Original Paper

Repeated Mechanical Thrombectomy in Recurrent Large Vessel Occlusion Acute Ischemic Stroke

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Key Words

Acute stroke · Cerebral ischemia · Recurrent event · Thrombectomy · Outcomes

Abstract

Background: Endovascular therapy has been proven effective for the treatment of large vessel occlusion strokes (LVOS). However, the feasibility and potential benefits of repeat thrombectomy for recurrent stroke is unclear. We aim to report our experience with repeat thrombectomy for recurrent LVOS. **Methods:** We reviewed our prospectively collected endovascular database for patients who underwent repeated mechanical thrombectomy. Baseline characteristics, procedural data and outcomes were evaluated. Patients with repeat thrombectomy were compared to patients with single thrombectomy. For patients with repeat thrombectomy, imaging and procedural variables were compared between first and last procedures. **Results:** Out of 697 patients treated within the study period, 15 patients (2%) had repeat thrombectomies (14 treated twice and one thrice). The mean age was 63 ± 15 years and 40% were males. The median time between the first and last procedure was 18 (1–278) days. Cardioembolism (66%) was the most common etiology, followed by intracranial atherosclerosis (13%) and large vessel atherosclerosis (6%). At 90 days after the last thrombectomy, 60% of patients achieved a modified Rankin Scale score of 0–2 and 20% were deceased. There were no statistically significant differences in demographics, stroke severity, time from last known normal to puncture, reperfusion rates, hemorrhagic complications, good clinical outcomes and mortality between patients who underwent repeat thrombectomy and those who had a single thrombectomy. **Conclusion:** In properly selected patients suffering recurrent LVOS, repeated mechanical thrombectomy appears to be feasible and safe. A previous thrombectomy should not discourage aggressive treatment as these patients may achieve similar rates of good clinical outcomes as those who undergo single thrombectomy.

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Introduction

Endovascular therapy has been proven effective for the treatment of large vessel occlusion stroke (LVOS) and has become the standard of care for patients presenting early in the therapeutic window [1]. Nearly 25% of stroke victims will have a recurrent event within 5 years [2]. However, the specific rate of LVOS recurrence is unknown.

Although repeated thrombolytic therapy has been reported safe and beneficial for recurrent strokes [3–6], the data regarding repeat thrombectomy (RT) is scarce and limited to a few case reports [7–9]; therefore, its safety and potential efficacy remain elusive. We aim to report our local experience with RT for recurrent LVOS. Our specific objectives are to (1) demonstrate the frequency of RT cases, (2) compare the clinical and procedural characteristics of patients that undergo RT and those who have a single thrombectomy, and (3) evaluate the safety and efficacy of RT.

Methods

This was a retrospective review of a prospectively collected database for RT cases between June 2012 and March 2016. Imaging and procedural variables were compared between first and last procedures. The RT cases were then compared to consecutive patients treated with single thrombectomy across a similar period. Successful reperfusion was defined as per modified Thrombolysis in Cerebral Infarction (mTICI) score 2b–3 [10]. Hemorrhagic complications were defined as per European Cooperative Acute Stroke Study (ECASS) criteria [11]. Good outcome was defined as per modified Rankin Scale (mRS) 0–2 at 90 days [12]. Alberta Stroke Program Early CT score (ASPECTS) was used to quantify infarct extent at baseline [13]. This study was approved by the local institutional review board.

Statistical Analysis

Continuous variables were reported as mean $\pm$ SD or median (IQR), as appropriate. Categorical variables were reported as proportions. Between groups, comparisons for continuous/ordinal variables were made with Student's *t* test, Mann-Whitney *U* test, paired *t* test, or ANOVA, as appropriate. Categorical variables were compared by χ^2 test or Fisher's exact test as appropriate. Significance is set at $p < 0.05$. Statistical analysis was performed using IBM® SPSS® Statistics 23 (IBM®, Armonk, N.Y., USA).

