

Repeated Endovascular Thrombectomy in Patients With Acute Ischemic Stroke

Results From a Nationwide Multicenter Database

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Background and Purpose—Patients with acute ischemic stroke treated with endovascular thrombectomy may be treated with repeat endovascular thrombectomy (rEVT) in case of recurrent large vessel occlusion. Data on safety and efficacy of these interventions is scarce. Our aim is to report on frequency, timing, and outcome of rEVT in a large nation-wide multicenter registry.

Methods—In the Netherlands, all patients with endovascular thrombectomy have been registered since 2002 (MR CLEAN Pretrial registry, MR CLEAN Trial [Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands], and MR CLEAN Registry). We retrospectively reviewed these databases for anterior circulation rEVT cases. Patient characteristics, procedural data, and functional outcome (modified Rankin Scale at 90 days) were analyzed.

Results—Of 3928 patients treated between 2002 and 2017, 27 (0.7%) underwent rEVT. Median time between first and second procedure was 78 (1–1122) days; 11/27 patients were re-treated within 30 days. Cardioembolism was the most common etiology (18 patients [67%]). In 19 patients (70%), recurrent occlusion occurred ipsilateral to previous occlusion. At 90 days after rEVT procedure, 44% of the patients had achieved functional independence (modified Rankin Scale score of 0–2), and 33% had died. Adverse events were 2/27 (7.4%) intracranial hemorrhage, 1/27 (3.7%) stroke progression, and 1/27 (3.7%) pneumonia.

Conclusions—In this large nationwide cohort of patients with acute ischemic stroke treated with endovascular thrombectomy, rEVT was rare. Stroke cause was mainly cardio-embolic, and most recurrent large vessel occlusions in which rEVT was performed occurred ipsilateral. Although there probably is a selection bias on repeated treatment in case of recurrent large vessel occlusion, rEVT appears safe, with similar outcome as in single-treated cases. (*Stroke*. 2020;51:526-532. DOI: 10.1161/STROKEAHA.119.027525.)

Key Words: cardio-embolic ■ functional outcome ■ repeated thrombectomy ■ stroke

Research has shown that ≈25% of all patients with stroke will have a recurrent stroke within 5 years.¹ The risk of a recurrent large vessel occlusion (LVO) after endovascular treatment (EVT) is largely unknown, but could be significant, as patients with LVO stroke often have a high-risk vascular profile, including atrial fibrillation. A meta-analysis of the large EVT trials showed that the risk of recurrent stroke within 90 days in EVT treated patients was 3-fold compared with the control group (5% versus 1.3%), but stroke subtype was not reported.²

Now that the use of EVT for LVO is growing worldwide, physicians will likely be faced with patients presenting with

recurrent LVO who are eligible for repeat EVT (rEVT). To date, few publications have reported on repeated EVT, and it is unclear whether rEVT could still be safe and effective in patients who suffered from previous stroke. Three case reports describe short-term recurrent LVO after EVT, being treated successfully with rEVT.^{3–5} In 3 single-center case series with relatively small numbers of rEVT, this also appeared to be feasible and safe.^{6–8}

Our aim is to report on rEVT cases from a large nationwide multicenter database that includes all EVT-treated stroke cases in the Netherlands from 2002 to 2017. We compare

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clinical, imaging, and procedural data between consecutive procedures and assess whether rEVT in case of recurrent LVO is safe and effective.

Methods

Patient Selection

We retrospectively reviewed data on patients treated with EVT, collected from 19 stroke centers in the Netherlands from October 2002 till November 2017. This cohort included patients from 3 datasets: MR CLEAN pretrial (2002–2013),⁹ MR CLEAN trial (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; 2010–2014),¹⁰ and MR CLEAN registry (2014–2017).¹¹

The MR CLEAN pretrial is a registry of all consecutive patients with acute ischemic stroke treated with EVT in the Netherlands. The registry started in October 2002 and continued until a center started participation in the MR CLEAN trial (last center in October 2013). The institutional review board from the coordinating institution approved registration and use of the data.

The MR CLEAN trial is a multicenter randomized clinical trial of treatment with EVT plus usual care versus usual care alone (control group) in patients with acute ischemic stroke and a proximal intracranial arterial occlusion, enrolling patients from December 2010 till March 2014. A central medical ethics committee and the research board of each participating center approved the study protocol. All patients or their legal representatives provided written informed consent before randomization. Patients randomized to the control group were excluded for the current study. It was not allowed for patients included in the MR CLEAN trial to be re-included in case of recurrent LVO during the follow-up period of 3 months.

