysis, but not multivariate analysis, is used in this study because of the small sample size.

5. Conclusion

The benefit of IAT in acute ICA occlusion was stronger in patients with better collateral and the success of IAT was also a key to good clinical outcome.

Conflicts of interest

We declare that there are no conflicts of interest relevant to this study.

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References

1. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372(1):11–20.
2. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med.* 2015; 372(11):1019–1030.
3. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med.* 2015;372(24):2285–2295.
4. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med.* 2015; 372(11):1009–1018.
5. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med.* 2015;372(24):2296–2306.
6. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387(10029):1723–1731.
7. Kappelhof M, Marquering HA, Berkhemer OA, et al. Intra-arterial treatment of patients with acute ischemic stroke and internal carotid artery occlusion: a literature review. *J Neurointerv Surg*. 2015;7(1):8–15.
8. Seet RC, Wijdicks EF, Rabinstein AA. Stroke from acute cervical internal carotid artery occlusion: treatment results and predictors of outcome. *Arch Neurol*. 2012;69(12):1615–1620.
9. Gliem M, Lee JI, Barckhan A, et al. Outcome and treatment effects in stroke associated with acute cervical ICA occlusion. *PLoS One.* 2017;12(1):e0170247.
10. Menon BK, d'Esterre CD, Qazi EM, et al. Multiphase CT angiography: A new tool for the imaging triage of patients with acute ischemic stroke. *Radiology*. 2015;275(2):510–520.
11. Badhiwala JH, Nassiri F, Alhazzani W, et al. Endovascular thrombectomy for acute ischemic stroke: A meta-analysis. *JAMA*. 2015;314(17):1832–1843.
12. Geoffroy CG, Hilton BJ, Tetzlaff W, et al. Evidence for an age-dependent decline in Axon regeneration in the Adult Mammalian Central Nervous System. *Cell Rep*. 2016;15(2):238–246.
13. Manwani B, Liu F, Xu Y, et al. Functional recovery in aging mice after experimental stroke. *Brain Behav Immun.* 2011;25(8):1689–1700.
14. Becker DE. Antithrombotic drugs: pharmacology and implications for dental practice. *Anesth Prog*. 2013;60(2):72–80.
15. Del Brutto VJ, Chaturvedi S, Diener HC, et al. Antithrombotic therapy to prevent recurrent strokes in ischemic cerebrovascular disease: JACC Scientific Expert Panel. *J Am Coll Cardiol*. 2019;74(6):786–803.
16. Camargo EC, Furie KL, Singhal AB, et al. Acute brain infarct: detection and delineation with CT angiographic source images versus nonenhanced CT scans. *Radiology*. 2007;244(2):541–548.
17. Yaghi S, Willey JZ, Cucchiara B, et al. Treatment and outcome of hemorrhagic transformation after intravenous alteplase in acute ischemic stroke: A scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2017;48(12): e343–e361.