Results

Fifteen (2%) of 697 patients who underwent endovascular treatment for acute ischemic stroke (AIS) over the study period were treated with RT. Fourteen patients were treated twice and one thrice (table 1; fig. 1). The mean age at the time point of first thrombectomy was 62.7 years. The median time interval between both endovascular treatments was 18 (1–278) days. The mean last known normal to puncture time interval was 245 ± 99 min for the first procedure and $486 \pm 1,131$ min for the last procedure ($p = 0.44$). The mean baseline National Institute of Health Stroke Scale (NIHSS) was 15.9 ± 6.1 for the first and 21.2 ± 7.2 for the last thrombectomy ($p = 0.03$). The mean ASPECTS was 8 ± 1.65 for the first and 8.36 ± 1.55 ($p = 0.41$) for the last procedure. Hospitalized patients ($n = 5$) had nonsignificant shorter time from last known normal to puncture in the last procedure as compared to nonhospitalized patients ($n = 10$, 111 ± 25 vs. $801 \pm 1,340$ min, $p = 0.14$), but outcomes were comparable. Successful reperfusion was achieved in 14/15 patients after the first thrombectomy and in all patients after RT. No vascular complications were identified. No parenchymal hemorrhage was observed after the first procedure and two were noted after the repeated intervention. The rate of good clinical outcome at 90 days in RT patients was 60% and their 90-day mortality rate was only 20%. Stroke etiology was the same for first and recurrent

Table 1. Demographic, clinical, neuroradiological and procedural parameters as well as outcome measures before and after each procedure

Case	Age ^a / sex	Stroke etiology	Time between procedures, days	Procedure characteristics									
				proce- dure	baseline mRS	NIHSS	ASPECTS	site (side)	LKN to puncture, min	device	mTICI	bleed	90-day mRS
1	55/M	APS	26	1st	0	18	9	M1 (L)	103	TA+SR	2b	none	2
				2nd	2	13	10	M1 (L)	113	TA	2b	none	1
2	82/F	CE	12	1st	0	20	9	M1 (R)	284	TA+SR	2b	none	5
				2nd	0	16	9	M1 (L)	130	SR	3	none	6
3	60/M	ICAD	18	1st	1	14	10	VB	257	ICS	3	none	2
				2nd	2	15	10	VB	133	TA+ICS	2b	none	2
4	52/F	CE	278	1st	0	28	8	M1 (L)	203	TA	3	none	1
				2nd	0	20	9	M1 (R)	596	TA+SR	3	PH-2	4
5	32/F	CE	616	1st	0	9	9	M1 (L)	270	TA	2b	none	1
				2nd	3	12	8	M1+M2 (R)	240	TA	2b	none	1
				3rd	0	12	8	M1 (L)	202	TA+SR	2b	none	1
6	61/M	ICAD	1	1st	0	12	10	M1 (R)	475	TA	2b	none	2
				2nd ^b	0	13	–	M1+M2 (R)	–	SR+ICS	2b	none	2
7	57/F	CE	15	1st	2	18	8	M3 (R)	269	TA	2a	none	3
				2nd	2	33	6	M1 (L)	250	SR	2c	a-SAH	3
8	78/F	CE	915	1st	0	13	8	M1 (R)	215	SR	3	none	1
				2nd	1	19	10	ICA-T (L)	1,628	SR	2b	none	2
9	84/F	CE	1	1st	2	13	6	ICA-T (R)	204	SR	3	none	6
				2nd	2	21	10	E-ICA+ICA-T (L)	90	TA+SR	3	none	6
10	61/F	CE	32	1st	1	23	5	M1 (L)	225	TA	2c	Hi-2	1
				2nd	3	31	8	M1 (R)	218	TA+SR	2c	none	1
11	63/F	LVA	<1	1st	1	18	9	E-ICA+M1 (L)	573	SR	2b	none	2
				2nd	1	19	5	E-ICA+M2 (L)	125	SR+ECS	2b	PH-2	2
12	62/M	CE	876	1st	1	21	6	M1 (L)	264	SR	3	Hi-2	4
				2nd	4	35	9	M1 (R)	4,389	SR	3	Hi-1	6
13	51/F	FMD	<1	1st	0	16	6	ICA-T+M1 (R)	125	TA+SR	3	none	1 ^c
				2nd	0	17	7	ICA-T+M2+M3 (R)	90	SR	2b	none	1 ^c
14	54/M	CE	3	1st	3	14	7	ICA-T (L)	335	SR	3	none	2 ^d
				2nd	3	25	8	M1 (R)	140	SR	3	none	2 ^d
15	89/M	CE	214	1st	0	2	9	M1 (R)	166	TA	2b	none	1
				2nd	1	21	8	ICA-T (R)	316	SR	3	none	5 ^e