The MR CLEAN registry is a prospective, observational study in the Netherlands of all patients treated with EVT from March 2014. The study protocol has been evaluated by a central medical ethics committee and permission to carry out the study as a registry was granted.

The MR CLEAN pretrial, trial, and registry datasets contain patients who underwent EVT for acute ischemic stroke with LVO in the anterior circulation in the Netherlands from 2002 to 2017. After merging these 3 datasets, patient duplicates were extracted.

We excluded patients who showed no LVO on digital subtraction angiography at initiation of the procedure because of spontaneous recanalization or initial misdiagnosis, as our aim was to report on actual performed thrombectomy.

We arbitrarily divided rEVT into early (≤ 30 days) and late re-treatments (>30 days) to trace possible distinct patterns in patient characteristics that may contribute to recurrent LVO.

Clinical Characteristics

Demographic and clinical data were recorded including age, sex, National Institutes of Health Stroke Scale score, time elapse between first and subsequent EVT procedure, use of antiplatelets or anticoagulants, and cardiovascular risk factors such as hypertension, hypercholesterolemia, diabetes mellitus, and atrial fibrillation. Risk factors were obtained from patient records.

Intervention Procedure

EVT consisted of arterial catheterization with a microcatheter to the level of occlusion, followed by mechanical thrombectomy or thrombus aspiration, or both, with or without delivery of a thrombolytic agent. Mechanical treatment could involve thrombus retraction, aspiration, wire disruption, or use of a retrievable stent. The method of EVT was left to the discretion of the local interventionist. Standard treatment procedure did not include intracranial balloon angioplasty or intracranial stenting.

Radiological Assessment

All obtained images were stored and analyzed by an imaging core laboratory. Successful reperfusion was defined as per modified

Thrombolysis in Cerebral Infarction score 2b or 3.¹² Symptomatic intracranial hemorrhage on follow-up imaging was scored according to the Heidelberg criteria.¹³

Stroke Etiology

We used the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) criteria to categorize cause into large artery atherosclerosis, cardioembolism, or undetermined cause (2 or more causes identified, negative or incomplete evaluation).¹⁴ A patient was considered to have large artery atherosclerosis stroke if there was $>50\%$ atherosclerotic stenosis or occlusion at the bifurcation of the carotid artery on the symptomatic side.

Outcome

The primary outcome was functional outcome at 3 months (based on the modified Rankin Scale score), ranging from 0 (no symptoms) to 6 (death).¹⁵ Secondary outcome measures included National Institutes of Health Stroke Scale at 24 hours, postprocedural modified Thrombolysis in Cerebral Infarction score, and complications that occurred during intervention, hospital stay, or during 3 months of follow-up.

Statistical Analyses

Continuous variables were reported as mean \pm SD or median (interquartile range), as appropriate. Categorical variables were reported as proportions. We compared procedural data and imaging data between consecutive EVT procedures, and then compared patient characteristics of the rEVT cases to the patient profile of single EVT cases, for which we used the cohort of the MR CLEAN registry 2014 to 2017. Standard statistics were used for comparisons between groups. STATA (version 14.1) was used for all statistical analyses. Source data will not be made available because of legislative issues on patient privacy, but detailed analytic methods and study materials, including log files of statistical analyses, will be made available to other researchers on request to the first author.

Results

Patient Characteristics and Outcome

We identified 27 out of 3928 patients with acute ischemic stroke (0.7%) who underwent 2 EVT procedures due to recurrent LVO in the anterior circulation (Figure). The mean age at the time of the first EVT procedure was 72 (± 16 , range 25–97) years. The median time interval between first and second EVT was 78 days (range, 1–1122) days. Median

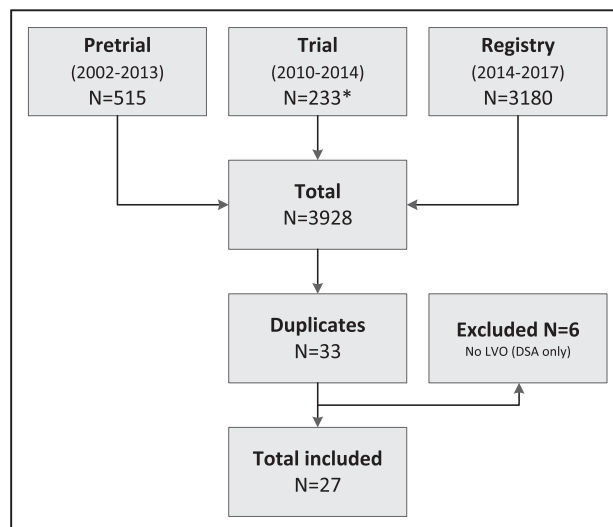


Figure. Flowchart Patient Selection. DSA indicates digital subtraction angiography; and LVO, large vessel occlusion. *Intervention group only.

baseline National Institutes of Health Stroke Scale at admission was 14 (interquartile range, 10–16) for the first procedure, and 17 (interquartile range, 12–21) for the second procedure. Nine out of 27 (33.3%) patients were not functionally independent (modified Rankin Scale score >2) when undergoing the second EVT procedure.

Procedural characteristics per case are shown in Tables 1 and 2, with distinction of early rEVT (41%, Table 1) and late rEVT (59%, Table 2). Both in patients with early retreatment and in patients with late retreatment, ≈70% of the re-occlusions occurred ipsilaterally. Overall, there were less device attempts (mean, 1.5±0.8 versus 2.1±1.7) and less procedural complications

Table 1. Early Recurrent LVO

Case	Sex/ Age*	Time Between EVT (d)	Baseline Characteristics				Procedural Characteristics					Outcome				
			Risk Factors	AT	ASPECTS	Pre mRS	Occlusion Site	Device Attempts	Complications	Onset to Groin (Min)	Post- TICI	NIHSS 0 h	NIHSS 24 h	SAE	mRS	TOAST
1	M, 63	1	AF, MI	VKA (INR 1.9)	7	1	M1+M2, right	2	No	223	3	17	3	Pacemaker Infection	4	CE
				VKA (INR1.7)	8	4	ICA-T+M1, right	5	M1 stayed TICI: 1	330	2A	17	17		4	CE
2	F, 25	1	CM	No	10	1	ICA-T right	1	No	135	2B	16	7	No	1	CE
				No	10	1	M1, right	6	No	187	2B	15	5	No	1	CE
3	F, 82	4	HT, AF, smoking	No	9	0	M1, left	2	No	120	2B	10	2	No	4	CE
				AP	9	1	M1, left	1	Dissection ICA left	158	2A	16	15	No	4	CE
4	F, 79	6	HT, HC, AF	VKA (INR1.7)	9	0	M1, left	1	No	135	3	12	0	No	0	CE
				VKA (INR1.7)	9	1	M1, left	1	No	170	3	2	0	No	0	CE
5	F, 69	6	AF, MI, HT, smoking	No	10	1	M2, right	2	No	336	2B	8	0	No	6	CE
				Heparin	10	1	M2, left	2	No	75	3	19	8	No	6	CE
6	F, 93	6	DM	AP	10	2	M2, right	1	No	253	2A	19	4	No	2	LAA
				AP	9	4	M2, right	1	No	180	3	17	3	No	2	LAA
7	M, 85	9	HT, DM, HC	No	9	3	M1, right	1	No	300	3	13	7	No	6	LAA
				AP	10	4	M1, left	2	No	237	2B	22	6	No	6	LAA
8	F, 97	11	HT, HC, AF	AP	10	1	M2, left	2	Perforation	250	3	5	16	SAH	5	CE
				AP, Heparin	10	1	M1, right	...	No	147	2B	14	11	No	5	CE
9	M, 71	13	AF, CM	VKA (INR1.8)	10	0	M2, right	1	No	135	3	14	0	No	2	CE
				AP	4	1	ICT-T, right	4	Perforation	135	3	17	2	No	2	CE
10	F, 71	13	AF, HC, MI	AP	9	0	M1, right	1	No	193	2B	5	0	Infection without focus	0	CE
				DOAC	9	0	M1, right	3	No	125	1	12	1	No	0	CE
11	F, 72	23	HT, HC	AP	9	0	M1, left	3	No	105	3	22	10	No	3	Unknown
				AP	5	0	M1, left	0, no access	No	...	0	23	21	No	3	Unknown

AF indicates atrial fibrillation; AP, antiplatelets; ASPECTS, Alberta Stroke Program Early CT Score; AT, antithrombotics; CE, cardio-embolism; CM, cardiomyopathy; DM, diabetes mellitus; DOAC, direct oral anticoagulation; EVT, endovascular thrombectomy; HC, hypercholesterolemia; HT, hypertension; ICA, internal carotid artery; LAA, large artery atherosclerosis; MI, myocardial infarction; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SAE, serious adverse event; SAH, subarachnoid hemorrhage; TICI, Thrombolysis in Cerebral Infarction; TOAST, Trial of ORG 10172 in Acute Stroke Treatment classification; and VKA, vitamin K antagonist.