APS = Antiphospholipid syndrome; a-SAH = asymptomatic subarachnoid hemorrhage; CE = cardioembolic; ECS = extracranial stenting; E-ICA = extracranial internal carotid artery; F = female; FMD = fibromuscular dysplasia; Hi = hemorrhagic infarction; ICAD = intracranial atherosclerotic disease; ICA-T = internal carotid artery terminus; ICS = intracranial stenting; L = left; LKN = last known normal; LVA = large vessel atherosclerosis; M = male; PH = parenchymal hemorrhage; R = right; SR = stentriever; TA = thromboaspiration; VB = vertebrobasilar. ^a Age at first procedure. ^b The patient remained symptomatic with an NIHSS of 12–13 and was taken back to the angiography suite for further clot retrieval. ^c mRS at 2 months. ^d mRS at discharge. ^e Patient had a third recurrent stroke (not amenable to endovascular treatment) 2 weeks after discharge and was transferred to hospice.

strokes, and was categorized as cardioembolic in 66% of the patients, followed by intracranial atherosclerotic disease (13%), and extracranial atherosclerosis (6%).

Patients with RT were comparable to those who had a single thrombectomy in terms of clinical, procedural and outcome parameters except for higher rates of hypertension ($p = 0.01$) and anticoagulation ($p = 0.001$) (table 2).

Discussion

We report the largest series of patients undergoing repeat mechanical thrombectomy for recurrent LVOS, and demonstrate that RT is feasible and appears to be safe and effective in properly selected cases.

Fig. 1. A 32-year-old woman with triple thrombectomy (table 1, case No. 5). **a** Patient presenting with acute left hemiplegia and aphasia: pre-procedure noncontrast computed tomography (CT) (left), pre- and post-procedure angiography (middle) and follow-up CT (right). **b** Twenty months later, new-onset right leg weakness: pre-procedure CT perfusion (left), pre- and post-procedure angiography (middle) and follow-up CT (right). **c** Six weeks after the second intervention, new-onset left side weakness and aphasia: pre-procedure CT perfusion (left), pre- and post-procedure angiography (middle) and follow-up CT (right).

Considering that nearly 1 in 4 patients will have a recurrent stroke within the first 5 years following an AIS [2], and that LVOS accounts for nearly 50% of all strokes [14], the need for further validation of repeat thrombectomy becomes apparent. Although repeated systemic thrombolysis has been reported to be safe and efficient for patients presenting with a recurrent AIS [3–6], its use carries the limitations inherent to tissue plasminogen activator (t-PA) including bleeding risk mostly if the recurrence is relatively early on [15]. Intravenous

Table 2. Comparison between patients with repeated treatment and patients with single procedure