*Age of patient on date of first procedure.

Table 2. Late Recurrent LVO

Case	Sex/ Age*	Time Between EVT (d)	Baseline Characteristics				Procedural Characteristics					Outcome				
			Risk Factors	AT	ASPECTS	Pre- mRS	Occlusion Site	Device, Attempts	Complications	Onset to Groin (Min)	Post TICI	NIHSS 0 h	NIHSS 24 h	SAE	mRS	TOAST
1	F, 8	37	HT, HC, AF, Smoking	AP	10	0	Distal M1, left	2	No	270	3	16	0	No	6	CE
				AP	10	3	Distal M1, left	6	No	167	2B	21	22	No	6	CE
2	M, 51	40		No	...	0	M1, right	1	No	...	3	14	1	No	2	CE
				AP	...	2	M1, left	1	Vasospasm	...	3	23	1	No	2	CE
3	F, 78	78	HT, HC, AF, DM, smoking	VKA (INR2.0)	10	3	M1, left	1	No	303	2B	16	3	No	3	CE
				VKA (INR1.3), AP	10	3	ICA-T, left	5	No	190	3	20	23	No	6	CE
4	F, 88	128	HT, DM	No	7	3	ICA-T, right	1	No	175	3	19	13	No	3	LAA
				AP	10	4	M1, left	2	No	315	3	19	37	No	6	LAA
5	M, 51	183	HT, DM, HC, MI, smoking	AP	5	0	ICA-T right	1	No	275	3	14	9	No	3	CE
				AP	10	3	M2, left	1	No	225	2B	15	10	No	3	CE
6	F, 90	193	HT, AF	VKA (INR1.6)	9	2	ICA-T, left	1	No	169	3	12	0	No	4	CE
				VKA (INR1.7)	10	4	ICA-T, left	1	No	265	3	25	12	No	6	CE
7	F, 85	200	HT, HC, MI	AP	10	1	Distal M1, left	1	No	185	2A	4	3	No	3	Unknown
				AP	5	3	Distal M1, left	2	Perforation	275	2A	24	24	ICH	6	Unknown
8	M, 60	212	AF	VKA (INR3.2)	...	0	M1, left	3	No	...	3	23	0	No	1	CE
				VKA (INR 2.5)	...	1	M1, right	3	No	...	3	21	25	Stroke progression	6	CE
9	M, 75	228		No	...	0	M1, right	2	No	...	3	10	0	No	1	LAA
				AP	...	0	M1, right	1	No	...	3	6	1	No	1	LAA
10	F, 80	295	HT, AF	No	10	1	M1, right	2	No	205	3	12	2	Pneumonia	3	CE
				DOAC	10	2	M2, right	1	No	183	2B	12	6	No	5	CE
11	M, 61	352	Smoking	No	9	0	Distal M1, right	4	No	165	2B	16	4	No	2	Unknown
				No	8	2	ICA-T, right	1	No	140	3	15	6	No	3	Unknown
12	F, 71	728	HT, AF, DM	VKA (INR2.5)	10	0	Prox M1, right	1	No	158	3	11	4	No	3	CE
				VKA (INR1.5)	10	2	M1, right	1	No	275	3	40	25	No	6	CE
13	M, 56	741	HT, HC, AF, MI	VKA (INR2.9)	10	0	M1, left	1	No	115	3	20	2	No	0	CE
				DOAC	8	1	M1, right	1	No	235	2B	10	1	No	2	CE
14	M, 62	833	MI	Unknown	M2, right†	1	No	...	2A	7	3	No	2	CE
				Unknown	M2, right†	1	No	...	2A	8	3	Pneumonia	2	CE
15	F, 80	1051	HT, HC	No	10	0	M1, right	1		205	2	12	4	No	2	Unknown
				No	10	0	ICA-T, right	2	No	145	2A	10	1	No	1	Unknown

(Continued)

Table 2. Continued

Case	Sex/ Age*	Time Between EVT (d)	Baseline Characteristics				Procedural Characteristics					Outcome				
			Risk Factors	AT	ASPECTS	Pre- mRS	Occlusion Site	Device, Attempts	Complications	Onset to Groin (Min)	Post TICI	NIHSS 0 h	NIHSS 24 h	SAE	mRS	TOAST
16	F, 72	1122	HT, HC, MI	No	10	0	M1, left	1	No	220	2B	15	6	No	1	Unknown
				No	9	0	Prox M1, left	1	No	270	3	5	3	ICH	0	Unknown

AF indicates atrial fibrillation; AP, antiplatelets; ASPECTS, Alberta Stroke Program Early CT Score; AT, antithrombotics; CE, cardioembolism; DM, diabetes mellitus; DOAC, direct oral anticoagulation; EVT, endovascular thrombectomy; HC, hypercholesterolemia; HT, hypertension; ICA, internal carotid artery; ICH, intracranial hemorrhage; LAA, large artery atherosclerosis; MI, myocardial infarction; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SAE, serious adverse event; TICI, Thrombolysis in Cerebral Infarction; TOAST, Trial of ORG 10172 in Acute Stroke Treatment classification; and VKA, vitamin K antagonist.

*Age of patient on the date of first procedure.

†Occlusion site assessed by treating radiologist, no blinded core laboratory assessment.

(1 patient versus 4 patients) during the first EVT procedure compared with the second. All of the procedural complications during second EVT occurred in ipsilaterally treated patients.

Table 3 shows the patient characteristics of the rEVT cases (second procedure) compared with single-EVT cases. Slightly more women were treated with repeat EVT compared with single-treated patients, though this difference was not significant (63% versus 48%; $P=0.12$). More patients in the rEVT group had a history of atrial fibrillation (52% versus 24%; $P<0.01$), myocardial infarction (30% versus 14%; $P=0.02$), and about twice as many patients were using secondary prevention at the time of the repeated EVT compared with the single-treated patients (statin: 73% versus 35%, $P<0.01$; antiplatelet: 54% versus 31%, $P<0.01$; anticoagulants: 41% versus 16%, $P<0.01$). The outcome after rEVT was comparable to the outcome after single EVT in terms of functional independence (modified Rankin Scale score <2 44% versus 41%), National Institutes of Health Stroke Scale 24 hours (6 versus 10), successful recanalization (74% versus 66%), and complication rate (symptomatic intracranial hemorrhage, 7.4% versus 5.9%; stroke progression, 3.7% versus 10%; pneumonia, 3.7% versus 11%). Mortality rate was slightly higher after rEVT (33% versus 29%), but the difference was not statistically significant ($P=0.62$).

The outcome of rEVT in ipsilateral recurrences ($n=19$) compared with rEVT in contralateral recurrences ($n=8$) are shown in Table I in the [online-only Data Supplement](#). Overall slightly better outcome was seen in ipsilaterally treated patients in terms of modified Rankin Scale (median 3 versus 5.5), functional independence (47% versus 25%), and mortality (26% versus 50%), though none of these differences were statistically significant.

Stroke Cause

Stroke cause could be identified in 22 (81%) out of 27 patients with rEVT (Tables 1 and 2). According to the TOAST classification, stroke cause was mainly cardioembolic for both early and late recurrent LVO (73% and 63%, respectively) and for both the ipsilateral recurrences (63%) as the contralateral recurrences (75%).

Discussion

This retrospective nationwide multicenter study describes rEVT cases in the Netherlands from October 2002 till November 2017.

The frequency of rEVT in our study was 0.7% of all EVT procedures, which is lower than in previous single center case series (2% and 1.4%).^{6,7} However, in our study, we excluded all posterior LVO's, and it was not allowed for patients included in the MR CLEAN trial (2010–2014) to be re-included in case of recurrent LVO during the follow-up period of 3 months. Therefore, possible early recurrent EVT was not performed or not registered during the study period.

Another explanation for the low rate of retreatment might be selection. Previous studies reported restenosis rates after EVT on standard magnetic resonance angiography follow-up after 3 to 12 months up to 9%; however, all of these restenosis were reported to be asymptomatic.^{16,17} A study on very early reocclusions (<48 hours) on follow-up imaging after EVT showed a recurrence rate of 16/711 (2.3%), but only 3 out of 711 (0.4%) were re-treated.¹⁸ This is similar to our rate of early (<30 days) repeated EVT cases: 11/3928 (0.3%). It is clear that these do not reflect all recurrent LVO's. Especially in early reocclusions, there might be a selection bias on repeated treatment, as vessel imaging and rEVT are often not considered in persistent poor or deteriorating neurological status during the acute stroke phase.