	Repeated thrombectomy (last procedure) (n = 15)	Single thrombectomy (n = 557)	p value
Age, years	63.4±15.01	65.4±14.61	0.61
Gender, male	6 (40%)	303 (54.4%)	0.3
Hypertension	15 (100%)	408 (73.4%)	0.01
Dyslipidemia	5 (33.3%)	230 (41.4%)	0.6
Atrial fibrillation	8 (53.3%)	199 (35.9%)	0.18
Diabetes	2 (13.3%)	129 (23.2%)	0.53
Smoking	3 (20%)	107 (19.3%)	1.00
Anticoagulation	8 (53.3%)	75 (16.3%)	0.001
Glucose	122±28	136±55	0.08
INR	1.49±0.79	1.11±0.36	0.11
SBP	138±23	148±32	0.12
Baseline NIHSS	21.21±7.27	17.9±6.4	0.11
ASPECTS	8.36±1.55	8±1.7	0.35
Stroke etiology			0.3
Cardioembolic	10 (66.7%)	277 (51.3%)	
LVA	1 (6.7%)	100 (18.5%)	
ICAD	2 (13.3%)	42 (7.8%)	
Other	2 (13.3%)	32 (5.7%)	
Undetermined	0 (0%)	89 (16.5%)	
Stroke location			
ACA	0 (0%)	16 (2.9%)	1.00
MCA-M1	9 (60%)	244 (43.8%)	0.29
MCA-M2/M3	0 (0%)	98 (17.6%)	0.08
ICA terminus	2 (13.3%)	77 (13.8%)	0.32
Extracranial ICA	0 (0%)	15 (2.7%)	1.00
Vertebrobasilar	1 (6.7%)	53 (9.5%)	1.00
Tandem	3 (20%)	70 (12.6%)	0.42
Procedure			
LKN to puncture	486±1,131	325±297	0.60
Stentriever	13 (86.7%)	470 (84.4%)	1.00
Reperfusion			
mTICI 2b--3	15 (100%)	484 (87.2%)	0.23
mTICI 3	6 (40%)	263 (47.5%)	0.61
Parenchymal hemorrhage	2 (13.3%)	49 (8.8%)	0.63
mRS 0--2 at 3 months	9 (60%)	236 (46.5%)	0.43
Mortality 90 days	3 (20%)	114 (22.5%)	1.00

ACA = Anterior cerebral artery; ICA = internal carotid artery; ICAD = intracranial atherosclerotic disease; INR = international normalized ratio; LKN = last known normal; LVA = large vessel atherosclerosis; MCA = middle cerebral artery; SBP = systolic blood pressure.

t-PA re-administration has also been associated with severe immune reactions [16, 17]. The majority of our patients had a cardioembolic etiology, which has been described in the literature to be more prone to stroke recurrence with a risk varying between 1 and 22% and a mean time between the 2 events of 12 days [18]. Contrarily to extracranial atherosclerosis, the rate of intracranial atherosclerotic disease was higher than usually reported [19, 20], and was probably due to a selection bias since our database only includes LVOS treated via endovascular therapy.

Mechanical thrombectomy has proven to be superior to systemic thrombolysis alone in recent clinical trials for LVOS [1] and may be considered as a potential option for patients presenting with a recurrent stroke. Data regarding the repeated use of intra-arterial treatment

(IAT) is limited to a total of 5 cases [4, 7–9]. Four of these patients underwent 2 IAT and one was treated thrice. Mechanical thrombectomy with stentrievers was performed in 5 out of the 11 procedures and intra-arterial thrombolytic injection was the main treatment in 3 procedures. The mean age was 60.8 ± 12 , three were male and the median time between procedures was 6 (2.5–165) days. All patients were successfully reperfused and there were no procedure-related complications following the repeated treatment with good outcomes achieved in 40% of the cases. It is also noteworthy that 4/5 patients in the above-mentioned case reports had a contraindication to intravenous t-PA at the time of the repeated intervention. Our study confirmed these preliminary findings and showed that when compared with patients that had only one intervention, properly selected RT patients (whether presenting with an early re-occlusion or with completely separate ischemic event) behaved similarly and had high rates of successful reperfusion, acceptable incidence of hemorrhagic complication rates, and high rates of good clinical outcomes.

There are important limitations to our study, mostly inherent to the retrospective design and relatively small sample size. However, to our knowledge, this is the first systematic analysis and represents the largest report on this topic. In our study, only 2% of the IAT treated patients had recurrent LVOS amenable to a second endovascular treatment. This rate is lower than expected and likely underestimates the true frequency of the problem. There are many factors that might have led to a potential underestimation including the fact that patients with recurrent strokes who were severely disabled after their initial stroke were presumably deemed noncandidates for RT. Moreover, it is likely that there were recurrent strokes that were in territories too distal for IAT, responded to intravenous t-PA, already had large/complete infarcts upon presentation, or were seen in other stroke centers.

Conclusions

In properly selected patients suffering from recurrent LVOS, repeated mechanical thrombectomy appears to be feasible and safe. A previous thrombectomy should not discourage aggressive treatment as these patients may achieve similar rates of good clinical outcomes as those who undergo single thrombectomy.

Disclosure Statement

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