Stroke cause was mainly cardioembolic (67%), which is in line with the findings from the previous case series on rEVT (66%, 43%, 87%).^{6–8} In our series, most patients were on secondary prevention at the time of the recurrent LVO. However, in patients using anticoagulants, international normalized ratio often was not in the therapeutic range, which may have contributed to a recurrent event.

In $\approx 70\%$ of the repeated EVT cases, recurrent LVO occurred in the same hemisphere, while in previous studies, the ipsilateral recurrence rate was much lower (36%, 50%, 43%). We hypothesize that certain vascular territories are more susceptible for reocclusion because of differences in vascular anatomy and blood flow, and that emboli will travel the route of least resistance.¹⁹ Furthermore, animal studies have found histological evidence of local vessel damage after EVT treatment which could make the vessel susceptible to reocclusion.^{20,21} We did not perform standard MR angiography follow-up; therefore, we are uncertain if vessel wall damage as result of thrombectomy or other intracranial vasculopathies may have contributed to reocclusion. However, no vessel abnormalities were reported by the interventionists.

The outcome of rEVT was comparable to the outcome of single EVT in terms of functional independence, reperfusion

Table 3. Characteristics of Patients With Repeated EVT vs Patients With Single EVT (MR CLEAN Registry March 2014 to Nov 2017)

	Repeated EVT Cases (2nd Procedure) n=27	Single EVT Cases n=3157*	P Value
Age, y, median (IQR)	74 (62–86)	72 (61–80)	0.25
Male sex, n (%)	10 (37%)	1648 (52%)	0.12
NIHSS, median (IQR)	17 (12–21)	16 (11–19)†	0.39
Premorbid mRS, median (IQR)	1 (1–3)	0 (0–1)	<0.01
Clinical localization: left hemisphere, n (%)	13 (48%)	1674 (53%)‡	0.81
Intravenous alteplase treatment, n (%)	10 (37%)	2417 (77%)	<0.01
Onset to groin, min, median (IQR)	185 (147–265)§	195 (150–250)¶	0.96
Medical history			
Atrial fibrillation, n (%)	14 (52%)	744 (24%)¶¶	<0.01
Hypertension, n (%)	17 (63%)	1616 (52%)#	0.27
Myocardial infarction, n (%)	8 (30%)	435 (14%)***	0.02
Diabetes mellitus, n (%)	6 (22%)	505 (16%)††	0.39
Intoxication and medication			
Current smoking, n (%)	6 (22%)‡‡	672 (21%)§§	0.88
Statin use, n (%)	19 (73%)	1083 (35%)¶¶¶	<0.01
Antiplatelet use, n (%)	14 (54%)	970 (31%)¶¶¶	<0.01
Anticoagulation, n (%)	11 (41%)	500 (16%)##	<0.01
Stroke cause***			
CE	18 (66.7%)	455 (33.1%)	<0.01
LAA	4 (14.8%)	185 (13.5%)	0.84
Undetermined	5 (18.5%)	670 (48.7%)	<0.01
Outcome			
mRS at 90 d, median (IQR)	3 (2–6)	3 (2–6)†††	0.85
mRS score 0–2 at 90 d, n (%)	11 (44%)	1194 (41%)†††	0.72
NIHSS 24 h, median (IQR)	6 (2–18)	10 (4–17)‡‡‡	0.35
Mortality at 90 d, n (%)	9 (33%)	855 (29%)†††	0.62
Successful reperfusion (mTICI 2B–3)	20 (74%)	1720 (66%)§§§	0.37
siCH	2 (7.4%)	187 (5.9%)	0.75
Stroke progression	1 (3.7%)	326 (10%)	0.26
Pneumonia	1 (3.7%)	352 (11%)	0.22

CE indicates cardioembolism; EVT, endovascular thrombectomy; IQR, interquartile range; LAA, large artery atherosclerosis; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; and siCH, symptomatic intracranial hemorrhage.

*Registry part I+part II (n=3180) minus 23 second EVT cases. †n=3126, missing in 51 patients; ‡n=3155, missing in 2 patients; §n=21, missing in 5 patients; ¶n=3143, missing in 14 patients; ¶¶n=3115, missing in 42 patients; #n=3091, missing in 66 patients; ***n=3091, missing in 64 patients; ††n=3133, missing in 24 patients; ‡‡n=21, missing in 5 patients; §§n=2422, missing in 735 patients; ¶¶¶n=3085, missing in 72 patients; ¶¶¶n=3117, missing in 40 patients; ##n=3123, missing in 34 patients.

***Only available for Registry part 1 (March 2014 to June 2016), TOAST missing in 111 patients out of 1488 patients.

†††n=2948, missing in 209 patients; ‡‡‡n=2833, missing in 324 patients; §§§n=2631, missing in 548 patients.

rate, and complication rate. There might be some selection bias regarding the patients with rEVT, as they may have been selected based on a more favorable clinical profile. However, one-third of our patients receiving rEVT were not functionally independent when undergoing second EVT treatment. Mortality rate was slightly higher after rEVT compared with the single-treated patients (33% versus 29%). An explanation may be that physicians and patient’s care givers more often lean to palliative care in case of clinical deterioration when

patients already suffered from previous stroke. Though all procedural complications of the second EVT occurred in ipsilaterally treated patients, the outcome of these patients was slightly better compared with the outcome of the patients treated for a contralateral recurrent LVO. This finding of a slightly worse outcome for patients who suffered a stroke in both hemispheres could be considered expected. However, 7 out of the 8 patients with contralateral recurrent stroke were functionally independent at the time of the second LVO. The case series of

Bhogal et al⁸ report similar outcome for patients treated for contralateral LVO's. We agree with the authors that a larger sample size is needed before conclusions can be drawn.

A case series has limitations in its interpretation and conclusions. As we stated before, based on our cohort of rEVT, we are unable to make any statements on recurrent LVO, as our study did not use standard follow-up imaging. We could just describe recurrent LVOs that were treated with rEVT. Furthermore, there probably is a selection of patients with LVOs who were retreated. Especially for very early retreatments this could limit our conclusions as we had only 2 retreatment cases <48 hours. Finally, we note that our study covers a long time period of 2002 to 2017. During this period, stroke logistics have changed, treatment indication has been broadened, and EVT procedures have improved.

Conclusions

In future, we expect an increase of repeat EVT as the implementation of EVT has already led to a substantial increase of procedures and the indication for EVT is expanding.^{22,23} In our case series, the outcome of repeated EVT was comparable with single EVT, underlining its safety and effectiveness. Despite selection bias, and although early repeat EVT may be underrepresented in our cohort, we recommend that repeat EVT should not be withheld in patients with acute ischemic stroke due to recurrent LVO.

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Disclosures

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References

- Mohan KM, Wolfe CD, Rudd AG, Heuschmann PU, Kolominsky-Rabas PL, Grieve AP. Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis. *Stroke*. 2011;42:1489–1494. doi: 10.1161/STROKEAHA.110.602615
- Emprechtlinger R, Piso B, Ringleb PA. Thrombectomy for ischemic stroke: meta-analyses of recurrent strokes, vasospasms, and subarachnoid hemorrhages. *J Neurol*. 2017;264:432–436. doi: 10.1007/s00415-016-8205-1
- Laible M, Möhlenbruch M, Hacke W, Bendszus M, Ringleb PA, Rizos T. Repeated intra-arterial thrombectomy within 72 hours in a patient with a clear contraindication for intravenous thrombolysis. *Case Rep Vasc Med*. 2015;2015:872817. doi: 10.1155/2015/872817
- Lee Y, Yi H, Kim BM, Kim DJ, Kim SH, Nam HS, et al. Recurrent cardioembolic stroke treated successfully with repeated mechanical thrombectomy within the acute index stroke period. *J Clin Neurol*. 2015;11:275–278. doi: 10.3988/jcn.2015.11.3.275
- Fandler S, Deutschmann H, Fazekas F, Gatteringer T. Repeated endovascular treatment of early recurrent proximal middle cerebral artery occlusion: case report and brief review of the literature. *Front Neurol*. 2018;9:289. doi: 10.3389/fneur.2018.00289

- Bousslama M, Haussen DC, Rebello LC, Grossberg JA, Frankel MR, Nogueira RG. Repeated mechanical thrombectomy in recurrent large vessel occlusion acute ischemic stroke. *Interv Neurol*. 2017;6:1–7. doi: 10.1159/000447754
- Weber R, Stracke P, Chapot R. Time point, etiology, and short-term outcome of repeated mechanical thrombectomy due to recurrent large vessel occlusion. *Front Neurol*. 2019;10:204. doi: 10.3389/fneur.2019.00204
- Bhogal P, AlMatter M, Hellstern V, Pérez MA, Ganslandt O, Bätzner H, et al. Mechanical thrombectomy for recurrent large vessel occlusion. *J Clin Neurosci*. 2019;66:107–112. doi: 10.1016/j.jocn.2019.05.010
- Rozeman AD, Wermer MJ, Vos JA, Lycklama à Nijeholt GJ, Beumer D, Berkhemer OA, et al; MR CLEAN Pretrial Study Group. Evolution of intra-arterial therapy for acute ischemic stroke in the Netherlands: MR CLEAN pretrial experience. *J Stroke Cerebrovasc Dis*. 2016;25:115–121. doi: 10.1016/j.jstrokecerebrovasdis.2015.09.002
- Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al; MR CLEAN Investigators. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11–20. doi: 10.1056/NEJMoa1411587
- Jansen IGH, Mulder MJHL, Goldhoorn RB; MR CLEAN Registry Investigators. Endovascular treatment for acute ischaemic stroke in routine clinical practice: prospective, observational cohort study (MR CLEAN Registry). *BMJ*. 2018;360:k949. doi: 10.1136/bmj.k949
- Zaidat OO, Yoo AJ, Khatri P, Tomsick TA, von Kummer R, Saver JL, et al; Cerebral Angiographic Revascularization Grading (CARG) Collaborators; STIR Revascularization Working Group; STIR Thrombolysis in Cerebral Infarction (TICI) Task Force. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. *Stroke*. 2013;44:2650–2663. doi: 10.1161/STROKEAHA.113.001972
- von Kummer R, Broderick JP, Campbell BC, Demchuk A, Goyal M, Hill MD, et al. The heidelberg bleeding classification: classification of bleeding events after ischemic stroke and reperfusion therapy. *Stroke*. 2015;46:2981–2986. doi: 10.1161/STROKEAHA.115.010049
- Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in acute stroke treatment. *Stroke*. 1993;24:35–41. doi: 10.1161/01.str.24.1.35
- van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke*. 1988;19:604–607. doi: 10.1161/01.str.19.5.604
- Eugène F, Gauvrit JY, Ferré JC, Genric JC, Besseghir A, Ronzière T, et al. One-year MR angiographic and clinical follow-up after intracranial mechanical thrombectomy using a stent retriever device. *AJNR Am J Neuroradiol*. 2015;36:126–132. doi: 10.3174/ajnr.A4071
- Enomoto Y, Takagi T, Matsubara H, Tsujimoto M, Yamauchi K, Yoshimura S, et al. Delayed stenosis in the intracranial vessels following endovascular treatment for acute stroke. *J Vasc Interv Radiol*. 2015;26:1814–1819. doi: 10.1016/j.jvir.2015.08.014
- Mosimann PJ, Kaesmacher J, Gautschi D, Bellwald S, Panos L, Piechowiak E, et al. Predictors of unexpected early reocclusion after successful mechanical thrombectomy in acute ischemic stroke patients. *Stroke*. 2018;49:2643–2651. doi: 10.1161/STROKEAHA.118.021685
- Zbornikova V. Long term follow-up of unilateral occlusion of the internal carotid artery including repeated tests of vasomotor reactivity by transcranial doppler. *Neurol Res*. 2006;28:220–224. doi: 10.1179/016164105X39969
- Gory B, Bresson D, Kessler I, Perrin ML, Guillaudeau A, Durand K, et al. Histopathologic evaluation of arterial wall response to 5 neurovascular mechanical thrombectomy devices in a swine model. *AJNR Am J Neuroradiol*. 2013;34:2192–2198. doi: 10.3174/ajnr.A3531
- Yuki I, Kan I, Golshan A, Sohn J, Murayama Y, Vinters HV, et al. A swine model to analyze arterial structural changes induced by mechanical thrombectomy. *AJNR Am J Neuroradiol*. 2013;34:E87–E90. doi: 10.3174/ajnr.A3221
- Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al; DEFUSE 3 Investigators. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378:708–718. doi: 10.1056/NEJMoa1713973
- Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al; DAWN Trial Investigators. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2018;378:11–21. doi: 10.1056/NEJMoa1706442